The philosophy of behavioural genomics: analysis of criteria for the conceptual mapping of research in the genomics of human behaviour

Volume 1 of 2

Submitted by Richard Julian Holdsworth to the University of Exeter as a thesis for the degree of Doctor of Philosophy in Genomics and Society, May 2009.

I certify that all material in this thesis which is not my own work has been identified and that no material has previously been submitted and approved for the award of a degree by this or any other University.

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ABSTRACT

This is a philosophical enquiry into scientific research that studies the causes of behaviour, principally human, using the findings, techniques or tools of genomic science. The objectives, concepts and methods of eight selected disciplines are analysed: biomolecular archaeology, evolutionary biomechanics, molecular neurobiology, Down syndrome research, human behavioural ecology, behavioural genetics, human evolutionary genetics and human developmental genetics. Nine semi-structured interviews were conducted with leading researchers in these fields. The results are analysed in terms of a set of fourteen criteria, chosen to illustrate diversity in the conceptual approaches of the researchers concerned. Some of these, for example, put the accent in their work on phylogeny rather than ontogeny. Some study the action of nuclear genes; some concentrate on mitochondrial DNA. The results are also plotted in a Criterion Matrix. The researchers spoke as individuals, not as representatives of their discipline. In parallel, sources in the literature as well as the interviews were used to generate a Genomic Workbench Analysis Model, identifying the different regions of the human and other genomes used by different disciplines in their research. The process of enquiry is presented as a conceptual mapping of the putative field of behavioural genomics. The two principal tools of the method – the Criterion Matrix and the Genomic Workbench Analysis Model – convey a picture of rich and complex diversity among the target disciplines. It is concluded that this diversity is inconsistent with a two-clusters model such as might have been suggested in the past by a polarisation of the nature-nurture debate along a single axis. Other conclusions of the conceptual mapping study are presented. A suggestion is made for the future development of a field of behavioural environomics.

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PART A: THE SCOPE OF THE RESEARCH PROJECT

Chapter A1 – Purpose and description of the project

The character of the enquiry

This is a philosophical enquiry into research in behavioural genomics. 'Behavioural genomics' is given a wide interpretation here. By it is meant the study of the causes of behaviour, principally human behaviour, using the findings, techniques or tools of genomic science.

It must be stressed at the outset that the mere choice of the topic for the enquiry does not already imply any particular assumption concerning the influence of genes on human behaviour. It does contain, indirectly, the assumption that some scientists are investigating that possibility, in many of its various ramifications. However the choice of topic implies, no less, that there are other scientists who are using the evidence of genomic analysis to investigate important questions, strongly relevant to the phylogeny or the ontogeny of human behaviour, where the influence of genes on behaviour is not the matter at issue. When we come to consider research into molecular neurobiology, for instance, we shall find a discipline that draws on genomic evidence to answer questions about the organisation and development of the neuronal structures essential for behaviour. That is not the same thing as taking any particular position on the influence of genes on behaviour. Another example: modern techniques of comparative genomic analysis can assist in the formation of hypotheses about speciation among the hominids - and in particular the close human family, the hominins - that again help us to understand the evolution of characteristic behavioural features of our species, such as upright bipedal locomotion.[1] We shall also be considering research that, while it uses the evidence of the human genome, does not necessarily use the part of the genome that comprises the genes. Such research, in

[1] For the possibilities and problems of molecular phylogenetics see Ridley, Mark, 2004, pp.423-470.

the context of anthropology and archaeology, can yield evidence about prehistoric migration, settlement and nutrition – in other words, about the emergence of forms of behaviour that we may now tend to think to be, or to have been typical of the human species.

From the examples just given it will indeed be clear that, in this enquiry, both the terms 'behavioural' and 'genomics' are given wide latitude of reference. That is the intent of the project: to take a wider look than is habitual at a number of different ways in which the evidence of the comparatively young science of genomics can be adduced in the task of trying to understand the causes of human behaviour, where 'causes' may be proximate or ultimate – may mean either phylogenetic, ontogenetic or even cultural causes, and where 'behaviour' may cover not only attributes of personality but also many of the anatomical, physiological and biomechanical traits that are immanent in the phenomenology to which our customary use of language attaches the label 'behavioural'.

The present research project has been conducted over the period 2002-2009. It therefore began soon after the public announcement of the sequencing of the human genome in February 2001 and continued during a period when a number of scientific disciplines directly or indirectly concerned with the origins of human behaviour were developing their use of new genomic methods, tools and data.

During this period 'behavioural genomics' has not been the name of a recognised, autonomous scientific research discipline. At the time of writing we may say that, as a term, it would be more likely to occur in the title of a multidisciplinary conference than in the name of an academic department.

In order to understand the background to this research it is relevant to know that the work has been conducted as a PhD project at the ESRC[2] Centre for Genomics and Society, Egenis, at the University of Exeter, England. Egenis is one of the four partners comprising

[2] Economic and Social Research Council.

the ESRC Genomics Network, EGN. The network and its partner organisations were created in 2002. EGN is

> dedicated to examining the development and use of the science and technologies of genomics. The activities of the EGN span the whole field of genomics, covering areas as diverse as plant and animal genetics, embryonic stem cell research, and associated health applications.[3]

The specific task of Egenis is "studying the meaning and social implications of contemporary genomic science".[4] Specifically, the Director of Egenis, the philosopher Professor John Dupré, has stated that the aims of Egenis

> include understanding what the whole language of the subject means, as well as exploring the slippages in meaning as the key terms from genomic science diffuse into other areas of expertise (for example legal) and the general public. Then we wish to apply that understanding to more specific issues such as the impact of genomics on specific crucial areas of human activity such as medicine, the food chain and the environment.[5]

The specific issue chosen for the present work has been the impact of genomics on research into the origins of human behaviour. In that context there are specific areas where the advance in genomic knowledge runs the risk of provoking a 'slippage in meaning'. The risk can arise in two ways: first, if we slip into the habit of simply re-labelling as 'genomics' everything that we used to call 'genetics', and second, if we give this treatment, specifically, to the term 'behavioural genetics'.

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[3] EGN website: http://www.genomicsnetwork.ac.uk/aboutus/ . (Consulted 10 July 2008).
[4] Ibid.
[5] Egenis website: http://www.genomicsnetwork.ac.uk/egenis/aboutus/ourmission/ . (Consulted 10 July 2008). The passage is quoted there from *Social Sciences*, newsletter of the ESRC.

The scope of reference of 'behaviour' and 'genomics'

How one views the putative subject of behavioural genomics depends on how one understands the ideas of 'behaviour' and 'genomics', respectively. The position taken here is that, for the present purpose, one's understanding of these concepts should be as wide as reasonably possible. We have said that the aim is to take a fresh look at this subject-area. It would be inconsistent with this aim to begin by making a large number of a priori exclusions. In designing the research project, the assumption was made that different research disciplines would have different ideas to offer, on these as well as other points. Therefore, it must be an important aim of the research to harvest these ideas. The general idea has been for the disciplines – or, more precisely, individual researchers in different disciplines - to speak for themselves.

'Genome', 'gene' and the disciplinary 'workbenches'

Having said that, we must address the question of what is meant by the terms 'genome' and 'gene'.

First, what is 'behavioural *genetics*'? Rowe and Jacobson (1999) put the matter in the following way:

> Behavioural genetics is a field concerned with variation, with why one individual differs from another. One hypothesis holds that genetic differences among people are a source of their behavioural differences.[6]

Does any of this change if we shift the context from 'genetics' to 'genomics'? The science of genomics has been described as "the mapping, sequencing and analysis of genomes".[7] In trying to answer the question various points must be reconciled. Among them is this one:

[6] Rowe and Jacobson, 1999, p.12.
[7] Jobling et al, 2004, p.24.

that the enlargement of the sphere of interest to the genome, which encompasses the entirety of an organism's DNA, invites attention to parts of the genome that are not genes.

Scientists have had difficulty in determining the number of genes in the human genome. Before the sequencing of the human genome was completed it was common to assume that the number was around 100,000. Since the completion of the Human Genome Project, the number of genes now looks much smaller than it did before. In 2004, Nüsslein-Volhard put the matter in the following way:

> The big surprise was that the number of genes in the mammals, human and mouse, at about 32,000, did not especially markedly exceed that of fly and worm. On average a human gene consists of 27,000 base pairs and about 10 exons of 100 base-pairs each, while the introns are ten times as long.[8]

According to Brown (2007), there are about 35,000 genes in the human nuclear genome: in other words, the DNA in the nucleus of human cells.[9] However, other workers have put the figure lower, and it may be that there would currently be a large measure of agreement on a figure of around 21,000 to 23,000.

There would appear to be three chief reasons to take an interest in the number of genes in the human genome. First, there is the sheer surprise felt by researchers at the comparatively low figure that sequencing the human genome disclosed. Second, the low tally seems to emphasise the fact that genes make up only a small proportion of the total nuclear DNA. The proportion may lie in the region of only 2-3%. Third, there is the challenge of conceptualising the development of so large and complex an object as the human organism from such a relatively small number of genes.

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[8] Nüsslein-Volhard (2004), pp. 167-8. Christiane Nüsslein-Volhard won the Nobel prize for medicine in 1995. In the passage cited, 'fly' and 'worm' refer to fruit-fly and nematode respectively. The passage is translated from German by the present author.

[9] Brown, T.A., 2007, p.

However, these three points, simple as they seem, beg a number of trickier questions. To begin with, the proportion of the genome taken up by genes is not just a function of the number of the genes, but also of their length. This was hinted at in the quotation from Nüsslein-Volhard given above. A more fundamental problem – if you wish to count or measure a gene – is to know what a gene is. Precisely this point has become a point of debate in recent years.

A concise summary of the modern debate may be found in an article in *Nature* by Pearson (2006). She reports that

> The first of the complexities to challenge molecular biology's paradigm of a single DNA sequence encoding a single protein was alternative splicing, discovered in viruses in 1977 [...]. Most of the DNA sequences describing proteins in humans have a modular arrangement in which exons, which carry the instructions for making proteins, are interspersed with non-coding introns. In alternative splicing, the cell snips out introns and sews together the exons in various different orders, creating messages that can code for different proteins. Over the years geneticists have also documented overlapping genes, genes within genes and countless other weird arrangements [...].[10]

The more researchers understand about phenomena such as alternative splicing the more difficult it becomes for them to cling to the idea of a gene as a discrete parcel of information carrying from one generation to the next all the instructions necessary for the assembly – via the processes of transcription and translation - of one particular protein molecule. To say what idea should replace that one is more difficult. In an empirical study, Stotz, Griffiths and Knight (2004) found some evidence of variation in the way biologists conceptualised the gene. Indeed, the situation they revealed was even more complex in that they found:

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[10] Pearson (2006), p. 399.

> Our general results for the whole subject population are consistent with Fogle's suggestion that the classical molecular gene concept continues to function as something like a stereotype for biologists, despite the many cases in which that conception does not give a principled answer to the question of whether a particular sequence is a gene (Fogle, 2001).[11]

These authors also reported the view of Falk that

> this may be a general model for thinking about 'gene concepts'. Biologists across all fields accept that there is a material basis for heredity, with DNA molecules at its core, but their different structural definition of a gene (explicit or implicit) reflects which functions of DNA elements are relevant to research questions in specific fields.[12]

Rose (2005), traces the modern shake-up in thinking on the nature of the gene to the work of Barbara McClintock on 'jumping' genes in maize. Her work, conducted in the 1930s, showed that genes could relocate themselves to "different sites in the chromosome map".[13] Her findings only achieved widespread acceptance in the 1980s.[14] Looking at the current debate, Rose considers that a significant distinction is to be made between the differing conceptions of the gene held, respectively, by 'Theoreticians' and 'Biologists'. For the former (for instance, Dawkins),[15] the gene is "isolated in the cell nucleus, magisterially issuing orders by which the rest of the cell is commanded".[16] For the latter, genes "are in constant dynamic exchange with their cellular environment". Tabulating some of the key differences, Rose characterises the 'theoretician' view as:

> Gene seen as unitary and indivisible, rather as atoms were before the days of nuclear physics

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[11] Stotz *et al*. 2004. 671
[12] Stotz *et al*. cite this as a personal communication from Falk.
[13] Rose (2005), p. 125.
[14] Barbara McClintock won the Nobel Prize for Medicine in 1983.
[15] Ibid., p. 121.
[16] Ibid, p. 125.

whereas, for the biologists,

> Genome fluid: DNA strands subject to alternative reading frames, splicing and editing processes[17]

A quotation from Barnes and Dupré (2008) makes the link between the debate about new conceptions of the gene and that concerning gene number:

> And more generally, the identification of more and more complexly organised, efficient forms of transcription and splicing is being used to account for how in humans around a million proteins may be produced from little more than twenty thousand so-called genes.[18]

At the same time, Barnes and Dupré, like Stotz et al. in the 2004 article cited above, are aware that there may be a dislocation between the current state of debate on the nature of gene and genome on the one hand and, on the other, the models of these concepts in the heads of people who have to operationalise them in various practical and professional settings. (There may even, of course, be a difference between what people say and what they do). These people would range from laboratory researchers to "Medical and legal professionals" trying to make sense of the new science both on their own behalf and on behalf of "patients or clients".[19]

Barnes and Dupré conclude that we perhaps need to accept the emergence of a social distribution of "genetic knowledges," different sets of shared beliefs all of which are authoritative to some degree in some contexts.[20] At the same time we need to bear in mind that all are working within a "division of technical and epistemic labor". Within such a division of labour, "there has to be a distribution of epistemic and cognitive authority

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[17] Ibid., p. 126
[18] Barnes and Dupré (2008), p. 56.
[19] Ibid., p. 68.
[20] Ibid., p.69.

existing in parallel to the distribution of knowledge". As individuals, we do not simply rely on what knowledge we may happen to have, but rather we make use of the division of epistemic labour to turn to the sources of expert knowledge that it affords. That knowledge and authority are distributed under a division of labour – distributed, that is, and not centralised – may be accepted. As Holdsworth (1994) has argued:

> A professional is a knowledge based worker in a defined domain. By the exclusive definition of that domain, the professional has knowledge which other people do not have. In other words, the knowledge pool in a society is not homogeneous: it is heterogeneous, and therefore structured.[21]

There is, first, an imbalance of knowledge: for instance, between the medical professional who offers the pill and the patient who swallows it. However, this imbalance is constructive, to the extent that the heterogeneity of the knowledge pool provides us with opportunities to be, in some situations, the person accepting the epistemic authority of someone else, and in other situations, to be the person exercising the epistemic authority. That, at any rate, is the picture when things are going well.

Here, we shall take note of Barnes and Dupré's idea of the social distribution of genetic knowledges and indicate our own strategy in this area. In the present enquiry we shall have to take other differences in concept and method among the disciplines studied as well as their ideas of gene and genome. Indeed, the latter will loom larger or smaller according to the discipline under study. Our approach, therefore, will be to try to identify the characteristic 'workbench' of a given research discipline. This will be defined more fully in subsequent chapters, but the idea will bundle objectives, methods and concepts. Notably, it will be used as a way to identify what the exponents of a discipline regard as their targets of attention in gene and genome.

We cannot leave this topic without touching on two other points. The first is this. We have just been considering what a gene may or not be, and how much of the human genome is

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[21] Holdsworth (1994), p.43.

accounted for by genes coding for enzymes and other proteins. We saw that the great majority of the genome is non-coding DNA. However, just because the remainder of the nuclear genome is 'non-coding' or 'non-recombining' does not mean that it is pointless to analyse it. There are two main reasons for this. First, recent years have seen significant advances in the analysis of DNA *other* than nuclear genes to glean information about such important matters as prehistoric migrations and the onset of the Neolithic revolution: the adoption by humans of farming and a settled way of life. It has been possible to make informative inferences on such topics from patterns of mutation in non-recombining sequences of DNA on the Y-chromosome, inherited through the male line. Another useful resource here was been the DNA in the mitochondria – energy-yielding organelles that exist in the cytoplasm of the cell and not the nucleus. This DNA is inherited through the female line. Second, there has been a re-assessment of the role of some of the 'non-coding' regions of the human genome, since it can have a function in controlling the action of genes.[22] In any case, much more of the non-coding DNA is transcribed into RNA than was previously supposed.[23]

This brings us on to the other point. There used to be a temptation to define the genome as the complete set of all the genes of a given organism. However, once it became clear that the genes only occupied a small proportion of the DNA of the organism, that non-gene regions of DNA could have a role in controlling genes, and that there was useful information to be gathered from non-coding and non-recombining regions of DNA, there were good reasons to shift the definition of 'genome' from 'all the genes' to 'all the DNA' of the organism. However, when discussing the function of the DNA we also need to discuss messenger RNA (as well as other kinds of RNA) and proteins. The full set of these is referred to, respectively, as the 'transcriptome' and the 'proteome'. The 'genome', then, is certainly not identical to the 'transcriptome', especially since one sequence of transcribed DNA may, according to circumstances, give rise to more than one sequence of mRNA. Nevertheless, if one wishes to describe the function of the genome – the DNA – it is necessary to refer to the function of the RNA, of proteins, and of other non-DNA objects.

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[22] Carroll (2008), p. 76.
[23] Barnes and Dupré (2008), p. 81.

Therefore the subject of genomics – and, by extension, that of 'behavioural genomics' - must be allowed to refer to these entities also.

The involvement of a plurality of disciplines

The advent of 'genomics' has, then, in some sense enlarged the scope for researchers to explore the possibility that DNA evidence could assist them in their studies of the origins of human behaviour. Such researchers are not to be found isolated in any one single scientific discipline. It is precisely the aim of the present work to probe the way data and methods from genomics have permeated the disciplines working, in their different ways, on the origins of human behaviour.

True, as we shall discover, certain workers in the fields of behavioural genetics and psychiatric genetics have put forward a conception of 'behavioural genomics' that they find illuminating for their fields. In other words, they have proposed a distinct usage as a term of art in those disciplines. The merit of this step is that it introduces rigour in an area that might otherwise be left vague. However, as we shall also see, the two disciplines named are not the only ones that are using findings of genomic science in researches into the origins of human behaviour.

The conceptual mapping exercise

The first purpose of the present work is to examine some of the concepts and methods of some of these disciplines in order to show the different ways in which they are using genomics in their research. As will be explained in due course, this task has been conceived of as a 'mapping' exercise. The task is to make a conceptual map of the spaces occupied by specific disciplines in the general research field.

It would be possible to describe and compare the disciplines in – for instance – sociological or economic terms. However, the approach adopted here has been to analyse the concepts,

assumptions, theories and methods employed by the various disciplines. This is primarily a philosophical task, and the project has been conceived in philosophical terms.

To speak of a 'map' here is to employ a metaphor. The aim is to help the reader to gain an understanding of the breadth and diversity of (at least some of) the specialised disciplines working in the general area that we have called 'behavioural genomics'. They resemble each other, or distinguish themselves from each other, by the concepts and methods that they apply. As an aid to understanding, a diagram will be presented that enables the reader to visualise the similarities and differences among the concepts and methods applied in the work of nine researchers from different disciplines. This diagram, for reasons to be explained, will be termed the 'Criterion Matrix'. The result of this process is not intended to be the presentation of a definitive chart of the research effort in behavioural genomics, but rather of a tool that can help readers orient themselves in a new and rich research terrain.

The disciplinary division of labour: a spontaneous network?

When one has once been made aware that a plurality of scientific research disciplines are working on a range of aspects of the origins of human behaviour, using concepts and methods that partly differ and partly overlap, it becomes difficult to indulge in an exclusive partisanship for any single approach. The general field is seen to be so wide, yet so complex, that it becomes hard to conceive a successful research strategy in terms other than those of a disciplinary division of labour. The disciplines involved will tend to constitute – whether spontaneously or deliberately – a network that provides the only realistic chance of capturing the significant features of the phenomena under study. This, at least, is a hypothesis worth exploring. It may prove to be over-optimistic. The subsequent development of the argument in these pages may help us to reach a judgment on this point.

That observation, obvious as it may be, is also relevant to a possible reaction on the part of the reader to the breadth of disciplines selected for study here. For so long, whenever the words 'behaviour' and 'genetics' have been mentioned in proximity to one another, people

have tended to assume that the only issue on the agenda could be that of assessing the influence of genes on behaviour. Surveying the account of behavioural genomics put forward in the present work, some readers may at first feel that some contrivance is being practised on them. They may feel that the wide, multidisciplinary interpretation of 'behavioural *genomics*' being developed here is somehow factitious: that it is getting away from 'the main point'. All that can be said in response is that, here, the point is to try and push previous expectations to one side, to the extent that this is possible, and look in an open way at the different uses to which genomic evidence is in fact being put by various scientific research disciplines interested in the origins of human behaviour, where the phrase 'causes of human behaviour' is not arbitrarily constrained.

The research interviews

Notwithstanding the philosophical orientation of this research project, it has included an empirical element. The author conducted nine research interviews with researchers in eight of the relevant disciplines. This part of the project was important to its chances of success, but it was not 'empirical' research in the direct sense. The selected disciplines were not envisaged as a statistical sample; the individual researchers were not selected as being representative of their research community, and the results of the interviews have not been analysed statistically, or even regarded a suitable for such treatment.

Rather, the interviews were conceived as a means of assisting and checking the author's understanding of the aims and methods of the 'target' disciplines, and as a means of generating fruitful ideas about the whole thematic area of the use of the findings of genomic research in the investigation of the origins of human behaviour. *Summary of the principal objectives of the research*

The first two objectives of the thesis research, then, were:

1. to undertake the conceptual mapping exercise, and
2. to reflect on the results.

To these was added a third:

3. inspired by Objectives 1 and 2, to identify themes in this area that
    a. would merit further analysis, and
    b. would serve to connect the enquiry to current debates in the philosophy of biology.

As regards Objective 3, two questions in particular emerged from the conceptual mapping exercise that, for the author, stood out as deserving further study. In each case, what suggested them for treatment was the fact that they seemed in danger of falling through the net of partially overlapping disciplines treated in this project. They were

a) the question of a serviceable concept of 'behaviour' for the purposes of biology, and

b) the question of how to integrate the environment into the picture or pictures of the causes of human behaviour being generated within behavioural genomics.

The detection of diversity

In this project, priority is placed, rather, on the detection of diversity in the research efforts in the general area of the origins of human behaviour. The validity of the different efforts is not 'operationally' placed in doubt here. All claims to knowledge deserve to be treated sceptically. But the operational approach here is to accept as a general rule that the practitioners of the research disciplines brought under study are going ahead on the assumption that the concepts and methods they apply are reasonably serviceable for their own purposes. This is not to replace the attempt to argue that some of the approaches are invalid with that of trying to show, rather vacuously, that 'all are equally valid'. Rather, it is to prioritise the point of interest – for present purposes – as the diversity more than the validity. The sequencing of the human genome provides, it might be thought, a unified DNA model of our species. Has it resulted in a unified approach to the study of the origins

of human behaviour? It is, in fact, the idea of a unified picture in this sense that will be treated sceptically here. The diversification in the ways that researchers are using the DNA model, and in the different types of inference that they draw from it, are phenomena worth analysing in their own right.

No enquiry is undertaken without any starting expectations. In the present case, the chief expectation was that, in looking at the general field of the use of genomic evidence to investigate the origins of human behaviour one would find a picture of considerable diversity. It was expected that the number of research disciplines active in the field would be rather high, and that they would differ significantly among themselves in the features that might attract the attention of philosophy: in their assumptions, objectives, methods, theories and terminology. With the project completed, it can be said that this expectation has been met.

In one way, this is hardly a surprising result. Soon after the project was started the early literature searches suggested that this would be the case. The interesting part has been analysing the diversity and testing the boundaries of the intellectual domains that go to make up the conceptual map of the area.

The legacy of the nature-nurture debate

The expectation of diversity went hand in hand with a conjecture that diversity would prove to be a healthy phenomenon. This was because of the unhelpful tendency of the nature-nurture debate to cause a polarisation in views about the origins of human behaviour. When the protagonists in a debate yield to the temptation to fall back on the principle that 'Those who are not with us are against us', the result is that subtle distinctions come to be blurred over, and positions that display quite subtle differences are clumsily clustered together in one or other of the binary lumps.

At the outset of this study it was conjectured that this binary fundamentalism could not survive exposure to the rich diversity of intellectual procedures and positions that would be

disclosed by the conceptual mapping exercise. Whether this conjecture was justified is something that later chapters of this thesis may show. Many readers would perhaps see it as an advance if debate could move on from a polarised conflict about first, and last principles, to a debate about candidate models of interactionism in all their subtlety and diversity. Indeed, they probably consider that this is where the debate is now at.

In general, the researchers whose work is considered in this study show little disposition to discuss the nature-nurture debate, and no wish to locate their own work in that context. With perhaps a few exceptions, they do not even particularly see themselves as working on models of interactionism. Rather, they are pursuing quite clear lines of research using the new ideas, techniques and tools that have become available to them in recent years. They have no desire to get bogged down in sterile debates of the past.

Focus on the epistemological rather than the ethical

The primary interest in mapping the target research domain is to describe and analyse its features as a system for the acquisition of knowledge. At the same time, the pursuit of investigation into the origins of human behaviour is a value-laden project. No human individual can take enough distance from the subject of human behaviour, and in particular its genomic dimensions, to claim otherwise with justification. The moral issues are more numerous and varied than might be supposed at first glance. Apart from the cluster of topics around the vexed question of genetic determinism, one might mention issues of genetic screening, of humans' relationships with other hominoid and animal species, the ownership of genes and genomes, the right to collect and analyse DNA sequences susceptible of yielding data about ethnicity or kinship, access to different types of healthcare, and numerous others.

The ethical analysis of these questions is a specialist task that cannot be relegated to the status of an 'add-on' to a research project such as the present one. At the same time the issues are too important to be ignored. An author approaching the subject of behavioural genomics should show alertness to these issues. On the other hand, it is unwise for an

author who is not an expert in their ethical analysis to claim to speak with authority upon them. The solution adopted here will be two-fold. First, it is made clear that the present work does not claim to present an ethical analysis of the moral issues in question. Second, the author will, however, attempt to signal the existence of ethical controversies where these become salient in the course of the discussion in these pages.

In addition, it can be helpful to indicate useful texts for further reading. Ethical issues arising from the debate about behavioural genetics were examined in a report by the Nuffield Council on Bioethics in 2002 entitled *Ethics of behavioural genetics*. For a critical account of eugenic ideas, there is Kevles (1995): *In the name of eugenics*.

The structure of the thesis

Having delivered these preliminary considerations, it remains to indicate the structure of this thesis. It is organised in six parts, in the following way:

Part A: The scope of the research project
Part B: The method of the enquiry
Part C: The criteria: evidence of the interviews
Part D: The conceptual map
Part E: Clarifying 'behaviour' and 'environment'
Part F: Conclusions

Chapter A2 - General statement of the 'conceptual mapping' approach

The target field: 'behavioural genomics'

The general target area for the enquiry is the whole field of research into the causes – proximate and ultimate - of human behaviour that draws (or plausibly could draw) on the findings of genomic science to support its investigations. This 'target field' is potentially vast domain. The first methodological challenge, therefore, has been to think of ways to bring the subject within a manageable compass. Before we begin on that topic, however, there is a matter of terminology to explore.

The thesis being explored here is that the 'behavioural genomics' is the name we should reserve for the target field as a whole: that its use should not be limited to any one discipline occurring in the field. This is one of the tasks of the conceptual mapping exercise: to help us probe the field in sufficient detail to arrive at a conclusion on this point.

The 'landmark' strategy and the 'target disciplines'

We have been talking about the target field as if it were unmapped territory that now needed to be 'explored'. In a sense, however, it would be absurd to maintain that the field as whole was 'unknown territory'. Many of the research disciplines working within it have produced work that attracts attention outside the boundaries of their own scientific communities. There have been widely-reported findings and widely-discussed controversies. Nevertheless, at any given point in time it may be difficult to hold in mind an accurate picture of the field as a whole. This is particularly so at the present time, at the end of the first decade of the 21st century, when the impact of the major advances in genomic science of the past 20 years or so is being felt. New research disciplines have emerged, and older ones have been transformed. Boundaries have shifted.

The method is bound to be conditioned by the fact that this type of enquiry has had few precursors. The expansion of the methods and scope of genomic science is still so recent as to present significant features of novelty. To take one example, the use of ancient DNA for the purposes of research in palaeoanthropology goes back not much more than twenty years. It was in 1985, for example, that Svante Pääbo published two papers on research into DNA taken from Egyptian mummies.[24] The techniques of this new branch of scientific enquiry did not spring into life fully formed. It has taken years for the new techniques to be refined and perfected – a process that is still continuing. It also takes time for the implications and possibilities of new research methods to be appreciated and exploited. It takes further time for results to emerge and for comparative studies to become feasible. It can take more time still for methods and results to cross-fertilise from one discipline to another. There has to be a chance for ideas to sort themselves out, and for workers in different disciplines to come to conclusions about the usefulness of the new methods for their own branch of enquiry. Now seems to be a good time to take stock of developments. However, the comparative novelty of the phenomena to be surveyed means that the appropriate methods of investigation are not ready to hand.

For our purposes, it has been desirable to try to put the field as a whole into perspective. It was also desirable that this should be a fresh perspective. Our way of looking at the field should not be conditioned, more than was inevitable, by the controversies of the past. The first step in developing the methodology for the present study was therefore to decide to proceed as though the field was indeed unknown territory. The second step was to think about how to go about mapping it.

There was a difficult balance to strike. Although it was desired to bring the whole field into one perspective, the idea of attempting a comprehensive, detailed survey of all the research efforts being conducted in the general field was not feasible and never came into consideration as a method for the present enquiry. The aim was understanding, not completeness, and besides the resources did not exist for that kind of operation.

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[24] Pääbo, 1985a and 1985b. For a brief summary of Pääbo's contribution to the critique of certain early claims made for ancient DNA, see Jones (2001), pp.24-25.

An alternative strategy might have been to take a sub-set of relevant research disciplines and treat them as a sample of the whole population. On reflection, however, this did not appear to be a promising approach. In contexts where it is appropriate, the statistical approach makes it possible to make generic inferences about a whole population of phenomena from consideration of a smaller sample of specific cases. But a geographer setting out to map a terrain does not only wish to know that it comprises, say, 40% of hills and 10% of bodies of fresh water. She also needs to know that there is a hill in one specific place and a lake in another. Her general picture of the whole terrain will emerge from this type of structured information. A priority will be to characterise the relief of the terrain by selecting salient landmarks and measuring their altitude and their relative distances and bearings.

The method of 'conceptual mapping' adopted in the present study comes closer to the latter model than to any other. A sub-set of disciplines is chosen, and their respective relations to a set of criteria are established and compared. The selected disciplines are the landmarks from which conceptual bearings are taken.

Conceptual mapping

Naturally, to speak of a 'conceptual map' is to use a metaphor. The metaphor is consistent with other figurative usages that we might commonly employ. If we were to talk of the 'space' that a given idea or theory occupies in contemporary debate we might not be using a well-defined technical concept – a precise 'term of art' – but we could be reasonably confident of being understood. Similarly, we could refer to a scientific discipline as having 'boundaries'. That would not imply that the boundaries were necessarily firm in outline, or impermeable, or free from fuzziness or overlap, but it would convey a potentially useful notion for helping us to locate some specimen idea or form of argument or strategy of enquiry.

To suggest, however, that we could resolve all the data of the present enquiry into a two-dimensional chart like a map of the counties of England would be to take the metaphor too far. The most we can achieve is a method for translating verbal information received from practitioners of different types of research into some form of graphic trace that we can explore and discuss. The graphic trace will take the form of a certain kind of diagram, to be known as 'the Criterion Matrix'.

Questions as criteria

The tool selected for this purpose is what we are calling the 'Criterion Matrix'. The practical advantage of this method is that the matrix can be built up, row by row, from the answers given by each interviewee to the questions posed during the interview.

Each question is to be thought of as a 'criterion'. It might be asked: 'A criterion of what?' They are criterion of comparison. They are designed to articulate a set of critical conceptual issues that either separate or assimilate the concepts and methods that form part of the research practice of each interviewee. They are criteria of differentiation or uniformity. But precisely because they can serve to differentiate, they are a tool for disaggregation. Why is this important? There are two reasons. Let us look at these before considering the Criterion Matrix.

The task of analysis is a quest for diversity

The first reason is a reason in principle. It is that the job of analysis has not been done until the variance in the target phenomena has been mined. In putting the matter in this way, we are reflecting a distinction that Blackburn (1996) has expressed in the following manner:

> More generally, the phenomenal aspects of things are the aspects that show themselves, rather than the theoretical aspects that are inferred or posited in order to account for them.[25]

Blackburn formulated that distinction in a passage in which he was characterising the treatment of 'phenomena' in Kantian metaphysics. However, its use in the present context is not intended to evoke any particular philosophical doctrine or practice, but rather the distinction that a physicist makes between observations at the *phenomenological* level and scientific accounts at the *theoretical* level. When we speak here about a particular 'phenomenology' what we shall mean is a set of observed phenomena identified by the observer as potentially apt for treatment at the theoretical level. A tract of terrain observed from the air exhibits, in this sense, a certain phenomenology. Remember, the 'phenomenology' is the observed aspect of the terrain. Now, the observer may become possessed of an instrument – say, a telescope – that enables her to observe the phenomena on the ground with increased resolution. The view of the terrain now displays greater differentiation. At this point, the trained observer begins to notice features of relief and vegetation that will enhance her theoretical-level account when she comes to formulate it.

In this imaginary example, greater resolution discloses greater differentiation in the phenomena under observation. Conversely, the degree of differentiation is an index of the degree of resolution. This is not to claim that diversity is somehow more valuable than uniformity. It is to point out that an appearance of uniformity may be misleading. What looks like uniformity at a low level of resolution may turn out to be diversity at a higher level of resolution.

The second reason for seeking out diversity in the subject-matter of the present research project is a historical one. This is a point that we noted in Chapter A.1 concerning the legacy of the nature-nurture debate. As long as that debate is regarded as a zero-sum conflict, then by definition only two 'camps' are permitted. The result is that 'outliers' among the disciplines studying the causes of human behaviour are deemed, whether on reasonable grounds or not, to adhere to one or other of the two camps. This tendency

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[25] Blackburn, Simon (1996): The Oxford dictionary of philosophy, OUP, Oxford, entry for 'phenomenon', p.285.

towards the amalgamation of points of view that, in reality, show significant variance conflates – and therefore destroys – the information that careful observers would need to build up an accurately structured picture of the intellectual terrain. To counteract this tendency, we need a method of study that will tend to disaggregate the phenomena that have been subject to this arbitrary and ultimately misleading amalgamation. Notice that, once the method has been successfully applied, there are no 'outliers' any more. Each discipline occupies just that place in the terrain that it has.

The Criterion Matrix

We have explained that, in the interviews, researchers were asked to a respond to a set of questions. For example, the interviewee was asked, with respect to her own research, '*The main concern is phylogeny or ontogeny?*'. So, if one interviewee replies 'phylogeny' and another replies 'ontogeny' we have not merely a piece of information, but one that serves to separate their respective research activities conceptually. The question is a criterion. We shall come to the content of the questions in a later chapter. For the time being, let us just assume that a given interviewee is asked a set of four questions. The results could be arranged in the form of a matrix with one row and four columns, as shown in the following figure:

Table A2.01. Example of a row in the Criterion Matrix

	Question 1	*Question 2*	*Question 3*	*Question 4*
Interviewee				

As a general rule, however, the questions were so phrased as to invite one of two possible answers, as in the example just given. In some other cases the question called for a

'Yes/No' answer. The matrix was therefore presented in the manner shown in Figure 00 below, where sample responses have been shaded in for illustrative purposes.

Table A2.02. Illustration of the method of the Criterion Matrix (1)

	Question 1		*Question 2*		*Question 3*		*Question 4*	
	Answer 1	*Answer 2*	*Answer 1*	*Answer 2*	*Answer 1*	*Answer 2*	*Answer 1*	*Answer 2*
Interviewee								

Having obtained results for one interviewee, the method is to go on and obtain results for a second and subsequent interviewee, and to add these to the Criterion Matrix in the following way (Fig. 00).

Table A2.03. Illustration of the method of the Criterion Matrix (2)

	Question 1		*Question 2*		*Question 3*		*Question 4*	
	Answer 1	*Answer 2*	*Answer 1*	*Answer 2*	*Answer 1*	*Answer 2*	*Answer 1*	*Answer 2*
Interviewee 1								
Interviewee 2								
Interviewee 3								

The 'target field', the 'candidate disciplines' and the 'target disciplines'

To summarise, we identified the 'target field' as "research into the causes – proximate and ultimate - of human behaviour that draws (or plausibly could draw) on the findings of genomic science to support its investigations". In order to implement the conceptual mapping method, it was necessary to enumerate a set of relevant disciplines that could take on the required role of landmarks in that broad terrain.

The process of selecting disciplines and interviewees will be described in later chapters (A.3 and B.2). Here it may simply be stated that the process involved making an initial 'long-list' of disciplines that might potentially come into consideration – 'candidate disciplines' – and those that were eventually selected, the 'target disciplines'. One researcher from each target discipline was to be selected for interview.

Two possible limitations of the project

It was clear from the start that, as a survey of such a rich and complex field, the research project had two possibly serious limitations. First, there was the abundance of disciplines. It was not going to be possible to survey them all. As will be shown, at the outset of the project the author identified more than fifty disciplines that could have been considered as candidates for inclusion in the study. No doubt it would have been possible to add to that list, if this had seemed useful, but practical considerations made it necessary to reduce the number of disciplines to be brought under the study, rather than to increase it. The second limitation was that, even working on a reduced list of disciplines, there was no possibility that the author of the research, a philosopher, could do full justice to the detail and subtlety of research that was occupying the full-time professional activities of hundreds of scientists, each one of them highly specialised in their various domains.

To balance the first of these two points it must be stressed that the research project was not conceived as a managerial survey, still less as an audit. At the outset, at least, the author

rather resembled an ecologist engaged on research into the species-richness of a biome, whose chief concern is not to overlook any example. That was how the list of fifty-plus was drawn up. It was with some reluctance that the list was subsequently pared down. However, the reluctance was mitigated by the fact that the author was after all not an ecologist but a philosopher, and in the last analysis his quest was not for specimens of disciplines, but rather for specimens of ideas, arguments and issues generated by the activities of the disciplines.

Concerning the second point – the impossibility of the author of the project becoming expert in each of the research disciplines studied - three things may be said. The first is that this problem would have faced anyone attempting this project, since nobody could be an expert in all the disciplines examined. The second observation is that the author, as a philosopher of science, has been trained to be sensitive to the aims and methods of different forms of scientific enquiry. Finally, it has been a key element of the method adopted here, not merely to rely on the author's reading of the literature of the various disciplines, but to go and talk to their practitioners. This, as will be seen, has given researchers in a selected number of disciplines a chance to express their own views of their subjects and to correct possible misconceptions in the mind of the author of the research.

Conceptual mapping by criteria

The sub-title of this project speaks of the 'analysis of criteria for the conceptual mapping of research in the genomics of human behaviour.' This draws attention to the fact that the role of the criteria as conceptual tools for discriminating among the target disciplines was only part of their function in this project. It was also clear that the criteria would have a significance in themselves, since there was likely to be an element of surprise in discovering, in the event, which criteria would turn out to be really informative and which would not. Therefore the method of research must permit both an ex-ante and an ex-post analysis of the criteria. That is to say, it would be necessary to start with a set of criteria to be taken into the conceptual mapping exercise and then at a later stage try and evaluate how fruitful the criteria had proved to be. The discussion of the criteria, accordingly, will begin

in Chapter B.1, where we shall set out the criteria that were used in the interview process and give reasons for the choice of each.

Summary of the method

The method adopted in the research may be outlined in the following steps:

1. Examination of the literature in order to draw up a 'long-list' of disciplines that came into the target category: scientific research disciplines that are drawing – or might well draw – on findings of genomic science in order to assist them in the investigation of the origins of human behaviour, broadly conceived;

2. Deriving a shorter list of researchers working in target disciplines who might be suitable to be interviewed for the purposes of the project;

3. Identifying criteria and drafting the outline of a graphical representation termed a 'Criterion Matrix';

4. The conduct of nine semi-structured interviews with selected researchers;

5. Processing the output of the interviews, notably (a) Edited Excerpts of the transcripts of the interview recordings, and (b) a Criterion Matrix for each researcher based on their responses during the interview;

6. Submission of the Edited Excerpts and Criteria Matrices to the nine researchers interviewed for comment and approval;

7. Written discussion of the output of the interview and Criterion Matrix process in the Thesis (Part C);

8. Construction of the Conceptual Map, in the form of a global matrix compiled from the separate Criteria Matrices; discussion of the same (Part D);

9. Discussion of specific themes selected by the author as meriting further study (Part E).

The possibility of alternative conceptual maps

It is possible that alternative conceptual maps of this research territory could be produced. However, the aim here has been to fashion an analytical tool that might be useful in probing the subject matter and disclosing interesting and suggestive facets of it, without aspiring to set out a uniquely valid and accurate image of the whole field of research. The aim is to offer this analytical tool for evaluation and possible use and improvement by other researchers.

Chapter A3 – Initial review of candidate disciplines

Selecting disciplines for study: general criteria

In this chapter we shall take a first look at candidate disciplines for the present enquiry. Here, and in a later chapter (B2), we shall see that from a somewhat large number of possible choices a comparatively small set of disciplines was ultimately chosen for further study.

In the initial phase, when the 'long-list' was to be established, there were two general criteria:

1. The search was for scientific research disciplines that, on generous definitions, could be said to be engaged in research into the causes of human behaviour;

2. They should be disciplines that drew on the results of genomic science in their research, or might reasonably be considered candidates to do so.

These criteria are simply stated, but behind them stand a number of questions. The first concerns the definition of 'discipline'. For the purposes of the project in hand it would have been self-defeating to exclude branches of research from consideration simply because they did not meet some uniform model. The quest was for areas of research in which the investigators were using the fruits of recent advances in genomic science – directly or indirectly – to further enquiry into the origins of human behaviour. The idea was to delineate the ways in which such knowledge could be used for that purpose, was in fact being used, or might come to be used.

Scientific research is not organised according to standard models, or at any rate the practice does not always follow the models as rigorously as the lay person might expect. The name given to a community of researchers in a given area of enquiry may imply, and is certainly

often meant to imply the existence, in that area, of a solid, well-corroborated body of exact knowledge. However, it may also have some other character or function. For instance, it may reflect aspiration rather than reality: it may be the name of a school or a movement that seeks to underpin its credentials by putting up a metaphorical brass plate outside its door.

In quest of the causes of human behaviour

The overriding considerations for the choice of disciplines in the present case were that the researchers in that field should

1. in some sense be involved in the quest for the causes of human behaviour, whether proximate or ultimate causes, and that
2. there should be something useful to say about the relationship of their work to research in genomics.

It is, in fact, very difficult to define what counts as a cause of human behaviour. Indeed, it is difficult to define behaviour. This means, among other things, that different researchers are operating with different conceptions of behaviour and its causes. Moreover, these differing conceptions may – indeed do – impel researchers from different disciplines to embrace, or to eschew a 'behavioural' vocabulary. The main questions here are too large to be analysed exhaustively in the present work, but we need a modus operandi for dealing with them. In summary, the method to be adopted here is the following:

1. to be inclusive with respect to the conception of behaviour and its causes used by different disciplines: to be more ready to collect new cases than to attempt to disqualify them on narrow grounds of definition;
2. to come back to the general problem of the concept of behaviour in Part E of the thesis.

In the biological context there is interest in causes that can be gathered together under two headings: phylogeny and ontogeny. Ontogeny is the development of traits of morphology or behaviour during the life-time of the individual. The causes of such development may be of many different kinds. Phylogeny is the evolutionary history of traits. To speak of a phylogeny of behaviour does not entail the view that all observable behaviour is caused by evolution and genetics: only that some of it is. Examples in modern humans might be upright bipedal walking, the eye-blink reflex or the basic capacity for linguistic communication. Probably no example that one could think of is free from controversy, but some have proved more controversial than others. At the outset of the present research project, the first instinct was to speak of the 'origins' of human behaviour. However, without intending to do so, this might have seemed to weight the enquiry more towards phylogeny than was actually warranted. That is the reason for preferring the term 'causes'.

The discipline defined by its workbench

The characteristic activities of a research discipline cannot always be ascertained by an outsider from first principles alone. A given discipline may bear a name that suggests a rather wide field of enquiry, but on inspection we may well find that the real areas of focus are quite strictly limited by critical constraints, often concerning access to technology or the limited availability of evidence. The research that *is* being done turns out to be the research that *can* be done with the aid of particular instrumentation or particular types of probably rare material, such as fossilised hominin bones or ancient DNA.

The discipline, in the sense in which we are using the term here, is largely defined by its 'workbench'. It is not just a community of researchers. It is that community working to a research agenda targeting characteristic types of evidence and using characteristic methods and technologies.[26] We could think of the 'workbench' as a finite area of laboratory space where a researcher works on the evidence that is to hand with the instruments that are within reach, pursuant to a research agenda constrained by the availability of time and

[26] For an instructive account of a discipline dependent on the availability of research technology, see the account of the early days of X-ray crystallography in the biography of Dorothy Hodgkin by Ferry (1998).

resources. To some, this characterisation may seem excessively pragmatic. However, this characterisation of the 'work-bench' is also, to a significant degree, a characterisation of the conceptual space in which the researcher functions. Unless we discipline ourselves, as observers, to apprehend the researcher's room for intellectual manoeuvre as bounded by the material constraints that we have just itemised, we shall not come close to understanding the thinking processes that give rise to the science. We stress this notion of the 'workbench' here because it is relevant to the development of genomic science.

The long-list

The early research for the thesis yielded the list set out in Table A3.01 below. In reproducing this early listing the author has faced, and resisted the temptation to 'clean up' the selection in the light of hindsight. It would indeed now be possible to remove some ambiguities and possible irrelevancies from this initial selection in order to make it more coherent and more finely targeted. However, this would not be a good procedure. It is more valuable to present the initial list, reflecting as it does some of the uncertainties that were inherent in the original conception of the project.[27]

Table A3.01. Long-list of disciplines in principle capable of giving rise to hypotheses in human behavioural genomics (*51 disciplines listed in alphabetical order*)

Ancient biomolecules research	Evolutionary genetics	Neuroscience
Anthropological linguistics	Evolutionary psychology	Ocularmotor physiology
Anthropology	Genetics	Osteoarchaeology
Archaeozoology	Human evolutionary studies	Otolaryngology
Auditory anatomy/physiology	Human genetics	Palaeoanthropology
Behavioural ecology	Human palaeoecology	Palaeoethnobotany
Behavioural genetics	Mammalian evolution	Palaeontology
Behavioural genomics	Molecular behavrl. genetics	Philosophy
Behavioural neurogenetics	Molecular neurobiology	Physical anthropology
Biological anthropology	Molecular phylogenetics	Primatology
Biomechanics	Molecular psychiatry	Psychology
Comparative behavrl. genetics	Motor control	Psychophysiology
Cultural phylogeny	Motor physiology	Quantitative behavrl. genetics
Cytogenetics	Neurobiology	Sociobiology
Ethnobiology	Neurology	Sociology
Ethology	Neurophysics	Speech physiology
Evolutionary anthropology	Neurophysiology	Zooarchaeology

[27] The list as given was the one included in the author's presentation to the ISHSSB meeting in Vienna in 2003.

Possible inconsistencies and anomalies in the long-list

Looking at the long-list, one may feel that there is a certain problem of inter-comparability among some of the disciplines named. 'Genetics' sounds much broader than, say, 'molecular phylogenetics'. At what level do we intend to pitch our analysis? Should we not have organised the list so as to ensure that all the candidate disciplines resemble each other in their general scope? There is something in this, although the requirement is easier to state than to satisfy. However, the real answer is that the long-list has a different function to perform than the short-list. Setting out the long-list is a heuristic exercise, rather than an analytical one.

Causes of behaviour, or prerequisites for it?

It would be self-deluding to think that the disciplines could be diverse in their aims, concepts and methods and yet fundamentally 'the same'. The divergences are symptomatic, in many cases, of radical differences in perspective. That does not necessarily mean contradictions, but simply different angles of approach to the subject-matter. For example, we could try distinguishing between a discipline like behavioural genetics, which seems to be directly concerned with causes of behaviour, and, say, neurophysiology which, except in the case of abnormalities, seems to be more concerned with the generic pre-requisites for behaviour than its specific causes. Perhaps, then, there is a distinction to be drawn between 'causation' disciplines and 'infrastructure' or 'substrate' ones. However, pursuing such a distinction would give no promise of a useful outcome.

Plausibility of genomic reference

One distinction that did deserve attention here was that between disciplines that drew on the findings of genomics and those that did not. The main aim of the research project was to

consider the role of genomic evidence in the study of the causes of human behaviour. At the same time, it was rather difficult to set a priori limits to the scope of this remit. That accounts for the presence in the list of disciplines such as sociology and psychology. To state at the outset of the project that these disciplines had been excluded on the grounds of the irrelevance of genomics to their subject-matter would have been to pre-empt almost all of the most interesting questions likely to feature in the research.

However, to allow the in-principle possibility of the relevance of a particular discipline and actually finding something concrete to say about that discipline's actual use of genomic evidence were quickly seen to be two different things. When one is considering, for instance, molecular phylogenetics, one can at once go into a description of things like the technique of hybridisation that is used to ascertain the molecular distance between the DNA of given species, and the way phylogenetic trees are constructed from such findings.

The conclusion drawn from these considerations was that the distinctive contribution that the present research project could make concerned the interface between the ideas generated in the target disciplines and their operationalisation in the context of some distinctive research practice. That conclusion would guide the final choice of target disciplines.

At the same time there were some genuine border-line cases that presented aspects too interesting to be overlooked. There is the case of cultural phylogenetics, which does not directly invoke genomic evidence, but which brings about a conceptual alignment of cultural phenomena with biological phylogenetics. This alignment was not an identification. Cultural phylogeny is held separate from biological phylogeny. Language trees are held separate from gene trees. However the respective ideas are brought into a structured relation that is fruitful of hypotheses in the fields of evolutionary anthropology and human behavioural ecology. It is an example of what we referred to in an earlier chapter as the task of establishing conceptual bearings between the landmarks in our target terrain. Accordingly, the requirement that target disciplines draw on the evidence provided by genomics was slightly relaxed: from a requirement that they should actually so draw, to

the requirement that there was an active plausibility about their being in a conceptual relation to genomics.

Pioneers in the field: Laland and Brown

The study by Laland and Brown (2002) is an important work in the field. However, their objectives are to be carefully distinguished from those of the present work. Their primary interest is in evolutionary accounts of human behaviour. Looking at the literature this subject has generated they rightly diagnose it as source of both sense and nonsense; indeed, they chose to highlight this in the title they gave to their book: *Sense and nonsense – Evolutionary perspectives on human behaviour*. At the risk of oversimplifying their analysis one can note that Laland and Brown were concerned by the sometimes extreme reactions for and against the exposition of Sociobiology by Edward O. Wilson in his work *Sociobiology: the New Synthesis*, published in 1975.[28] In a section sub-headed 'Taking the middle ground', they mention with approval what they see as the balanced position taken by John Maynard Smith, first, in a review in 1975 that referred to Wilson's book "as making 'a major contribution' to an understanding of animal behaviour" and, second, in an interview in 1981 in which Smith "confessed to finding some of Wilson's views on human behaviour 'half baked', or even 'silly'.

Laland and Brown themselves declare their intention

> to follow Maynard Smith's lead and take the middle ground between the positions of advocates of evolutionary approaches to the study of human behaviour and their critics.[29]

Concerning their own position they say

> We hope that we have also provided a balanced, central view, which outlines the positive features of evolutionary methods but does not shy away from stating where

[28] Among reviews of this work, see: Holdsworth (1976).
[29] Laland and Brown, 2002, p.6.

> we find the arguments suspect, and remains vigilant to the dangers of irresponsible biologizing. Some researchers appear to believe that all aspects of behaviour can be described by reference to human evolutionary history. We do not take this line, and believe that alternative explanations of human behaviour must be considered.[30]

The intentions of the present work are similar. However, the modus operandi differs from that of Laland and Brown. The research 'approaches' or 'schools' selected for study by Laland and Brown were the following:

1. Human sociobiology
2. Human behavioural ecology
3. Evolutionary psychology
4. Mimetics
5. Gene-culture co-evolution.

As would be the case with any attempt to carve up the total field of the study of the origins of human behaviour – including the present one – this one results in a heterogeneous set of component approaches. For instance, Laland and Brown themselves admit that few contemporary researchers actually proclaim themselves 'human sociobiologists'.[31] Sociobiology has perhaps more been a spirit that has moved a number of scientists rather than a formal discipline. Does that matter? In some ways, not at all. However, in the present research project an effort is being made to discern the distinctive 'workbench' of the selected target disciplines: more specifically, their genomic workbenches. Sociobiology has no specific genomic workbench.

If the following distinction has any validity then it helps to explain the slightly different emphasis between this research project and that of Laland and Brown. Sociobiology, evolutionary psychology and mimetics (the theory of the meme as cultural replicator) have something of the character of programmes for the biologicisation, or naturalisation of the study of human social and cultural phenomena. Among the disciplines chosen for the present study, by contrast, the need for such a programme hardly arises. This study will

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[30] Ibid.
[31] Laland and Brown (2002), p.22.

focus on research disciplines that are already embedded in the matrix of the life sciences. This distinction is not a hard-and-fast one, and it might be contested, but as an indication of where the emphasis has been placed it may be serviceable.

This concludes the initial look at the long-list of potential target disciplines for the study. The process of making the final choice of target disciplines will be described in Chapter B2.

Chapter A4 – Genomic workbenches: introduction

Introduction

In the previous chapter we suggested that a scientific research discipline may be characterised in terms of its 'workbench': a finite area of laboratory space (or fieldwork camp or research vessel, etc.) where a researcher works on the evidence that is to hand with the instruments that are within reach, pursuant to a research agenda constrained by the availability of time and resources. We shall now take a first look at this idea in the specific context of disciplines working in behavioural genomics. The idea of the workbench is intended to capture the element of the contingent in scientific practice.

Early genetic workbenches: the pea and the fruit-fly

Of all the millions of species in the terrestrial biosphere that propagate themselves genetically a small sub-set have contributed disproportionately to the history of genetic science. The first example to come to mind is that of the pea-plants studied by Gregor Mendel. The choice of the pea as genetic 'workbench' sounds unremarkable enough, but it was no doubt quite heavily constrained by the circumstances of monastery life. Later choices by subsequent researchers would not have to have met those criteria, but were conditioned by others, no less pressing. Barnes and Dupré (2008) have emphasised the suitability of the experimental animal chosen by Thomas Hunt Morgan: *Drosophila melanogaster*, or the fruit-fly.[32]

> As so often happens in biology, one of Morgan's greatest achievements had proved to be his choice of an organism to work with and his organization of systematic work around it. The fruit fly *Drosophila melanogaster* was almost perfectly suited

[32] Barnes and Dupré (2008), p. 27.

> to the development of genetics. Although work in the fly rooms remained tedious and laborious, as so much highly successful science tends to be, and thousands of hours had to be spent examining flies one by one and sorting them into categories according to traits of interest, research now moved forward relatively rapidly. Most importantly, the fly could be bred easily; the life cycle was only a few weeks; it had a suitable suite of natural variations for study;[33] and its chromosomes were particularly suitable for microscopic examination.

Training and induction: the example of a course in biocomputing

Training and the process whereby new recruits are inducted into a discipline are important aspects of the workbench. By the 1990s, important aspects of genetic research had transferred to information-technology platforms. Holdsworth (1999) has cited[34] the example of a recruit to the discipline of biocomputing who reported her reflections and experiences in the newsletter of her scientific network (Thonnard, 1996). First, Thonnard observes that

> molecular biologist[s] rely more and more often on computer aided sequence analysis tools [...]. [For] example, they need computer programs to compare DNA and protein sequences, to search for coding regions in DNA sequences, to predict the secondary and tertiary structure of DNA, RNA and proteins.[35]

This shows some of the changes in evidence and methods at the workbench. Thonnard also goes into another highly relevant factor: training. A researcher at a Belgian institution, she learned biocomputing skills by taking part in an on-line interactive biocomputing course organised by the University of Bielefeld in Germany.[36]

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[33] The authors here refer the reader to Kohler (1994).
[34] Holdsworth (1999), pp.89-90.
[35] Thonnard (1996), p. 6.
[36] Virtual School of Natural Sciences – BioComputing Division (VSNS-BCD), University of Bielefeld. Homepage: http://www.techfak.uni-bielefeld.de/bcd/welcome.html (Consulted 20 December 2008).

The 'evidence to hand'

In characterising the idea of the workbench we have spoken of 'the evidence to hand'. It is very important to remember, when discussing the disciplines at work in the target field we are calling 'behavioural genomics', that evidence is a problem. That is to say, the availability of evidence is a problem. If the public impact of the sequencing of the human genome were to have given the impression that, suddenly, scientists have all the evidence they need then this would be a serious misapprehension. Rather, each community of scientists is busy in its own area cross-referencing the genomic evidence (where this exists) with other categories of evidence. The categories are often peculiar to the disciplines, as is the part of the human or other genomes that provides the material for study in each specific context.

The progression of the argument in this chapter goes from the problem of the 'evidence to hand' to the configuration of the workbench. In configuring its own workbench, a given research community selects the categories of evidence that it feels it can work with conveniently and appropriately. Inevitably, a discipline has a distinctive point of view on the evidence: not necessarily a distorted point of view, but just a point of view.

Categories of evidence must work across disciplinary boundaries. They are generated, or 'made', within the space occupied by one discipline; they are used in that discipline, and then their transferability is checked as they enter the conceptual space of, first, neighbouring and then more remote disciplines. It remains to add the obvious point that, in any given time-slice, we will find a more complex situation than this initial picture implies. At a given point in time, particular categories of evidence will be at different stages of this process and will therefore occupy intermediate states. Many will be the subject of controversy, inside or outside a particular discipline.

Evidence in palaeoanthropology

Palaeoanthropology may be understood as the study of the fossilised remains of hominins. It is a science that can yield substantial information about the origins of some traits of modern human behaviour such as upright bipedal walking and working with tools. The fossil record is growing, as new discoveries are made,[37] but it remains incomplete. Accordingly, palaeoanthropology must use the double strategy of (a) widening the range of the evidence that it can adduce, and (b) using technology to derive ever more information from the evidence that it has. Palaeoanthropology has always worked alongside archaeology to permit a cross-referencing between fossils and the associated material culture. More recently, advances in research at the molecular level have enriched the store of both palaeontological and archaeological evidence, partly, but not only, by furnishing the evidence of DNA.

Direct DNA evidence of humans is only available for approximately the past 50,000 years – if it can be retrieved at all. The upper limit for any animal is not much higher. See M. Jones (2001):

> In the meantime, however, the time frame for ancient DNA analysis stretches back not much further than the Siberian woolly mammoth, 50,000 – perhaps as much as 100,000 – years. [38]

Meanwhile, the application of the recent technology of CT scanning (computerised tomography), originally developed in medicine, has provided palaeoanthropologists with "unprecedentedly detailed internal images of fossils".[39] Computerised tomography was originally developed in medicine, but has now also become a vital tool in palaeoanthropology.

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[37] Stringer and Andrews (2005), p. 6.
[38] Jones, M. (2001), p. 37.
[39] Ibid., p. 42.

Palaeoanthropology is vitally interested in classification. Working out the phylogeny of the hominin genera and species requires accurate taxonomy. However, accuracy is difficult to achieve, precisely because of the paucity of fossil evidence. The most important skeletal find in Britain in recent years – the discovery of Boxgrove man in West Sussex in 1993 – comprised one tibia, or shin-bone. In 1995, two human incisor teeth were found at the same site. They both belonged to an individual of the same species as the owner of the tibia: *Homo heidelbergensis*. That species lived in Africa and Europe in the Middle Pleistocene, about 500,000 years ago. One of the scientists of the Boxgrove Project has commented:

> These three finds now join the Swanscombe skull fragments and teeth from the Pontnewydd cave as the only pre-anatomically modern human remains from the British Isles.[40]

This statement points up very clearly the scantiness of the fossil record. Exactly how surprising we ought to find it depends, of course, on whether we expect to find the remains of archaic humans in 'Britain' at periods that pre-date the presence of Anatomically Modern Humans (*Homo sapiens*). Scientists' knowledge of what human species lived when and where depends on what fossils, of what age, have been found in which locations.

The workbench of molecular phylogenetics

It might be asked whether some of these questions could be answered with the aid of genomic evidence. The answer is that it could, if the evidence were accessible. The science of molecular phylogenetics is able to distinguish the lines of descent of different hominid species – i.e., species of Great Ape - where DNA evidence is available. A characteristic technique of molecular phylogenetics is the construction of phylogenetic trees by the molecular distance method. This is a measure of the dissimilarity of given nucleotide sequences. As Mark Ridley explains, a characteristic method is hybridisation:[41]

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[40] See website at: http://matt.pope.users.btopenworld.com/boxgrove/sitehomo.htm (Consulted 10 December 2008).

[41] Ridley, Mark (2004), p. 441.

> For example, the molecular distance between two whole DNA molecules, from two species, can be measured by DNA hybridisation. [...]. The DNA of [a] pair of species is "denatured": the double-stranded molecule is made into two single strands, usually by heating the molecule up The single strands of DNA from the two species are allowed to join up and form double-stranded hybrid DNA. This hybrid molecule is then in turn denatured by heating it up. The crucial measurement is how hot you have to make the hybrid DNA before it will separate into two single strands. The more similar the DNA of the two species is, the stronger the bond between them, and the higher the temperature required to separate them.

So, for hybridisation, DNA of both of the two target species is required. This means that inferences from molecular phylogenetics are feasible with a much greater time-depth than 500,000 years, if the aim is to compare the ancestry of two extant species: for instance, *Homo sapiens* and *Pan troglodytes*, the chimpanzee. However, all the putative human ancestors of *Homo sapiens* are extinct. One of these has quite recently been eliminated as an ancestor – so it is widely accepted – and that is *Homo neanderthalis*. For this finding to be made it was necessary for the researchers to gain access to Neanderthal fossil bones and to devise a means of extracting and analysing DNA from them.[42]

DNA hybridisation is not the only technique used in molecular phylogenetics. Brown (2007) states that other early techniques included immunological data and protein electrophoresis patterns, but that

> today most comparisons are made between DNA sequences. Groups of sequences are first aligned and polymorphisms identified. This information is converted into numerical data, such as a distance matrix, which can be analysed mathematically to reconstruct a tree showing the evolutionary relationships between the sequences.[43]

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[42] Krings *et al*. (1997).
[43] Brown (2007), p. 620.

The typical output from molecular phylogenetics is a phylogenetic tree, which may be either a species tree or a gene tree. Because of the large quantities of data involved, phylogenetic trees are generated by computers using specialised software applications.

The workbench of palaeoanthropology

The team of researchers who carried out the research on Neanderthal DNA just referred to made their analysis of mitochondrial DNA. We shall come back to this in a moment.

Studying human DNA lineages that can be cross-referenced with geographical, environmental and cultural markers yields data of relevance to topics in anthropology such as patterns of settlement and migration, the spread and diversification of languages, the transition from hunter-gathering to farming and the emergence of social and cultural practices.

Let us note in passing that this means it is vital for this type of research to take into account the ecological context.

Inferences of the kinds just mentioned can be made when it has been possible to establish the presence or absence, in an individual or a population, of the known variations of a genetic polymorphism. The first of these to be defined was the ABO blood group system. However, this type of research was pre-genetic. It was only considerably later that exact methods were developed using what are now regarded as the ‘classical’ genetic markers, notably the blood group genes and those responsible for immunological functions such as the immunoglobins and the human leukocyte antigen – or HLA – complex. Table A4.01 itemises some of the milestones on the way to the emergence of DNA lineages as evidence on anthropology.

Table A4.01. The emergence of DNA lineages as evidence in anthropology – A select chronology of relevant developments	
1786	Sir William Jones states common Indo-European language source for Sanskrit, Greek and Latin
1900	Landsteiner discovers ABO blood group system
1919	Hirschfelds' Lancet paper uses WWI blood group data in quest for human origins
1953	Watson and Crick: structure of DNA
1971	Cavalli-Sforza and Bodmer: The genetics of human populations
1983	Mullis and Faloona invention of PCR
1987	Cann, Stoneking and Wilson article in Nature on mitochondrial DNA and evolution
1991	Ötzi: 5,300 year old preserved human body
1997	Pääbo et al: mtDNA from Neanderthal bones
2000	Underhill et al. letter to Nature Genetics on Y chromosome sequence variation and the history of human populations (NRY)
2001	Publication of draft human genome

Non-coding and non-recombining regions in DNA

Random mutations occurring in DNA – for instance, nucleotide substitutions – if they occur at regular intervals, can serve as a molecular clock for timing changes in the genome of a species. If members of the species happen to disperse across the land-masses of the globe, then the process supplies spatial as well as temporal coordinates for events in the phylogeny of the species. Putting the situation at its simplest, if one population splits, and some individuals disperse in one direction, and the others in another, then although at first they will both exemplify the genomic variation existing at the split - i.e., the set of mutations accumulated at that point - as soon as the next round of mutations kicks in, the two lineages will begin to diverge. In time to come, the DNA of each will yield evidence of that historical divergence. That will not be the case, however, if the mutations affect genes in a manner that could in turn affect the viability of the phenotype. In these circumstances, we would expect natural selection to eliminate deleterious mutations. Phylogenetically, then, they are erased from the record and can no longer serve to mark distinct clades. If the mutation is favourable, selection will bias gene frequencies in the opposite direction.

Viewed purely as an aid to phylogenetic research, we would like the system to preserve the patterns of polymorphism intact across the generations. Not only natural selection, but even recombination works against this. However, there are certain classes of DNA that can escape the direct impact of natural selection either because they do not code for any protein that turns up in the phenotype or because they are exempt from the process of recombination, or both. Examples may be found in mitochondrial DNA of the control region and non-recombining DNA sequences on the Y-chromosome.

Mitochondrial DNA is inherited only through the maternal line and therefore never exists in the two-chromosome, or diploid state and thus escapes recombination. Moreover, mtDNA accumulates nucleotide substitutions at an overall rate roughly an order of magnitude greater than the rate at which they accumulate in nuclear genes.[44] The rate is even higher in the portion of the control region of mtDNA called hypervariable segment 1, or HVS 1.[45]

This relative rapidity of mutation enhances, as it were, the resolution of the technique that analyses the un-recombining mitochondrial haplotype, questing for differences in sequences – i.e., lineages. The researcher can be comparatively confident in attributing the differences to

> the overall accumulation of mutations during the time that the sequences have diverged from a common ancestor,

making it possible

> to define the relationship between groups of sequences in terms of a tree of ancestral relationships.[46]

If the rate of mutation in the control region is taken (Sykes, 1999) "at about 1 substitution in 10,000 years", then as Sykes has explained:

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[44] Ward (1999) in Sykes (1999), p.143.
[45] Ibid.
[46] Ibid., p.144.

> If two individuals differ at only one position in the control region this means that, on average, their common maternal ancestor lived about 10,000 years ago. Differences at two positions push that time back to about 20,000 years and so on.[47]

An early and pioneering paper that demonstrated the power of mtDNA analysis was the article published in Nature in 1987 by Cann, Stoneking and Wilson under the title 'Mitochondrial DNA and human evolution'.[48] This research used the whole mitochondrial genome and not just the control region. On this basis the authors drew up a phylogenetic tree – they called it a 'dendrogram' – that charted the branchings of lineages.

The two most famous aspects of this tree are (1) the deep split between the cluster of African lineages at bottom right, and all the rest, and (2) the implication of a single female ancestor for everyone in the tree – indeed for everyone. This ancestor came to be referred to, somewhat misleadingly, as 'Mitochondrial Eve'.

The paper gave decisive impetus to the 'Out of Africa' hypothesis, implying that this movement had started within the last 150,000 years. So recent a date was widely held to undermine the claims of the multi-regional hypothesis whereby contemporary humans resulted from dispersed evolutionary processes.

Mitochondrial DNA sequencing from the hypervariable segment was used in the study by Svante Pääbo and his team on the original Neanderthal specimen in 1997.[49] They found that the average deviation of the replicate Neanderthal sequences was estimated as 26 substitutions, whereas a typical difference for modern humans would be eight, and the average number between modern humans and chimpanzees would be 55.[50,51]

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[47] Ibid., p.104.
[48] Cann *et al*. (1987).
[49] Sykes (1999), p.vi, preface. The specimen is held at the Rheinisches Landesmuseum in Bonn.
[50] Jones, M. (2001), pp.60-61.
[51] See also for mtDNA, and Neanderthal research, Jobling *et al*. (2004), pp. 252-263, especially for Neanderthals, 260. Also Brown (2007), pp. 614-6.

Y chromosome research

Because the majority of the DNA on the Y chromosome does not recombine (there are exceptions – the so-called 'pseudoautosomal' regions),[52] Y chromosome polymorphisms, by definition found in the male line, can also be used as markers. As Wells (2002) has put it,

> The Y turns out to provide population geneticists with the most useful tool available for studying human diversity. Part of the reason for this is that, unlike mtDNA, a molecule roughly 16,000 nucleotide units long, the Y is huge – around 50 million nucleotides. It therefore has many, many sites at which mutations may have occurred in the past. As we saw [...], more polymorphic sites give us better resolution – if we only had Landsteiner's blood types to work on, everyone would be sorted into four categories: A, B, AB and O. To put it another way, the landscape of possible polymorphisms is simply much larger for the Y. And critically, because of its lack of recombination, we are able to infer the order in which the mutations occurred on the Y – just like mtDNA.[53]

A given mutation serves as a 'marker' which labels a particular lineage. An example is the marker known as 'M168'. Wells (2002) explains the case in this way:

> By mapping these markers on to the map of the world, we can infer details of past migrations. Following the order in which the mutations occurred, and estimating the date and any demographic details (such as population crashes or expansions), we can gain an insight into the details of the journey. And the first piece of evidence comes from one man in particular, who had a rather important, random mutation on his Y-chromosome between 31,000 and 79,000 years ago. He has been named,

[52] Jobling *et al*. (2004), p. 38.
[53] Wells (2002), p. 43.

> rather prosaically, M168. More evocatively, he could be seen as the Eurasian Adam – the great ... great-grandfather of every non-African man alive today.[54]

The plotting of markers and lineages gives rise to two types of graphic representation. First, it permits the construction of trees, in which the mutations form the nodes and the lineages the branches. Second, as indicated by Wells in the passage above, the occurrence of the markers in space and time can be plotted on geographical maps to show the dispersal of given lineages around the world. For instance, one of the figures in Wells (2002) is a map of the world with the caption 'The spread of Y-chromosome lineages around the world'.[55] Starting with M168, it presents the trajectories of 13 Y-chromosome lineages as arrowed tracks moving and branching across the continents. A legend assigns approximate dates to the generation of each marker. Thus we see the trajectory of M168 (50,000 Years Ago) moving up from East Africa into the Arabian Peninsula and branching, so as to send M130 (50,000 YA) along the southern, coastal route to East Asia and M89 (45,000) northwards into the Middle East, itself to branch between M172 (10,000), piercing up into South-East Europe, and M9 (40,000) heading into Central Asia. According to this Y-chromosome map, M9 was the track that led to a branching in the steppes at M45 (35,000) that permitted M173 (30,000), moving west, to effect the initial *Homo sapiens* entry into Europe, while M242 (20,000) went east across Siberia. The entry into the Americas, the map suggests was by two lineages pushing east over what is today the Bering Strait: M3, a marker downstream from M242, and the M130 lineage, finally working its way northwards from South-East Asia.

This mapping illustrates how Y-chromosome analysis has helped to contribute to topics such as the origins of modern human settlement in Australia and the Americas, the settlement of Europe, and the Neolithic migration into Europe from the Middle East. Apart from geographical markers like the continents themselves, this research uses other environmental markers including not only the material culture of the people under study, but also the genomes of species of flora and fauna that humans have brought under cultivation and domestication.

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[54] Wells (2002), pp. 70-71.
[55] Wells (2002), pp. 182-3.

The kind of research we have been talking about is providing evidence on two important fronts. It clarifies the relationship between different hominid species, notably Neanderthals and modern humans (Pääbo, 1997). Findings of bio-archaeological research relevant to migration, nutrition, disease, the transition to farming and the relationship between genetic and linguistic diversity contribute to our understanding of the behavioural dimension of the adaptation of modern humans to their environments (Sykes, ed., 1999; Martin Jones, 2001; Jobling, Hurles and Tyler-Smith, 2004).

Table A4.02. Selected examples of mtDNA and Y-chromosome analysis referenced in the secondary literature

Date	*Researchers*	*Research*	*Secondary references*
1985	Pääbo S.	'Molecular cloning of ancient Egyptian mummy DNA', *Nature*, Vol. 314, pp. 644-5.	Jones, M. (2001), p. 243.
1987	Cann, R.L., Stoneking, M. and Wilson, A.C.	Cann, R.L., Stoneking, M. and Wilson, A.C. (1987): 'Mitochondrial DNA and human evolution', *Nature* 325: 31-36.	Olson (2002), p. 244.
1995	Sykes B.C. *et al*.	'The origins of the Polynesians: an interpretation from mitochondrial lineage analysis', American Journal of Human Genetics, Vol. 57, pp.1463-75.	Jones, M. (2001), p. 255.
1996	Underhill, A. *et al*.	'A pre-Columbian Y chromosome-specific transition and its implications for human evolutionary history', *Proceedings of the National Academy of Science USA*, Vol. 93, pp. 196-200.	Jones, M. (2001), p. 262.
1997	Krings, M., Stone, A., Schmitz, R.W., Krainitzki H., Stoneking, M. and Pääbo, S.	'Neandertal DNA sequences and the origin of modern humans', *Cell*, 90, 1997, pp. 19-30.	Jobling *et al*. (2004), p. 266.
2000	Underhill, P.A., Shen, P., Lin, A.A. *et al*.	Y chromosome sequence variation and the history of human populations, *Nature Genetics*, 26, 2000, pp. 358-361.	Jones, M. (2001).
2000	Chen Y-S, Olckers A., Schurr T.G., Kogelnik A.M., Huoponen K. and Wallace, D.C.	'mtDNA variation in the South African Kung and Khwe – and their genetic relationships to other African populations', *Am. J. Hum. Genet.*, 66, pp. 1362-1383.	Olson (2002), p. 245. Jobling, Mark *et al*. (2004), p. 265.

Criticism of mtDNA and Y-chromosome research

Jobling *et al*. (2004) have discussed 'Early controversies about 'mitochondrial Eve''.[56] At issue were certain criticisms of the paper by Cann et al. (1987) that had put the 'mitochondrial Eve postulate on the table. The more serious points, as formulated by Jobling *et al*., were:

- most of the 'African' DNA samples were from African-Americans: only two of the 20 were born in sub-Saharan Africa. Are they representative of African mtDNAs?

- the method used to generate the tree was not guaranteed to find the most parsimonious tree. Different, more parsimonious, trees might exist;

- the method used to locate the root (midpoint rooting) placed it at the midpoint of the longest branch. This could be unreliable if, for example, the rate of evolution was higher in Africa than elsewhere. Outgroup rooting is preferred.[57]

However, Jobling *et al*. (2004) concluded that

> Despite these criticisms, subsequent studies have supported the major conclusion of Cann et al.: that is, a recent African origin for mtDNAs.[58]

Olson (2002) has reported scientists' warnings about the interpretation of mtDNA sequences. He speaks of the need to keep in mind two "caveats" when interpreting mitochondrial DNA sequences. The first is this:

> Larger populations tend to create greater diversity in DNA, and until the last few millennia, more humans lived in Africa than anywhere else. Surely some of the

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[56] Jobling *et al*. (2004), Box 8.7, 'Early controversies about 'mitochondrial Eve'', p.255.
[57] Ibid.
[58] Ibid.

> extra diversity seen in the DNA of Africans today arises from their greater numbers over all of human history.[59]

The second caveat runs as follows:

> Also, studies of mitochondria sample just a small part of our DNA. Geneticists tend to use mitochondrial DNA as an indicator for what has happened with the rest of our DNA, since it tells an exceptionally clear story. But different parts of the genome tell somewhat different stories, and these different accounts are still being compared and synthesized.[60]

Another line of criticism of the use of mtDNA and Y-chromosome evidence to reconstruct human origins came in a 2006 article by Garrigan and Hammer.[61] The issue here is time-depth.

Evidence in behavioural genetics

Let us now turn to evidence in behavioural genetics: the study of the influence of genes on behaviour. One might have said 'the *possible* influence' of genes on behaviour. However, it will not be disputed that there is genetic influence on the ontogeny of much motor activity in non-human animals and at least some in humans, such as posture, locomotion and mastication. The challenge, as ever, is to piece together a balanced and accurate picture.

The quest for evidence must overcome the obstacles presented at both the first- and second-order levels. The difficulties involved in finding evidence are both of the practical kind and of the theoretical. The latter amount to the problem of deciding what shall count as evidence in this context.

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[59] Olson (2002), p.38.
[60] Ibid. In the notes to the page on which this passage occurs (p. 245, re p.38), Olson refers the reader to discussions of these caveats in Weiss (1998), Relethford (1998) and Hawks *et al*. (2000).
[61] Garrigan, Daniel, and Hammer, Michael F. (2006): 'Reconstructing human origins in the genomic era', *Nature Reviews Genetics*, Vol.7, September 2006, pp.669-680.

Suppose the aim is to discover the reason for differences among human individuals in the development of some behavioural trait. Scientists cannot, fortunately, do breeding experiments on humans, nor can they just pluck people at random out of the population, ascertain what genes they have and then compare their behaviour. In the first place, their methods of genomic analysis are not yet so well-developed to make this kind of rapid, whole-genome comparison feasible. This situation can change with advances in technology. However, there are also problems with the exact observation and measurement of behaviour. In real life, people are behaving in all sorts of different ways at once. To observe and measure the selected trait requires it to be isolated, and this may render the procedure artificial and unrealistic.

A consequence of these difficulties has been that behavioural geneticists have concentrated a large part of their enquiries on pairs of identical twins. In such cases the genomic and genetic identity is assumed, and inferences are made from similarities or differences of behaviour. This concentration on twins has by now a long history. The first serious twin studies started in 1924,[62] long before methods of genomic analysis were available.

Evidence of 'behaviour'

As regards the observation and measurement of behaviour, precision is not the only issue facing behavioural geneticists. There is also the issue of standardisation of data. This brings us back again to the problem of the replicable description of behaviour. The problem was well characterised in Nuffield (2002), using the following example.

In Paragraph 3.16, the following point is argued:

[62] Plomin et al (2008), Ch. 5.

Any description of a human action can be set at a level that includes information about the biological characteristics of the individual. For example, the following descriptions could all correctly refer to the same act:

- The man's brain sent messages to his leg muscles.
- The man's brain leg muscles contracted and then relaxed.
- The man moved his leg.
- The man kicked the dog.

A further problem is our relative ignorance of development processes.

The workbench of behavioural genetics

We have spoken of behavioural genetics as "the study of the influence of genes on behaviour". Presented in this way, it sounds like a broad field, as indeed it is. However, as we probe it we shall find, as ever, that the workbench of behavioural genetics is more narrowly focused. An initial constraint is one that has already been imposed by the terms of reference of the present study: for present purposes we are primarily concerned with human behavioural genetics. There is a large literature on behavioural genetics. As far as the aims and methods of behavioural genetics are concerned, attention should be drawn to the successive volumes produced by Plomin and co-workers since. These and other texts will help us to identify the lenses of the 'virtual microscope' of behavioural genetics.

In 2002, a study published by the Nuffield Council on Bioethics in the United Kingdom under the title *Genetics and human behaviour: the ethical context* introduced behavioural genetics in the following way:

> Human behaviour is influenced both by the genes that we inherit and the environment in which we live. With the significant advances in our knowledge of genetics and publication of the draft sequence of the human genome, the focus of research has moved once again towards understanding the biological contribution to behaviour. Some researchers are attempting to locate specific genes or groups of

genes, associated with behavioural traits and to understand the complex relationship between genes and the environment. This is called research in behavioural genetics. In contrast to the research into the genetic basis of diseases and disorders, researchers in behavioural genetics investigate aspects of our personalities such as intelligence, sexual orientation, susceptibility to aggression and other antisocial conduct, and tendencies towards extraversion and novelty-seeking.

Nuffield then looked at the operational benchmarks. The chief distinction to be drawn in the methodology of research into behavioural genetics is that between quantitative genetics and molecular genetics.

As the Nuffield study explains:

- Quantitative genetics involves statistical methods that attempt to distinguish the effects of genetic and environmental factors on variation in certain behavioural traits, which can be quantitatively measured, between groups of individuals.

- The subjects of the research are usually twins, siblings, adopted children, and families.[63]

By contrast, the Nuffield report said of molecular genetics:

- Research in molecular genetics tries to identify variation in particular genes that influences behaviour, by examining the DNA of individuals.[64]

[63] Nuffield, p. xxiii.
[64] Ibid.

The focus on heritability

For exponents of behavioural genetics, the 'quantitative' domain of their research practice maps to 'population genetics'. They are interested in variation in the population at the phenotypic level, and variation in the gene pool. A key concept here is 'heritability', which Plomin *et al*. (2008) have defined as follows:

> **heritability** The proportion of phenotype differences among individuals that can be attributed to genetic differences in a particular population.[65]

It is often stressed by exponents of behavioural genetics that knowing "the proportion of phenotype differences among individuals that can be attributed to genetic differences in a particular population" is not the same thing as knowing the proportion of the behavioural make-up of a given human individual that is due to heredity – i.e., to the individual's genetic make-up.

Plomin *et al*. (1980) sought to clarify three possible misconceptions about heritability. In a section headed 'What Heritability Is Not', they said that

1. "*Heritability Is Neither Constant Nor Immutable*". The term "does not indicate an eternal truth concerning the phenotype, for it can vary from population to population and from time to time. It is a population parameter, a true character of a population, analogous to the population mean and variance. If the population changes, you can expect its parameters to change accordingly."

2. "*Heritability Does Not Refer to One Individual*". Here what the authors wrote is so helpful in explaining their view that we shall quote it in full: "Heritability is a descriptive statistic that applies to a population. If we say that height has a heritability of 0.80, that means that 80 percent of the variation in height observed in

[65] Plomin *et al*. (2008), p. 416.

this population at this time is due to genetic differences. It obviously does not mean that an individual who is 5 feet tall grew to the height of 4 feet as the result of genes and that the other 12 inches were added by the environment. However, if an individual from this population were 10 inches taller than average, one could estimate (rather imprecisely) that 80 percent of this deviation was due to genetic effects and that 20 percent was due to environmental influence. The same reasoning, of course, applies to behavioural traits".

3. "*Heritability Is Not Absolutely Precise*". Plomin *et al*. comment that heritability "is a descriptive statistic: like all descriptive statistics, it involves error. Correlations, for example, involve a range of error that is partly a function of the size of the sample from which the estimate is made".[66]

Twin and adoption studies

As the Nuffield study pointed out, research in quantitative behavioural genetics usually focuses on twins, siblings, adopted children, and families. As Nuffield put it, the aim is "to distinguish the effects of genetic and environmental factors on variation in certain behavioural traits, which can be quantitatively measured, between groups of individuals".[67]

Plomin *et al*. (2008) explain the interest in twin studies in the following way:

> Francis Galton (1876) studied developmental changes in twins' similarity, but one of the first real twin studies was conducted in 1924 in which identical and fraternal twins were compared in an attempt to estimate genetic influence (Merriman, 1924). This twin study assessed IQ and found that identical twins were markedly more similar than fraternal twins, a result suggesting genetic influence. Dozens of subsequent twin studies of IQ confirmed this finding. Twin studies have also been

[66] Plomin *et al*. (1980), pp. 225-6.
[67] Nuffield (2002), p. xxiii.

> reported for many other psychological dimensions and disorders; they provide the bulk of the evidence for the widespread influence of genetics in behavioral traits.[68]

Adoption studies are conducted for the following reasons. As Plomin *et al*. (2008) point out, certain behaviours 'run in families'. How can the researcher determine whether the reasons for this are genetic or environmental? Behavioural geneticists consider adoption to be an analytically useful condition because (1) it "creates pairs of genetically related individuals who do not share a common family environment", and also (2) it "produces family members who share family environment but are not genetically related".[69]

There can be variations on the basic models of twin and adoption studies. An example is the 'twins reared apart' model that has been investigated, notably, by Bouchard.[70] Such an approach combines the twin study and adoption study approaches.[71]

Linkage and association studies

Turning from quantitative behavioural genetics to molecular behavioural genetics, perhaps the easiest case to visualise is that of the mutation that rearranges or repeats a sequence of genetic DNA, so causing a behavioural disorder that is descends in a family according to Mendel's laws of inheritance. Such a case may, for example, involve the substitution of a single base in a nucleotide sequence. This is called a 'point mutation'. Examples of 'Mendelian' disorders with an impact on behaviour are phenylketonuria (PKU), Huntington's disease and Fragile X syndrome.

There are other disorders, however, that do not have such a simple cause, but are considered by geneticists to result from complex interactions among a number of different genes and environmental factors. Indeed, Sherman and Waldman (1999) observe that

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[68] Plomin *et al*. (2008), p. 78, Box 5.3, 'The Twin Method'.
[69] Ibid., pp. 70-1.
[70] Ibid., p. 158.
[71] Ibid., p. 80.

"virtually all psychiatric disorders and behavioural traits can be considered complex traits from a genetic perspective".[72] They go on:

> Given their non-Mendelian transmission pattern, the lack of a simple one-to-one genotype-phenotype relationship, reduced penetrance of any putative liability-increasing alleles, and the presence of phenocopies, psychiatric disorders and behavioural traits must be approached using contemporary molecular genetic analytic methods.[73]

Sherman and Waldman distinguish "four approaches currently used to find genes involves in complex traits: linkage analysis, allele-sharing methods, linkage disequilibrium methods, and experimental crosses using animal systems". They state:

> All depend on the co-segregation of the trait with some genetic marker of known location, be it an anonymous piece of DNA or a gene of known function. The putative trait gene and the genetic marker will be transmitted together from parent to child when they lie close together on the chromosome (i.e., are "linked"), so close that recombination does not often separate them. Recombination is a natural process that occurs during meiosis and causes genetic material to be exchanged between the maternally and paternally derived chromosomes of a homologous pair.[74]

The authors explain:

> The closer together two genetic markers are, the smaller the chance that recombination will occur between them. A measure of the genetic distance between two markers and/or genes is related to the recombination fraction, or the proportion of meioses in which recombination between the two markers would occur.
>
> When genetic markers are close together (i.e., tightly linked), or perhaps part of the same gene, the probability of recombination is negligible and characteristics of the

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[72] Sherman and Waldman (1999), p. 38.
[73] Ibid.
[74] Ibid., pp. 38-9.

> surrounding DNA (i.e., the allele polymorphisms) will be preserved from generation to generation. This phenomenon of the association of specific alleles of a genetic marker with the trait is called *linkage disequilibrium*.[75]

The particularity of the idea of 'linkage' is to describe a situation in which a "putative trait gene" and a genetic marker have a better-than-random chance of being transmitted together from the parental generation to the offspring because of their physical proximity on the same chromosome. It can also occur, however, that specific alleles go forward to the next generation in association with genetic markers that occur at different locus, perhaps on different chromosomes. This latter phenomenon is not to be expected a priori, because of the independent assortment of alleles during meiosis. When genes are in close proximity to each other, this factor tends to overcome the principle of independent assortment: hence 'linkage'. When gene and marker are associated despite *not* being in close proximity we have a phenomenon that defies random expectation: this is called 'linkage disequilibrium'.

It has been found that it is sometimes possible to discern a pattern of association between a trait (for instance, a disease) and a genetic marker that is stronger in a population showing the trait than it is in a population of controls. This fact has permitted the development of a technique known as the 'association study'.

Linkage and association studies are the basic tools of molecular behavioural genetics. The characteristic reference group for linkage studies is the family; that for association studies is the set of persons affected by the disorder.

Quantitative Trait Loci

There are some phenotypic traits that organisms just do or do not have, and there are others that may be present to a greater or lesser extent: in other words, they are phenomena that may vary in magnitude or intensity along a scale. Redness in tomatoes and height in

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[75] Ibid., p.39.

humans are examples that are often given. They may be called 'quantitative traits'. Where they result from the expression of genes, the genes may be referred to as 'quantitative trait loci', or 'QTLs'. As we have seen, the attention of behavioural geneticists has gone beyond single-gene effects to complex interactions among numbers of genes. As Plomin *et al*. (2008) put it,

> During the past decade, however, quantitative genetics and molecular genetics have begun to come together to identify genes for complex, quantitative traits. Such a gene in multiple-gene systems is called a quantitative trait locus (QTL). Unlike single-gene effects that are necessary and sufficient for the development of a disorder, QTLs contribute like probabilistic risk factors. QTLs are inherited in the same Mendelian manner as single-gene effects; but, if there are many genes that affect a trait, then each gene is likely to have a relatively small effect.[76]

According to Jobling et al. (2004), a QTL

> is usually defined as a polymorphic genetic locus identified through the statistical analysis of a continuously distributed trait (such as plant height or animal body weight). These traits are typically affected by more than one gene, as well as by the environment.

They comment:

> The QTL concept has been expanded to include traits that are not continuously distributed, such as schizophrenia or diabetes in humans, since the risk of developing these disorders is usually assumed to reflect a continuously distributed susceptibility function. In these contexts QTLs are really no different from the complex genetic phenotypes discussed [in Chapter 14].[77]

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[76] Plomin *et al*. (2008), p. 92.
[77] Jobling et al. (2004), Box 10.7, p. 331.

Be this as it may, exponents of behavioural genetics consider QTLs to be a key element in the workbench of the discipline.

Personality research

In Part III of Nuffield (2002), the authors reviewed the evidence for the inheritance of behavioural traits under four headings: "Intelligence", "Personality", "Antisocial behaviour" and "Sexual orientation". These concepts can be further broken down. Although there is not space here to go into all the details of the subject, it may be helpful to mention two points. First, the report notes that tests of intelligence may come in the form of five different types of test, among others, namely:

- measures of abstract reasoning or 'fluid' intelligence;
- vocabulary and general knowledge, or 'crystallised intelligence';
- visuo-spatial ability;
- retrieval or memory;
- speed of processing.[78]

Secondly, as far as personality was concerned, the authors of the report adopted what has been called the 'Big Five' model, which separates personality into the following five traits:

- neuroticism,
- introversion-extraversion
- agreeableness,
- conscientiousness,
- openness to experience, and (according to some methodologies)
- impulsivity, or sensation-seeking.

[78] After Nuffield (2002), pp. 70-71.

Research into intelligence or 'cognitive ability'

It would be impossible in a short space to summarise fairly the treatment of the topic of human intelligence in behavioural genetics and the criticisms that have been voiced against it. Our limited task here is to identify some aspects of the topic that feature in the workbench of the discipline of behavioural genetics as pursued by its exponents, including some of the tools that they employ.

In behavioural genetics, the term 'general cognitive ability' – or, simply, '*g*' - is often preferred to 'intelligence'. Plomin *et al*. (2008) consider that

> The phrase *general cognitive ability* to describe *g* is preferable to the word *intelligence* because the latter has so many different meanings in psychology and in the general language (Jensen, 1998).[79]

The idea behind *g* is that when people are given tests of various different cognitive abilities there is some intercorrelation among the results.[80] This suggested to Charles Spearman (Spearman, 1904) that there was an ability common to the various specialised abilities, and he called this *g*. As Plomin *et al*. (2008) explain, the use of *g* therefore entails a hierarchical model of cognitive abilities. General cognitive ability (*g*) stands at the top, branching down to the next level – that of the specific cognitive abilities - which in turn branches down to the various different tests that may be employed to investigate the specific abilities.

This conceptual structure rests on a basis of tests, referred to as 'psychometric' tests. Plomin *et al*. (2008) explain:

> Most people are familiar with intelligence tests, often called IQ tests (intelligence quotient tests). These tests typically assess several cognitive abilities and yield total scores that are reasonable indices of *g*. For example, the Wechsler tests of

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[79] Plomin et al. (2008), pp. 147-8. The reference is to Jensen, A.R. (1998): *The g factor: The science of mental ability*, Westport, CT, 1998.
[80] Ibid., p. 147.

> intelligence, widely used clinically, include ten subtests such as vocabulary, picture completion (indicating what is missing in a picture), analogies, and block design (using coloured blocks to produce a design that matches a picture). In research contexts, *g* is usually derived by using a technique called factor analysis that weights tests differently, according to how much they contribute to *g*. This weight can be thought of as the average of a test's correlations with every other test.[81]

The authors add:

> A test's contribution to g is related to the complexity of the cognitive operations it assesses. More complex cognitive processes such as abstract reasoning are better indices of g than less complex cognitive processes such as simple sensory discriminations.[82]

Comparative behavioural genetics

Behavioural genetics has made use of other species in its investigation of intelligence (and of other topics). Experiments have been conducted on the ability of strains of rats and mice to learn their way through mazes. Selective breeding has been used to produce strains of 'maze-bright' and 'maze-dull' rats.[83]

A different use of an animal model is the breeding of so-called 'knock-out' mice, in which the activity of one or other gene is suppressed in order to study the effects. This technique has been used in the investigation of the genetics of behavioural disorders. An example of the use of the technique in relation to a particular disorder – Neurofibromatosis Type 1 – is discussed in Plomin *et al*. (2008).[84]

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[81] Ibid., p. 148.
[82] Ibid.
[83] Ibid., pp. 149-155.
[84] Ibid., pp. 127-8.

A third type of approach is that of comparative genomics. An interesting example is research that has been done on the gene FOXP2. The issue here was a rare mutation of the gene in question that resulted in severe speech and language impairment in members of three generations of a particular family. The evolution of the gene is discussed in Carroll (2005).[85] He writes:

> The gene that is mutated in this family has been identified and is called *FOXP2*. The protein FOXP2 is a transcription factor, a tool kit protein that binds to DNA and regulates the expression of other genes. This mutation changes one amino acid in FOXP2, and this one change appears to knock out the FOXP2 protein function. Because these patients also carry one copy of the normal *FOXP2* gene, they still have some FOXP2 function.

Carroll next turns to the question whether the FOXP2 gene is "a novel, uniquely human gene". He answers in the negative.

> No, *FOXP2* is not at all unique to humans. The gene has been identified in a bunch of primates, rodents, and a bird. This distribution is typical of human tool kit genes, in that most, if not all, have counterparts in other species. In fact, the human FOXP2 protein differs at only 4 out of 716 positions from that of the mouse, at 3 positions from the FOXP2 of the orang-utan, and at just 2 positions from those of the gorilla and chimpanzee. This is a smaller amount of change in sequence than most proteins show, indicating that there has been a lot of pressure to conserve the FOXP2 protein sequence throughout mammalian evolution.

At first sight, this might not be thought to be particularly good evidence for a role for the FOXP2 gene in things so specific to humans as speech and language. Carroll advances two considerations that serve to modify that view. First, he refers to the phenomenon known as the 'selective sweep'. This is an effect of natural selection. It occurs when there has been a mutation in a nucleotide sequence and when the mutation has been favoured by natural

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[85] Carroll (2005), pp. 274-6.

selection. These events do not only concern the precise point where the mutation occurred, but also the variation in nucleotide sequences neighbouring the mutation. The selection of the particular variant created by the mutation, as it were, sweeps clean the neighbouring variation.

Carroll explains the next step in the argument:

> From the pattern of reduced variation at a gene relative to its neighbours, geneticists can tell if a gene has experienced a selective sweep. The signal of a selective sweep at the human *FOXP2* locus is one of the strongest at any human gene. This is a good indication that for some period of the past 200,000 years, during the evolution of our species, mutations in the *FOXP2* gene were favoured and spread throughout *H. sapiens*.

This, so the argument goes, sets up FOXP2 as a locus that could deliver something that other species have not got: that is, a faculty for speech and language. As we saw, there are two "coding differences" between human and chimp here. Are these the source we are seeking? Carroll is cautious:

> While it is possible that these could be responsible, there are hundreds more differences in noncoding DNA around *FOXP2*, in switches and regions that affect the place and amount of *FOXP2*expression. It is very difficult to pinpoint the changes that might have been meaningful to human evolution with current technology. My money is on the noncoding regions because tinkering with switches of the *FOXP2* gene would allow fine tuning of *FOXP2* expression in the formation of neural networks. It is known that *FOXP2* is expressed in many sites in the developing human brain. It is also expressed in the counterparts of these regions in the mouse, so FOXP2 would appear to have a widespread role in mammalian brain development. It is not clear yet precisely what FOXP2 does in development, but it is likely that it affects how subregions of the brain form and connect with other parts.

This example has been considered at length for a number of reasons.[86] The attention to the possible role of noncoding regions of DNA is interesting. So is the consideration of a gene that is very similar in a number of different animal species. Finally, it is noteworthy that this gene came to attention as a possible factor in the evolution of speech and language because of a marked case of 'individual differences' affecting a single family.

[86] For further details of the FOXP2 gene, see OMIM, No. 605317.

PART B: THE METHOD OF THE ENQUIRY

Chapter B1 – Criteria for distinguishing between different disciplines in the field

Aim of the chapter

In this chapter we shall present and discuss the criteria that were used in the conceptual mapping exercise. The task was, primarily, to devise a set of criteria that could serve either to assimilate or to separate the target disciplines. It was, however, crucial to the exercise that the assimilations or separations facilitated by the criteria should be significant. The point of the exercise was to illustrate the fact that people with a certain similarity of objectives could nevertheless differ in their specific goals, and in the concepts and methods they employed on the way to attaining these. A good way of doing this was to show that there were some quite simple but serious ways in which the approaches of selected research disciplines could differ. At the same time the approach needed to make room for the pragmatic. Not all differences in 'workbench' practice are at the highest conceptual level. They may reflect practical constraints such as the availability of funding, access to facilities or traditions of training and recruitment.

An important point to bear in mind is that whatever set of criteria was chosen it could never be exhaustive. The procedure implemented here was not the same as a written questionnaire exercise. Each interview was expected to last for about one hour. That is not a very long time to explore the intellectual world of an active scientific researcher in a complex discipline. To say that the interviews were 'semi-structured' was accurate. Their value could easily have been reduced by being over-structured. Rather, it was necessary to have a back-bone of criteria that could be developed, discussed and complemented during the conversation with the researcher.

Criteria discussed in the first round of interviews: Criteria 1 to 8

There was an initial set of eight criteria that were used as the basis for the first round of interviews. The inventory of criteria was allowed to grow as the interviewing progressed.

Criterion 1: '*Does the research cover all hominids or only* Homo sapiens*?*'

It seemed that the aim of pointing up differences in approach could usefully start by asking a researcher in a given discipline the simple question: '*Does the research cover all hominids or only* Homo sapiens*?*' This question is 'simple' and 'pragmatic' in that, although it potentially invokes some weighty themes, for the individual practitioner it boils down to a relatively concrete enquiry concerning her operational agenda – in other words, her workbench. Like many questions, it becomes less simple the longer one has to meditate on it. It serves as a good curtain-raiser on the subject of this enquiry since it serves as a reminder that the modern science of genomics does indeed offer the data and techniques that enable the scientist to bring other hominid and hominin species as well as *Homo sapiens* within the scope of an investigation into the origins of human behaviour.

It is necessary to say a word about taxonomy. Whereas 'hominid' was formerly used to refer to *Homo sapiens* and archaic humans, the modern awareness of our closeness to the Great Apes has resulted in their being classed as 'hominids', while the term 'hominin' is kept for humans and chimpanzees. The relevant terms are used here in the following way:

Table B1.01. Hominid taxonomy

Classification	*Taxon*	*Explanation*
Order	Primates	
Superfamily	Hominoids	Apes: Hominidae and Hylobatidae (Gibbons)
Family	Hominids	The Great Apes – orangutans, gorillas, chimpanzees, humans
Subfamily	Hominins	Human (*Homo*) and chimp (*Pan*)
Genus	*Homo*	*Homo sapiens* and extinct species and genera that palaeoanthropologists deem to be 'human' or 'human ancestor'. Examples: *H. habilis, H. ergaster*, *H. erectus*, *H. neanderthalensis*, and the genera *Australopithecus*, *Paranthropus* and *Ardipithecus*

Criterion 2: '*Is behaviour studied in the ecological setting – or in the laboratory or clinic?*'

At first sight, Criterion 2 is another that can be dealt with on a pragmatic level. Again, on one level at least, it is an operational question. It asks the researcher whether, as a matter of scientific practice, she habitually pursues her enquiries in the lab, in a clinical setting, or in the ecological context of the organisms under study.

However, this was not the main reason for advancing this criterion. The proposition that both heredity and environment contribute to the causation of human behaviour is so widely accepted as to amount to little more than a truism. Yet there is something strange here. The proposition as just stated places great weight on the relation between the human organism and its environment. This is, by definition, an ecological relation. Therefore the proposition concerning heredity and environment seems to assume that it is important to pay attention to the ecological relation between the human organism and its environment. However, it is not so clear that people are as swift to characterise that apparent assumption as a 'truism' – or even as a 'truth' - as they are in the case of the original proposition. Criterion 2 might offer a chance to explore the extent to which given interviewees were engaging with the ecological dimension of the subject.

To speak of an organism's relation with the environment as an ecological relation does not commit one to a specific view on the relative weight to be accorded, respectively, to heredity and environment in the causation of behaviour. The ecological relation is a relation between the phenotype and its environment. The question of what causes the behaviour shown by the phenotype as this interaction with the environment is played out is not pre-empted by this way of setting out the problem.

Criterion 3: '*Is the focus on species-typical traits or on individual differences?*'

The expression 'human behaviour' can easily be understood to mean 'the behaviour of *Homo sapiens* in general'. That understanding underlies what we mean when we talk about the behaviour of humans by comparison with other species: for instance, chimpanzees.

Indeed, turning that observation around, when we read the phrase 'chimpanzee behaviour' our first response is almost certainly to take the writer to mean 'the behaviour typical of chimpanzees'. A moment's reflection shows, however, that it does not have to be taken that way. In the study of human behaviour it may be of high interest to study, for example, the behaviour of the small proportion of individuals who suffer from some particular genetic disorder.

In the latter case the subject of study is the 'different' individual. Inherited psychiatric disorders do not provide the only context within which a researcher may decide to focus on individual differences. To take an alternative example, Burling (2005) has argued that the evolution of complex, fine-tuned language in humans may have been due to natural selection favouring people who had leadership qualities, including the quality of eloquence. Since leaders often have more offspring than other members of the social group, Burling argues, this could have been a way for language gradually to enhance its subtlety and richness.[87] Whether or not one actually agrees with Burling's argument, it is an interesting one in the present context. Burling focuses on individual differences, but he does so in order to develop a hypothesis concerning a trait – subtle and rich language – that comes to be the possession of the wider group.

By contrast, it is possible to be interested in individual differences in behaviour, not for what they will ultimately tell us about the wider group, or indeed the whole species, but rather as a way of trying to explain the differences that have been observed between people in such matters as personality traits and intelligence. This seemed to be the characteristic orientation of behavioural genetics. We have already seen how Rowe and Jacobson (1999) characterised behavioural genetics as "a field concerned with variation, with why one individual differs from another".[88]

[87] Burling (2005), pp. 190-2.
[88] Rowe and Jacobson, 1999, p.12. The quotation was cited in Chapter A.1 above, Footnote 5.

Criterion 4: '*Does the research typically draw on the findings of genomics?*'

The point of this question was to discover whether, and how far, the research in question actually made use of the findings of genomic science. This and Criteria 5 and 6 were intended to probe the ways in which genetic evidence is being used by various disciplines.

A negative response to Criterion 4 was not in itself evidence of irrelevance. In the planning of the interview series it was always intended to leave room for responses that might not fit neatly into a preconceived conceptual or methodological framework.

Criterion 5: '*Is the research on genes or other DNA? If 'other': mtDNA or Y-chromosome?*'

In Chapter A4, the point was made that different disciplines working in the general area of behavioural genomics could have different 'genomic workbenches'. They might concentrate on genes (in the various understandings of that term), notably nuclear genes, or they might be interested in other regions of the human genome. Criterion 5 was therefore necessary in order to help characterise the workbench of the researcher being interviewed.

Criterion 6. '*Is there research on the DNA of non-human/hominid species? If so, animals or plants?*'

As has been explained, the primary focus of the present study is human behavioural genomics. However, the human genome cannot meaningfully be studied in isolation from other genomes. Moreover, the study of particular animal genomes can be part of the workbench of a discipline, even, that in general puts the emphasis on humans. This is the case when model species such as mice are studied.

A different approach is the study of the evolution of animal and also plant species that have been associated with humans and their behaviour. Biomolecular archaeology, for instance, has been concerned with the DNA of species of plant and animal brought under domestication by humans, notably in the Neolithic Revolution that saw the emergence of agriculture (Jones, Martin, 2001).

Criterion 7: '*Is there research on other biomolecules? If so, proteins or other?*'

This criterion was intended to put the question of DNA in perspective. It is all very well to ask researchers whether they have an interest in DNA. They could answer 'yes' to that question while, in fact, having even more salient points of focus elsewhere: different types of RNA, protein or whatever.

It was also simply considered interesting to uncover cases of the adduction of biomolecular evidence other than that of DNA.

Criterion 8: '*Does the research use environmental markers?*'

By 'environmental marker' is meant here some signal in the environment that can, or conceptually could be correlated with a biological signal: for instance, fossilised bones or teeth, or a DNA sequence. The idea is easiest to grasp in the case of prehistoric archaeology. A case in point would be when a particular type of lithic industry (stone tool-making detritus) is found in association with fossilised hominin remains. Another instance would be the identification of a particular type of dwelling in association with human remains from which DNA could be extracted. Pollen can be an environmental marker. Its study is named 'palynology', and Roberts (1989) has stated that

> Palynology is the single most important branch of palaeoecology for the late Pleistocene and Holocene.[89]

The DNA of plants and animals that characterised the environment of earlier human populations can also serve as an environmental marker: so in certain circumstances a DNA sequence of one species can be an environmental marker for a DNA sequence in another.

It is an interesting question how far this concept of an environmental marker may validly be extended. Does it, for example, include the idea of an environmental 'factor' in behavioural ontogeny? On the one hand, the latter case seems at first sight to be more fluid and more complex than the former. On the other hand, the 'simplicity' of the first case is largely illusory. To revert to the case of palynological evidence, this may help us to understand the environment that conditioned the lives of earlier human populations, or it may be a way of tracing the impact on the environment made by these populations. The interactions can be complex and difficult to discern. As Roberts puts it:

> The interpretation of pollen records in terms of past human impact is, if anything, more difficult than it is for climate. Many former land-uses, such as hunting-fishing-foraging in Mesolithic Europe, have no modern analogue for comparison. Furthermore, it is often the indirect consequences of human impact that are most obvious palynologically (Edwards, 1979; 1982).[90]

The potential complexity of the issues raised by this criterion was finally decided to be a good reason for including it.

Criteria discussed in subsequent interviews: Criteria 9 to 14

On the basis of experience with the first series of interviews, it was decided to add certain new criteria. As has already been explained, the list of interviewees was not being regarded

[89] Roberts (1989), p. 22.
[90] Ibid., p. 27.

as a statistical sample. In adding new criteria as the interview series progressed there was a loss of standardisation in the interview protocol. However, there was a realistic prospect of this (in the circumstances) minor disadvantage being off-set by a greater advantage: that of enriching the exchanges with the interviewees and adding value to the output of the interview process.

Criterion 9: '*The main concern is phylogeny or ontogeny?*'

The purpose of this criterion was to explore more deeply the motivation and objectives of the interviewee's research, especially research drawing on genomic evidence. Also, it might turn out that there was a difference in perspective on the role of genomic evidence between scientists looking at their subject from the points of view of phylogeny and ontogeny respectively. If so, posing this question would help to bring this out and to give some insight into these different perspectives.

In the wider debate about the pertinence of genomic evidence to the study of the causes of human behaviour it may be that the weight of attention has shifted too far towards ontogenetic questions. By adopting this criterion, it would be possible to open the project to the phylogenetic perspective: or rather, since this openness was already acquired, to emphasise it explicitly. The project concerned concepts and methods. It would be interesting to see to what extent different concepts and methods flowed from the phylogenetic/ontogenetic distinction. It might also be interesting to discover whether that distinction was considered to be a significant one for the discipline in question. The literal significance is clear, but its implications for each discipline were not self-evident.

Criterion 10: '*Does the research draw on fossil evidence?*'

Different concepts and methods certainly flow from another distinction: that between researchers who have to have recourse in their work to fossil evidence and those who do not. Yet the subject-matter investigated by each may be the same: for instance,

encephalisation in human or precursor human species, or modes of bipedal locomotion. How much difference does it make to have to draw one's inferences from fossil remains, and how much does it matter?

The advance of genomic science has increased the inventory of methods available to archaeologists and palaeoanthropologists by adding new molecular methods. Two ways in which this has happened spring to mind: the emergence of molecular phylogenetics, and the success of researchers in accessing ancient DNA. These developments have – so one would hypothesise – have had a proportionately greater impact on researchers whose enquiries are constrained by the limitations of the fossil record than on others.

Criterion 11: '*Is Newtonian mechanics relevant to the research?*'

This criterion was inspired by the discussion in the second interview, the one with John Hutchinson, a researcher in the field of evolutionary biomechanics. He specialises in the study of how large animals stand and move: for instance, elephants and dinosaurs. Dr Hutchinson gave the opinion that the recourse to physics – in the form of Newtonian mechanics – was one of the key points that differentiated evolutionary biomechanics from other disciplines under study here.

Criterion 12: '*Is the research intended to have a clinical application?*'

As a general point, it might be observed that the professional, economic or social motivation of research lay rather within the scope of a sociological or economic investigation than a philosophical one. However, discussion with interviewees and reflection on that discussion suggested that it would be perverse to ignore the existence of factors that could have a large impact on the research agenda of a discipline. To proceed as though a research agenda was solely the product of the interplay of epistemic imperatives would itself be a distortion.

The economic factor is the expectation that research likely to yield results of clinical applicability will have a better chance of funding than that which solely serves to advance knowledge. Thus research into the nervous system of the sea-slug may well be undertaken for the benefits that it may yield to neurology, with an ultimate human application in mind, rather than out of a consuming curiosity about the natural history of the sea-slug. At the same time, this type of prioritisation is not irrational. It does not necessarily place the researcher in a self-contradictory position.

Taking into account the possibility of a clinical application for one's research is not only a matter of economics. There is also philanthropy. This may be individual philanthropy – 'What can I do to help?' – or collective philanthropy – 'What can our profession or our country do to help?' This dimension of the question was particularly stimulated by a passage in the interview with Smith, the molecular neurobiologist, that will be discussed later.[91]

Criterion 13: '*Does the research use cultural markers, e.g., surnames?*'

The idea of reference to environmental markers had already been incorporated in the list of criteria. It became clear that this ought to be complemented by the idea of a cultural marker. The issue was the existence of cultural phenomena that might usefully be cross-referenced by researchers with genomic phenomena of various kinds. A classic example is language. Language is passed down from one generation to another, but not genetically. The transmission of language is effected culturally. It shows a tendency to reflect biological inheritance, but with exceptions. The upshot is that tracing linguistic inheritance and tracing biological inheritance, and comparing the two, can be a fruitful area of enquiry.

The same thing can be said about surnames. Once again, the inheritance of surnames is connected to biological inheritance, although the two mechanisms are not a perfect match. The acquisition of surnames is subject to social rules that vary from one culture to another,

[91] See Chapter C13 below.

and which are frequently marked by gender differences. Jobling et al. (2004) have discussed linguistic evidence for genetic admixture in human populations, making the point that spoken languages themselves are not the only source of linguistic evidence. As they point out,

> surnames and place names (**toponymy**) are both capable of revealing the hybrid nature of a population. For example, English towns have names derived from Celtic, French (Norman) and Scandinavian languages as well as from Anglo-Saxon.[92]

Criterion 14: '*Does the research offer economic or social benefits?*'

Having introduced a criterion of clinical applicability (Criterion 12), it was logical to ask the further question, whether the research offered economic or other social benefits. The reasons were similar to those in the former case. There was no plan to turn the research project into a socio-economic audit. There was, nevertheless, a point of difference to be noted from the criterion of clinical applicability. If you are told that a scientist is studying, say, the development of the human brain it comes as little surprise to learn that there may be benefits from the research for the diagnosis and perhaps treatment of some neurological disorders. The link between some of the research discussed in the interviews and particular socio-economic benefits may be less predictable and therefore all the more interesting to elicit. It may be evidence of socio-economic drivers at work behind the research, but it may also be evidence of human ingenuity.

[92] Jobling *et al*. (2004), p. 377.

Chapter B2 – The selection of disciplines and interviewees

The task

Once the conception of the research project had been worked out and preliminary research had been conducted, the next step was to select a sub-set of disciplines for more detailed study and to identify researchers who would be suitable, and available for interview. It was never intended that the scope of the project should be limited to the work of the selected disciplines and interviewees. What was intended was that the chosen disciplines and researchers could serve to illustrate the general field. The subject of the project was behavioural genomics. Focusing attention on a sub-set of disciplines and researchers was a way into the subject: it was not meant to exhaust it.

The role of the interviewees in the procedure: examples, not samples

A further word must be said on the role of the interviewees in the procedure. It could be summed up in the phrase: 'examples, not samples'. In fact, there were two putative roles that it was considered better to avoid. One was the role of 'sample', in the statistical sense. The other was the role of 'representative', in the sense of 'spokesperson'.

As we saw in Chapter A3, it was possible to draw up a long-list of 50 potential target disciplines, each of which undoubtedly displays some internal variation in practice. In the case of the current research project, practical constraints put a limit of about twelve on the number of researchers to be interviewed, and in the end the actual number of interviewees was nine. These numbers were too small to permit the set of interviewees to be treated as a sample of the whole field. Taking into account the fact that it was planned to have only one interviewee per chosen discipline, the interviewees could not even validly be regarded as a sample of their own research community. Thus any idea of treating the set of interviewees as a statistical sample was discarded. This had an influence on the interview procedure

itself, since it meant that the responses to the questions on the various criteria could not be validly treated in the same way as answers to a questionnaire might have been and subjected to statistical analysis.

The view might have been taken that a sample of one could have had a useful role to play as part of a qualitative analysis, if the person concerned could be regarded as a 'representative' of his or her discipline. The word 'representative' can be used in different ways. One of these ways is in the sense of a representative of a country at an international meeting. Such a person is a plenipotentiary, with delegated powers. This sense was inappropriate in the present case. The interviewees were not meant to be representatives of their disciplines, in the sense of being 'spokespersons' or 'delegates'. To be representatives in this sense they would need credentials, and who was to validate these?

At the same time it would have been perverse systematically to avoid leaders of their research communities. The ideal person should be a leader of research in the given field, in the sense of having experience, not just of active involvement, but of an initiative-taking role in the setting and execution of a research agenda. A 'leader' in this sense is neither a validated spokesperson (one sense of 'representative'), nor just any researcher plucked at random (another sense). Such people are 'examples', but not 'samples' of the researchers in their discipline. They are chosen for being potentially interesting examples: people whose knowledge and experience equip them to describe what it is like to do their kind of research - and not just 'describe', but give illuminating insights into their research practice and the ideas that drive it. They cannot commit others to the ideas that they express. They are not 'spokespersons' in that sense. But they can illuminate their field for an interested outside enquirer.

The short-list not necessarily a sub-set of the long-list

The long-list of potential target disciplines set out in Chapter A3 was a product of an initial survey of the field of behavioural genomics. It could be described as 'raw data'. Within and among the disciplines listed there were further potential distinctions and sub-divisions that

could be made, as well as overlaps that could be noted. The selection of a short-list of disciplines was not just a matter of taking a sub-set of the original 50, but of refining the analysis of the disciplines as well.

Choosing disciplines for study or researchers for interview?

As between choice of disciplines and choice of interviewees, then, the priority was given to the disciplines, in the interests of ensuring adequate thematic coverage. The second step was the identification of potential interviewees. After that came two further steps: first, the sending of requests for interviews to selected researchers and, second, revision of the list of interviewees and interview requests in the light of feedback from those originally contacted. Inevitably, the establishment of the final list of interviewees was influenced to some extent by issues of availability or willingness on the part of certain persons. A separate factor was one of manageability. Some disciplines, earmarked provisionally for further study, were dropped from the list because of a fear that the list of interviewees might become too long to be manageable.

Overlap among disciplines and thematic coverage

The fact that only a comparatively small sub-set of all the potential target disciplines could be selected for further study, and for supplying examples for the interview series, might have prejudiced the completeness thematic coverage of the research project. Indeed, to some extent this was inevitable. However, there was a countervailing factor, and this was the overlap among disciplines. To take an imaginary example, Interviewee *X* is an example of a researcher from Discipline *A*. However, it is a well-known fact that Discipline *A* overlaps considerably with Discipline *B*, or that Researcher *X* was originally trained in the older Discipline *C*, or that Researcher *X* has participated in (perhaps led) inter-disciplinary research initiatives with both Disciplines *A* and *B*. The upshot is that *X* can speak with substantial intellectual authority about the three disciplines *A*, *B* and *C*.

Did selecting a discipline for further study entail an interview?

We have spoken about selecting disciplines for further study and about selecting examples of researchers in the various disciplines as interviewees. Did this amount to the same thing? Were only those disciplines for which interviewees were found become the objects of further study? The short answer is 'yes'. At the same time account must be taken of what we have already said here about thematic coverage. So once the interviewees had been identified it became necessary to concentrate on the preparation of the interviews, their conduct, and on the treatment of the output. However, this did not mean that the scope of the entire field of behavioural genomics was suddenly confined to the immediate concerns of eight or nine disciplines. It was considered that the set of disciplines chosen provided adequate thematic coverage to serve as a basis for discussion of topics that pervade the whole field of behavioural genomics.

At the post-interview stage a further widening of the scope of the project was effected when it came to analysing the topics within the general field of behavioural genomics that were not receiving their due share of attention. These were the gaps in the multidisciplinary division of labour. This is a matter we shall return to in later chapters.

Initial ideas about the choice of disciplines

Reviewing the long-list in the light of further literature research, a set of 20 possible target disciplines was identified. These are itemised in Table B2.01 below.

Table B2.01. List of 20 potential target disciplines	
Behavioural ecology	Human developmental genetics
Behavioural genetics	Human evolution
Behavioural pharmacogenomics	Human evolutionary genetics
Biogeochemistry	Human genetics
Biomolecular archaeology	Human intelligence research
Cognitive neuroscience	Molecular mechanisms underlying behaviour
Developmental psychopathology	Molecular neurobiology
Down Syndrome research	Niche construction theory
Evolutionary biomechanics	Palaeoanthropology
Evolutionary psychology	Psychiatric genetics

This list of 20 was the short-list for the final choice. The next task was to reduce the 20 to a more manageable number. The target was a figure between six and ten. In the end eight disciplines were selected. There were nine interviews because the first interviewee from evolutionary biomechanics mentioned the names of other researchers in the field whose work was more directly relevant to humans, and one of these suggestions was followed up successfully.

The reasons for dropping some of the 20 from the final list of eight included the following: overlap between disciplines, lack of availability or willingness on the part of selected interviewees, positive prioritisation of certain other disciplines on the basis of particularly promising and useful contributions to the literature, and the simple, pragmatic need to reduce the total number of interviews.

The number of persons to whom requests for interview were sent was 14. Although there were some potential interviewees who did not respond positively to the request for their participation, these were few in number (four). In general the responses from selected interviewees were encouraging. Tribute is gratefully paid to the constructive cooperation shown by the nine eventual interviewees.

The nine researchers with whom interviews were arranged, and the disciplines that they exemplified, are listed in Table B2.02 below. They are listed in the order in which they

were interviewed. In the column headed 'Discipline', the respective entries are the disciplines which they were selected by the author of the project as exemplifying. They are not necessarily, in this table, self-descriptions. After the table has been given there will be short descriptions of the reasons for choosing each of the respective researchers.

Table B2.02. Researchers selected for interview, with disciplines

Researcher	*Affiliation*	*Discipline*
Jones, Martin K.	George Pitt-Rivers Professor of Archaeological Science, University of Cambridge.	Biomolecular archaeology
Hutchinson, John	Lecturer in Veterinary Basic Sciences, Royal Veterinary College (Reader, 2008).	Evolutionary biomechanics (Large animals)
Smith, Christopher U.M.	Department of Vision Sciences, University of Aston.	Molecular neurobiology
Buckley, Susan	Emeritus Professor of Developmental Disability Psychology, Department of Psychology, University of Portsmouth, and Director of Research and Training Services, Down Syndrome Educational Trust.	Down Syndrome research
Mace, Ruth	Professor of Anthropology, University College London (UCL); (Fellow of the British Academy, 2008).	Human behavioural ecology
McGuffin, Peter	Professor of Psychiatric Genetics and Dean of the Institute of Psychiatry at the Maudsley Hospital, London.	Behavioural genetics
Jobling, Mark A.	Wellcome Trust Senior Research Fellow in Basic Biomedical Science, Professor of Genetics, Department of Genetics, University of Leicester.	Human evolutionary genetics
Lindsay, Susan	Professor of Human Developmental Genetics, Institute of Human Genetics, University of Newcastle upon Tyne.	Human developmental genetics
Crompton, Robin Huw	Professor, Primate Evolution and Morphology Group (PREMOG), Department of Human Anatomy & Cell Biology, School of Biomedical Sciences, University of Liverpool.	Evolutionary biomechanics (Hominids)

Martin Jones

Martin Jones is the professor of archaeological science at Cambridge. He is a former chairman of the Ancient Biomolecule Initiative and the Science-based Archaeology Strategy Committee. His work, *The molecule hunt: Archaeology and the search for ancient DNA*,[93] was a valuable resource during the preparation of the current project.

Professor Jones' biography exemplifies some of the difficulties involved in classifying scientists according to their disciplines. He is patently an 'archaeologist', but it is also highly pertinent that he works in 'archaeological science'. At the same time, on his website he describes himself as working in 'archaeobotany' and 'archaeogenetics'.

John Hutchinson

Dr John Hutchinson is a researcher in evolutionary biomechanics who specialises in locomotion in large animals, including elephants and dinosaurs. He was identified by a web-search as a researcher interested in the evolution of bipedal gait. The present author had decided to explore the topic of bipedal gait for the following reasons. It seemed important to establish the point that when we are talking about human behaviour we are not only referring to the functioning of the higher cognitive faculties, or to motor behaviour apparently mediated by those faculties. When we do concentrate on the higher cognitive faculties we can slip into thinking that the fact that humans walk upright on two legs is trivial. Yet it is something that is characteristic of our species, that has evolved, and that – by leaving our arms and hands free for other behaviour – is a prerequisite for much behaviour mediated by the higher cognitive faculties. In other words, the fact that humans walk upright on two legs, and that they have the skeleto-muscular infrastructure that facilitates this, are not just miscellaneous facts about human motor physiology: they are important truths about the behavioural repertoire of the human species.

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[93] Jones, Martin (2001).

To say that bipedal gait is characteristic of humans does not mean that it is exclusive to them. Among other species to have shown bipedal locomotion were many dinosaurs. Hutchinson and co-workers had, in particular, written papers on the locomotion of *Tyrannosaurus rex*: for instance, a letter to *Nature* with Garcia in 2002 entitled 'Tyrannosaurus was not a fast runner', and an article in *Nature* with Gatesy in 2006, 'Beyond the bones: How did dinosaurs stand and move? Computer simulation and other methods have told us much about how dinosaurs did and did not move, but they have not yet reached their full potential'. Hutchinson and Gatesy explained, notably, how researchers trying to determine how Tyrannosaurus moved work by a process of successive exclusion, applying a "range of kinematic (motion-based or geometric) and kinetic (force-based) criteria" to help them to exclude the movements that would have been "unrealistic".[94]

These and other points emerging from the interview had general applicability for evolutionary biomechanics. Their significance was not confined to dinosaurs. In addition, Hutchinson was able to name other researchers with a more particular interest in hominins. This led to the successful approach to Robin Crompton (see below).

Chris Smith

A thesis concerning the ontogeny of behaviour necessarily has some neuroanatomical and therefore developmental presuppositions. These cannot be made explicit without some account of what is going on at the genomic level: for instance in the processes of gene expression in the ontogeny of the neuroanatomy and the environmental interactions susceptible of influencing these. Here 'environmental' can refer to both the external environment of the organism and the internal, cellular environment.

The foregoing considerations, in slightly different forms, underlay the choice of two disciplines that did not specifically have behaviour as their subject-matter, but which were

[94] Hutchinson and Gatesy (2006), p. 293.

profoundly concerned with the molecular account of the neural and developmental prerequisites for behaviour. These disciplines were molecular neurobiology and human developmental genetics. The researchers selected for interview were, respectively, Chris Smith and Susan Lindsay.

Dr Chris Smith was selected to exemplify the discipline of molecular neurobiology. He was the author of *Elements of molecular neurobiology* (2nd edition 1996, 3rd edition 2002).[95] Smith was Dean of Faculty of Life and Health Sciences at the University of Aston from 1991 to 1994. Since 1996 he has been Honorary Visiting Fellow in the Department of Vision Sciences, and latterly Sessional Lecturer in the Department of Optometry, School of Life and Health Sciences.

Sue Buckley

Professor Sue Buckley is the Director of Research and Training Services at what was formerly called the 'Down Syndrome Educational Trust' and is now (since May 2008) 'Down Syndrome Education International'. On the DSEI website, Down syndrome is explained in the following terms:

> **Down syndrome is the result of a genetic variation**
>
> Each cell in the body usually has 23 pairs of chromosomes (46 in total). Individuals with Down syndrome have an additional copy of chromosome 21 in all or some of the cells in their body (making 47 chromosomes in total).
>
> There are three main types of genetic variation that cause Down syndrome:
>
> - Trisomy 21 - all of the cells in the body have an extra copy of chromosome 21. This is the most common type of Down syndrome, found in at least 9 out of 10 people with the condition.

[95] The 2nd edition was used in the preparation of the interview.

- Translocation - all of the cells in the body have additional chromosome 21 genetic material attached to another chromosome. Only around 1 in 20 people with Down syndrome have the translocation form of the condition.
- Mosaic - only some of the cells in the body have extra chromosome 21 genetic material. Only around 1 in 50 individuals with Down syndrome have the mosaic form of the condition.[96]

Down syndrome is a significant cause of intellectual impairment. Down syndrome research was selected for further study here because it is a relatively common disorder (occurring in about 1 in 1,000 live births in the UK) that affects behaviour. As a general point, it was considered desirable to include at least one widely-recognised genetic disorder in the set of research fields chosen for further study. Down syndrome, which can affect cognitive faculties and motor behaviour, was considered an appropriate choice.

Sue Buckley is a leading researcher and educator in Down syndrome. She is Emeritus Professor of Developmental Disability Psychology in the Department of Psychology, University of Portsmouth.

Ruth Mace

Ruth Mace is Professor of Evolutionary Anthropology at University College London, where she is also Convenor of the Human Evolutionary Ecology Group. She co-edited *The evolution of cultural diversity: A phylogenetic approach* (2005). In her preface to that book, she said that it "arose proximally out of a session at the Human Behaviour and Evolution Society annual meeting" that was held at UCL in 2001. Concerning her own professional background, Professor said in the preface that

> In my case, I trained as an evolutionary ecologist working in zoology, then moved into human behavioural ecology.[97]

[96] From the Down Syndrome Education international website at: http://www.downsed.org/our-work/down-syndrome/incidence/ (Consulted 9 February 2009).

On the website of the Human Evolutionary Ecology Group at UCL, it is stated that

> We study human behaviour and life history as adaptations to local environments - which includes not only **human behavioural ecology** but also the related areas of **reproductive ecology**, **evolutionary demography**, **evolutionary medicine** and **cultural evolution**.[98]

The disciplines and specialisations that have just been mentioned offer a rich nomenclature, highly promising to the researcher interested in the conceptual mapping of behavioural genomics. However, the main reason for wishing to interview Ruth Mace was to explore what is understood by an ecological approach to human behaviour. A second reason was to clarify the 'evolutionary' and 'phylogenetic' perspectives of a discipline, or cluster of disciplines, that – so it seemed from the preparatory research – did *not* typically draw directly on the findings of genomics.

Articles by Mace that provided background for the interview included Holden and Mace (2003) – 'Spread of cattle led to the loss of matrilineal descent in Africa: a coevolutionary analysis' - and Gibson and Mace (2006) – 'An energy-saving development initiative increases birth-rate and childhood malnutrition in rural Ethiopia'.[99] In 2008 Professor Mace was elected a Fellow of the British Academy.

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[97] Mace et al. (2005), p. *v*.
[98] Human Evolutionary Ecology Group, UCL, at: http://www.ucl.ac.uk/heeg/ (Consulted 13 March 2007 and 6 February 2009).
[99] See also Pagel and Mace (2004) and Mace and Holden (2005).

Peter McGuffin

Peter McGuffin is Professor of Psychiatric Genetics and Dean of the Institute of Psychiatry at the Maudsley Hospital, London. He was a co-author of the work *Behavioral genetics in the postgenomic era*, with Robert Plomin, John C. Defries and Ian W. Craig (2003), which was consulted during the literature search phase of the project. McGuffin has cooperated with Plomin and other co-authors in the writing and editing of a series of five editions of the work *Behavioural genetics*. The most recent edition appeared in 2008.[100] Another reason for approaching McGuffin was that the present writer had heard him speak at the 4th EMBO/EMBL Joint Conference on Genetics, Determinism and Human Freedom in Heidelberg in 2003.[101]

On the basis of the writings just mentioned, McGuffin was selected as a researcher from the discipline of behavioural genetics. At the same time it will be noted that the chair he holds is one in psychiatric genetics. When it came to the actual interview, as we shall see, McGuffin proposed a self-description that was different from both of these.

Mark Jobling

Mark Jobling is Professor of Genetics at the University of Leicester. He was one of the authors (with Matthew Hurles and Chris Tyler-Smith) of the work, *Human evolutionary genetics – origins, peoples and disease* (2004). This was another valuable resource during the preparation of the current project. The purpose of the work was summarised by its authors in the following way:

> This book provides an extensive introduction to the analysis of human genomic variation from an evolutionary perspective. The fundamental concepts underpinning

[100] Plomin *et al*. (2008).
[101] 4th EMBO/EMBL Joint Conference on Genetics, Determinism and Human Freedom, 14-15 November 2003, Heidelberg, Germany.For a concise conference report, see Armandola (2004).

anthropological, medical and forensic applications of human diversity studies are all explored with illustrative examples.[102]

Jobling's research projects at Leicester have included 'The Y chromosome as a marker for the history and structure of human populations'. This was conducted under a Wellcome Trust Senior Fellowship in Basic Biomedical Science from August 1999 to July 2004.

Susan Lindsay

The reasons for selecting the discipline of human developmental genetics for further were touched on above, in the section on Chris Smith. The researcher selected for interview in this case was Susan Lindsay. She is Professor of Human Developmental Genetics at the University of Newcastle upon Tyne.

Lindsay and her colleagues are engaged in gene expression studies during early human development. The Newcastle team have been the coordinators of the Developmental Gene Expression Map (DGEMap) project (2005-2009) under the European Union's Sixth Framework Programme. This is described as "the first ever "Design Study" for a pan-European research infrastructure dedicated to the analysis of gene expression patterns in early human development".[103] The Institute of Human Genetics at Newcastle and the Institute of Child Health at University College London are the resource managers for the MRC-Wellcome Trust Human Developmental Biology Resource (HDBR), "an ongoing collection of human fetal material ranging from 4 to 12 weeks of development". HDBR makes tissue samples available to the international scientific community and also conducts an *in situ* hybridisation service.[104]

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[102] Jobling et al. (2004), Preface, p. xvii.
[103] DGEMap website: http://www.dgemap.org/ (Consulted 9 February 2009).
[104] HDBR website: http://www.hdbr.org/ . Consulted 9 February 2009.

Robin Crompton

Robin Crompton is a professor in the Department of Human Anatomy & Cell Biology, School of Biomedical Sciences, University of Liverpool, where he leads the Primate Evolution and Morphology Group (PREMOG). He was selected for interview for his research in evolutionary biomechanics. Specifically, on the basis of the interview with John Hutchinson (see above), Crompton was selected as a researcher well-placed to talk about the evolutionary biomechanics of hominids.

Examples of Crompton's work consulted before the interview included the articles by Crompton and Wang (2004) on 'The role of load-carrying in the evolution of modern body proportions' and that by Carey and Crompton (2005) on 'The metabolic costs of 'Bent-Hip, Bent-knee' walking in humans'. These papers brought out, *inter alia*, the bioenergetic dimension of human behaviour, a topic that, it was felt, had not always received its due measure of attention, at least in some disciplines.

That concludes this brief, initial survey of the selected interviewees. This chapter closes with a general point about the final list of researchers.

Manageability: the geographical aspect

It will be seen from the list of interviewees given in Table B2.02 that only researchers at British research institutions were interviewed. At the outset of the project, the idea of selecting some interviewees at research institutions in other European countries was considered. However, the logistical arrangements that were needed to set up and conduct the interview series represented a significant management task. Including researchers from outside the United Kingdom would have added to the practical difficulty of bringing the task to a successful conclusion. That said, if this had been a research project on a larger scale, the inclusion of interviewees from other European countries would have been desirable. The same applies to researchers from other countries as well, but in widening the

choice of researchers in this way one would also, almost inevitably, be lengthening the list of potential interviewees. The temptation to launch the project as a full-scale survey of the international effort in behavioural genomics might become great, but that is something that the present project never aspired to be.

Chapter B3 – Planning and method of the interviews

Introduction to the chapter

The method for constructing a conceptual map of behavioural genomics has now been explained, as have the criteria for analysing the selected research disciplines. We have seen how nine researchers were selected for interview, exemplifying the disciplines selected for further study. This chapter explains the modus operandi of the interview series.

The purposes of the interviews

Each interview had two main purposes:

1. To enhance the author's general understanding of the aims, methods and concepts of each discipline as practised by the researcher interviewed, and
2. Specifically, to talk through, with the researcher being interviewed, the set of criteria devised by the author for distinguishing between the aims, concepts and methods of the selected disciplines.

The output from the interviews

The usable output from the interview process was also intended to be dual:

1. There would be a verbal record of the interview , and
2. There would be a graphical presentation of the results of the discussions over the criteria, termed here the 'Criterion Matrix'.

Each interview was recorded, and the recording was subsequently transcribed. It was considered neither appropriate nor practical to incorporate the full transcripts of the

interviews into the present thesis. The chief practical reason was that they were too long. Also, some of the content was repetitive, as when the interviewer explained his research project to each of the interviewees. However, the transcripts had a purpose to serve as supporting evidence for the views attributed to the interviewees in the thesis. The course of action decided upon was to edit the transcripts, excising passages that were not germane to the flow of the discussion and inserting sub-headings to provide points of reference for the reader: notably, sub-headings indicating the passages in which the various Criteria were discussed. The resulting document was called the 'Edited Excerpts'. It was decided to print the Edited Excerpts of each interview in full in an appendix to the thesis. This meant that where a point from an interview was discussed in the main body of the thesis, the relevant passage in the Edited Excerpts for that interview could be referenced. As an extra guarantee of the fidelity of the Edited Excerpts these were sent to the interviewees for approval.

As regards the Criterion Matrix, this was described in Chapter A2. Briefly, it is a matrix in which the mapping criteria form the column-headings, and the titles of the respective disciplines serve as the names of each row.

The approach to the interviewee

The initial approach to each selected interviewee took the form of an email explaining the research project and requesting that individual's cooperation in a research interview. Since this series of interviews constituted research with living subjects, a request for approval was submitted to the Ethics Committee of the School of School of Humanities and Social Sciences, University of Exeter. The request for approval was accompanied by a form entitled 'Information/consent form for interviews'. The project was approved by the Committee at its meeting of 19 June 2006.[105]

[105] HuSS School Ethics Committee approval reference: 19.06.06/4vi.

Between the interviewee's acceptance of the request for an interview and the holding of the interview itself, the author sent the researcher concerned the list of criteria to be discussed, in the form of a blank Criterion Matrix.

The semi-structured character of the interviews

The interviews were 'semi-structured'. First, as has just been stated, each interviewee received a Criterion Matrix in advance. In the Criterion Matrix most of the squares were left blank so that they could be filled in during the interview. However, a token square was completed in advance to illustrate the method and to prompt discussion. Taking the interviewee through the criteria enumerated in the Criterion Matrix provided the structural backbone of the interview. However, there were other elements in the architecture of each interview which, overall, looked as follows:

1. The interviewer's introduction

   The interviewer introduces himself, his research institution and the character, aims and method of his own research project;
2. Procedural questions

   Procedure is explained and agreed (notably as regards approval of the transcript and summary of the interview, and the question of identification or anonymity of the interviewee);
3. The interviewee's description of the research

   The interviewee describes his or her research discipline, and the work that he or she does;
4. General discussion of concepts and methods

   There may follow a discussion of some issues arising from this research in the light of the description just given, drawing also on relevant literature;
5. Examination of the criteria

   This is a one-by-one process. The interviewer takes the interviewee through each criterion in the Criterion Matrix, discussing issues as they arise (see the section 'The list of criteria', below);

6. General and concluding discussion

   There is an opportunity towards the end of the interview to review any questions that may not yet have been fully explored, including any comments by the interviewer on the set of criteria selected.

There was some variation in the order of these component parts from one interview to another. in some cases components were conflated: for example, the 'General discussion of concepts and methods' and the 'Concluding discussion'. As far as points like these are concerned, it has not been considered indispensable to force the Edited Excerpts to fit a single, inflexible template.

The evolution of the list of Criteria

The inventory of criteria was permitted to evolve as the series of interviews progressed. This did not upset the methodology, since the original set of eight questions put to the first interviewee (Jones) proved serviceable and robust. None of these criteria was so severely challenged by an interviewee as to require dropping from the list.

Accordingly, all nine interviewees were asked the first eight questions set out in the Criterion Matrix explained in Chapter B1 above:

1. Does the research cover all hominids or only *Homo sapiens*?
2. Is behaviour studied in the ecological setting – or in the laboratory or clinic?
3. Is the focus on species-typical traits or on individual differences?
4. Does the research typically draw on the findings of genomics?
5. Is the research on genes or other DNA? If 'other': mtDNA or Y-chromosome?
6. Is there research on the DNA of non-human/hominid species? If so, animals or plants?
7. Is there research on other bio-molecules? If so, proteins or other?
8. Does the research use environmental markers?

This list was subsequently extended, as has already been explained. The following six criteria were added:

9. The main concern is phylogeny or ontogeny?
10. Does the research draw on fossil evidence?
11. Is Newtonian mechanics relevant to the research?
12. Is the research intended to have a clinical application?
13. Does the research use cultural markers, e.g., surnames?
14. Does the research offer other economic or social benefits?

This completes the description of the planning and method of the interviews. In the next chapter we shall briefly describe the conduct of the interviews.

Chapter B4 – The conduct of the interviews

Schedule of the interviews

The nine interviews were held over the period from Monday, 22 January 2007 to Wednesday, 11 July 2007. With one exception, the conversations took place at the interviewee's institution. Details of the schedule are given in the following table (Table B4.01).

Table B4.01. Schedule of the interviews

Researcher	*Date and time*	*Length*	*Venue*
Jones	22 Jan, 14:00	0 hr 54 min 39 sec	Department of Archaeology, University of Cambridge
Hutchinson	5 Feb, 11:00	0 hr 40 min 57 sec	Royal Veterinary College, Hawkshead Campus, North Mymms
Smith	7 Mar, 11:00	1 hr 43 min 51 sec	Department of Vision Sciences, University of Aston
Buckley	9 Mar, 10:30	1 hr 39 min 42 sec	The Down Syndrome Educational Trust, The Sarah Duffen Centre, Southsea
Mace	15 Mar, 11:30	1 hr 20 min 01 sec	Department of Anthropology, University College London
McGuffin	16 Mar, 14:00	0 hr 51 min 28 sec	Institute of Psychiatry, King's College London, De Crespigny Park, London
Jobling	4 Jun, 14:00	1 hr 11 min 41 sec	Department of Genetics, University of Leicester
Lindsay	20 Jun, 15:00	1 hr 20 min 24 sec	Institute of Human Genetics, University of Newcastle upon Tyne
Crompton	11 Jul, 11:00	0 hr 28 min 34 sec	University of Liverpool and Neuhäusgen, Luxembourg, by Skype

Interviewing in person or by telephone?

It was decided at the outset to hold the interviews in person, rather than by telephone. The author considered that the personal encounter offered the advantages of more natural circumstances. In attempting to hold a serious conversation with someone it is desirable to build a certain personal rapport, and it was felt that this would be achieved more easily and more quickly in a face-to-face meeting. However, an exception was made in one case. The

final interview, with Crompton, was conducted by the Skype Internet telephony system at the suggestion of the interviewee as a time-saving measure. The author agreed to this suggestion because of the value of the opportunity to interview this researcher. This raises the question of whether the 'exception' should have been the rule from the outset. The answer would be in the negative, since it is most unlikely that all the interviewees would, at that time, have had convenient access to Skype. The alternative would have been to fall back on the conventional telephone system, which was regarded as inferior to a face-to-face meeting. It is true that Skype had some positive features that make this or some similar system of Internet telephony an option worth considering for future research purposes:

1. Making a recording of the conversation was convenient; all that was needed was appropriate software (in this case 'Powergramo');
2. Skype communication can be visual as well as acoustic, if a webcam is used; in the case being discussed, only the interviewee was equipped with a webcam; so the interviewer could see him, but he could not see the interviewer;
3. The use of a headset leaves the speakers' hands free for making notes or finding references, which is commonly not the case with a conventional telephone;
4. On balance, the holding of the interview over Skype comes nearer to the experience of a personal encounter than a conventional telephone conversation would do, if webcams are used; in these circumstances the cost advantage of a Skype interview by comparison with a journey to, in this case, Liverpool needs to be carefully weighed.

On the subject of recording, all the interviews were recorded, using a digital recorder.[106]

The interview format in practice

The conception and planning of the interview series has been described. The content of the conversations will be analysed in Part C of this thesis. Meanwhile it may be helpful here to

[106] Olympus DS-2300.

conclude Part B with some remarks on the general usefulness of the 'interview series' method as it was applied in the present research project.

First, the method as conceived stood up in practice to the requirements that were made of it. The plan to hold a series of interviews with researchers exemplifying a sub-set of disciplines in the broad field of behavioural genomics was executed. The practical arrangements for meeting at the specified time and place worked successfully in all cases. There were no problems with the recordings. The design of the interview format proved realistic. The procedure that comprised sending the interviewee the Criterion Matrix in advance and then talking it through in the interview proved satisfactory. The length of the interview (median: 1 hour 12 minutes) was adequate to allow for the interviewer to introduce his project, for the interviewee to explain her research, for the two of them to go through the list of criteria and also to have a reasonably substantial general discussion. This was achieved in every case. Apart from a few specific comments on individual criteria, no interviewee expressed criticism of the interview method as it was designed and executed here. Cooperation from the researchers interviewed was excellent.

One hour is not long to summarise somebody's professional work. On the other hand an hour can be quite a long time for a researcher to sacrifice from her schedule. The interview time-span of about one hour was more of an opportunity than a constraint. However, the time necessary for transcribing and editing the verbatim record of the interview was a real constraint. The nine Edited Extracts together reached a total of 75,000 words. It was a considerable task to identify specialist terms and proper names mentioned by the interviewers, and to look up allusions to the literature to find precise references. For these reasons it would have been unrealistic to have increased either the number of interviews or the length of each one.

Flexibility in the organisation

As has already been mentioned, some flexibility was built into the organisation of the interviews. This applied to the choice of interviewees, to the addition of new criteria while

the series was in progress, and to the order in which different sections of an interview were taken. Reasons for taking a flexible approach have already been given. As regards the choice of interviewees, in the event only one (Crompton) was added during the series as a result of feedback from an earlier interviewee (Hutchinson). The author would have been ready in principle to have added other researchers to the list in this way in justified cases, but the constraints of practical organisation began to tell against this.

Concerning the addition of new criteria, it was held that the benefits of flexibility outweighed those of standardisation, in view of the fact that a statistical analysis of the responses of the interviewees did not come into the picture. The following table – Table B4.02 – shows which questions were put to each of the interviewees.

Table B4.02. Questions answered by each interviewee

Interviewee	
Jones	1-8
Hutchinson	1-8
Smith	1-12
Buckley	1-12
Mace	1-13
McGuffin	1-13
Jobling	1-14
Lindsay	1-14
Crompton	1-14

This completes the account of the planning and conduct of the interviews. In Part C we shall turn to an analysis of their content.

PART C: THE CRITERIA: EVIDENCE OF THE INTERVIEWS

Chapter C1 – Introductions to the researchers and their disciplines

Aims and structure of Part C

We now come to the content of the interviews conducted with the nine researchers over the period January to June 2007. The methodology has been explained, and in Chapter B.1 we presented the set of criteria that would be used as questions in the interviews and thus serve as a basis for the conceptual mapping exercise. In Part C we report and discuss the interviewees' answers to the questions and their contributions to the discussion. We shall not present separate narratives or summaries of each interview. Readers who wish to learn how each interview unfolded may turn to the Annex, where they will find the Edited Excerpts from each interview transcript.

Except in the case of this opening chapter, the presentation in Part C will focus on the criteria rather than the individual researchers. Chapters C2 to C15 will take the 14 criteria one by one and report and discuss their treatment in the interviews.

In the early stages of each interview, the interviewer (Holdsworth) gave the researcher being interviewed the opportunity to give a succinct account of her research, and to characterise the discipline within which she was working. Accordingly this opening chapter, Chapter C1, is devoted to a presentation of these introductory accounts.

In addition to the researcher's self- introduction and the subsequent discussion of the criteria, there was also some opportunity in each interview for general discussion. These passages gave rise to a number of themes not directly covered by the criteria. A selection of these will be described and discussed in the final chapter of Part C: Chapter C16, 'Additional themes'.

Treatment of the criteria in Chapters C2 to C15

It will be convenient to have a standard method of presenting the material in the chapters dealing with the successive criteria. Accordingly we shall begin each chapter by presenting the Criterion Matrix for the criterion in question, displaying graphically the responses of each of the nine interviewees.

That done, the views expressed by the various researchers on the criterion in question will be reported and discussed. Not every criterion was equally pertinent to every discipline reviewed. The purpose in this section is to bring out what was salient for the criterion in the responses of the researchers interviewed.

The purpose of the criteria was to identify points of diversity among the researchers interviewed and their disciplines. The next section of each chapter presents a concise analysis of the diversity disclosed by the responses of the interviewees.

Finally, there will be a section offering an assessment of the criterion: that is, an assessment of its fruitfulness as a stimulus to discussion and its utility for separating or assimilating the disciplines under study.

In summary, the main sections of each chapter will be as follows:

1. The matrix for the criterion
2. Salient interviews
3. Analysis of diversity
4. Assessment of the criterion

Referencing the Edited Excerpts of the interviews

As has been explained, the Edited Excerpts of each interview are presented in Annex to the thesis. Timings are inserted in the text of the excerpts to assist navigation and reference.

Where the reader finds a figure at the end of a line – for example, 1.12.54 – this indicates how much of the interview had elapsed – in hours, minutes and seconds – by the time that point was reached. It has not been practicable to give a timing for every line of text. The method of referencing is to cite the name of the researcher interviewed, followed by the timing that falls nearest to the passage under reference, or an estimate.

We now pass to the self-introductions of the researchers interviewed. To the extent that is practicable within the analytical framework, the researchers' interview responses are given in their own words.

Martin Jones

The first researcher to be interviewed was the archaeologist Martin Jones. Holdsworth asked him (Jones 0.07.40) if 'biomolecular archaeology' was the accurate designation for his discipline. Was this what he would call it? Jones concurred. He was then asked how he would define or describe it. Jones replied that, typically, he would describe the trajectory of biomolecular archaeology in historical terms:

> that the things we've looked at have got smaller, so there's a large field of bioarchaeology that looks at bits and pieces like that lump of charcoal and bone and so forth. And through time, through microscopy we've kind of unpacked the information from the cells, and what's happened - for a series of reasons in the history of science – is that the potential to tap chemical evidence of a wide range of historical imprints has just mushroomed over the last, probably, twenty years now. [...]
>
> So, biomolecular archaeology covers anything using chemical information to try and elicit human pasts, and the methodologies to do that have just mushroomed. (Jones 0.09.12).

These methodologies will be explored in due course, when we turn to some of the specific criteria. Meanwhile, as a way of trying to define biomolecular archaeology from the outside, it is interesting to read how Jones replied when Holdsworth asked him what other research disciplines touch biomolecular archaeology at the edges, or overlap it.

> Well, there are a whole series of forms of anthropology and biological anthropology that are touching it. I think the way the subject unfolds is that - particularly in relation to DNA - there is a series of core archaeological questions, and what happens, you know, in each methodological change is you revisit the set of core questions to ask how they re-articulate themselves in relation to the new methods. Obviously archaeology as a general topic tries to explain pattern through its history - that's what it does - and so working with genetics - and DNA in particular - what you're doing is trying to re-articulate these questions in terms of a family tree, a map. That's what you're trying to do. So, I mean, it obviously touches on all fields of archaeology; it touches on Quaternary science quite a lot, and it touches on various types of anthropology. There are also obviously interfaces with things like historical linguistics now and that sort of thing. (Jones 0.12.00)

Holdsworth said he had made the assumption, from reading Jones' book *The molecule hunt*, that there was a close link with 'molecular palaeoanthropology'.[107] Jones agreed that this was so. (Jones 0.12.33).

As to Quaternary science, mentioned by Jones, this has been described in the following way on the website of the International Union for Quaternary Research (INQUA):

> The Quaternary Period spans approximately the last two million years of the Earth's history, an interval dominated by frequent changes in global climate that led to a succession of glacial and interglacial ages. Quaternary scientists study the complex environmental changes of the glacial ages and interpret them using analogies to present-day processes and environments. A major goal of these investigations is to document the pattern and timing of climatic changes in order to understand the causes of changing climate on various time scales. Such investigations are of prime importance: the Earth, influenced by human activities, is entering a time of unusually warm climate in which significant and potentially rapid environmental changes could pose major challenges for human habitability.[108]

Jones was asked if he saw biomolecular archaeology as a 'behavioural' discipline. This appeared to cause some difficulty: "I'm not sure, actually." Jones acknowledged that in his subject "we are exploring human behaviours, of course", but he hesitated to commit himself to the word 'behavioural': "I suppose, the way in archaeology it works is, we don't necessarily find ourselves moving down towards that taxonomy" (Jones 0.10.0). Jones

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[107] Jones, Martin (2001): The molecule hunt: Archaeology and the search for ancient DNA, 2001.

[108] International Union for Quaternary Research (INQUA) website: http://www.inqua.tcd.ie/about.html . The author of the passage is S.C. Porter.

admitted that this was "a bit of a vague answer". The topic was taken up again at the end of the interview. It also arose in the context of other interviews. For that reason, further discussion of it here will be reserved until Chapter C16, 'Additional themes'.

Asked if he could think of a criterion, other than those foreseen in the interview structure, that would serve separate his discipline from others in cognate areas (Jones 0.46.06), Jones replied that

> the interesting thing is – although it might seem obvious – that we like to explain patterns by a historical argument. I remember someone - this is going off at a tangent – he was actually a guy who was interested in the philosophy of economics, and he did a text called 'Story-telling and metaphor in economics'.[109] One of the things that he was arguing was that the way we explain anything is either by telling a story or building a model of it. So it may be, but it does strike me that the key thing that we do to explain pattern in people is we tell a very long story. That's how we explain things. So we're forever trying to explain things historically.
>
> *Holdsworth*: 'To explain pattern in people' – that's a good phrase – 'by telling a long historical story'. (Jones 0.47.14)
>
> *Jones*: Yes. I mean, it may be so self-evident to archaeologists, but nevertheless it is something that we do, and I notice we do. And when I do something in an inter-disciplinary collaboration I notice how much we do it, and how much that's part of our mind-set.

Contemplating Jones' account of the discipline of biomolecular archaeology one can imagine it situated on a map of inter-connecting and overlapping disciplines, featuring chemistry and biochemistry, palaeoanthropology and "a whole series of forms of anthropology and biological anthropology", archaeology, Quaternary science and historical linguistics. To these it might seem obvious to add 'genomics'. However, it will be wiser to reserve judgment on this point until we have had a chance to look at some of the criteria analysed later in Part C. A key question to signal in advance is this: should we think of 'genomics' as something 'out there' being pursued by specialists called 'genomicists', or is

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[109] A reference to a paper by Donald N. McCloskey entitled 'Storytelling in economics'. It was published as Chapter 4 of Don Lavoie (ed.): Economics and hermeneutics, Routledge, 1991. See the web page: http://books.google.com/books?hl=en&lr=&id=Azz33GC56iAC&oi=fnd&pg=PA61&dq=%22McCloskey%22+%224+Storytelling+in+economics%22+&ots=YqJS-pt06-&sig=Z27_E3Dt7nZAwTpMXNgcB0EEKb4 (Consulted 12 February 2008).

'genomics' rather something that people like biomolecular archaeologists do when they are, for instance, analysing a specimen of mitochondrial DNA?

One way of looking at the cluster of disciplines surrounding biomolecular archaeology might be to portray them as having a 'family resemblance'. It is doubtful, though, whether it is really useful to operate in this assimilative mode. If we picked out any single one of the disciplines catalogued above, we could make a new map for each of them, each time plotting the given discipline at the centre of a new family. This can be tried as a thought experiment, by picking out, say, Quaternary science or historical linguistics and imagining what very different sets of related disciplines would surround each of these. Once one has done the thought experiment, it becomes clear that there is no point in constructing a factitious family resemblance among clustered disciplines in a way that may mislead us into thinking that we have uncovered some essential affinity that binds them. No, it is more useful to continue to operate in disaggregating mode, drawing attention to the diversity among the disciplines by insisting on the criteria that separate them, while noticing the epistemic circumstances that tend to bring them into repeated contact. The diversity is the richness. Among other things, we may conjecture that the tendency of disciplines to propagate new disciplines, and of literatures to propagate new literatures, spontaneously serves to fill in the gaps in the division of labour in a field like behavioural genomics.

John Hutchinson

When John Hutchinson, whose subject is evolutionary biomechanics, was asked to describe his research, he replied: (Hutchinson 0.4.20)

> Broadly speaking I'm interested in how locomotor systems evolved in animals. A second part of my work is how size influences locomotion in animals, both in a comparative context between species, but also in an evolutionary context: how size influences locomotion as size changes during evolutionary time. So I have various projects going on, and on various groups of animals – taking them as case studies, if you will: this is what this lineage does, how size will influence locomotion and how the two of them evolved, in, like, dinosaurs and elephants. I've done a bit with crocodiles as well. (Hutchinson 0.05.10)

Hutchinson's approach to research was conditioned, and in some ways constrained by his concern with evolution and with the past. When he was asked whether, in the research which he had been doing, he drew greatly on genetic or genomic research (Hutchinson 0.12.35), he replied:

> I would say I pay attention to it, kind of because it's interesting. I'm an evolutionary biologist kind of first and foremost. I'm interested in evolution and in the past. The revolution in genomics is absolutely important. But for a lot of the groups I work on in the lab their members are extinct [...]

The findings of genomics were vital in setting what Hutchinson referred to as "the phylogenetic framework". Asked to suggest a criterion which strongly distinguished evolutionary biomechanics from other disciplines, Hutchinson said

> The things that stand out the most to me are that it uses the phylogenetic framework, that it uses physics. Those are the two things that basically, you know - physics plus phylogeny, really. (Hutchinson 0.36.00)

He explained that by 'physics' he meant, specifically, Newtonian mechanics, but also physics in general.

Chris Smith

In making his introduction, the molecular neurobiologist, Chris Smith, took an autobiographical perspective (Smith 0.05.00). This offered an interesting insight into the career trajectory – by no means self-evident - of the future author of the text-book *Elements of molecular neurobiology*:[110]

> [F]irst of all. I took long ago a degree in zoology at Birmingham. I then went on to take degrees in physics and maths at London, external in fact. And then followed that up with a postgraduate qualification in biophysics at Edinburgh. And ended up doing a PhD in neuroscience here. (Smith 0.05.40)

[110] Smith, 2002.

Holdsworth asked if the biophysics was in the context of neurobiology.

> No, it wasn't really. It was a department in Edinburgh. I was there in 1960/61. It was run by Jack Dainty,[111] who was himself a physicist, but interested in membrane transport. It was largely concerned with: transport of materials across membranes, the nature of membranes, but there were other aspects. Other people there talked about structures of proteins and radiology. So that's what I did there and I also learnt electron microscopy with Geoff Haggis in the Physiology Department. [...]
>
> And since that time I've been back at Aston here, and teaching, first of all in biological sciences, and subsequently over here in vision sciences – which is associated with neuroscience - and I've been very involved in doing the neurophysiology side of the courses. When I was in biology I did the palaeoanthropology courses as well and set up undergraduate degree programs in *Biology of Man and his Environment*. [...]
>
> Latterly my interest has focused on molecular neurobiology. I was very interested in molecular biology from the beginning, back in the 1950s and 60s – when Watson and Crick brought out their material. I was fascinated by molecular biology. My first books were on molecular biology [...] (*Architecture of the Body* (1964); *Molecular Biology: A Structural Approach* (1968)). And then I went on to do one on the brain, [...] *The Brain: Towards an Understanding,* (1970). And then I did another book, [...] called *The Problem of Life: The Origins of Biological Thought* (1976) - that was historical and philosophical (Smith 0.08.08).

Smith explained that he had been interested in the brain and the mind and how these related – "the classical 'hard problem', problem of mind (Smith 0.09.04).

> I've been trying – certainly in recent years – to get a grip on that. So my interest on the scientific side, then - having been interested in brain, taught the brain, taught molecular biology - is trying to put the two together, trying to understand how the neuroscientific understanding relates to our everyday lived-through experience – qualia etc. I've also published a book on the biology of sensory systems: *Biology of Sensory Systems*, Wiley, 2000.[112] [...]
>
> I start from the molecular end and do all the molecular stuff, and then I come on to talk about the actual sensory systems themselves from an evolutionary, molecular point of view. And there's a certain amount of philosophical discussion – I mean, it is the hard problem, the relation of mind to brain, which comes up over and over

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[111] Author, for example, of: Dainty, Jack (1963): 'The polar permeability of plant cell membranes to water', *Protoplasma*, Vol. 57, Nos. 1-4, March 1963, pp. 220-228.

[112] 2nd edn. due for publication in 2009.

> again if you're thinking about sensory systems and sensory biology: how does it relate to our everyday experience? (Smith 0.10.43) [...]

Smith said that, so far as molecular neurobiology was concerned, "that's trying to put together molecular biology and neuroscience". He had published the book *Elements of Molecular Neurobiology* (1st edn. 1989, 2nd edn. 1996; 3rd edn. 2002). He commented:

> And I suppose – obviously - it's pure science. I mean, that's my background – pure science - but I'm interested in seeing how that relates to medicine. The various neuropathologies often have a molecular basis. And that's just becoming apparent. So that's the application into human life which I seek – which I try to emphasise in those books. Partly because, I suppose, the major readership is likely to be in medical circles (Smith 0.12.10).

Sue Buckley

Sue Buckley explained the various dimensions of research in the field of Down syndrome, and how her own activities fitted into that context. Summarising what Buckley said in the interview, we could say that she outlined three types of scientific response to Down syndrome, each of which could be further sub-divided:

1. Intervention: the provision of services; conceiving and practising appropriate forms of intervention – i.e., methods of training and education designed to permit the individual Down Syndrome patient to flourish to the highest possible degree; a major goal is inclusion of Down Syndrome patients in education;

2. Intervention research: pursuing research into intervention: both the methods and the outcomes; such research will concern, for example, psychological development in the child;

3. Genetic research: investigation of the genetic basis and implications of Down syndrome, including research aimed at the possibility of future pharmacological therapies for some of the symptoms.

One might add a fourth element – 'pre-natal diagnosis' - which would be the development of ever more precise pre-natal diagnostic techniques. Some of the issues here were discussed in the interview. (Buckley 1.28.19)

Buckley explained that Down Syndrome Education International (DSEI), the organisation of which she is Director of Research and Training Services, is active in the first two of the three areas detailed above. She stressed that there was a high level of demand for the provision of services. This affected the balance of effort as between services and research. However, the experience on the intervention side was beneficial for the research:

> It does stand us in good stead. It gives us the opportunity to collect research information on children longitudinally, and children who are getting best practice in terms of intervention. So you make sure they're all receiving the same sort of intervention or education and then look at what's happening to their development. That's quite helpful, even if it's some sort of experimental study about memory training. At least we know that the children are getting the same sort of input to their development. (Buckley 0.01.38)

Buckley said she sometimes thought that "People would be quite happy if we did nothing but provide direct services" (Buckley 0.2.01),

> Whereas, you know, our reputation's really based on the research that we've done, which means we can provide more effective practice. We're just reviewing our five-year strategy, and we've been, [...] needless to say, thinking about that and looking at what everybody else is doing round the world, and we're still the only people who have this sort of emphasis on education and development (Buckley 0.02.33).

Pressed on this last assertion, Buckley claimed for her group that "we're the only research team who really are interested in practice outcomes, I think" (Buckley 0:02:45). She admitted that this might be "slightly harsh", but her point was that "if you read the vast majority of research" you found that

> People who want to understand their learning difficulties or their speech difficulties - so many of them, not all, but so many will not speculate [further] – you know. They're scared to do so, I think. They think it reduces their scientific credibility. It's OK to do experimental studies.

Let us pick out the threads of this discussion. It is interesting because it presents a challenge to a way of approaching this topic that one might have found natural. Such an approach might have begun in the following way. Down syndrome is a chromosomal, and therefore genetic disorder that has, among other things, a harmful effect on the patient's mental and behavioural capacities. In recent years there have been advances in genetic knowledge, as part of the 'genomic revolution'. It now becomes natural to ask whether scientists may dare to hope that further research on the genetics of the disorder could lead to the discovery of a 'cure', at least in the sense of delivering pharmacological therapies capable of mitigating or suppressing certain symptoms. The prospect of progress in this direction is so attractive that it seems reasonable to suggest that research of this type should receive funding.

However – a riposte might go - it will be years before successes of this kind are achieved, if they are achieved. The idea of a 'silver bullet' is illusory (Buckley 0:51:07). Meanwhile there is a population of patients who could benefit from entirely different forms of therapeutic intervention. These are largely educational, targeted, for example, at improving the patients' command of speech and language, as well as teaching them to read and write. The advantages of educational inclusion for Down syndrome children should be obvious, but to promote this demands intervention from an early age. If we take no action until, in an unknown number of years, pharmacological therapies become available, lives will have been wasted – or at least, vital life-opportunities will have been wasted. Naturally, educational interventions will continue, but in this area, too, knowledge does not stand still. Techniques of intervention need to be continuously developed and enhanced in the light of experience, and this demands a vigorous research effort of its own. This intervention research ought not to be starved of funds to pay for genetic research that may or may not one day yield the benefits that some people are claiming for it.

Finally, in considering both the first approach and the riposte, one must take into account the fact that the whole situation has a demographic and epidemiological context. Among the relevant factors – which do not necessarily all work in the same direction - are the availability of pre-natal diagnosis, terminations of pregnancy, advancing average age of primigravidae in many societies, and the incidence of multiple births from in vitro fertilisation.

So Buckley distinguished two basic approaches to Down syndrome research. One was the intervention research pursued by herself and her colleagues, which was trying to draw lessons from intervention outcomes. But then she commented:

> We have two research camps at the moment as it stands. In relation to understanding Down syndrome, you have some very high profile people across genetics and molecular biology, biochemistry. (Buckley 0.19.30)

So Buckley saw a divide between research teams like her own, interested in investigating practice outcomes, and the geneticists. The former approach tends to issue from a psychological tradition, or traditions. The focus may be on working memory, or on speech and language, or other issues in child development. However, the divisions did not end there. Buckley also sketched a division between two different approaches to research into the psychological dimension of Down syndrome study. On the one hand there were researchers who put their emphasis on studying the psychological questions themselves, while on the other there were researchers – like Buckley herself – who prioritised the lessons for effective practice. It might be thought that the one would feed smoothly into the other, but this was not necessarily the case.

As Buckley put it (Buckley 0.3.30),

> There's this sort of academic research strand. You can do the pure research, but they're very frightened about speculating about interventions, and even more about setting up studies [to evaluate] interventions, which for us [we prefer to do].
>
> There's a divide, you know, there's the people who do the academic research, who are mostly asking 'What's wrong?', 'What's different about people with Down Syndrome?' So they understand what's wrong, but won't take the next step. (Buckley 0.05.16)
>
> And then there's all those people involved in practice, like the vast majority of parents, who are trying to do something, regardless of whether there's the evidence, because there's loads of practitioner wisdom. If they write about it, the real toffee-nosed researchers don't accept it, because they haven't got a control group. (Buckley 0.05.37)

There were some researchers who were able to overcome this divide. Buckley cited the example of researchers at the University of York who were open to intervention work, which Buckley considered "unusual for academic departments". These were Maggy Snowling and Charles Hulme, whom she described as "the world's leading experts on the literacy issue, for all children". They were in the Psychology Department at York and led the Centre for Reading and Language there.[113] (Buckley 0.04.50)

In general, however, the tendency was that

> People publishing more academic stuff will go to the high prestige journals in their area. The child development ones that are high prestige. Disability ones that are high prestige, like what is just about to change its name: the *American Journal of Mental Retardation* - AJMR. They finally changed their name this year to 'intellectual' – they've dropped mental retardation, in favour of the 'intellectual and developmental disability'.[114]

At the same time there were good reasons to be proud of the place won for itself in the literature by her own organisation's publication:

> But when you run a journal called *Down Syndrome Research and Practice*,[115] which is identified in all the main search engine sites like Medline and so on – I mean, we've achieved that. (Buckley 0.8.46)

Ruth Mace

In her self-introduction, Mace presented herself as a behavioural ecologist. As we shall see, this was not the only label she might validly have worn. However, it was the starting-point. (Mace 0.05.40)

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[113] Centre for Reading and Language: http://www.york.ac.uk/res/crl/ (Consulted 17 August 2008).
[114] The organisation, American Association on Mental Retardation (AAMR), changed its name in 2006 to American Association on Intellectual and Developmental Disabilities (AAIDD). The AAIDD continues to publish two journals: (1) *American Journal on Mental Retardation* (AJMR), which retains that name despite the change in the name of the parent organisation, and (2) *Intellectual and Developmental Disabilities* (*IDD*). See http://aamr.allenpress.com/aamronline/?request=index-html (Consulted 1 October 2008).
[115] Website: http://www.down-syndrome.org/research-practice/ (Consulted 11 October 2008).

> Behavioural ecologists make a distinction between the proximate explanations of behaviour and the ultimate explanations of behaviour, in the sense that proximate are the sort of 'how' questions - of causation. Questions [like] whether or not something is nature or nurture, or what the genetic basis of it is, probably come into that category. And then you've got the 'why' questions, which include the phylogenetic history of the behaviour and the adaptive function of the behaviour – i.e., why did it evolve, how did it evolve? OK? That's what Tinbergen called his 'Four Why's', which are usually categorised into two different kinds of questions: the proximate questions and the ultimate questions.[116] And because behavioural ecologists have tended to focus on the ultimate questions more than the proximate questions, they're not – you know, they're interested in adaptive function, they're interested in the history of the behaviour - but that doesn't really require you to know, necessarily, that much about the genetics. (Mace 0.06.58)

In other words, human behavioural ecology did not really use genomic research "explicitly for the most part", although Mace added: "This isn't to say that we're not influenced by some of the lessons that are [there]."

Mace confirmed that behavioural ecologists have been mainly concerned with ultimate causes (Mace 0.07.20):

> The ultimate: i.e., how, how, how did, why did, you know, why, what is it, what is the adaptive advantage of behaving in this way – i.e., why is this behaviour being selected for? OK. You don't really need to know its genetic basis to answer that question. So even though it's an interest in how did behaviour evolve, you don't need to know much about genes to do that study. OK. So that's why it's kind of separate (Mace 0.08.00).

Holdsworth recalled that "the idea that linguistic phylogenetic trees somehow fit genetic ones without being caused by them is a rather well accepted idea", and supposed that behavioural ecologists built on that. (Mace 0.08.31) This gave Mace an opportunity to extend the thematic area covered by her research:

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[116] Tinbergen, N. (1963): 'On aims and methods of ethology', *Zeitschrift für Tierpsychologie*, Vol.20, 1963, pp.410-433. Tinbergen enumerates four basic questions for ethology or "the biological study of behaviour". These are (following Julian Huxley for the first three) causation, survival value, evolution and ontogeny. Note: the Bard-Rockefeller Program, a collaboration between Bard College and The Rockefeller University, has made a pdf of this article available among its Class Notes at: http://www.rockefeller.edu/bard/pdfs/week_02_tinbergen_on_aims_and_methods_of_ethology_zft_1963.pdf (Consulted 7 August 2008).

Yes, I'm just giving it to you very generally. Because there's lots of areas to my research. OK then, the cultural phylogeny. So geneticists have worked out, as you say, that you can use genes to make [estimates] about population history, and linguists have also been using language variation to look at population history, too. And we've been looking at language variation, and if you plug it into the same sorts of programs that really geneticists are using to build these trees - if you plug *language* variation, rather than *genetic* variation, into these programs, you can also build trees [of history]. And these seem to be very good models of population history. And they seem to work extremely well. I mean, the phylogeny-building programs are really designed to model the evolution of the species. (Mace 0.09.56)
[...]

And if you look at the genetic variation within a species it's a bit of a mess, because you've got inter-breeding, obviously, between all these different groups, and the trees don't come out brilliantly. If you use *language*, they always seem to come out better than if you use genes - more tree-like. And I think the reason we think – well, the reason I think that's found, is because - you know, when you have a language - OK, so language is evolving in some ways a little bit - linguistic diversity is always a little bit similar to the way genetic diversity evolves. I mean, it's a neutral phrase, but when populations get separated their languages start to diverge; they start to get different. The longer they've been separated the more different they become, as with genetic diversity. OK? (Mace 0.10.57)

Holdsworth: Yes.

Mace: But if you get migration between groups, then the genes get - obviously - very mixed up, but when you've got migration between groups, and you migrate into a new group, you bring your genes with you, but you probably don't bring your language with you, or at least your children will not speak your language. They'll speak the language of the group. So, I think that's why the integrity of the group is easier to maintain when you're looking at language than when you're looking at genetics. So we know that populations don't map out into nice genetic units very much at all: there might be certain markers in certain populations, but it is quite messy. Whereas with language it seems to lessen it. I think it's this process that - you know - language by definition has to be mutually intelligible for the members of your group, which therefore maintains the integrity of linguistic groups, which doesn't maintain the integrity of [genetic populations]. There's no reason why everyone has to have the same genes, but everyone living in that group does have to speak the same language, if they want to make themselves understood. (Mace 0.12.11)

So the phylogenetic tree programs, which were built really for looking at species diversity, don't work very well within species or in genes, because the groups aren't different enough, but they do seem to work really well on languages. So people are now, including us, using language diversity to makes these trees of population history. (Mace 0.12.33)

Holdsworth asked Mace: "would you say that the discipline you're working in is 'human behavioural ecology', or would you give it another name?" (Mace 0.16.10). Mace replied:

> I say it's 'human behavioural ecology', yes. I mean [some people] talked about 'cultural biology' [as if it's] kind of a subject, but, you know, that's not really using genes: it's using cultural data. But, I mean, the human behavioural ecologists don't really use genes, either. I mean, we're a completely evolutionary paradigm. We're testing for adaptation, and we're looking for the adaptive function of behaviour. So that's really a separate question from what genes programme. (Mace 0.16.40)

On the subject of cultural transmission,

> You know, your genetic parents are your parents: there's nothing you can do about that. But your cultural parents might be your friends or your age-mates or influential people on TV or your teachers or people you admire because they're prestigious in society, and they argue that these transmission processes can lead to the evolution of slightly strange variants (Mace 0.45.10).

Asked to cite some names in that field, Mace suggested

> Boyd and Richerson.[117] They're the prime examples, and still the most prolific, or their students. But they're kind of teaming up with the evolutionary economists[118] now, who are also, you know, doing very similar models. It's a very mathematical field. It's quite hard to do empirical work on cultural change. I mean, we're trying to with the phylogenetic stuff, but - most of the work in this field has been mathematical models of what can happen in theory, and they're actually quite hard to assess (Mace 0.45.45).

As to names in evolutionary economics, Mace mentioned Sam Bowles[119] and Herb Gintis.[120] A number of papers by Gintis, Bowles, Boyd and Richerson were about evolutionary economics and altruism, subjects which Mace described as being very fashionable at the moment (Mace 0.46.12).

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[117] Richerson, P.J., and Boyd, R. (2005): Not by genes alone: how culture transformed human evolution, University of Chicago Press, Chicago, 2005.

[118] For evolutionary economics, see, for example, Hodgson, Geoffrey M. (2002): 'Darwinism in economics: from analogy to ontology', *Journal of evolutionary economics*, 12, 2002, pp.259–281.

[119] Website of Sam Bowles at the Santa Fe Institute: http://www.santafe.edu/~bowles/ . (Consulted 5 August 2008).

[120] Website of Herb Gintis at the University of Massachusetts Amherst: http://people.umass.edu/gintis/ (Consulted 5 August 2008).

Another of Mace's interests was life-history theory. Holdsworth mentioned a paper on which Mace had worked on unexpected consequences of the introduction of taps in Ethiopia and the effect on fertility and malnutrition in children. The article combined the analysis of reproductive success with an energetic calculus. Mace commented (Mace 0.22.30):

> Yes, well that's another branch of my interests. That's kind of 'life-history theory'. Life-history theory is another branch of evolutionary ecology, really, or behavioural ecology – whatever you want to call it. Where it's to do with the timing of life-history events. You know, there's all these trade-offs. The energy that you put into parenting you can't put into other things. Do you have a few offspring in which you invest heavily, or more that you invest less heavily in? Do you spend time growing, or do you stop growing and start reproducing? Do you carry on reproducing, or do you stop reproducing and start looking after the children you already have? These are all life-history trade-offs, and people have worried about them across species: you know, why does one species have one life history and another species have another? [121] (Mace 0.23.23)

Asked to cite other literature in this area, Mace mentioned the work of the American researcher Kristen Hawkes.[122] (Mace 0.23.53)

From these pieces of self-introduction by Mace, one assembles a complex of interlocking disciplines or literatures: human behavioural ecology, cultural phylogeny, evolutionary economics and life-history theory.

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[121] Mace, Ruth (2000): 'Evolutionary ecology of human life history', *Animal Behaviour*, Vol.59, No.1, January 2000, pp.1-10.

[122] See Hawkes (2006) and Hawkes (2005). Kristen Hawkes, Distinguished Professor, Department of Anthropology, University of Utah: http://www.anthro.utah.edu/people/faculty/kristen-hawkes.html (Consulted 6 August 2008).

Peter McGuffin

The interview with Peter McGuffin began with an enlightening exchange concerning nomenclature.

> *Holdsworth*: I had put you down, as it were, as a researcher in behavioural genetics, although I might have also put you down as a researcher in psychiatric genetics, I imagine. (McGuffin 0.04.00)
>
> *McGuffin*: Yes.
>
> *Holdsworth*: So could I begin by just asking you where you position yourself, and to describe a little bit your type of research.
>
> *McGuffin*: I describe myself as a researcher in normal and abnormal behaviour. Mostly, because I'm a psychiatrist, I'm interested in abnormal behaviour, but I don't think you can actually study one without the other. (McGuffin 0.04.30)

Here we had a researcher who declared himself to be a psychiatrist, who acknowledged that he might be termed either a behavioural geneticist or a psychiatric geneticist, and who chose, finally, the description "researcher in normal and abnormal behaviour". McGuffin saw this behavioural range as a continuum:

> So - and I think this is a view commonly held among psychiatrists, not just biological psychiatrists, but most psychiatrists these days – that there's for all practical purposes a continuum between normal and abnormal behaviour. There's not a clear-cut distinction between them. And to some extent the dividing line is a bit arbitrary at times. (McGuffin 0.05.02)

Holdsworth asked if this conditioned McGuffin's approach to the genetic dimension of the enquiry. He agreed that it did. Holdsworth asked him for an example of a behaviour that might be called a disorder but which shaded off into the normal range. McGuffin replied:

> A very good example is depression. So there are very few among us who haven't had a day or two of feeling low, but for most people it doesn't interfere much with their lives, and they recover spontaneously. Then there are people at the other end of the spectrum who are absolutely devastated by depression with all the associated symptoms of sleep disturbance, weight-loss and all the rest of it, who have their lives seriously disrupted by it and require treatment – sometimes in-patient

> treatment. Then in the middle you've got people who have depressive symptoms that are sufficiently impairing for them to consult their GP or some other professional, but they don't actually come to the attention of psychiatrists. Well, as I say, while people have attempted to make a clear-cut distinction between depressive disorder and depressive symptoms and normal low mood, they've been hard-pressed to make any clear-cut distinction, so one seems to shade into the other. (McGuffin 0.06.19)

Holdsworth mentioned the title of a book he had seen in the display-cabinet downstairs. The title asked: 'Does schizophrenia exist?'[123] Was that a good question?

> Yes, it's a question with lots of shades of meaning, I think, because clearly, descriptively schizophrenia exists, and actually probably causes – well, it used to, anyway, result in more occupancy of hospital beds than any other disorder. [...]
>
> But the question is: is it one disorder or is it a grouping of dimensions? The question [...] arises [...]: is it absolutely distinct from what are called 'mood disorders'? Or are there some over-lapping phenomena – aetiological factors, for example bipolar disorder? Most of the current evidence is suggesting that yes, indeed, there are over-lapping aetiologies.
>
> *Holdsworth*: Depression and bipolar disorder you would call 'mood disorders'?
>
> *McGuffin*: Yes. (McGuffin 0.07.26)

Holdsworth asked McGuffin about the scope of behavioural genetics:

> *Holdsworth*: If one takes the expression 'behavioural genetics', at a quick count how many sort of sub-areas of that could one distinguish?
>
> *McGuffin*: There are two pretty big sub-areas. One is behavioural genetics in the traditional sense that deals with behaviour in a quantitative sort of way. And the main tools are statistics. Then there's behavioural genetics that's much more biological, where the focus is on finding genes and discovering what they do - at the molecular level. So, traditionally, I think behavioural genetics has been very much on the quantitative side. And to some extent that's why there has come up something of a split between people who call themselves 'behavioural geneticists' and people who call themselves 'psychiatric geneticists'. Because psychiatric geneticists by and large tend to be more interested in the hard-core biology, if you like. So there's a society called the International Society of Psychiatric Genetics. And much of the stuff that you'll see presented at meetings is about finding genes, doing functional genomics, looking at the biology of what actually happens when

[123] Maudsley Discussion Paper No. 12, *Does Schizophrenia exist?*, Institute of Psychiatry, London 2003.

> where there's a variation in a particular gene or set of genes. Whereas if you go along to the Behavior Genetics Association's meeting you'll find the people describing structural equations, models and various fancy stats approaches. (McGuffin 0.09.30)

Holdsworth asked if there were "thematic distinctions between people who are studying cognitive ability, the dimensions of personality, or indeed single-gene disorders?" McGuffin responded:

> Yes. Well, there are thematic distinctions, you're quite correct. But it depends where you position yourself, or whether you need to position yourself at all. I position myself pretty much across the spectrum, which is why I started off saying I work on normal and abnormal behaviour. I'm just helping Robert Plomin edit the latest edition of his book. I'm co-editor and have been for the last couple of editions. And that book is called 'Behavioural genetics' and it covers everything.[124] I'm also an editor of another book, called 'Psychiatric genetics', where the focus is very much on disorders, so [the scrutiny is on] disorders. But we have to have some discussion in there of things like cognitive ability and personality even in a book that deals mainly with disorders, because for reasons I've said I don't think you can have a complete discussion of disorders without a context of the genetics of normal behaviour. (McGuffin 0.11.06)

Holdsworth wanted to know whether it was correct that "Quantitative genetics infers the existence of genes from the statistical analysis. McGuffin replied "Yes" to that question. He agreed that it had been true for "a good long time", since it preceded not only molecular genetics but Mendelian genetics as well:

> So you could say the first person to systematically attempt to do quantitative genetics was Francis Galton, back in the late eighteen hundreds, 1860s. But of course you could go back further than that, and you could say that physicians – doctors interested in behaviour observed a long, long time ago that what used to be called insanity quite often ran in families. So that was a crude observation, but it was an observation nevertheless. And an important one. And you can even find instances, if you go eight miles down the road to the Bethlehem Royal Hospital, which is one of our associated hospitals, to their museum, you can pick up case-notes from the early 1800s, where there's a section in the front of the case-notes where the admitting doctor had to record of a patient: whether hereditary? There's a little question there: 'Whether hereditary?' (McGuffin 0.12.45)

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[124] Plomin *et al*. (2008).

And the methods of molecular research – linkage studies and association studies –precede the full sequencing of the human genome, did they not? McGuffin agreed:

> Yes. By quite a way, actually. [...] (McGuffin 0.13.00). The first observation of linkage is usually attributed to Morgan, who was a fruit-fly geneticist who spotted that some traits were linked in fruit-flies. Of course, Mendel hadn't seen that, and he [formed] his Law of Independent Assortment. Morgan and his followers found that that law wasn't always followed, and they made the inference that these traits were linked. Chromosomes were discovered, and the physical basis for linkage in other organisms was discovered. Methods for studying it in human beings were devised. So, one of the earlier methods was [that] of Lionel Penrose, who was actually a psychiatrist, but probably more famous for being a geneticist who proposed the first sib-pair linkage test. And there were various, well, really likelihood-based methods for inferring it in humans. And the big breakthrough was Newton Morton's devising the LOD score method in a landmark paper in 1955.[125] (McGuffin 0.14.14)
>
> Those people got into genetic analysis in a big way with physical traits, looking at – firstly, Mendelian disorders, and then looking at markers like blood-groups – later on, the HLA system. And in my own case, I got interested in the HLA system in the mid-1970s, when I'd just graduated from medical school and was working in cardiology, and everyone was becoming terribly [interested in HLA]. The HLA system is the major histocompatibility system in man. (McGuffin 0.14.54)
>
> Now known to be carried on a complex of genes on the short arm of Chromosome 6. We didn't know that in the early 1970s. But anyway it turns out that variants in the HLA system are associated with susceptibility to various common diseases, various types of arthritis, and Type 1 diabetes, and so on. Anyway, to cut a long story short, I got involved in the study of HLA and coronary heart disease, which turned out to be completely negative, but it got me turned on to the idea that you might be able to find genetic markers associated with [common] traits, so I did a study on schizophrenia, and I thought we'd found something on HLA and schizophrenia. That was an association study. And then was awarded a fellowship by the MRC to do what was one of the first linkage studies in schizophrenia. So I managed to get very good, generous help from a couple of really top labs: Hilliard Festenstein's very good HLA lab at the London Hospital,[126] and then there was a group at the Galton Lab at University College. There was somebody called Peter Cook[127] who ran the marker lab, and these were mainly markers – pre-DNA markers – markers based on electrophoresing proteins, really. How you can, you

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[125] Morton, Newton. E (1955): 'Sequential tests for the detection of linkage', *Am J Hum Genet*, 1955, 7:277-318. See also Morton, Newton. E (1995): 'LODs past and present', *Genetics*, 140: 7-12 (May, 1995).

[126] Demant, P. (1989): 'Hilliard Festenstein', *International Journal of Immunogenetics*, Vol. 16, No. 4-5, pp. 255-256, and David, Chella S. (1990): 'In memoriam' [Hilliard Festenstein], *Immunogenetics*, Vol. 31, No. 2, March 1990, pp. 63-64.

[127] Mentioned in Morton (1995), p.8.

> know, separate out various alleles by just separating the proteins on electrophoretic gels. And similarly, red cell blood types behave in a Mendelian fashion and can be used as genetic markers. So my PhD thesis was based on about 30 different marker types, which was the most you could do in those days. I calculated that you could cover about six per cent of the genome. So my magnificent PhD thesis, excluding a schizophrenia gene, essentially from six per cent of the genome!

Holdsworth suggested that the completion of the Human Genome Project had at least two beneficial effects from the point of view of this type of research. First of all, there was the sequencing data itself, but also it had improved the technology. McGuffin (0.17.37) saw the technological progress coming earlier:

> Yes. Well, the technology really started improving in leaps and bounds from the 1980s onwards. So, first of all, a type of marker called Restriction Fragment Length Polymorphisms were discovered, so that round about the end of the 80s we could really cover almost 100 per cent of the genome for linkage. So, for linkage you only need a few hundred markers to cover the genome. Then all the gaps were filled in with the new generation of markers called microsatellites, which mainly consist of dinucleotide repeats. (McGuffin 0.18.15) [...]
>
> Well, CA repeats[128] came in in a big way really towards the end of the 80s, early 90s. So, I can't remember the exact date now, but the Généthon from Paris - there's a lab in Paris, Généthon - published their microsatellite-based map in early 1990s.[129] So that really made it possible to, for sure, map any disease as Mendelian - or any non-Mendelian disease, where there's a genome-large effect. [...]
> Yes. So I was just sketching - what I can just say: even before 2001, which people usually mark as the time (you know, when *Nature*[130]and *Science*[131] published genome sequences and so on, at least partial genome sequences – partially annotated genome sequences – in the same week), so before all that we [had access to] all these other quite important discoveries: RFLPs, microsatellites and all that (McGuffin 0.19.36).

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[128] 'CA repeats': the type of microsatellite comprising dinucleotide repeats of the motif 'CA' . See Brown, T.A. (2007): Genomes 3, Garland Science Publishing, New York and London, p. 218.

[129] Gyapay, Gabor; Morissette, Jean; Vignal, Alain; Dib, Colette; Fizames, Cécile; Millasseau, Philippe; Marc, Sophie; Bernardi, Giorgio; Lathrop, Mark, and Weissenbach, Jean (1994): 'The 1993−94 Généthon human genetic linkage map', Nature Genetics, 7, 1994, 246-339.

[130] Lander, E.S., et al. (2001): 'Initial sequencing and analysis of the human genome', Nature, Vol. 409, pp. 860-921, 15 February 2001.

[131] Venter, J.C. et al. (2001): 'The sequence of the human genome', *Science*, Vol. 291, No. 5507, 1304-1351, 16 February 2001.

Holdsworth turned the discussion towards the term 'behavioural genomics'. He asked:

> Could I just ask you, for you – I know you've approached this subject in a short article in *Science* in 2001[132] - you've got a certain conception of what you could mean by 'behavioural genomics' as opposed to 'behavioural genetics' in your own field. Could you just say a word about that? (McGuffin 0.20.02)

Describing it as "a kind of slippery term really", McGuffin said that in his professional sphere it had a specific denotation:

> when I use it - or when colleagues I work with like Robert Plomin, on whose last book I am a co-author, use it - I think we're talking about – in addition to doing the traditional bottom-up approach, where you start off with the gene, study its sequence and structure, study the gene products, and then study the possible effects of the gene from that sort-of bottom-up route – you start with a whole organism – it might be man; it might be fruit-fly; it might be a rodent – and you study the behaviour of the organism, and you study the component traits of behaviour, some of which might be models for parts of disease like depression (you can never model depression completely in the animal, but you can model components of it) and then looking further down to then see what genes might be involved, and then see what pathways might be involved. So it's not so you don't do the bottom-up approach, but it's actually taking the whole-organism approach at the same time. And the attraction of taking the whole-organism approach is that you can then, not just study the consequences of anomalies in metabolic pathways, but you can actually study gene-environment interactions. So the centre that I'm still working in, but I was directing until I became Dean here three months ago, was called the MRC Social, Genetic and Developmental Psychiatry Centre, and the whole aim of that is really behavioural genomics. It's to put together social and other environmental factors and genetics in the development of psychiatric disorders. (McGuffin 0.21.56)

Holdsworth commented that this top-down perspective sounded different from the approach, for example, of the Genes to Cognition programme. McGuffin partly agreed:

> Yes, it is different. I mean – I'm on the steering group of the Genes to Cognition programme.[133] It's a very interesting programme. I think they do have some

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[132] McGuffin, Peter; Riley, Brien, and Plomin, Robert (2001): 'Genomics and behavior: Toward behavioral genomics', *Science*, Vol. 291, No. 5507, 16 February 2001, pp. 1232-1249.

[133] For a description of the Genes to Cognition (G2C) neuroscience research programme, see: http://www.genes2cognition.org/ (Consulted: 24 June 2008). See also here, footnote 12 below.

> elements of the top-down as well, because they are certainly modelling lots of stuff in animal models. (McGuffin 0.22.31)
>
> But it's true that a lot of what they do is looking at, in great detail, at pathways, particularly in their case what goes on at NMDA receptors, and all the complicated stuff that goes on in the post-synaptic density, which is the bit inside the cell that's attached to the NMDA receptor. So yes, I suppose that is a bit more, kind of, bottom-up, because it's setting up pathways and seeing what the consequences are. (McGuffin 0.23.02)

Mark Jobling

Holdsworth began the interview with Mark Jobling by referring to the book he had written with Matthew Hurles and Chris Tyler-Smith.[134] (Jobling 0.01.15).

> *Holdsworth*: The book is called *Human Evolutionary Genetics*. The first thing I wanted to ask you was whether that was just an appropriate title for a book, or whether you consider that to be the name of a subject.
>
> *Jobling*: Well, it certainly is an appropriate title for a book, and it mirrors the title of another book, called 'Human Molecular Genetics'. Do I think it's a subject? Well, it seems to be sort of becoming a subject in that you now see advertisements for, you know, a 'post-doc in human evolutionary genetics', which you didn't use to see. So I think it's pretty much becoming a subject, I would say. It's distinct from human genetics in general because of its evolutionary perspective. In a sense I take the Dobzhansky view that nothing in biology makes sense without evolution. And so it seems to me that evolution – an evolutionary aspect – is a given of any biological subject, so it seems almost unnecessary to have the 'evolutionary' bit in the title in a way, but operationally it really is becoming a subject, I think (Jobling 0.02.39). [...]
>
> Yes, I do think it's a good idea, yes, because much of human genetics is extremely medically focused on specific issues – sometimes extremely rare diseases, which are of course interesting, but I think that in order to understand diseases, for example, you need to have an evolutionary perspective. It's the frequencies of alleles that determine susceptibility to disease. And resistance to disease has an evolutionary framework behind it of population history and selection (Jobling 0.03.16).

Staying with the idea of a discipline of human evolutionary genetics, Holdsworth asked Jobling to describe how he saw it (Jobling 0.07.11).

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[134] Jobling *et al*. (2004).

> Well, in part it has to do with our history as a species, how we came to be – how the human species, however you define it, came to be - anatomically and behaviourally modern humans, and how we are related to other species - in particular the great apes, who are reasonably close in relation to us, and how we differ from them. And then it has to do with how our species came to be distributed around the world, and what the differences in genetic diversity are, if any, between us – between different populations. And it has to do with the genetic explanations for phenotypic differences. There clearly seem to be differences – differences in appearance, in particular in susceptibility to disease - between different populations. And then it has to do with the distribution of disease alleles within the population: diseases themselves, and what the evolutionary explanation for those disease distributions is. And within that there are various issues like the issue of population admixture: you know, there have been populations that have been separated for a thousand generations essentially that are now coming back together again; how one can recognise that moment and what its implications are. And again, within that, the consideration of the impact of various changes in human behaviour and lifestyle which have occurred in the past – a good example is the agricultural revolution, which clearly has had an enormous impact on us as a species, the census size of our species, the diseases to which we have been exposed, the distribution of alleles that are associated with cultural changes. And then I would take it right up to issues that would affect individuals (Jobling 0.09.26). [...]
>
> So, for example, if you are arrested by the police in this country for almost anything you have a DNA sample taken from you whether you like it or not, and you go into a database. So there is an evolutionary context to that: to understand the distribution of the alleles present within donors' DNA profiles that the police have obtained and how they differ between populations and sub-populations. So I would take it seriously as a subject, and I think that's why it's interesting to teach to undergraduates. It goes right from the origins of our own species or even the divergence with chimps, and the chimp-human common ancestor, right up to issues that are very current and have social implications of their own (Jobling 0.10.18).

Holdsworth asked Jobling what were some of the key methods of human evolutionary genetics? (Jobling 0.10.30).

> Well, the raw material, if you like, is DNA diversity. So you need to be able to tell the difference between different individuals at the DNA level. You need to be able to sample individuals and to define groups of individuals that you might call populations, and then you need to be able to analyse their DNA and detect differences and then interpret those differences. And to interpret those differences the methodology is the statistical methods of inference that you can use (Jobling 0.11.04).
>
> From comparing one group of people to another group of people at DNA level you can say something about the relationship between them in a meaningful way. So

> essentially you've got DNA technology. You have sampling, DNA technology and then statistical methodologies to say what the differences you see actually mean. There also some more medically important issues like phenotypic testing. If you're interested in disease alleles, you need to know when someone has a disease and when they don't. That can be surprisingly difficult to know when you come to think about complex diseases. And it can be surprisingly difficult because of heterogeneity – in other words, you get the same manifestation with maybe not the same genetic basis (Jobling 0.12.00).

This seemed to indicate that the evolutionary perspective really draws the boundary, in the sense that clinically-orientated research in medical genetics does not have this evolutionary focus. Jobling agreed that it did not, but pointed out that

> some people think that it should, particularly a guy called Randolph Nesse, who founded the field of evolutionary medicine as he calls it, and he's a medic – a proper medic – but he strongly believes that evolutionary thinking should be part of medical school training for people.[135] So taking an evolutionary perspective to medicine in general he believes is essential for fully developing someone who's training to be a doctor (Jobling 0.12.49).

Susan Lindsay

The next interview was with Susan Lindsay. Holdsworth asked her about human developmental genetics, and what sort of research she was doing (Lindsay 0.06.25). Lindsay replied:

> We are principally looking at the patterns of gene expression during development: so when and where genes are active or activated – turned on and then turned off, if they are, or maintained, and how that relates to the development of individual tissues or particular structures as the embryo develops, and my particular areas in the brain and looking at gene expression in the brain with an interest in, at the

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[135] Professor Randolph M. Nesse, M.D, The University of Michigan, at http://www-personal.umich.edu/~nesse/ (Consulted 11 August 2008). See Nesse, Randolph M., and Williams, George C. (1998): 'Evolution and the origins of disease', *Scientific American*, November 1998, pp.86-93. Ness and Williams were the authors of *Why We Get Sick: The New Science of Darwinian Medicine*, 1994. See also (1) Trevathan, Wenda R; Smith, E.O., and McKenna, James, eds. (2007): *Evolutionary medicine and health – new perspectives*, OUP, New York, 2007, and (2) Stearns, Stephen C., and Koella, Jacob C., ed. (2008) *Evolution in Health and Disease*, OUP, New York, 2nd edition, 2008. For Stearns as a leading author in the field of life-history theory, see the interview here with Ruth Mace, Annex XX, footnote.

> moment, producing an atlas and a gene expression map of the human embryonic brain (Lindsay 0.07.50).
>
> So one first thing is that: definition of embryo and foetus? I work on post-implantation development. Because 'human embryo' has come to mean pre-14 days, when human embryonic stem cells are developed. I do not work on human embryonic stem cells. That's pre-implantation (Lindsay 0.08.26).
>
> I work post-implantation. And I work from the time when - . The Central Nervous System starts as a tube, basically. It starts as a flat field, that rolls up.

Lindsay was referring to the neuroepithelial cells and their role in the development of the neural tube.

> Neuroepithelial, exactly. It rolls up, and it closes at both ends. And I work from about three and a half weeks of human development, at which point we have a fully closed tube (Lindsay 0.08.54).
>
> And then after that the major regions of the brain are developed through the rest of the embryonic period to about eight weeks. And then in the foetal period there's obviously a huge growth and further differentiation and development of the fine detail of all of the different brain regions, particularly in humans, cerebral cortex (Lindsay 0.09.24).
>
> So we do some work in foetal stages, but it's mostly in embryonic. So it's mostly in that three and a half to eight weeks of development (Lindsay 0.09.36).

Holdsworth asked about novel methods used in the research, such as 3D modelling. Lindsay replied:

> The 3D modelling is novel. The generation of gene expression data – finding out when a gene is active or inactive - is using very traditional methods. Immunocytochemistry, looking at proteins – that's something that's been done for a long time. What we do most of is looking at messenger RNA (Lindsay 0.10.03).
>
> So, messenger RNA is more difficult to look at (Lindsay 0.10.20), because everywhere - on our fingers, all over our skin, we have enzymes which break down RNA, and they're very resistant to all sorts of things that we might usually use to get rid of them. So the tissue has to be treated in quite careful and specific ways in order to preserve that messenger RNA (Lindsay0.10.48).
>
> Which is why the collection that we have here, which is part of a national collection held here and at the Institute of Child Health in London, that's one of the reasons why it's a valuable resource (Lindsay 0.11.08).

Holdsworth: It's a kind of reference resource? (Lindsay 0.11.10).

Lindsay: It's a resource for people to obtain material, but also as we get results we're sticking them into a database. [...] And then we try and grow that database. I hope. That's one of the ideas: to build it into a reference database for gene expression patterns (Lindsay 0.11.26).

Holdsworth asked Lindsay about another activity mentioned on Lindsay's website: 'Large-scale gene expression studies and analyses'. Lindsay explained:

Well, 'large-scale' means lots of different things to different people (Lindsay 0.11.40). Because with genomics you – if you were using micro-arrays and looking at all of the human genome on an Affymetrix chip or on other kinds of microarrays – these techniques are ones where we're looking at all human gene sequences (Lindsay 0.12.14).

That's one definition of large scale – you're looking at all of the genome. But in doing that you don't have any information about the – detailed information - about the spatial expression patterns: where, precisely, the gene is expressed (Lindsay 0.12.34).

Lindsay illustrated her explanation with an image shown on the PC screen. It showed a tissue section[136] (Lindsay 0.13.27). Lindsay used the image to illustrate two regularly-used techniques in her type of research: immunocytochemistry and in situ hybridisation.

OK. So these are the two techniques. This is the immunocytochemistry, looking for protein, and you can see this is a tissue section with the developing head at the top. And the embryo's curved round, so this is head and this is spinal cord; these are developing eyes, and you can see the signal in brown (Lindsay 0.13.50).

Holdsworth: That reminds me of the 3D images on your website (Lindsay 0.13.55).

Lindsay: Yes, but the 3D images are built up section by section from this kind of data. But you can see from here – and here's the gene expression pattern here for this particular gene. This was RNA in situ hybridisation. You get a very distinct and clear idea of where the gene is precisely expressed (Lindsay 0.14.24).

So, instead of protein this is messenger RNA. And it happens that the staining gives a purple stain rather than a brown one, which is just to do with the chemicals. But

[136] For a description of the techniques used in this research see the following article (with illustrations): Kerwin *et al*. (2004).

> this is showing where the mRNA for this particular gene is, and you can see it's in a very confined place (Lindsay 0.14.49).
>
> This is an Affymetrix chip here. So you could - and we have been trying – you can get a detailed idea of localisation by cutting out the tissue area that you're interested in and generating RNA and then putting that RNA on a chip (Lindsay 0.15.15).
>
> So the detailed spatial information which in situ hybridisation and immunocytochemistry give you - people are reconstructing by very precise microdissection. And then you can see that in this area that you've microdissected , and then screen the 20-odd thousand or however many sequences there are on an Affymetrix chip, I can say that in this region here are all the genes that are expressed (Lindsay 0.15.55).

So the two key techniques when working on tissue are: immunocytochemistry, which is a technique for detecting proteins using antibodies, and in situ hybridisation (ISH). The latter is a technique for detecting DNA or RNA sequences in tissue sections by hybridisation, using complementary DNA, or RNA (Lindsay 0.16.25). Lindsay further explained:

> So what that in situ hybridisation is - [...]. A short bit of DNA that matches the RNA of a specific gene (Lindsay 0.22.47). So it's finding RNA from a specific gene. And that particular gene happens to be expressed in a very specific place (Lindsay 0.22.57).
>
> *Holdsworth*: It's identifying it and localising it (Lindsay 0.23.00).
>
> *Lindsay*: Yes. And sticking to it. Because it's the linking of DNA and RNA. The whole idea of the Double Helix is that the bases pair with each other (Lindsay 0.23.18). [...] So if you have a complementary sequence they will identify and stick together (Lindsay 0.23.28).

Holdsworth asked how the images that Lindsay was showing had been created.

> [In] both cases what we have is an embryo embedded in a block of paraffin wax. And then very thin sections cut through the embryo, and then these sections mounted onto glass slides. And so what this is, is a section through an embryo (Lindsay 0.17.06).

Lindsay showed an example on the screen.

> This is a real section – a physical section through the embryo (Lindsay 0.17.49).
>
> [*Lindsay refers to a black shape in the image*]. The black block. And this has just been stained with a stain that identifies cell structure. What's called a histological stain. It's not a particular gene, it's just showing cells. And this is a view of the painted 3D model. But as you move through the structure you can see - look, this is the forebrain, this is the developing eye, this is the mid-brain, developing cerebellum, into the hind-brain and down into the spinal cord. That's the heart, and that's the liver (Lindsay 0.18.27).

To facilitate inspection of these areas of the embryonic brain, researchers now make use of a tool called Optical Projection Tomography (OPT). Lindsay explained that the advantage of this was

> that you've got a three-dimensional, digital model that you can section in any plane, and you can compare the sections in one plane to another (Lindsay 0.19.41). Because, as you can see, the developing brain has a lot of bending and folding, and the shape changes quite dramatically (Lindsay 0.19.54).

Thus the researchers are working either with tissue sections or with the 3D digital models offered by OPT. The latter has been explained in the following terms:

> Optical projection tomography (OPT) microscopy is a new technique which allows the 3D imaging of biological specimen over 1 cm across. It was initially developed with the hope of enabling accurate measurement of 3D shapes. However, it has proven to be a fast method for scanning the 3D distributions of gene expression patterns during embryo development.[137]

Summing up, Holdsworth asked Lindsay if her concern was with the expression of the genes concerned in the development of neurons (Lindsay 0.26.35). She answered:

> And other brain regions. Because it's not only the neurons that are important in shaping the brain and also in the function of the developing brain (Lindsay 0.27.01).

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[137] From the OPT homepage of the MRC Human Genetics Unit, Edinburgh, UK: http://genex.hgu.mrc.ac.uk/OPT_Microscopy/optwebsite/frontpage/index.htm (Consulted 9 October 2008).

> We're really concerned with expression of a whole variety of different genes during brain development, and our selection of the genes partly depends on - are they genes underlying particular genetic disorders (Lindsay 0.27.20).
>
> So there's a relevance to humans, or human beings, but in order to understand those we need also to need to know about patterns of key developmental genes (Lindsay 0.27.32).

Lindsay said it was known from mouse and other species

> that there are certain families of genes that are very important in the development of not only the brain, but all sorts of different organs, and quite often it's the same genes in different organs or different members of the same gene families. There are key gene families you can identify (Lindsay 0.27.56).

In amplification of the phrase "gene expression pattern", Lindsay said it meant "to define the regions, or cells, where a gene is either off or on (Lindsay 0.33.00).

Holdsworth opened the topic of behaviour.

> Now, obviously in some sense neuronal and other brain structures are a prerequisite for explaining behaviour, but is there any direct sense in which your research is looking at the development of behaviour? (Lindsay 0.34.43).

Lindsay's answer was

> I think the honest and real answer to that is no, because we're looking at a much earlier stage than that. Because, for example, this is going to be the cerebral cortex, where you - . What I was going to say –. It may be that other people that you talk to would argue about this, but I would imagine –. That's going to be the cerebral cortex – and that's where, as you develop into an adult, all the different sulci and gyri – they are a picture of the adult - we're getting to the adult brain! (Lindsay 0.35.23).
>
> So usually the map that people have of functions of the brain - the cerebral cortex is really showing, and that's where all our thinking power comes from. But I don't know how much of behaviour – certainly in lower animals too, but primates, behaviour would also be to do with reflex actions (Lindsay 0.35.51).
>
> And so how much of our behaviour would also be in our cerebellum, affecting how we move? And there may be lots of other places (Lindsay 0.36.03).

Robin Crompton

Robin Crompton's discipline is evolutionary biomechanics, as he explained (Crompton 0.02.04):

> Well, very briefly, I'm interested in the evolution of our locomotor system - that is, walking and other ways of moving around for our immediate relatives. And I'm interested in this from the fieldwork aspect, and also laboratory studies of biomechanics and locomotion.

Holdsworth had noticed that evolutionary biomechanics was often talked about as a way of explaining the form and function of organisms. He asked what Crompton thought of that description (Crompton 0.02.48).

> That's fair enough. I'm not sure that every kind of biomechanics researcher would use the same way. My meaning of biomechanics is quite specific and concentrated, and that's not always the case. People tend to sometimes use the word biomechanics interchangeably with 'function' which I don't think is appropriate. It's not exactly the same thing.

This led into a discussion of the concept of 'work' in Crompton's research. Holdsworth observed that, generally, in literature on the biology of behaviour, the term 'function' was often used rather vaguely, but in evolutionary biomechanics, and in some other areas, it could be replaced by the term 'work' (Crompton 0.03.37). Crompton responded:

> Well, when I use the term 'work' I'm using it very specifically. In fact, [...] I'm just writing a talker for a paper I'm giving next Monday, and there we do use the term 'work' in its Newtonian sense, purely. In the sense of Newtonian mechanics. And I'm not sure that a lot of people who use the word 'biomechanics' are all that familiar in my field with Newtonian mechanics. I'm not a physicist, I'm an anthropologist, but at least I've learnt enough to be able to, I hope, use words in an appropriate sort of way.
>
> *Holdsworth*: Yes, but that's interesting because you couldn't use the term 'work' to cover every meaning of the term 'function'.
>
> *Crompton*: No, certainly not.
>
> *Holdsworth*: You couldn't use it to cover every meaning of the term 'behaviour'.

Crompton: No.

Holdsworth: But in specific cases it may be the appropriate term to use.

Crompton: Yes, absolutely. I mean, for example, this paper I'm about to give, this is actually on prosimians, comparing the work done in crossing between two trees by leaping across to the work done against gravity if you climb down the tree, cross the ground and go up the next tree. So, that's a very specific use of 'work'. (Crompton 0.05.23)

Conclusion

In this chapter we have given an idea of how each researcher interviewed presented his or her discipline. It will have been seen that there was a considerable diversity of subject-matter, in the sense of the concepts and methods employed by the various researchers in their disciplines, as well as diversity in the manner of communicating this material, as well as a certain tendency to generate further diversity. In some cases the researcher concerned showed interests that spread from the discipline initially described into other disciplines and literatures.

Chapter C2 – Does the research cover all hominids or only *Homo sapiens*?

The matrix for the criterion

The first question asked whether the work of the researcher concerned was restricted to *Homo sapiens*, or whether it extended to other species related to our own. As we have already made clear,[138] 'hominids' here denotes the Great Apes: orangutans, gorillas, chimpanzees and humans. It could therefore include species coeval with *Homo sapiens* - like the chimpanzee, *Pan troglodytes* - putative ancestral species such as *Australopithecus afarensis* or *Homo erectus*, or other extinct but related species like *Homo neanderthalensis*.

Table C2.01. Matrix for Criterion 1:
'*Does the research cover all hominids or only* Homo sapiens*?*'

Researcher	*Discipline*	*Hom. sap.*	*Other*
Jones	Biomolecular archaeology	■	■
Hutchinson	Evolutionary biomechanics (dinosaur)		
Smith	Molecular neurobiology	■	
Buckley	Down Syndrome research	■	
Mace	Evolutionary anthropology	■	
McGuffin	Research into normal and abnormal behaviour	■	
Jobling	Human evolutionary genetics	■	■
Lindsay	Human developmental genetics	■	
Crompton	Evolutionary biomechanics (human)	■	■

[138] Chapter B1, above.

Salient interviews

For this criterion, the evolutionary perspective proved to be the determinant. The researchers for whom research into other hominids were clearly salient were Jobling (human evolutionary genetics) and Crompton (evolutionary biomechanics). For the other respondents, research into other hominids was either not relevant or was only marginally so.

When the biomolecular archaeologist Martin Jones was asked this question he replied that "in practice" the research had been, he would guess, "99% *Homo sapiens*", but in principle it was "not constrained to *Homo sapiens*". In these circumstances it was "probably about right" to record a 'Yes' for Homo sapiens, while indicating that the rubric 'All hominids' was also applicable (Jones 0.14.0).

Chris Smith pointed out that

> Well, molecular neurobiology is a very fundamental subject: it's going to cover all organisms – all organisms which have a nervous system. And that really amounts to practically all even down to the Cnidaria - the jellyfish - and so forth. They have nervous systems, so - (Smith 0.51.00).

Therefore, for Smith, the domain of molecular neurobiology covered *Homo sapiens* and all other animals, even if some were more important than others for neurobiological research. (Smith 0.51.30).

Holdsworth supposed that one could make a pragmatic distinction. The research was actually conducted in the context of modern humans, because of a lack of evidence for extinct species. Smith agreed that this was so (Smith 0.52.00):

> You can't do neurobiology on Neanderthal humans. Obviously you can look at their skulls and draw some conclusions about their intellectual capacities and so forth from that, but that's not molecular neurobiology – that's something different.

However the interview returned to the topic of Neanderthals later in an interesting way when the time came to discuss Criterion 10 on fossil evidence. This will be reported in Chapter C11.

Sue Buckley, answering from the point of view of her research into Down syndrome, replied (Buckley 1.17.12) that researchers in this field would take mice as comparative species rather than primates. To the best of her belief no researcher had created a trisomic chimpanzee. Looking into the matter after the interview, Holdsworth found no literature in this sense, but did come upon the article by McClure et al. (1969) describing an infant chimpanzee "with clinical, behavioral, and cytogenetic features similar to those in Down's syndrome".

Buckley said there were claims of historical evidence of Down syndrome:

> People argue there are paintings around of people with Down syndrome and babies with Down syndrome that go back [a long time]. Some famous paintings[139] (Buckley 1.18.06).

The reply from Ruth Mace, a behavioural ecologist, was

> Mostly *Homo sapiens*, but behavioural ecology can cover anything, from a *Drosophila* to a - you know (Mace 0.50.10).

Mace looked for the factor that demarcated human behavioural ecology. It occurred to her that the key criterion might lie in "the fact that they're all dead" – that is, the extinct human species that might lend themselves to comparison with *Homo sapiens*. This meant that if

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[139] See, for example: Levitas, A.S. and Reid, C.S. (2003) 'An angel with Down syndrome in a sixteenth century Flemish Nativity painting', *American Journal of Medical Genetics Part A*, Vol.116A, No.4, 1 Feb 2003, pp.399-405. This attracted a comment in: *Am J Med Genet A.*, 2004 Apr 15; 126A(2):220. A photographic reproduction of the painting is to be found in the following news report: 'Down Syndrome Through the Ages', *medGadget - Internet journal of emerging medical technologies*, Friday, 18 November 2005 at: http://medgadget.com/archives/2005/11/down_syndrome_t.html (Consulted 24 September 2008).

one's interest was in one of the extinct species then one's focus lay rather in the field of (as some people called it) 'human evolutionary ecology', rather than 'human behavioural ecology' (Mace 0.50.30).

> [If you're interested in] something like age at first reproduction, or age at menopause or something, it's more 'life history' than behaviour. So human evolutionary ecology is slightly broader. It might include, you know, the evolution of menopause, but then one of the hypotheses for the evolution of menopause is the 'Grandmother hypothesis' – i.e., grandmothering as an adaptation to stopping reproduction in yourself, but looking after your daughter, helping your daughter reproduce (Mace 0.51.32). [...]
>
> So it has a behavioural dimension, but human 'evolutionary' ecology is just slightly broader than 'behavioural' because 'behaviour', you know, might just imply a slightly narrower focus. So I guess if we're doing just 'behavioural' then we're mainly doing *Homo sapiens*, because it's the only extant species, whereas if you were doing human 'evolutionary' ecology - I mean, people have written papers on, you know, 'Did *Homo erectus* have menopause'[140] and this kind of thing. I suppose. I would tick mainly the first one: *Homo sapiens* (Mace 0.52.05).

The positive respondents: Mark Jobling and Robin Crompton

Turning to the explicitly positive respondents, Mark Jobling stated that "human evolutionary genetics covers other hominids – lots of hominids" (Jobling 0.14.53). When Holdsworth asked if there were any boundaries to this, Jobling's response was (Jobling 0.15.14):

> Are there boundaries within human evolutionary genetics? Not really, because I mean the taxonomy of hominids is always controversial and frequently changing. So I don't think you can rule any hominids out of human evolutionary genetics.

[140] See (1) O'Connell *et al*. (1999) on grandmothering, and (2) Aiello and Key (2002) on 'Energetic consequences of being a *Homo erectus* female'.

> Most of them are under debate. There's still a question mark over whether Neanderthal contributed genes to our gene pool of modern *sapiens*. And I think you can't rule out any other hominids, and they're all of interest.

The researcher who had the fullest contribution to make on this criterion was Robin Crompton (evolutionary biomechanics). We shall look at his comments in some detail.

Robin Crompton

First, Crompton quickly confirmed that his field of research covered all other hominids as well as *Homo sapiens* (Crompton 0.14.45). As far as the genomic perspective was concerned, Crompton's interest was indirect. His work drew on the latest findings of molecular phylogenetics:

> for example I've just been writing a big review of the hominoid - I mean, the ape and human - locomotive system, and obviously the recent information on genetic separation dates of humans and chimpanzees is relevant to that, and it's mentioned in the paper, but that's about as far as I take it (Crompton 0.17.00).

The paper he referred to was one entitled 'Locomotion and posture from the common hominoid ancestor to fully modern hominins, with special reference to the last common panin/hominin ancestor', co-authored with Vereecke and Thorpe, which appeared in *Journal of Anatomy* in April 2008.[141] In the interview Crompton explained that this was to be "a special issue on human evolution and modelling the lost common ancestor of humans and chimpanzees, edited by Bernard Wood[142] and Sarah Elton"[143] (Crompton 0.17.10).

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[141] Crompton *et al*. (2008). This issue of *Journal of Anatomy* in question published papers from the 2007 Winter Meeting of the The Anatomical Society of Great Britain and Ireland on the theme 'Human evolution: ancestors and relatives'. For an introduction to the issue, see: Wood, Bernard, and Elton, Sarah (2008).

[142] Bernard Wood is Henry R. Luce Professor of Human Origins at George Washington University, Washington DC.

[143] Dr Sarah Elton is Lecturer in Anatomy and a member of the Functional Morphology and Evolution Research Unit at the Hull York Medical School (HYMS).

Crompton gave examples of research projects that concerned both extinct human species and extant species of Great Ape. One theme he had selected for future study was the evolution of running. Another was "looking at the costs of moving on compliant supports". As Crompton explained,

> You know, I think the evolution of upright bipedal walking was in arboreal contexts in the trees. So it's obviously relevant to look at compliant supports. If our ancestors started upright bipedal walking in the trees, not on the ground - which is what I think - then we started doing it in a context of moving around on bendy branches. So if you tread on a branch, then you are actually imparting energy to the branch. If it's a small branch - small-diameter branch - then the branch can bend, and you're losing energy. And unless the rebound happens within your walk cycle, you lose the energy. So that's one of the things we need to look at (Crompton 0.13.05).

Crompton has already done work on this subject, based on observations of the Sumatran orangutan, *Pongo abelii*.[144] From the comment just given, it is clear that what interests Crompton is the possibility of applying his techniques of bioenergetic analysis both to extant and extinct species in order to derive an evolutionary account adequate for both. This point was well illustrated when Crompton was asked for further examples, and he cited work by himself and his colleagues on the Laetoli footprints in Tanzania, which are held to be the fossilised footprints of three individuals of the species *Australopithecus afarensis* (two probably female adults and a child). Crompton said he and his team (at PREMOG at the University of Liverpool)[145] were "trying to reverse engineer them and work out what the gait was from the footprints"[146] (Crompton 0.19.00).

Holdsworth said he had been particularly struck by Crompton's paper on 'The role of load-carrying in the evolution of modern body proportions' with Wang,[147] and by possibility of

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[144] Thorpe *et al*. (2007).
[145] PREMOG website: http://www.liv.ac.uk/premog/premog-research-current-laetoli.html (Consulted 12 March 2009).
[146] Although the current Laetoli project had not yet produced a publication, Crompton gave the following reference, which did mention the Laetoli footprints: Sellers *et al*. (2005).
[147] Crompton and Wang (2004).

making inferences from the skeleto-muscular data about an organism to its behaviour in the sense of tool utilisation or tool transport. He asked Crompton if he had done much study on tool utilisation. (Crompton 0.09.16). Crompton replied that he had not, although he had done some work with a colleague, John Gowlett,[148] "on the Acheulean industry and really looking at form and the scaling of form in handaxes in Africa". So I've done a little bit of archaeology, but not a lot (Crompton 0.09.30). The Acheulean industry is identified with the production of bifacial handaxes and is associated with *Homo ergaster* and *Homo erectus*, from about 1.7 million years before the present.[149]

Analysis of diversity

As remarked above, the root of the diversity among the responses here was the relative weight accorded by the various research disciplines to the evolutionary perspective on human behaviour. For the person conducting the interviews it was sometimes a strange experience to be asking researchers in disciplines with a clear ontogenetic focus whether their work took account of other hominids, including ancestral humans. It seemed almost like a wilful digression from their direct concerns – a capricious indulgence, perhaps, in a taste for the archaic. This was an inevitable effect of the chosen method and therefore only to be expected, given precisely that the method was designed to seek out diversity among the respondents. Nevertheless the effect was there. It was corrected, if that is the right word, by Crompton's replies.

Crompton, the evolutionary biomechanist, is concerned both with past and present: not just because the one leads into the other, but for other, specific reasons. First, he adduces the evidence, not only of extinct species, but also of extant species of Great Ape (and other primates). Second, he adduces evidence of the behaviour – notably locomotive behaviour – of present-day humans who participate in laboratory trials. Then comes the third reason, which underpins the other two but would be easy for the non-specialist to overlook. It is

[148] Professor John A.J. Gowlett, Professor of Archaeology and Evolutionary Anthropology, School of Archaeology, Classics and Egyptology (SACE), University of Liverpool. See: Crompton and Gowlett (1993), and Gowlett and Crompton (1994).
[149] Miller, Wood *et al*. (2006), p. 203.

that, for the purposes of evolutionary biomechanics, the 'environment' to which different species are constrained to adapt is largely constituted by unchanging physical measures. Most narratives of evolutionary adaptation have to take into account secular or periodic variation in environmental parameters reflecting changes in climate and the distribution of animals and plants. Here is, by contrast, a narrative about mass, gravity, momentum and velocity. It would be wrong to say that changes in the physical parameters of the terrestrial environment do not occur – one thinks of changes in the earth's magnetic field, for example – but in the case under study we are talking about laws of physics that have conditioned life forms throughout the history of the terrestrial biosphere. The cells of every tree that has lived have had to do the work of growth against the force of gravity. Considerations such as these make it interesting and feasible to make cross-species comparisons across very long time-spans. Yet, in a sense, the time-spans are irrelevant. Although *Australopithecus afarensis* is extinct, the shape of her foot is extant. It may validly be compared with other hominin foot-shapes on the basis of constant mechanical and energetic criteria.

Assessment of the criterion

The criterion served the purpose of detecting divergence of approach where this existed. The divergence was significant. The distinguishing factor was the pertinence, or otherwise, of the evolutionary perspective. This might be an appropriate moment to reflect that, in the context of various debates, the idea that human behaviour can or should be studied in an evolutionary perspective has occasionally been controversial. The controversy has to do with the notion that there is something that we might call 'human nature' that has been delivered to us across the generations by evolution. In the discussion of Criterion 1 in our interviews, however, this notion was never evoked by an interviewee, in either the positive or the negative sense. The interviewees who saw no need, in their own disciplines, to take into account other hominids, were describing the characteristics and exigencies of their professional work-benches as they knew them from everyday experience, not declaring a principle. This, at any rate, was the judgment of the interviewer.

Chapter C3 – Is behaviour studied in the ecological setting – or in the laboratory or clinic?

The matrix for the criterion

Criterion 2 gave scope for exploring the extent to which behaviour was being studied in its natural setting – more precisely, its ecological setting – and the extent to which it was being studied in the setting of the laboratory, or the clinic.

Table C3.01. Matrix for Criterion 2:
'Is behaviour studied in the ecological setting – or in the laboratory or clinic?'

Researcher	*Discipline*	*Ecol. setting*	*Lab/ clinic*
Jones	Biomolecular archaeology		
Hutchinson	Evolutionary biomechanics (dinosaur)		
Smith	Molecular neurobiology		
Buckley	Down Syndrome research		
Mace	Evolutionary anthropology		
McGuffin	Research into normal and abnormal behaviour		
Jobling	Human evolutionary genetics		
Lindsay	Human developmental genetics		
Crompton	Evolutionary biomechanics (human)		

Salient interviews

The responses on Criterion 2 tended to throw up two clusters: the field workers and the lab workers. The research of Jones, Mace and Crompton involves a significant measure of anthropological fieldwork. That of Smith, McGuffin and Jobling is done in the lab. Hutchinson belongs with the field-oriented group. Buckley's reply concerning research on

Down Syndrome was 'both' the ecological setting and laboratory research (Buckley 1.18.18), while Lindsay's reply was 'neither', since her research in human developmental genetics did not target 'behaviour' at all (Lindsay 0.47.22). We take the field workers first.

Martin Jones

For Jones, in biomolecular archaeology,

> Behaviour is studied in the ecological setting, I mean, even if one takes it off to a sample, there's a lot of work in the lab on the samples, but there's a guiding principle of all archaeology which is, 'if you want to understand the contents, you've got to understand the context' (Jones 0.15.08).

In the opening part of Jones' book (2001), in relating his own development as an archaeologist, Jones described himself as in the early days more or less casting aside the earth and vegetable detritus surrounding the artefacts, and then later moving his focus towards the analysis of the surrounding matrix and the wider environment. In the interview Jones acknowledged this and confirmed: "That's absolutely right: the ecological setting" (Jones 0.15.20).

John Hutchinson

Hutchinson was positive on the ecological context:

> In the work I do: yes. And quite a few people who study evolutionary biomechanics of hominids would concur. They're quite explicit about comparing the laboratory and ecological setting (Hutchinson 0.20.25).

Asked to cite researchers, Hutchinson mentioned two:

> Well, Robin Crompton again, you've got, to start with. He's doing a lot of work lately on hominid footprints, where they left them. But also there's kind of on the other end of the spectrum a guy named Daniel Schmitt. He's at Duke University in the States.[150] He's done a lot of very explicitly ecological work on primate locomotion, trying to look at how their adaptations are matched to their ecology and how locomotion is affected just by ecology (Hutchinson 0.21.20).

Ruth Mace

For the behavioural ecologist Ruth Mace the ecological setting had great importance:

> Yes, that's the defining feature, really, I would say (Mace 0.52.16).

The ecological perspective was present throughout the interview. Specifically, Mace gave clear examples of studies that she and colleagues had undertaken in which the interaction between environment and culture was analysed. A case in point was a study of patriliny among pastoralists in Africa:

> Pastoralists tend to be polygynous systems. In other words, individuals with lots of cattle can afford lots of wives – OK? - and the reason is, that it's a very good source of food. So, if you can marry a girl with a lot of cattle, you can have a lot of healthy children; there's going to be a lot of milk; it's much less hard work than farming. You know, it's a good deal all round. So if a man has lots of cattle, he can have very high reproductive success – because he can marry several wives, in fact, and that's often what you see in pastoralist societies. And because it so much favours your

[150] Dr Daniel Schmitt, Associate Professor, Department of Biological Anthropology and Anatomy, Duke University, Durham, North Carolina. Website: http://fds.duke.edu/db/aas/BAA/faculty/daniel.schmitt (Consulted 12 March 2009).See, for example, Schmitt *et al*. (2006).

> sons to have this cattle, then you get this kind of male-biased wealth inheritance. OK? So that's the explanation for why when societies gain cattle they become more patrilineal (Mace 0.21.04). [...]
>
> And then you can just test that and see whether it really happens, over evolutionary time. I mean, are societies that are adopting cattle becoming more patrilineal? And we find that they are. So you've built a model, and you make your prediction from it, and you test it using the data. [...] It's an adaptive model in that we're saying, you know, there's a functional reason why this society switched from being matrilineal to being patrilineal, which is the reason I just gave you, and then you test it. So we're saying rather than cultural variation being random or whatever, it's actually to do with individuals trying to maximise their reproductive success (Mace 0.21.52). [...] So that would be an example of a behavioural ecological model.

Robin Crompton

Crompton confirmed that, in his work on evolutionary biomechanics, behaviour was studied in the ecological setting (Crompton 0.15.02). As an example, he cited the work that he and colleagues had done about the origins of human upright walking. He said this had been informed by studies of orangutans in Sumatra. He cited their very recent paper in *Science* looking into that.[151]

In his self-introduction, Crompton had explained that, in addition to the fieldwork in the ecological setting, his research included "laboratory studies of biomechanics and locomotion" (Crompton 0.02.10).

We now turn to the cluster of laboratory workers who did not specifically prioritise the ecological setting.

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[151] Thorpe *et al*. (2007).

Chris Smith

For Chris Smith, it was clear that molecular neurobiology was a laboratory science (Smith 0.52.48):

> I think really you've got to say not in the ecological setting, but in the laboratory. Now let me think. I mean, obviously you can't make utterly sharp distinctions here, but for the vast majority it will be in the laboratory. And clinic? I think you'd really say it's a laboratory subject. As I said, the applications – the outcomes of molecular neurobiology - one would hope many of them can be applied – *applied* in the clinic. So if somebody came to you with a neurological condition, you might say, well, it's due to some defect in the channel protein in a particular neuron. Which is sometimes the case. But you wouldn't use them for that molecular neurobiological research (Smith 0.54.24).

Although molecular neurobiology as such was a laboratory science, the interaction between the organism and its environment was an important part of the discipline's subject-matter: the interaction, for example, between stimuli from the external environment on the one hand and, on the other, developing neurophysiological systems in the organism's CNS. In this context, Smith referred to

> the experimental evidence within the field of visual perception in particular, which shows how labile the visual cortex is with respect to early visual experience – lots of experiments on that. And also experiments which put experimental animals in poor and rich environments - that is, stimulus environments – showing that this also as a strong effect on the development of the cortex. So all of these things show that the brain is very open - certainly in its early development - to environmental effects. These early periods are known as the critical or sensitive periods, and in experimental animals such as cats and so forth they last a few months, but in humans, I think, something like 18 months. And different parts of the brain of course have different lengths of these sensitive periods. I think the linguistic areas are much more, you know, have a much longer period when they're open to

> environmental influence. Which isn't to say of course that there isn't a strong hereditary component in there as well. You've got the two things: you've got a core hereditary component, and this is going to be affected and influenced, moulded, by the environment in which it finds itself (Smith 0.17.42).

Peter McGuffin

To the question 'Is behaviour studied in the ecological setting?' McGuffin, the researcher 'in normal and abnormal behaviour', replied:

> Well, it is to some extent. So that a lot of my research has been, for example, looking at naturally occurring hazards, such as unpleasant life-events, and how they impinge upon people to make them depressed or not, and the extent to which those sort of naturally-occurring hazards interact, or co-act with genetic predisposition. So in that sense, if you call it 'ecological', yes, I think it is (McGuffin 0.25.19).

However, he agreed that his subject was also studied in the laboratory, and the clinic (McGuffin 0.25.35). In the analysis of McGuffin's responses on the criteria, it was agreed in this case to place the predominant emphasis on 'laboratory/clinic', with the ecological setting also pertinent "to some extent".[152] The interview returned to the role of environmental measures in McGuffin's research when it reached Criterion 8 on 'environmental markers'.[153]

It is relevant to recall that in behavioural genetics research laboratory work can be of at least two different kinds. Researchers on the molecular side are conducting genomic research. Those on the psychological side are often conducting tests of reasoning or rapidity of response. An example of the latter would be the work reported in the article by Posthuma

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[152] After each interview, the researcher concerned was sent by email for approval a 'Criteria graphic' summarising the criteria matrix as it emerged from his or her responses.
[153] See Chapter C9.

et al. (2001) entitled: 'Perceptual speed and IQ are associated through common genetic factors'. This is an examination of the 'inspection time' hypothesis, whereby

> Inspection time is defined as the minimum display time a subject needs to make an accurate perceptual discrimination on an obvious stimulus, and is often thought to reflect speed of apprehension or perceptual speed (Kranzler and Jensen, 1989).[154]

The basic setting for research of this type is a laboratory in which a human subject (for instance, a member of a pair of twins) is asked to inspect and identify a figure displayed on a computer screen. The time they take to do so is recorded, and their scores are correlated with other measures.

Mark Jobling

Mark Jobling sought clarification of the question (Jobling 0.16.22), asking:

> So you mean people in their own environments, as opposed to DNA in laboratories?
>
> *Holdsworth*: Or behavioural testing in laboratories.
>
> *Jobling*: Well, almost exclusively it's DNA analysis in laboratories, but there is a clinical aspect. So, for example, in lactose persistence, ideally people will be tested for lactose persistence in a direct way, but often that's not the case. I'd say, more often than not, behaviour was not studied in the ecological setting. (Jobling 0.17.04)

Holdsworth suggested that, nevertheless, the research was designed to elucidate behaviour in the environment. Jobling replied

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[154] Posthuma *et al*. (2001), p. 593.

> Well, it depends what you mean by 'behaviour', doesn't it? I mean, clearly, if you're interested in, for example, whether microcephalin haplotypes affect IQ, then you need to ask certain questions.[155] There's a gene called microcephalin, and a certain haplotype comes with high frequency in some populations relatively recently. It's expressed in the brain, and if you knock out the gene you get a small brain. But quite what it does normally we don't know. It spread very fast, very recently. And it's brain-expressed, so people were interested in whether it had some influence, and if carrying that haplotype made a difference to some easily measurable aspects of behaviour, and so they did an IQ test, and it doesn't. So there are those kinds of things. It's difficult. I can come up with more examples. Skin colour, for example (Jobling 0.18.11). [...]
>
> Pigmentation studies do measure skin colour. You can't do it without. If you are saying behavioural – behaviourally related research within human evolutionary genetics, then, yes, there is an ecological aspect. It depends again whether you mean something like an IQ test, or a skin-reflectance test. Does that count as an ecological setting or is it just the laboratory? (Jobling 0.18.46).

Holdsworth commented that this was interesting because from Jobling's book and other literature, one's thoughts are drawn to the accounts that are now given of prehistoric migrations, for example. He had already mentioned the investigation of the Neolithic revolution. All these things seemed to be closely concerned with the ecological setting of the humans concerned (Jobling 0.19.21). Jobling replied that

> They are, but we're interested there, in the case of the Neolithic revolution, in a past ecology. We can't revisit the times of the Palaeolithic and say what was the ecological setting at the time. So it's inferred from modern populations. So that's, in a sense, the problem with the subject: that you need to sample modern populations and infer something about the past. That process of inference is controversial and

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[155] For an account, inter alia, of the controversy that has surrounded some aspects of microcephalin research, see the article in Wikipedia, 'Microcephalin': http://en.wikipedia.org/wiki/Microcephalin (Consulted 12 August 2008). For an example of the literature, see: *Evans et al*. (2004).

> difficult. It doesn't matter whether you are a farmer now, or a City worker, or a lay-about or whatever you might be, to what your ancestors were doing ten thousand years ago. So we just sample, in a sense, in a behavioural, ignorant way: we just take people and then we classify them in some way - I suppose, Romanians or Basques or something like that, which again has its problems - and then we try and infer something about people who lived in the past from the DNA that their modern descendants carry. (Jobling 0.20.37)

Holdsworth pointed out that there was also contemporary evidence in the soil or in food residues. Although Jobling agreed that this was so, when Holdsworth suggested that this seemed to imply an ecological setting, Jobling commented:

> That's archaeology, though, isn't it? And, I mean, I think archaeology helps people who study human evolutionary genetics, but it can't be said to be part of human evolutionary genetics. It's another discipline that illuminates the question that we all might be interested in, whether we are archaeologists or prehistorians or linguists or whatever, so that you can make some kind of synthesis based on this, but I think nonetheless they are different things. So if you look at the human evolutionary genetics 'thing', that's about inheritance, really. It's about inheritance in a certain way. So it's a, you know, slightly odd word to see there: an 'ecological' setting. (Jobling 0.21.45)

Jobling observed that he was not himself an anthropologist. He had noticed that

> some anthropologists talk about ecology a lot, and some of them don't seem to be very interested. So there seems to be a school that sees ecology as being something to do with non-human species. Humans are somehow set aside. But there are anthropologists who see humans as very much in an ecological setting.

Jobling pointed out that there was a journal called *Molecular Ecology*, which was interesting for the reason that

> it never, never, never has any articles about human beings: always about pine trees or starfish or beetles or anything else but humans, as if humans are somehow apart - they don't have anything that could be called 'molecular ecology'. (Jobling 0.22.37)

Analysis of diversity

Viewed in one way, the distinction between studying human behaviour in its ecological context and studying it in the laboratory has the character of an important difference in principle. Viewed another way, it is just a contingent divergence of research practice: a difference in the respective workbenches of the field workers and the lab workers. If it is an issue of principle, its significance is not the same for everybody. Jobling even found a certain incongruity in the raising of this question, at least as far as human evolutionary genetics was concerned. Perhaps in the end his position was similar to that of the molecular neurobiologist, Smith. In Smith's subject, it seems both natural and necessary to take into account the interaction between the organism and its environment, but it also seems natural and inevitable that the work of the molecular neurobiologist is done in a lab.

What about behavioural genetics? McGuffin was certainly open to a certain conception of the 'ecological' setting. We heard him explaining that much of his research had been

> looking at naturally occurring hazards, such as unpleasant life-events, and how they impinge upon people to make them depressed or not, and the extent to which those sort of naturally-occurring hazards interact, or co-act with genetic predisposition. (McGuffin 0.25.19)

In due course, in the discussion of Criterion 8 ('environmental markers'), we will find him also ready to take into account environmental measures that may be associated with psychological disorders, ranging from smoking in pregnancy to

> housing conditions, deprivation, living in an area where most people don't have a car. (McGuffin 0.34.00)

There is a similarity here with something that Smith said when, in the passage we have already quoted from, he spoke about

> experiments which put experimental animals in poor and rich environments - that is, stimulus environments – showing that this also as a strong effect on the development of the cortex.

As we saw, Smith commented:

> So all of these things show that the brain is very open - certainly in its early development - to environmental effects. These early periods are known as the critical or sensitive periods, and in experimental animals such as cats and so forth they last a few months, but in humans, I think, something like 18 months. And different parts of the brain of course have different lengths of these sensitive periods. (Smith 0.17.42)

This idea, that there are "sensitive periods" in the story of the brain's early development, during which the brain is "very open ... to environmental effects", is clearly one with important implications, not only for molecular neuroboiology, but also for behavioural genetics. However, it is another matter to be able to specify just what these implications are, and how they work themselves out in neurophysiological development.

In the book on behavioural genetics that McGuffin recently published with Plomin *et al*. (2008), we find the statement that

> The goal of behavioural genetics is to understand pathways between genes and behaviour at all levels of analysis.[156]

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[156] Plomin *et al*. (2008), Box 15.2, Endophenotypes, p. 296.

The context of that statement is a 'box' devoted to a discussion of "endophenotypes". To explore deeply the specific significance of endophenotypes for the investigation of psychological disorders would lead us too far into a digression at this point. However, it so happens that the exposition of the concept in the box in question is generic rather than specific. The argument goes as follows. The pathways between genes and behaviour can be studied at various different levels of analysis. The highest level is that of the behaviour itself. An example of a lower level could be the brain, or traits of the brain – say, "neurotransmitter levels in the brain". Plomin *et al*. observe that

> Levels of analysis lower than behaviour itself are sometimes called endophenotypes where *endo* means "inside". It has been suggested that these lower levels of analysis, such as the brain, might be more amenable to genetic analysis than behaviour [...].[157]

These authors argue:

> Although less complex than behavioural traits, brain traits are nonetheless very complex, and complex traits are generally influenced by many genes of small effect [...]. Indeed, the most basic level of analysis, gene expression, appears to be influenced by many genes of small effect, as well as by substantial environmental influence.[158]

It is indeed interesting, and worth pointing out that behavioural geneticists have good reason to strive "to understand pathways between genes and behaviour at all levels of analysis" and may well further this goal by studying what are here called "lower levels of analysis", including "brain traits" and "gene expression". However, behavioural geneticists will not be the only people interested in trying to get a better understanding of these phenomena. Just to take two examples, the research of molecular neurobiologists such as Smith, or specialists in human developmental genetics like Lindsay, could just as well be directed at the same targets, if not for precisely the same reasons or motives. Such

[157] Here Plomin et al. (2008) cite Bearden and Freimer (2006) and Gottesman and Gould (2003).
[158] Ibid.

researchers could well see merit in undertaking a genetic analysis of aspects of the brain without being particularly aware that they were thereby settling for a 'lower level of analysis' than some other target of enquiry deemed significant by behavioural genetics. These reflections reinforce our view that it was right to include in the present study disciplines such as molecular neurobiology and human developmental genetics even though they did not explicitly have 'behaviour' on their workbench. The march of knowledge towards the "pathways between genes and behaviour" will not take us across the territory of one discipline alone.

Assessment of the criterion

Criterion 2 permitted us to probe the reasons for which different research disciplines do or do not study human behaviour in its ecological setting, but work remains to be done on what the 'ecological setting' really means in the respective contexts.

A moment ago we cited Plomin *et al*. (2008) as saying that "the most basic level of analysis, gene expression, appears to be influenced by many genes of small effect, as well as by substantial environmental influence". This statement exemplifies a feature about the debate over 'heredity and environment' that is sometimes overlooked. Much attention has understandably been given to what can truly be said about the influence of heredity – understood as the influence of genes – and to precise ways of talking about this. Much attention has been given, for instance, to the concept of 'heritability' which, as we have already seen,[159] has been defined by Plomin et al. as "The proportion of phenotype differences among individuals that can be attributed to genetic differences in a particular population".[160] If this proportion is 1:1 – i.e., the maximum heritability score of 1 - then by definition there is no room left for the action of environmental factors. But heritability is almost never 1. So we could say – and this is the point that it is easy to overlook – that the concept of heritability 'expects' a proportion of environmental influence. Now the concept

[159] Chapter A4.
[160] Plomin *et al*. (2008), p. 416.

of heritability is not free from controversy,[161] and we cannot hope to clarify all the issues it raises here. However, it is perhaps useful to point out that, when the debate is about heredity and environment, and if (in given circumstances) the chosen measure of the hereditarian component is heritability, then this requires to be complemented by a robust measure of environmental influence. That robust measure, however, is unavailable if we are not already in possession of a robust concept of the 'environment' – and a clear conception of the ways in which the environment can act on the phenotype. If part of the story needs to be told in terms of environmental influence, there needs to be something like a taxonomy of environmental influences, or rather perhaps, a taxonomy of modes of environmental interaction. One could call this an 'environome'.

[161] See the discussion in Barnes and Dupré (2008), from p.144.

Chapter C4 – Is the focus on species-typical traits or on individual differences?

The matrix for the criterion

The responses to Criterion 3 yielded the matrix displayed below in Table C4.01. From the matrix it will be seen that, although the preponderant interest among the researchers was in species-typical traits, there were significant exceptions.

Table C4.01. Matrix for Criterion 3:
'*Is the focus on species-typical traits or on individual differences?*'

Researcher	*Discipline*	*Spec.-typ.*	*Indiv. diffs.*
Jones	Biomolecular archaeology	■	■
Hutchinson	Evolutionary biomechanics (dinosaur)	■	
Smith	Molecular neurobiology	■	
Buckley	Down Syndrome research	■	
Mace	Evolutionary anthropology		■
McGuffin	Research into normal and abnormal behaviour		■
Jobling	Human evolutionary genetics	■	■
Lindsay	Human developmental genetics	■	
Crompton	Evolutionary biomechanics (human)	■	

Salient interviews

Martin Jones

Martin Jones thought it was "right to say species-typical traits (Jones 0.16.11). He acknowledged that there could be exceptions, and that "there are some elements of biomolecular archaeology that have homed in on the individual", but thought that these could not really be said to "stand out as interesting new departures when unquestionably the general drift, the drive behind the research is more towards the traits rather than the individual".

Holdsworth pointed out that the question of what the 'species-typical' is could prove problematical in the following sense. If we were to discover by the methods of biomolecular archaeology that a small group of people in the Fertile Crescent were the first to domesticate goats or something, well they weren't species-typical. But they ushered in an activity that was broadly typical (Jones 0.17.15). Jones expressed the view that, "in terms of capturing the essence of the question, and what kind of answers we're looking for, both of those, at least in our aspirations, is on the broadly typical".

Jones commented that

> The broad trend within archaeology is that – like all these things - the whole discipline goes backwards and forwards, and when I started out in archaeology, in the seventies, for its interest with general traits, to break away from overly individualistic history, if you see what I mean (there's a lot of history narrated with a great interest in an individual), and archaeology is one of those for me [i.e., a discipline with an interest in general traits], so it means you get to large groups and to ordinary people and so forth (Jones 0.19.00). [...]
>
> And like all these things, I mean, there's been in some fields of archaeology an interest in 'agency', and 'agency' can mean different things. I mean, for some of the American archaeologists in particular, the idea of agency is focusing on the idea that

> individual, you know, individual – unique men and so forth – can actually appear. Agency means something rather different and more sort of 'given' over here, but in America there's a sort of style of agency. There's a certain interest at the moment amongst some of my contemporaries in notions of, you know, agency, free will and history as part of conscious, meaningful actions and so forth. (Jones 0.20.00)

Among authors on agency theory, Jones cited one of his Cambridge colleagues, the American John Robb, who had written a book on agency[162], and in America, Kent Flannery. Then there was a book by Dobres and Robb.[163]

Holdsworth recalled that there had been a period in archaeology, for instance at the time of Schliemann, when "people were amazed at the idea that they might be getting at the history of named individuals" (Jones 0.21.00), to which Jones responded:

> That's right. And I think, possibly, on the one hand you have various trends there. On the one hand, you have that kind of theory of the past which emphasises named individuals, often of some rather central, powerful status, and then you have - both in history and in archaeology - a reaction against that, and an attempt to write stories of ordinary people and the common man and so forth. [...]
>
> The, sort of, named individual is almost an obstacle rather than anything else. But then more recently you have ideas of agency which are not necessarily related to finding the elite and how they did everything, but, you know, finding the agency of other people and so forth.

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[162] See also John Robb: 'Steps to an archaeology of agency', Paper presented at the Agency Workshop, University College London, November 2001. Robb was at that time at the Department of Archaeology, University of Cambridge. For the text of the paper, see: http://www.arch.cam.ac.uk/~jer39/jer39-steps-to-archaeology-of-agency.html (Consulted 12 February 2008).

[163] Dobres and Robb (2000).

John Hutchinson

Hutchinson, the specialist in the evolutionary biomechanics of large animals such as dinosaurs, said

> Most of us would typically focus on the species, but where we can we look at individuals. It's pretty hard. Sometimes you just don't have the sample size to look between individuals, but in hominid research I think people have done. I've seen quite a few studies that have been pretty careful about individual variation, and that's like one of the disputes over these dwarf hominids in Flores: is this some sort of disease - individual variation - or does it represent them being a different species? (Hutchinson 0.22.43).

He added:

> In my kind of work individual variation is something to be checked for and factored out but not a major focus of work. Sometimes you just can't even cope with it, because if you get two individuals what can you say about individual variation?

Chris Smith

Faced with the question 'Is the focus on species-typical traits or individual differences?' Species-typical traits?' Smith's reaction was to say "Not sure what you mean".

Holdsworth offered an example.

> In research on intelligence, for example, people are usually looking for the reasons why some people are more intelligent than others. On the other hand, to go back to biomechanics, if your question is 'Why do human beings walk upright on two legs?', that's a 'species-typical' trait - arguably (Smith 0.55.25).

Smith: Yes. 'Is the *focus* on species-typical traits or individual differences?' I would probably go for individual differences, I think, in molecular neurobiology. Let me think. You see, there's a certain amount of – it's difficult to say, actually. Not a very good categorisation, I think, for our purposes (Smith 0.56.00). Holdsworth welcomed this criticism.

Smith said:

There's a lot of research done on *Aplysia*, which is an aquatic mollusc, and Nobel Prizes have been won. They're looking there at *Aplysia* as a model organism for understanding learning and memory, and that goes down to the molecular level.[164] There's a significant tranche of neurobiology - molecular neurobiology, if you wish - done on that organism. And the trait they're looking for is the withdrawal of the siphon beneath the mantle in response to a stimulus, and looking at conditioned reflexes. That conditioned reflex in *Aplysia* of course is species-typical. It's typical of that particular species, but you're looking – but you're using that species-typical phenomenon to do some molecular biology, trying to get down to how the molecules interact together to produce that conditioned reflex, with the hope of getting some insight into human memory and reflexes - conditioned reflexes. This is one of the things about molecular neurobiology: one looks for the model organism - the organism with which you can actually attack the problem most easily in. So you have a lot of organisms you can examine, but because the investigation is at a fundamental, molecular level, always with the hope of generalising the outcome to understand the human condition (Smith 0.58.24).

Holdsworth: But, for example, take what we discussed earlier about research into neuronal development. Surely, aren't you asking, 'How does this work in human beings?', rather than 'How does it work in Chris Smith?'

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[164] For concise accounts of relevant research on the sea slug *Aplysia californica*, see Clark, William R., and Grunstein, Michael (2000): Are we hardwired? – The role of genes in human behaviour, OUP, Oxford, 2000, pp.118-124, and Greenfield, Susan A. (1995), pp.78-80.

Smith accepted that argument:

> Oh well, that's absolutely true, yes. So in that case that's species-typical – *Homo sapiens*. But you might say, 'Well, why have *I* got such and such a condition?' – if I had some neuropathology, and you haven't, so there are individual differences, and you'd find in many cases that this is due to a particular molecular defect in my neurobiology compared with yours (Smith 0.59.16).

Holdsworth asked if Smith meant: "So it's individual with relation to pathologies?" Smith's reply was:

> Yes, and this is a source of very considerable interest. It was obscure, before molecular neurobiology came along. And this is one of the interesting things about the sea-urchin research which I mentioned to you before. In the sea-urchin, some of the genes there are the same as those which, on mutation, cause human deafnesses, for example, and blindnesses (the Usher syndromes) (Smith 1.00.02).
>
> *Holdsworth*: Really?
>
> *Smith*: Yes, it's that general. So, to answer that question – a bit of both, really, I think (Smith 1.00.28).

When the Criteria Graphic for the Smith interview came to be finalised, the choice went to 'species-typical'.

Sue Buckley

For Sue Buckley (Buckley 1.18.32),

> The focus is on 'species-typical' traits, I would say. Though not exclusively. But there's been much more of a focus on how do people with Down syndrome differ

> from people with the right number of chromosomes. I think definitely 'species-specific'.

It is also true that, in the interview, consideration was given to the issue of the case-study in Down syndrome research. These were studies of the developmental history of individuals. However, in terms of the answer by Buckley just reported, such case-studies might be taken as individual examples of generic phenomena. The purpose of an individual case-study is not only to disclose facts about the individual, but to instance the individual as evidencing characteristics of wider significance.

Another question is whether these characteristics of wider significance should be described as 'species-typical', when Down syndrome patients account for only a small proportion of people. For instance, in the United Kingdom, the incidence of Down syndrome has been put at around 1 in 1,000 live births.[165] One answer might be to use the expression 'population-typical', referring to the population of patients. However, this may not be necessary or even helpful if we acknowledge the need to bring out the fact that it is typical of the species to contain populations of patients – and not only Down syndrome patients at that.

Ruth Mace

Ruth Mace was at first inclined to say that the focus in behavioural ecology was on individual differences (Mace 0.54.40). When this answer was probed, she responded by saying:

> Yes. Well, it's actually on both. If you're interested in 'How did menopause evolve?', then obviously that's a species-typical trait, but you might approach it by asking, as we do when we are dealing with traditional populations with high mortality, are children with grandmothers more likely to survive than children

[165] 'Down syndrome - incidence and cause', article posted on the Downsed International website: http://www.downsed.org/our-work/down-syndrome/incidence/ (Consulted 26 March 2009).

> without grandmothers? OK, that might be the kind of analysis that you would do (Mace 0.55.14).

The argument here is about the evolution of a post-menopausal grandmotherly role that enabled the young children in a family to flourish. For Mace, this concerned the differences between individuals,

> because you're looking at variation in behaviour to see what works. Is there a fitness advantage to having a grandmother? You compare children who do have grandmothers and don't have grandmothers, and you see which ones are more likely to die (Mace 0.56.25).

Mace linked this example to the problems of method facing researchers doing human behavioural ecology.

> [T]he animal behavioural ecologists can obviously do experiments. They can experimentally manipulate things, which we can't do. So you have to look for, as it were, natural experiments. So that question about the grandmothers: if you use a natural population, you can actually look. You know, just by chance half of them will have grandmothers; half of them won't.

Mace referred to a second example.

> Or with the water pump. That was a natural experiment. Some villages had taps put in them; some villages didn't, and we could compare (Mace 0.57.08).

Holdsworth asked if her argument was that it didn't make sense in this case to say it's a species-typical trait to have a tap in your village: "You're examining precisely the differences between the situation where you do have the tap or you don't have a tap". Mace replied:

> Yes. We're getting data from individuals. So I'd say I think we do study individual variation. There's not much you can do by comparison across species, because there's only one species of humans. [There are] comparisons with other apes (Mace 0.58.02).

This brought Mace to her conclusion on this criterion:

> Yes. My research is on individual differences, because, you know, you're also looking at how people in one ecological setting might behave differently from people in another ecological setting. So, you know, whereas an evolutionary psychologist might be interested in a mental module as a human universal, a behavioural ecologist is kind of interested in positing why some people are doing something different than others (Mace 0.59.08).

Peter McGuffin

When the question was put to Peter McGuffin, he replied:

> Yes, my own research is very much on individual differences. (McGuffin 0.25.40)

Holdsworth questioned whether this had to be true for all research into the genetics of behaviour. He referred to the Genes to Cognition programme (G2C), [166] and to the chapter by Grant about the programme in the book that McGuffin had co-edited on *Behavioural genetics in the post-genomic era*.[167] Holdsworth's question was

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[166] 'Genes to Cognition' (G2C) is "a neuroscience research programme that studies genes, the brain and behaviour in an integrated manner, established to elucidate the molecular mechanisms of learning and memory, and shed light on the pathogenesis of disorders of cognition": http://www.genes2cognition.org/ (Consulted 26 March 2009).

[167] Plomin, Robert *et al*. (2003), pp. 123-138, Chapter 8 by Grant, Seth G.N.: 'An integrative neuroscience program linking mouse genes to cognition and disease'.

> whether there was a distinction there, and that type of research is really looking at the genetic – if you like - infrastructure of everybody. (McGuffin 0.26.29)

To this McGuffin replied:

> I suppose it is, yes. But the only research I've personally been involved with that's to do with cognition *has* been to do with individual differences: so, for example, a study with Robert Plomin on ways of looking at what genetic differences there may be between individuals who are one extreme on the distribution of IQ with individuals who are slap-bang in the middle range or sometimes individuals who are at the low end. So that's an example of where the individual difference approach is (McGuffin 0.27.06).

Narrowing the focus, Holdsworth made the point that there was a great deal of research effort going into individual differences in IQ – or 'g', as it is often called. A question on this brought the following exchange:

> What about research into intelligence as something that the whole species has? (McGuffin 0.27.34).
>
> *McGuffin*: It would require a different type of experiment! [...]
>
> *Holdsworth*: [...] But can you think of any research discipline that's doing it?
>
> *McGuffin*: Well, yes, there are – there are geneticists who are interested in differences between genomes, and quite a lot of bioinformatics experts who are interested in differences between genomes, and you could argue that that's how you might find the genes – quote – 'for' speech and human-style cognition. By comparing humans with –
>
> *Holdsworth*: Chimpanzees.

McGuffin: Yes, chimpanzees (McGuffin 0.28.20).

McGuffin did not suggest any specific literature on "differences between genomes", as it was not his field. After the interview Holdsworth located a survey article by Morley and Montgomery that argues for the potential importance of animal models in the study of human cognition, concentrating on mouse and *Drosophila melanogaster*.[168]

The issue of whether researchers were more interested in the species-typical than in individual differences arose spontaneously in a different part of the interview, when Holdsworth opened the issue of the relationship between behavioural genetics and cognitive science (McGuffin 0.43.15). He cited a paper by de Geus *et al*. (2001), which had been published as an editorial in a special issue of *Behavior Genetics* in 2001 devoted to the genetics of cognition. The editorial expressed the view that

> As yet an unfortunate gap exists between behavior genetics and cognitive neuroscience. Behavior genetics, through its sophisticated statistical modelling in twin and family studies, focuses mainly on individual differences in cognitive ability. Cognitive neuroscience tends to focus on species universals in specific cognitive operations, isolated by clever experimental design, and located in the time and (brain)space by modern imaging techniques. Both parties could gain from a complementary approach.[169]

Holdsworth referred to this view that there ought to be, but at the time there was not more interaction between the discipline of behavioural genetics and cognitive neuroscience, and asked McGuffin if this was a fair comment? He replied:

> I suppose it is. The trouble is that what we need in genetics a lot of the time is accurate and repeatable information on a very large number of subjects, and the

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[168] Morley and Montgomery (2001). This article was published in a special issue of *Behavior Genetics* on the genetics of cognition.

[169] de Geus, et al. (2001), p. 493.

> sorts of things that turn on cognitive neuroscience experts are doing small, precise studies on, you know, groups of individuals (McGuffin 0.44.25). [...]
>
> And very often cognitive neuroscientists are more interested in species-typical behaviours rather than individual differences.

McGuffin gave an example of an existing point of contact between behavioural genetics and cognitive science:

> I mean, we have people who work in the MRC SGDP[170] Centre who are normally speaking – could be classed as cognitive neuroscientists - people like Francesca Happé.[171] Now, she's interested in individual differences in traits that may be associated with the autism spectrum. Her work is involved in putting forward theories such as 'weak central coherence'.[172] 'Weak central coherence', I understand, is when individuals are very good at having an eye for detail, and attention for detail, but aren't particularly good at seeing the overall big picture, which is said to characterise people within the autism spectrum, because often they're very, very good at, you know, proof-reading, for example, but not very good at extracting the overall meaning of the paragraph that they've just proof-read. You can treat that as a quantitative trait. And you could do twin-studies on it, as she and Robert Plomin are doing.[173] Or map the genes, if you're confident that that place is helpful (McGuffin 0.46.29).

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[170] Social, Genetic and Developmental Psychiatry Centre.
[171] Dr Francesca G. Happé, Reader in Cognitive Neuroscience.
[172] Booth *et al*. (2003).
[173] See, for instance, Happé *et al*. (2006), and Ronald *et al*. (2006).

Mark Jobling

Holdsworth put the question about species-typical traits and individual differences to Mark Jobling, asking him if the question made sense in the context of human evolutionary genetics (Jobling 0.22.51). Jobling replied positively, and this led into the following exchange:

> It does make sense, and I would say definitely both. Because we are both interested in what makes humans different from, for example, chimpanzees, and we are very much interested in what makes one human or one human population different in some respects from others (Jobling 0.23.10).
>
> *Holdsworth*: And what makes one individual different.
>
> *Jobling*: What makes one individual different.
>
> *Holdsworth*: That's species, population and individual. (Jobling 0.23.23)
>
> *Jobling*: Yes.

Holdsworth asked Jobling if he found it "comfortable to deal with the idea of 'species-typical' traits". He answered, "Yes, I think so". Asked to think of examples of human species-typical traits, Jobling suggested "capacity for a complex language" (Jobling 0.24.03). He agreed that bipedal locomotion could be another example, although birds also did that. It depended "how tightly you want to draw your kind of region of comparison", but there were "quite a lot of things".

As another perspective on the species-typical, Holdsworth sought clarification on two expressions that Jobling had used in the interview: 'anatomically modern humans' and 'behaviourally modern humans'. Were these the same thing? Jobling replied (Jobling 0.25.03):

> No, not at all. And, I mean, it's, again, not a subject for geneticists, in a sense. It's a subject for palaeontologists. Because it's clear that you see evidence of anatomical modernity earlier than you see evidence of behavioural modernity. And behavioural modernity is associated with things like burial practices, making tools, certain things like the use of ochre in graves, the production of sort of art, and evidence of certain kinds of living, in the past. So you have anatomical modernity and then later on you see these things cropping up, and the problem always of course is one of dating these things and also the survival of the evidence. With human fossils and evidence of past human behaviour the evidence is extremely scarce. There just isn't very much of it. And so it's very much influenced by individual finds. Many of those are very controversial, because people disagree about what some of those things are. So there does appear to be a time-difference between being anatomically modern and behaviourally modern. But how real that is, I'm not entirely sure. I think it could be to an extent artefactual, based on dating problems and just general scarcity of evidence. But I'm not an expert on that. (Jobling 0.26.36)

Susan Lindsay

For Susan Lindsay, the focus of human developmental genetics was clear: "It would be species-typical" (Lindsay 0.47.23). She explained:

> So if we were then taking information from another stage in development in human life-span or from other animals we would go looking for something that's generally true in humans (Lindsay 0.47.46). [...]
>
> There may well be differences – individual to individual, or embryo to embryo - but we wouldn't have sufficient numbers there to be able to pull those out (Lindsay 0.48.00).

Robin Crompton

Robin Crompton was also clear about the focus of evolutionary biomechanics (Crompton 0.15.02):

> Species-typical, I'm sure. Largely. Yes (Crompton 0.16.07).

Analysis of diversity

The responses of the researchers illustrated a real difference in practice between disciplines in which there was a focus on the species-typical and those where the emphasis was placed on individual differences. However, the starkness of the focus varied somewhat from case to case. If we look at the two researchers who went for individual differences – Mace and McGuffin – it was McGuffin who gave his 'individualistic' research orientation the sharper profile. One recalls that McGuffin had earlier identified himself as "a researcher in normal and abnormal behaviour" with, as a psychiatrist, a special interest in abnormal behaviour (McGuffin 0.04.30). A researcher could live up to that self-description and still be interested in species-typical behaviour. It was noteworthy that the question about the idea of research that saw intelligence as "something that the whole species has" did not evoke a particularly positive response from McGuffin.

Where Mace was concerned, one might wonder whether the topic was rather 'individual circumstances' than 'individual differences', with the attendant question of what difference this might make. In fact, it is fair to point out that 'individual differences' may come in different epistemic shapes and sizes. We attempt to illustrate this by listing examples in Table C4.02 below.

Table C4.02. Denotations of 'individual differences'	
Denotation of 'individual differences'	*Example discussed in interview, if any*
Pathology	Flores controversy (Hutchinson)
	Neuropathies (Smith)
	Autism spectrum (McGuffin)
Human personality differences	
Human intelligence differences	'g': general cognitive ability
Situational differences	Children with or without grandmothers (Mace)
	Populations with or without water taps (Mace)

The discussion with the archaeologist, Martin Jones, was interesting. Jones saw a reaction in history and archaeology against "that kind of theory of the past which emphasises named individuals, often of some rather central, powerful status" towards "an attempt to write stories of ordinary people and the common man and so forth". Certainly one can recall cases in archaeology where the object of study has been a named individual with "central, powerful status". One thinks of Egyptian pharaohs, for example. To the non-specialist, and indeed to many specialists no doubt, the interest in figures like Tutankhamen has seemed paradigmatic of archaeology, or a certain tendency within it. The idea that archaeology may recently have been moving its focus onto the 'species-typical' is suggestive.

Jobling came up with an actual instance of a human, species-typical trait, in the "capacity for a complex language". It was refreshing to deal with a clear example. Jobling's answers also added a dimension to the subject, moving it away from the stark choice between 'individual' and 'species' by bringing in the level of the population as well.

Assessment of the criterion

The expression 'individual differences' was used by Darwin in the *Origin* and other works. The subject claims a section of its own early in Chapter II, 'Variation under nature'.[174] Darwin wrote:

[174] Darwin (1928), pp. 51-53.

> No one supposes that all the individuals of the same species are cast in the same actual mould. These individual differences are of the highest importance for us, for they are often inherited, as must be familiar to everyone; and they thus afford materials for natural selection to act on and accumulate, in the same manner as man accumulates in any given direction individual differences in his domesticated productions.[175]

In emphasising the significance of individual differences under natural selection, Darwin was counteracting what he saw as an erroneous tendency, in his day, to overlook variability that happened to be inconvenient to classificatory schemes. He wrote:

> It should be remembered that systematists are far from being pleased at finding variability in important characters, and that there are not many men who will laboriously examine internal and important organs, and compare them in many specimens of the same species.[176]

However, at the present day science has developed molecular methods that have influenced the orientation of research. As Barnes and Dupré (2008) have put it:

> The methods and techniques now available to molecular geneticists allow them to study DNA in the laboratory as one ingredient in the functioning and regulation of cellular chemical processes, with the aim not primarily of explaining differences but of throwing light on the "normal" functioning of cells and organisms.[177]

This shift provides a good reason for using the distinction between 'species-typical' and 'individual differences' as a criterion here. At the same time, the application of this criterion in its uninflected binary form is not without problems. We saw Jobling's

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[175] Ibid., p.51.
[176] Ibid., pp. 51-52.
[177] Barnes and Dupré (2008), p. 8.

introduction of a third factor, the population. We also saw that the goal of studying individual differences can be further broken down into sub-divisions of that concept.

It was not always clear how to apply the criterion even in its basic, binary form. This provoked criticism from Smith that this was "Not a very good categorisation, I think, for our purposes (Smith 0.56.00)." On the other hand, Jobling expressed himself as comfortable with the idea of the species-typical. On balance, the conclusion is probably that this criterion served its purpose as a conceptual probe, helping the enquiry to dig out the diversity in the respective positions.

Chapter C5 – Does the research typically draw on the findings of genomics?

The matrix for the criterion

The responses to Criterion 4 yielded the matrix displayed below in Table C5.01.

Table C5.01. Matrix for Criterion 4:
'*Does the research typically draw on the findings of genomics?*'

Researcher	*Discipline*	*Yes*	*No*
Jones	Biomolecular archaeology		
Hutchinson	Evolutionary biomechanics (dinosaur)		
Smith	Molecular neurobiology		
Buckley	Down Syndrome research		
Mace	Evolutionary anthropology		
McGuffin	Research into normal and abnormal behaviour		
Jobling	Human evolutionary genetics		
Lindsay	Human developmental genetics		
Crompton	Evolutionary biomechanics (human)		

Salient interviews

In setting the objectives of the present study on disciplines within the field of behavioural genomics it was assumed, not that the target disciplines all drew directly on the findings of genomics, but that they should stand in some relation to genomics that it would prove fruitful to characterise. A number of the researchers interviewed readily answered 'Yes' to this question (Jones 0.22.20, Smith 1.00.30, McGuffin 0.28.35, Jobling 0.31.38 and Lindsay 0.48.34). However, Jones and Jobling had observations to add to this answer, while the replies of Buckley and Crompton were nuanced in different ways, and those of

Hutchinson and Mace were mainly negative. We shall assume that the positions of Smith, McGuffin and Lindsay call for no amplification here and pass to a brief consideration of the supplemented, nuanced or negative responses.

Martin Jones

Having agreed that his research in biomolecular archaeology typically drew on the findings of genomics, Martin Jones was quick to make the following clarification:

> I think, one thing actually is that - to elaborate on that - that they don't just *draw on* the findings: their actual practice is rather steered by the progress of genomics. And the reason for that is – it will vary on your list,[178] but on our list, in our departments, the sums of money, the volume of research are such that we have to be responsive to fields with more money. So, for example, on the anthropological front, it's inevitable that we will respond to what medical research is doing, even if it has different objectives. And in looking for the spread of agriculture, it's inevitable we respond to what genetic breeding and genetic modification is doing, simply because the scale of activity in those fields is just something that we kind of hang onto by the skirt-tails. And a new departure in either of those fields, that may have nothing to do with the human past, will nevertheless have an impact on even the questions we're asking because there are new questions we can ask (Jones 0.24.03).

The idea that the progress of genomics is not just something that biomolecular archaeology draws on, but rather may be seen as a steering force, is worth probing. Holdsworth asked if Jones could mention a specific example.

> Yes, I can. If we go, say, to the origins and spread of agriculture - some projects that I'm involved with - you have a sequence there of activity that, as you rightly perceived, in order to build the family tree and tell the story, we work heavily on

[178] I.e., among the different research disciplines under study here.

non-coding regions, and so with plants in particular we find some non-coding regions at the edge of some genes people are studying. But within something like barley breeding there's, well, as you can imagine, tremendous interest in genes that will affect how much – produce, or - ?

Holdsworth: Yield (Jones 0.25.11).

Yield. Exactly! Or something like that. So, they would explore particular genes that will prompt us to ask questions about how those genes worked in the past. And as I said, the gene is chosen for entirely different reasons, because there's money in it. And so, if - There's, for example, barley, and its field that spreads furthest north, and in the spread of agriculture barley comes into the Arctic Circle, and to do that it has to switch a gene off. That gene's job is to tell it what season it is. Basically, when the gene is switched on, it just tells the plant to do nothing and hibernate, because it's cold and horrible. So you've got to switch that one off. And so there are some very interesting questions to ask about the spread of agriculture north, which is prompted by research into a gene that was chosen in order that barley farmers or brewers or whatever could follow their objectives. The same with medicine. I mean, we're obviously moving into a field now where because the genomics is done the proteomics are being done, and so there's going to be more and more work on how genes - how DNA sequences become genes and become proteins, and the particular sequences that are studied will be driven by pressing medical questions, pressing food questions and we'll find ourselves hovering around the edges asking what we can learn from that (Jones 0.27.02).

Holdsworth asked for an example in the medical context. Jones said

Yes, exactly, I can think of a very good example there. I mean, various forms of disease susceptibility in the system is something there's great interest in lactose intolerance and coeliac disorders, which you know are obviously an issue of whether you can digest milk or flour. 'Coeliac' disorders. It's a problem with

gluten. And so those are ones that are researched because they're medical or dietary issues (Jones 0.28.05).

Holdsworth asked, "But how does archaeology come into that?", to which Jones replied:

> Well, both the ability to drink milk or the ability to eat grass-seeds is tied up ecologically with agriculture. I mean, the reason we have problems with both is probably that, you know, palaeolithic hunter-gatherers – there was more meat in their diet. On a time-scale that we're still trying to work out, both - you know, ground-up grass-seeds, i.e. cereals, and milk of other animals - is something that we've only had for a short period of evolutionary history. So, in a sense it's not surprising that there are genotypes that have trouble digesting it. Whereas you wouldn't find human genotypes having that much trouble digesting meat, because there's a long idea of what meat is. So the history of resistance or tolerance of it can be explored in order to understand the history of cattle domestication or cereal domestication (Jones 0.29.16).

Holdsworth asked whether, for the archaeological enquiry into that subject, Jones was looking both at genes and at non-coding regions.

> Yes, and also other forms of information like just cattle bones in the archaeological record. And so you hit it from a variety of angles. What you get from the modern genetic information is - if you're lucky - a distribution map that will show you tolerance of milk is much stronger in North Europe and much weaker in East Asia and – well, obviously, lots of variations. So you get a modern genetic map, and then you can use, kind of, phylogenetic methods to build a family tree of those genes and then try and relate it to time and space. And, as you say, for that you're using non-coding material. And then there are the archaeological records, and sites with animal bones in, and sites with lots of mature female cows in, that suggest there might have been milking, and so on and so forth. So those would be two examples. I mean, again if there were money too, I mean, if there was a surge of research in alcohol dehydrogenase, that too would be something that one could explore,

> because the history of alcohol is something quite interesting in terms of archaeology.
>
> *Holdsworth*: But that hasn't happened yet?
>
> *Jones*: There hasn't really been a study on it. I mean, that's - if you like - a sort of study waiting to happen, you know, because alcohol-related genes probably themselves preserve, you know, a good deal of historical information about how old alcohol consumption is within our species (Jones 0.31.08).

John Hutchinson

In the interview with the evolutionary biomechanist John Hutchinson, who specialises in large animals, there were two opportunities to discuss this question. When he was asked (Hutchinson 0.10.26) whether, in the research that he had been doing, he drew greatly on genetic or genomic research, he replied:

> I would say I pay attention to it, kind of because it's interesting. I'm an evolutionary biologist kind of first and foremost. I'm interested in evolution and in the past. The revolution in genomics is absolutely important. But for a lot of the groups I work on in the lab their members are extinct, so there's no genomic information, and there may never be. So what genomics has to offer varies for people, but for the questions I want to ask there's just nothing there. But in terms of broad relationships of animals it's useful to a point – and important – but so far there's no way to connect, like, genomics research and factors related to locomotion. You see, in my work it's just too much of a leap, but yes, there are connections there, but I haven't ever explored them (Hutchinson 0.11.50).

Holdsworth asked Hutchinson if the recent developments in the accessibility of ancient DNA had not greatly helped in his line of work (Hutchinson 0.11.57).

> No, I mean, I think it's a limitation of the method that getting DNA after a couple of thousand, or a couple of hundred thousand years, is pretty much impossible. So, you just can't reach that far in the past. I mean, you're talking about lineages that were around 230 and at least 65 million years ago – far beyond the reach – far beyond the limit of preservation of biomolecules. Almost nothing is left. Occasionally you find little bits of keratin, or other durable proteins that are still relatively intact, but as far as DNA, you don't even find a base-pair yet that is usable. There is no dinosauric DNA. There is no extinct elephant DNA. Very recent mammoths - for mammoth researchers it's been useful, actually. People have learned a bit about the evolution of mammoths and modern elephants to draw a very closely related group of species, and for those animals there is ancient DNA. There is ancient mammoth and maybe a little bit of mastodon DNA, so that stuff is useful. And there's very controversial evidence of dwarf elephant DNA that's recently come out. That's some of the oldest DNA on record: 800,000 years old, if it truly is DNA. So that's interesting (Hutchinson 0.13.28).

Holdsworth: And the kind of time-scale that you're often working with?

> As old as 230 million years. That would be the older stuff I might be working on. That's way, way, way beyond - . But genomics still deals with major phylogenetic relationships of groups, and that's something I use a lot of. I need to know phylogenetic relationships of major lineages, and that includes living animals. So there's been a lot of research done on using genomes of crocodiles and birds and lizards to see how they're related to each other. And I draw on that research because it forms the evolutionary framework behind my work (Hutchinson 0.14.23). [...]
>
> But then filling in the picture takes information from outside genomics. It takes morphological evidence (Hutchinson 0.15.00).

Specifically on Criterion 4 - 'Does the research typically draw on the findings of genomics?' – Hutchinson's answer was:

> [W]here it's most relevant is in determining the relationships of major groups of animals and that's - [...] Yes, phylogenetic relationships (Hutchinson 0.24.00).

Sue Buckley

We have already seen that, for Sue Buckley, the situation in Down syndrome research is complicated by the existence of two main tendencies in the research, which may be broadly termed the genetic – "you have some very high profile people across genetics and molecular biology, biochemistry" (Buckley 0.19.00) - and the psychological. The focus of her own research lies within the latter. The former she sometimes referred to as "the basic science side". Buckley's interview was interesting for the number of question marks it put against the assumption that genomic research is the natural motor for progress in the understanding of Down syndrome and its effects. For example, Buckley argued as follows:

> On the - I mean what we call the basic science side of the fence, the people [are] looking at what does a gene on chromosome 21 code for, and then looking also at the - they've got ideas about which the genes might be that are causing some of the effects (Buckley 0.26.31).

> They are trying to also take account of what we see as the developmental phenotype, what sort of behavioural changes there are, developmental changes, [...], to try and inform where they're looking for markers. Two kinds of issues around that. I'm sure you don't want to expand your interview, but of course there's a lot of excitement about epigenetics [179] (Buckley 0.26.59).

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[179] See Cavalli, Giacomo (2006). The paper reviews the meeting on 'Epigenetics and Chromatin Remodeling in Development' organised by Renato Paro and Peter Fraser at Keystone (CO, USA) on 19-23 January 2006. Conference programme: http://www.keystonesymposia.org/Meetings/viewPastMeetings.cfm?MeetingID=784&CFID=2571555&CFTOKEN=74494846 (Consulted 18 September 2008). The website of the Human Epigenome Project is at: http://www.epigenome.org/index.php . It cites, among others: Novik *et al*. (2002). See also: Holliday (2006) and Kiefer (2007).

> And the fact that gene action will not be an automatic sort of read-out activity (Buckley 0.27.06).
>
> Genes can be turned on or off or they can be modified. So, if you like, there's the basic scientists, and then there are people into developmental research, whether that's psychologists, educators, therapists and so on. And the cognitive neuroscientists would be on the psychology side of the fence usually, looking at - , understanding in quite detailed ways, the way brain function is reflected in the skills we've actually got, what tasks you can learn and so on (Buckley 0.27.37).

Buckley, then, was weaving quite a complex picture, bringing together diverse threads such as genetics, epigenetics, developmental psychology and cognitive neuroscience. She made the point that all of these contributing branches of knowledge had their role to play:

> One of the anxieties people have is that - people on the psychological, developmental side of the fence - that the geneticists don't understand that development is development: that we change over time (Buckley 0.27.52).
>
> There may be issues about epigenetics, but whatever coding is going on early on, most of the things that we see any child develop are learned by observed social interaction with people. It doesn't matter what their genes set them up to do, if you shut them up in a room on their own they won't develop (Buckley 0:28 10).
>
> Human development isn't fixed at birth, and it's not like watering a bulb. Food and water is not enough to make it grow. Learning to talk, learning to move, learning to socially interact, smile, understand social interaction, everything that goes on from day one assumes interaction with warm, loving and socially competent people around you (Buckley 0.28.34).
>
> You're not going to learn to talk if people don't talk to you. So one of the things that I think is problematic is that the people on the basic science side of the fence frequently don't seem to know anything about development (Buckley 0.28.48). [...]

> There's far more plasticity around brain development. But brain development is driven by activity after birth. And so their models are too simple for what they're looking for (Buckley 0.29.00).

Buckley mentioned, as an example of a British psychologist who had worked with trisomy children, and who had "talked about the difficulties of the basic scientists understanding development", Annette Karmiloff-Smith[180] (Buckley 0.31.30).

Buckley stated that her own organisation was planning to host a meeting for researchers from different approaches. She said "we're going to hold a seminar in October to bring these two camps together" (Buckley 0.29.06). Holdsworth asked what she thought were the prospects for getting the two sides to talk. Buckley replied:

> Not sure, but we've had excited, positive responses from people on both sides of the fence. We're going to bring Bill Mobley, who's the leader of the research team at Stanford, here. William Mobley. [...] He leads the group at Stanford doing the Down syndrome research, and I happened to be in Denver last week and met up with him (Buckley 0.31.03).

Holdsworth asked how many people would be involved. Buckley said:

> Probably about forty. Partly because, although we could restrict it to a smaller number of key people we would invite to prepare papers and circulate in advance and so on, because the aim is to set the agenda for research for the next ten years. So that we could deliver short-term gains for people, mid-term gains, research that's going to have outcomes that will improve things for people in the next five to ten years (Buckley 0.32.36).

[180] An example of Karmiloff-Smith's recent writing on 'atypical development' is: Karmiloff-Smith (2007).

> Because that's our mission here. We focus on research that's likely to have an impact and to change things in the near term for people (Buckley 0.32.50).

Buckley was critical of what she saw as over-optimistic claims by the basic science side. She made two points emphasising the extreme complexity of the tasks in hand. Her first point related to the relation between genotype and phenotype in the Down syndrome case:

> But we want to bring people from both sides together because some of the leading people are writing about the genotype, because they're on that side. But talk about the phenotype turns around alterations to the skeleton. They've got a slightly different shaped head, motor skills in learning, heart defects - the sort of structural, physical defects that are there from birth, that are fixed - right? (Buckley 0.29.58). [...].
>
> Researchers on the basic science side acknowledge that learning and memory and language are issues, but are not quite ready to deal with that directly. And, of course, if you start to look at the genetics of anything to do with learning to talk, learning to read, and so on, you're talking about complex interactions of genes across all the chromosomes (Buckley 0.30.21).

In other words, once you look deeply into the developmental issues the problem can be seen to go much wider than chromosome 21 alone. The second point was the sheer complexity of the genes on chromosome 21 itself, where "You have got some 300 genes on Chromosome 21 that are being triplicated" (Buckley 0.37.0).

Against this background, Buckley was sceptical about some claims attributed to the geneticists: "And these people have on their website that there's going to be cures and treatment [...]" She said she had read a claim that researchers "had effectively returned the learning capacity of a trisomic mouse to normal with a particular drug" (Buckley 0.34.55)[181].

[181] No source cited.

Holdsworth asked if the issue here was gene therapy rather than drugs. Buckley replied:

> No. This is looking at synapse function and learning. But of course that's the end-point, OK? Gene therapy is not just about switching genes off, it's knowing what they code for (Buckley 0:35:10).

> So these people are suggesting quite clearly on their website there will be treatments within five to ten years. And we don't believe it. I mean, we just don't believe it (Buckley 0:35:57).

Buckley affirmed that

> there is no doubt that the people doing the genetics and, as I say, molecular biology stuff imply – they talk about little bits of stuff that they've looked at and imply it's going to be easy to reverse the effects of this gene, I suppose (Buckley 0:36:32).

Buckley instanced work by Mobley's team at Stanford on synapse action and said:

> It might be possible to improve synapse action with some sort of therapeutic medication, drugs. But still many people would say 'not very widely'. And, of course, if you look at genetic conditions from single genes - [...], cystic fibrosis, muscular dystrophy, people have known about the genes for anything between ten and twenty years for those conditions, and we're still without the treatment (Buckley 0.37.46).

Buckley went on to say that she would like to issue a challenge to some of the genetic researchers:

> to see if they can come up with anything in ten years' time. All right? They're studying mice. And the claim that that's going to transfer quickly - . Now, for a number of years, people have been able to collect – create mouse models that have

some of the mouse analogue of what's on human chromosome 21, and it's chromosome 16 in mice (Buckley 0.40.39).

Now, there are several versions of trisomic mice, and there's a woman in London, whose name I've forgotten, who last year was in the press because she had managed to implant some of human chromosome 21 into mice. So not just triplicating their own chromosome -16 - but implanting some of human chromosome 21[182] (Buckley 0.40.58).

And again, people have got very excited, and there's appeals out to help fund the mice. If you read it, first of all most of these mice died. It's extremely difficult to create these mice and have them live. And they're mosaics. They're what we call 'mosaics' (Buckley 0.41.18).

Now, most children with Down syndrome are straight-forward trisomies. Over 95 per cent have three copies of chromosome 21 (Buckley 0.41.30). [...]

Over 95 per cent of children diagnosed with Down syndrome have the straight-forward trisomy. They've got an extra copy of 21. A small group are mosaic (Buckley 0.41.43).

The physical person with Down syndrome has an extra copy of the chromosome in every cell in their body. It was there at the point of conception, and it's been there ever since. It's most commonly in the egg cell. It can arise in the sperm, but that's unusual. It's in the egg cell, and it's in every cell in the body thereafter (Buckley 0.42.08).

But there are some children that are mosaic, which simply means they don't have it in every cell. So something happens after the first cell division. They have some normal cell lines and some trisomic cell lines (Buckley 0:42:20).

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[182] O'Doherty *et al*. (2005).

> And they are typically less affected, but not always. Now this mouse which has been created in London is mosaic. You try to implant human chromosome it doesn't get to all cells. So: interesting, but we're not sure how interesting (Buckley 0:42:43).

Buckley's conclusion was clear:

> OK. Because I think the – the magic bullet appeal – of understanding the genetics is pulling all the money in that direction (Buckley 0.44.24).
>
> Whereas we think all the big gains for folks with Down Syndrome come from good healthcare, understanding more about why they find it difficult to learn to talk, etc. (Buckley 0.44.37).

Ruth Mace

When asked 'Does the research typically draw on the findings of genomics?', Mace's answer was

> I would say no. [...]. I'm not saying that we're not completely uninfluenced by genetic research. It's interesting to know about, but I wouldn't say that we need to - I mean, Darwin didn't even know about genes (Mace 0.59.52).

What Mace was getting at was that cultural evolution and cultural phylogeny may be studied without direct reference to the findings of genomics. Human behavioural ecology has a certain indirect relationship with aspects of genomics to the extent that cultural phylogenies can be related, positively or negatively, with anthropological phylogenetic trees.

Mace brought up a second point, however, that did touch on the prospects for the direct use of genomic data by human behavioural ecology:

The other thing that's going on, as I'm sure you're aware, is this. Actually, I'll backtrack slightly. If you're interested in the mating system of some group or other, which is the kind of thing anthropologists and behavioural ecologists are interested in, obviously if we could get everyone's DNA, we would learn an awful lot about their mating system. We would learn, how monogamous are people, how polygynous are they? You know, who wins? Do children tend to be all from the same father, or do they tend to be actually all from different fathers, or [what]? (Mace 1.01.39).

And, of course, the ethical hurdles of doing that kind of research are practically insurmountable. So we would love to have DNA, but basically you're hanging yourself if you say you're going to do something like that. It's got worse and worse, and you're getting these ethics panels. It's becoming - . I just had a huge grant come down for no reason whatsoever, because I wanted to ask women about their contraceptive history. It's just not something that I've ever had any problem with before. But, you know, ethics panels are esoteric. And if someone on the panel – you know, they have lay members on them - and if someone thought it's not really acceptable to ask Ethiopian women about their contraceptive history there's not much you can do about it. So that was a bit weird. But, you know, people have tried to work out how much paternity uncertainty there is, and things like that. So we could use DNA data to help answer certain questions. On the whole we don't, because that data isn't –. I mean, I think it's crazy. So, for example, it would be possible to take a British sample, and say, OK, the proportion of UK children fathered outside wedlock is *x* (Mace 1.03.08). [...]

Obviously, you have to scrupulously maintain the anonymity of any sample that you use, but at the population level, I don't think that's a controversial question, to be honest. But I think this must be part of your work. In a way, you know, the ethical climate round anything to do with DNA has gone completely bonkers. I mean, in parts of the world it's basically closed down any kind of anthropological genetic research work whatsoever (Mace 1.03.54).

So, there are things I would love to know. Like we've done this long-term study in The Gambia; we've done this long-term study in Ethiopia, and I would love to have everyone's DNA and be able to say who's actually related to who. And it would tell me an awful lot about the social system and the mating system and everything else, and everyone's reproductive success, but because I'm dealing with humans I can't do that.

But if you wanted to use it to ask anthropological questions about mating systems and all this sort of stuff, and paternity - . I mean, bird behavioural ecologists use it all the time. They collect DNA from chicks, and they say 'Oh, right, in this pair extra-pair copulation's going on here, and actually the female mated partially with her mate, but she's also got two from the next door, you know, great tits or whatever it is what they're studying,[183] and they've done tons of studies like that which have told us about mating systems or, you know, polyandrous dunnocks[184] tend to have two partners and one of them is more genetically successful than the other. Now, we can ask people in surveys – you get data all the time about who are your children, blah, blah, blah. But you wouldn't be allowed, I think. I mean, I don't know (Mace 1.05.53). [...]

But it would be a useful tool, if we could use it. Just because the animal behavioural ecologists have made extensive use of genetics. I mean someone's doing it: some of the evolutionary economists now. You can still do it in behavioural genetics, obviously. And some of the evolutionary economists are now interested in different genes that give you different responses in economic games. But in an anthropological context I just don't think you would ever get – at the moment – you would not get permission to do this. So people don't, and it isn't because they don't want to know. It's because they don't want a stink. An ethics committee sank a huge three-year grant that I should have got. And I wasn't doing anything that was remotely controversial except, you know, DNA! For some reason, DNA was very,

[183] For instance, see: Norris and Blakey (2008).
[184] For instance, see: Burke, Davies, Bruford and Hatchwell (1989).

very controversial. And you could imagine that if your anonymity was not respected - (Mace 1.07.19).

[I]f you could do paternity testing, for some questions in human behavioural ecology that would be very interesting, but because it's personal information that they're very unlikely to get, I'm not aware of anyone using that kind of information.

Mark Jobling

Mark Jobling's answer to the question, 'Does the research typically draw on the findings of genomics?', was forthright and positive (Jobling 0.31.38):

Yes. Much more so now than it did in the past, but very much so now, yes.

In expanding on this, Jobling emphasised the progress in the technology:

Well, I think that, in the past, studies of DNA – the parts you need for human evolutionary genetics - were very much small-scale studies, because of the technology. So we would tend to study a very small bit of the genome – one that was of interest for some reason or another, and what's happened since that time is that pretty much the whole genome has been sequenced, and so now we have the raw material there to discover variation across the entire genome rather than in a little bit of it, and to sort of explore hypotheses about patterns of variation of one piece of DNA compared to the other, for example. So it's now, you know, possible to do that on a very large scale. The technology was there to sequence the genome - that's been done. But now the technology exists to analyse variation in very many segments of the genome simultaneously (Jobling 0.32.53) [...] using a technology like SNP typing.[185]

[185] See the section on 'SNP typing methods' in Jobling *et al*. (2004), pp. 96-101.

> In the past we would type, say, 20 or 30 SNPs in the β-globin gene. But now you can type a million SNPs across the whole genome, including the β-globin ones, if you want. So what you have is a very rich context in which to look at variation in one place that you might be interested in: you have the context of all the rest. Or you can look, simply for its own sake, at genome-wide variation. And what you get away from is locus-specific effects. Any one bit of the genome is a, is a specific locus - for example, of the β-globin gene. And that will have experienced locus-specific effects due to selection, for example in relation to malaria[186] (Jobling 0.33.51).

Holdsworth asked Jobling for an example to elucidate the phrase 'locus-specific effects'. Jobling suggested:

> Well, a good example would be if you took the lactose gene, and you used that as a marker to investigate human population relationships, you would come up with a picture which reflects - not how people migrated and how generally similar or dissimilar they are - but you would come up with a picture which reflects very strong selection for lactose persistence with the practice of agriculture and milk-drinking.[187] So you would find great similarities between populations which are generally rather dissimilar, because what you are seeing is the strong force of positive selection in maintaining that allele at a high frequency in populations that are otherwise rather distantly related, simply because they happened to drink milk (Jobling 0.34.52).

Jobling offered further examples:

> So that would be a locus-specific effect. Similarly, malaria resistance: you would look at the sickle-cell gene, sickle-cell variant, and you would see if you typed that marker, you'd see great similarities in populations that had been exposed to malaria.

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[186] See the review article: Williams, Thomas N. (2006): 'Red blood cell defects and malaria', *Molecular & Biochemical Parasitology*, 149, 2006, pp.121–127.
[187] For lactase persistence, see Jobling et al. (2004), pp. 414-421. See also Ingram *et al*. (2007).

> So if you were then to type the whole genome in some general way, you'd see a much more - if you like - an average and a more reliable picture of similarities between populations, or dissimilarities between populations, because selection is locus-specific. It's interested in a little bit of DNA which does a particular job. For example, it's interested in a bit of DNA that stops lactase being switched off after weaning, or the bit of DNA that disrupts β-globin, which means that malarial parasites can't get into the red blood cells. But the rest of the genome is going its own sweet way. It will be evolving not under a specific selective force. There may be lots of other, different ones, acting elsewhere. But on the whole it's just providing a reasonably neutral - if you like - picture of the relationships between different populations (Jobling 0.36.14).

Jobling concluded:

> So we are right now able to have a genome-wide rather than a locus-specific picture, because of the advances in sequencing being there and the technology being there to analyse variation. And what's going to happen soon is that we'll be able to completely re-sequence human genomes, relatively cheaply. And that will make a big difference, because instead of looking at specific sites of variation you might be able to take someone's genome and just throughput the whole thing. And the Holy Grail that people talk about is the 'thousand-dollar genome'. So you could take someone's genome and sequence the whole shebang, instead of looking at little bits of variation (Jobling 0.37.00).

Robin Crompton

To the question whether his research typically drew on the findings of genomics, Robin Crompton replied:

> I'm not sure if you asked me to define genomics I'd be able to help. To the best of my understanding of it: slightly. But I'm really not sure that I know what genomics actually is (Crompton 0.16.07).

Holdsworth tried to illustrate the point in the following way:

> Well, if we were talking to somebody in behavioural genetics they might be talking about genes, but people in palaeoanthropology are tracing lineages in mitochondrial DNA or on the Y-chromosome.

To this Crompton responded:

> OK, if we're talking at that level, I suppose the answer is yes, inasmuch as for example I've just been writing a big review of the hominoid - I mean, the ape and human - locomotive system, and obviously the recent information on genetic separation dates of humans and chimpanzees is relevant to that, and it's mentioned in the paper, but that's about as far as I take it.

This was the article we have already referred to here, in Chapter C2, above. It was published in the special issue of *Journal of anatomy* on human evolution and modelling the lost common ancestor of humans and chimpanzees, edited by Bernard Wood and Sarah Elton.[188]

[188] Crompton *et al*. (2008).

Analysis of diversity

The various different replies to this question showed among other things how easily affected scientific research agendas can be by external factors. Jones made a point of describing the link between the research agenda of biomolecular archaeology and medical and agricultural priorities. Buckley saw a strong impact of economic factors on the divided domain of Down syndrome research. Mace clearly identified the social, by extension economic factors inhibiting DNA analysis in the identification of family relationships by researchers in human behavioural ecology. Jobling stressed the importance of advances in technology to the growth of knowledge in human evolutionary genetics.

Assessment of the criterion

In a research project on behavioural genomics it might have seemed superfluous to ask the researchers in their interviewers whether, in their work, they drew on the findings of genomics. The results show how wrong such an assumption would have been. Criterion 4 was an effective tool for analysing unexpected difficulties in the application of the new science.

Chapter C6 – Is the research on genes or other DNA? If 'other': mtDNA or Y-chromosome?

The matrix for the criterion

The responses to Criterion 5 yielded the matrix displayed below in Table C6.01.

Table C6.01. Matrix for Criterion 5:
'*Is the research on genes or other DNA? If 'other': mtDNA or Y-chromosome?*'

Researcher	*Discipline*	*Genes*	*mtDNA Y-chrom.*
Jones	Biomolecular archaeology		
Hutchinson	Evolutionary biomechanics (dinosaur)		
Smith	Molecular neurobiology		
Buckley	Down Syndrome research		
Mace	Evolutionary anthropology		
McGuffin	Research into normal and abnormal behaviour		
Jobling	Human evolutionary genetics		
Lindsay	Human developmental genetics		
Crompton	Evolutionary biomechanics (human)		

Salient interviews

The phrasing of this criterion involved a necessary simplification. As we saw in Chapter A1, the concept of the gene is a complex one to handle. For Barnes and Dupré (2008),[189] 'ontological authority' has shifted from the gene to the genome. Against this background, the division of the genome into 'genes' and 'other DNA' may appear crude. However, that

[189] Barnes and Dupré (2008), p. 8.

division was only a starting-point. It created the opportunity for the separate interviews to probe the issues in greater detail.

In the event, a number of the respondents felt able to give a simple and concise answer to this question. Among those whose discipline specialised in research into human nuclear genes, and did not feel the need to add much to this statement, were Buckley, Smith and Lindsay. Lindsay put her response this way:

> We are not really looking at mitochondrial DNA. So there are genes in human nuclear DNA. Y-chromosome? We might do, we haven't as yet. We have certainly looked at a number of genes on the X-chromosome. And that's because a number of those underlie different mental retardation syndromes (Lindsay 0.49.10).

McGuffin expanded a little on the theme of mtDNA research, as we shall see. Jones was predominantly concerned with the non-recombinant forms of DNA, while the work of Jobling in human evolutionary genetics spanned both categories. Hutchinson, Mace and Crompton had previously explained that their work involved little or no direct genomic research.[190]

The only respondent to give a straight 'yes' to both work on genes and work on mtDNA and Y-chromosome sequences was Jobling, the researcher in human evolutionary genetics. However, before coming to his interview we shall first consider that with Martin Jones.

Martin Jones

That Martin Jones' research in biomolecular archaeology involved the study of 'other DNA' than just human nuclear genes could hardly have been in doubt given a certain familiarity with his book, *The molecule hunt* (Jones 2001). A passage from that work serves as an introduction to that theme:

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[190] See Chapter C5, above.

> As methods of sequencing DNA molecules and reading their genetic code came on stream in the 1970s, the tacit assumption had been that the existence of DNA was subservient to that of the whole organism and its evolutionary battles. One of the surprises was how little of the stuff seemed to be engaged in those battles. It transpired that 'coding genes' – the sequences of DNA actually used to build proteins and thus engage in the outside world – make up as little as 10 per cent of the DNA within the cell's nucleus. The other 90 per cent reproduce without any connection to the trials and tribulations to which the whole organism is exposed. These emerging non-coding regions were ideal for charting evolutionary patterns independently from natural selection.[191]

The methods of DNA analysis that involve study of the non-coding and non-recombinant sequences of DNA have already been discussed[192]. What a passage such as this reminds us, however, is the sense of surprise that came with the realisation that 'other DNA' – i.e., the non-coding, non-recombining sort – could provide a rich source of phylogenetic information and, moreover, comprised the great majority of the genome.

In the passage already quoted from, Jones went on to say that

> These non-coding regions are the best source we have for independently tracking lineage and generating a molecular clock. We can predict that on the average a particular stretch of DNA is likely to accumulate a new change every few hundred generations, or few thousand years.[193]

Assuming (for the time being) that discrepancies in this random process are – in the long term - "absorbed into a relatively uniform rate", then, if the researcher focuses on a particular stretch of DNA,

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[191] Jones (2001), p. 49.
[192] See the section 'Non-coding and non-recombining in DNA' in Chapter A4.
[193] Ibid.

> two closely related individuals will have almost identical sequences, and increasingly distant relatives will have increasingly disparate sequences. The sequences thus form the basis for the construction of phylogenetic trees, but this is not an entirely self-contained process. At some stage, these molecular projections of evolution had to be anchored on some real dates, bringing them back to the archaeological and geological records.[194]

This makes the point that the opportunities for research using non-coding, non-recombining DNA sequences is not merely a convenient method for archaeology to use. It is a way by which biomolecular archaeology makes a vital contribution to the whole enterprise of developing the DNA molecular clock. However, as we shall see from the Jones interview here and from the Jobling interview in a moment, scientists are also finding ways to derive evidence from genes. In the Jones interview, the discussion of Criterion 5 came just after an exchange in which Jones had spoken of the possibility that

> if there was a surge of research in alcohol dehydrogenase, that too would be something that one could explore, because the history of alcohol is something quite interesting in terms of archaeology. [...]
>
> There hasn't really been a study on it. I mean, that's - if you like - a sort of study waiting to happen, you know, because alcohol-related genes probably themselves preserve, you know, a good deal of historical information about how old alcohol consumption is within our species (Jones 0.31.08).

So, coming on to Criterion 5 - 'Is the research on genes or other DNA? If 'other': mtDNA or Y-chromosome?' – Holdsworth asked if one should also consider ticking the 'gene' box here (Jones 0.31.08), to which Jones responded:

> Well it's very - kind of - emergent. It has a signal 'Not at the moment, but coming soon' - if you know what I mean.

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[194] Ibid.

As an additional point, Jones suggested also taking account of 'autosomal non-coding DNA', which he said was very important, especially in relation to "crop-related stuff and plants". If there were such an additional column at this point in the Criterion Matrix, Jones suggested, it would need to be filled in for biomolecular archaeology and left blank for molecular palaeoanthropology. To Holdsworth's request for clarification on the context in which this was relevant, Jones replied:

> To plants. [...] Crop - any plants, actually. But crops are the ones that count. I mean, the key thing is they have mitochondria, but plant mitochondria are a bit wild in the evolutionary timescale. [...]
>
> They just evolved very weirdly. And there's also - I mean, you don't want to complicate this list – but you also want - there's also chloroplast DNA. But I think if you've got 'autosomal non-coding DNA' in a box then that should cover the plants (Jones 0.33.13).

Mark Jobling

Holdsworth asked Jobling: "Now what about 'genes' or 'non-recombinant sequences': mitochondrial DNA and Y-chromosome? (Jobling 0.37.23). Jobling replied that he and his colleagues were definitely interested in all of those things, while hinting at the limitations of these avenues of research:

> So, mitochondrial DNA and Y-chromosomes are interesting because they escape recombination and don't get reshuffled every generation. That means that they're relatively straightforward-to-interpret patterns of diversity. You see modern individuals in terms of how they came to be that way – their ancestry – you don't have them reshuffling in each generation. But they are only two loci – genetic locuses. Mitochondrial DNA and the Y: those are just two pictures, if you like, of the evolutionary process. And it's very much only part of the story (Jobling 0.38.13).

Holdsworth asked how the story could be filled out with autosomal DNA. Jobling's answer was:

> Well, any segment of DNA that doesn't undergo recombination has its own history, because it comes down – it coalesces back at some point to a single ancestor. Those ancestors didn't all live in the same place, and they didn't all live at the same time. So, to provide a rich picture of human history through DNA you need to look at a lot of them – to look at their history. Because if you look at – if you take one at random, you will find, for example, that it may have a relatively recent origin in Asia. If you look at another, you might find it has a very ancient origin in Africa (Jobling 0.39.00). [...]
>
> But, because each segment of DNA has its own evolutionary history, each one has its own past. I mean, each one has its own place of origin. So, if you look at just one, that's fine, that's the history of that piece of DNA, but to what extent it reflects the history of our species may be another matter. So you need to look at a lot, and that means Y-chromosomes and mitochondrial DNA on their own are just two pictures of the evolutionary process. OK, they may happen to represent the species picture as well, but they may not. I mean, it's striking. If you look at humans, chimps, gorillas and orangutans, then we have a phylo- , an accepted phylogeny for the relationship between those species, but orangutans and the rest are – orangutans are a sister clade of the rest, and the gorillas are a sister clade of chimps and humans, but if you take any piece of DNA it can give you a different tree. It can give you a tree that shows that gorillas are the most ancient branch. And then come orangs and then humans and chimps (Jobling 0.40.19). [...]
>
> Jobling: Or you can even get ones that place humans as the most ancient. From one sequence. And that's fine, but what you need to do is look at a lot of them, and then you get a true picture – or a truer picture (Jobling 0.40.37).

Holdsworth asked about an article by researchers from the University of Arizona published in *Nature Reviews Genetics* the previous September?[195] This seemed to be a criticism of relying on mtDNA and Y-chromosome sequences (Jobling 0.41.39). Jobling responded:

> Well yes, well absolutely, yes. I think it's fair to criticise. Indeed what we're doing at the moment - I've been traditionally a Y-chromosome researcher in my own research - although we continue to use it, we're moving towards using the output of the HapMap Project.[196] That's the genome-wide project which looks at haplotype structure of the whole genome, and what it allows you to do is identify regions of DNA within the autosomes that have never historically undergone any recombination. They're like little 'Y-chromosomes' embedded in the autosomal DNA. So they haven't had recombination, but they have had a history. You can then use those as you might use a Y-chromosome. You can build a tree and so on and so forth. (Jobling 0.42.30)

In summary, Holdsworth suggested, what Jobling was saying was that the 'traditional' mtDNA and Y-chromosome approaches "are only as good as they are, and not better". They could be supplemented by evidence from the autosomal DNA, which is possible now because of the high-powered systems for investigating it. It would not have been possible a few years ago. Jobling replied (Jobling 0.43.02):

> Yes. And because of the HapMap project, which certainly wouldn't have been possible a few years ago because it required the analysis of, I think, about 3.1 million markers – about 3.1 million SNPs - for a population. That's been extremely helpful, because we didn't have to do any work: it's all available. Just with a genome browser you can – you can actually take down that data and use it and find these bits of DNA (Jobling 0.43.27).

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[195] Garrigan and Hammer (2006). I am grateful to Maureen O'Malley of Egenis for bringing this paper to my attention.

[196] The International HapMap Project. Website: http://www.hapmap.org/ (consulted 14 January 2008). See also: Thorisson *et al*. (2005).

Holdsworth asked if we had already seen, so to speak, 'corrections' of the picture that was emerging. Or did Jobling expect us to? The answer was

> Well, I don't think we are, no. So I think that – I think it unlikely that the generally-held view that there was an African origin for modern humans is going to be overturned by the new genetic methods (Jobling 0.44.01). [...]
>
> I think that very unlikely. What seems to be happening is that most – if we look at these little bits of DNA within the genome that are non-recombining – that have not recombined in the past - the majority of them are of African origin. Which is kind of what we expected. So I think we're getting a richer picture by having more markers and more systems to look at, but I don't think it's likely to overturn the general view that is held at the moment (Jobling 0.44.34).

Holdsworth asked if Jobling could confirm that this was not going to eliminate the validity of mitochondrial DNA and Y-chromosome research. Jobling said:

> No. I mean, both mitochondrial DNA and Y-chromosomes have the trees – the phylogenies have African roots, for example. And I think those both do reflect the species history. They needn't necessarily have done so, but they did (Jobling 0.45.05).

Holdsworth raised the question about time-depth, also mentioned in Garrigan and Hammer (2006). Jobling agreed that this was a concern.

> Yes. That's a difficult one. I mean, mitochondrial DNA and Y-chromosomes have a low effective population size, as we say. So for every one Y-chromosome in a global population there are four copies of chromosome 1, for example. And that means that there are just fewer of them out there, and that the time at which they will coalesce to a common ancestor is proportional in number. That's the time we expect them to coalesce to the common ancestor. And so when we look at mitochondrial and Y-chromosome ancestry for time-depth it's very shallow. That

doesn't necessarily reflect the species time-depth. It's variable. It may do, but it's unlikely. I mean, it depends what estimates you use, but one estimate of Y-chromosome time-depth is about 60,000 years. That clearly can't be the species time-depth. That's too young, based on palaeontological evidence. (Jobling 0.46.13)

Holdsworth: Which would be between 150 and 200,000 years.

Jobling: Something like that. Whereas autosomal markers we expect to, on average, to coalesce to something around about four times as old as the Y-chromosome and mitochondrial, which may actually pre-date the species origin. [...]There are autosomal [sequences] with coalescence times of about [800,000 years], or even older (Jobling 0.46.46). [...]

A species is not descended from one individual, but from a group. [...]. So before you can try and reach the event of a speciation, you've got a group of individuals who contain diversity themselves. To go back to the time of the speciation, you sample everybody, look at the histories of their people's DNA. Some of them will go back quite a long way. A pair of chromosomes - a pair of individuals in the population will themselves have a coalescence time that might be hundreds of thousands of years. And if those lineages survive them through the speciation event to modern times, and you now look at the time-depth, you're going to find that ancient time-depth that was already separating those lineages, plus the time that's elapsed since speciation - which is, say 200,000 years. So you can find sequences which have – which are really ancient in their time-depth. On average, they will be younger than the species, but it is possible to find lineages which have very, very old genetic histories (Jobling 0.47.55).

Holdsworth went back to the point at which Jobling had talked about HapMap and finding autosomal sequences that in their history had not in fact been subject to recombination, and asked whether there was a special term for that (Jobling 0.48.11). Jobling said there was not

an accepted term. They were normally referred to as 'haplotype blocks'[197] (Jobling 0.48.21).

Chris Smith

When the question was put to Chris Smith he first gave a definite reply and then paused a moment for reflection (Smith 1.01.00):

> Well, for molecular neurobiology, I'm thinking that it's got to be genes on nuclear DNA. So it's not really going to be much involved in mitochondrial or Y chromosome. Well, is that absolutely true? Let's have a look. I've got a list here somewhere, I think.

Smith referred to a table in the 3rd edition of his *Elements of molecular neurobiology*. The table set out the chromosomes, indicating the loci of various neuropathologies:

> With the exception of the Y-chromosome each has at least one gene locus responsible for a neuropathology. I don't think we've got a Y-chromosome pathology, but I'm surprised if there isn't one. Now, you see, all of these chromosomes, with apparently that exception, do have genes which when defective lead to a neuropathology - these are the genes. Just a single nucleotide change causes the various pathologies, which I've written down here (Smith 01.02.24). [...]
>
> *Holdsworth*: Still, the emphasis – (Smith 1.03.00).
>
> *Smith*: Yes, the emphasis - that's right – the emphasis is on nuclear DNA. Anyway, the vast preponderance... Mitochondrial DNA – I'm not sure about whether that has a significance in molecular neurobiology. Don't know about that. Don't like to say.

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[197] Gabriel *et al*. (2002).

Holdsworth: Anyway, it's not preponderant.

Smith: No.

Holdsworth explained that this criterion served to "bring out the fact that in anthropological and biomolecular archaeology contexts people are looking at the mutations precisely in the parts of the DNA that don't recombine" (Smith 1.04.06), so that the lineage can be followed over a long period.

Smith wondered again if there could be a relevance to molecular neurobiology, but came down against the idea:

> I mean, I'm not aware that it's neurobiological, though it could well be, of course. In other words, does it affect the brain? I mean, the mitochondrial stuff is really tracing lineages, as you say - trying to find the origins of *Homo sapiens sapiens*. Similarly, with some of the Y-chromosome work. It is also lineages, trying to find origins in East Africa, which is not specifically related to brain size, though you could argue – I suppose - . So, I think, on the whole, the latter two columns are not of great interest to molecular neurobiology (Smith 01.05.10).

Peter McGuffin

Asked whether his research typically drew on the findings of genomics, McGuffin had replied with a straight "Yes" (McGuffin 0.28.30). His answer was the same when the interviewer moved on to the next question: whether that meant human nuclear genes. Holdsworth pointed out that in some other disciplines, it might mean mitochondrial DNA. McGuffin said

> Yes, well, we have done some work on mitochondrial DNA (McGuffin 0.29.00).

Asked in what connection, he replied:

> Well, just looking at mitochondrial DNA in schizophrenics compared with controls. So in one of our early linkage studies - actually, not the very early one, but one in the 1990s - we had quite a lot of what appeared to be maternal transmission. There are lots of explanations of maternal transmission other than mitochondrial DNA, but it did make some mitochondrial DNA experts interested in what we were doing. And it also made us interested in it, too. Yes, essentially we looked at the mitochondrial DNA of schizophrenics, and we found actually differences compared with controls. We haven't followed that up because he differences weren't all that striking, but the findings are still there and need to be looked at again by someone (McGuffin 0.30.01).[198]

McGuffin said he had not done any research using the Y-chromosome (McGuffin 0.30.25).

Analysis of diversity

A rich range of targets for research emerged from the discussions of this criterion. As well as predictable uses for human gene sequences, human mtDNA and non-recombinant Y-chromosome sequences, Jones adduced alcohol-related genes, viewed as a potential source of "a good deal of historical information about how old alcohol consumption is within our species", autosomal non-coding DNA in crop plants, and chloroplast DNA. (The information that archaeology derives from the history of plants is relevant to behaviour because it can be cross-referenced to behavioural characteristics such as diet, migration, agriculture and settlement).

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[198] Marchbanks *et al*. (2003). This article is cited in, among others, Bandelt *et al*. (2005).

Jobling discussed the limitations as well as the advantages of research into mtDNA and Y-chromosome sequences. He described how these methods could now be supplemented by evidence from the autosomal DNA, which had become possible with the development of the high-powered systems for investigating it that are now available to the HapMap project.

McGuffin showed that mtDNA analysis had at least been entertained in the context of psychiatric genetics.

Assessment of the criterion

The original purpose of the criterion was to probe the distinction between methods of DNA analysis targeting genes and those targeting non-recombinant sequences such as mtDNA and Y chromosome sequences. In the event, it captured the additional diversity in research practice that has here been described.

Chapter C7 – Is there research on the DNA of non-human/hominid species? If so, animals or plants?

The matrix for the criterion

The responses to Criterion 6 yielded the matrix displayed in Table C7.01 below.

Table C7.01. Matrix for Criterion 6:
'*Is there research on the DNA of non-human/hominid species? If so, animals or plants?*'

Researcher	*Discipline*	*Animals*	*Plants*
Jones	Biomolecular archaeology	■	■
Hutchinson	Evolutionary biomechanics (dinosaur)		
Smith	Molecular neurobiology	■	
Buckley	Down Syndrome research	■	
Mace	Evolutionary anthropology		
McGuffin	Research into normal and abnormal behaviour	■	
Jobling	Human evolutionary genetics	■	■
Lindsay	Human developmental genetics	■	
Crompton	Evolutionary biomechanics (human)		

Salient interviews

The matrix shows that a number of disciplines use evidence from the other animal species. The most unequivocal negative reply to this question came from the human behavioural ecologist, Mace, whose answer was a straight 'No' (Mace 1.00.00). Two researchers expressed an interest in plant DNA. These were Jones (biomolecular archaeology) and Jobling (human evolutionary genetics).

Starting now with those researchers whose discipline made use of laboratory animals, Buckley referred back to the research done on trisomic mice (Buckley 1.23.24). She said that these had "been artificially created to be models for trisomy 21". McGuffin and his colleagues also worked with mouse. He said it was "Mainly mice in our centre, but we collaborate with other groups who use rats" (McGuffin 0.30.48). Lindsay said that there was not research on the DNA of non-human species "directly within my group", but "a lot of mouse developmental genetics" was done. Other model animals used were zebra fish and, in terms of the brain, (chicken) chick and rat (Lindsay 0.49.46).

Neither of the two evolutionary biomechanists, Crompton or Hutchinson, did any research into the DNA of non-human or –hominid species (Crompton 0.18.02; Hutchinson 0.24.40). In the case of Hutchinson, we had already seen in Chapter C5 that Hutchinson's use of genomic findings was limited by the chronology, since his work on dinosaurs took the time-frame back to about 230 million years ago. However, he did mention the utility for phylogenetic purposes of research – actual or potential – into the DNA of ("very recent") mammoth, and mastodon (Hutchinson 0.13.00), and living elephants, crocodiles, birds and lizards. Such research helps to clarify "major phylogenetic relationships of groups", which is important for Hutchinson's work (Hutchinson 0.14.23). Asked specifically to respond to about Criterion 6 - 'Is there research on the DNA of non-human species?' (Hutchinson 0.24.40), his answer was "Not directly, but, yes, again for phylogenetic research it has potential too."

We shall now consider the responses of Jobling, Smith and Jones in greater detail.

Mark Jobling

Asked this question - 'Is there research on the DNA of non-human/hominid species? If so, animals or plants?' – Jobling introduced the topic of comparative genomics, at first with reference to inter-hominid comparisons, but also bringing in other primates and other taxonomic groups:

> Yes. There's the subject of comparative genomics. Comparative genomics seeks to illuminate the genetics of one species by looking at the genomes of other species (Jobling 0.49.02). [...]
>
> One aspect is comparing human genomes with those of chimps and bonobos and gorillas and so on. We can learn quite a lot about patterns of diversity in our own genomes by looking at – by using as a reference point genomes of other species. So we can understand, for example, that there are differences between the human and the chimp genome. And the question is: did those differences arise from the lineage that led to chimps or the lineage that led to humans? So now the macaque genome – the rhesus macaque genome - is published, so it provides a reference-point, which we can compare humans and chimps from each other, but then also with an out-group: the rhesus macaque. And you can say, OK, well, chimps and rhesus macaques have the same DNA base at this position; humans have a different one; so it's a human-specific change. And you may find that rhesus macaques and humans have the same base at this position; chimps have a different one; so it's a chimp-specific change. That's quite useful – to be able to know, of the many differences between humans and chimps, which ones have occurred on our lineage, and which ones occurred on theirs, for example. So it's then interesting to compare human diversity with the diversity among different chimps, different gorillas, different orangutans, that have different histories and different behaviours (Jobling 0.50.31).

Holdsworth sought clarification:

> Sorry, when you say 'among different' - different *populations*?

Jobling replied:

> Yes. Or a group. There's a study done, for example, of Y-chromosome diversity in chimpanzees, or in gorillas, and you see very different patterns than you see in humans, which reflect their different histories. Then moving away from primates, then, a lot of studies have been done of diversity of species that are commensal, or

humans have been associated with: so, for example, JC polyoma virus or *Helicobacter pylori*. JC polyoma is a virus.[199] I don't even know what it does to you, but a lot of people carry it around. And you can look at the diversity of its DNA sequence to provide another picture of human migration and contact (Jobling 0.51.24).[200] [...]

More recently, people have looked at *Helicobacter pylori* strains and how they vary in different human populations, to give an indication of how long that bacterium's been associated with humans and whether it provides a picture of diversity similar to that of human being genes diversity. And then there are domesticated animals and plants that a lot of people have looked at to see evidence of how agricultural practices were adopted, and when they were adopted, by looking at the genomes of maize or rice or wheat, or cows or sheep or goats or any of these (Jobling 0.52.17).

Chris Smith

Smith, the molecular neurobiologist, had already referred to one model animal before the interview reached Criterion 6 specifically (Smith 0.56.00). This was the sea hare, *Aplysia*:

There's a lot of research done on *Aplysia*, which is an aquatic mollusc, and Nobel Prizes have been won. They're looking there at *Aplysia* as a model organism for understanding learning and memory, and that goes down to the molecular level.[201] There's a significant tranche of neurobiology - molecular neurobiology, if you wish - done on that organism. And the trait they're looking for is the withdrawal of the siphon beneath the mantle in response to a stimulus, and looking at conditioned reflexes. That conditioned reflex in *Aplysia* of course is species-typical. It's typical of that particular species, but you're looking – but you're using that species-typical

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[199] "JC virus (JCV) is a double-stranded DNA polyomavirus co-evolving with humans since the time of their origin in Africa" (Pavesi, 2005).
[200] See also Jobling et al. (2004), p.369.
[201] For concise accounts of relevant research on the sea slug *Aplysia californica*, see Clark and Grunstein (2000), pp. 118-124.

> phenomenon to do some molecular biology, trying to get down to how the molecules interact together to produce that conditioned reflex, with the hope of getting some insight into human memory and reflexes - conditioned reflexes. This is one of the things about molecular neurobiology: one looks for the model organism - the organism with which you can actually attack the problem most easily in. So you have a lot of organisms you can examine, but because the investigation is at a fundamental, molecular level, always with the hope of generalising the outcome to understand the human condition (Smith 0.58.24).

When Question 6, concerning research on non-human species, was put to him, Smith replied (Smith 01.05.10) that

> molecular neurobiology rather takes the DNA for granted, you know, as another research area. What we are interested in - you're given the genome, and, you know, there are a large number of them now, on the databases. And how do those genomes affect – you know, code for proteins in the brain? So I wouldn't have thought molecular neurobiologists are going to actually research on the DNA (Smith 01.06.08).

Holdsworth rephrased the question. Using the same wording as in an earlier criterion, he asked whether research in molecular neurobiology drew on the findings of such research (Smith 1.06.34). Smith's reply this time was positive:

> Yes. Sure, sure. In that case, the answer is yes. (*Referring to his book*). I've got a nice little table here, you see – Table 6.2 – which shows the number of proteins in the nervous system of humans, *Drosophila* and *Caenorhabditis* – and to get that number you have to know the genomes of *Drosophila*, *Caenorhabditis* – that's the little nematode worm – and humans. So we are interested in those other genomes, certainly, though we wouldn't, I think, as molecular neurobiologists research - do research into the DNA. So yes. Plants? No, I would say not. Animals, yes, but plants no. For fairly obvious reasons, I think! (Smith 1.07.35).

Anticipating the discussion of the next criterion - Criterion 7, 'Is there research on other biomolecules?' – we should also briefly mention here Smith's citing of research analysing the proteins of potassium channels. Such research uses the bacterium *Streptomyces lividans* as a 'model' organism. Smith explained that the research "was done on bacteria because you can get large quantities of the channel material for X-ray diffraction" (Smith 1.11.00). Holdsworth commented that Criterion 6, which referred to 'animals' and 'plants', should perhaps have had a third column in the Criterion Matrix, for 'microbes'.

Martin Jones

When the question, 'Is there research on the DNA of non-human species - either animals or plants?', was put to Martin Jones (Jones 0.33.20), he replied: "Absolutely so, both". This reply reflected, notably, the work of biomolecular archaeologists on the DNA of species of animal and plant that have come under domestication by humans and thus provide evidence for important aspects of human behaviour. When discussing the previous criterion – Criterion 5 on the general relevance of the findings of genomics - we already had occasion to cite passages from the Jones interview relevant to these points.

In Jones (2001), numerous and varied examples are given of animal and plant species that have had their DNA studied by molecular archaeology. Among the former are 30,000-year-old horse frozen in the Siberian ice,[202] 1,000-year-old sacrificial llamas and alpacas preserved in desiccated conditions at El Yaral, Peru,[203] and aurochs specimen such as that from Çatal Hüyük in the Konya Plain of southern Turkey, "one of the earliest sites to show evidence of cattle husbandry".[204] The same work also discusses the study of the lineages of domesticated plants by analysis of the chloroplast genome, for instance those of maize,[205] rice[206] and wheat.[207] Jones further cited work on the DNA of bacteria. Among pathogens,

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[202] Jones (2001), p. 119. Here Jones is citing work by Adrian Lister and Helen Stanley (Lister *et al*., 1999).
[203] Ibid., p. 122, citing work by Stanley, Kadwell and Wheeler (1994).
[204] Ibid., p. 124, citing work by Dan Bradley. On aurochs DNA, see Edwards, Bradley *et al*. (2007).
[205] Ibid., pp. 98-101.
[206] Ibid., pp. 102-4.
[207] Ibid., p. 96.

he mentioned research into *Mycobacterium tuberculosis*,[208] into *Yersinia pestis*, the plague bacterium deemed to have caused the medieval Black Death and other outbreaks of plague,[209] and into DNA of the bacterium *Treponema pallidum*, the agent of venereal syphilis, taken from the four-centuries-old remains of Maria of Aragon, a notable woman of the Renaissance in Italy.[210] Jones also pointed out that the action of bacteria associated with humans could also be benign, such as that of the *Clostridium* detected by Rollo (1999) in the gut of a mummified young woman from the ancient Inca capital at Cuzco in Peru.[211]

Analysis of diversity

From the answers given by the interviewees to this question, and from the associated literature, a long list of diverse species was generated, each of which – through its DNA - has a role to play in the account of human behaviour. Apart from the Great Apes, the rhesus macaque was cited. Some of the species mentioned were model organisms studied in the laboratory for their contribution to our understanding of neurobiology: animals such as mice, rats, chicks and sea hares. Some others were species, extinct or extant, in which DNA analysis can serve to clarify phylogenetic relationships. Here one recalls the list resulting from the talk with the evolutionary biomechanist, Hutchinson, which included mammoth, mastodon, elephant, crocodile, birds and lizards. Then there were the commensal species mentioned by Jobling and Jones, where the history of the DNA complements the knowledge that science has gained from other sources concerning human migration, settlement, diet and farming. These included - as well as cows, sheep and goats - horse, alpaca, llama and aurochs. Jobling *et al*. (2004) cited a commensal lizard (*Lipinia noctua*) that was "presumably a stowaway on ocean going canoes" of early Polynesian migrants.[212] The commensal species included domesticated crop plants, such as maize, rice, wheat.

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[208] Ibid., pp. 223-7. Jones cites Spigelman and Lemma (1993) and Arriaza *et al*. (1995).
[209] Ibid., pp. 221-3. Jones cites Drancourt et al. (1998).
[210] Ibid., pp. 217-8. Jones cites Rollo and Marota (1999).
[211] Ibid., p.230.
[212] Jobling *et al*. (2004), p. 369.

Three of the researchers referred – in their interviews or in their writing – to the DNA analysis of microbes associated with humans. Jobling mentioned JC polyoma virus (a DNA virus) and the bacterium *Helicobacter pylori*. Smith cited the bacterium *Streptomyces lividans* as a 'model' organism used in molecular neurobiology. Jones (2001) referred to work by various authors on the bacterial pathogens *Mycobacterium tuberculosis*, *Yersinia pestis* (plague) and *Treponema pallidum* (syphilis), as well as on the bacterium *Clostridium*.

The diversity in the organisms chosen for research corresponded to a significant degree to a diversity of approach and method among the various disciplines studied, as will already have been apparent from the examples cited above.

Assessment of the criterion

The rich diversity of the DNA brought under study in this context was a striking result. Genomic analysis is, by definition, molecular analysis. But once the door has been opened onto the molecular level of analysis it cannot be closed again. Conceptually, the taxonomic boundaries that divide up the subject matter of biology become permeable. Human genomics ceases to be specific to the human genome alone. Its study ceases to be a monogenomic study. It opens itself up in three ways: first, there is the comparison with phylogenetically related species; then there is the analysis of the DNA of species with a life-history that is intertwined with that of humans; third, there is a phenomenon that we could call a 'licence to draw analogies'. One thinks of the examples given by the molecular neurobiologist, Chris Smith. These were the sea hare, *Aplysia*, and the bacterium *Streptomyces lividans*.

Chapter C8 – Is there research on other biomolecules? If so, proteins or other?

The matrix for the criterion

The responses to Criterion 7 yielded the matrix displayed below in Table C8.01.

Table C8.01. Matrix for Criterion 7:
'Is there research on other biomolecules? If so, proteins or other?'

Researcher	*Discipline*	*Protein*	*Other*
Jones	Biomolecular archaeology		
Hutchinson	Evolutionary biomechanics (dinosaur)		
Smith	Molecular neurobiology		
Buckley	Down Syndrome research		
Mace	Evolutionary anthropology		
McGuffin	Research into normal and abnormal behaviour		
Jobling	Human evolutionary genetics		
Lindsay	Human developmental genetics		
Crompton	Evolutionary biomechanics (human)		

Salient interviews

The interviews to be chiefly considered here are Jones, Smith and Lindsay. The responses on this criterion by McGuffin and Jobling respectively were instructive but concise.

As to the other researchers interviewed, Mace and Crompton each replied with a simple negative. Buckley said 'Yes' to proteins and to 'others' (Buckley 1.24.02), thinking of certain neurotransmitters (of which the ester, acetylcholine would be an example). John Hutchinson's response was positive, within limits:

> Well, for phylogenetics work. And occasionally you get some weird preservation, like you occasionally get some dinosaurs preserved with keratin and other proteins. Not really relevant for learning their locomotion, but it is relevant for understanding their biology (Hutchinson 0.25.53).

Martin Jones

When Holdsworth asked Martin Jones the question - 'Is there research on other biomolecules? If so, proteins or other?' – Jones distinguished between the reply from biomolecular archaeology and that from molecular palaeoanthropology, saying:

> [In] biomolecular archaeology, both proteins and 'other' are definitely the case. In molecular palaeoanthropology it's certainly the case at the moment that DNA is, yes, the main thing. Whether or not information from proteins will come back into play is hard to say (Jones 0.35.18).

Holdsworth asked how that could that happen in molecular palaeoanthropology, conceptually. Jones put it this way:

> Conceptually, you see, the issue of where it might come back is early hominids and things that, say, are between one and two million years old. And at the moment for stuff of that age you can't really get DNA out in a terribly convincing way. You might be able to check its existence there. You can get protein out, but not very informative protein. It's not an easy prediction which is the better biomolecule, once those explorations have been sorted out. I mean, if DNA survived in a form that could be studied in really early hominids then it would be better than protein, but it may be the case that proteins survive in a reasonable way better. So, basically, if you've got, say, a one-and-a-half-million-year-old hominid bone, you may be able to detect DNA immunologically, but what you can do with it is open to question. There may be collagen and osteocalcine – two proteins - that you can convincingly extract, and in the osteocalcine there may or may not be variation which is

> informative. But I'm really speculating here. I'm just elaborating rather verbosely on the fact that, although within anthropology it's DNA at the moment, the door is not closed (Jones 0.37.18). [...]
>
> I think it's when methodologies change. I mean, think at the moment you could predict that stuck in the sides of very old bones there are bits of DNA and protein evidence that are there, but our current methods can't get them out and read their sequence. And it's crystal-ball-gazing to really establish when that'll change, or what'll change (Jones 0.38.06).

Referring to the history of protein research in these contexts, Holdsworth recalled that in Jones (2001), Jones had mentioned[213] the research by Sarich and Wilson into the blood plasma proteins, the serum albumins, published in 1967.[214] That research had built on the finding that

> The strength of the cross-reaction between human anti-serum and chimp serum provided a measure of the sequence similarity of two proteins that performed precisely the same function, but in different, albeit related, species.[215]

As Jones had explained,

> By considering a variety of species, they demonstrated that the levels of difference between albumin proteins seemed well ordered, and came up with series of time estimates for different episodes in the human evolutionary story.[216]

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[213] Jones (2001), pp. 45-7.
[214] Sarich and Wilson (1967).
[215] Jones (2001), p. 45.
[216] Ibid., p. 46.

In the interview, Jones commented:

> Yes. I mean, that's the other interesting thing. Before DNA molecular studies were there, protein had a longer history. And the same thing of 'feeding off' medical research happened. So you can go back for example to the First World War and the study of blood groups, which is a protein study with a clear genetic determinant. And on the one hand we've got research into it in terms of a contemporary medical problem, but then there's a spin-off. Those are that the geography of As, Bs and Os reflect the history of our species and its spread across the globe.
>
> *Holdsworth*: Could you call it almost a kind of proxy genetic study?
>
> *Jones*: It's a proxy – yes exactly. Absolutely. I mean it's clear that, it's a simple Mendelian system, so it's a very sound proxy. And I guess the only limitations on it, really, are that with proteins you're always dealing with coding regions. You're always dealing with something that's engaged in ecological stuff, and so those As, Bs and Os are there to resist diseases. Diseases are different in different parts of the world, so the picture you get might be environmental rather than phylogenetic (Jones 0.40.02).

Reference was made in the preceding chapter to Jones' interest in plant DNA. In connection with this, it is relevant at this point to note another place in the literature where Jones and his co-workers underlined the importance of other biomolecules in the molecular archaeological study of plants. The citation is an article by Brown, Allaby and Jones (1993) on the biomolecular archaeology of wheat. The article concluded with the following paragraph:

> In the longer term further major advances will be achieved if studies with ancient wheat DNA can be combined with equivalent work on the lipid, protein and carbohydrate contents of archaeological seeds. One limitation of ancient DNA is that it can provide little or no information on the physiological status of the

> organism whose remains are being studied. With wheat seeds, for example, ancient DNA studies will not be able to provide much information on the nutritional value of the grain, as this is determined by the identities and amounts of the seed proteins, lipids and carbohydrates, which in turn depend on the level of activity displayed by the relevant genes, a factor that cannot be assessed simply by analysing ancient DNA molecules. Should it prove possible in the future to use preserved remains to make meaningful estimates of the protein, lipid and carbohydrate contents of wheat seeds, then the biomolecular archaeology of plants will truly have come of age.[217]

Chris Smith

Chris Smith stressed the importance of the study of proteins for his discipline:

> 'Is there research on other biomolecules' in molecular neurobiology? The answer to that is yes, there is. Proteins are of very great significance: in fact, of more significance than the DNA. Because all the channel proteins and all the rest – the synapses and the axons and all the rest of it - all work on proteins, which we need to analyse. And recent Nobel Prizes have been obtained for analysing the proteins of potassium channels (Smith 1.09.15).

Asked for an example of a Nobel prize-winner in this area, Smith replied:

> MacKinnon is the one I was thinking about. I think he got the Nobel Prize in 2003 or 2004.[218] Anyway, a huge and wonderful development, really. Finding the structure of one of these channel proteins at this resolution: this is 2-ångström resolution (Smith 1.10.50). [...]

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[217] Brown, Allaby and Jones (1993), p. 71.

[218] Roderick MacKinnon, winner of the Nobel Prize in Chemistry, 2003. The text of his Nobel lecture on 'Potassium Channels and the Atomic Basis of Selective Ion Conduction', delivered in Stockholm on 8 December 2003, is available at the following website (Consulted 6 December 2007): http://nobelprize.org/nobel_prizes/chemistry/laureates/2003/mackinnon-lecture.html .

> But it's interesting here, of course, which is partly the reason why I find the question just a little bit difficult to answer. For this work was done on bacteria. It was done on bacteria because you can get large quantities of the channel material for X-ray diffraction. The bacterium (*Streptomyces lividans*) is an example of a 'model' organism. It has (so far) proved impossible to extract sufficient quantities of channel protein - sufficient quantities to analyse with X-ray diffraction techniques – from animal nervous systems. One has to transfer the knowledge, the exact structural knowledge obtained from the bacterial preparation, to understand the functionally similar channels known to exist in animal nervous systems (Smith 1.11.35). [...]
>
> Well, in that case - and also in some of the sensory physiology - you're using bacteria as model organisms. Simple organisms. Simple – that is, as simple as it can be - to work out the basics of what's happening in more complex entities such as ourselves. This has been one of the great themes of molecular biology (Smith 1.12.09).

Holdsworth asked about other molecules as well as proteins, and Smith mentioned carbohydrates and lipids.

Peter McGuffin

When McGuffin was asked, 'Is there research on other biomolecules? If so, proteins or other?' (McGuffin 0.30.48), his answer was:

> Yes, particularly in recent areas, we've got into pharmacogenetics. And we have a big pharmacogenetics study on the go, looking at the effects of anti-depressants. And so we're working with proteomics experts (McGuffin 0.31.20).
>
> *Holdsworth*: And other biomolecules?
>
> *McGuffin*: No, not really, no. That's mainly it: proteins (McGuffin 0.31.33).

McGuffin was a co-editor of the work *Psychiatric Genetics and Genomics*, published in 2002, which discusses pharmacogenetic studies relevant to psychiatry, and in particular the prospects for the individualization of treatment.[219]

Mark Jobling

Jobling, when asked the question about 'other biomolecules' (Jobling 0.52.18), replied:

> Well, genetics is essentially about DNA. So it's very DNA-centric. The question that you might ask is, OK, there's a change in the DNA, but does it have a functional effect – what is the functional consequence? And that could involve studies of protein, or studies at the RNA level to ask what differences there are. But I think it's very much DNA-centred (Jobling 0.52.59).

Susan Lindsay

The theme of RNA came to the fore again in the interview with Susan Lindsay. Was there research on other biomolecules?

> Yes. Proteins and now other kinds of – there's now non-coding RNA (Lindsay 0.50.09).
>
> And that's very recent in terms of recognising this as an area of importance for regulating gene expression (Lindsay 0.50.25).
>
> So there's a point of turning a gene on and off, that's at the DNA level, but then fine-tuning or fine-controlling that – the RNA, and turning the RNA into protein - that can be done by non-coding RNAs, and in fact the turning the gene on and off at

[219] McGuffin, Owen and Gottesman (2002).

> the DNA level, we're finding it's being done by RNAs as well as by proteins (Lindsay 0.50.58).
>
> Have you heard of micro-RNAs? So these are whole sets of RNAs that people are just discovering [...] (Lindsay 0.51.11). [...]
>
> 'Micro'-RNAs. And these are non-coding RNAs, but they regulate specifically the activation of genes. I don't know if they regulate turning some genes off, they may do, I just don't know (Lindsay 0.51.32).

Analysis of diversity

Jobling's response was a reminder that genomic research is DNA-centric for good reason, and yet some of the other replies showed that, if we see the rise of genomics as part of a molecularisation of these branches of biology, there is no a priori boundary that confines research to DNA and DNA alone if 'chemical information', as Jones has called it, can be gathered from other molecules. Archaeology is epistemologically interesting because it is usually operating in circumstances where evidence is sparse, and where the interpretation of the evidence is hardly ever self-proclaimed, but must be inferred using great ingenuity. This means that it will exploit all types of molecular evidence for which valid methods of analysis are available.

Assessment of the criterion

This criterion served as a check on the possible assumption that researchers professing an interest in genomics would be exclusively interested in DNA. In this task, the various responses on different families of protein, as well as the mentioning of RNA by Jobling and by Lindsay were salutary.

Chapter C9 – Does the research use environmental markers?

The matrix for the criterion

The responses to Criterion 8 yielded the matrix displayed below in Table C9.01.

Table C9.01. Matrix for Criterion 8:
'*Does the research use environmental markers?*'

Researcher	*Discipline*	*Yes*	*No*
Jones	Biomolecular archaeology		
Hutchinson	Evolutionary biomechanics (dinosaur)		
Smith	Molecular neurobiology		
Buckley	Down Syndrome research		
Mace	Evolutionary anthropology		
McGuffin	Research into normal and abnormal behaviour		
Jobling	Human evolutionary genetics		
Lindsay	Human developmental genetics		
Crompton	Evolutionary biomechanics (human)		

Salient interviews

The concept of an 'environmental marker', though not self-evident to every researcher interviewed, brought out an interesting range of responses. No great relevance was found, however, to the work of the molecular neurobiologist, Chris Smith, or to that of Sue Buckley, from Down syndrome research, although she had a wry comment to make:

> So it's no, I think then. Although some people have looked at whether, if you keep your mice in rich circumstances, they do better. What a surprise! Children in rich

> circumstances may do better. But, I mean, 'no', I think really there (Buckley 1.25.04).

This specific question did not attract much discussion in the interview with Ruth Mace (Mace 1.12.51), although the theme of adaptation to the environment was ubiquitous in the conversation with her as a researcher in human behavioural ecology.

We shall take the other researchers in turn.

Martin Jones

The first researcher to have the question put to him was Martin Jones, Holdsworth explaining (Jones 0.40.02):

> Environmental markers being something like a site – you know, a cave, or a dwelling-site - or an artefact. Or a heap of oyster-shells, or something like that.
>
> *Jones*: Absolutely. It's very closely contextualised by the environment.
>
> *Holdsworth*: But, in biomolecular archaeology, logically you take into account what I've just called 'environmental markers', but is there theoretical work on the inter-relationship between the biomolecular markers and environmental markers (Jones 0.41.13)?
>
> *Jones*: It's an interesting question. And I think the answer is: in time there ought to be, but it's pretty underdeveloped at the moment. There's a great interest - in the wider field of archaeology - in site-formation processes that will explore those issues at different levels. So for example, if you're excavating a town which has buildings in it, and the buildings in it have rubbish tips, and the rubbish tips have bones in them, then there's been quite a lot of discussion at various levels of how the bones relate to the pit, how the pit relates to the house, how the house relates to - and so on. And there pretty much ought to be the same thing in relation to

> biomolecular archaeology, but I would be wrong to suggest that was a highly developed field (Jones 0.42.22).

Holdsworth asked if this was a direction in which things might go in the future. Jones thought it was. He said:

> I mean, there's - if you like - a sort of trajectory that things happen in these fields. I mean, one of the things that you see first with some new methodologies like this is that the first stage is to some extent 'headlining' - that a new method is applied to a high-profile problem, and a quick route to interesting results comes into being. Certain elements of the methodology then become more routine, and they're repeatedly asked of different sites and different materials and build a more collective picture. And once they've become routine, I think questions about connection between different data categories become part and parcel of research activity. So [that's how] it happens. It certainly happened in ancient DNA (Jones 0.43.42). [...]

John Hutchinson

The topic initially came up in the interview with John Hutchinson in the context of a discussion of evidence in molecular phylogenetics, relevant to evolutionary biomechanics (Hutchinson 0.14.23). Hutchinson had just explained that the picture supplied by DNA analysis – where that was feasible – had to be filled in by "information from outside genomics": it also required morphological evidence. Holdsworth asked: "Is there any way that environmental markers can be useful?" At first, Hutchinson wondered if he meant radioactive isotopes. Holdsworth said, no, he "was thinking the geological characteristics of sites, or actual signs of the presence of the organisms at the time when they lived (Hutchinson 0.15.10)". Hutchinson came up with an example:

> There are footprints. That's a major source of information. Extremely important. There are thousands of them (Hutchinson 0.15.15). [...]

> Oh yes, I mean any one animal could leave thousands of footprints in its lifetime but only one skeleton. So we actually have more footprints than there are specimens of animals.
>
> *Holdsworth*: Which is particularly useful for somebody studying locomotion.
>
> *Hutchinson*: Absolutely, yes. It's the only direct evidence of behaviour you normally have. That's right. The problem is you can never tell what species made the footprint. It's normally only very general details: well, this is a big, two-legged animal – something like that. So it's limited in its ability to give you very much to draw on (Hutchinson 0.15.53).

Holdsworth asked if there was "any way of cross-referencing other factors so you can narrow down the choice?" Hutchinson said that, to a degree, there was.

> By knowing what animals were present in a given area at a given time, you can kind of narrow down your list of likely candidates, but then you're always kind of left wondering, well, what if – given our fossil record limitations - what if there was another animal there which we just don't know about, and it made the footprint? It makes it very hard. We know all too well how incomplete the fossil record is. We may know the skeleton of an animal from Africa, and we find footprints in America. Even though that animal in Africa lived at the same time, it couldn't have made those footprints in America. And then later on you find that it *was* there in America – you just didn't find any fossils of it yet. The field is so young. We just haven't found everything (Hutchinson 0.16.46).

Later the discussion reached Criterion 8 - 'Does the research use environmental markers?' – and it was agreed that footprints would indeed fall within that classification (Hutchinson 0.25.53). Hutchinson then brought up another example:

> And also fossils. People who dig up fossils always pay attention to what kind of sedimentological setting they're preserved in, because that tells you was the animal in a desert versus a swamp, or things like that (Hutchinson 0.26.29). [...]
>
> Well, pretty much every dinosaur discovery out there is always carefully detailed. A good researcher carefully describes the geological setting: was this a river that this animal was preserved in, a flood plain, a forest? Knowing the ecological setting is very important (Hutchinson 0.27.02). [...]

Holdsworth asked Hutchinson if he could cite him a reference to some of his own work that involved footprints. Hutchinson replied that although he had not done direct research on footprints, he had discussed the topic in review articles or similar. He cited a paper by Farlow[220] and himself and others in American Zoologist in 2000. [221] That paper went through some of the footprint evidence. (Hutchinson said a 'pdf' was available on his website).[222]

Holdsworth asked if Hutchinson could say a bit more about what inferences you can draw from footprints. Hutchinson said:

> You can tell kind of the general posture of the animal: was it standing with its feet very close together or widely spaced apart? You can figure out relatively speaking how fast it was moving: whether it was moving at the same speed or speeding up, accelerating or slowing down – based on the distance between footfalls. And you can sometimes tell if an animal was limping: if it leaves kind of asymmetrically spaced footprints, with one step being longer – the right leg taking longer steps than the left leg - or something like that. Occasionally you find evidence of specific behaviour (Hutchinson 0.29.13).

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[220] Professor James O. Farlow, Professor of Geology, Department of Geosciences, Indiana-Purdue University at Fort Wayne, Indiana.
[221] Farlow *et al*. (2000).
[222] The url is: http://www.rvc.ac.uk/AboutUs/Staff/jhutchinson/Publications.cfm (Consulted 3 March 2008).

Peter McGuffin

When Holdsworth put Criterion 8 - 'Does the research use environmental markers?' - to Peter McGuffin (McGuffin 0.31.33), the reply was:

> Yes, very much. Depends what you mean by 'markers'. Certainly uses environmental measures.

Asked for an example, McGuffin offered the following:

> Well, I mentioned earlier life events and depression, but we also have an interest in early childhood trauma. And we have an interest in physical environmental measures, like smoking in pregnancy.

Holdsworth asked about dietary questions. McGuffin replied:

> Dietary, yes, we haven't – at least, I haven't done much about diet, but I have done a little bit. And certainly when I was starting out and had my interest in HLA, one can make a nice story about food allergy and mental illness. In fact, all - everything I did on that turned out to be negative. [...]
>
> I was quite interested at one stage in looking at food antibodies in schizophrenia. There's another story linking – associating, rather, schizophrenia with coeliac disease, which is a disorder where you get – essentially - atrophy of the gut's lining, and it seems to be related to allergy to certain foods, particularly foods that contain gluten. People with coeliac disease make antibodies against gluten. So I did a study looking at antibodies against gluten and its effects, and we didn't find any!

Holdsworth asked about things like housing conditions.

> Yes, OK. I suppose that's back to ecological measures again. Yes, certainly: housing conditions, deprivation, living in an area where most people don't have a

car. We certainly use those types of measures. And there's no doubt they have a small but significant effect in some behaviours - particularly anti-social behaviours (McGuffin 0.34.00).

Holdsworth: Really?

McGuffin: Well, by 'effect' I mean there's an association.

Asked for an example, McGuffin replied:

Oh, yes. I supervised an MSc when I was in Cardiff looking at ecological indices of deprivation.[223] These are things like the Jarman Index and the Townsend index which are based on things like measures of where you live, how many people have a car, how many people are unemployed and that sort of stuff. So there are interesting indices that people have made: public health doctors and GPs. And the study showed there was a substantial influence of those measures on behaviour, particularly anti-social types of measures, conduct disorders and so on. Subsequently, I later supervised a PhD thesis on anti-social behaviours in children and adolescents, where we found much the same thing: that measures of deprivation have a small but significant effect that you couldn't throw out of your model when you're trying to explain individual differences in the severity of a disorder[224] (McGuffin 0.35.28).

Holdsworth asked about the workplace environment. Had that been taken into account (McGuffin 0.35.34)? McGuffin said

It hasn't been taken into account much in my own research except in a very broad way: so, for example, looking at socio-economic status. No. So that's not looking at workplace environment as such, but it's actually looking at, you know, where

[223] Koppel and McGuffin (1999).
[224] Thapar and McGuffin (1996).

> people come in socio-economic bands. Which we actually found, in adults with depression, despite what some other people have found, didn't have any influence (McGuffin 0.36.03).
>
> *Holdsworth*: Right. Interaction with technology?
>
> *McGuffin*: Let me think. Don't think I've done anything on that (McGuffin 0.36.15).

Mark Jobling

When this criterion was raised with Mark Jobling (Jobling 0.53.05), he asked:

> What do you mean by 'environmental markers'?

Holdsworth again mentioned the archaeological example. There was the fact that specimens of bone or DNA are found in some environmental matrix. Then there were settlement sites. Jobling's comments from the point of view of human evolutionary genetics were as follows:

> Well, in that sense, yes. I mean, if you were studying ancient behaviour - . [...]. Yes. Mostly, environmental objects are people. So all you do is sample people, in some sense. So we don't, in our work, use environmental markers, I'd say. But in terms of studies of Neanderthal bones – well, OK, yes (Jobling 0.54.08).

Holdsworth suggested that "the whole concept of phylogeography implies some spatial location", to which Jobling replied:

> Yes, you have a box in the freezer with a hundred tubes in, and the box is called, for example, 'Basques'. I've got several of those. And so in some sense you regard those people as the Basques. So that locates them geographically and culturally, and it tells you what language they speak. And you, well, organise them and file them in

> a filing-cabinet or something which has a sheet, or set of sheets, that refers to those samples, and you have a consent form for each one of those people, and they self-define as 'Basques'. They give their first language as Basque, and they tell you that they were born in such a village or such a place, and that their father was born in the same place – with mother and grandmother, grandfather both sides, and that's your environmental marker (Jobling 0.55.06). [...].
>
> That allows you to place a person, in some sense, in a place or a population, but you don't necessarily have to go there, of course, but you have information which allows you to say, OK, this box of DNA samples is a distinct set.

Susan Lindsay

Susan Lindsay cast her reply to the question, 'Does the research use environmental markers?', in the perspective of human developmental genetics.

> No we don't. We would certainly like to be able. I'm sure we will in the future try and look at gene-environment interaction, but it is difficult to do that (Lindsay 0.51.57).

Holdsworth asked how that could conceivably emerge in Lindsay's area (Lindsay 0.52.05). The reply was:

> I think we would need to generate - if we were doing it in human - cell lines – from particular areas of the brain say - and then we could ask whether exposing these cell lines to particular changes in glucose, or oxygen - or you could ask about – [...] these kind of environmental factors. I suppose then you could ask about pesticides, or things that you might worry would have toxic effects during development (Lindsay 0.52.43).

Robin Crompton

After an initial request for clarification, Robin Crompton gave a positive response.

> *Crompton*: What do you mean by an 'environmental marker'?
>
> *Holdsworth*: Well, habitat sites, tools.
>
> *Crompton*: Yes is the answer to that. Yes.
>
> *Holdsworth*: Any particular examples you want to give? For example, fossilised footprints.
>
> *Crompton*: Yes, because we are working currently on the Laetoli footprints and trying to reverse engineer them and work out what the gait was from the footprints. So that's a major current project I've got on at the present moment (Crompton 0.19.00).[225]

Analysis of diversity

In the Jones interview, a point of interest that arose was the question of the conceptual relationship between a piece of DNA evidence and the environmental markers with which it was associated. Jones recognised this as a potentially fruitful area of further research. No doubt this question – and indeed the whole idea of an 'environmental marker' – had a sharper outline for the archaeologist than for researchers in some other disciplines because of the archaeologist's need to exploit sparse evidence to the full by exhaustively cross-referencing given specimens and the context of their discovery. On the other hand, one

[225] Further information available on the website of PREMOG at the University of Liverpool (Primate Evolution and Morphology Group), previously cited, at: http://www.liv.ac.uk/premog/premog-research-current-laetoli.html (Consulted 8 April 2009).

might ask which research discipline studying the causes of human behaviour did not suffer from a paucity of evidence – at least, of useful evidence.

The reply of McGuffin was interesting, particularly when he spoke of "ecological indices of deprivation". McGuffin made a distinction, or left open the possibility of a distinction between an 'environmental marker' and an 'environmental measure'. It will be recalled that he explained that the 'ecological indices' were

> things like the Jarman Index and the Townsend index which are based on things like measures of where you live, how many people have a car, how many people are unemployed and that sort of stuff. So there are interesting indices that people have made: public health doctors and GPs.

Possibly, one might decide that a statistic concerning car ownership in a given residential area was an 'environmental measure', but that the second-hand Ford Focus belonging to a particular individual living in that place was an 'environmental marker'. Alternatively, it might be regarded as a 'social' or 'cultural' marker. It would be idle to pretend that strict rules of nomenclature were already in place to cover every example of this nature. What is interesting is McGuffin's conception of such indices as 'ecological'. This evokes the idea that the individual actor in any human situation is in a perpetual interplay with a rich matrix of contextual factors – whether we want to call them 'environmental', 'social' or 'cultural'.

Assessment of the criterion

The responses to Criterion 8 underlined the point that DNA evidence on its own is not enough. What the researcher can read off from the DNA evidence depends on the collateral evidence of environmental markers. To some extent, there were differing notions of what an 'environmental marker' might be.

An interesting theme to emerge was that of the 'contextualisation' of behaviour, or of evidence of behaviour. In his interview, Jones spoke of the archaeological specimen as

being “very closely contextualised by the environment”. If the interpretation just given above to McGuffin’s response to Criterion 8 is accurate, then here too we see a concern for the contextualisation of behaviour. We also see the interesting reflex of labelling this interplay as ‘ecological’. Going back to the responses to Criterion 2 - ‘Is behaviour studied in the ecological setting – or in the laboratory or clinic?’ – we also saw that there McGuffin was open to the role of environmental factors, such as “naturally occurring hazards”. At that point in the discussion we also looked to the literature of behavioural genetics for illustration of some of the laboratory research in that discipline. Looking back on the example taken – laboratory tests designed to assess subjects’ perceptual speed (this was not an example taken from McGuffin’s own research) – one might now wish to ask how, or to what extent research of that character was, or ought to be ‘contextualised’ in the sense we have just been considering here.

Chapter C10 – The main concern is phylogeny or ontogeny?

The matrix for the criterion

This was one of the four new criteria added after the first two interviews (with Jones and Hutchinson respectively).The responses to Criterion 9 yielded the matrix displayed below in Table 10.01.

Table C10.01. Matrix for Criterion 9:
'*The main concern is phylogeny or ontogeny?*'

Researcher	*Discipline*	*Phyl.*	*Ont.*
Jones	Biomolecular archaeology	■	
Hutchinson	Evolutionary biomechanics (dinosaur)	■	
Smith	Molecular neurobiology		■
Buckley	Down Syndrome research		■
Mace	Evolutionary anthropology		
McGuffin	Research into normal and abnormal behaviour		■
Jobling	Human evolutionary genetics	■	
Lindsay	Human developmental genetics		■
Crompton	Evolutionary biomechanics (human)		

Salient interviews

For a number of the researchers it was possible to give a simple, unqualified reply to this question. On the ontogeny side, these were Buckley (Buckley 1.25.27), McGuffin

(McGuffin 0.36.20) and Lindsay (Lindsay 0.53.0). On the phylogeny side, there were Jobling (Jobling 0.56.05) and Jones.[226]

Crompton quite bluntly said 'Neither'. We may briefly expand on his reply, and those of Hutchinson, Smith and Mace.

Robin Crompton

Asked whether the main concern in his research in evolutionary biomechanics was phylogeny or ontogeny, Crompton replied:

> Neither. Sorry! (Crompton 0.19.15)

He went on to explain:

> It's function. I'm interested in function. I'm not interested in relationships, and I'm not really interested in development. I mean, I obviously have to deal with them, but I'd rather do it from a safe distance. So neither, I'm afraid.

John Hutchinson

When John Hutchinson, the other evolutionary biomechanist was interviewed, this question had not yet entered the set of criteria. However, as we have already seen, Hutchinson was strongly interested in the way that genomics "deals with major phylogenetic relationships of groups". He said

> I need to know phylogenetic relationships of major lineages, and that includes living animals (Hutchinson 0.14.00).

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[226] In the case of Jones, the response to this criterion communicated by email after the interview.

This aspect of his work was so important, indeed, that when he was asked for a criterion that strongly distinguished evolutionary biomechanics from other disciplines being studied here, he offered these two candidates:

> The things that stand out the most to me are that it uses the phylogenetic framework, that it uses physics. Those are the two things that basically, you know - physics plus phylogeny, really (Hutchinson 0.36.00).

Chris Smith

Smith approached this question from "a strong medical perspective" (Smith 1.16.30) and this led him to the following conclusion:

> So I think that the ontogenetic area - the development of the individual – human, in this case – is the most important thing.

At the same time he recognised that

> Genomics of course will also illuminate the evolutionary process, we talked about the sea urchin for instance, and we talked of the genomics of mitochondrial DNA. Indeed the evolutionary insights provided by molecular biology and neurobiology have proved fascinating: the whole area known as 'evo devo' where palaeontology and molecular embryology come together is fascinating (Smith 1.17.19).[227]

However, on "a normal day in the lab", as Holdsworth put it, the molecular neurobiologist agreed that his aim would be "to try to find some way [to] ameliorate neurological conditions", which meant that the focus would be on ontogeny.

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[227] For a recent introductory account of evo devo, see Carroll (2005).

Ruth Mace

When Ruth Mace, the human behavioural ecologist, was asked whether her main concern was phylogeny or ontogeny (Mace 1.13.15), she replied:

> Well those would both be. I would say the *main* concern is adaptive function. But, you know, people are interested in phylogeny, and they are interested in ontogeny. [...].
>
> I mean, some behavioural ecologists are not interested in phylogeny or ontogeny. I happen to be quite interested in phylogeny. But I'm really interested in population history, which is – I mean, I'm interested in cultural phylogeny (Mace 1.14.14).

We have already seen examples of the behavioural ecologist's interest in cultural phylogeny – for example, the cultural phylogeny of language or of styles of artefact. However, Mace was anxious to stress her interest in 'function', saying:

> Well, I'm certainly interested in the development of behaviour. Phylogeny is evolutionary history. And they're both separate questions from 'What is its function?' - which is what human behavioural ecologists are primarily, mainly concerned with.

Holdsworth suggested that, as far as phylogeny and ontogeny went, it was perhaps "a bit of each", but Mace was not satisfied:

> Or neither, really. I would say the main concern was neither of those. The main concern was the adaptive function. You don't need to know the phylogeny or the ontogeny to know that (Mace 1.15.05)

Analysis of diversity

The diversity of perspective between those interested, respectively, in phylogeny and ontogeny was duly noted. Beyond that, it was interesting to receive the 'Neither' responses of the evolutionary biomechanist, Crompton, and the behavioural ecologist, Mace. Each from the point of view of their own discipline advanced the argument that, for the analysis of function, it was not necessary to prioritise either the phylogeny or the ontogeny.

Assessment of the criterion

The responses to the criterion confirmed that when we ask about the ways in which various disciplines are using genomics to study the causes of human behaviour we must remember that some are working from a phylogenetic perspective and some from an ontogenetic one. In the past a great portion of the nature-nurture debate has involved an assumption that ontogeny was the focus of interest. At the same time – and Crompton and Mace's answers showed this - it was interesting to note that by no means all the respondents fitted into the binary framework of the question as posed.

There was a special validation of the power of this criterion in the response of Hutchinson. For him only two criteria were needed to profile the discipline of evolutionary biomechanics: phylogenetics and physics.

Chapter C11 – Does the research draw on fossil evidence?

The matrix for the criterion

The responses to Criterion 10 yielded the matrix displayed below in Table C11.01.

Table C11.01. Matrix for Criterion 10:
'*Does the research draw on fossil evidence?*'

Researcher	*Discipline*	*Yes*	*No*
Jones	Biomolecular archaeology		
Hutchinson	Evolutionary biomechanics (dinosaur)		
Smith	Molecular neurobiology		
Buckley	Down Syndrome research		
Mace	Evolutionary anthropology		
McGuffin	Research into normal and abnormal behaviour		
Jobling	Human evolutionary genetics		
Lindsay	Human developmental genetics		
Crompton	Evolutionary biomechanics (human)		

Salient interviews

Criterion 10 was added to the list after the interviews with Jones and Hutchinson had already taken place. The idea that some disciplines were marked by the appeal to fossil evidence emerged from these initial interviews, one with a biomolecular archaeologist and the other with an evolutionary biomechanist having a strong interest in extinct species. It became apparent that this was a criterion for differentiating the workbenches of disciplines interested in the study of behaviour. Although Jones and Hutchinson had not specifically

been interviewed on this criterion their respective positions on it were obvious, and were in any case confirmed in the follow-up to the interviews.

Researchers who draw on fossil evidence by this fact share some common concerns. The same cannot necessarily be said of those who do not. In the latter category were Smith, Buckley, Mace, McGuffin and Lindsay. In only two of these instances was the negative reply nuanced. In the case of Lindsay it was lightened by humour:

> *Lindsay*: And we don't draw on fossil evidence! A fossil in situ hybridisation – I mean, yes! Maybe. Maybe one day! (Lindsay 0.53.10).

In the case of Smith there was a proviso concerning the neurobiology of Homo neanderthalensis that acquired additional resonance from subsequent events. We shall come to this in a moment.

The interviews we shall consider are those with Hutchinson, Smith, Jobling and Crompton.

John Hutchinson

Asked to reflect on criteria that might serve to distinguish evolutionary biomechanics from some other disciplines, Hutchinson responded as follows:

> Let's see if I can think of anything else that's intrinsic. I guess, if you want to separate archaeology, anthropology and other evolutionary approaches, dealing with fossils, I guess, would become a relevant criterion, because archaeology, kind of by definition, doesn't involve fossils, per se, it's kind of post- , or pre-fossil material, whereas palaeoanthropology I think would involve fossils (Hutchinson 0.38.21). [...]

> That kind of gets into the question of definitions: how you define the difference between archaeology and palaeoanthropology. I would say a lot of people would say, well, 'fossils' draws the line.

The extent to which archaeologists would concur with this remains to be established. The question lies outside the scope of this discussion. However, the quotation is interesting in that it puts forward the idea of the use of fossils as evidence as providing a criterion for the conceptual mapping of different disciplines, and it confirms the importance of fossils for "other evolutionary approaches" such as Hutchinson's own – that of evolutionary biomechanics.

At the same time, Hutchinson clearly pointed to the major problem associated with fossil evidence, namely the incompleteness of the fossil record. When discussing the evidential value of footprints, Hutchinson had remarked that

> The problem is you can never tell what species made the footprint. It's normally only very general details: well, this is a big, two-legged animal – something like that. So it's limited in its ability to give you very much to draw on (Hutchinson 0.15.53).

Holdsworth asked if there was any way of cross-referencing other factors so as to narrow down the choice. Hutchinson replied:

> You can to a degree, yes. By knowing what animals were present in a given area at a given time, you can kind of narrow down your list of likely candidates, but then you're always kind of left wondering, well, what if – given our fossil record limitations - what if there was another animal there which we just don't know about, and it made the footprint? It makes it very hard. We know all too well how incomplete the fossil record is. We may know the skeleton of an animal from Africa, and we find footprints in America. Even though that animal in Africa lived at the same time, it couldn't have made those footprints in America. And then later

on you find that it *was* there in America – you just didn't find any fossils of it yet. The field is so young. We just haven't found everything (Hutchinson 0.16.46).

Chris Smith

To the question about fossil evidence in molecular neurobiology, Chris Smith's initial response was largely negative. However, he quickly qualified this reaction (Smith 1.18.30):

> Not a great deal, no. Not yet! If they dig up one of these nice mammoths in Siberia, sufficiently well preserved, we might get some interesting things. And of course, I mean, one shouldn't dismiss it. We're just talking in 2007, you know. A few years down the track we might be able to get Neanderthal DNA and see if the FOXP2 gene – the one that is alleged to have something to do with speech[228] - is represented there or not. It might be a small variation, but, of course, of huge significance – from the general point of view, understanding who we are, how we got here (Smith 0.19.39).

Holdsworth recalled the thesis that *Homo sapiens* is not descended from the Neanderthals. Smith commented:

> No, but you might say that linguistic ability – related to the the development of this particular gene which is alleged to be significant in speech occurred – this is the hypothesis - occurred in humans but not in Neanderthals, and consequently gave humans an advantage (Smith 1.20.14).
>
> *Holdsworth*: Ah, it would be interesting to find out if they had *not* got it?
>
> *Smith*: Well, it would be interesting to find out if the Neanderthals had *not* got the gene with the sequence we have. [...] Whether or not the gene is present in its

[228] FOXP2: see Chapter A4 above.

> contemporary sequence, the matter is of molecular neurobiological interest, insofar as speech is a feature of brain. (Smith 1.20.46)

Smith had spoken of possible future developments "a few years down the track" from 2007. This was prescient, although developments seem to have come even more quickly than he anticipated. On 12 February 2009 it was announced that a first draft genome of the Neanderthal genome had been completed. A press release stated that the research project had been conducted by the Max Planck Institute for Evolutionary Anthropology, Leipzig, Germany, and the 454 Life Sciences Corporation, Branford, Connecticut, USA. The project was directed by Prof. Svante Pääbo, Director of the Institute's Department of Evolutionary Anthropology.[229] The press release added that

> In order to aid in the analysis of the Neanderthal genome, Dr. Pääbo has organized a consortium of researchers from around the world that plans to publish their results later this year. They will look at many genes of special interest in recent human evolution, such as FOXP2, which is involved in speech and language in modern humans, as well as genes such as the Tau locus and the microcephalin-1, implicated in brain aging and development, respectively.

In his presentation to the press conference, Pääbo explained that research into Neanderthals was not merely interesting for its own sake, or even (only) for the opportunity to make direct comparisons between modern humans and Neanderthals. It enriched the study of the phylogeny of modern humans by bringing the time to a last common ancestor down from perhaps 5 to 7 million years (humans and chimpanzees) to about 400,000 years (modern humans and Neanderthals), thus making it possible to be much more precise in the dating of mutations traced in modern humans.

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[229] Pääbo, Svante *et al*. (2009): http://www.eva.mpg.de/english/press-kit-neandertal.htm (Consulted 18 April 2009). Links from the webpage cited lead to the Press Release and also to a Press Conference Livestream of Pääbo's presentation.

Mark Jobling

When this question was put to Mark Jobling, the researcher in human evolutionary genetics, the answer was unequivocal (Jobling 0.56.05):

> Yes. Certainly. Strongly. And I think that it's as we say in our book: there are different records of the past. The genetic record is one, and that's what is our focus, but there are the other records. The palaeontological record is another very important one. We want to know to what extent the genetic record is giving a similar picture to the other kinds of records: the archaeological record, the palaeoclimatological record, the fossil record (Jobling 0.56.53).

The topic of fossil evidence had already come up in the interview, in an exchange about the relation between the two concepts, mentioned by Jobling, of 'anatomically modern humans' and 'behaviourally modern humans'. Holdsworth had asked if these were the same thing, and Jobling replied (Jobling 0.25.03):

> No, not at all. And, I mean, it's, again, not a subject for geneticists, in a sense. It's a subject for palaeontologists. Because it's clear that you see evidence of anatomical modernity earlier than you see evidence of behavioural modernity. And behavioural modernity is associated with things like burial practices, making tools, certain things like the use of ochre in graves, the production of sort of art, and evidence of certain kinds of living, in the past. So you have anatomical modernity and then later on you see these things cropping up, and the problem always of course is one of dating these things and also the survival of the evidence. With human fossils and evidence of past human behaviour the evidence is extremely scarce. There just isn't very much of it. And so it's very much influenced by individual finds. Many of those are very controversial, because people disagree about what some of those things are. So there does appear to be a time-difference between being anatomically modern and behaviourally modern. But how real that is, I'm not entirely sure. I

> think it could be to an extent artefactual, based on dating problems and just general scarcity of evidence. But I'm not an expert on that (Jobling 0.26.36).

Holdsworth observed that some of the traits that Jobling had mentioned were ones which people cited when they were trying to distinguish between *Homo sapiens* and Neanderthals. Jobling replied:

> But Neanderthals buried their dead. I mean, clearly Neanderthals were - are anatomically distinct from *sapiens*. So you have that distinction. I think when people look on the lineage what they see is the lineage, which is anatomically similar to us, and they'd assume that these people may have been our ancestors, and then they look at behavioural modernity among them. So it doesn't mean to say that other anatomically distinct humans didn't have behaviours that we would regard as typical of, you know, humans. So, tool-making and the use of beads and things like that. There is evidence that Neanderthals did that (Jobling 0.27.40).[230]

Holdsworth noted that there was controversy about whether in fact Neanderthals copied *Homo sapiens*. Jobling's response was:

> Yes. I think 'Who knows?' is the answer to that. Because, again, the evidence is so thin that you can build a career on a fragment of skull. There's a strong pressure for people in the field to come up with something rather surprising or interesting rather than something rather humdrum or similar to what somebody else found. That's one of the problems in palaeontology, I think (Jobling 0.28.09). [...]

[230] Jobling et al. (2004), pp.247-248.

On this criterion Crompton was also unequivocally positive. Asked by Holdsworth 'Does the research draw on fossil evidence? (Crompton 0.19.30), the evolutionary biomechanist replied:

> Absolutely. Yes.

This is the reply one would have expected from the co-author of a paper we have already referred to,[231] on 'Locomotion and posture from the common hominoid ancestor to fully modern hominins, with special reference to the last common panin/hominin ancestor'.[232] This article contains an extensive review of the fossil evidence for the subject it discusses.[233]

Elsewhere in the interview, Crompton indicated that there could be differences of palaeontological emphasis in the study of fossilised bones. His interest in them was as a source of evidence of function, rather than as clues to systematic. This point came up during a discussion of Crompton's use, in the context of evolutionary biomechanics, of the physical concept of work (Crompton 0.05.59). Holdsworth noted that not all authors gave it such a central place in their analysis. As an example he cited a book by Chris Stringer and Peter Andrews - *The complete world of human evolution* (2005) – that nowhere mentioned the term, or the concept 'work'. Crompton explained that

> They come from a very different tradition than I come from.
>
> *Holdsworth*: How would you describe that?

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[231] Chapter C2 above.
[232] Crompton, Vereecke and Thorpe (2008).
[233] Ibid., pp. 511-35.

> *Crompton*: Well, Peter Andrews in particular is quite an old-fashioned comparative anatomist. Both of them are really concerned with relationships amongst animals, not function at all. It's not their strong point. What they actually do these days is phylogenetics and systematics. Function is not their area of research at all. They're concerned with phylogenetics, systematics, relationships - establishing relationships amongst fossil species and things like that (Crompton 0.07.31).

Reference has already been made in the present chapter to certain difficulties associated with the use of fossil evidence. Hutchinson mentioned the incompleteness of the fossil record. Jobling pointed out that the scarcity of what fossil evidence we do have means that research is "very much influenced by individual finds", many of which are, in any case, "very controversial".

In his writing, Crompton has drawn attention to another limitation of fossil evidence – albeit one that can be made good by complementing it with other techniques.

Carey and Crompton (2005) is an article on 'The metabolic costs of 'bent-hip, bent-knee' walking in humans'. The research reported in the article concerned the likely gait of *Australopithecus afarensis*, based on the skeleton known to science as AL-288-1 and to the public as 'Lucy'. It is, of course, difficult to infer behaviour such as gait from incomplete fossilised skeletons. It was a premise of Carey and Crompton's research that different candidate gaits entail different metabolic energy costs, and that these will therefore be subject to the action of natural selection:

> The measure most pertinent to natural selection, however, is more likely to be the complete, physiological, or metabolic energy cost.[234]

In other words, metabolic energy cost gives scientists a measure that can be used for the purpose of comparing hypothesized gaits. However, as Carey and Crompton immediately go on to say,

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[234] Carey and Crompton (2005), Abstract, p. 25.

We cannot measure this parameter in a fossil.

What these researchers did was to model different gaits using human subjects in the laboratory. The chief aim was to test one particular hypothetical gait - 'bent-hip, bent-knee' (BHBK) walking - which could be seen as an evolutionary half-way stage between forms of arboreal locomotion and the upright bipedal gait characteristic of modern humans. The results they reported showed that in BHBK walking energetic efficiency was halved when compared with "normal upright posture" while thermal stresses and water loss were doubled. They inferred that "short bursts of locomotion in a BHBK gait may well have been possible", but argued on the basis of their results that "as a consequence of the high thermal and muscular loads this would induce, a long period of recovery (150% of activity time) would be needed post-exercise".[235]

In this literature it is to be noted that where 'metabolic' energy costs are cited this is a necessary specification, since other energy inputs and outputs are involved in human behavior as well as those that take the form of chemical energy. Carey and Crompton's research on gait was an analysis of "the joint motion typical of normal human bipedalism" and other hypothesised gaits. The hypotheses could be tested, among other things, from the "skeletal proportions" known from fossil evidence.[236] Researchers working in this area are able to calculate the energy balance of human motor behavior to a high degree of resolution as we may deduce from the statement by Carey and Crompton that, in different gaits under study, there may be variation

> in the possibility of energy conservation by exchange of potential and kinetic energies, the mechanism which is known to be the basis of the efficiency of human bipedal walking.[237]

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[235] Ibid., p. 38.
[236] Ibid., p. 26.
[237] Ibid.

In Crompton's research, then, fossil evidence is integrated with data gathered from trials with living human subjects – and also with data gathered in the field from the study of contemporary hominoids. Concerning these last, Crompton and his colleagues have written:

> The locomotor ecology and biomechanics of the living apes remain a surprisingly underutilized resource – even when several of our hominoid cousins are in immediate danger of extinction in the wild.[238]

Analysis of diversity

The discussions of Criterion 10 illustrated a wide variety of research objectives, methods and practice, ranging from total disinterest in fossil evidence to a significant level of dependence on it. Jobling put the matter in context when he noted that there are "different records of the past" and that the genetic record can fruitfully take its place alongside other records: the palaeontological, the archaeological and the palaeoclimatological.

Assessment of the criterion

If the interviews were consistent with Jobling's vision of there being different records of the past, however, it is also true to say that they exemplified different visions of the route to the present. The criterion did not merely serve to identify the disciplines having a fascination with the archaic. What makes the difference is the evolutionary dynamic, manifested by the research of Crompton and similar workers. As we have just seen, Crompton is an authority on the fossil evidence for the evolution of hominoid locomotion, yet his research world is a compound workbench that combines evidence of the archaic with direct observation of living hominoid cousin species in the wild and behavioural trials with human subjects in the laboratory.

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[238] Crompton, Vereecke and Thorpe (2008), p. 503.

This criterion highlights the issue of chronological focus in the study of the causes of human behaviour. A case in point was that of the latest research by Pääbo and others on the Neanderthal genome and its implications for the time-depth of methods of molecular phylogenetics.

Chapter C12 – Is Newtonian mechanics relevant to the research?

The matrix for the criterion

The responses to Criterion 11 yielded the matrix displayed below in Table C12.01.

Table C12.01. Matrix for Criterion 11:
'*Is Newtonian mechanics relevant to the research?*'

Researcher	*Discipline*	*Yes*	*No*
Jones	Biomolecular archaeology		
Hutchinson	Evolutionary biomechanics (dinosaur)		
Smith	Molecular neurobiology		
Buckley	Down Syndrome research		
Mace	Evolutionary anthropology		
McGuffin	Research into normal and abnormal behaviour		
Jobling	Human evolutionary genetics		
Lindsay	Human developmental genetics		
Crompton	Evolutionary biomechanics (human)		

Salient interviews

This was another criterion added to the list after the first two interviews (with Jones and Hutchinson, respectively). Negative responses were given by Jones, Smith, Buckley, Mace, McGuffin and Jobling. Buckley's negative was slightly qualified, and Smith's permitted a brief digression on physics in general and quantum physics in particular. Hutchinson and Crompton were positive, while Lindsay described one area of her research in which the criterion was relevant. In the case of Buckley, it was agreed that Newtonian mechanics was relevant to the human motor skills that were studied in connection with Down syndrome,

although Buckley doubted whether in fact any researchers had "come at it from that sort of direction" (Buckley 1.27.30). Naturally, no behaviour is exempt from the laws of physics, so saying that a given researcher's response was 'negative' in this context merely means that, for that discipline, Newtonian mechanics was not an area of proactive enquiry but rather what Smith called "a background assumption" (Smith 1.27.20).

It was the interview with Hutchinson that paved the way for the adoption of this criterion, so we shall look at the relevant passages in that conversation in a moment. The relevance of Newtonian mechanics to evolutionary biomechanics was succinctly confirmed afterwards in the interview with Crompton, who simply remarked (Crompton 0.20.00):

> Highly relevant. Crucial.

We shall also take a brief look at the responses of Lindsay and Smith.

John Hutchinson

The topic first arose in the interview with Hutchinson. It came up spontaneously, rather than in response to a specific question. This was when Hutchinson was asked what criteria might serve to characterise evolutionary biomechanics. As we have already had occasion to note (in Chapter C10), Hutchinson chose to mention the discipline's twin focus on phylogeny and physics, adding:

> Newtonian mechanics, I guess, would be the most specific way of phrasing it (Hutchinson 0.36.15).

Earlier in the interview, there had been some discussion of the relation between evolutionary biomechanics and physics, specifically touching on the significance in this context as gravity as a selective pressure. An example might be the role of gravity in the evolution of the posture and locomotion of a large animal like a hippopotamus. Hutchinson commented that

> one of the things about my work is I work on larger animals in which gravity plays an even larger role. As you move to the smaller end of the scale other forces become more important, like viscous and fluid forces. So again gravity becomes pretty important there (Hutchinson 0.31.31).

Elsewhere in the discussion, Holdsworth asked Hutchinson whether he would agree that many disciplines that work on human behaviour often did not take into account bioenergetics or biomechanics (Hutchinson 0.9.25). Hutchinson replied:

> Sure, I think – well, it's a matter of specialisation. A lot of people don't consider anything outside of their specialty. It's kind of hard. The extremely specialised nature of science today is that everyone's so specialised in what they do. Rarely, you find someone who does everything just right. But, yes, it's true in general. It takes a lot of training to really properly interpret mechanics and physiology; so a lot of people either intentionally or unintentionally shy away from it (Hutchinson 0.10.02).
>
> *Holdsworth*: Yes, and yet it's easy to see that it could be important in the evolution of hominid and human behaviour.
>
> *Hutchinson*: Well, I think for hominids it's certainly gotten more attention than it has in most other groups, but maybe that's just a factor of a lot of research in general being concentrated there (Hutchinson 0.10.26).

Susan Lindsay

To the question about the relevance of Newtonian mechanics to human developmental genetics, Lindsay replied:

> Newtonian mechanics. Well, that's a possible yes (Lindsay 0.53.13).

If we had a way – and we don't do this, but one of the things that's obviously very interesting, is what regulates or shapes growth. And from the brain perspective the starting – or the point where we start looking at is a tube. And that tube then bends at specific places, and also structures grow out of it (Lindsay 0.53.56). [...]

So these lateral ventricles, so these structures here – this is kind of the remains of the tube where it's been bent, and these lateral ventricles that are going to, in human, expand enormously – actually to grow right up and cover the whole of the rest of the brain basically, apart from the cerebellum – apart from this bit right at the back (Lindsay 0.54.18).

I'm sure that that the forces – that there will be forces of just physically pushing out and expanding – and that the role of pressure will make a difference in how rapidly – and maybe the shape – that these lateral ventricles expand (Lindsay 0.54.45).

And we know that's true, because if with some disorders where the skull - because usually the skull in humans – well, the skull - there's room for expansion. Because after babies are born, the skull still keeps expanding, which allows the brain to expand (Lindsay 0.55.02).

So if you have a situation where the skull fuses early, there isn't any further, I mean, the brain stops growing (Lindsay 0.55.12). [...]

So there are disorders where the brain sutures fuse, and then the - .

Holdsworth: Could you mention the name of such a disorder?

Lindsay: Craniosynostosis. And there are a number of these. And the effect on brain development is that usually and unfortunately the patients are mentally retarded. So the brain doesn't develop properly. So the mechanical and physical forces are important (Lindsay 0.55.52).

> And there may well also be an evolutionary dimension. In the sense there must have been a period when it was – when obviously the brain expanded, but there must also have been a mechanism to allow the skull to expand as well (Lindsay 0.57.09). [...]
>
> So it may be that – well, presumably in chimps also the skulls, the sutures don't fuse. So maybe they just didn't fuse for a longer and longer period in development, which then allowed the brain to expand (Lindsay 0.57.44).

Chris Smith

When the molecular neurobiologist Chris Smith was asked about the relevance of Newtonian mechanics (Smith 1.21.45), he replied:

> No. I think the answer to that is 'no', but you might put in quantum theory, which probably is relevant. Because we're right down at the molecular level, and of course the chemical bond is a quantum phenomenon. But even that, I think, is below the level with which molecular neurobiologists are concerned. So I think the answer is 'no'.

Holdsworth recalled that Smith's list of publications included work in that area. He asked Smith what line he had developed (Smith 1.23.00).

> Well, what I was doing was a historical account, because if you're interested in mind/brain issues you'll know that people like Penrose, a mathematician down at Oxford, and a number of other quite eminent physicists – and particularly the quantum physicists of the 1920s and 30s – the early quantum physicists at the start of the subject – believed that their break-through at that level of physics – of matter theory - would provide a solution to the age-old brain/mind problem: how are 'matter' and 'mind' related? And because they – because the quantum physicists believed that consciousness is implicated in the dynamics of matter at that level – a

very curious thing - they thought there would be a tie-up. So I wrote a paper on that early thought which, in my view, came to nothing in the 1920s and 30s (Smith, 2006). And my more recent paper has been on where we are today, in the 21st century, on that issue (Smith, 2007). And I still think that we've not got there yet. Partly because I think there's a big divide between people who've been trained up in physics and have gone into quantum physics and those who've been trained up in neurobiology. And the quantum physicists don't understand the complexity of the synapse, which is where they think these quantum effects occur (Smith 1.25.10).

Holdsworth: Sorry, who don't understand?

Smith: The quantum physicists, because they're not in the area. They're using an incorrect model there, I think. And the neurobiologists, of course, are not sufficiently able to understand the mathematics of quantum physics to be able to counter the physicists' theories adequately. Now, I can't pretend to understand quantum physics at any level either, but I did take a physics degree, maths degree in my youth. So I've got a little bit of grip on it. And so I've tried to produce a paper that shows the difficulties and mutual misunderstandings. I think the mind/body problem – mind/brain problem - is a real issue. I'm not sure whether we can find a solution – whether it's soluble by us, so to speak, by human beings (Smith 1.26.18). [...]

Anyway, so that was obviously a question about Newtonian mechanics. As far as molecular neurobiology is concerned it's just a background assumption (Smith 1.27.20).

Analysis of diversity

The chief source of diversity in the responses to this criterion was the simple fact that evolutionary biomechanists are bound to take a professional interest in the interplay between skeleto-muscular systems and mechanical forces. But how 'simple' is this fact? Is

it a ‘simple’ fact that other professional students of the causes of behaviour tend to neglect these phenomena? One answer is to agree that the topic may validly be placed on the shelf marked ‘background assumptions’. Another answer may be the one suggested by Hutchinson:

> It takes a lot of training to really properly interpret mechanics and physiology; so a lot of people either intentionally or unintentionally shy away from it (Hutchinson 0.10.02).

Assessment of the criterion

The criterion served to draw out a difference between biomechanics and other disciplines that, as we have just seen, may either be a banal, contingent fact about respective workbenches, or the sign of a profound fault-line running across the study of behaviour.

Chapter C13 – Is the research intended to have a clinical application?

The matrix for the criterion

The responses to Criterion 12 yielded the matrix displayed below in Table C13.01.

Table C13.01. Matrix for Criterion 12:
'*Is the research intended to have a clinical application?*'

Researcher	*Discipline*	*Yes*	*No*
Jones	Biomolecular archaeology		
Hutchinson	Evolutionary biomechanics (dinosaur)		
Smith	Molecular neurobiology		
Buckley	Down Syndrome research		
Mace	Evolutionary anthropology		
McGuffin	Research into normal and abnormal behaviour		
Jobling	Human evolutionary genetics		
Lindsay	Human developmental genetics		
Crompton	Evolutionary biomechanics (human)		

Salient interviews

This was the fourth of the set of new criteria added after the interviews with Jones and Hutchinson had taken place. Therefore this criterion was not discussed directly with those researchers. The interview with Jones did give rise to the interesting passage quoted below. In the follow-up to the interview, Jones volunteered a negative answer to the question whether his research was 'intended to have a clinical application'. The topic did not come up at all in the interview with Hutchinson, and the relevant boxes in the Criterion Matrix at this point are therefore shaded in grey. Looking at the wider context of Hutchinson's work,

it is pertinent to recall that his institution is a veterinary college and that research in his field contributes to knowledge of the biomechanics of large animals.

This criterion was added, not out of any intention to conduct a utility audit of the research investigated, but rather to capture any signs of a tendency for clinical priorities to influence research agendas in the target disciplines.

Martin Jones

The key passage (for present purposes) in the interview with the biomolecular archaeologist Martin Jones came during the discussion of Criterion 4: 'Does the research typically draw on the findings of genomics?' Jones responded as follows:

> I think, one thing actually is that - to elaborate on that - that they don't just *draw on* the findings: their actual practice is rather steered by the progress of genomics. And the reason for that is – it will vary on your list, but on our list, in our departments, the sums of money, the volume of research are such that we have to be responsive to fields with more money. So, for example, on the anthropological front, it's inevitable that we will respond to what medical research is doing, even if it has different objectives. And in looking for the spread of agriculture, it's inevitable we respond to what genetic breeding and genetic modification is doing, simply because the scale of activity in those fields is just something that we kind of hang onto by the skirt-tails. And a new departure in either of those fields, that may have nothing to do with the human past, will nevertheless have an impact on even the questions we're asking because there are new questions we can ask (Jones 0.24.03).

Chris Smith

When the question - 'Is the research intended to have a clinical application?' - was put to him directly, Chris Smith, the molecular neurobiologist, replied (Smith 1.18.14):

Yes. I think the answer to that is affirmative.

Elsewhere in the interview, Smith offered a personal view of the motivation behind his work. This came during the discussion of Criterion 9, 'The main concern is phylogeny or ontogeny?' (Smith 1.15.42). Holdsworth had just reassured Smith that he was not being interviewed as a spokesperson for his discipline. Smith said (Smith 1.16.05):

> Well, I would say personally it's the ontogenetic which is the main focus. I'm interested in knowing 'how'. I've got a strong medical perspective. My feeling is that for the privilege of studying molecular neurobiology you must put something back into the taxpayer's pocket, so to speak, and I think that payment back is in the medical area. So I think that the ontogenetic area - the development of the individual – human, in this case – is the most important thing. Genomics of course will also illuminate the evolutionary process, we talked about the sea urchin for instance, and we talked of the genomics of mitochondrial DNA. Indeed the evolutionary insights provided by molecular biology and neurobiology have proved fascinating: the whole area known as 'evodevo' where palaeontology and molecular embryology come together is fascinating (Smith 1.17.19).

The matter came up again later, in the general and concluding discussion. Holdsworth noted that Smith had well expressed his conception of the link with the clinical realm, in the sense that Smith considered that it was highly desirable that molecular neurobiology could generate findings of potential practical use in the clinical context (Smith 1.36.22). He went on to ask Smith a question about the direction of research in molecular neurobiology. In his opinion, did it tend to be influenced or orientated in accordance with clinical objectives? Smith answered:

> To some extent. You see, molecular neurobiology is an expensive thing to do. You've got to have a lab; you've got to have a lot of equipment; you've got to have research students. So you've got to get money from somewhere. And the money'll come from a grant from the grant-forwarding authorities. And these will not support

> work they don't see some outcome from. It's not their money they're distributing: it's the public's money they're distributing. And so, in that sense, they want to see an outcome in the medical field, I think. I mean, that's not going to be always the case, and sometimes the connection to medicine is somewhat difficult to see. I mean, take the case that I've just talked about, the potassium channel for which MacKinnon got his Nobel Prize, worked out from a bacterial system. You might think, looking at it, well what on earth has that got to do with anything medical? How is that going to help someone who's suffering from a neurological condition? It's a long set of steps to get to the answer. But in fact it's very, very vital - in my view - to understand these channels: how they work, and how they may go wrong. When they go wrong you get the neuropathology. They're called 'channelopathies', and there are quite a lot of channelopathies around. I think the criticism is that although there are a lot of different channelopathies about, they are individually fairly rare. They're not like malaria or one of these other conditions that affect millions upon millions of people. They're rather minority interests. And I think the criticism is that putting a lot of money and effort into that, which is probably going to affect perhaps a few hundred people in Great Britain, is perhaps questionable, when you might have put it into malaria or obesity or whatever (Smith 1.39.24).

Sue Buckley

When Sue Buckley, from Down syndrome research, was asked this question - 'Is the research intended to have a clinical application?' – she replied (Buckley 1.25.27):

> Again, it depends what you mean, doesn't it? There's another whole piece of this. Well, first of all, of course, there's been quite a lot of work on Down syndrome patients' health-care needs. So they get their cardiac surgery, etc. They get their thyroids tested and get thyroxin, if they need it. And they get their hearing tested. So there's been a piece looking more closely at their health-care and medical needs, where obviously there can be an application. That obviously hasn't been linked to genetics (Buckley 1.26.03). [...]

> So there's obviously a clinical application for health-care. There's educational application from what we do. There's educational therapy. Now some people would put therapy under a broad clinical heading. But clearly there are educational and therapeutic possibilities (Buckley 1.26.26).
>
> Now, as I've told you already, the people who are studying the genes claim that there will be drug treatments, but nobody's anywhere near anything like that at the moment in my view. So there are no proven outcomes at all (Buckley 1.26.45).

Elsewhere in the interview the discussion touched on indirect reasons for undertaking research into the effects of the trisomy on chromosome 21: in other words, opportunities for studying other areas of clinical interest that are bound up with Down syndrome. Buckley (1.20.20) mentioned the following example:

> One of the things I should tell you is some of the reasons for the interest of the geneticists in Down Syndrome is that they are at an increased risk of getting Alzheimer's – or thought to be. It's a bit controversial. OK? They seem to be at more risk of ending up with an Alzheimer's dementia, though some people argue it's a knock-on consequence of more rapid ageing: so by 50 they're more like a 70-year-old. So some people say the rates of dementia at 50 – well, some people would say it's a 30-year shift – that their rates of dementia at 50 may be similar to the rest of the population at 80 (Buckley 1.21.12).
>
> Which puts a slightly different shine on what you're looking at: if it's some sort of accelerated ageing, or if it's something specific to getting dementia. The brains have plaques and tangles in that look like Alzheimer's for the majority of people with Down syndrome, though they don't all get the symptoms, so that plaques and tangles on their own don't predict Alzheimer's. [...] (Buckley 1.21.35).
>
> The reason I'm telling you that is that's one of the reasons money pours into looking at chromosome 21, hoping that it will tell us something about the causes of

> Alzheimer's-type dementia in the rest of us: that there's something on chromosome 21 that might be relevant (Buckley 1.21.50).

Buckley went on to cite other links between the trisomy and medical conditions likely to be of interest to researchers.

> Similarly, half the children have structural cardiac defects at birth; so people interested in why children should be born with cardiac defects have also been interested in chromosome 21.
>
> People with Down syndrome are almost unheard of in terms of getting solid tumorous cancers. Solid tumours (Buckley 1.22.21). [...]
>
> They also don't get their arteries clogged up. They've arteries like babies as old people. In other words, they don't get arteriosclerotic disease. So there's some pluses as well as some minuses. So you can see, people interested in just some of those things are interested in what's happening on chromosome 21 (Buckley 1.22.43).
>
> So there's a lot of interest in the genetics of chromosome 21 for a whole variety of reasons. Yes. Not just because of an interest in improving things for people with Down syndrome (Buckley 1.22.57).
>
> And some of those people might be doing – some of them will certainly be looking for individual differences in genetic material on chromosome 21 that might explain why half of them have perfectly normal hearts and the other half don't. [...] (Buckley 1.23.22).

Ruth Mace

When Ruth Mace, from human behavioural ecology, was asked the question - 'Is the research intended to have a clinical application?' (Mace 1.15.13) – she replied:

> It's not intended to. I mean, I think it can. You know, there's this kind of branch of evolutionary medicine where people are trying to say that evolutionary principles can be relevant. So I wouldn't - . I would say 'no' to that, for the most part (Mace 1.15.33).

So, although Mace decided on a negative response in general, she did refer to the literature on evolutionary medicine. We had occasion to refer to the work in this area of Randolph Nesse and other authors in Chapter C1 during the introduction to the research of Mark Jobling in human evolutionary genetics.[239]

Peter McGuffin

Peter McGuffin was broadly positive, but in his reply he to tried to make a distinction, saying

> it's intended to have a clinical relevance, if not an application. So, an application - application is difficult. There are some people who view the sort of research I do as terribly applied, but those are people who do extraordinarily basic research on molecules or organisms or, you know, cells in vitro and nothing else. My more clinical colleagues regard me as a basic scientist, so I've got stuck in the middle. Well, yes, of course, most of my research has been funded by the Medical Research Council, so it has medical, clinical applicability in the broader sense (McGuffin 0.37.24).

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[239] Nesse and Williams (1994, 1998), Trevathan et al (2007) and Stearns and Koella (2008).

Mark Jobling

Mark Jobling also wanted to make a distinction (Jobling 1.01.55) in connection with his research:

> It certainly has a clinical interest. I think it would be too strong to say that it has a clinical application. But it is interested in the history of human populations and all genetic causes of disease - or all genetic influences on disease - that come to be distributed in populations because of our evolutionary history. Some through neutral processes like drift, and some through non-neutral processes like selection or migration. So a general understanding of those things, I think, is important if you want to - for example - learn about the genes that influence Type 2 diabetes susceptibility (Jobling 1.02.47).
>
> *Holdsworth*: Right. So medicine could perhaps find information of interest coming out of human evolutionary genetics?
>
> *Jobling*: Yes. Definitely (Jobling 1.03.01).

Susan Lindsay

Before the interview with Susan Lindsay reached Criterion 12 there had already been some discussion of how her research contributed to the understanding of disorders. Holdsworth had asked if it was correct to say that Lindsay was concerned with the expression of the genes involved in the development of neurons, to which she added:

> And other brain regions. Because it's not only the neurons that are important in shaping the brain and also in the function of the developing brain (Lindsay 0.27.01).

> We're really concerned with expression of a whole variety of different genes during brain development, and our selection of the genes partly depends on - are they genes underlying particular genetic disorders? (Lindsay 0.27.20). [...]
>
> So there's a relevance to humans, or human beings, but in order to understand those we need also to need to know about patterns of key developmental genes (Lindsay 0.27.32).
>
> We know from mouse and other species that there are certain families of genes that are very important in the development of not only the brain, but all sorts of different organs, and quite often it's the same genes in different organs or different members of the same gene families. There are key gene families you can identify. (Lindsay 0.27.56).

When it came to the direct question, whether her research was intended to have a clinical application, Susan Lindsay answered:

> In the very long term, it is. One would expect that the expression patterns that we see might help to inform the mechanisms behind different aspects of brain development, but it's not directly clinical (Lindsay0.58.47).

Holdsworth suggested that, on the basis of what she had said, Lindsay's research was already contributing to the understanding of disorders, and she agreed:

> Yes. We are looking directly at genes that are mutated in human disorders. Yes (Lindsay 0.59.04).

Robin Crompton

To the same question, Robin Crompton replied succinctly, and with a different emphasis (Crompton 0.20.04):

> I'm not interested in the clinical application, to be honest, but yes, it would – it is likely to. If it has a clinical application, that's fine, but I really regard myself as a pure scientist (Crompton 0.20.54).

Analysis of diversity

The diversity in the responses to Criterion 12 was structured along various different axes. There were those who avowed an intention of clinical applicability and those who disclaimed it. Among those who avowed it, there was diversity of view as to whether the accurate term in their case was clinical 'application' or 'relevance' or 'interest'.

Both McGuffin and Crompton, from their respective disciplines, found that to answer the question precisely it was necessary to invoke – perhaps even to defend? – the researcher's status as a 'basic' or 'pure' scientist.

Jones and Smith seemed to find it natural that research in their separate fields should be influenced by priorities on the medical research agenda. Jones couched his analysis of the situation in realistic, economic terms. Smith portrayed the situation both in economic and in ethical terms. He hinted at the existence of a tacit contract between the researcher and society. The researcher enjoyed the freedom to devote his professional life to the study of interesting problems in molecular neurobiology, while society provided the opportunity and the means for this. Smith drew the conclusion that this placed the researcher under a moral obligation:

> for the privilege of studying molecular neurobiology you must put something back into the taxpayer's pocket, so to speak, and I think that payment back is in the medical area (Smith 1.16.20).

Buckley drew attention to the way the situation might be characterised by the existence of parallel research goals. Research into a disorder such as Down syndrome might target the disorder itself, in a way that offered a chance to benefit future potential Down syndrome patients, or it might target aspects of the syndrome that appeared to offer a chance to benefit other potential patient-groups in the wider community.

Assessment of the criterion

This criterion was about agenda-setting. It raised issues that it would have been wrong to neglect.

Chapter C14 – Does the research use cultural markers, e.g., surnames?

The matrix for the criterion

The responses to Criterion 13 yielded the matrix displayed below in Table C14.01.

Table C14.01. Matrix for Criterion 13:
'*Does the research use cultural markers, e.g., surnames?*'

Researcher	*Discipline*	*Yes*	*No*
Jones	Biomolecular archaeology		
Hutchinson	Evolutionary biomechanics (dinosaur)		
Smith	Molecular neurobiology		
Buckley	Down Syndrome research		
Mace	Evolutionary anthropology		
McGuffin	Research into normal and abnormal behaviour		
Jobling	Human evolutionary genetics		
Lindsay	Human developmental genetics		
Crompton	Evolutionary biomechanics (human)		

Salient interviews

The fullest responses to this criterion came from Mace and Jobling. The question was not put in the interviews with Jones, Hutchinson, Smith or Buckley. However, Jones subsequently volunteered a positive response.

McGuffin, Lindsay and Crompton were negative in their response. Crompton said: "Probably no" (Crompton 0.20.54). Before giving his negative answer (McGuffin 0.38.45),

McGuffin asked for clarification of the idea of a 'cultural marker'. On the spur of the moment, the interviewer sought for an example from anthropology and suggested "things like certain types of ritual or ceremony". In the light of hindsight one might be able to think of alternative examples that might have elicited a more positive response. Other cultural markers that came up in the interviews included languages and surnames.

Ruth Mace

When asked, 'Does the research use cultural markers?', Ruth Mace's reply was a simple "Yes" (Mace 1.16.04). In fact the issue of cultural markers had already arisen spontaneously more than once in the interview before the discussion arrived at Criterion 13. This was perhaps not surprising in a conversation with a researcher in human behavioural ecology who has published work on cultural phylogenetics.

An early exchange on the topic went as follows. Holdsworth had just put the following question (Mace 0.12.33):

> Of course language is presumably the most important cultural marker, but you're interested in others as well. Could you give me some examples?

Mace replied:

> Well, I mean, one of the reasons we were interested in building trees is because we're interested in cultural evolution. And again, evolutionary biologists have come up with models where, if you know the tree - the historical tree - you can ask: is it co-evolving with another trait? OK, you can ask this every time we see the evolution of something like monogamy or polygyny, or some cultural trait we're interested in, or some behavioural trait we're interested in. So for example we did a study on matrilineal kinship versus patrilineal kinship in Africa. And is that co-evolving with cattle? So, we built a tree of the Bantu, which is – we were interested

> in about 60 to 80 groups in Africa[240] using language, and then we mapped onto that tree which groups were matrilineal, which groups were patrilineal, which groups had cattle, and which groups didn't have cattle. And you can use these methods called 'phylogenetic comparative methods' which can tell you whether matriliny is – well, in this case we showed that patriliny and pastoralism – i.e., keeping cattle – were evolving together. So if a culture acquired cattle they were more likely to become patrilineal (Mace 0.14.14).

Holdsworth asked for a clarification:

> And when you say 'evolving' you mean *culturally* evolving?

Mace answered:

> *Culturally* evolving. Yes. Now of course there might be genetic evolution in there too, because we also know that when you become a pastoralist you start evolving, for example, lactose tolerance. So you can use these methods to look at, you know, gene-culture co-evolution, or you can look at culture-culture co-evolution. So pastoralism and patrilineal kinship is cultural co-evolution. We've also used the technique to look at pastoralism and the lactose gene, and you can see that there there's gene-culture co-evolution: i.e., when groups acquire livestock they evolve the ability to digest lactose as an adult, which [indigenous human groups] can't do. [This helps us to understand an aspect of the history of pastoralism.] (Mace 0.15.14).

Later in the interview there was discussion of another type of cultural marker. Holdsworth raised an example mentioned by Mace in a written work, that of basket-weaving methods (Mace 0.28.25).[241] Mace replied:

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[240] The number was 68: Holden and Mace (2003), pp. 2427-8.

[241] Jordan and Shennan (2005) in Mace *et al*. (eds.) (2005). See also Jordan and Shennan (2003).

> Yes, that's not my work - just citing someone else's - but they were arguing – that's going back to the phylogenetics - rather than just using language you can use some other traits as well. I mean, archaeologists have always done this. They've found bits of pots and said, well, these pots look like this and the pots don't look like that, so we think this is a different population from the ones here. I mean, I think language is a much better marker if you've got it, you know. But obviously archaeologists have to use whatever they can find (Mace 0.29.01). [...]
>
> They were just trying to measure all these traits of the baskets, and trying to work out if they could make trees out of the basket similarities in the same way we'd been making trees out of language similarity.

Holdsworth noted one possible criticism of the cultural phylogenetic tree approach. It had been said that the approach works if you can assume that the culture is transmitted longitudinally, but it works less well if you have to take into account that it can be transmitted horizontally (Mace 0.29.44). Mace's response was this:

> Yes. That's true. Well, the question is what history are you trying to study. It may be a cultural history. Some groups almost get swallowed up by other groups: i.e., they gain their language, and then that group is almost lost. It's almost submerged into the other group. So if what you're interested in is the cultural history, you know, it might not be the genetic history, but it might still be quite a good model of the cultural history, if you see what I mean. But they might not be exactly the same, because it is possible that certain groups just get, kind of, run over almost by other groups and end up speaking their language. And once they're speaking their language they lose their own cultural identity altogether and just become part of this wider group. But the tree-building programs are based on the idea of vertical transmission, so it's true that they don't work too well if there's too much horizontal transmission (Mace 0.31.19).

Holdsworth asked if there were other cultural equivalents to the reported phenomenon of a steady loss of language diversity in the world. Were there other cultural markers about which one could say the same thing? Mace said:

> Well, it depends if we believe that genetic diversity and language diversity are prone to similar things like barriers – populations being separated. It doesn't matter if they were separated by mountain ranges or rivers or distance or what have you, those kinds of things can cause separation (Mace 0.32.05).

Holdsworth recalled a diagram about barriers that had been published in an article in *Nature* co-authored by Mace.[242] Taking up this point, Mace said:

> Yes, exactly. I mean, we don't know the exact causes, but it's evidence that there are ecological processes involved. So if you look at species diversity in North America like we did in that article, you know, you get certain patterns. So, in certain parts of North America, especially towards further south, or on the coast, they've got very high species diversity. These are areas where ecologically there's tons of diversity. Then you go up to the north, and species diversity goes right down (Mace 0.32.44). [...]
>
> You get big ranges and big areas. OK? That's a well-known phenomenon. Ecologists have noticed that rule for ever. We know the tropics are incredibly diverse, and the northern climes are much less diverse. And interestingly enough if you plot linguistic diversity you get exactly the same thing. So in the tropics you've got very small areas, and there you can go over the hill and there's another language being spoken, and you go over the next couple of valleys, and there's another language being spoken. Whereas you go north, and there's this huge language area where people are migrating large distances. So you do get this latitudinal gradient. This is looking at native American languages - obviously, not now – it's all English now apart from a few pockets – but pre-colonisation there was indeed this

[242] Pagel and Mace (2004).

latitudinal gradient, which is suggestive that there are some parallels between processes that give rise to species diversity and processes that give rise to diversity in linguistic groups. And exactly what they are I don't think we really know, but it does suggest that similar processes are going on. Barriers to gene flow, for example, could cause species to diverge, we think, and obviously in modern times it's just so much easier to travel or to transmit ideas across barriers. Migration basically means that those barriers are being broken down, so it's not really surprising that we're losing both linguistic and cultural diversity now, because the diversity arises when groups get separated, and they start going off in different directions. And when they're not separated then you're going to get more assimilation (Mace 0.34.39). [...]

So we think that, like, 10,000 years ago there were, you know, ten thousand languages or whatever, and then it's gone down to six thousand, and, you know, it'll probably end up going down to two or three languages if we carry on at the rate we're going! Because you know there's a kind of global reason why it's useful to speak English, or in parts of the world where it's useful to speak Chinese - and maybe Spanish in parts of the world, you know, Arabic, Russian - and that'll probably be it. Because it's all changed. But when you were living in a small group that was just farming a particular area and had largely hostile relationships with neighbouring groups it was completely different. So linguistic diversity has definitely gone down. Once agriculture started actually we started getting much bigger language groups as well. So people think the peak of linguistic diversity was back when we were all hunter-gatherers, and it's been going down since then. And then globalisation – recent globalisation – is probably speeding it up even faster (Mace 0.35.47).

Mark Jobling

When Holdsworth put this question to Mark Jobling, the researcher in human evolutionary genetics, he gave 'surnames' as an example of a cultural marker, aware that Jobling had himself done work in that area (Jobling 0.57.24). Jobling replied:

> Yes, it does. We use surnames, in some of our research.[243] There are studies that use language, studies that use religion, also, as a way of sub-dividing populations. And studies which use lifestyle, so, in the sense of nomadic or sedentary, or farming or hunter-gathering, or something like that. Milk-drinkers and non-milk drinkers (Jobling 0.58.02).[244]

Asked for any particular reflections on surnames, Jobling responded:

> Well surnames is a rather specialised branch, but I think it's interesting, because it in principle allows you access to the past in a way that you can't get with other things, because surnames are heritable cultural markers. And you can put them together with a heritable genetic marker and start to find out what patterns of those heritable genetic markers were like in the past, and how much they've changed in the last few hundred years. It will only work in a society where you have heritable patrilineals, though - which is most. But the time-depths vary a lot. It's rather limited, generally (Jobling 0.59.00).

Jobling turned to the example of languages.

> Language is often used, but language can change pretty rapidly. OK, we know about some of the language changes that have occurred. We know that Hungarians, not

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[243] See, for example: King, Turi E., Jobling, Mark A. *et al*. (2007).

[244] For lactose tolerance, see Jobling *et al*. (2004), pp. 414-21. This topic also arose in the interview with Mace (Mace 0.15.15). Mace mentioned the work of Mark Thomas and Dallas Swallow, who were co-authors, for instance, of Ingram, C.J. et al. (2007).

that long ago - about a thousand years ago - spoke an Indo-European language, and now they speak a Finno-Ugric, a Uralic language (Jobling 0.59.25). [...]

So if you look at the genetics of Hungarians, to my knowledge there's no evidence that would cluster them with other Uralic speakers. And then Turks speak a Turkic language. But again, fifteen hundred years ago they didn't speak a Turkic language. And then we classify the people of Iberia. We have the Basques and then everyone else, but it's a subject of great debate as to what the languages were like before the Roman Empire. The Romans were very good at lots of things, but one of them was spreading Latin everywhere. So we see the influence of that here. Virtually, English is a sort of bastard language made up of all sorts of different things, whereas some languages are very clearly the way they are because of the Romans, and Romanian is one of them (Jobling. 1.00.21). [...]

So languages can change pretty fast. So as a cultural marker that can be a problem. Religion: I don't think I have much comment on that. Never use that as a divisor. Some people do, though – certainly people who are interested in the history of Jewish populations do. And, you know, there are papers about the genetics of Samaritans and all sorts of people. And Buddhists in Ladakh, and people like that, looking at some aspect of their genetics.

Holdsworth raised the point that sometimes groups were of interest because they had distinctive dietary practices (Jobling 1.01.08). Jobling concurred.

They do. They also often have odd disease spectra. It seems to me that what the cultural things do is simply lead to a certain amount of population isolation, small effective population size. Religions tend to exclude people who aren't in the religions, so by definition they lead to small effective population size. And then you've got an isolate, and in that isolate you can have high frequencies of disease. So Ashkenazi Jews are a good example, because they do have quite a lot of

otherwise rather rare diseases: Tay-Sachs disease, for example (Jobling 1.01.52).[245]

Analysis of diversity

There was indeed notable diversity between those researchers for whom cultural markers were of no relevance, such as Smith and Lindsay, and others for whom they were of capital importance, such as Mace, Jobling and the archaeologist, Jones. There was also a possible area of uncertainty in between, perhaps including McGuffin, the student of normal and abnormal behaviour, for whom the relevance of cultural markers is largely a matter of how such markers are defined.

Assessment of the criterion

Stepping back from this criterion for a moment, one might justly observe that the issue of 'cultural markers' is a huge one for the study of human behaviour. Its ramifications reach deep into more and wider areas of study than are encompassed by the present study. As part of a conceptual mapping exercise it was right to plant a flag on this part of the territory, without claiming to have explored it exhaustively.

At the same time the criterion was useful for bringing out significant aspects of human behavioural ecology and human evolutionary genetics.

[245] Jobling et al (2004), p.392.

Chapter C15 – Does the research offer other economic or social benefits?

The matrix for the criterion

The responses to Criterion 14 yielded the matrix displayed below in Table C15.01.

Table C15.01. Matrix for Criterion 14:
'*Does the research offer other economic or social benefits?*'

Researcher	*Discipline*	*Yes*	*No*
Jones	Biomolecular archaeology		
Hutchinson	Evolutionary biomechanics (dinosaur)		
Smith	Molecular neurobiology		
Buckley	Down Syndrome research		
Mace	Evolutionary anthropology		
McGuffin	Research into normal and abnormal behaviour		
Jobling	Human evolutionary genetics		
Lindsay	Human developmental genetics		
Crompton	Evolutionary biomechanics (human)		

Salient interviews

Criterion 14 was added to the matrix after the interview with McGuffin had taken place. Accordingly, the question was not treated in the interviews with Jones, Hutchinson, Smith, Buckley, Mace or McGuffin, although Jones subsequently volunteered a positive response. It was discussed in the interviews with Jobling, Lindsay and Crompton, each of whom gave a positive response.

Mark Jobling

When the question was put to Mark Jobling, the researcher in human evolutionary genetics, his answer was (Jobling 1.03.10):

> Well, I don't see there's a strong aim to have economic or social benefits. I think that one thing our field does do that's socially beneficial is that it's a good field to engage the public. It contributes towards public understanding of science, because everyone has a natural interest in their own origins, or nearly everyone does. If there's a subject with an interest in human origins, it's usually of interest to people, generally speaking (Jobling 1.04.01).

Susan Lindsay

When Susan Lindsay was asked about possible economic or social benefits of her research in human developmental genetics (Lindsay 0.59.06), she replied:

> Social benefits I think would be at the training level. So the three-dimensional models and the expression patterns and the capturing of expertise within the database or within the anatomy painting – all of that is to do - we do use on an ad hoc basis for training people, and you can – we would hope to do more of that. I think training and, yes, capturing expertise, would be the benefits (Lindsay 0.59.52).

Robin Crompton

When this question was put to the evolutionary biomechanist, Robin Crompton, he answered.

> Quite positively. All the work that we do on the foot, for example, is highly relevant to, well, to orthopaedics, to sport science, design of shoes – running shoes – that sort of thing (Crompton 0.21.06).

Holdsworth explained that he was

> not doing a kind of social utility audit. It's just I'm interested to know the things that are favourable to your kind of research, or the things that give them a boost, whether there are fashions, or trends or funding issues.

Crompton replied:

> Yes, obviously, I mean, every time you write a grant application to the national grant agencies we have to have a section 'applicability' and benefit to the country – that sort of thing (Crompton 0.21.41).

Analysis of diversity

The three respondents cited above gave three different replies, each interesting in its own way. Jobling cited the impetus given to the public understanding of science from recent research into the genetic origins of individuals and communities. Such research has indeed had a wide popular resonance. It is worth reflecting that this whole phenomenon has grown up as a result of the advances in genomics. It connects with important issues of personal

and social identity that have attracted study, not least because of their significance in legal and regulatory contexts.[246]

Assessment of the criterion

This criterion was intended to be complementary to the one concerning potential clinical applications (Criterion 12). The few findings it yielded were not such as to transform the picture of the various target disciplines or their practitioners, but its insertion has served as a reminder that there is a link between the topics under study here and social and economic factors that deserve to be borne in mind.

[246] See, for example, Hauskeller, Christine (2004), an article that "examines different ways in which concepts of identity in relation to genetic and genomic knowledge are currently employed in regulatory discourses".

Chapter C16 – Additional themes

Introduction

In the end, as we have seen, 14 criteria went into the Criterion Matrix that provided the conceptual structure of the series of nine interviews. No list of 14 criteria could have captured every imaginable issue arising in the field of behavioural genomics, and it was inevitable that some possible themes for discussion received no, or incomplete coverage. Examples may already have occurred to the reader. In the present chapter – the last of Part C – we look at three additional themes that, though mentioned in some of the interviews, in the opinion of the present writer merit further consideration. The ones chosen are

1. The concept of behaviour;
2. The currency of evolutionary adaptation;
3. The concept of the environment.

The concept of 'behaviour'

The interviews disclosed divergent views on the concept of behaviour. It became apparent that researchers differed in their use of the term 'behaviour' to denote the same phenomena. The most conspicuous example was the question, put to Jones and Jobling, as to whether farming was 'behaviour'. This was a pertinent question because the introduction of agriculture about 10,000 years ago – the Neolithic Revolution – was arguably a major change in human behaviour, if indeed we may refer to it in those terms. It left an imprint on patterns of human migration and settlement that, as we have already seen, can be picked up by the analysis of, for example, mtDNA and non-recombinant Y chromosome DNA.

In the interview with Jones, Holdsworth asked him if he saw biomolecular archaeology as a 'behavioural' discipline (Jones 0.09.12). Jones replied:

> I'm not sure, actually. I mean, the word - we are exploring human behaviours, of course, but I'm not sure that that would be the - . I suppose, the way in archaeology it works is, we don't necessarily find ourselves moving down towards that taxonomy. I mean, that's a bit of a vague answer.

The hesitancy to commit to the term 'behaviour' received an echo when Holdsworth returned to the topic later in the interview. Holdsworth asked Jones if he would describe farming as a behaviour (Jones 0.49.00). This received the answer:

> I would describe it as a 'practice'. I think on reflection there may be a history of how behaviour has come into archaeology. A behavioural subject that we would be very much aware of is behavioural ecology. And so with that comes a baggage of - more of behaviour as a Darwinian trait. And I suppose by saying 'practice' we're keeping our options open about whether it's a Darwinian trait or whether it needs to be explained in some other way. I think – yes - that the word 'behaviour', for reasons that may be very local to archaeology, comes with quite a lot of baggage. [...] (Jones 0.50.01).

> Within archaeology, if we talk about a 'behavioural' thing – so, if you or I were to start here talking about a 'behavioural' response, there would be a sub-text to that, and it's a kind of trace of, kind of, doubt there for various reasons. And so, for example, some people would believe that of farming. Some people would argue that's how you explain farming: that basically it's a form of adaptation to a Holocene environment. And if, for example, you feel that farming is not sufficiently explained in that way and may be a sort of polycausal thing, or only explained at a higher level of generality, then one might tend not to use the word 'behaviour' just for that reason alone. But that may be a rather local usage of 'behaviour' – I don't know (Jones 0.51.00).

Holdsworth suggested that it was an easy stage to go from saying that it was a form of adaptation to a Holocene environment, to saying that it was a form of 'behavioural' adaptation. Jones replied:

> Exactly - if you argue, as some people would, that that's why farming has come into being - because it's a process of adaptation, you know, a process of selection of hunter-gatherers and farmers being separately selected. And by using the word 'practice' rather than 'behaviour' then it kind of opens the way to explore other models, really.
>
> *Holdsworth*: Not selected by natural selection, though.
>
> *Jones*: No. I mean, to use the word 'behaviour' nudges it in the direction of natural selection, I would say. [...] But that may be very local usage.
>
> *Holdsworth*: Because of the perspective of behavioural ecology? (Jones 0.52.00).
>
> *Jones*: Yes. I think largely, yes. [...] It's one of the things I haven't taken sort of taken apart. I'm conscious that the usage of the word behaviour would have that added baggage. And –
>
> *Holdsworth*: But would you agree - now seeing it from some other perspective, like social psychology or sociology - with the argument that farming led to, in the end, permanent settlements, and it's arguable that led to stratification of society?
>
> *Jones*: Yes.
>
> *Holdsworth*: It would seem natural at that stage to say that it was a causal factor in the emergence of certain patterns of social behaviour.
>
> *Jones*: Yes, that would be perfectly reasonable.

Holdsworth: For some people it would have a Darwinian implication, and for some people it would not (Jones 0.53.01).

Jones: Yes. Absolutely, I entirely take your point. And if I hadn't any constraints connected with being an archaeologist, and I think about how I might use the word 'behaviour' in the pub, I can see that it's probably quite a local discourse. You know how these words can have a bit of baggage in a local discourse, don't they?

Reflecting on Jones' remarks, one sees that at least some scientific archaeologists, while deeply interested in the biological dimension of their work, might feel there was no advantage in getting involved in the controversies that have been engendered by various attempts to 'Darwinise' the study of human behaviour and human society. To ask whether such reticence is either justified or helpful is probably beside the point. The debates on these matters are not yet closed, and to expect archaeologists, with quantities of empirical evidence waiting to be sifted, to have much time to spare for predicting their outcomes is not especially realistic.

It is interesting to compare these exchanges from the Jones interview with passages in the interview with Mark Jobling, whose subject is human evolutionary genetics. First, the general question about 'behaviour':

Holdsworth: How strict do you think one ought to be, or can be over the use of the term 'behaviour'?

Jobling: Well, I don't know that I've ever thought about how strict one ought to be about it (Jobling 0.29.36).

Holdsworth: I mean, is farming a behaviour?

Jobling: Yes. I would say that it is. I mean, we tend to talk about 'cultural practices'. For example in our book, but those are 'behaviours' in a sense. I've never felt at all strongly you that should draw distinctions between what is a

behaviour and what isn't. I know that's because of my background. I've never studied behavioural genetics, for example, or psychology. People in this department work on behaviour in flies - fruit flies. They work on circadian rhythms, and aggression, and things like that. So they have proper terminology, and they will probably use the word 'behaviour' in a very clear and precise way, but I guess that I use it in rather an imprecise way (Jobling 0.30.31).

Holdsworth: Well, as I said, my approach is pluralist. It's merely an attempt to find out how people are using it. You can imagine that some people who are in another field, when they think of behaviour they might think 'Oh: extroversion/introversion, neurosis or gender orientation'.

Jobling: Well, I suppose I'm rather generalist in that case. And I would say that things that people do are behaviour. That would cover you know painting, farming, killing other people, sailing across the sea (Jobling 0.31.09).

Holdsworth: Technology?

Jobling: Yes, an element of technology. Religion [...] (Jobling 0.31.30).

The case of the researcher in human behavioural ecology, Ruth Mace, is also instructive here. The questions about the general definition of behaviour and about the specific case of farming were not put to Mace in her interview, as they were superfluous. The studies she herself had worked on, and which she cited in the interview, were sufficient indication. Research such as that linking cattle-ownership and patriliny showed that farming practices such as livestock husbandry were the natural subject matter of human behavioural ecology – were, in other words, certainly 'behaviour'.

Another perspective is exemplified by the work of Crompton and like-minded researchers in evolutionary biomechanics. This is the conception of 'behaviour' as 'work' in the sense which that concept has in physics. We have already had occasion to quote the following passage from the Crompton interview (Crompton 0.03.37):

> Well, when I use the term 'work' I'm using it very specifically. [...] I'm just writing a talker for a paper I'm giving next Monday, and there we do use the term 'work' in its Newtonian sense, purely. In the sense of Newtonian mechanics. And I'm not sure that a lot of people who use the word 'biomechanics' are all that familiar in my field with Newtonian mechanics. I'm not a physicist, I'm an anthropologist, but at least I've learnt enough to be able to, I hope, use words in an appropriate sort of way.

All work has to be paid for by the dissipation of useful energy. The useful energy that the organism generates within itself from the food it eats is metabolic energy. Those who study the evolution of motor behaviour such as locomotion, like Crompton and Hutchinson, realise that different gaits are likely to incur different rates of energy dissipation. It would be pointless to hypothesise a gait that used up so much of the available metabolic energy that none was left over for other work necessary to survival. The description of a given organism moving at a given gait therefore connects the following factors, among others: availability of food (energy intake from outside the organism), locomotion at the given gait (the work output), and dissipation of waste heat into the surroundings. This description, or energy budget, is not limited to events inside the organism. It conveys a picture, not just of the individual organism, but of that organism situated in its environment: that is, in a matrix of ecological relations. We should bear this in mind as we approach the second additional theme: that of the 'currency' of adaptation.

The 'currency' of adaptation

If the adaptation of an organism or group of organisms to the environment is real, it ought to be possible to quantify it – but in what units of measurement? Since Darwin published the *Origin*, number of offspring has been treated as the principal criterion of adaptation, but reproductive success is not the only imaginable criterion. Biomass, for example, could serve as an alternative. The choice of criterion depends to a large extent on the purpose of the calculation. Observers coming to their research from differing functional perspectives may evaluate adaptation in differing 'currencies'.

Holdsworth raised this topic with Ruth Mace (Mace 0.16.40), observing that

> it's possible to have more than one idea of how adaptation, as they say, 'cashes out'. One popular measure is reproductive success. Would you align yourself with that, or do you think there are other measures of adaptation? What are the criteria for saying 'This is well adapted'? (Mace 0.17.18).

Mace replied:

> Yes, it would be reproductive success. That's the first option – right? - natural selection. If you're talking about cultural evolution you might talk about an idea being good at making copies of itself - in other words, being influential at transmitting itself to others. But normally when we talk about 'adaptive' we do just mean it enhances your reproductive success, yes.

Holdsworth asked if, for Mace, it could also mean the successful replication of an idea, some cultural pattern. (Mace 0.18.00). Her answer was:

> Well, it depends what you're talking about. If you're trying to understand the spread of a cultural idea, you know, it might spread because the individuals that had that idea left more descendants, and they also inherited the idea. That's the simplest explanation. Or it might spread because - you know, it's the whole meme debate. Some ideas have properties that are very good at spreading themselves, so even if they're not very good for your reproductive success, so long as they have properties which cause you to persuade other people to believe in them then they themselves will spread.
>
> *Holdsworth*: I thought you introduced the word 'meme' with a certain amount of caution (Mace 0.18.52).

Mace: Well, I did really. I mean, most behavioural ecologists – I think what we tend to do is, sometimes we're measuring reproductive success, or sometimes we're measuring a currency that we think approximates to reproductive success. If you can't get data on reproductive success, though – yes, so it would be – [I can't think at the moment]. But for example, when we were interested in kinship systems, we proposed that - it's a slightly complicated argument - but if you've got cattle, it [enables] you. Pastoralists tend to be polygynous systems. In other words, individuals with lots of cattle can afford lots of wives – OK? - and the reason is, that it's a very good source of food. So, if you can marry a girl with a lot of cattle, you can have a lot of healthy children; there's going to be a lot of milk; it's much less hard work than farming. You know, it's a good deal all round. So if a man has lots of cattle, he can have very high reproductive success – because he can marry several wives, in fact, and that's often what you see in pastoralist societies. And because it so much favours your sons to have this cattle, then you get this kind of male-biased wealth inheritance. OK? So that's the explanation for why when societies gain cattle they become more patrilineal (Mace 0.21.04). [...]

And then you can just test that and see whether it really happens, over evolutionary time. I mean, are societies that are adopting cattle becoming more patrilineal? And we find that they are. So you've built a model, and you make your prediction from it, and you test it using the data. [...] It's an adaptive model in that we're saying, you know, there's a functional reason why this society switched from being matrilineal to being patrilineal, which is the reason I just gave you, and then you test it. So we're saying rather than cultural variation being random or whatever, it's actually to do with individuals trying to maximise their reproductive success (Mace 0.21.52). [...] So that would be an example of a behavioural ecological model.

Holdsworth also raised the topic with Crompton (Crompton 0.07.31):

In the theories of human behaviour that come one's way looking at the literature on – how shall I put it? – the 'biologicisation' of the study of human behaviour, there is

a lot of attention paid to what you might call the 'propagation calculus', the chances of successful reproduction, the spread of the genes.

Crompton: Yes.

Holdsworth: There's comparatively little on the bioenergetic calculus – energy conversion (Crompton 0.08.09).

Crompton: Not that many people in my field have adopted a biomechanical or energetic perspective, so that, yes, it's unusual.

Holdsworth expressed particular interest in a paper on 'The role of load-carrying in the evolution of modern body proportions' that Crompton had co-authored with Wang,[247] and the inferences from the skeleto-muscular data about an organism to its behaviour in the sense of tool utilisation or tool transport. He asked if Crompton had done much study on tool utilisation (Crompton 0.09.16). Crompton replied:

Tool utilisation - no I haven't. I've actually done a little bit of work with a colleague on the Acheulean industry and really looking at form and the scaling of form in handaxes in Africa. So I've done a little bit of archaeology, but not a lot.

Crompton told Holdsworth the colleague in question had been John Gowlett.[248] Holdsworth went on to mention another of Crompton's articles, this one on 'bent-hip, bent-knee' walking in humans. In it, Crompton had mentioned the 'metabolic costs'. Holdsworth asked if this was another case where Crompton had been rather unusual in adopting this approach such an approach (Crompton 0.10.15). He answered:

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[247] Crompton and Wang (2004).

[248] Professor John A.J. Gowlett, Professor of Archaeology and Evolutionary Anthropology, School of Archaeology, Classics and Egyptology (SACE), University of Liverpool. See the following articles: Crompton and Gowlett (1993), and Gowlett and Crompton (1994).

> Yes. My 1998 paper – this is the 1998 paper I presume you're talking about[249] - that one actually wasn't able to even predict metabolic cost. That was just an estimate from mechanical cost. These days what we're doing - we had a paper with Bill Sellers in *J. Royal Soc. Interface* - we're actually using a different kind of dynamic modelling with which we can actually predict metabolic cost, and actually we've done it for walking, and now for running. So we can actually verify. We can actually do studies, model human walking and running and compare predicted costs to experimental costs measured in the lab. So things have moved on an awful lot since that 1998 paper. (Crompton 0.11.03).
>
> *Holdsworth*: Actually I was thinking of the paper with Carey in 2005[250] (Crompton 0.11.07).
>
> *Crompton*: Oh right, OK. Well that was the follow-up to the 1998 paper. Because the first reaction to the 1998 paper was to say: 'Oh, it's just a computer model, what's it go to do with reality?' Tanya Carey did a PhD with me in which we actually measured the costs of 'bent-hip, bent-knee' walking in humans – which was obviously the closest we could get.

Holdsworth asked what future contribution to anthropology could be expected from Crompton's approach. Crompton said:

> Yes, well the next big exercise is to – well, there's two things – one is to move on to looking at the evolution of running in a similar sort of way. So that's probably for the next five years or so. That's one direction we'll be going in. Also, looking at the costs of moving on compliant supports. You know, I think the evolution of upright bipedal walking was in arboreal contexts in the trees. So it's obviously relevant to look at compliant supports. If our ancestors started upright bipedal walking in the trees, not on the ground - which is what I think - then we started doing it in a context of moving around on bendy branches. So if you tread on a branch, then you

[249] Crompton *et al*. (1998)
[250] Carey and Crompton (2005)

> are actually imparting energy to the branch. If it's a small branch - small-diameter branch - then the branch can bend, and you're losing energy. And unless the rebound happens within your walk cycle, you lose the energy.[251] So that's one of the things we need to look at (Crompton 0.13.05).

The energy in the rebounding branch can help an orang-utan propel itself upward and/or forward. Notice that this energy is not metabolic energy but kinetic energy. It can be exploited by the organism using metabolic energy and kinetic energy to position itself correctly to make use of the potential elastic energy in the branch.

Above, we cited Crompton referring to an article written with Sellers and others in *J. Royal Soc. Interface* (Sellers *et al*., 2005). The subject was 'Stride lengths, speed and energy costs in walking of *Australopithecus afarensis*: using evolutionary robotics to predict locomotion of early human ancestors'. The article begins with this statement:

> The adoption of bipedalism as the preferred mode of terrestrial locomotion is a fundamental step in divergence of the human lineage from that of other African apes.[252]

It goes on to explain the energetics of human walking, in the following terms:

> Human walking is characterized by extended postures of the hip and knee joints so that gait is relatively 'stiff'. This 'stiff' gait brings about out-of-phase oscillations of the kinetic and potential energies of the centre of mass (CM) which permit energy to be exchanged between the two states conserving up to 70% of the energy of one stride for use in the next.[253]

The energetics of human walking may be compared with the bipedal walking of other hominids:

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[251] See: (1) Thorpe, Crompton and Alexander (2007), and (2) Thorpe, Holder and Crompton (2007).
[252] Sellers *et al*. (2005), p. 431.
[253] Ibid.

> Bipedally walking chimpanzees by contrast use 'compliant' gaits where knee-flexions are sufficient and long-lasting enough to bring the oscillations of kinetic and potential energies of the CM into phase, eliminating mechanical energy exchange, and thus increasing metabolic costs. When walking bipedally the orang-utan does maintain extended hip and knee joints (Crompton et al. 2003) and up to 52% energy exchange occurs, but no ape appears to be able to combine extended hindlimb posture with the long strides and high stride frequencies that are required for fast bipedal walking.

Crompton *et al*. concluded that

> All other things being equal, our data suggest that 1.0 m s^{-1} was the optimal walking speed for *A. afarensis*.[254]

At that speed, the predicted cost of locomotion from their model was 5.8 J kg^{-1} m^{-1} (2.9 J kg^{-1} m^{-1} net), the net figure being the gross figure adjusted for the metabolic cost of standing still and "energy costs not associated with the musculoskeletal system (such as by the liver, brain, etc.)" while at rest.[255]

What has been said here is an inadequate account of the research that has just been briefly described. Nothing has been said, for example, about the techniques of 'evolutionary robotics' that Crompton, Sellers and their colleagues have developed and used. These are modelling and computer simulation techniques summarised in Sellers *et al*. (2003) as "genetic algorithms, pattern generators and mechanical modelling".[256] Nor has anything been said about the use made of fossil data in, for example, Sellers *et al*. (2005), which drew on the AL 288-1 'Lucy' skeleton and on the Laetoli footprints. However, this does not affect the main reason for citing the research, which is to point out that it gives its account of human (and other hominid) behaviour in the currency of the joule. It is an energetic, or

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[254] Sellers *et al*. (2005), p. 438.
[255] Ibid.
[256] Sellers *et al*. (2003), Summary, p. 1127. See also Sellers *et al*. (2005).

strictly a 'bioenergetic' account. It is, of course, a biomechanical account, but the biomechanics and the bioenergetics cannot be dissociated. The analysis, for example, of the forces acting on a moving organism is necessarily at the same time an analysis of the work that the organism must do to keep moving, and therefore also of the energy that it requires for this locomotion.

Sellers *et al*. (2003) make the following instructive observation:

> One major difficulty of all modelling approaches is the conversion of the mechanical work calculated from these models to metabolic energy consumption, which is the ecologically more important parameter.[257]

In other words, it is the bioenergetic measure that is needed if the behaviour under study is to be accurately situated in its ecological context.

The concept of the environment

The third additional theme that was selected for discussion in this, the closing chapter of Part C, was the concept of the environment. This topic was not neglected in the interviews. It was touched on in the interviews under two criteria: Criterion 2, 'Is behaviour studied in the ecological setting – or in the laboratory or clinic?', and Criterion 8, 'Does the research use environmental markers?' We discussed the responses in Chapters C3 and C9 above.

In Chapter C3, in the section headed 'Assessment of the criterion', we wrote:

> The observation that we need a robust concept of the 'environment', and "a clear conception of the ways in which the environment can act on the phenotype" will be greeted by some as a truism. We shall just note two points (for later development) that place question marks against such a judgment. First, there is the fact that we do

[257] Sellers *et al*. (2003), p. 1128. The authors add: "Fortunately Minetti and Alexander (1997) derived a formula from empirical data of Ma and Zahalak (1991) that allows this conversion.

> not yet have an environome. Second – and the responses here to Criterion 2 show this – we do not have a consensus on whether 'environment' can be taken just to mean 'everything that is out there', or whether the use of the term 'environment' commits us to a strictly ecological conception of relations between organisms and their surroundings. We shall attempt to explore the implications of these points in Part E [...].

Accordingly, at the present juncture, we shall content ourselves with signalling the need to analyse the concept of the environment in the context of behavioural genomics.

The philosophy of behavioural genomics: analysis of criteria for the conceptual mapping of research in the genomics of human behaviour

Volume 2 of 2

Submitted by Richard Julian Holdsworth to the University of Exeter as a thesis for the degree of Doctor of Philosophy in Philosophy, May 2009.

I certify that all material in this thesis which is not my own work has been identified and that no material has previously been submitted and approved for the award of a degree by this or any other University.

(signature) .....

PART D: THE CONCEPTUAL MAP

Chapter D1 – The Criterion Matrix

Introduction

We have now analysed the content of the interviews. In Part C, each chapter was prefaced by a Criterion Matrix for the responses of the various interviewees to the criterion in question. In this, the opening chapter of Part D, we shall present and comment on a global Criterion Matrix for the whole series of interviews.[258]

The first objective of this project has been to develop a conceptual map of the general research field of behavioural genomics, using material from the literature and from the series of interviews. It has already been explained that to speak here of a conceptual 'map' is to employ a metaphor. It is not a map in a literal sense. Rather it is an attempt to derive, from the material, a structured method for visually presenting similarities and separations among the concepts and methods of the target research disciplines. In order to accomplish this, it was necessary to devise a method suitable to the task, and the semi-structured interviews, the criterion matrices and the workbench analysis have been the chosen tools.

In Chapter D2 we shall briefly review the genomic workbenches. Chapters D1 and D2, therefore present the results of the conceptual mapping exercise. The final chapter of Part D – Chapter D3 – will be devoted to some concluding thoughts on the putative field of behavioural genomics.

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[258] Partly based on the author's presentation at ISHPSSB at the University of Exeter on 27 July 2007.

The Criterion Matrix

Now we turn to the global Criterion Matrix. This is set out as Table D1.01 below. The detailed results of the discussion of the 14 criteria in the nine interviews do not need to be repeated here. They have been examined in the separate chapters of Part C. Now we have an opportunity to draw any general lessons from the Criterion Matrix that may strike us.

The principal lesson of the Matrix is the remarkable diversity that it discloses among the target disciplines. It would be tendentious to call this a 'finding', since we have just explained that our investigation here has not had the character of an empirical study. Moreover, it was an avowed purpose of this research to disaggregate the conceptual concretions that we saw, from the outset, as one of the most unfortunate consequences of the nature-nurture stalemate. That the conceptual mapping exercise should come up with evidence of diversity among the disciplines – in objectives, in concepts and in methods – is in itself no surprise. What is interesting is the detail of this diversity, and its structure.

Intersecting axes of polarisation

There are many situations in life in which we are inclined to regret the polarisation of a debate. These are the situations in which the opinions of the disputants are deemed to aggregate themselves into two mutually exclusive positions. There are four things wrong with allowing this process to happen:

1. It lumps together, at either end of the axis of polarisation, opinions that ought, if everyone were being conscientious in their analysis of the situation, to be carefully distinguished;
2. It disguises the fact that the axis of polarisation is not just a line linking two irreducible masses, but rather a spectrum of intermediate shades of opinion;
3. It incurs the risk of dogmatic escalation, whereby each difference in emphasis, method or practice is elevated to the level of a doctrinal confrontation, and

4. It over-simplifies, to the extent that it characterises the situation in terms of a single axis of polarisation in a single plane, rather than a plurality of axes of polarisation, intersecting with each other in different planes and at different angles.

The aim of our procedure in the present study has been to help restore detail and structure to the conceptual map of behavioural genomics. As regards point 4 in the above list, the criteria set out in the Criterion Matrix may be regarded as alternative axes of polarisation, the intersections amongst which go to build up our overall conception of the field of behavioural genomics. An example is provided by Criterion 10: whether or not the research draws on fossil evidence. There is no ‘good’ or ‘bad’ about using fossil evidence, but it is a difference that we ought to be aware of for its own sake.

Table D1.01. The Criterion Matrix for the whole interview series
Bright green: assent. Pale green: 'to some extent'. NA: not asked.

	1 Research into all hominids or only *Homo sapiens*?		2 Behav-iour studied in the ecologic al setting?		3 Focus on species-typical traits or individ. differ-ences?		4 Does the research draw on the findings of gen-omics?		5 Genes or other DNA?		6 Researc h on DNA of non-human/ hominid species?		7 Researc h on other biomol-ecules?		8 Does the research use environ-mental markers ?		9 The main concern is phyl-ogeny or ontog-eny?		10 Does the research draw on fossil evid-ence?		11 Relev-ance of Newton -ian mech-anics?		12 Does the research use cultural markers ?		13 Researc h intende d to have a clinical applic-ation?		14 Other econ-omic or social benefits ?	
	Hom. sap.	Other	Ecological	Lab	Species	Individual	Yes	No	Genes	mtDNA, Y	Animals	Plants	Proteins	Other	Yes	No	Phylogeny	Ontogeny	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Jo																												
Hu																							NA	NA	NA	NA	NA	NA
Sm																							NA	NA			NA	NA
Bu																							NA	NA			NA	NA
Ma																											NA	NA
Mc																											NA	NA
Jb																												
Li																												
Cr																												

The pitfalls of the diplomatic instinct

Although one may regret the polarisation of a debate, notably a debate about natural phenomena, the instinct to be diplomatic and look for a compromise may lead us astray. The underlying natural phenomena may not be so accommodating. But in any case, the problem in any situation of uncertainty is not just that one may be wrong in one's empirical hypotheses. That can always happen. The problem is 'unforced errors' at the conceptual level. For example, if it is the case that, in some situation, a complex question has been falsely reduced to a single axis of polarisation, with all the harmful consequences envisaged in our list of four points above, then seeking a compromise along that false axis of polarisation cannot yield a satisfactory result. If the polarisation is false, the compromise cannot be true.

To protect ourselves against error of this kind, our first care must be to see that our way of conceptualising the problem is sufficiently diversified to preserve the maximum amount of the structure inherent in the phenomena we are studying. This has been the consideration behind the development and application here of the tool we have called the Criterion Matrix.

Questioning assumptions

Part of the function of the Criterion Matrix is to remind us of things that may have been known already, but that may have been overlooked, perhaps because they were taken for granted. One example is Criterion 9, which separated researchers according to whether their discipline was primarily concerned with phylogeny or ontogeny. In the minds of some people, to mention 'behaviour' in the same sentence as 'gene' or 'genome' may automatically trigger an assumption that what is on the agenda is a thesis about the influence of genes during the development of the individual. If so, it is salutary to recall that there are researchers for whom this is not the case, simply because ontogeny is not the

focus of their enquiries. It is helpful to be reminded that not everyone is trying to do the same thing at the same time.

The impact of molecularisation

The same point applies to the diversity we found in the responses to Criterion 3: whether the focus was on species-typical traits or on individual differences. In psychiatric genetics there can be very good reasons for wishing to understand why one individual – for instance, an individual suffering from a disorder – is not like others. Equally, in palaeoanthropology there may be good reason for wishing to know what the members of an extinct human species typically had in common. The point is obvious, almost to the point of triviality –but not quite. Something has made a difference.

What has made the difference has been the molecularisation of so many of the crucial disciplines in this area. Palaeoanthropology, for example, used to be the study of human fossilised skeletal remains. It is still that, but in addition it is the study of human and hominid DNA, whether this is DNA retrieved from fossilised bones or the DNA of living organisms. By virtue of the molecularisation of sciences such as phylogenetics and palaeoanthropology – which is a comparatively recent phenomenon - there has been a proliferation of disciplines using DNA. As the Criterion Matrix illustrates, these disciplines are using different types of DNA in different ways in the pursuit of different objectives.

The risk of anachronism

Comparing the situation today with the situation before this wave of molecularisation, one can look back to a time when researchers with the one objective of looking into genes for the causes of human behaviour had the field to themselves. But that time has gone. To act and talk today as if it was still with us is to be anachronistic. It is to be doubly anachronistic, since it is not only the 'new' DNA disciplines that have experienced molecularisation. Behavioural genetics and psychiatric genetics have themselves been

'molecularised' in the sense that those disciplines have also seen their workbenches transformed by the new ideas, new data and new methods brought onto the scene by the maturation of genomics. An especially important reference here is what McGuffin had to say in his interview about the transforming effect of new technology:

> The pace of change and development in technology is absolutely breath-taking. So, we're just about to embark on a study of depression using the new Affymetrix 500k chip, which has dropped in price dramatically. So you can look at 500,000 SNPs in one, you know, in one experiment quite quickly, and they've just brought out a million k chip – a million chip, a million-SNP chip - 1,000k, and I think it's not going to be too long before we can see pretty rapid whole-genome sequencing, you know, being feasible and affordable on a large-scale. So I think that we're going to discover [...] those genes that have a small effect on behaviour. You know, at the moment the level of resolution with linkage is pretty poor: you can only pick up genes with comparatively big effects. It's much better with association, particularly if you've got a very large grid of markers, but with the ability to sequence whole genomes affordably, I think you'll be able to detect more of the genes effectively (McGuffin 0.41.19).[259]

Contact and overlap with related disciplines

Before closing this chapter, we shall briefly review the coverage of disciplines in the present study. In the interview series, only a small sub-set of possible disciplines from the general field of behavioural genomics was chosen for study. Also, it was a rule of the procedure that the researchers spoke for themselves: they were not assumed to be spokespersons for their discipline. At the same time, from the depth of their own previous training and experience, several of the researchers interviewed were able to speak with a significant degree of authority about the research done in disciplines (or literatures) other

[259] See Plomin et al. (2001).

than the their own principal discipline. There were, therefore, principal disciplines and additional disciplines. According to the interviewees' self-reports, their principal research disciplines were the eight enumerated in the list given in Table D1.02 below.

Table D1.02. The disciplines of the researchers interviewed: initial list (8)

Discipline	*Discussed in the interview with:*
Biomolecular archaeology	Jones
Down syndrome research	Buckley
Evolutionary biomechanics	Crompton, Hutchinson
Human behavioural ecology	Mace
Human developmental genetics	Lindsay
Human evolutionary genetics	Jobling
Molecular neurobiology	Smith
Research into normal and abnormal behaviour	McGuffin

Further to these, one could identify, from the interviews, 12 additional disciplines or literatures. These are enumerated in Table D1.03 below.

Table D1.03. The disciplines of the researchers interviewed: list of additional disciplines (12)

Discipline	*Discussed in the interview with:*
Anthropology	Crompton
Anatomy	Crompton
Behavioural genetics	McGuffin
Behavioural pharmacogenomics	McGuffin
Cultural phylogenetics	Mace
Evolutionary anthropology	Mace
Evolutionary economics	Mace
Evolutionary medicine	Jobling, Mace
Life history research	Mace
Molecular phylogenetics	Crompton, Hutchinson
Molecular palaeoanthropology	Jones
Psychiatric genetics	McGuffin

We now pass to a discussion of the disciplinary workbenches. This will be the subject of Chapter D2.

Chapter D2 – The genomic workbenches

The aim of this chapter

This chapter argues for a multidisciplinary understanding of the field of behavioural genomics. Within this multidisciplinary understanding there is room for a surprising amount of diversity, as will be shown. Possibly, a simple approach to this issue might have been to maintain that 'behavioural genomics' is just an up-to-date version of 'behavioural genetics' and that recognising this fact requires nothing more than a slight adjustment to our terminology. Let us call this 'the simple transition model'. However, after seeing the large amount of diversity in the concepts and methods of the target disciplines set out in the Criterion Matrix, it becomes impossible to sustain such a simplistic approach. The advances in genomics of the past two decades has transformed existing disciplinary workbenches and created new ones. The overall picture is not simple but complex. In this chapter we shall try to build up a picture of at least some of this complexity, taking the task step by step. We shall offer a selection of models of increasing complexity to arrive at the overall picture. We make a start in Table D2.01, where we present Model 1: the simple transition model. In subsequent tables we shall present a succession of models of increasing complexity.[260]

Table D2.01. Behavioural genomics workbenches - Model 1: The simple transition model

Research discipline	*Human genome 'workbench'*
Behavioural genetics	Genes

[260] Based on the author's presentation to the Amsterdam conference, April 2008.

Could any part of the human genome provide researchers with evidence concerning the origins of human behaviour? As we have seen, researchers in the discipline known as 'behavioural genetics' answer 'yes'. Using statistical methods and molecular methods they are interested in the possibility that certain genes can have an influence on aspects of human behaviour. However, genes – as is now well-known - are only a small part of the totality of human nuclear DNA. As we saw in Chapter A1, the number of genes may be around 21,000 and 23,000, and they may comprise only 2 to 3 per cent of human nuclear DNA.

Here we are looking at things in the following way. If the totality of the human genome is a work area for scientists interested in the origins of human behaviour we could expect to find that different research communities have set up different 'workbenches' within that area.

Let us first note that researchers interested in the genetic aspects of the ontogeny of human behaviour do not necessarily call themselves 'behavioural geneticists'. They may call their work 'research into individual differences', or 'research into normal and abnormal behaviour'. As the interview with Peter McGuffin showed, there is overlap among various formulations. Among others, they include psychiatric genetics.

We can begin to diversify the simple transition model by adding psychiatric genetics, as we do in Table D2.02. Here and in the subsequent tables in this series we display the latest discipline to be added to the model in bold characters.

Table D2.02. Behavioural genomics workbenches - Model 2: Beginning to diversify the simple transition model		
Research discipline	*Human genome 'workbench'*	*Additional clarification/examples*
Behavioural genetics	Genes in nuclear DNA	The quest for QTLs[261] Recombinant DNA
Psychiatric genetics	Genes in nuclear DNA	Disorders from mutations Polygenic effects[262] Recombinant DNA

Behavioural geneticists and Psychiatric geneticists have interests that overlap, yet can be separated. Behavioural geneticists are often interested in the quest for single genes of the type known as 'Quantitative Trait Loci' that might combine to influence, say, the degree of given personality traits. Psychiatric geneticists are interested in disorders, whether caused by mutations in genes or by the polygenic effect of numbers of genes. In all the cases mentioned so far, the interest is in genes, and therefore in recombinant DNA.

The methods of psychiatric genetics are arguably pertinent to the study of addiction, depending on one's view of what addiction is. An article by Goldman *et al*. (2005) exemplifies the use made of the concept of 'polygenicity', which it defines as "A model of genetic determinism in which many alleles function in combination to produce a phenotype".

In Models 1 and 2 we have been concerned with research into the possibility of genetic influence on human behaviour. In addition to such research there are other types of genomic enquiry that can yield data pertinent to the causes of human behaviour. One example is molecular phylogenetics, including molecular phylogeography (Model 3, Table D2.03). The genomic workbenches in these cases may be nuclear genes, but they may also be non-recombinant sequences in the mitochondrial DNA and on the Y-chromosome.

[261] Plomin, Defries and McGuffin (eds.) (2003).
[262] Goldman *et al*. (2005).

Table D2.03. Behavioural genomics workbenches - Model 3: Introducing non-recombinant DNA and phylogenetic trees		
Research discipline	*Human genome 'workbench'*	*Additional clarification/ examples*
Behavioural genetics	Genes in nuclear DNA	Example: QTLs Recombinant
Psychiatric genetics	Genes in nuclear DNA	Mutations/Polygenic Recombinant
Molecular phylogenetics/ Human evol. genetics[263]	**Genes/mtDNA/ Y-chrom.**	**Phylogenetic trees**[264,265,266] **Phylogeography** **Non-recombinant DNA**

Molecular phylogenetics as such is not, of course, a research discipline principally concerned with the origins of human behaviour. However, its emergence has provided valuable tools for other disciplines that work in that area.

Genomics has provided new taxonomic criteria at the molecular level: hopefully, more precise than those involving morphological comparison. As a result, Molecular phylogenetics makes it possible to draw up:

- Species trees, and
- Gene trees.

These are not identical. A node in a species tree is a speciation event. A node in a gene tree is an ancestral mutation that is most unlikely to have been a speciation event. Although called 'gene trees', they are often constructed from mtDNA or non-recombinant Y-chromosome data. Molecular phylogenetics obviously goes far beyond the human species. A discipline, or thematic area, that covers the principles of human molecular phylogenetics as well as many related topics is 'Human Evolutionary Genetics'. Since there is an authoritative book on this subject by Jobling, Hurles and Tyler-Smith (2004), this subject is

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[263] Jobling *et al*. (2004)

[264] Brown (2007), pp. 595-620.

[265] Ridley, Mark (2004), Chapter 15, 'The reconstruction of phylogeny', pp. 423-70. See pp. 440-2 on how "the molecular distance between two whole DNA molecules, from two species, can be measured by DNA hybridization".

[266] Pagel (1999) is a review article.

being used as a point of reference here. As the name implies, Human Evolutionary Genetics is concerned with the evidence of genes - as well as of the non-recombinant DNA sequences already mentioned.

Now we come back to the origins of human behaviour, as we consider the way the types of data and technique we have just been considering have been taken up by palaeoanthropology. In Model 4 (Table D2.04) we take account of the use of mtDNA and non-recombinant Y chromosome evidence in palaeoanthropology.

Table D2.04. Behavioural genomics workbenches - Model 4: Adducing the evidence of mtDNA and the Y-chromosome in palaeoanthropology

Research discipline	*Human genome 'workbench'*	*Additional clarification/examples*
Behavioural genetics	Genes in nuclear DNA	Example: QTLs
Psychiatric genetics	Genes in nuclear DNA	Mutations/Polygenic
Human evolutionary genetics	Genes/mtDNA/Y-chrom.	Phylogenetic trees Phylogeography
Palaeoanthropology [≤ 40,000 years]	**Mitochondrial genome**[267,268,269,270]	**HVS 1** **Non-recombinant**
	Y-chromosome[271]	**Nuclear DNA, but non-recombinant**

To be more specific about mitochondrial DNA, the workbench of choice is the Control Region of the circular mitochondrial DNA molecule, and notably the segment of the Control Region known as 'Hyper-Variable Segment 1' (HVS 1).

Research on mitochondrial DNA and the Y chromosome has been used for investigating the migrations of early Anatomically Modern Humans, including migration out of Africa, for the dating of human specimens, and for helping to trace economic or cultural developments such as the Neolithic Revolution – the adoption of agriculture. It has also

[267] Cann, Stoneking and Wilson (1987).
[268] Jobling *et al*. (2004), p. 255, 'Early controversies about 'mitochondrial Eve'.
[269] Works providing an introduction to mtDNA analysis in palaeoanthropology include Sykes (1999) and, for the non-specialist, Sykes (2001, 2006).
[270] Garrigan and Hammer (2006).
[271] Introductory works on Y chromosome analysis in anthropology include Wells (2002, 2006).

been used to try to establish the relationship – or lack of one – between *Homo sapiens* and *Homo neanderthalensis*. Knowledge on all these points enlarges our knowledge of the behaviour of prehistoric and later members of our species. To that extent, this is evidence that can be adduced in the study of the origins of human behaviour.

A note on time-depth is necessary. It has been possible to extract mtDNA from bones of Neanderthals that were about 38,000 years old. However, the evidence thus obtained has been used as the basis for inferences and calculations that yielded the hypothesis that *Homo neanderthalensis* and *Homo sapiens* had a common ancestor some 500,000 years ago.

The use of mtDNA and Y chromosome sequences for palaeoanthropological research has received wide attention. Such sequences are preserved from disruption by natural selection. However, it has come to be realised that this is also true of various types of autosomal gene sequence. This topic came up in the interview with Jobling, when he said:

> I've been traditionally a Y-chromosome researcher in my own research - although we continue to use it, we're moving towards using the output of the HapMap Project.[272] That's the genome-wide project which looks at haplotype structure of the whole genome, and what it allows you to do is identify regions of DNA within the autosomes that have never historically undergone any recombination. They're like little 'Y-chromosomes' embedded in the autosomal DNA. So they haven't had recombination, but they have had a history. You can then use those as you might use a Y-chromosome. You can build a tree and so on and so forth (Jobling 0.42.30).

Bearing this in mind, we shall introduce a Model 5 which includes autosomal genes (Table D2.05).

[272] The International HapMap Project. Website: http://www.hapmap.org/ (consulted 14 January 2008). See also: Thorisson *et al*. (2005)

Table D2.05. Behavioural genomics workbenches - Model 5: Adducing the evidence of mtDNA and the Y-chromosome – and of genes - in palaeoanthropology		
Research discipline	*Human genome 'workbench'*	*Additional clarification/examples*
Behavioural genetics	Genes in nuclear DNA	QTLs
Psychiatric genetics	Genes in nuclear DNA	Mutations/Polygenic
Human evolutionary genetics	Genes/mtDNA/Y-chrom.	Phylogenetic trees Phylogeography
Palaeoanthropology [≤ 40,000 years]	Mitochondrial genome	HVS 1 Non-recombinant
	Y-chromosome	Nuclear DNA, but non-recombinant
	Genes in nuclear DNA	**Blood grp./HLA**[273] **Recombinant**

The entry for palaeoanthropology has been revised in this slide to include genes as well as non-recombinant sequences. This type of research received its early impetus from study of human blood groups. The ABO blood group system has been called "the first human genetic polymorphism to be defined".[274] In immunology, the Human Leukocyte Antigen (HLA) system is highly polymorphic.

So far we have considered direct use of the findings of genomic research. There is also indirect use by other disciplines. In Model 6, we add two of these: evolutionary biomechanics and human behavioural ecology.

The evolution of one of the most characteristic behavioural attributes of humans – upright bipedal walking – is studied by evolutionary biomechanics. Researchers in evolutionary biomechanics do not conduct research directly on DNA. However, they draw on the research of other scientists who do, in the sense that their evolutionary hypotheses adduce the evidence of molecular phylogenetics in distinguishing the species whose behaviours they wish to compare. For instance, the article on the origins of human bipedalism cited in Table D2.06 – by Thorpe, Holder and Crompton – cites chimpanzees, bonobos, gorillas and orangutans as well as humans.

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[273] Cavalli-Sforza (2000).

[274] Jobling *et al*., 2004, p.51.

Table D2.06. Behavioural genomics workbenches - Model 6: Phylogenetic trees as a tool		
Research discipline	*Human genome workbench*	*Additional clarification/examples*
Behavioural genetics	Genes in nuclear DNA	QTLs
Psychiatric genetics	Genes in nuclear DNA	Mutations/Polygenic
Palaeoanthropology [≤ 40,000 years]	Mitochondrial genome	HVS1
	Y-chromosome	Nuclear DNA/non-recomb.
	Genes in nuclear DNA	Blood group/HLA
Evolutionary biology	Genes/mtDNA/Y-chrom.	Phylogenetic trees
Evol. biomechanics[275]	**(Hominoids)**	**Phylogen. trees as tool**
Behavioural ecology	**None**[276,277]	**Cultural phylogen. trees**[278,279]

The case of human behavioural ecology is interesting. Even though research here may not involve any direct use of genomic evidence, use is made of the technique of phylogenetic tree-making to establish *cultural* phylogenetic trees. Language trees, for example, are not genetically-bound, but they resemble and may even track molecular phylogenetic trees. Researchers in this area use the same or similar software to build their trees as is used by researchers in molecular phylogenetics.

Now we come to RNA. In Chapter A1 we argued that our discussion of the genome must certainly not restricted to the genes alone, and indeed could not be limited to the DNA, for the reason that it is impossible to draw a complete picture of the function of DNA without referring to RNA and protein, to the transcriptome and the proteome. Then in Chapter C8, when we looked at the 'Other biomolecules' criterion, we saw that the researcher in human developmental genetics, Susan Lindsay, was deeply interested in microRNAs (miRNAs), which she described as non-coding RNAs that regulate the activation of genes (Lindsay 0.51.32). More generally, Großhans and Filipowicz (2008), is a helpful article in *Nature* on small RNAs. We add RNA in Model 7 (Table D2.07).

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[275] Thorpe, Holder and Crompton (2007).
[276] Brown (2007), p.604: 'Technical note 19.1' on software for phylogenetic analysis.
[277] 'Computational phylogenetics', Wikipedia article (Consulted 3 April 2008).
[278] Mace et al. (eds.) (2005).
[279] Pagel and Mace (2004).

Table D2.07. Behavioural genomics workbenches - Model 7: Looking at RNA		
Research discipline	*Human genome workbench*	*Additional clarification/examples*
Behavioural genetics	Genes in nuclear DNA	QTLs
Psychiatric genetics	Genes in nuclear DNA	Mutations/Polygenic
Palaeoanthropology [≤ 40,000 years]	Mitochondrial genome	HVS1
	Y-chromosome	Nuclear DNA/non-recomb.
	Genes in nuclear DNA	Blood group/HLA
Human evol. genetics	Genes/mtDNA/Y-chrom.	Phylogenetic trees/Phylogeography
Evol. biomechanics	(Hominoids)	Phylogen. trees as tool
Behavioural ecology	None	Cultural phylogen. trees
Human developmental genetics	**Transcriptome mRNA miRNA (non-coding)**	**Gene expression in early brain development**

Researchers in the discipline of Human developmental genetics are interested in gene expression in early brain development. Even if they might not declare themselves as working on 'the causes of human behaviour', progress in their field is a prerequisite for a full understanding of the ontogeny of human behaviour. The emphasis on gene expression means that the research focuses on the transcriptome – in other words, on RNA. Specific workbenches are messenger RNA, and also micro-RNA. miRNA does not code for proteins, but has the function of regulating gene expression. The article by Helge Großhans and Witold Filipowicz on 'The expanding world of small RNAs' explains the aims of micro-RNA research and argues that:

> Molecular cell biology has long been dominated by a protein-centric view. But the emergence of small, non-coding RNAs challenges this perception. These plentiful RNAs regulate gene expression at different levels, and have essential roles in health and disease.[280]

On the subject of the workbench of human developmental genetics, as we saw in Chapter 8, another significant aspect is 3D modelling in research into early human brain development. An interesting account of this is to be found in Kerwin *et al*. (2004).

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[280] Großhans and Filipowicz (2008). The quotation is from the sub-title of the article.

In talking about genomes we have, in the main, been talking about the human genome. However, as we saw in Chapter C7, the genomes of many other species of animals, and of plants, yield evidence relevant to the study of humans. In model 8 (Table D2.08), we have inserted information about the other genomes that feature in the genomic workbenches of the target disciplines. It is highly appropriate to add biomolecular archaeology at this point, because of the wide range of genomes that it has adduced.

Table D2.08. Behavioural genomics workbenches - Model 8: Genomes of other species

Research discipline	*Genome workbenches*	*Additional clarification/examples*
Behavioural genetics	Human/ Mice/Drosophila	Genes, including QTLs
Psychiatric genetics	Human/Mice Zebrafish	Mutations/Polygenic Zebrafish/cocaine addiction[281]
Palaeoanthropology [≤ 40,000 years]	*H. sap.*: mtDNA *H. neandertal.*: mtDNA	HVS1
	H. sap.: Y-chromosome	Nuclear DNA/non-recomb.
	H. sap.: genes	Blood group/HLA
Human evolutionary genetics	Genes/mtDNA/Y-chrom.	Phylogenetic trees
Evol. biomechanics	(Hominoids)	Phylogen. trees as tool
Behavioural ecology	None	Cultural phylogen. trees
Human dev. genetics	DNA/RNA in human/mouse/monkey	Dev. gene expression
Biomolecular archaeology[282]	***Homo sapiens*** **Horse/Cow/Dog mtDNA** **Rice chloroplast DNA** **Mycobacterium DNA**	**Migration/Farming**[283] **Domestication dates** **Radiation** **Maize, wheat** **Tuberculosis**

Even when *Homo sapiens* is the main focus of study scientists may need to go to other species for evidence of human behaviour. Advances in knowledge of numerous animal and plant genomes may be adduced. As we have already seen, evidence for the feeding behaviour of prehistoric humans can be gleaned from research into plant lineages. Evidence concerning the domestication and breeding of certain animals helps to track developments in the behaviour of human individuals and social groups. Ancient DNA has provided evidence relevant to the domestication by man of species of animals and plants, and thus to the Neolithic revolution. Work has been done on the mitochondrial DNA of dogs, horses

[281] Darland and Dowling (2001).
[282] Jones interview, Annex 1. See also Jones (2001) and (2007).
[283] Brown (1999).

and cattle.[284] In crop plants, there has been work on genes of maize and chloroplast DNA of rice. Terry Brown pioneered work on the ancient DNA of wheat.[285] As early as 1993, Spigelman and Lemma published an article on 'The use of the polymerase chain reaction (PCR) to detect *Mycobacterium tuberculosis* in ancient skeletons' in the International Journal of Osteoarchaeology.[286] Knowing about the pathogens that have assailed humans at different periods contributes to our knowledge of how they lived.

In the final model Model 9, (Table D2.09) we take the opportunity to add the remaining two target disciplines not so far mentioned in these models: molecular neurobiology and Down syndrome research. With these additions, we create a model that summarises our analysis of the genomic workbenches of all the target disciplines. Naturally, there is much that is missing from this summary. It can only be an indication. But in succinct form it sufficiently illustrates the complexity and diversity of the field. For this reason, we entitle Model 9 'The Genomic Workbench Analysis Model'. As such, Model 9 is intended to complement the Criterion Matrix as set out in Table D1.01. Together they form the graphic presentation of the conceptual map.

[284] Jones (2001), pp.111, 120 and 115, respectively.
[285] Brown (1999). See also Jones (2001), p.105.
[286] See Jones (2001), p. 226.

Table D2.09. Behavioural genomics workbenches - Model 9: The Genomic Workbench Analysis Model		
Research discipline	*Genome workbenches*	*Additional clarification/examples*
Behavioural genetics	Human/ Mouse/Drosophila	Genes, including QTLs
Psychiatric genetics	Human/Mouse Zebrafish	Mutations/Polygenic Zebrafish/cocaine addiction
Palaeoanthropology [≤ 40,000 years]	*H. sap*.: mtDNA *H. neandertal.*: mtDNA	HVS1
	H. sap.: Y-chromosome	Nuclear DNA/non-recomb.
	H. sap.: genes	Blood group/HLA
Human evolutionary genetics	*H. sap*.: Genes/mtDNA/ Y-chromosome Gorilla, chimpanzee *Helicobacter pylori* JC polyoma virus	Phylogenetic trees Genomes of commensal species
Evol. biomechanics	(Hominoids)	Phylogen. trees as tool
Behavioural ecology	None	Cultural phylogenetic trees
Human dev. genetics	DNA/RNA in human/mouse/monkey	Developmental gene expression
Biomolecular archaeology	***Homo sapiens*** **Horse/Cow/Dog mtDNA** **Rice chloroplast DNA** **Mycobacterium DNA**	**Migration/Farming** **Domestication dates** **Radiation** **Maize, wheat** **Tuberculosis**
Molecular neurobiology	***Homo sapiens*** ***Aplysia*** ***Drosophila*** ***Caenorhabditis***	***Aplysia*: conditioned reflexes**
Down syndrome research	***Homo sapiens*** **Mouse**	**Trisomic mice**

Behavioural genetics and behavioural genomics as seen by McGuffin

Finally for this chapter we give another element of the workbench for behavioural genetics. This is the characterisation of behavioural genomics as a specific, 'top-down' approach to the subject-matter of behavioural genetics.

Table D2.10 'Behavioural genomics' seen from Behavioural genetics/Psychiatric genetics: McGuffin on combining the 'Bottom up' and 'Top down' approaches

Bottom up	*Top down*
• "the traditional bottom-up approach,where you start off with the gene, • study its sequence and structure, • study the gene products, • and then study the possible effects of the gene from that sort-of bottom-up route".	• a top-down approach, where "you start with a whole organism – it might be man; it might be fruit-fly; it might be a rodent – • and you study the behaviour of the organism, and you study the component traits of behaviour, some of which might be models for parts of a disease like depression [...] • and then looking further down to then see what genes might be involved, and then see what pathways might be involved".

Source: Research interview with Peter McGuffin, Professor of Psychiatric Genetics and Dean of the Institute of Psychiatry at the Maudsley, London, 16 March 2007.
See also: Peter McGuffin, Brien Riley and Robert Plomin (2001): 'Toward behavioural genomics', Science, Vol. 291, Issue 5507, 1232-1249, 16 February 2001.

Chapter D3 - Behavioural genomics

Introduction

The criterion matrix and the analysis of the genomic workbenches have vividly illustrated the diversity that marks the research disciplines that we have studied here. These, the two principal tools of the conceptual mapping methodology, have fulfilled their function. We may now draw some conclusions for the postulated research field of behavioural genomics.

The lessons of the earlier parts of the thesis

In the earlier parts of this thesis we considered the broad field of behavioural genomics by studying a sub-set of its putative disciplines. In doing this we did not assume that there is, or ought to be a recognisable, and recognised science of 'behavioural genomics'. What we did was to investigate a number of the different ways in which the methods and findings of genomic science are being used by various research disciplines to further their investigation of the causes of human behaviour. In making a conceptual map of the disciplines studied, drawing attention to features that distinguished them from each other, or gave rise to overlap, we found significant diversity of approach. We by no means assumed that all the disciplines studied were consciously embarked on a common intellectual enterprise demanding the close coordination of concepts and methods. Our initial assumptions went rather in the opposite direction: in the direction of an exercise in disaggregation. From the outset, we saw a need to counteract a harmful tendency that we attributed to the legacy of the nature-nurture debate. This was the polemical instinct to divide the world into two opposing camps and, by doing this, incautiously to lump together in one or other of only two clusters research orientations that, if conscientious accuracy had been the goal, ought rather to have been painstakingly disentangled.

This was the motive for the construction and application of the set of criteria that were introduced here as the principal tool of the conceptual mapping exercise. If the reader will think back to the way these criteria were discussed in the successive interviews with researchers in the target disciplines, it will, we think, be clear that the criteria served this, their main purpose. With the diverse responses of the researchers to each of the criteria set out and analysed in systematic fashion, it is plain that the validity of any attempt to aggregate them at the opposing ends of a single axis of polarity has been definitively negated. Instead, there were cross-cutting polarities, as a glance at the Criterion Matrix (Table D1.01) will show. Some disciplines studied behaviour in the ecological setting and some in the laboratory; some disciplines focused on species-typical behaviour and some on individual differences; some disciplines focused on phylogeny and some on ontogeny, and so on. With the plots of these responses laid out on the conceptual map, the illegitimacy of any simplistic attempt to aggregate the disciplines into 'friend or foe' groupings is starkly illustrated.

Two pictures of disciplinary diversity

The Criterion Matrix and the Genomic Workbench Analysis Model (Table D2.09) are the principal output of this enquiry. They constitute the conceptual map. They are two pictures, from two dfferent angles, of the same phenomenon: the diversity that marks the objectives, concepts and methods of the disciplines that in principle might be candidates for a general research field of behavioural genomics. The pictures are so rich and so complex as to show that

1. The diversity among the disciplines cannot be captured by a two-clusters model implied by a binary polarisation of approach;
2. There is no formal, organised research domain of behavioural genomics at the present time;
3. To the extent that an unstructured field of behavioural genomics exists, it may at most be conceived of as an informal network that exemplifies the model of a spontaneous division of labour, but it is a network with gaps.

Respecting diversity

If we endorse this lesson of the conceptual map, then, we commit ourselves to a respect for diversity. There is an implication here for our subsequent use of the term 'behavioural genomics'. Once aware of what the conceptual map has to tell us, if we persist in referring to 'behavioural genomics' then we cannot validly mean by this term a single, homogeneous school of thought. Rather, we must mean a broad terrain of research effort, marked internally by a significant degree of inter-disciplinary diversity of concept and method – not excluding outright disagreement. This may strike us as unusual, even paradoxical. 'Behavioural genomics' is being proffered as a singular term, but one that refers to a diverse set of phenomena. Logically, this is possible, but taxonomically – when we are talking about the hierarchy of sciences, theories, schools, disciplines and so on – it is a challenge to our preconceptions. To give a name to a field of research is conventionally a way of labelling its distinctive unity of aim and method, not a way of signalling its internal differentiation. At the same time it would be wrong to exaggerate the degree of heterogeneity involved here. What the target disciplines of behavioural genomics (as presented here) have in common is that their concepts and methods stand in some significant relation to the concepts and methods of genomic science. It is interesting that they have this in common. It is interesting, for example, that advances in genomics have given new tools to the biomolecular archaeologist, just as it is interesting that they have enhanced the power of molecular phylogenetics to clarify the species-relationships germane to the work of the evolutionary biomechanist.

The conceptual map: formulating conclusions to this point

The conceptual mapping exercise enables us to add detail to our preliminary conclusions in the following way:

1. A significant number of research disciplines are using the methods and/or data of genomic science – directly or indirectly – to help them study the causes of human

behaviour. We selected eight research disciplines for special study (the 'target disciplines'). That we should only be considering a sub-set of the possible disciplines was inevitable in view of the practical constraints on the scope of the project. Nevertheless, we identified another twelve disciplines as touching or overlapping with the target disciplines.

2. The target disciplines exhibited diversity in their objectives, concepts, methods and practice, as illustrated by the two expressions of the conceptual map presented in this work: the Criterion Matrix and the Genomic Workbench Analysis Model.
3. From the conceptual map we see that investigation of the causes of human behaviour drawing on genomic science exhibits more diversity and complexity than can be captured by the two-cluster model implied by a binary polarisation of approach.
4. There is no formal, organised research domain of 'behavioural genomics' at the time of writing. At most one may refer informally to a field of behavioural genomics comprising disciplines such as those that have been considered in the present work.
5. Among the target disciplines, there is no single lead discipline in the field of behavioural genomics recognised as such by the others. There is no one discipline among them to which the others see themselves as the intellectual heirs.
6. The field of behavioural genetics has generated a certain conception of behavioural genomics, but this is not necessarily generalisable to other disciplines.
7. There is no commonly agreed research agenda for behavioural genomics.
8. To the extent that an unstructured field of behavioural genomics exists, it may at most be conceived of as an informal network that exemplifies the model of a spontaneous division of labour, but it is a network with gaps.

Centrifugal and centripetal forces

The conclusions just listed firmly support a heterogeneous conception of behavioural genomics, but they do it so firmly that, by the end, behavioural genomics has hardly any homogeneity left: scarcely enough to sustain it as a recognisable field of research activities.

Clearly, the centrifugal forces are strong here. Perhaps, even as we try to analyse it, the idea of behavioural genomics as a research field is spinning out of our grasp. Are there any centripetal forces to counteract this tendency?

We are under no obligation to find any. The present research project has not been a quest for a field of behavioural genomics, but a quest for the diversity manifested by the separate disciplines that have come under study here. If it has been successful, then perhaps it has undermined the chances of identifying behavioural genomics as a unitary field. However, the idea that the term 'behavioural genomics' might have something real to refer to cannot just be shrugged off. Early in the opening chapter of this thesis we located the work in the category of those "exploring the slippages in meaning as the key terms from genomic science diffuse into other areas". The similarity of the terms 'behavioural genetics' and 'behavioural genomics' is a tacit invitation to execute or condone a multiplicity of slippages of meaning. As we said a moment ago, there is a job to be done in determining what behavioural genomics is, and what it is not.

Among the researchers interviewed for this research, there was considerable interest in the project. There was at also a reluctance to get embroiled in open-ended controversies. As far as the nature-nurture debate was concerned, Mace was explicit about the need to avoid falling back into it:

> Because, you see, let's not get back into nature-nurture because it's so boring. Because everything is both. Everything is both. Genes expect to be in a certain environment. If you don't put them in the environment they expect to be in, you get weird organisms (Mace 0.41.00). [...]
>
> The environment that you're in is going to have an influence on how you're going to develop, and your genes are going to have an influence on how you develop, and some things are going to be at one end of the spectrum, and some things are going to be at the other end of the spectrum, and some things are going to be in the middle, but exactly where they are – you know, it depends on how variable your environment is for a start! So it's actually a bit of a sterile debate. But whether or not behaviour is adaptive is a separate question from whether or not it's nature or nurture (Mace 0.41.42).

The Sysiphus principle – no rolling back

Not all the researchers interviewed would have expressed their views in precisely the same way as Mace, but not one of them expressed any enthusiasm for pursuing the nature-nurture debate. The reticence of the researchers in the face of these open-ended debates – that about the possible Darwinist implications of the use of the term 'behaviour' is another that we have already mentioned – has its pragmatic side as well as its philosophical, but that does not necessarily mean there are not good philosophical reasons for respecting it. If one aspires to casting some of these issues in a fresh light, there are very good reasons for trying to avoid quite a number of conceptual quagmires, of which one might select the following as especially hazardous:

1. the nature-nurture impasse and the two-clusters model;
2. social Darwinism;
3. anthropomorphism, and
4. mind/body dualism.

Pushing one's boulder up the mountain and preventing it from rolling back into these inconvenient places is a Sisyphean task. We must bear this in mind if we are to move forward.

Behavioural genomics as a metafield

We have asked whether behavioural genomics is a unitary field of research. This is really many questions in one, because there can be a number of different models for a unitary field. The one we can discard immediately, for reasons that will have become obvious, is the model of the single research discipline. That one is clearly not applicable here. Perhaps we could say, though, that behavioural genomics is a 'metafield', under which the separate research disciplines are somehow collected. However, giving it this name is not necessarily the same thing as giving it substance.

One solution might be to promulgate a 'federal' model of behavioural genomics, whereby each of the separate disciplines maintains its own identity and rights while being, for some purposes, treated as a component of the wider phenomenon. Searching for analogies, one might consider the modern evolutionary synthesis itself, which linked evolution, genetics and population genetics.[287] However, that was a true, dynamic synthesis of constituent elements that, given the chance to interact, truly created a whole that was greater than the sum of its parts. Whether, for example, the target disciplines that we have studied here can fulfil the same role with respect to a behavioural-genomic synthesis is a question worth deliberating upon, but not one that can receive an immediate, conclusive answer. An interesting question that would need to be answered first is how many of the disciplines would wish to be regarded as candidates for the synthesis. Moreover, would a general consensus be obtained on the composition of the synthesis? These are valid questions, deserving of future discussion, but it would be wrong to suggest that the research carried out for the present project imposes definitive answers to them at this stage.

To conclude this chapter we shall briefly mention one further considerations of a centripetal character: the idea of a spontaneous division of labour.

The spontaneous division of labour

There is, fortunately, no superior authority in the world of research that can dictate to the scientific disciplines concerned exactly what role each shall play in the pursuit of knowledge concerning the subject-matter of behavioural genomics. There is no authority that has the acknowledged right to impose a division of labour in this sense upon the disciplines hypothetically concerned. It remains conceivable, however, that by the scope of the activities of each touching or overlapping, even in an unplanned way, they insensibly spread the meshes of an epistemic network that can create a division of labour 'effect'. It

[287] Huxley (1942).

would be a spontaneous division of labour, not perhaps intended by the presumed participants, yet performing a real function.

If there is any substance to this idea, then it makes a virtue of a thing that some people might have seen as problematic. The concept of a division of labour presupposes specialisation among the participants. The participating disciplines, in other words, should not all be engaged on the same sort of research using the same methods. For specialisation, diversity is a requirement.

An imbalance of knowledge as between genome and environment

Even if we take a positive view about the spontaneous division of labour, there is another aspect of the situation to be taken into account. This is that the genomic areas of the picture have by now been painted in to a much higher level of detail than the environmental areas. Knowledge of the genome is more structured than knowledge of the environment – at least, of those features of the environment that are likely to be pertinent to a model of interaction. To put it bluntly, science has the genome, but it does not have an environome. Is this asymmetry inexorably fated, or is it something that we can take action to change? Is it an eternal verity – or a problem to be solved? In the remaining chapters of this thesis we shall treat it as a problem to be solved. We shall examine some strategies for solving it.

Impulses towards a clearer and more systematised conception of the environment in this context have come from differing sources. In the work edited by Plomin *et al*. (2003), *Behavioural genetics in the postgenomic era*, the editors stressed the importance of the environment in the following terms:

> Although most chapters in this book concentrate on genetics, it should be mentioned at the outset that quantitative genetic research is at least as informative about nurture as it is about nature. In the first instance, it provides the best available evidence for the importance of the environment in that the heritability of complex traits is seldom greater than 50%. In other words, about half of the variance cannot be explained by genetic factors. [...]

> The present book's focus on genetics is not intended to denigrate the importance of environmental influence or to imply biological determinism. In many ways, it is more difficult to study the environment than genes. There is no Human Environome Project – indeed, environmental research is pre-Mendelian in the sense that the laws of environmental transmission and even the units of transmission are unknown.[288]

Plomin himself had already published a monograph on the environment as it figures in the concerns of behavioural genetics in 1994, in which he expressed a similar point:

> For the environment, there is nothing comparable to the laws of heredity worked out by Mendel, to DNA, or to the triplet code. How is the environment transmitted and translated? What are the units of environment? Although much remains to be learned about genetics, understanding of genetic processes seems to be light years ahead of our understanding of environmental processes.[289]

Between 1994 and 2003 it would not be true to say that there had been no attempts at all to clarify the mode of function of the environment in these contexts. It was in 2000 that Lewontin published his influential work, *The triple helix* – Gene, organism and environment. In this he argued that

> Taken together, the relations of genes, organisms, and environments are reciprocal relations in which all three elements are both causes and effects. Genes and environment are both causes of organisms, which are, in turn, causes of environments, so that genes become causes of environments as mediated by the organisms.[290]

With these quotations we close this chapter, which was entitled 'behavioural genomics'. In the single chapter of the next part of the thesis, Part E, we shall try to draw together some of these threads. We shall briefly discuss the prospects for the environome.

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[288] Plomin *et al*. (2003), p. 11.
[289] Plomin (1994), p. 26.
[290] Lewontin (2000), pp. 100-1.

PART E: BEHAVIOUR, WORK AND THE ENVIRONOME

Chapter E1 – Behaviour and environment: towards environomics?

Behaviour, environment and environome

In earlier chapters of the thesis we have argued that the analysis of the idea of behavioural genomics is rendered additionally problematical because of the fuzziness of the concepts of 'behaviour' and 'environment'. This emerged from the discussion of 'Additional themes' in Chapter C16.

As regards the environment in particular, in Chapter D3, we found Plomin (1994) asking "What are the units of environment?", and we saw Plomin *et al*. (2003) noting the lack of an 'environome'. At the end of our discussion of Criterion 2, on research in the ecological context, we spoke of the need for a taxonomy of modes of environmental interaction and suggested that this, when we had it, could be called an environome.

In the present chapter we shall briefly look at the feasibility of bringing these threads together – behaviour, environment and environome. This is not a problem that we aspire to solve here, but it deserves to be approached. Perhaps, in the study of the causes of human behaviour, it is a more urgent task to come at the subject-matter from the environomic, rather than the genomic end. Notwithstanding the serious efforts that have already gone into elucidating interaction with the environment, perhaps there is still something to be gained from further detailed exploration of what is denoted by the very term, 'environment'.

Different conceptions of 'environment'

In the discussion of human behaviour and its environment we are at an uncomfortable stage between the entirely general and the consensually specific. We find much generality in parallel with a range of alternative specificities. In the conception of the evolutionary biomechanist the environment may be a tree with springy branches through which a hominid is seeking to locomote with the lowest possible dissipation of energy. For the quantitative behavioural geneticist conducting an adoption study, the environment may mean the family circle. For the human behavioural ecologist, it may be a socio-cultural system like patriliny. At this point we are faced with a choice: to respect the diversity and leave it at that, or to make an attempt at precision. Here we shall explore the second of these options.

From the economy of nature to ecology

A good starting-point is the science of ecology, in which the concept of the environment has a relatively clear and developed role. All living things are enmeshed in a web of ecological relations, often depicted as a food web. In describing these relations, ecology has a system of concepts that serve to give specific structure to the general idea of the environment: ecosystem, biome, biotope and habitat. These are not mere labels, but dynamic concepts that capture the structure of cause and effect in ecological relations.

Ecology is not just a qualitative description of natural history in action, but a precisely quantified account of 'the economy of nature' – a phrase that was used by Charles Darwin and occurs several times in the *Origin*, for example in this passage:

> Though Nature grants long periods of time for the work of natural selection, she does not grant an indefinite period; for as all organic beings are striving to seize on each place in the economy of nature, if any one species does not become modified and improved in a corresponding degree with its competitors, it will be

> exterminated. Unless favourable variations be inherited by some at least of the offspring, nothing can be effected by natural selection.[291]

Darwin also made use of the metaphor of the web:

> I am tempted to give one more instance showing how plants and animals, remote in the scale of nature, are bound together by a web of complex relations.[292]

The modern conception of ecology: the energetic dimension

However, it is developments that have occurred since Darwin's day that have established the intellectual authority of ecology. In particular, it is the integration of thermodynamic and energetic ideas that have established its importance. What has happened is that concepts, laws and parameters have been introduced from physics that enable the 'economy of nature' to be analysed with precision. This type of analysis considers the total amount of energy entering an ecosystem in the form of sunlight, quantifies the green plant growth resulting from this by photosynthesis and proceeds to give an account of the subsequent energy flow through the different levels of structure in the ecosystem.

Trophic levels

What has just been provisionally termed 'levels of structure' is conventionally referred to in ecology as a hierarchy of 'trophic levels'. If we imagine a food chain, with particular species stationed at nodes along the chain where (as 'producers') they provide sustenance to other species by being consumed by them ('consumers'), then each of these nodes represents a trophic level. We can think of this as a 'feeding level'.

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[291] Darwin (1928), p. 99.
[292] Ibid., p. 75.

The hierarchy of the levels emerges naturally from an interaction of physics and statistics. Although the reasoning here is well known, there are good reasons for insisting on it. The first part of the argument has been clearly expressed by Dowdeswell (1984), in a section of his text entitled 'Energy conversion':

> All ecosystems are subject to the First Law of Thermodynamics. This states that whereas energy may be converted from one form into another, it can neither be created nor destroyed. In other words, the total energy intake through primary producers must be accounted for either through assimilation by primary and secondary consumers or dissipation through waste products and losses to the atmosphere through respiration.[293]

The Second Law of Thermodynamics ensures that at each level a proportion of the energy converted by consumption is will indeed be dissipated. In other words, although this energy cannot be 'destroyed' it can, as it were, be taken out of circulation. So, on the far side of each trophic level there is a smaller quantity of useful energy available than there was before that level was reached. It follows that

> the biomass of producers must always be greater than that of primary consumers, while this in turn will invariably exceed that of secondary consumers.[294]

Credit for realising that energy conversion yields an efficiency ratio between each successive trophic level is given to Ray Lindeman, whose pioneering paper on 'The trophic-dynamic aspects of ecology' was published in the journal *Ecology* in 1942.[295]

Lindeman helped to give the subject a conceptual framework that enabled it to be validly assimilated to physics. People often talk about the reduction of biology to physics – sometimes with chemistry as an intermediate stepping-stone – but they need to remember that the issue is not only the reduction of biological objects to physical objects (for instance, particles), but also other classes of phenomenon, including processes, patterns, events or effects - or trophic levels and efficiency ratios.

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[293] Dowdeswell (1984), p. 51.
[294] Ibid.
[295] Lindeman (1942).

Trophic levels as a cascade of energy conversions

Much of the interest in the science of ecology lies in considering particular instances of trophic levels, such as the feeding of predators like lions or eagles on their prey, but of course the power of the concept lies in its abstraction. The food chain is more than just a hierarchical list of species, in which the higher feed on the lower. It is better thought of as a cascade of energy conversions. That is the nature of the 'environment' in which particular organisms live their lives. This is the conceptual space in which the life-span of an organism may be plotted.

Energy budget and temperature-criticality

Descriptions of living systems – and, where relevant, their behaviour - are accountable in terms of the laws of thermodynamics. These are inherent in the concept of the energy budget (or, in the case of humans, energy balance). These concepts link directly to those of heat and temperature. For instance, Blaxter (1989) has defined energy budgeting as

> [...] a careful accounting of the energy consumed in food, losses of energy from the body in excreta, heat produced by metabolism and the retention in or secretion from the body of energy represented by organic compounds."[296]

Hardy (1979) defined 'energy balance' in terms of the following equation:[297]

> TOTAL ENERGY INTAKE =
>
> HEAT PRODUCTION + WORK OUTPUT + ENERGY STORAGE

The measurement of the temperature of a living system by an observer is a report on the state of that system. We are used to the truth of this in medical contexts, but it is true in

[296] Blaxter (1989), p.23.
[297] Hardy (1979), p. 18.

other biological contexts as well: for example, in the case of the growth of a plant in a given location and soil. In some given case, say in winter or spring, there may be a cascade of effects for other members of the food web.

Temperature and genomes

Temperature is critical in genomics. At first sight, it may seem a digression to mention this at the present point, but let us wait and see. It tells us something significant to know that the human organism (among others) survives at a body temperature of 37° C. This is significant in the context of the organism's environmental temperature. It is also significant in the context of the environmental temperature of, for instance, the bacterium, *E. coli*, bearing in mind that the *E. coli*'s natural environment is the intestines of mammals such as humans.[298] This is especially so in view of the fact that

> The *E. coli* DNA polymerase I enzyme has an optimum reaction temperature of 37° C.[299]

However, at a temperature of 75° or above the protein unfolds. It 'denatures', in the sense that heating destroys its enzymatic activity. These are features which have made the enzyme a convenient tool for certain molecular biological techniques. However, it is not the most convenient enzyme for all such purposes: for instance, not for the Polymerase Chain Reaction (PCR) technique for DNA amplification. As Brown explains,

> [...,] PCR requires a thermostable DNA polymerase – one that is able to function at temperatures much higher than 37°C. Suitable enzymes can be obtained from bacteria such as *Thermus aquaticus*, which live in hot springs at temperatures up to 95°C, and whose DNA polymerase I enzyme has an optimum working temperature of 72°C.[300]

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[298] Brown, p. 37.
[299] Ibid.
[300] Ibid.

So the temperature-criticality of *Taq* DNA polymerase, just like that of the *E. coli* DNA polymerase I enzyme, has been set by evolution. It is a calibration effected by interaction between the respective organisms and their characteristic natural environments. To speak of these things here, then, is not a digression from our theme – anything but.

The environment as a space in which energy conversions occur

We have been sketching a picture of the environment as a space, first and foremost, in which incidents of energy conversion occur. This is a space which requires to be understood in the abstract, by the laws of physics, but which also presents us with a familiar, phenomenological surface. This is the difference between the ecosystem understood by the scientist as a complex cascade of energy conversions and the way observers apprehend the functioning of the trophic levels in everyday terms: a dolphin catching a mullet or a woodpecker pecking out a grub.

Behaviour and work

Where does human behaviour fit into this picture? Earlier in this thesis we have had opportunities to consider the writings of Crompton and his co-workers on the behaviour of several species of primate, including humans, viewed as work. By this we mean work in the sense of physical science: the application of a force to an object so as to move the object in the direction of the force. Crompton's work on, for example, orangutans optimising the energy balance of their locomotion through the trees of the Sumatran forest by capitalising on the springiness of the branches is illuminating here. So too is his technique of studying the *Australopithecus afarensis* fossil footprints at Laetoli both by measurement and modelling of the footprints themselves and by computer analysis of laboratory trials with human subjects. Behaviour understood as work fits seamlessly into the energetic conception of the environment.

Triangulation

In Chapter C9 we considered the role of environmental markers in different areas of research and, in particular, archaeology. The biomolecular archaeologist, Martin Jones, was asked if there was "theoretical work on the inter-relationship between the biomolecular markers and environmental markers (Jones 0.41.13)". Jones replied:

> It's an interesting question. And I think the answer is: in time there ought to be, but it's pretty underdeveloped at the moment.

It is a challenge to think how environmental markers might be conceptually integrated into the study of human life at certain times and places in cases where the written evidence of history is unavailable. Let us assume that for a particular system to be selected for study the researcher starts with biological evidence of human life (for instance fossilised bones or a DNA sequence) at a location having certain spatial coordinates. In addition there will be 'environmental markers' in the sense that the system will be associated with physical objects and processes in its vicinity (even inside it) that can yield information about it. To summarise, therefore, we may say that – in the context under review - a system apt for study comprises DNA in given spatio-temporal coordinates associated with environmental markers. Provisionally, for the simple reason that it comprises three elements – the DNA, the coordinates and the markers - we shall call it the *triangulation method* for integrating the evidence of environmental markers

What inferences does the triangulation method permit?

Let us step back for the time being and stay with the triplet: DNA, spatio-temporal coordinates, and environmental markers. What inferences does the triangulation method permit from the types of evidence usually available?

The environmental markers include sites of habitation and artefacts such as tools. We may assume that the experienced archaeologist can often discern in such markers the evidence

of generalised tendencies or ‘cultures’. To a greater or lesser extent they can be treated as cultural symbols, which may be ‘read’ as such by competent researchers. At the same time these same articles may – indeed in certain circumstances must – be regarded as physical objects. In this context they will be assessed for their physical measurements and properties.

It is possible, although there is not time to develop the argument here, that ‘environmental’ markers should be reinterpreted as ‘energetic’ ones. A given marker could be regarded as a token of the work that went into making it and getting it to that location: for example, a stone tool of some transported raw material. Seeing things in this light sets the subject-matter in the context of the cascade of energy conversions.

What could an environome be?

A simpler way to start the project might be to say we are looking for a way to plot and fix the environmental profile of a given organism or group of organisms. We could call this an environmental taxonomy – or environome. Having got so far, we could then look around for the additional features that would transform the environome from a simple verbal list of factors and properties to a serviceable conceptual tool.

Much of this work has already been done, albeit under other auspices. For example, whenever an ecologist charts the food web for a given ecosystem, she is drawing a profile of the environmental relations of the species concerned. This can serve at least as a prototype, or proto-model of the sort of thing an environome could be. Notice that it is already much more than a verbal list. It reflects the underlying dynamic provided by ecological science. Ecology serves as its dynamic conceptual substrate. For instance, if we have such a food web and are then given some fresh information about the ecosystem – say, that all the owls in it have died as the result of the bioaccumulation of poisonous pesticides – we can in principle make predictions about future changes in the ecosystem, occurring at different trophic levels. Therefore the food web is a dynamic conceptual tool. This is something that we should require of an environome.

Let us think about some ways of systematising thought about the environment, and interactions with it, that we might view as proto-models of the environome.

Bronfenbrenner's ecological model

Plomin (1994) expressed interest in an ecological model of the developing human individual's environment proposed by Bronfenbrenner.[301] Plomin summarised the model in the following way:

> The model consists of four levels. The *microsystem* involves proximal interactions that directly involve the child. The *mesosystem* is a system of microsystems in the sense that developmental effects involve interactions among microsystems such as home and school. The *exosystem* refers to interactions between settings in which at least one setting does not directly involve the child, such as interactions between the home and the parents' workplace. The *macrosystem* refers to the overall system of microsystems, mesosystems, and exosystems that characterize a culture or subculture. The model emphasizes that interactions can occur between and within levels.[302]

Adding Bronfenbrenner's model to that of the food web, already mentioned, we now have two proto-models. In Table E1.01 below, we have collected a few more.

[301] Plomin (1994), p. 34, cites Bronfenbrenner (1989). See also Bronfenbrenner (1994).
[302] Plomin (1994), p. 34.

Table E1.01. Environomic proto-models: select examples		
Proto-model	*Source*	*Reference*
Food web charts	Ecological literature	*Passim.*
Ecological systems theory	Bronfenbrenner	Plomin (1994), p. 34.
Psychiatric enviromics	Anthony	Anthony (2001).
Normally occurring environmental and behavioural influences on gene activity	Gottlieb	Oyama et al. (2001), p. 49.
Discussed in the present work		
Triangulation with environmental markers	Holdsworth	Chapter E1 above.
The LEC inventory (Environmental loci of energy conversion)	Holdsworth	Chapter E1 below.

The reference in Table E5.01 to Anthony (2001) is to a paper that argues for a research effort in psychiatric enviromics, to be

> planned as a deliberately complementary search for specific environments or environmental processes and conditions that promote mental health and reduce the occurrence of psychiatric disturbances.[303]

The Gottlieb reference in Table E5.01 is an example of a of an attempt to systematise environmental influence on gene activity. It cites a table that Gottlieb compiled in order to illustrate a paper in which, he said,

> the main purpose here is to place genes and genetic activity firmly within a holistic developmental-physiological framework, one in which genes not only affect each other and mRNA but are affected by activities at other levels of the system, up to and including the external environment.[304]

Gottlieb's table is headed 'Normally occurring environmental and behavioural influences on gene activity'.[305] In it, he cites examples of environmental signals or stimuli that, acting on animals of given species, result in alterations in gene activity. One example that he gives

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[303] Anthony (2001).
[304] Gottlieb (2001), p. 48.
[305] Ibid., p. 49.

is the case of songbirds, such as canaries and zebra finches) hearing conspecific song, which has been reported to result in an alteration in forebrain mRNA.[306] Another example is the influence of the light-dark cycle on hamsters, which is reported to result in alteration in pituitary hormone mRNA and reproductive behaviour.[307] Gottlieb's general comment on the research results summarised in his table is this:

> The fact that normally occurring environmental events stimulate gene activity during the usual course of development in a variety of organisms means that genes and genetic activity are part of the developmental-physiological system and do not stand outside of that system.[308]

The idea of environmental loci of energy conversion (LECs)

Finally, we briefly propose another route to a proto-model arising from the idea of the cascade of energy conversions. To do so, we consider what happens at the point where the energy conversion occurs.

The organism interacts with the environment. If something is transacted – if something happens – there is conversion of energy. A woodpecker eats an insect, or an orangutan steps on a branch. To meet environmental pressures, the organism must multiply the instances of energy conversion in interaction with the environment that work out positively for its energy budget. Let us say that each instance has its *locus* somewhere in the environment of the organism. To be literally accurate we might call this the *Environmental Locus of Energy Conversion*, or ELEC. Since this is cumbersome, we shall shorten it to Locus of Energy Conversion, or LEC – always bearing in mind that this is a locus in the environment and not a locus on a chromosome.[309]

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[306] Here Gottlieb cites Mello, Vicario and Clayton (1992).
[307] Gottlieb cites Hegarty *et al*. (1990).
[308] Gottlieb (2001), p. 48.
[309] LEC is pronounced 'leck'.

We could say that the trunk of a tree is a LEC for a woodpecker, or more precisely that the trunk of a tree supplies the woodpecker with a number of LECs. Notice we are not saying that the trunk of the tree supplies the woodpecker with insects. We are saying that it supplies loci for the coming together of (a) the woodpecker with its beak, (b) the bark of the tree and (c) insects, in interactions in which the woodpecker transacts metabolic energy used up in pecking-work for the nutritive energy delivered by eating insects. The concept of the LEC is not restricted to the behaviour of animals, but it is clearly of potential use in the analysis of behaviour.

Since animals vary in their feeding habits and much other behaviour, different species, populations and even individuals will have distinct LEC inventories. The differences in these inventories will reflect both genetic endowment and environmental context. However, the scientific warranty for the accuracy of the LEC inventory is not the organism's DNA, but the laws of thermodynamics. A LEC inventory is a thermodynamically accountable behavioural profile.

The case for the LEC inventory as a proto-model for the environome has been sketched here as a contribution to a debate that deserves to be opened. If it is reductionist, it at least describes a new reductionist trajectory: reduction to the joule, not the gene.

PART F: CONCLUSIONS

Chapter F1 – Summary of conclusions

General conclusions of this study

To summarise the general conclusions of this study, these were:

1. the developments in genomic science of the past twenty years, important as they have been, have not given birth to a new science of 'behavioural genomics';

2. in particular, it would not be valid to make a simple extrapolation from 'behavioural genetics' to 'behavioural genomics': there is no science of 'behavioural genomics' that is just a scaled-up version of 'behavioural genetics';

3. the modern rise of genomic science has facilitated the adoption of molecular methods in general, and genomic methods in particular, by a significant number of scientific research disciplines studying the causes of human behaviour and topics closely related thereto; these have been referred to here as the 'target disciplines', since some of them were targeted for special study under this research project;

4. the target disciplines exhibit diversity in their objectives, concepts and methods; they show too much diversity to be collected together under a single heading of 'behavioural genomics'; this picture of diversity emerged from the conceptual map of the disciplines derived under this project from literature study and interviews;

5. the target disciplines include behavioural genetics, which, however, ought itself also to be seen as a diversified subject-area, comprising, for example, behavioural genetics, psychiatric genetics and behavioural pharmacogenetics;

6. it is true that the target disciplines are connected by the fact that they study the human genome, directly or indirectly, but they tend to study different areas of the genome, with differing ends in view: in the terminology adopted here, they have chosen different 'genomic workbenches';

Conclusions concerning the conceptual map

In a set of interim conclusions set out in Chapter D3, we considered what lessons could be drawn from the conceptual mapping exercise - as illustrated by the two expressions of the conceptual map presented in this work, the Criterion Matrix and the Genomic Workbench Analysis Model - with respect to the past tendency, under the influence of the nature-nurture controversy, to divide scientific opinion into two mutually exclusive clusters.

9. From the conceptual map we see that investigation of the causes of human behaviour drawing on genomic science exhibits more diversity and complexity than can be captured by the two-clusters model implied by a binary polarisation of approach;
10. There is no formal, organised research domain of 'behavioural genomics' at the time of writing: at most one may refer informally to a field of behavioural genomics comprising disciplines such as those that have been considered in the present work;
11. Among the target disciplines, there is no single lead discipline in the field of behavioural genomics recognised as such by the others: there is no one discipline among them to which the others see themselves as the intellectual heirs;
12. It is possible that a sense of common membership of a wider field of behavioural genomics has been inhibited among the target disciplines because the apparent linguistic analogy between 'behavioural genomics' and 'behavioural genetics' may have given the impression that the choice of the name already pre-empts choices concerning theoretical and methodological orientations; we can call this 'the name factor';

13. The discipline of behavioural genetics has generated a certain conception of behavioural genomics, but this is not necessarily generalisable to other disciplines.
14. There is no commonly agreed research agenda for behavioural genomics.
15. To the extent that an unstructured field of behavioural genomics exists, it may at most be conceived of as an informal network that exemplifies the model of a spontaneous division of labour, but it is a network with gaps.

Broader conclusions: 1 – Behaviour and work

The study carried out here has disclosed a lack of consensus on the understanding of two concepts crucial to consideration of a putative research field of behavioural genomics: 'behaviour' and 'environment'. To take behaviour first:

1. The term 'behaviour' is used in differing ways in the target disciplines: some include it in their very name while some seek to avoid using the term at all;
2. In certain contexts, for example in evolutionary biomechanics, 'behaviour' is often conceived of in similar terms to 'work' in the physical sense;
3. It is a conclusion of the present study that the applicability of the physical sense of 'work' to 'behaviour' has been under-explored in the case of other disciplines.

Broader conclusions: 2 – Towards environomics

Although concepts such as 'genome' and 'gene' do not have a single, clear definition that is held to by all scientists in all disciplines, their use is not arbitrary, and researchers in one discipline usually get enough clues from their own usage and practice to understand usage in others: there is moderate to high inter-disciplinary transferability of genomic concepts.
The same cannot be said for concepts of the environment; their transferability is vitiated by two contradictory tendencies: one is an assumption of generality in the reference of 'environment' when thinking of other researchers' disciplines, and the other is an assumption of specificity when thinking of one's own. We conclude that there is moderate

to low inter-disciplinary transferability of environmental concepts. This gives rise to the following further conclusions:

1. Given that the study of behaviour, the study of evolution and the study of genomics all presuppose that an organism is in some relation to an external environment, there is an obligation to clarify the ideas of environment and relations with the environment;
2. Contrary to widespread assumptions, there is at the present time at least as great an opportunity to improve the inter-disciplinary transferability of concepts in the area of the environment than there is in the area of the genome;
3. What is currently lacking is a viable concept of an 'environome', understood as a dynamic taxonomy of the environment: 'dynamic' in the sense that it must be more than a verbal list of environmental features; it must present a classification sensitive to the dynamics of some underlying science chosen as a system of reference;
4. For the purpose of deriving an environome, the appropriate system of reference is ecology, understood as the science of the flow of energy through the ecosystem;
5. This does not mean that all the disciplines studying the causes of behaviour in general, and human behaviour in particular, must be superseded by ecology: rather, ecology provides the epistemic warrant for future inter-disciplinary transfers of environmental concepts, leaving the disciplines free to generate and operationalise environomes in terms of their characteristic orientations and methods;
6. In environomics, as here conceived, the epistemic warrant lies in the ability to translate environomes back into ecological terms if necessary: it is a requirement for accountability, whereby, if the account is called in, it is to be provided in ecological terms;
7. An argument has been sketched for a concept of an environmental locus of energy conversion (LEC), offering the possibility of testing the idea that a LEC inventory might be appropriate to serve as a proto-model for an environome;
8. Environomics does not suffer from 'the name factor': its underlying science is energetics, not genetics; in environomics, reduction is to the joule, not the gene.

APPENDIX

EDITED EXCERPTS FROM THE INTERVIEW TRANSCRIPTS

1. Research interview with Professor Martin Jones – Edited Excerpts

Interviewed: Professor Martin Jones, George Pitt-Rivers Professor of Archaeological Science, University of Cambridge.
Interviewer: Richard Holdsworth, PhD candidate, Economic and Social Research Council (ESRC) Centre for Genomics in Society, Egenis, University of Exeter.
Date and time of interview: Monday, 22 January 2007, 14.00.
Place: Department of Archaeology, Cambridge.
Total length of the recording: 54 minutes 39 seconds.

The interviewee's description of the research 0.07.40

Holdsworth: May I ask you then, to begin with: do you see your discipline as being 'biomolecular archaeology'? Is that what you would call it? Is that the right designation?

Jones: Yes, I think that's a good expression. Like all young disciplines, a few words get bandied about, but that's the good one, yes.

Holdsworth: Briefly, how would you define it or describe it?

Jones : The way to describe it, really – I mean, typically, I would describe something historically: that the things we've looked at have got smaller, so there's a large field of bioarchaeology that looks at bits and pieces like that lump of charcoal and bone and so forth. And through time, through microscopy we've kind of unpacked the information from the cells, and what's happened - for a series of reasons in the history of science – is that the potential to tap chemical evidence of a wide range of historical [imprints] has just mushroomed over the last, probably, twenty years now.

Holdsworth: Right.

Jones: So, biomolecular archaeology covers anything using chemical information to try and elicit human pasts, and the methodologies to do that have just mushroomed. 0.09.12

Holdsworth: Right. Do you see it as what some people might call a 'behavioural' discipline?

Jones: I'm not sure, actually. I mean, the word - we are exploring human behaviours, of course, but I'm not sure that that would be the - . I suppose, the way in archaeology it works is, we

don't necessarily find ourselves moving down towards that taxonomy. I mean, that's a bit of a vague answer. Do you want to elaborate on the question, or - ?

Holdsworth: Well, if we may, we'll come back to it. As I said, I'm interested in the conceptual mapping of the subject. My dissertation is called 'The *philosophy* of behavioural genomics'. My approach is: 'what are the ideas, the assumptions, the methodologies, the theories?' To define your field from the outside, what other research disciplines are touching it at the edges or overlapping it?

Jones: Well, there are a whole series of forms of anthropology and biological anthropology that are touching it. I think the way the subject unfolds is that - particularly in relation to DNA - there is a series of core archaeological questions, and what happens, you know, in each methodological change is you revisit the set of core questions to ask how they re-articulate themselves in relation to the new methods. Obviously archaeology as a general topic tries to explain pattern through its history - that's what it does - and so working with genetics - and DNA in particular - what you're doing is trying to re-articulate these questions in terms of a family tree, a map. That's what you're trying to do. So, I mean, it obviously touches on all fields of archaeology; it touches on Quaternary science quite a lot, and it touches on various types of anthropology. There are also obviously interfaces with things like historical linguistics now and that sort of thing.

Holdsworth: Yes. I made the assumption – naturally, from reading your book *The molecule hunt* - that there is a close link with what we could call 'molecular palaeoanthropology'.[310]

Jones: Yes. 0.12.33

Examination of the criteria

Holdsworth: Now, the idea is that along the top (*of the diagram called the 'Criteria Graphic', which Holdsworth is looking at with Jones*) we've got a set of criteria that can be used to separate given disciplines. And this afternoon, as a basis for our conversation, I thought we'd take the top two, 'biomolecular archaeology' and what I call here 'molecular palaeoanthropology'.

Jones: Sure.

Holdsworth: The other names are in there just for your information. These are ones that I'll be exploring with other people at other times. I'm aiming to come up with something like this. (*Shows him an example*), which should be a kind of picture of diversity. I wondered if we could discuss some of the criteria and see whether you think they're valid or not.

Jones: Yes, OK. (Just before) 0.14.00

Criterion 1: *'Does the research cover all hominids or only* Homo sapiens*?'*

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[310] Jones, Martin (2001): *The molecule hunt: Archaeology and the search for ancient DNA*, London, 2001.

Holdsworth: 'Does the research cover all hominids or only *Homo sapiens*?'

Jones: In practice, it's been, I guess, 99% *Homo sapiens*, but in principle it's not constrained to *Homo sapiens*. So the way you've done it there (*Jones points to the provisional diagram in the draft 'Criteria Graphic'*), with the green [shading in the '*Homo sapiens*' box] and the question mark [under 'Other hominids'], is probably about right.

Criterion 2: *'Is behaviour studied in the ecological setting – or in the laboratory or clinic?'*

Holdsworth: Good. We're off to a good start. The next criterion is one that certainly separates some disciplines: 'Is behaviour studied in the ecological setting, as opposed to in the laboratory or in a clinical setting?'

Jones: Behaviour is studied in the ecological setting, I mean, even if one takes it off to a sample, there's a lot of work in the lab on the samples, but there's a guiding principle of all archaeology which is, 'if you want to understand the contents, you've got to understand the context'. 0.15.08

Holdsworth: Yes, that was something which came over strongly in the first and opening part of your book. In describing your own development as an archaeologist, you describe yourself as in the early days more or less casting aside the muck surrounding the artefacts, and then moving towards the analysis of the – well, I won't use the word 'muck' again.

Jones: Ha, ha. Absolutely, yes. That's absolutely right: the ecological setting.

Criterion 3: *'Is the focus on species-typical traits or on individual differences?'*

Holdsworth: Another criterion that separates some disciplines that is perhaps a little more tricky is that some disciplines would say that they were investigating individual differences in behaviour, and some would say that they were going for species-typical traits. 0.16.11

Jones: Yes. And I think, again, it's right to say species-typical traits. I mean, it's like one of these things – as soon as one's said it, one can think of the exceptions, you know, and there are some elements of biomolecular archaeology that have homed in on the individual, but it doesn't really stand out as interesting new departures when unquestionably the general drift, the drive behind the research is more towards the traits rather than the individual.

Holdsworth: Right. Yes, there were two points that occurred to me there: one was that the question of 'species-typical' is actually problematical, because if we discover by the methods of biomolecular archaeology that a small group of people in the Fertile Crescent were the first to domesticate goats or something, well they weren't species-typical. But they ushered in an activity that was broadly typical. 0.17.15

Jones: Yes. And I think, in terms of capturing the essence of the question, and what kind of answers we're looking for, both of those, at least in our aspirations, is on the broadly typical.

Holdsworth: Yes. Would it be fair to say in fact that in your discipline you're distinctly not on the outlook for interesting exceptions, or is that going too far?

Jones: It might be going too far.

Holdsworth: Can you think of any examples?

Jones: Of interesting exceptions?

Holdsworth: Yes: that have attracted the attention of researchers in your area.

Jones: Well, I suppose there's been some interest – it's partly 'interesting exceptions' – there's been some interest in 'special events' - you know, things relating to cometary impacts and so forth, but even those – . 0.18.15

Holdsworth: Volcanic eruptions?

Jones: Exactly, even those can set you - when they're handled – they're handled as a *set* of volcanic eruptions, if you see what I mean.

Holdsworth: Yes.

Jones: The broad trend within archaeology is that – like all these things - the whole discipline goes backwards and forwards, and when I started out in archaeology, in the seventies, for its interest with general traits, to break away from overly individualistic history, if you see what I mean (there's a lot of history narrated with a great interest in an individual), and archaeology is one of those for me [i.e., a discipline with an interest in general traits], so it means you get to large groups and to ordinary people and so forth.

Holdsworth: Yes. 0.19.00

Jones: And like all these things, I mean, there's been in some fields of archaeology an interest in 'agency', and 'agency' can mean different things. I mean, for some of the American archaeologists in particular, the idea of agency is focusing on the idea that individual, you know, individual – unique men and so forth – can actually appear. Agency means something rather different and more sort of 'given' over here, but in America there's a sort of style of agency. There's a certain interest at the moment amongst some of my contemporaries in notions of, you know, agency, free will and history as part of conscious, meaningful actions and so forth.

Holdsworth: Oh. Could you mention an author who - ? 0.20.00

Jones: Yes. One of my colleagues, John Robb, has written a book on agency.[311] In America, Kent Flannery – his book's quite interesting.

Holdsworth: John Robb is British, is he?

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[311] See also John Robb: 'Steps to an archaeology of agency', Paper presented at the Agency Workshop, University College London, November 2001. Robb was at that time at the Department of Archaeology, University of Cambridge. For the text of the paper, see: http://www.arch.cam.ac.uk/~jer39/jer39-steps-to-archaeology-of-agency.html (Consulted 12 February 2008).

Jones: Well, he's American. [He is in the Department of Archaeology here at Cambridge], but he works at Cambridge now. And then there's a book by Dobres and Robb.[312]

Holdsworth. Yes, in the sort of - in inverted commas - 'the heroic epoch' of archaeology – Schliemann and all that sort of thing – people were amazed at the idea that they might be getting at the history of named individuals. 0.21.00

Jones: That's right. And I think, possibly, on the one hand you have various trends there. On the one hand, you have that kind of theory of the past which emphasises named individuals, often of some rather central, powerful status, and then you have - both in history and in archaeology - a reaction against that, and an attempt to write stories of ordinary people and the common man and so forth.

Holdsworth: Right.

Jones: The, sort of, named individual is almost an obstacle rather than anything else. But then more recently you have ideas of agency which are not necessarily related to finding the elite and how they did everything, but, you know, finding the agency of other people and so forth.

Holdsworth: Right. Well, I'd better check that in the literature.

Jones: Yes, absolutely. It's a slightly complicated area.

Holdsworth: I can tell! 0.22.02

Jones: I'm sure in a number of these disciplines you'll probably find you'll get, kind of, discussion within the discipline.

Holdsworth: Yes, of course. That's why I made the point that you're not considered as a spokesman.

Jones: No, absolutely.

Criterion 4: *'Does the research typically draw on the findings of genomics?'*

Holdsworth: Well, the next question seems simple enough to answer: 'Does the research typically draw on the findings of genomics?'

Jones: I think 'yes' is the answer there. Yes.

Holdsworth: It's more, or less true as you go down the list of other disciplines.

Jones: Yes.

Holdsworth: They're selected because they mostly do, but -

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[312] Dobres, Marcia-Anne and Robb, John (eds.) (2000): Agency in Archaeology, Routledge, 2000.

Jones: I think, one thing actually is that - to elaborate on that - that they don't just *draw on* the findings: their actual practice is rather steered by the progress of genomics. And the reason for that is – it will vary on your list, but on our list, in our departments, the sums of money, the volume of research are such that we have to be responsive to fields with more money. So, for example, on the anthropological front, it's inevitable that we will respond to what medical research is doing, even if it has different objectives. And in looking for the spread of agriculture, it's inevitable we respond to what genetic breeding and genetic modification is doing, simply because the scale of activity in those fields is just something that we kind of hang onto by the skirt-tails. And a new departure in either of those fields, that may have nothing to do with the human past, will nevertheless have an impact on even the questions we're asking because there are new questions we can ask.
0.24.03

Holdsworth: Yes, I see. Can you think of a specific example?

Jones: Yes, I can. If we go, say, to the origins and spread of agriculture - some projects that I'm involved with - you have a sequence there of activity that, as you rightly perceived, in order to build the family tree and tell the story, we work heavily on non-coding regions, and so with plants in particular we find some non-coding regions at the edge of some genes people are studying. But within something like barley breeding there's, well, as you can imagine, tremendous interest in genes that will affect how much – produce, or - ?

Holdsworth: Yield. 0.25.11

Jones: Yield. Exactly! Or something like that. So, they would explore particular genes that will prompt us to ask questions about how those genes worked in the past. And as I said, the gene is chosen for entirely different reasons, because there's money in it. And so, if - There's, for example, barley, and its field that spreads furthest north, and in the spread of agriculture barley comes into the Arctic Circle, and to do that it has to switch a gene off. That gene's job is to tell it what season it is. Basically, [when] the gene is switched on, it just tells the plant to do nothing and hibernate, because it's cold and horrible. So you've got to switch that one off. And so there are some very interesting questions to ask about the spread of agriculture north, which is prompted by research into a gene that was chosen in order that barley farmers or brewers or whatever could follow their objectives. The same with medicine. I mean, we're obviously moving into a field now where because the genomics is done the proteomics are being done, and so there's going to be more and more work on how genes - how DNA sequences become genes and become proteins, and the particular sequences that are studied will be driven by pressing medical questions, pressing food questions and we'll find ourselves hovering around the edges asking what we can learn from that. 0.27.02

Holdsworth: Good. Can you think of an example there in the medical context?

Jones: I'm thinking about that, but I'm trying to think back. Yes, exactly, I can think of a very good example there. I mean, various forms of disease susceptibility in the system is something there's great interest [in] - in lactose intolerance and coeliac disorders, which you know are obviously an issue of whether you can digest milk or flour. 'Coeliac' disorders. It's a problem with gluten. And so those are ones that are researched because they're medical or dietary issues. 0.28.05

Holdsworth: But how does archaeology come into that?

Jones: Well, both the ability to drink milk or the ability to eat grass-seeds is tied up ecologically with agriculture. I mean, the reason we have problems with both is probably that, you know, palaeolithic hunter-gatherers – there was more meat [in their diet]. On a time-scale that we're still trying to work out, both - you know, ground-up grass-seeds, i.e. cereals, and milk of other animals - is something that we've only had for a short period of evolutionary history. So, in a sense it's not surprising that there are genotypes that have trouble digesting it. Whereas you wouldn't find human genotypes having that much trouble digesting meat, because [there's a long idea of what meat is]. So the history of resistance or tolerance of it can be explored in order to understand the history of cattle domestication or cereal domestication. 0.29.16

Holdsworth: For the archaeological enquiry into that subject, are you looking both at genes and at non-coding regions?

Jones: Yes, and also other forms of information like just cattle bones in the archaeological record. And so you hit it from a variety of angles. What you get from the modern genetic information is - if you're lucky - a distribution map that will show you tolerance of milk is much stronger in North Europe and much weaker in East Asia and – well, obviously, lots of variations. So you get a modern genetic map, and then you can use, kind of, phylogenetic methods to build a family tree of those genes and then try and relate it to time and space. And, as you say, for that you're using non-coding material. And then there are the archaeological records, and sites with animal bones in, and sites with lots of mature female cows in, that suggest there might have been milking, and so on and so forth. So those would be two examples. I mean, again if there were money too, I mean, if there was a surge of research in alcohol dehydrogenase, that too would be something that one could explore, because the history of alcohol is something quite interesting in terms of archaeology.

Holdsworth: But that hasn't happened yet?

Jones: There hasn't really been a study on it. I mean, that's - if you like - a sort of study waiting to happen, you know, because alcohol-related genes probably themselves preserve, you know, a good deal of historical information about how old alcohol consumption is within our species. 0.31.08

Criterion 5: *'Is the research on genes or other DNA? If 'other': mtDNA or Y-chromosome?'*

Holdsworth: Thank you. If we come onto the next segment, at the top the question is: 'Genes or other DNA?' And that's split between 'genes', meaning genes in the human nuclear DNA, or - two other possibilities mentioned here – 'mitochondrial DNA', 'Y-chromosome'. So, I shouldn't necessarily have left the 'genes' box blank.

Jones: Well it's very - kind of - emergent. It has a signal 'Not at the moment, but coming soon' - if you know what I mean.

Holdsworth: 'Watch this space'. 0.32.00

Jones: 'Watch this space', exactly. And, the other thing: you might want to add a column too, actually, and that is 'autosomal non-coding DNA', which - especially in relation to, well, in

relation to crop-related stuff and plants – is very important. And that would be filled in for biomolecular archaeology and blank for molecular palaeoanthropology.

Holdsworth: So, especially in relation to, did you say – ?

Jones: To plants.

Holdsworth: Crop plants?

Jones: Crop - any plants, actually. But crops are the ones that count. I mean, the key thing is they have mitochondria, but plant mitochondria are a bit wild in the evolutionary timescale.

Holdsworth: Yes?

Jones: They just evolved very weirdly. And there's also - I mean, you don't want to complicate this list – but you also want - there's also chloroplast DNA. But I think if you've got 'autosomal non-coding DNA' in a box then that should cover the plants. 0.33.13

Holdsworth: But you mention the chloroplast DNA in your book.

Jones: Yes.

Criterion 6: *'Is there research on the DNA of non-human/hominid species? If so, animals or plants?'*

Holdsworth: Good. Now, is there research on the DNA of non-human species - either animals or plants?

Jones: Absolutely so, both. And I think, in terms of molecular palaeoanthropology, you've probably defined how you're using 'human', haven't you, in your [research]? Or you will in your dissertation.

Holdsworth: Yes.

Jones: Not everybody's using it in the same way. That's just something I warn you. But I think you can choose. I mean some people use 'human' just for *Hom. sap. sap*. Some people use it for all of *Homo* and so on. And so I think you'll get away with making clear what your definition is and sticking to it. 0.34.05

Holdsworth: Yes.

Jones: So, on some definitions of human, people might want to put Neanderthal DNA [...]. But that you can cover just by clarifying your own definition.

Holdsworth: Thank you for drawing attention to that. It is rather a key point.

Criterion 7: *'Is there research on other biomolecules? If so, proteins or other?'*

Holdsworth put the next question: 'Is there research on other biomolecules? If so, proteins or other?'

Jones: [In] biomolecular archaeology, both proteins and 'other' are definitely the case. In molecular palaeoanthropology it's certainly the case at the moment that DNA is, yes, the main thing. Whether or not information from proteins will come back into play is hard to say. 0.35.18

Holdsworth: How could that happen, conceptually?

Jones: Conceptually, you see, the issue of where it might come back is early hominids and things that, say, are between one and two million years old. And at the moment for stuff of that age you can't really get DNA out in a terribly convincing way. You might be able to check its existence there. You can get protein out, but not very informative protein. It's not an easy prediction which is the better biomolecule, once those explorations have been sorted out. I mean, if DNA survived in a form that could be studied in really early hominids then it would be better than protein, but it may be the case that proteins survive in a reasonable way better. So, basically, if you've got, say, a one-and-a-half-million-year-old hominid bone, you may be able to detect DNA immunologically, but what you can do with it is open to [question]. There may be collagen and osteocalcine – two proteins - that you can convincingly extract, and in the osteocalcine there may or may not be variation which is informative. But I'm really speculating here. I'm just elaborating rather verbosely on the fact that, although within anthropology it's DNA at the moment, the door is not closed. 0.37.18

Holdsworth: Do you mean that, with time, as specimens are gathered and analysis proceeds, and people see the kind of variation - ?

Jones: I think it's when methodologies change. I mean, think at the moment you could predict that stuck in the sides of very old bones there are bits of DNA and protein evidence that are there, but our current methods can't get them out and read their sequence. And it's crystal-ball-gazing to really establish when that'll change, or what'll change. 0.38.06

Holdsworth: It's conceptually possible.

Jones: Conceptually possible, yes.

Holdsworth: That's interesting. In your book you mentioned the case of Wilson's investigation of the serum albumins.

Jones: Yes. I mean, that's the other interesting thing. Before DNA molecular studies were there, protein had a longer history. And the same thing of 'feeding off' medical research happened. So you can go back for example to the First World War and the study of blood groups, which is a protein study with a clear genetic determinant. And on the one hand we've got research into it in terms of a contemporary medical problem, but then there's a spin-off. Those are that the geography of As, Bs and Os reflect the history of our species and its spread across the globe.

Holdsworth: Could you call it almost a kind of proxy genetic study?

Jones: It's a proxy – yes exactly. Absolutely. I mean it's clear that, it's a simple Mendelian system, so it's a very sound proxy. And I guess the only limitations on it, really, are that with

proteins you're always dealing with coding regions. You're always dealing with something that's engaged in ecological stuff, and so those As, Bs and Os are there to resist diseases. Diseases are different in different parts of the world, so the picture you get might be environmental rather than phylogenetic. 0.40.02

Criterion 8: *'Does the research use environmental markers?'*

Holdsworth: Good. Well, the next one's one for you. 'Does the research use environmental markers?'

Jones: Yes. Ha, ha!

Holdsworth: Environmental markers being something like a site – you know, a cave, or a dwelling-site - or an artefact. Or a heap of oyster-shells, or something like that.

Jones: Absolutely. It's very closely contextualised by the environment.

Holdsworth: But, in biomolecular archaeology, logically you take into account what I've just called 'environmental markers', but is there theoretical work on the inter-relationship between the biomolecular markers and environmental markers? 0.41.13

Jones: It's an interesting question. And I think the answer is: in time there ought to be, but it's pretty underdeveloped at the moment. There's a great interest - in the wider field of archaeology - in site-formation processes that will explore those issues at different levels. So for example, if you're excavating a town which has buildings in it, and the buildings in it have rubbish tips, and the rubbish tips have bones in them, then there's been quite a lot of discussion at various levels of how the bones relate to the pit, how the pit relates to the house, how the house relates to - [and so on]. And there pretty much ought to be the same thing in relation to biomolecular archaeology, but I would be wrong to suggest that was a highly developed field. 0.42.22

Holdsworth: Is it a direction in which things might go in the future?

Jones: I think so. I think what happens [is this]. I mean, there's - if you like - a sort of trajectory that things happen in these fields. I mean, one of the things that you see first with some new methodologies like this [is that] the first stage is to some extent 'headlining' - that a new method is applied to a high-profile problem, and a quick route to interesting results comes into being. Certain elements of the methodology then become more routine, and they're repeatedly asked of different sites and different materials and build a more collective picture. And once they've become routine, I think questions about connection between different data categories become part and parcel of research activity. So [that's how] it happens. It certainly happened in ancient DNA. 0.43.42

Holdsworth: That was a good phrase you used then – "different data categories".

Jones: Yes, absolutely.

Holdsworth: Sorry, you were going to give an example.

Jones: Well, I was going to say, I mean, a simple example which isn't in this field is in radiocarbon dating. You know, the first radiocarbon dates are high-profile articles dating the Dead Sea Scrolls or something like that. And the second phase is for radiocarbon dating to get built into a routine dating method. And it's when it gets built into a routine dating method when people ask procedural questions or transformation questions, like - hang on, let's take each aspect of this data and ask what problems, biases there could be with them, and how we could get in control of those biases. So it's almost like a three-step thing. 0.45.10

Holdsworth: Yes, so there were three steps: from the 'headline news' of radiocarbon dating –

Jones: Yes: to the repeated application to less 'headline' but probably more profound questions. And the third step was, if you like, methodological interpretive research to fine-tune issues of how the data curve relates to the question being asked.

General and concluding discussion

Holdsworth: Good, well we've exhausted the list of criteria I've come up with so far. I don't know if off-hand you can think of any to add to the list, that separate your discipline from others in cognate areas. 0.46.06

Jones: I mean, the interesting [thing is – although it might seem obvious] – that we like to explain patterns by a historical argument. I remember someone - this is going off at a tangent – he was actually a guy who was interested in the philosophy of economics, and he did a text called 'Story-telling and metaphor in economics'.[313] One of the things that he was arguing was that the way we explain anything is either by telling a story or building a model of it. So it may be, but it does strike me that the key thing that we do to explain pattern in people is we tell a very long story. That's how we explain things. So we're forever trying to explain things historically.

Holdsworth: 'To explain pattern in people' – that's a good phrase – 'by telling a long historical story'. 0.47.14

Jones: Yes. I mean, it may be so self-evident to archaeologists, but nevertheless it is something that we do, and I notice we do. And when I do something in an inter-disciplinary collaboration I notice how much we do it, and how much that's part of our mind-set.

Holdsworth: Do other people treat you as being – excuse the word – 'funny' in some way for being so interested in the past?

Jones: Well, I suppose if it's in the context of collaboration, I think the collaborators sympathise! You collaborate if you regard the archaeology as a rather interesting angle. So for example

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[313] Apparently a reference to a paper by Donald N. McCloskey entitled 'Storytelling in economics'. It was published as Chapter 4 of Don Lavoie (ed.): Economics and hermeneutics, Routledge, 1991. See the web page:
http://books.google.com/books?hl=en&lr=&id=Azz33GC56iAC&oi=fnd&pg=PA61&dq=%22McCloskey%22+%224+Storytelling+in+economics%22+&ots=YqJS-pt06-&sig=Z27_E3Dt7nZAwTpMXNgcB0EEKb4
(Consulted 12 February 2008).

at the moment I collaborate with people who are primarily concerned with crop breeding. 0.48.06

Holdsworth: Of course, if you were to collaborate with geologists they would regard your interests as being ultra-modern.

Jones: That's right. Absolutely.

Holdsworth: I mean, oddly enough there's less of a – let me put it this way - an antiquarian flavour to biomolecular archaeology than there would be to, say, mediaeval history.

Jones: Yes, absolutely.

Holdsworth: Largely a question of time-frames appropriate to the the discipline.

Jones: That's right. Absolutely. And we would look for patterns on different time-scales. That's right.

Holdsworth: Just quickly to return to the subject of the definition of behaviour, but with an example, would you describe farming as a behaviour? 0.49.00

Jones: I would describe it as a 'practice'. I think on reflection there may be a history of how behaviour has come into archaeology. A behavioural subject that we would be very much aware of is behavioural ecology. And so with that comes a baggage of - more of behaviour as a Darwinian trait. And I suppose by saying 'practice' we're keeping our options open about whether it's a Darwinian trait or whether it needs to be explained in some other way. I think – yes - that the word 'behaviour', for reasons that may be very local to archaeology, comes with quite a lot of baggage.

Holdsworth: That you want to avoid? Or you, so to speak, delegate to other disciplines? 0.50.01

Jones: Within archaeology, if we talk about a 'behavioural' thing – so, if you or I were to start here talking about a 'behavioural' response, there would be a sub-text to that, and it's a kind of trace of, kind of, doubt there [for various] reasons. And so, for example, some people would believe that of farming. Some people would argue that's how you explain farming: that basically it's a form of adaptation to a Holocene environment. And if, for example, you feel that farming is not sufficiently explained in that way and may be a sort of polycausal thing, or only explained at a higher level of generality, then one might tend not to use the word 'behaviour' just for that reason alone. But that may be a rather local usage of 'behaviour' – I don't know. 0.51.00

Holdsworth: But I mean, if you say it's a form of adaptation to a Holocene environment, it's an easy stage to say it's a form of 'behavioural' adaptation.

Jones: Exactly - if you [argue], as some people would, that that's why farming has come into being - because it's a process of adaptation, you know, a process of selection of hunter-gatherers and farmers being separately selected. And by using the word 'practice' rather than 'behaviour' then it kind of opens the way to explore other models, really.

Holdsworth: Not selected by natural selection, though.

Jones: No. I mean, to use the word 'behaviour'nudges it in the direction of natural selection, I would say.

Holdsworth: I see.

Jones: But that may be very local usage.

Holdsworth: Because of the perspective of behavioural ecology? 0.52.00

Jones: Yes. I think largely, yes.

Holdsworth: Ah, that's interesting.

Jones: It's one of the things I haven't taken sort of taken apart. I'm conscious that the usage of the word behaviour would have that added baggage. And -

Holdsworth: But would you agree - now seeing it from some other perspective, like social psychology or sociology - [with] the argument that farming led to, in the end, permanent settlements, and it's arguable that led to stratification of society?

Jones: Yes.

Holdsworth: It would seem natural at that stage to say that it was a causal factor in the emergence of certain patterns of social behaviour.

Jones: Yes, that would be perfectly reasonable.

Holdsworth: For some people it would have a Darwinian implication, and for some people it would not. 0.53.01

Jones: Yes. Absolutely, I entirely take your point. And if I hadn't any [constraints connected with] being an archaeologist, and I think about how I might use the word 'behaviour' in the pub, I can see that it's probably quite a local discourse. You know how these words can have a bit of baggage in a local discourse, don't they?

Holdsworth: Absolutely. I read a perfectly serious text twenty or thirty years back saying that 'behavioural science' had become a more popular expression in America than 'social science' because of possibilities of confusion with 'socialism'.

Jones: Mm. Interesting.

Holdsworth: I'm not saying it was the case, but this was argued. As I said at the beginning, the nomenclature of disciplines is subject to a lot of historical accident.

Jones: Mm. 0.54.00

Holdsworth: Well, thank you very much. I think we've gone through the agenda. I don't know if there are any other points that you'd like to come back on or volunteer or correct?

Jones: No, that's fine. I hope it's been helpful.

Holdsworth: Enormously. Thank you very much.

Jones: Not at all. And if you wanted to kind of bounce anything by email or something – I mean, just if you wanted further input or anything, you know. I wish you well in your research.

Holdsworth: Thank you very much.

0:54:39

2. Research interview with Dr John R. Hutchinson – Edited Excerpts

Interviewed: Dr John R. Hutchinson, Lecturer (now Reader) in Veterinary Basic Sciences, Royal Veterinary College, Hawkshead Campus, North Mymms, Herts, AL9 7TA.
Interviewer: Richard Holdsworth, PhD candidate in the Economic and Social Research Council (ESRC) Centre for Genomics in Society, Egenis, University of Exeter.
Date and time of interview: Monday, 5 February 2007, 11.00.
Place: Royal Veterinary College, Hawkshead Campus.
Total length of the recording: 40 minutes 57 seconds.

The interviewee's description of the research 0.03.00

Holdsworth: I've read your *Nature* paper –

Hutchinson: The dinosaur locomotion one recently?

Holdsworth: Yes - which was very much a methodological paper.[314]

Hutchinson: Yes.

Holdsworth: And I'm very interested in the kind of inferences which you, for example, think it's valid to make from the palaeontological data, which nowadays of course includes, as well as bones, DNA.

Hutchinson: Right, yes.
[...] 0.03.45-0.04.00

Holdsworth: So, first of all would you mind just briefly describing typically the research that you're engaged in? 0.4.20

Hutchinson: Broadly speaking I'm interested in how locomotor systems evolved in animals. A second part of my work is how size influences locomotion in animals, both in a comparative context between species, but also in an evolutionary context: how size influences locomotion as size changes during evolutionary time. So I have various projects going on, and on various groups of animals – taking them as case studies, if you will: this is what this lineage does, how size will influence locomotion and how the two of them evolved, in, like, dinosaurs and elephants. I've done a bit with crocodiles as well.
0.05.10

Holdsworth: To what extent would you say size was a factor in hominid evolution?

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[314] Hutchinson, John R. and Gatesy, Stephen M. (2006): 'Beyond the bones', *Nature* 440, 292-4 (16 March 2006). The article carried the secondary headline: 'How did dinosaurs stand and move? Computer simulation and other methods have told us much about how dinosaurs did and did not move, but they have not yet reached their full potential'.

Hutchinson: It's a bit outside my area of expertise, but I've read some of the literature, and it seems like there's been a general size increase throughout hominid evolution with some kind of exceptions on side branches, but I don't think it's played a huge role. Size increase hasn't been that big. I mean, there has been a doubling of height or so. Compared to other groups I work on, it's a very modest size increase.

Holdsworth: But are there criteria you can identify for deciding in some way whether we have the optimum size? 0.06.05

Hutchinson: Well, I guess to know what criteria would be relevant it would be important to know what was meant by 'optimum'. That's a very tricky issue: optimum size for what?

Holdsworth: For example, for bipedal locomotion. 0.06.28

Hutchinson: Even then it kind of gets into what's optimum there in terms of: is it metabolic cost during walking, or running speed, or what are you choosing as your criterion? It gets pretty hairy. Yes, I don't know. Those kinds of questions are addressable at a specific level, but -.

Holdsworth: Well, in other species, I'm sure you can think of examples where particularly large size or particularly small size seems to have evolved in response to particular selection pressures. You've got elephants, for example. What meaningful can be said about the very large size of elephants?

Hutchinson: Well, kind of the classic story that I think most people think is probably true is that elephants evolved very, very large size very early on, in kind of a classical pattern of herbivores evolving a large body size perhaps to escape predation at an adult age. Once they get so big that it's hard for any predator to take them down, they become immune to predation - as adults, anyway. So that's kind of the classic story for why elephants became so big: that size offers protection against predation. But there are other factors, like monopolising resources or being able to have a large home range. Those kind of things, they're important too. 0.08.30

Holdsworth: And you mentioned metabolic cost. Is that intimately related to gait?

Hutchinson: Oh, definitely. Cost of locomotion - yes. Metabolic cost of just standing there is still related to biomechanics somewhat, for animals standing still. They still need muscular energy to keep them from falling down. So yes, it's very much connected to locomotor biomechanics in terms of walking energetics. 0.09.04

Holdsworth: A point that interests me is that many disciplines that work with, on human behaviour often don't take into account bioenergetics or biomechanics for consideration. Would you agree with that? 0.9.25

Hutchinson: Sure, I think – well, it's a matter of specialisation. A lot of people don't consider anything outside of their specialty. It's kind of hard. The extremely specialised nature of science today is that everyone's so specialised in what they do. Rarely, you find someone who does everything just right. But, yes, it's true in general. It takes a lot of training to really properly interpret mechanics and physiology; so a lot of people either intentionally or unintentionally shy away from it. 0.10.02

Holdsworth: Yes, and yet it's easy to see that it could be important in the evolution of hominid and human behaviour.

Hutchinson: Well, I think for hominids it's certainly gotten more attention than it has in most other groups, but maybe that's just a factor of a lot of research in general being concentrated there. 0.10.26

Holdsworth: And in the research which you've been doing, do you draw a lot on genetic or genomic research?

Hutchinson: I would say I pay attention to it, kind of because it's interesting. I'm an evolutionary biologist kind of first and foremost. I'm interested in evolution and in the past. The revolution in genomics is absolutely important. But for a lot of the groups I work on in the lab their members are extinct, so there's no genomic information, and there may never be. So what genomics has to offer varies for people, but for the questions I want to ask there's just nothing there. But in terms of broad relationships of animals it's useful to a point – and important – but so far there's no way to connect, like, genomics research and factors related to locomotion. You see, in my work it's just too much of a leap, but yes, there are connections there, but I haven't ever explored them.

Holdsworth: The recent developments in the accessibility of ancient DNA have not greatly helped in your line of work? 0.11.57

Hutchinson: No, I mean, I think it's a limitation of the method that getting DNA after a couple of thousand, or a couple of hundred thousand years, is pretty much impossible. So, you just can't reach that far in the past. I mean, you're talking about lineages that were around 230 and at least 65 million years ago – far beyond the reach – far beyond the limit of preservation of biomolecules. Almost nothing is left. Occasionally you find little bits of keratin, or other durable proteins that are still relatively intact, but as far as DNA, you don't even find a base-pair yet that is usable. There is no dinosauric DNA. There is no extinct elephant DNA. Very recent mammoths - for mammoth researchers it's been useful, actually. People have learned a bit about the evolution of mammoths and modern elephants to draw a very closely related group of species, and for those animals there is ancient DNA. There is ancient mammoth and maybe a little bit of mastodon DNA, so that stuff is useful. And there's very controversial evidence of dwarf elephant DNA that's recently come out. That's some of the oldest DNA on record: 800,000 years old, if it truly is DNA. So that's interesting. 0.13.28

Holdsworth: And the kind of time-scale that you're often working with?

Hutchinson: As old as 230 million years. That would be the older stuff I might be working on. That's way, way, way beyond - . But genomics still deals with major phylogenetic relationships of groups, and that's something I use a lot of. I need to know phylogenetic relationships of major lineages, and that includes living animals. So there's been a lot of research done on using [genomes] of crocodiles and birds and lizards to see how they're related to each other. And I draw on that research because it forms the evolutionary framework behind my work. 0.14.23

Holdsworth: Yes.

Hutchinson: But then filling in the picture takes information from outside genomics. It takes morphological evidence.

Holdsworth: Is there any way that environmental markers can be useful?

Hutchinson: You're thinking, like, radioactive isotopes?

Holdsworth: No, I was thinking the geological characteristics of sites, or actual signs of the presence of the organisms at the time when they lived. 0.15.10

Hutchinson: There are footprints. That's a major source of information. Extremely important. There are thousands of them. 0.15.15

Holdsworth: Really?

Hutchinson: Oh yes, I mean any one animal could leave thousands of footprints in its lifetime but only one skeleton. So we actually have more footprints than there are specimens of animals.

Holdsworth: Which is particularly useful for somebody studying locomotion.

Hutchinson: Absolutely, yes. It's the only direct evidence of behaviour you normally have. That's right. The problem is you can never tell what species made the footprint. It's normally only very general details: well, this is a big, two-legged animal – something like that. So it's limited in its [ability to give you] very much to draw on.
0.15.53

Holdsworth: Is there any way of cross-referencing other factors so you can narrow down the choice?

Hutchinson: You can to a degree, yes. By knowing what animals were present in a given area at a given time, you can kind of narrow down your list of likely candidates, but then you're always kind of left wondering, well, what if – given our fossil record [limitations] - what if there was another animal there which we just don't know about, and it made the footprint? It makes it very hard. We know all too well how incomplete the fossil record is. We may know the skeleton of an animal from Africa, and we find footprints in America. Even though that animal in Africa lived at the same time, it couldn't have made those footprints in America. And then later on you find that it *was* there in America – you just didn't find any fossils of it yet. The field is so young. We just haven't found everything.
0.16.46

Holdsworth: Interesting these recent discoveries in Australia: deposits of bones of ancient fauna.[315]

Hutchinson: Yes. Oh, it's a kind of Ice Age thing. Pretty recent.

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[315] 'Ancient Nullarbor megafauna thrived in dry climate', Western Australian Museum Media alert, 25 January 2007, available at http://www.museum.wa.gov.au/AncientNullabormegafuana.asp (Consulted 29 February 2008). This referred to the following letter in *Nature*: Prideaux, Gavin J, et al. (2007): 'An arid-adapted middle Pleistocene vertebrate fauna from south-central Australia', *Nature* 445, 422-425 (25 January 2007).

Holdsworth: I know it's not your field, but do you interact at all with people doing research into hominids? 0.17.23

Hutchinson: Yes. There are a couple of groups in the UK that I talk to a fair amount, one of which I try to set up collaborations with.

Holdsworth: Oh. Do you mind telling me who they are? 0.17.37

Hutchinson: Yes, there's a guy named Bill Sellers up in Manchester who does a lot of hominid locomotion and energetics research, doing a lot of simulation of hominid locomotion.[316] And Robin Crompton at the University of Liverpool.[317] He's kind of the top guy in that area, hominid locomotor research, especially in the UK. Bill Sellers as well does a lot. So those are the top two. I get to talk to those guys a fair amount. And then there's also another researcher here at the college, Rachel Payne, who has worked a bit on hominid locomotion.[318] Functional anatomy, yes. And she is working with those guys. It's all kind of a rather incestuous family of hominid locomotor researchers who've all worked under the same supervisor, Robin Crompton.
0.18.40

Examination of the criteria

The interview then passed to a consideration of the Criterion Matrix.

Holdsworth: So, my quest is for criteria that can categorise and separate different disciplines, of which these are some examples. I think all the ones here are going to be covered by my research. And first of all I'd like to take a look at the criteria with you, and you can tell me whether you think they're valid.

Hutchinson: Mm, hm.

Holdsworth: And we could have a look at where evolutionary biomechanics fits in.

Criterion 1: *'Does the research cover all hominids or only* Homo sapiens*?'* 0.19.33

Holdsworth: So, first of all we're interested in knowing - and here perhaps this is not so applicable to you? - 'Does the research cover all hominids or only *Homo sapiens*?' That's of obvious relevance in separating some of the other fields.

Hutchinson: Sure.

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[316] Dr Bill Sellers, Lecturer in Integrative Vertebrate Biology, Faculty of Life Sciences, University of Manchester.

[317] Professor Robin Huw Crompton, Primate Evolution and Morphology Group (PREMOG), Department of Human Anatomy & Cell Biology, School of Biomedical Sciences, University of Liverpool. *Note*: Professor Crompton was also interviewed in the context of the present research.

[318] Dr Rachel C. Payne, Research Fellow, Structure and Motion Lab, The Royal Veterinary College, Hawkshead Campus, North Mymms.

Criterion 2: *Is behaviour studied in the ecological setting – or in the laboratory or clinic?*

Holdsworth: 'Is behaviour studied in the ecological setting?'

Hutchinson: Yes.

Holdsworth: Because there are other disciplines - .

Hutchinson: In the work I do: yes. And quite a few people who study evolutionary biomechanics of hominids would concur. They're quite explicit about comparing the laboratory and ecological setting.

Holdsworth: As part of their method? 0.20.25

Hutchinson: Yes, I know some people that do look at that. Yes.

Holdsworth: Could you give me any guide to the literature?

Hutchinson: Well, Robin Crompton again, you've got, to start with. He's doing a lot of work lately on hominid footprints, where they left them. But also there's kind of on the other end of the spectrum a guy named Daniel Schmitt. He's at Duke University in the States.[319] He's done a lot of very explicitly ecological work on primate locomotion, trying to look at how their adaptations are matched to their ecology and how locomotion is affected just by ecology. 0.21.20

Criterion 3: *'Is the focus on species-typical traits or on individual differences?'*

Holdsworth: 'Is the focus on species-typical traits or on individual differences?' 0.21.53

Hutchinson: Mm. Most of us would typically focus on the species, but where we can we look at individuals. It's pretty hard. Sometimes you just don't have the sample size to look between individuals, but in hominid research I think people have done. I've seen quite a few studies that have been pretty careful about individual variation, and that's like one of the disputes over these dwarf hominids in Flores: is this some sort of disease - individual variation - or does it represent them being a different species?

Holdsworth: I see, yes. 0.22.43

Hutchinson: In my kind of work individual variation is something to be checked for and factored out but not a major focus of work. Sometimes you just can't even cope with it, because if you get two individuals what can you say about individual variation?

Criterion 4: *'Does the research typically draw on the findings of genomics?'*

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[319] Dr Daniel Schmitt, Associate Professor, Department of Biological Anthropology and Anatomy, Duke University, Durham, North Carolina.

Holdsworth: 'Does the research typically draw on the findings of genomics?'

Hutchinson: For my work, yes and no, I guess. I mean, mostly in my day to day work, no, but certainly it's relevant at a certain level. 0.23.28

Holdsworth: Sort of, as it were, theoretically relevant?

Hutchinson: It's just, like I said, where it's most relevant is in determining the relationships of major groups of animals and that's -

Holdsworth: Phylogenetics?

Hutchinson: Yes, phylogenetic relationships. 0.24.00

Criterion 5: *'Is the research on genes or other DNA? If 'other': mtDNA or Y-chromosome?'*

Holdsworth: Maybe this is not so relevant. For some of the disciplines on the list it's important to distinguish between genes in the nuclear DNA and - .

Hutchinson: Yes. So again, phylogenetically, the first two would be often used, but I haven't seen many studies that have used the Y-chromosome. Of course that's for human chromosome studies.

Holdsworth: Yes.

Hutchinson: You would not expect to see it used in bird studies.

Criterion 6: *'Is there research on the DNA of non-human/hominid species? If so, animals or plants?'*

Holdsworth: 'Is there research on the DNA of non-human species?' 0.24.40

Hutchinson: Not directly, but, yes, again for phylogenetic research it has potential too.

Holdsworth: I mean, interesting work has been done in a much more modern time-scale in biomolecular archaeology on the origins of domestication in animals and plants.

Hutchinson: Sure, yes.

Holdsworth: And they can interact between the two – well, between the three: animals, humans and plants. 0.25.19

Hutchinson: Yes.

Holdsworth: Because the archaeological sites show what plants have been consumed, and whether they were domesticated or not.

Hutchinson: Mm,hm.

Criterion 7: 'Is there research on other bio-molecules? If so, proteins or other?'

Holdsworth: 'Is there research on other biomolecules?'

Hutchinson: Well, for phylogenetics work. And occasionally you get some weird preservation, like you occasionally get some dinosaurs preserved with keratin and other proteins. Not really relevant for learning their locomotion, but it is relevant for understanding their biology. 0.25.53

Criterion 8: '*Does the research use environmental markers?*'

Holdsworth: And a question I already asked: 'Does the research use environmental markers?'

Hutchinson: By that you mean: you would say footprints would fall within that classification? And also fossils. People who dig up fossils always pay attention to what kind of sedimentological setting they're preserved in, because that tells you was the animal in a desert versus a swamp, or things like that.

Holdsworth: Ah yes, well, that's a clear case, isn't it? A very good example. 0.26.29

Hutchinson: Yes, that's definitely important.

Holdsworth: Can you think of a particular example off-hand?

Hutchinson: Well, pretty much every dinosaur discovery out there is always carefully [detailed]. A good researcher carefully describes the geological setting: was this a river that this animal was preserved in, a flood plain, a forest? Knowing the ecological setting is very important. In terms of understanding the locomotion that's a whole other can of worms, but - . 0.27.02

Holdsworth: Can you give me a reference to some of your own work that involves footprints?

Hutchinson: I guess some of my work has discussed it. I haven't done actual hands-on footprint research. It's more or less other people do it, and I read their literature and synthesise it into what I do. But I've discussed it in review articles and stuff. There are - let's see – what would be the most relevant? The paper by myself and – actually, the first author is a guy named Farlow.[320] In 2000. And that's a paper that goes through some of the footprint evidence.

Holdsworth: Where was that published?

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[320] Professor James O. Farlow, Professor of Geology, Department of Geosciences, Indiana-Purdue University at Fort Wayne, Indiana.

Hutchinson: That was in American Zoologist.[321] There is actually a 'pdf' available on my website.[322]

Holdsworth: Thank you. Could you tell me a bit more about what inferences you can draw from footprints?

Hutchinson: You can tell kind of the general posture of the animal: was it standing with its feet very close together or widely spaced apart? You can figure out relatively speaking how fast it was moving: whether it was moving at the same speed or speeding up, accelerating or slowing down – based on the distance between footfalls. And you can sometimes tell if an animal was limping: if it leaves kind of asymmetrically spaced footprints, with one step being longer – the right leg taking longer steps than the left leg - or something like that. Occasionally you find evidence of specific behaviour.

General and concluding discussion 0.29.13

Having concluded the examination of the criteria, a general and concluding session of discussion provided an opportunity to range over some other themes. Holdsworth began by raising the relation between evolutionary biomechanics and physics.

Holdsworth: With regard to biomechanics - I'm putting this as a question because I'm certainly not an expert in the subject - but part of it seems to me to be about the physics of an organism just being.

Hutchinson: Yes.

Holdsworth: Us standing, or sitting.

Hutchinson: Yes. 0.29.38

Holdsworth: And when we're standing the legs have to do work. And the muscles are holding the skeleton in the right posture - to optimise the work and the energy which is used.

Hutchinson: Mm,hm.

Holdsworth: But it's also about locomotion, about movement – and it has to be about both.

Hutchinson: Yes. 0.30.10

Holdsworth: But what seems to me to be somewhat unusual about biomechanics, and I'm thinking about evolutionary biomechanics, is that among the selective pressures – the pressures of natural selection – there are simply the laws, the direct application of the laws of physics, which when you stop and think about it is a bit rare in terms of the evolution of other physiological systems in plants and animals, where they can be mediated by various forms of perception or chemoreception, and things like that.

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[321] Farlow, James O., Gatesy, Stephen M., Holtz, Thomas R., Jr, Hutchinson, John R., and Robinson, John M. (2000): 'Theropod locomotion', Amer. Zool., 40:640–663 (2000).

[322] http://www.rvc.ac.uk/AboutUs/Staff/jhutchinson/Publications.cfm (Consulted 3 March 2008).

Hutchinson: I see.

Holdsworth: But if you're a hippopotamus standing on four legs it's gravity undiluted -

Hutchinson: Yes. Pretty important.

Holdsworth: - that evolution has to select for.

Hutchinson: And one of the reasons - one of the things about my work is I work on larger animals in which gravity plays an even larger role. As you move to the smaller end of the scale other forces become more important, like viscous and fluid forces. So again gravity becomes pretty important there. 0.31.31

Holdsworth: From the human point of view - hominids and humans - a point that interests me is this. When we talk about behaviour, people think about – they think about movement.

Holdsworth: They think about cerebration, and the connection of that and the movement that people make. They often forget, I think, behaviour such as manual behaviour and the things that people do with their hands. I came across a very interesting book – it's a little old now, in fact it's out of print – 'The biomechanics of the hand' by somebody called Brand,[323] who was very interesting because his knowledge was scientific, but also resulted from the fact that he'd worked for many years in India doing operations on the hands of leprosy sufferers -

Hutchinson: Oh, wow.

Holdsworth: - to restore manual function. In this book he mentions at one point that the – I don't know how to put this correctly – that the muscles in the hand have evolved in such a way that implies a relationship with objects external to the body. It's not just a capacity, which people often talk about, the fact that we have a hand that's capable of grasping, but the structure of the muscles is actually so to speak expecting an interaction with an external object.

Hutchinson: Interesting. I guess that makes sense in an evolutionary context.

Holdsworth: Can we see that in other species? Climbing animals, for example?

Hutchinson: Oh, absolutely, yes. The literature is full of descriptions of adaptations for climbing and swimming, flight, a lot of animal systems, a lot of the evidence you see, especially behind the head, is adaptations for interactions with their environment. 0.34.08

Holdsworth: Sorry, what do you mean: 'behind the head'?

Hutchinson: When I teach students, I take them to a museum and say, if you're looking at a skeleton, don't just look at the head, which often they focus on – you know, the teeth, the jaws, everything, but often they miss what's going on in the back of the animal, the details

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[323] Brand, Paul W. (1985): Clinical mechanics of the hand, St. Louis, 1985.

of how the post-cranial skeleton changes and how that reflects what the animal's life involved. 0.34.34

Holdsworth: Right.

Hutchinson: So the [anatomy] [holds] reflections of interactions with the environment. Especially the feet: in a bipedal animal they tell you quite a bit about the animal. 0.34.51

Holdsworth now guided the conversation back to issues of method.

Holdsworth: Have you any comments to make on this set of criteria that I introduced? 0.35.00

Hutchinson: No, I can't see anything wrong with it. It's not something I'm terribly familiar with, like what the epistemological procedures are you would take in order to make a good one versus a not so good one.

Holdsworth: Well, it's no mystic process. It's just a process of asking people like yourself. I mean, is there a criterion which, for example, strongly distinguishes evolutionary biomechanics from something else on the list?

Hutchinson: The things that stand out the most to me are that it uses the phylogenetic framework, that it uses physics. Those are the two things that basically, you know - physics plus phylogeny, really. 0.36.00

Holdsworth: 'Phylogenetic framework'?

Hutchinson: Yes.

Holdsworth: Do you mean physics in the sense that we discussed it earlier?

Hutchinson: Yes, yes. Newtonian mechanics, I guess, would be the most specific way of phrasing it. But physics – that's just, well - .

Holdsworth: But I mean, that is, if I may say so, intensely interesting, because [*Indicating other disciplines occurring lower down on the page of the Criterion Matrix*] when you're looking at something down here - . Let's take an example – psychiatric genetics. We're not going to start talking in terms of Newtonian mechanics.

Hutchinson: No, no!

Holdsworth: I mean, it's not to say that one approach is more valid than the other – not at all. What I'm interested in doing is mapping the diversity.

Hutchinson: Right. 0.37.03

Holdsworth: Because sometimes people come to this subject under the influence of older ways of looking at things and they don't realise that there's more diversity than at first appears.

Hutchinson: Sure, yes.

Holdsworth: As I say, there's no mystery to my method. It's a simple matter of cataloguing the things which are distinctively characteristic of some scientific disciplines and then showing that, neither better nor worse, they happen to differ from other methods and approaches.

Hutchinson: Let's see if I can think of anything else that's intrinsic. I guess, if you want to separate archaeology, anthropology and other evolutionary approaches, dealing with fossils, I guess, would become a relevant criterion, because archaeology, kind of by definition, doesn't involve fossils, per se, it's kind of post- , or pre-fossil material, whereas palaeoanthropology I think would involve fossils. 0.38.21

Holdsworth: Yes.

Hutchinson: That kind of gets into the question of definitions: how you define the difference between archaeology and palaeoanthropology. I would say a lot of people would say, well, 'fossils' draws the line.

Holdsworth: Yes. That's very helpful, too. Good, well thanks very much. I think we've covered the ground. 0.39.03

Hutchinson: Good. Cool.

Holdsworth: And I think I'll follow up, at any rate in the literature, some of the names which you've kindly given me. I might even go and see one or other.

Hutchinson: Yes. They're nice guys to talk to.

Holdsworth: Oh well, that's fine. Good. Oh, and – I explained in my email I would do a transcript of this interview and send it to you for your OK. That was one thing. For my actual dissertation I shall be making a summary. Would you like to see that?

Hutchinson: Sure, I love reading this stuff.

Holdsworth: Good.

Hutchinson: I'm kind of an amateur philosopher myself, so I like to read these kinds of things.

Holdsworth: Well, that's great. But you're being modest, aren't you? You're involved in the theory of biology.[324]

Hutchinson: Well, sure, I'm a scientist – any scientist worth his salt is kind of a part-time philosopher.

Holdsworth: But some are more interested in theoretical and methodological issues than others.

Hutchinson: Yes.

Holdsworth: Good. Thank you.

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[324] Dr Hutchinson is an Associate Editor of the *Journal of Theoretical Biology*.

0.40.57

3. Research interview with Dr Christopher U.M. Smith – Edited Excerpts

Interviewed: Dr Christopher U.M. Smith, Department of Vision Sciences, University of Aston
Interviewer: Richard Holdsworth, PhD candidate in the Economic and Social Research Council (ESRC) Centre for Genomics in Society, Egenis, University of Exeter
Date and time of interview: Wednesday, 7 March 2007, 11.00
Place: Department of Vision Sciences, University of Aston, Birmingham
Total length of the recording: 1hour 43 minutes 51 seconds.

The interviewee's description of the research 0.05.00

Smith: Well, my background, first of all. I took long ago a degree in zoology at Birmingham. I then went on to take degrees in physics and maths at London, external in fact. And then followed that up with a postgraduate qualification in biophysics at Edinburgh. And ended up doing a PhD in neuroscience here. 0.05.40

Holdsworth: Was the biophysics in the context of neurobiology?

Smith: No, it wasn't really. It was a department in Edinburgh. I was there in 1960/61. It was run by Jack Dainty, who was himself a physicist, but interested in membrane transport. It was largely concerned with: transport of materials across membranes, the nature of membranes, but there were other aspects. Other people there talked about structures of proteins and radiology. So that's what I did there and I also learnt electron microscopy with Geoff Haggis in the Physiology Department. But it was a useful diploma, in fact. And since that time I've been back at Aston here, and teaching, first of all in biological sciences, and subsequently over here in vision sciences – which is associated with neuroscience - and I've been very involved in doing the neurophysiology side of the courses. When I was in biology I did the palaeoanthropology courses as well and set up undergraduate degree programs in *Biology of Man and his Environment*. But that's a few years ago now. Latterly my interest has focused on molecular neurobiology. I was very interested in molecular biology from the beginning, back in the 1950s and 60s – when Watson and Crick brought out their material. I was fascinated by molecular biology. My first books were on molecular biology, published by Faber and Faber (*Architecture of the Body* (1964); *Molecular Biology: A Structural Approach* (1968)). And then I went on to do one on the brain, which – [there's] a rather tattered copy over there - also by Faber and Faber (*The Brain: Towards an Understanding,* (1970)) And then I did another book, this time for Macmillan, called *The Problem of Life : The Origins of Biological Thought* (1976)*'* - that was historical and philosophical. 0.08.08

Holdsworth: Right.

Smith: That was published back in the 1970s. I'm now, in my retirement, trying to develop that area. Probably you've met me at some of these conferences and heard me talk about some of these historical and philosophical ideas.

Holdsworth: Yes, that's true. I attended your presentation in Vienna. ('The origins of molecular neurobiology: the role of the physicists': IS/HSSPB, Vienna, 2003)

Smith: Right. Yes, that was molecular biology, that's right – or molecular neurobiology – **r**eally the historical case – a session I organised commemorating the 50th anniversary of the Watson and Crick paper. But I've been interested in the brain and the mind – how do the two relate? - the classical 'hard problem', problem of mind. I guess as a philosopher you're familiar with that.

Holdsworth: Yes. 0.09.04

Smith: I've been trying – certainly in recent years – to get a grip on that. So my interest on the scientific side, then - having been interested in brain, taught the brain, taught molecular biology - is trying to put the two together, trying to understand how the neuroscientific understanding relates to our everyday lived-through experience –qualia etc. I've also published a book on the biology of sensory systems: *Biology of Sensory Systems*, Wiley, 2000. In fact that one there is a Russian translation of it.

Holdsworth: Does that deal with transduction?

Smith: Yes. I start from the molecular end and do all the molecular stuff, and then I come on to talk about the actual sensory systems themselves from an evolutionary, molecular point of view. And there's a certain amount of philosophical discussion – I mean, it is the hard problem, the relation of mind to brain, which comes up over and over again if you're thinking about sensory systems and sensory biology: how does it relate to our everyday experience? 0.10.43

Holdsworth: And of course the issue of perception.

Smith: It's a pity I haven't got the English edition [here]! (*Laughter*). I can't read the Russian. But - that was what I published in the year 2000. And in fact I'm about to do a 2nd edition of that one. [Wiley/Blackwell, in press, due late 2008]. So, so far as molecular neurobiology is concerned - that's trying to put together molecular biology and neuroscience – that came out in *Elements of Molecular Neurobiology* (1st edn. 1989, 2nd edn. 1996; 3rd edn. 2002) And I suppose – obviously - [it's] pure science. I mean, that's my background – pure science - but I'm interested in seeing how that relates to medicine. The various neuropathologies often have a molecular basis. And that's just becoming apparent. So that's the application into human life which I seek – which I try to emphasise in those books. Partly because, I suppose, the major readership is likely to be in medical circles.

Holdsworth: Yes. 0.12.10

Smith: You mentioned palaeoanthropology and mitochondrial DNA and so forth - I must say I haven't really done a great deal on these topics. I mean, I've got a sort of layman's appreciation. But [I haven't] expert knowledge on that. Now, does that give you a sort of overview? 0.12.44

Holdsworth: Yes. Thank you. That's a very good introduction.

General discussion of concepts and methods 0.12.47

Holdsworth: Perhaps we could then move a bit into the area of brain development and what is the role of the genes. [Reading *Elements of molecular neurobiology*], I've picked out a few

points that seemed to me particularly interesting. First of all, you rule out completely any form of genetic preformationism. And you say that the small number of human genes, which became smaller between the 2nd and the 3rd edition of the book -

Smith: Yes. This is one of the interesting things about genomics actually, isn't it?

Holdsworth: Yes.

Smith: That the number of genes which are present in the human genome is so small. There are only about twenty-odd thousand genes there. You know, compared with the older thoughts – [which] were that as one went through the evolutionary process, you increased the number of genes in the genome - it seems not to have been the case. And I don't think we really know why that is. It was a surprise. 0.14.08

Holdsworth: Yes. You also say that genetic preformation is out, even allowing for things like differential splicing, polyprotein sub-division, mRNA editing, and so on. So you're saying: even allowing for the fact that the cell has ways of shuffling around the available genetic material, we still couldn't predict all the 10^{14} synapses.

Smith: I think that is true. Yes, it's still my view. I think it's the usual view. It's not hard-wired in that sense. There isn't a blueprint - in the genes – from which you could then determine how all the various synapses are distributed. 0.15.12

Holdsworth: There may once upon a time have been people with a naïve view of genetic determinism who imagined it would turn out to be different.

Smith: To be predictable?

Holdsworth: Yes. 0.15.31

Smith: Yes, there might have been. But I think that there's so much evidence against that now, both from the point of view of the numbers which you've just quoted and we've just talked about, but also from the experimental evidence within the field of visual perception in particular, which shows how labile the visual cortex is with respect to early visual experience – lots of experiments on that. And also experiments which put experimental animals in poor and rich environments - that is, stimulus environments – showing that this also as a strong effect on the development of the cortex. So all of these things show that the brain is very open - certainly in its early development - to environmental effects. These early periods are known as the critical or sensitive periods, and in experimental animals such as cats and so forth they last a few months, but in humans, I think, something like 18 months. And different parts of the brain of course have different lengths of these sensitive periods. I think the linguistic areas are much more, you know, have a much longer period when they're open to environmental influence. Which isn't to say of course that there isn't a strong hereditary component in there as well. You've got the two things: you've got a core hereditary component, and this is going to be affected and influenced, moulded, by the environment in which it finds itself. 0.17.42

Holdsworth: Right, so you'd lay emphasis on the need for a good epigenetic account of what's going on? 0.17.56

Smith: Yes. It depends. If we're talking about development of the brain, it is of course a hugely complex thing – as I guess you know if you've started to read through the literature. Perhaps I didn't put an awful lot about early development in my second edition, because that was published - when was it? – sort of mid-nineties, I think.

Holdsworth: 1996.

Smith: Yes, 1996 - somewhere about then.

Holdsworth: And then reprinted. 0.18.25

Smith: Then reprinted. This one, the third edition, is 2002, and between 1996 and 2002 there was a huge development in understanding of epigenetics, as you say. And in this edition, I've got – I've developed – that area. I also put an entirely new chapter on genomics

Holdsworth: In the second edition there's already a chapter on epigenetics.

Smith: Yes. In the second edition I also had a chapter called ''Genetics of the Brain'. In the third edition I re-wrote that and called it 'Developmental Genetics of the Brain'

Holdsworth: I'm going to make a note of the new title of the chapter.

Smith: It's a difficult topic; here's a lot of confusion – I found it difficult myself to sort it out. I hope I managed to do it. By developmental genetics of the brain I mean how the genes control the early development of the brain, which is fascinating, but very intricate and difficult to sort out. I hope, as I say, I've sorted it out for [the reader]. These books are really for third-year students, and perhaps postgraduates. The epigenetics: yes, here I have a chapter on epigenetics, and I don't think I've changed that an awful lot in the new edition. You know, it's interesting - here you've got the songbirds, for example. And you find here that we get - not so much a moulding of what is there - but you get a whole new set of new neurons developing when they learn their song, and so forth. So different animals do it in different ways… 0.21.18

Holdsworth: There was part of your treatment of the subject in the second edition I was very interested by – the part concerning the morphopoietic field, or the early genetic landscape. 0.21.37

Smith: That's right. [*Looking at the book.*] Now, we might as well have a look at that. That's right. This is the second edition, isn't it?

Holdsworth: That's the one. It's around page 385.

Smith: Right, OK. I don't suppose I changed it very much. Yes. I've got the same sort of figures in the 3rd edition. They're full of Waddington's ideas.

Holdsworth: Could you talk me through that a bit? 0.22.08

Smith: The notion is that you've got gradients of chemicals going in different directions, in which the neurons develop. You've got three chemical gradients: X, Y, Z. . They create a complex environment. You take any point in this volume, and you've got three chemical gradients

developing or present. At any point you'll have a different concentration of chemicals, or distribution – what would be the better word? 0.23.19

Holdsworth: Concentration?

Smith: It's the amount of one chemical, of the other chemical - X, Y and Z. The mixture – perhaps it's the best word – the mixture will be different in any particular part of this volume, and consequently will affect the nature of the cells developing. So that's what I'm half-way trying to say here.
0.23.50

Holdsworth: Yes.

Smith: The idea that comes out of Waddington, in 1957, when he's writing about genetics. (Waddington, 1957, *The Strategy of the Genes*, Allen and Unwin)

Holdsworth: So this will promote the growth or differentiation of the cells.

Smith: It'll affect the differentiation of the cells.

Holdsworth: Yes.

Smith: Not so much the growth, but the differentiation. It will affect how they develop into one form of cell or another, and so on. Because all the cells in the brain are dissimilar. None of them - no one cell is identical to another. It depends where in the brain they are. And, I mean, this is one of the great differences between brains, I suppose, and computers. The elements of computers are all identical. 0.24.27

Holdsworth: Yes.

Smith: Whereas in the brain that's not so. And, of course, this variation goes all the way down to the molecular level: the actual molecular structure of the membranes, for example, of different neurons, and, indeed, in different parts of a single neuron. In that sense, I think, it's almost unbelievably complicated, and whether we shall ever get - .

Holdsworth: It's interesting, because actually if one was designing a microprocessor, I suppose you'd throw up your hands in horror at the idea that you were going to manufacture it in such a way that each component was different from the next. 0.25.41

Smith: You wouldn't be able to do it. No, that is true. There is a sort of holistic phenomenon – a feature of the brain which, you know, isn't analysable in the same way that a computer is. There, you just take the different parts and just put them together in different ways.
0.26.05

Holdsworth: Right.

Smith: It's all controlled by - . That's the 'epigenetic landscape' idea, I suppose, that the whole – here you've got a holistic idea. The whole thing – the whole – controls the parts.

Holdsworth: Right.

Smith: You can have a, sort of, downward causation. 0.26.28

Holdsworth: Do you think that's true? Or probably true? Do you think it is?

Smith: I think it is true, yes.

Holdsworth: And there's a passage in one of the books on the brain by Susan Greenfield which caught my attention. She's criticising the view, which a lot of people assume, that the best model for the brain and its neurons is indeed a circuit-wiring diagram such as you might find in an information-processing machine. And to counter that she says, actually, the brain is much more like a 'soup' of chemicals.[325] 0.27.24

Smith: Yes, well, I think you'd have to go somewhere in between those. Ha, ha! Yes, I mean you can have a sort of virtual brain. You can model the brain, as we all know. You can model the - not the anatomy, but you can model the output. I mean, we have these chess-playing devices, which model the way in which humans play chess. They can beat most humans at chess, can they not? But that's just the behaviour of the thing. But the actual way in which that outcome is produced is, I think, radically different. And so Susan Greenfield I think is perhaps saying that - although of course one wouldn't say that the brain is a 'soup', very far from it, it is highly structured - but the structure is far more intricately complex and down to the molecular level.

Holdsworth: Yes. 0.28.25

Smith: That's the difference it seems to me between brains and computers. Computers are made of silicon chips, which are themselves just sort of homogeneous metal artefacts, whereas in the brain you go all the way down – down to the protein molecules, and it's very interesting in fact because one gets into questions about chemistry. You talk about a molecule of salt - sodium chloride. All sodium chloride molecules are the same: NaCl. But if you look at a protein molecule – one of the proteins in the brain, perhaps one of the transmitter proteins, such as the acetylcholine receptor. There are lots and lots and lots of these. But they differ. You talk about the acetylcholine receptor, which is a protein. There are lots of different acetylcholine receptors. You can't say, as you could with the salt molecule, that all sodium chlorides are the same – certainly not acetylcholine receptors. There are several dozen different ones. And similarly with the majority of protein molecules. The terminology is not the same as in the case of simple chemicals. The term 'acetylcholine receptor' does not refer to a single molecular structure but to a class of similar (but not identical) structures. 0.30.20

Holdsworth: Yes.

Smith: You use a term to describe a protein molecule, but it's a class of molecules you're really talking about. And these vary from one part of the brain to another.

Holdsworth: They vary in their spatial configuration?

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[325] Citation currently being checked by the interviewer in: Greenfield, Susan A. (1995): Journey to the centers of the mind, W.H. Freeman and Co., New York, 1995, and in other works by the same author.

Smith: Yes. In their structure. The structure of protein molecules varies. And this, as I say, is different from the computer's silicon chips, which are all the same.

Holdsworth: Right.

Smith: So, it's heterogeneous right down into the protein molecules.

Holdsworth: The structure of the protein molecules is sometimes talked about as 'structural chemistry'. 0.31.00

Smith: Well, yes, that's the – that's the science which studies the three-dimensional structure of protein molecules, yes. Structural chemistry. Yes, I mean, it is, obviously, a matter of chemistry. But the way the atoms are put together in the molecule, how they are positioned, which amino acids are involved, say, is going to be different in the different protein molecules. 0.31.29

Holdsworth: Right. Could I ask you for your views on the pertinence of information technology talk in these contexts? It's come under quite a bit of criticism in the context of genes and genomics. When you're talking about molecular neurobiology, you could bring information theory terminology in through two different doors, if you wanted to. One would be the gene as information. And the other would be processing in the neurons as information processing such as seems to be familiar to us from computers. Do they amount to the same thing? Are they valid? Are they equally valid? 0.32.42

Smith: Well, I'm not sure at the philosophical level how to answer that question. All I can say is that, as you know, the information which the genes hold is held in a structural form in the sequence of nucleotides. Information in the brain is the contrast you want to make. So, is the information in the brain held in a structural form? 0.33.32

Holdsworth: What I was saying is, a lot of people, including yourself, I believe, would tend to say that a signal in a neuron, and what happens to it, is an instance of information processing.

Smith: Well, I think I would probably say the information processing was a matter between a population of neurons, or a matter of what is being done in a population of neurons: information *processing*.

Holdsworth: Mm, hm. 0.34.07

Smith: I mean, the gene itself: you wouldn't talk about information processing in the context of a gene, would you?

Holdsworth: Well, processes like transcription and translation.

Smith: Yes, well that's true. But that's a sort of cellular matter, isn't it? You've got the sort of blueprint held in the – an orthodox way of looking at it, I suppose – held in the nucleotide sequences that constitute the gene. And from that you've got a complex set of biochemical reactions which transcribe that information, and you get the transcript, the messenger RNA, which is then going to be chopped up in different ways and so forth so on and then put together, and ultimately finds a ribosome, which then translates the information in that messenger RNA into a protein, which then does the work of whatever cell it's in. So that sequence is a set of biochemical processes – very complex processes. 0.35.17

Holdsworth: Mm, hm.

Smith: You might say that that is analogous to the action of a population of neurons, which may be taking visual input and - .

Holdsworth: Right. I think the point I wanted to draw attention to was that – forgetting about the neurons now, and the population of neurons, but looking just at the cellular processes, there's now quite a lot of criticism of the idea of the gene as a blueprint, and a tendency to suggest that over-reliance on information-theoretical terminology tends to perpetuate the blueprint assumption - and tends to entail what is ultimately a preformationist conception of the function of the gene. 0.36.18

Smith: Mm.

Holdsworth: Whereas what we really want – I'm interpreting now the views in the literature – what we really want is a more complex picture which takes into account – it's sometimes called Developmental Systems Theory[326] - which takes into account everything that's going on around this situation in the developing organism, and how even events in the internal and external environment switch genes on and off. 0.37.04

Smith: Oh yes. Yes, yes. But you're still thinking of the gene as holding the blueprint. And as I was just sketching – you know, it's saying the same thing, really –when I sketched the very complex set of biochemical reactions by which the information in the gene is translated into, ultimately, protein structure, and the protein will then do whatever job it is designed to do. But that sequence of biochemical reactions is your information processing. That's how I would see it. I'm aware that there is a criticism of genes as being information stores. But, for myself, I take a rather simple view of it, as I've just described. Genes have many different functions, of course. Some genes switch others on and others off - it's certainly not simple - but I like to hold onto the simple notion that the sequence of nucleotides – the old Watson and Crick idea, in fact - does hold the necessary information to start the whole thing off. But not on its own – no, the cell is a huge, complex chemical factory. And it will obviously be affected by, you know, hormones or whatever it is outside in the - what for the cell is the external environment. That is just the body. And the body itself of course will be affected by what we normally would regard as the external environment, and that will perhaps switch the hormones on and off. 0.38.51

Holdsworth: Right.

Smith: A good example is photoperiod. In many animals this switches on pineal melatonin secretion. This is a good example of the external environment ultimately affecting (controlling) detailed molecular biology. And ultimately this molecular biology - in the pinealocytes - controls the reproductive cycles of many (non-human) animals

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[326] See (1) Griffiths, P. and Gray, R. (1994): 'Developmental systems and evolutionary explanation', Journal of Philosophy, Vol.91, No.6, pp.277–304, and (2) Oyama, Susan; Griffiths, Paul E., and Gray, Russell D., Eds., (2001): Cycles of contingency: Developmental systems and evolution, MIT Press, Cambridge, Mass., 2001.

Holdsworth: So now we've rejoined the picture we were talking about when you were explaining the epigenetic landscape.

Smith: Yes, in a way

Holdsworth: You end up with a gradient of chemicals: a number of gradients.

Smith: Yes.

Holdsworth: And their interplay –

Smith: That's right.

Holdsworth: - influences the development of the neurons.

Smith.: Of the neurons. I always say that that's a starting-point. So, if you look at the literature on the developing understanding of the genetics of early development, it's hugely complex. And, I mean, that epigenetic landscape is just how we begin, but - and I think as a global idea it's fine - but then you need to go down to the detail, and the detail does show that some of these early genes – you know, those we call the homeobox genes – which start the whole thing off, which give you the dorsoventral axis– and anterior-posterior axis - those absolutely crucial things – and the segmentation - go back hundreds of millions of years in time. Very ancient forms. I mean, it's by showing that the same genes occur in a wide spectrum of animals - both vertebrates and invertebrates – you can take them back to the Cambrian, pre-Cambrian period – that's five hundred, six hundred million years ago. So there is a firm basic plan at the very beginning, which we can't change, really, because if anything goes wrong with that then the whole thing just falls apart. Development – developmental process will abort: produce nothing which is viable.

Holdsworth: Yes. 0.41.14

Smith: Coming back, really, to where you started, you have your basic core. And we're talking about evolutionary processes now, which can hardly be changed. And when you add on bits and pieces it's – I think it was – I think - Francois Jacob who talked about 'tinkering'? 'Evolutionary tinkering'? Have you come across this idea? That that's what happens in the evolutionary process: there's no, sort of plan or foresight or crystal-balling as to how things are going to turn out. Tinkering. Like a gypsy encampment, tinkering bits on - fine if it works, throw it away if it doesn't. It's not taken down to the beginning and redesigned. Evolution's like that. 0.42.00

Holdsworth: Yes, it's curious. As somebody once said: the interplay between chance and necessity.

Smith: Yes. Jacques Monod. Yes.

Holdsworth: Because you've been talking about what seems to be an irreducible minimum handed down across the generations, the millennia.

Smith: The aeons. Yes.

Holdsworth: On the other hand, there is the phenomenon - and that made me think of Richard Dawkins's book, *The Ancestor's Tale*[327] - where he actually takes us back to the various speciations and genetic differentiations which have taken place in evolutionary history. And at the same time he mentions things like the fact that vision has evolved separately in a large number of different cases. 0.43.07

Smith: Yes.. This is the classical problem, isn't it? About evolution. It's the one which Charles Darwin said it made him go cold all over. When people say: how did the eye evolve? because it seems that – you know, it's either perfect or it won't work at all?[328]

Holdsworth: Yes.

Smith: If any small part of it isn't there it won't work. So how can it be explained? - does it evolve in one great jump? Or could it have occurred, as Darwin and orthodox biologists believe, in a number of small steps? And that is what Darwin – what Dawkins is pointing out: that there are lots – if you look at the animal kingdom – there are huge numbers of different eyes.

Holdsworth: Yes.

Smith: From the very simple – just eyespots – up to our complex eyes, which of course are not the only complex eyes – the only design in the animal kingdom. The octopus – the cephalopods – have also very good vesicular eyes such as we have, and insects have got a totally different design – the arthropods - they've got a totally different way of organising out their eyes, which are conceivably just as effective - for them. 0.44.26

Examination of the criteria

Holdsworth: Good. Could we turn our attention, if you don't mind, to the graphic I sent you, which systematises – or attempts to systematise – a series of criteria which can help to distinguish between the ways in which various scientific disciplines make use, or do not make use, of the findings of genomic science. 0.45.12

[*During the following exchanges, while talking, the speakers have in front of them copies of a draft Criterion Matrix for molecular neurobiology, to which they refer, sometimes calling it 'the graphic'.*]

Smith: Right.

Holdsworth: And this may bring us back - in the course of our conversation on this graphic – it may bring us back to some of the themes we've already looked at.

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[327] Dawkins, Richard (2004): The ancestor's tale: a pilgrimage to the dawn of life, Weidenfeld and Nicholson, London, 2004 .

[328] Darwin discusses the evolution of the eye in Chapter 6 ('Difficulties of the theory') of *The origin of species* (6th edition, 1872), in a section entitled 'Organs of extreme Perfection and Complication'. This section will be found on pp167-170 of the 6th edition, as reprinted in the Everyman edition published by Dent, London, 1928.

Smith: Yes.

Holdsworth: Now, the point is that – I think – the number of disciplines that are somehow working on the origins or development of human behaviour and drawing on evidence from genomic research – defining 'behaviour' broadly and defining 'genomics' broadly - is quite large, and perhaps to some people that they would be quite surprised at the number of disciplines that could be brought into the list.

Smith: Indeed. 0.46.15

Holdsworth: And I'm interested to investigate this phenomenon, and also to show – if indeed it's the case - that the various disciplines have different objectives, make different assumptions, have different methods and, in short, are using different ideas.

Smith: Yes, now when you talk about 'behavioural genomics', I mean, could you say 'behavioural genetics' there? 0.46.52

Holdsworth: Well, thank you for that question. It gives me the opportunity to explain that I'm using it – not everybody would do the same – but I'm using it to refer not just to behavioural genetics but to everything which in some way links human behaviour and the findings of genomic research.
0.47.16

Smith: Right. Because the genome, of course, refers to the whole –

Holdsworth: Precisely. Yes.

Smith: - genetic complement which we have.

Holdsworth: All the DNA whether it's that small percentage which is nuclear genes, you know, coding for proteins or not.

Smith: Well that's right. I mean, but the human genome, as we know, is the however many it is, 22,000 genes, which were published in 2003. And similarly, you've got a lot of other organisms which have had their genomes published in the last decade or so [329]. I noticed they've sequenced the genome of a sea-urchin quite recently. The interesting thing there was that that rather lowly organism has genes which are similar to ones which we have in our bodies.[330] 0.48.18

Holdsworth: Yes:

Smith: And some of these genes when they go wrong, produce pathologies in ourselves, and one of the, I think, interesting points about genomes in that sense is that it does allow us to find

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[329] There is a 'List of sequenced eukaryote genomes' in Wikipedia at: http://en.wikipedia.org/wiki/List_of_sequenced_eukaryotic_genomes#Other_Animals (Consulted 23 February 2008).

[330] Sodergren, Erica, et al. (Sea Urchin Genome Sequencing Consortium) (2006): 'The Genome of the Sea Urchin *Strongylocentrotus purpuratus*', *Science*, 10 November 2006, Vol.314. No.5801, pp.941 – 952.

organisms which we can manipulate and investigate with a view to having some medical importance for ourselves, if the genes are the same, even though they're separated by a vast length of time. 0.48.55

Holdsworth: Yes.

Smith: So that's - . When you said 'behavioural genomics' up there, I just wondered if that was what you were really thinking about, but it appears not. 0.49.08

Holdsworth: No.

Criterion 1: '*Does the research cover all hominids or only* Homo sapiens*?*'

Smith: Ha, ha. 'Does the research cover all hominids or only *Homo sapiens*?' Well, molecular neurobiology is a very fundamental subject: it's going to cover all organisms – all organisms which have a nervous system. And that really amounts to practically all even down to the Cnidaria - the jellyfish - and so forth. They have nervous systems, so - .

Holdsworth: Right. There's going to be a column later on [in the Criterion Matrix] for putting in other animal species.

Smith: Ah, OK. Yes, so the answer to that is, yes it does.

Holdsworth: Certainly for *Homo sapiens*. 0.51.10

Smith: *Homo sapiens* and other. I think it's all organisms (except, of course, the plants and fungi), really. Some of course are more important than others for neurobiological research. But in essence all of them I think are covered.

Holdsworth: I suppose one could make a pragmatic distinction. I mean, the research is actually conducted in the context of modern humans, because we haven't got –.

Smith: Oh well, that's true. Yes.

Holdsworth: But the relevance obviously extends to - . 0.52.00

Smith: I think that's true. You can't do neurobiology on Neanderthal humans. Obviously you can look at their skulls and draw some conclusions about their intellectual capacities and so forth from that, but that's not molecular neurobiology – that's something different.

Holdsworth: Whereas for comparison with another discipline, if you were looking at evolutionary biomechanics, the fossil evidence is direct.

Smith: That would be. Yes. That would be relevant. So it's *Homo sapiens sapiens*. But not other hominidae – no. No, I think not. 0.52.48

Criterion 2: '*Is behaviour studied in the ecological setting – or in the laboratory or clinic?*'

Holdsworth: The next question: 'Is behaviour studied in the ecological setting? Or in the laboratory? In a clinical setting?'

Smith: I think really you've got to say not in the ecological setting, but in the laboratory. Now let me think. I mean, obviously you can't make utterly sharp distinctions here, but for the vast majority it will be in the laboratory. And clinic? I think you'd really say it's a laboratory subject. As I said, the applications – the outcomes of molecular neurobiology - one would hope many of them can be applied – *applied* in the clinic. So if somebody came to you with a neurological condition, you might say, well, it's due to some defect in the channel protein in a particular neuron. Which is sometimes the case. But you wouldn't use them for that molecular neurobiological research. 0.54.24

Criterion 3: '*Is the focus on species-typical traits or on individual differences?*'

Smith: 'Is the focus on species-typical traits or individual differences?' Species-typical traits? Not sure what [you mean].

Holdsworth: Well, let me give you an example. In research on intelligence, for example, people are usually looking for the reasons why some people are more intelligent than others. On the other hand, to go back to biomechanics, if your question is 'Why do human beings walk upright on two legs?', that's a 'species-typical' trait - arguably. 0.55.25

Smith: Yes. 'Is the *focus* on species-typical traits or individual differences?' I would probably go for individual differences, I think, in molecular neurobiology. Let me think. You see, there's a certain amount of – it's difficult to say, actually. Not a very good categorisation, I think, for our purposes. 0.56.00

Holdsworth: That's fine! We want a few criticisms. They're very welcome!

Smith: There's a lot of research done on *Aplysia*, which is an aquatic mollusc, and Nobel Prizes have been won. They're looking there at *Aplysia* as a model organism for understanding learning and memory, and that goes down to the molecular level.[331] There's a significant tranche of neurobiology - molecular neurobiology, if you wish - done on that organism. And the trait they're looking for is the withdrawal of the siphon beneath the mantle in response to a stimulus, and looking at conditioned reflexes. That conditioned reflex in *Aplysia* of course is species-typical. It's typical of that particular species, but you're looking – but you're using that species-typical phenomenon to do some molecular biology, trying to get down to how the molecules interact together to produce that conditioned reflex, with the hope of getting some insight into human memory and reflexes - conditioned reflexes. This is one of the things about molecular neurobiology: one looks for the model organism - the organism with which you can actually attack the problem most easily in. So you have a lot of organisms you can examine, but because the investigation is at a fundamental, molecular level, always with the hope of generalising the outcome to understand the human condition. 0.58.24

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[331] For concise accounts of relevant research on the sea slug *Aplysia californica*, see Clark, William R., and Grunstein, Michael (2000): *Are we hardwired? – The role of genes in human behaviour*, OUP, Oxford, 2000, pp.118-124, and Greenfield, Susan A. (1995), pp.78-80.

Holdsworth: Right. But, for example, [take] what we discussed earlier about research into neuronal development. Surely, aren't you asking, 'How does this work in human beings?', rather than 'How does it work in Chris Smith?'

Smith: Oh well, that's absolutely true, yes. So in that case that's species-typical – *Homo sapiens*. But you might say, 'Well, why have *I* got such and such a condition?' – if I had some neuropathology, and you haven't, so there are individual differences, and you'd find in many cases that this is due to a particular molecular defect in my neurobiology compared with yours. 0.59.16

Holdsworth: So it's individual with relation to pathologies?

Smith: Yes, and this is a source of very considerable interest. It was obscure, before molecular neurobiology came along. And this is one of the interesting things about the sea-urchin research which I mentioned to you before. In the sea-urchin, some of the genes there are the same as those which, on mutation, cause human deafnesses, for example, and blindnesses (the Usher syndromes). 1.00.02

Holdsworth: Really?

Smith: Yes, it's that general. So, to answer that question – a bit of both, really, I think. 1.00.28

Criterion 4: '*Does the research typically draw on the findings of genomics?*'

Holdsworth: 'Does the research typically draw on the findings of genomics?'

Smith: On your wide definition of genomics - on any definition of genomics - it will do, yes.

Criterion 5: '*Is the research on genes or other DNA? If 'other': mtDNA or Y-chromosome?*'1.01.00

Smith: Well, for molecular neurobiology, I'm thinking that it's got to be genes on nuclear DNA. So it's not really going to be much involved in mitochondrial or Y chromosome. Well, is that absolutely true? Let's have a look. I've got a list here somewhere, I think. (*Referring to a copy of* Elements of molecular neurobiology*, 3rd edition, that he is holding*). Table 6.3: you see, here are the chromosomes. With the exception of the Y-chromosome each has at least one gene locus responsible for a neuropathology. I don't think we've got a Y-chromosome pathology, but I'm surprised if there isn't one. Now, you see, all of these chromosomes, with apparently that exception, do have genes which (when defective) lead to a neuropathology - these are the genes. Just a single nucleotide change causes the various pathologies, which I've written down here. 01.02.24

Holdsworth: I can't remember - is that also in the second edition?

Smith: No, 3rd edition. I put this in – it's a new chapter - on genomics. This is, as I say, fairly recent work. It wasn't available for the second edition. So, yes, that might be worth-while your having a look at some time. But even that of course is now out of date in 2007.

Holdsworth: Still, the emphasis – 1.03.00

Smith: Yes, the emphasis - that's right – the emphasis is on nuclear DNA... Anyway, the vast preponderance... Mitochondrial DNA – I'm not sure about whether that has a significance in molecular neurobiology. Don't know about that. Don't like to say.

Holdsworth: Anyway, it's not preponderant.

Smith: No. The first column is preponderant, and the other two are not very significant.

Holdsworth: Good. It's just to bring out the fact that in anthropological and biomolecular archaeology contexts people are looking at the mutations precisely in the parts of the DNA that don't recombine. 1.04.06

Smith: Yes, that's true.

Holdsworth: So that they can be traced over – the lineage can be followed over a long period.

Smith: That's true.

Holdsworth: Haplotypes.

Smith: Yes.

Smith: But when would that - ? I mean, I'm not aware that it's neurobiological, though it could well be, of course. In other words, does it affect the brain? I mean, the mitochondrial stuff is really tracing lineages, as you say - trying to find the origins of *Homo sapiens sapiens*. Similarly, with some of the Y-chromosome work. It is also lineages, trying to find origins in East Africa, which is not specifically related to brain size, though you could argue – I suppose - . So, I think, on the whole, the latter two columns are not of great interest to molecular neurobiology. 01.05.10

Criterion 6. '*Is there research on the DNA of non-human/hominid species? If so, animals or plants?*'

Holdsworth: Now, 'Is there research on the DNA of non-human species?'

Smith: On the DNA? Well, you see, molecular neurobiology rather takes the DNA for granted, you know, as another research area. What we are interested in - you're given the genome, and, you know, there are a large number of them now, on the databases. And how do those genomes affect – you know, code for proteins in the brain? So I wouldn't have thought molecular neurobiologists are going to actually research on the DNA. 01.06.08

Holdsworth: I've been perhaps guilty of an imprecision here. I should have perhaps used the same wording as in an earlier column, when I said, 'Does the research *draw* on the findings...? 01.06.34

Smith: Yes. Sure, sure. In that case, the answer is yes. (*Referring to his book*). I've got a nice little table here, you see – Table 6.2 – which shows the number of proteins in the nervous system of humans, *Drosophila* and *Caenorhabditis* – and to get that number you have to know the genomes of *Drosophila*, *Caenorhabditis* – that's the little nematode worm – and humans.

So we are interested in those other genomes, certainly, though we wouldn't, I think, as molecular neurobiologists research - do research into the DNA. So yes. Plants? No, I would say not. Animals, yes, but plants no. For fairly obvious reasons, I think! 01.07.35

Holdsworth: I maintain that there is some benefit in stating the obvious.

Smith: Oh yes!

Holdsworth: And in biomolecular archaeology people can draw conclusions about things like the origins of farming among modern humans from studying the genomes of domesticated animals and plants. 1.08.08

Smith: Yes, I can agree with that. But, I think in the case of molecular neurobiology the study of plant genomes – although I suppose there is a certain, peripheral interest in fly-catching plants and so forth, - is not really significant. Molecular neurobiologists are interested in how nervous systems work at the molecular level.

Criterion 7: '*Is there research on other biomolecules? If so, proteins or other?*'

Smith: 'Is there research on other biomolecules' in molecular neurobiology? The answer to that is yes, there is. Proteins are of very great significance: in fact, of more significance than the DNA. Because all the channel proteins and all the rest – the synapses and the axons and all the rest of it - all work on proteins, which we need to analyse. And recent Nobel Prizes have been obtained for analysing the proteins of potassium channels. 1.09.15

Holdsworth: Could you mention the name of a Nobel prize-winner?

Smith: Yes, I certainly could. [*Leafing through his volume, Smith comes upon an image that he brings to Holdsworth's attention.*] This is the sort of structure which the X-ray diffraction yields. Now let me see. Let's go to 'channels'. MacKinnon is the one I was thinking about. I think he got the Nobel Prize in 2003 or 2004.[332] Anyway, a huge and wonderful development, really. Finding the structure of one of these channel proteins at this resolution: this is 2-ångström resolution. 1.10.50

Holdsworth: What page is that?

Smith: This is - well, it comes after page 304 - a little colour insert. But it's interesting here, of course, which is partly the reason why I find the question just a little bit difficult to answer. For this work was done on bacteria. It was done on bacteria because you can get large quantities of the channel material for X-ray diffraction. The bacterium (*Streptomyces lividans*) is an example of a 'model' organism. It has (so far) proved impossible to extract sufficient quantities of channel protein - sufficient quantities to analyse with X-ray diffraction techniques – from animal nervous systems. One has to transfer the knowledge,

[332] Roderick MacKinnon, winner of the Nobel Prize in Chemistry, 2003. The text of his Nobel lecture on 'Potassium Channels and the Atomic Basis of Selective Ion Conduction', delivered in Stockholm on 8 December 2003, is available at the following website (Consulted 6 December 2007): http://nobelprize.org/nobel_prizes/chemistry/laureates/2003/mackinnon-lecture.html .

the exact structural knowledge obtained from the bacterial preparation, to understand the functionally similar channels known to exist in animal nervous systems. 1.11.35

Holdsworth: So I should have had a third column in the earlier question: 'animals', 'plants' –

Smith: - 'microbes'. Well, in that case - and also in some of the [sensory] physiology - you're using bacteria as model organisms. Simple organisms. Simple – that is, as simple as it can be - to work out the basics of what's happening in more complex entities such as ourselves. This has been one of the great themes of molecular biology. 1.12.09

Holdsworth: Right. Are there other molecules as well as proteins? Yes, of course.

Smith: Yes. Carbohydrates. Yes, indeed. Lipids

Criterion 8: '*Does the research use environmental markers?*'

Smith: 'Does the research use environmental markers?' I doubt it does. I don't think it does. No, to my way of thinking the answer to that is 'no'. Unless you can - .

Holdsworth: I can't think. Of course this is a question again for the biomolecular archaeologists and the palaeoanthropologists.

Smith: Yes, I guess it must be. 1.13.00

Holdsworth: Who study settlement sites and tools and so on.

Smith: Yes, indeed. You see, you've got down at the bottom here 'psychiatric genetics'. I think you'll find when – I don't know if you're interviewing somebody on this yet –

Holdsworth: Not yet.

Smith: - or it's to come, you may find some of his answers, or her answers, may coincide with some of mine. Because, as I said, my feeling is that molecular neurobiology is going to be hugely important in medicine in the coming years. It'll allow us to personalise medicine. We'll be able to - I hope - detect the variation between different people and direct the medical treatment, the therapy, more accurately. At the moment it's 'One size fits all' very often in medicine.

Holdsworth: Ah?

Smith: Knowing the precise reason why something is going wrong at the molecular level makes it possible, it seems to me, to tailor a precise drug to affect that individual, different from that which might affect a second individual. 1.14.15

Holdsworth: So that's – that's surely the answer to the earlier question on individual differences.

Smith: It could be, yes.

Holdsworth: The research is relevant to both the search for species-typical traits –

Smith: Yes.

Holdsworth: - and, actually to the extent that it's successful there, it will help to explain individual differences.

Smith: Yes, to an extent. I think that's right. I'd go along with that, yes. But remember, we're all different at the molecular level.

Holdsworth: And your phrase 'to *personalise* the medicine' is the key there.

Smith: Right. As I say, you may find a point of interest when you speak to your psychiatric geneticist. I mean, obviously molecular neurobiology is a materialistic subject. I mean, it will look at what is causing the problem - the neurological problem. But neurological problems have a psychiatric dimension, frequently. So you may find there's a connection. 1.15.20

Criterion 9: '*The main concern is phylogeny or ontogeny?*' 1.15.42

Holdsworth: Are we more interested here in phylogeny or ontogeny?

Smith: More interested? Well, I can say – these are rather personal views, of course. 1.16.05

Holdsworth: I meant to say at the beginning, as part of my method - and I'm sorry I didn't at the outset - you're not being treated as 'the spokesperson'.

Smith: Well, that is what I'm not. That I am not. Right. Well, I would say personally it's the ontogenetic which is the main [focus]. I'm interested in knowing 'how'. I've got a strong medical perspective. My feeling is that for the privilege of studying molecular neurobiology you must put something back into the taxpayer's pocket, so to speak, and I think that payment back is in the medical area. So I think that the ontogenetic area - the development of the individual – human, in this case – is the most important thing. Genomics of course will also illuminate the evolutionary process, we talked about the sea urchin for instance, and we talked of the genomics of mitochondrial DNA. Indeed the evolutionary insights provided by molecular biology and neurobiology have proved fascinating: the whole area known as 'evodevo' where palaeontology and molecular embryology come together is fascinating. 1.17.19

Holdsworth: Right. I mean, a normal day in the lab, so to speak: the focus is - ?

Smith: In my case, would be to try to find some way ameliorate neurological conditions.

Holdsworth: So here we'd be talking about the ontogeny?

Smith: Yes, I mean, ten or twelve years ago, when I was doing Alzheimer's disease that's what I was concerned with.

Holdsworth: You were working in Alzheimer?

Smith: I was interested in Alzheimer's, yes. And we're still a long way from getting anywhere with that, but that would seem to me an estimable thing to do in molecular neurobiology.

Criterion 12: '*Is the research intended to have a clinical application?*'

Holdsworth: So that is also relevant to the next question: 'Does the research in your discipline have, or aspire to have, clinical application?'[333] 1.18.14

Smith: Yes. I think the answer to that is affirmative.

Criterion 10: '*Does the research draw on fossil evidence?*'

Holdsworth: The next one may not be so positive: 'Fossil evidence?'

Smith: Fossil evidence?

Holdsworth: Yes.

Smith: For molecular neurobiology? Well.

Holdsworth: Perhaps not much!

Smith: Not a great deal, no. Not yet! If they dig up one of these nice mammoths in Siberia, sufficiently well preserved, we might get some interesting things. And of course, I mean, one shouldn't dismiss it. We're just talking in 2007, you know. A few years down the track we might be able to get Neanderthal DNA and see if the FOXP2 gene – the one that is alleged to have something to do with speech - is represented there or not. It might be a small variation, but, of course, of huge significance – from the general point of view, understanding who we are, how we got here. 0.19.39

Holdsworth: That is obviously intensely interesting. Some people think they've shown that we're not descended from the Neanderthals.

Smith: No, but you might say that linguistic ability – related to the development of this particular gene which is alleged to be significant in speech occurred – this is the hypothesis - occurred in humans but not in Neanderthals, and consequently gave humans an advantage. 1.20.14

Holdsworth: Ah, it would be interesting to find out if they had *not* got it?

Smith: Well, it would be interesting to find out if the Neanderthals had *not* got the gene with the sequence we have..

Holdsworth: Yes.

Smith: Whether or not the gene is present in its contemporary sequence, the matter is of molecular neurobiological interest, insofar as speech is a feature of brain. 1.20.46

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[333] In fact Holdsworth altered the order of the questions here to make the natural link with the 'clinical application' criterion.

Criterion 11: '*Is Newtonian mechanics relevant to the research?*' 1.21.45

Holdsworth: Next question. There are only two more on this list. You may wonder why I'm asking it. 'The relevance of Newtonian mechanics'.

Smith: 'The relevance of Newtonian mechanics'.

Holdsworth: That was suggested because it separates out, for example, biomechanics from other disciplines.

Smith: No. I think the answer to that is 'no', but you might put in quantum theory, which probably is relevant. Because we're right down at the molecular level, and of course the chemical bond is a quantum phenomenon. But even that, I think, is below the level with which molecular neurobiologists are concerned. So I think the answer is 'no'.

Holdsworth: Did I see on your publications list you've written something on that topic?

Smith: Yes. In that area. 1.23.00

Holdsworth: What line did you develop?

Smith: Well, what I was doing was a historical account, because if you're interested in mind/brain issues you'll know that people like Penrose, a mathematician down at Oxford, and a number of other quite eminent physicists – and particularly the quantum physicists of the 1920s and 30s – the early quantum physicists at the start of the subject – believed that their break-through at that level of physics – of matter theory - would provide a solution to the age-old brain/mind problem: how are 'matter' and 'mind' related? And because they – because the quantum physicists believed that consciousness is implicated in the dynamics of matter at that level – a very curious thing - they thought there would be a tie-up. So I wrote a paper on that early thought which, in my views, came to nothing in the 1920s and 30s. ('The "Hard Problem" and the quantum physicists, Part 1: the first generation', *Brain and Cognition, 61*, 181-8 (2006)). And my more recent paper has been on where we are today, in the 21st century, on that issue ('The 'Hard Problem" and the quantum physicists, Part 2: modern times', *Brain and Cognition, <doi:10.1016/j.bandc.2007.09.004>*). And I still think that we've not got there yet. Partly because I think there's a big divide between people who've been trained up in physics and have gone into quantum physics and those who've been trained up in neurobiology. And the quantum physicists don't understand the complexity of the synapse, which is where they think these quantum effects occur. 1.25.10

Holdsworth: Sorry, who don't understand?

Smith: The quantum physicists, because they're not in the area. They're using an incorrect model there, I think. And the neurobiologists, of course, are not sufficiently able to understand the mathematics of quantum physics to be able to counter the physicists' theories adequately. Now, I can't pretend to understand quantum physics at any level either, but I did take a [physics degree, maths degree] in my youth. So I've got a little bit of grip on it. And so I've tried to produce a paper that shows the difficulties and mutual misunderstandings. I think the mind/body problem – mind/brain problem - is a real issue. I'm not sure whether we can

find a solution – whether it's soluble by us, so to speak, by human beings. Anyhow, that's the most recent one I've done. 1.26.18

Holdsworth: And when does that appear?

Smith: 2007/2008: see above

Holdsworth: Still, that does sound intensely interesting.

Smith: Anyway, so that was obviously a question about Newtonian mechanics. As far as molecular neurobiology is concerned it's just a background assumption. 1.27.20

General and concluding discussion

Holdsworth: That concluded the criteria. I did have a suggestion for a further criterion from another researcher, along the following lines. Are we interested in autosomal, non-coding DNA, such as would be relevant in the case of the study of crop plants?

Smith: 'Autosomal, non-coding DNA'. Now this means it's not coding for particular 'structural' proteins, presumably, but it's one of these sections of DNA which is concerned in switching on/off, switching off other genes. Is that the sort of thing you're thinking of here? I'm a little bit unclear again as to what is 'autosomal, non-coding'. The thing is, as you may know, the DNA has regions which are thought to be just junk – for instance, the introns, [as distinct from] the exons, which are actually coding. Now, if you're talking about introns, which are – yes, I suppose you would define them as 'autosomal, non-coding DNA' - well, I don't know much about crop plants, but I'm not aware we know what the introns are actually doing, except spacing out the exons. So I think the answer as far as I'm concerned, as a non-representative neurobiologist, is no, we're not. 1.29.17

Holdsworth: Is it talking about repeats?

Smith: Well, if you're talking about that, then I suppose I have to reverse my opinion, and say yes. But I don't think that's non-coding. You see, one of the very interesting things are trinucleotide repeats. [*Smith consults his book.*] Let me just see if I can - . Can't find it. . I have written a paper for a publication on the history of neuroscience which deals with the impact of molecular biology on clinical neurology. And I talk about some of these things that I've been boring you with on the significance of neurobiology in the clinic. And one of these things is trinucleotide repeats. Expansion diseases. Have you come across them? There are about a dozen of them: Fragile X, Huntington's disease, Friedreich's ataxia, Spinobulbar muscular atrophy - a number of pathologies. Faulty DNA replication. Extra nucleotides are sometimes added – sometimes many hundreds of them, in fact - and this causes an incorrect protein to be transcribed, or transcribed and translated, and causes these diseases: fragile X [for example]. These are just increases in the number of nucleotides stuck on the end of the normal gene. So in that sense, if that's what we're thinking about, yes, we are very interested in that. But I don't think it's non-coding. It would be coding. It's an extra. It's a repeat. ca 1.32.00

Holdsworth: I'm not sure whether that [last] one's going to make it to the final list of criteria.

Smith: Right. Well, I think what comes out of it is that it's very difficult to get your criteria, isn't it? Don't you find that?

Holdsworth: That's the essence of my task, in a way. But on the other hand, I don't want to be 'essentialist' about it. I mean, I don't want to peddle the view that there's some ideal science of behavioural ontogeny.

Smith: That's right. I mean, this is what you're trying to get away from. I mean, this method tries to canalise it into particular columns, doesn't it? I mean, in fact, it's very, very fluid. In the end, it's very difficult to find a border-line to these subjects. I mean, in fact, all the questions which you've asked me, and I've tried to answer: it seems to be a vague area, which one is gradually cutting out. 1.33.07

Holdsworth: Yes. Even if it's difficult to decide which side to fall, there'll be a tendency for some people to fall that way, and some people in another discipline to fall that way.

Smith: Yes. You're absolutely right. There's going to be overlap. We were talking about the Neanderthals – the issue of speech, for example. That obviously comes into your evolutionary genetics and your molecular palaeoanthropology. So there's some significant overlap, and as I've said, psychiatric genetics at the bottom there. I think you'll find that will relate quite well. It should do, anyway. 1.34.00

Holdsworth: Yes, but of course psychiatric genetics is - [and here I make an assumption], because I haven't yet interviewed somebody from the area - but I take it it's a discipline very much driven by clinical imperative.

Smith: Yes, indeed. And that is so. And you'll probably find it's much more – well, we shouldn't talk about it really because you're going to speak to [another researcher] about it – but it's statistical. You know, you're taking large samples, whereas in molecular neurobiology, of course, is not in that sense statistical. You're taking particular samples from one organism or another and looking at it from a molecular point of view, just putting it through chromatography or whatever techniques you want - X-ray diffraction and so on, electron microscopy. You're not surveying large populations, in the sense that psychiatric genetics might do. You know, if you're looking at depression, I think one of the things – I shouldn't really muddy the waters here, should I? [You'll see what the psychiatric geneticist says] - but one of the ways of looking at clinical depression is – or has been - is to take large surveys of a group of people like Old Order Amish in the States who have been isolated and inbred for generations, and looking at patterns of heredity to establish genetic bases for the symptoms.[334] And not going down to the molecular level. 1.35.56

Holdsworth: Yes. In molecular neurobiology, you – if I may say so - very well expressed your conception of the link with the clinical realm, in the sense that you think it's highly desirable that molecular neurobiology can generate findings that can be of practical use in the clinical context. 1.36.22

Smith: I think so.

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[334] Although the genetics of the Amish have been studied for the results of inbreeding, it is not clear that depression is one of the disorders concerned.

Holdsworth: Is the direction of research in molecular neurobiology - in your opinion does it tend to be influenced or orientated in accordance with clinical objectives?

Smith: To some extent. You see, molecular neurobiology is an expensive thing to do. You've got to have a lab; you've got to have a lot of equipment; you've got to have research students. So you've got to get money from somewhere. And the money'll come from a grant from the grant-forwarding authorities. And these will not support work they don't see some outcome from. It's not their money they're distributing: it's the public's money they're distributing. And so, in that sense, they want to see an outcome in the medical field, I think. I mean, that's not going to be always the case, and sometimes the connection to medicine is somewhat difficult to see. I mean, take the case that I've just talked about, the potassium channel for which MacKinnon got his Nobel Prize, worked out from a bacterial system. You might think, looking at it, well what on earth has that got to do with anything medical? - how is that going to help someone who's suffering from a neurological condition? It's a long set of steps to get to the answer. But in fact it's very, very vital - in my view - to understand these channels: how they work, and how they may go wrong. When they go wrong you get the neuropathology. They're called 'channelopathies', and there are quite a lot of channelopathies around. I think the criticism is that although there are a lot of different channelopathies about, they are individually fairly rare. They're not like malaria or one of these other conditions that affect millions upon millions of people. They're rather minority interests. And I think the criticism is that putting a lot of money and effort into that, which is probably going to affect perhaps a few hundred people in Great Britain, is perhaps questionable, when you might have put it into malaria or obesity or whatever.

1.39.24

Holdsworth: True, but of course in a completely different context there is a debate about what people call 'orphan drugs', where there are so few sufferers that it doesn't generate a market that will repay the pharmaceutical company for their investment.

Smith: Exactly.

Holdsworth: Are there 'orphan areas' of molecular neurobiology?

Smith: In other words, areas which I think should be researched and which are not being funded?

Holdsworth: Yes.

Smith: That's probably what you're saying, isn't it? And the answer to that is that there probably are, but being someone who's no longer really doing the work, I can't really say that's the case. I mean, you ask people who are in the lab, and they'll obviously have special interests. They'll say 'I'm not being funded, and my work I should be – the work is absolutely essential, and it is an orphan area!' But I'm not sure.

1.40.25

Holdsworth: It's not my job to analyse the economics of the situation. I just wondered: are there areas where it would be interesting, but so far the resources haven't been available?

Smith: I can't answer that question, I just don't know. I think if you can make a case – you know, I mean people are always criticised because there's never enough money – certainly on this side of the Atlantic and I guess on the other side – to go round, and people who don't get their submissions funded are going to say, you know, this jolly well ought to be researched.

But, you know, I have a certain faith in the people who make these grant awards, and I think they probably do as good a job as they can.
1.41.12

Holdsworth: And in any case, there is a kind of – would you agree? – I seem to distil this from what you said before - there's a kind of magnetism in the air which takes the research at least some of the time to where the medical interest is.

Smith: Yes. I think so, yes. From the process of, as I say, funding the research, I think you've got to go through that circuit: the Medical Research Council etc[335]

Holdsworth: And, as you say, that's a laudable process.

Smith: I don't see there's any other way of doing it. It's public money. You can do it yourself, I mean, as you might have done in the 19th century with just one person. I mean, Darwin with his earthworms and his barnacles and so forth, he was able on his own – he financed himself. He was a wealthy man. You can't do that now, not in molecular neurobiology. In some subjects you might be able to. That's what's happened to science: it's become huge. And there are dangers in that. 1.42.27

Holdsworth: Actually, today, if you costed Darwin's trip on the Beagle, he got quite a lot of funding.

Smith: If you costed it – yes, he would. He got a cabin! He had to put up with Fitzroy, but apart from that!

Holdsworth: Good. Well, thank you very much, Chris.

Smith: Well, thank you for coming up, anyway. I hope it's been of some use to you, and it's been interesting to talk it through, anyway. I don't generally get the opportunity to talk in general terms about the subject. 1.43.08

Holdsworth: Good. Well, it is an attempt to put different disciplines which have *something* in common - to see them in one context.

Smith: That's right.

Holdsworth: And to notice the special characteristics of each.

Smith: Yes.

Holdsworth: Good.

Smith: Well, as I said, the motivation is dual. I find the subject of molecular neurobiology fascinating. I also think that it must have a medical pay-off. 1.43.51

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[335] Cf. Lewontin, Richard (2000): The triple helix: gene, organism and environment, Harvard, Cambridge, Mass., 2000, p.128: "In general scientists do what they know how to do and what the time and money available to them allow them to do".

4. Research interview with Professor Sue Buckley – Edited Excerpts

Interviewed: Professor Sue Buckley, Emeritus Professor of Developmental Disability Psychology, Department of Psychology, University of Portsmouth, and Director of Research and Training Services, Down Syndrome Educational Trust.
Interviewer: Richard Holdsworth, PhD candidate in the Economic and Social Research Council (ESRC) Centre for Genomics in Society, Egenis, University of Exeter.
Date and time of interview: Friday, 9 March 2007, 10.30.
Place: The Down Syndrome Educational Trust, The Sarah Duffen Centre, Belmont Street, Southsea, PO5 1NA, United Kingdom.
Total length of the recording: 1 hour 39 minutes 42 seconds.

The interviewee's description of the research 0.00.00

Buckley: When we started doing research, we grew a bit. We'd always provided a service to families in the health district, and that just sort of grew, I mean we've people come from up to seventy to eighty miles away now.

Yes, on the whole I try to discourage it. I mean, we would prefer people not to need to do that - that their local services were so good that they didn't feel they'd get something extra here.

We'd rather be putting our effort into training people and putting good information out there so they'd get good services where they live, but that doesn't stop us from having children here. And the fact is that we both do this early intervention programme and then we also provide direct support to the schools. We have an outreach service – one of our psychologists. It's only the City of Portsmouth schools now, and they actually pay for that, but we do a lot of training and support for inclusion in education. 0.01.06

It does stand us in good stead. It gives us the opportunity to collect research information on children longitudinally, and children who are getting best practice in terms of intervention. So you make sure they're all receiving the same sort of intervention or education and then look at what's happening to their development. That's quite helpful, even if it's some sort of experimental study about memory training. At least we know that the children are getting the same sort of input to their development. 0.01.38

Yes, so the service side – we've always said, you know, it keeps our hand in, it keeps us in contact with practitioners and parents first hand, but we've reduced it [so it doesn't take over].

People would be quite happy if we did nothing but provide direct services, I think sometimes. 0.2.01

Whereas, you know, our reputation's really based on the research that we've done, which means we can provide more effective practice. We're just reviewing our five-year strategy, and we've been, [...] needless to say, thinking about that and looking at what everybody else is doing round the world, and we're still the only people who have this sort of emphasis on education and development. 0.02.33

Holdsworth: Really?

Buckley: Who actually do something.

Holdsworth: You're the *only* people?

Buckley: Well, we're the only research team who really are interested in practice outcomes, I think.

Holdsworth: Really? 0:02:45

Buckley: Well, that's perhaps slightly harsh, but if you read the vast majority of research. I'm in conversation with the leading researchers. People who want to understand their learning difficulties or their speech difficulties - so many of them, not all, but so many will not speculate further – you know. They're scared to do so, I think. They think it reduces their scientific credibility. It's OK to do experimental studies. Working memory would be a good case in point. I know the key researcher - the leading, probably the most knowledgeable person in the world on working memory in children with Down syndrome. 0.3.30

Holdsworth: In which country is that person?

Buckley: Here. I've never managed to persuade him to comment on potential intervention, to approve it. There's this sort of academic research strand. You can do the pure research, but they're very frightened about speculating about interventions, and even more about setting up studies [to evaluate] interventions, which for us we prefer to do. Well, a lot of academic researchers don't necessarily have the contacts. Not true any more. University of York: Maggy Snowling and Charles Hulme are the world's leading experts on the literacy issue, for all children. They're open to intervention work, which is unusual for academic departments. 0:04:24

They're at the University of York. Psychology Department. And they have a Centre. I think it's called the Centre for Language and Reading.[336] 0.04.50

There's a sort of – there's a divide, you know, there's the people who do the academic research, who are mostly asking 'What's wrong?', 'What's different about people with Down Syndrome?' So they understand what's wrong, but won't take the next step. 0.05.16

And then there's all those people involved in practice, like the vast majority of parents, who are trying to do something, regardless of whether there's the evidence, because there's loads of practitioner wisdom. If they write about it, the real toffee-nosed researchers [don't accept it, because they haven't got a control group]. 0.05.37

There's a psychologist who has seen all the inclusion work here, who came in yesterday to do a school visit, and she talked to me. This was about a boy - a little lad of about eight doing brilliantly in one of our primary schools. We would have not had him down at first as a child with Down syndrome. 0.06.05

He's reading as well as other children in his class, and he's surprised us with the progress he's made in the last three years at school. Quite dramatically. Well, if we write that up it'll be, oh well, just as an anecdotal case study. And it's very difficult. I mean, it deters teachers

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[336] Centre for Reading and Language: http://www.york.ac.uk/res/crl/ (Consulted 17 August 2008).

and speech therapists and so on from writing up their findings – because you have the toffee-nosed researchers, academics, who just look down their noses at what they've got to say. The rest of us know, of course, they are getting it right. 0.06.40

If you really want to find out how to make progress with children, you don't read academic papers by experts reviewing the research literature on language development. We've written practical reviews, but they totally ignore them. We've written for practitioners, with references in the back, about the conclusions you can draw from this research – what you're actually going to transpose. People don't even notice. 0.07.10

Holdsworth: You have a series of research publications. I ordered this one, which interested me: 'Motor development for individuals with Down syndrome – An overview'.[337] Are there in fact journals where one would publish academic research in the traditional mould, so to speak? 0:07:49

Buckley: People publishing more academic stuff will go to the high prestige journals in their area. The child development ones that are high prestige. Disability ones that are high prestige, like what is just about to change its name: the *American Journal of Mental Retardation* - AJMR. They finally changed their name this year to 'intellectual' – they've dropped mental retardation, in favour of the 'intellectual and developmental disability'.[338] But when you run a journal called *Down Syndrome Research and Practice*,[339] which is identified in all the main search engine sites like Medline and so on – I mean, we've achieved that. 0.8.46

Holdsworth: Mm.

Buckley: There are a lot of people - . They won't get university brownie points for publishing with us. You know, there's a rating system for high-prestige journals. 0.08.56

But we try hard to get second-hand summaries of what they do. I mean, we either write summaries ourselves, or - . We're just totally revamping that. We probably can get much more practical stuff. We'll run case studies. You know the big people need to know what we're doing, aside from the traditional research stuff, which we also publish. 0:09:25

Holdsworth: Much of what you're telling me is quite surprising, although I suppose in another way it's not surprising. But is it not then regarded as OK to write up case studies? 0.09.41

Buckley: Well, there are case studies and case studies. You can have your case report which would be partially anecdotal and might have some standardised measures in it, or might be entirely anecdotal. We would have to have standardised data on this [chart] we're talking about - using one of our local schools - but we don't go in for a lot of that. You know, much of our

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[337] Sacks, Ben and Buckley, Sue: 'Motor Development for Individuals with Down Syndrome - An Overview', Downsed. Information at: http://shop.downsed.org/entry.aspx?id=300100000034 (Consulted 12 October 2008).

[338] The organisation, American Association on Mental Retardation (AAMR), changed its name in 2006 to American Association on Intellectual and Developmental Disabilities (AAIDD). The AAIDD continues to publish two journals: (1) *American Journal on Mental Retardation* (AJMR), which retains that name despite the change in the name of the parent organisation, and (2) *Intellectual and Developmental Disabilities* (*IDD*). See http://aamr.allenpress.com/aamronline/?request=index-html (Consulted 1 October 2008).

[339] Website: http://www.down-syndrome.org/research-practice/ (Consulted 11 October 2008).

information, of course, is contributing to their IEPs - Individual Educational Plans - and practical teaching programmes. It's a lot about collecting standardised data. 0.10.21

So, there's a journal called *Cognitive neuropsychology* which is very posh. I read a copy of a paper there last year. People we know. It was on the perception of a child with Down syndrome, who was an exceptional reader.[340] 0.10.39

Holdsworth: On one child?

Buckley: Well, against the backdrop of about 13 or 14 other pupils with Down Syndrome that they'd collected to provide a sort of normative group, although actually [they were more asking] to recruit them. They were looking for more able children. 0.10.56

Holdsworth: Sorry, who were the authors?

Buckley: A student called Margriet Groen. I think she's from Holland. Her supervisor is Dorothy Bishop at the University of Oxford, who's very well known. 0.11.14

And then Glynis Laws, who was a research fellow here with us, went to Oxford to work with Dorothy and is now at the University of Bristol. Kate Nation, who is also at Oxford but was a student with Maggy and Charles in York. She's an expert on reading comprehension. And they did some rather clever things.[341] 0.11.36

They took this youngster who we know, because we've worked with her since she was two. That would have been worth a cursory mention! [...] I had a dialogue with the authors, which I'll come back to in a moment. They took this little one – well, she's not little now, she's ten or eleven now. She was about eight or nine when they collected this data. They looked at her scores across a whole string of language, literacy, experimental measures, against this other group with Down syndrome. 0.12.08

And then they draw on data they've collected on children whose reading age is an appropriate level, who've got the decoding skills, but have poorer reading comprehension than we would like. Their comprehension, particularly for story text, lags behind their actual technical reading ability. 0.12.28

So she had data on typical children like that.

Holdsworth: You mean some who could read what's written on the page – read out loud for example - but not necessarily take in the full meaning.

Buckley: Yes. So what you see with these children is: if it's literal text like a text-book [...] they'll probably be all right. If it's story material that requires more [inputting from the world of

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[340] Groen, Margriet A.; Laws, Glynis; Nation, Kate, and Bishop, Dorothy V.M. (2006): 'A case of exceptional reading accuracy in a child with Down syndrome: Underlying skills and the relation to reading comprehension', *Cognitive Neuropsychology*, Vol.23, No.8, December 2006, pp.1190-1214. This article cites Buckley, S. (1985): 'Attaining basic educational skills: Reading, writing and number', in Lane, D. and Stratford, B. (Eds.), *Current approaches to Down's Syndrome*, Holt, Rinehart and Winston, London, 1985, pp. 315–343.

[341] Checking would be helpful re this account of the Groen et al case-study, on this and the following pages.

knowledge] to understand the characters and so on then they struggle. So it depends what sort of text you give them. [...] 0.12.59

They did a very clever piece of work, involving lots of other data that they happened to have, that they could compare her with. Now, they consider that a case-study. 0.13.26

It's highly technical. A huge number of tests that they gave her to do. Not us telling her: she can read and write at the age-appropriate level. And she could do it a jolly sight better than they described in this article, in fact. 0.13.40

Because they were using [...] questioning. But her mental age measures are given as very low – below the third percentile on visual – on verbal and non-verbal mental age. That's chronologically age-appropriate reading ability, and much better spoken language [...]. Now this young lady's actually very competent. She's holding her own in regular education. She's socially very competent. I mean, her family are very confident. They give her support. 0:14:09

But the, kind of, appalling mental age measures they've put in! I've got no idea what they mean. Whether she was having a bad day, or - . But they don't reflect her ability to function in the real word in any sense at all. 0:14:23

But that's a very considerate case study. Very technically well-planned. A lot of detailed norms to test data and so on. 0:14:44

But when I wrote to them they described her exceptional skills, but there were two issues at the end, which I felt the discussion just left hanging, because, by their account, she had exceptional reading ability – i.e., age-appropriate - good literal comprehension, but not quite so good comprehension when you need [meaning], much better clarity of speech and spoken language than is typical for a child with Down Syndrome - it wouldn't be entirely age-appropriate, but very good – and, according to them, these very poor mental age scores. 0.16.00

A bit like these autistic children with exceptional attainments. Totally uneven profile. And it raises all sorts of issues that are current in developmental debates, about modularity in development. How can you have some areas where apparently your cognitive functions are poor and others where you're functioning at age-appropriate level? 0.16.19

They even comment that that is worth exploring, as if it would surprise you! Neither do they comment on whether any of the interventions she'd received could possibly have anything to do with it. I mean, they don't even comment that that would be worth investigation. When I wrote to them saying I was disappointed I got them quite hot and bothered. 0.16.43

Because I said, you know, how could you just kind of stop at that point, describing this unusual profile? They could at the start when the parents told them they were teaching her to read at three. They comment that that might have something to do with it. So maybe it's appropriate. 0.17.01

When people look at autism – at the people with very special abilities, like they can tell you all the bus time-tables, and do calculations, against the backdrop of not being able to look

after themselves, people will say, well, [...] you know, they like to have something they can do well. 0.17.20

That still doesn't entirely explain why those bits of the brain function so well [for them]. But it does explain why they become so expert: they don't think about anything else, and they just practice. 0.17.33

Well, they haven't even made that sort of comment. You know: has a lot of attention been given to building up a literacy skill, as well as other things? [...], but the way we do it is always to use it to improve their spoken language, as well as to teach them to read. 0.17.48

We've organised a meeting in October to bring these people together – to bring a small number of cutting edge researchers together to debate what we know on what we should be doing in the next ten years across the, sort of, psychology and educational research field. And we'll have some geneticists there. 0.18.14

One of the responses I got from Dorothy Bishop to my saying 'Why didn't we comment on what might be - how she could be like this?' She just said, Oh well, it's probably the particular alleles [on the gene on the extra copy of] Chromosome 21 that she got. And I thought, give me a break, you know, you only [can do this] if somebody teaches you. And yes, you might have better potential than the next child with Down syndrome. [But to suggest we can answer it by] looking at their genes! A psychologist - a cognitive psychologist [...]. Totally potty! 0:18:50

Holdsworth: Well.

Buckley: It links a bit, probably, to what you really want to talk about. We have two research camps at the moment as it stands. In relation to understanding Down syndrome, you have some very high profile people across genetics and molecular biology, biochemistry. And you have the high-profile research teams with research money. I can give you websites you can go and have a look at. One of them is called the Down Syndrome Research and Treatment, or Treatment and Research Foundation at Stanford University. [...].[342] 0:19:41

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[342] Down Syndrome Research and Treatment Foundation (DSRTF). The website is at http://www.dsrtf.org/ . From the website it is not apparent that DSRTF is institutionally linked to Stanford University. However, the website carries a news item dated 21 April 2008 headed 'DSRTF Awards New $880,000 Research Center Grant to Stanford School of Medicine Researchers'. The opening sentences read as follows: "The Down Syndrome Research and Treatment Foundation (DSRTF) is pleased to announce the award and funding for a major new $880,000 DSRTF Research Center Grant to researchers at the Center for Research and Treatment of Down Syndrome and Neuroscience Institute at the Stanford University School of Medicine. This newly awarded DSRTF Center Grant significantly extends and builds upon the more than $2.8 million DSRTF has previously generated to support researchers at the Stanford Center since 2004. Past DSRTF support led to dramatic research breakthroughs in defining specific mechanisms responsible for cognitive impairment in Down syndrome and resulted in the identification of new potential drug targets for improving cognitive function.
"The highly collaborative research programs funded by this DSRTF grant are directed by William Mobley, MD, PhD, Professor and Director of the Stanford Center and Neuroscience Institute; Craig Garner, PhD, Professor of Psychiatry and Behavioral Sciences; Daniel Madison, PhD, Associate Professor of Molecular and Cellular Physiology; and Isabella Graef, PhD, Assistant Professor of Pathology." (Consulted 15 September 2008).

A group of families have set up this Down Syndrome Research and Treatment Foundation to raise money for the research team at Stanford who are looking at biochemistry and genes. 0.19.52

And this is [something that's not generally known: that they're] raising money from families. 0:19:59

Holdsworth: So that was Stanford. We were discussing the first of the two camps, as it were.

Buckley: Well, yes, there's a whole group of researchers. There's a mouse model for Down syndrome, in fact there's more than one. There are trisomy mice, and there have been trisomy mice for the last 15 years, I should think. 0:20:37

The chromosomal abnormality

Holdsworth: Could you just, for my benefit, explain the chromosomal abnormality? 0:20:47

Buckley: Yes. OK. Well children with Down syndrome have three copies of Chromosome 21, instead of two.

Holdsworth: That's what they call the 'trisomy'.

Buckley: 'Trisomy'. Yes, they've got three copies of Chromosome 21. We now know, I think, about all the genes on Chromosome 21. I mean, in the last ten years or so there's been a huge genome project, you know, to unravel the human genome. To try to figure out all the genes on every chromosome, and then figure out what they code for. 0:21:19

[*Excised*: The interviewer's introduction to his research project.]

General discussion of concepts and methods 0:25:50

Buckley: OK. Well there are three papers, some of which we could lay our hands on quite quickly for you, where people are trying to link the genotype to the phenotype. 0:26:04

On the - I mean what we call the basic science side of the fence, the people [are] looking at what does a gene on Chromosome 21 code for, and then looking also at the - they've got ideas about which the genes might be that are causing some of the effects. 0:26:31

They are trying to also take account of what we see as the developmental phenotype, what sort of behavioural changes there are, developmental changes, [...], to try and inform where they're looking for markers. Two kinds of issues around that. I'm sure you don't want to expand your interview, but of course there's a lot of excitement about epigenetics .[343] 0.26.59

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[343] See Cavalli, Giacomo (2006). The paper reviews the meeting on 'Epigenetics and Chromatin Remodeling in Development' organised by Renato Paro and Peter Fraser at Keystone (CO, USA) on 19-23 January 2006. Conference programme: http://www.keystonesymposia.org/Meetings/

And the fact that gene action will not be an automatic sort of read-out activity. 0.27.06

Genes can be turned on or off or they can be modified. So, if you like, there's the basic scientists, and then there are people into developmental research, whether that's psychologists, educators, therapists and so on. And the cognitive neuroscientists would be on the psychology side of the fence usually, looking at - , understanding in quite detailed ways, the way brain function is reflected in the skills we've actually got, what tasks you can learn and so on. 0.27.37

One of the anxieties people have is that - people on the psychological, developmental side of the fence - that the geneticists don't understand that development is development: that we change over time. 0.27.52

There may be issues about epigenetics, but whatever [coding] is going on early on, most of the things that we see any child develop are learned by [observed] social interaction with people. It doesn't matter what their genes set them up to do, if you shut them up in a room on their own they won't develop. 0:28 10

Human development isn't fixed at birth, and it's not like watering a bulb. Food and water is not enough to make it grow. Learning to talk, learning to move, learning to socially interact, smile, understand social interaction, everything that goes on from day one assumes interaction with warm, loving and socially competent people around you. 0:28.34

You're not going to learn to talk if people don't talk to you. So one of the things that I think is problematic is that the people on the basic science side of the fence frequently don't seem to know anything about development. 0.28.48

[...] There's far more plasticity around brain development. But brain development is driven by activity after birth. And so their models are too simple for what they're looking for. And we're going to hold a seminar in October to bring these two camps together. 0:29.06

Holdsworth: Really?

Buckley: Yes. We're planning that at the moment. I'm wondering where I'm going to find enough money to do it on the scale I would like to, but we'll definitely do it, because on a small scale we could fund it anyway. And we can use this building. 0.29.19

But we want to bring people from both sides together because some of the leading people are writing about the genotype, because they're on that side. But talk about the phenotype turns around alterations to the skeleton. They've got a slightly different shaped head, motor skills in learning, heart defects - the sort of structural, physical defects that are there from birth, that are fixed - right? 0.29.58

[...]. Researchers on the basic science side acknowledge that learning and memory and language are issues, but are [not quite ready to deal with that directly]. And, of course, if

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viewPastMeetings.cfm?MeetingID=784&CFID=2571555&CFTOKEN=74494846 (Consulted 18 September 2008). The website of the Human Epigenome Project is at: http://www.epigenome.org/index.php . It cites, among others: Novik *et al*. (2002). See also: Holliday (2006) and Kiefer (2007).

you start to look at the genetics of anything to do with learning to talk, learning to read, and so on, you're talking about complex interactions of genes across all the chromosomes. 0.30.21

So the two groups live in slightly different worlds, if we're not careful. One is the psychology - . 0.30.33

Holdsworth: Can they talk? Can they talk to each other? Have they got a common language?

Buckley: Not sure, but we've had excited, positive responses from people on both sides of the fence. We're going to bring Bill Mobley, who's the leader of the research team at Stanford, here. William Mobley. He's a very high-prestige scientist. Whole string of credits to his name. He leads the group at Stanford doing the Down syndrome research, and I happened to be in Denver last week and met up with him. 0.31.03

David Patterson, who heads up the Eleanor Roosevelt Research Institute at the University of Denver, and who's got a long history on the basic science side, he's going to come. There are quite a lot of key people who know a lot about it. But they are basic scientists. I'm not quite sure how the dialogue will go!

But one of the psychologists in this country who's worked with trisomy children is Annette Karmiloff-Smith. 0.31.30

I could give you a couple of her papers as well. She's talked about the difficulties of the basic scientists understanding development. [...]. 0.32.06

Holdsworth: How many people are you trying to bring together?

Buckley: Probably about forty. Partly because, although we could restrict it to a smaller number of key people we would invite to prepare papers and circulate in advance and so on, because the aim is to set the agenda for research for the next ten years. So that we could deliver short-term gains for people, mid-term gains, research that's going to have outcomes that will improve things for people in the next five to ten years. 0.32.36

Because that's our mission here. We focus on research that's likely to have an impact and to change things in the near term for people. And so we've put a peer research partner together as part of our current development strategy. 0.32.52

We've enlarged our Advisory Board for Down Syndrome Research and Practice. We'll probably work better with experienced figures. But I would also like to be able to invite a few of the brightest doctoral students around to benefit from this discussion. Kind of forty if we have it here is probably the limit. 0.33.15

We want to look at where, you know, where we should be going with development and educational research and its implications for therapy. And I mean we have some pretty good ideas about what that is now, and that's why we're working with research partners who are at the cutting edge – a phrase I get told off for using here. 0:33:48

We know who's doing the work in all this stuff, who's doing the literacy stuff, who's good and so on. We've got all of those. 0:33:58

Because we can tap, we hope, some very rich families and so on, as well as research councils. But we want to bring people together, particularly to discuss this problem that so much is talked about the genes and the molecular biology. 0:34:25

And these people have on their website that there's going to be cures and treatment, and it hit the press only last week while I was away. The people at Stanford put something out to say that they had effectively returned the learning capacity of a trisomic mouse to normal with a particular drug. The fact that most of these drugs, well – . 0:34:55

Holdsworth: Drugs? Not gene therapy?

Buckley: No. This is looking at synapse function and learning. But of course that's the end-point, OK? Gene therapy is not just about switching genes off, it's knowing what they code for. 0:35:10

So you may move a little bit further along the chain. When you see what proteins they code for, you may be able to do something at that point – if it's over-expressed. And [...] GABA receptors are trying to block them because they're over - I think they've got it right – they're over-excitatory. 0:35:29

So it follows on from knowing something about the genes and what the genes code for, but it's not trying to actually predict that gene action. It's a bit further along the chain. 0:35.41

So these people are suggesting quite clearly on their website there will be treatments within five to ten years. And we don't believe it. I mean, we just don't believe it. 0:35:57

Holdsworth: This is Mobley's team? 0:35:59

Buckley: Yes. I think most of the claims have actually come from him in the last few years. There is no doubt that the people doing the genetics and, as I say, molecular biology stuff imply – they talk about little bits of stuff that they've looked at and imply it's going to be easy to reverse the effects of this gene, I suppose. 0:36:32

You have got some 300 genes on Chromosome 21 that are being triplicated. The notion it's going to be easy doing that, to the rest of us, even those of us who [...]. And so nobody's saying 'I shouldn't keep that line of research up', because for example Mobley's lot, what they've been doing is looking at synapse action. It might be possible to improve synapse action with some sort of therapeutic medication, drugs. But still many people would say 'not very widely'. And, of course, if you look at genetic conditions [from single genes] - [...], cystic fibrosis, muscular dystrophy, people have known about the genes for anything between ten and twenty years for those conditions, and we're still [without the treatment]. 0.37.46

Holdsworth: Yes, I see. 0.37.48

Buckley: So from our point of view, one of the things people into gene research [at the moment] [do] - they exaggerate. I'm not sure whether they do it deliberately to get money. But I think they [put out more than is possible]. Our parents are very vulnerable to them. The people - [by the way,] they do get grants from, obviously, research councils, particularly [in the States]. 0.38.19

[...]. 0.38.49

But I think they hold out hope that is a little beyond careful, scientific judgment. They launched a two-million-pound fund-raiser last week on the back of this. The parents' groups supported it. 0.39.04

Holdsworth: What? Sorry?

Buckley: The parents' groups are supporting them in a two-million-dollar fund-raising campaign last week on the back of this bit of research. 0.39.11

So, I mean, yes of course it's terribly important to keep studying the genetics and the biochemistry, but I don't think it's always been done in a very ethical fashion. I think it was a PR thing, looking for the money, to make unrealistic claims about how quickly a cure may be found. 0.39.44

Holdsworth: That's quite tough talk. 0.39.46

Buckley: Yes. I think you need to take a look at their website to see what I mean. [...] Stanford, if you looked on every research page and wait for the rotating pictures to stop, it actually says they're going to improve the speech, language and memory of children with Down syndrome. 0.40.04

I'd actually like to issue a challenge to them, to see if they can come up with anything in ten years' time. All right? They're studying mice. And the claim that that's going to transfer quickly - . Now, for a number of years, people have been able to collect – create mouse models that have some of the mouse analogue of what's on human Chromosome 21, and it's Chromosome 16 in mice. 0.40.39

Now, there are several versions of trisomic mice, and there's a woman in London, whose name I've forgotten, who last year was in the press because she had managed to implant some of human Chromosome 21 into mice. So not just triplicating their own chromosome - 16 - but implanting some of human Chromosome 21. 0.40.58

And again, people have got very excited, and there's appeals out to help fund the mice. If you read it, first of all most of these mice died. It's extremely difficult to create these mice and have them live. And they're mosaics. They're what we call 'mosaics'. 0.41.18

Now, most children with Down Syndrome are straight-forward trisomies. Over 95 per cent have three copies of Chromosome 21. 0.41.30

Holdsworth: Sorry, what percentage?

Buckley: Over 95 per cent of children diagnosed with Down syndrome have the straight-forward trisomy. They've got an extra copy of 21. A small group are mosaic. 0.41.43

The physical person with Down syndrome has an extra copy of the chromosome in every cell in their body. It was there at the point of conception, and it's been there ever since. It's most commonly in the egg cell. It can arise in the sperm, but that's unusual. It's in the egg cell, and it's in every cell in the body thereafter. 0.42.08

But there are some children that are mosaic, which simply means they don't have it in every cell. So something happens after the first cell division. They have some normal cell lines and some trisomic cell lines. 0:42:20

And they are typically less affected, but not always. Now this mouse which has been created in London is mosaic. You try to implant human chromosome it doesn't get to all cells. So: interesting, but we're not sure how interesting. 0:42:43

Holdsworth: Do you remember the name of the researcher?

Buckley: It'll come to me in a minute. [...] 0:43:01

But, you know, one of the other issues, which links to what you're asking about, is families are extremely vulnerable to the message there's a cure round the corner. 0.43.20

Holdsworth: Yes, I can see that.

Buckley: Any condition which is difficult to treat and technically doesn't have a cure - . People are after the magic bullet.

Holdsworth: If necessary, I ought to correct a misapprehension. I'm not specialising in the ethical aspects of this topic. 0.43.37

Buckley: Yes, OK.

Holdsworth: But something that does interest me very much is the extent to which, in your opinion, there are gaps in the research coverage, which may be caused by a shortage of funding or the way funding is allocated. I'm looking at the epistemic dimension. You know, are there bits of the subject that are losing out where more research would be desirable? 0.44.04

Buckley: Do you mean in terms of research into the genes, specifically?

Holdsworth: Not only.

Buckley: OK. Because I think the – the magic bullet appeal – of understanding the genetics is pulling all the money in that direction. 0.44.24

Whereas we think all the big gains for folks with Down syndrome come from good healthcare, understanding more about why they find it difficult to learn to talk, etc. 0.44.37

Holdsworth: Presumably there's a shortage of money.

Buckley: Oh, absolutely. Absolutely.

Holdsworth: I saw something on your website. It was your paper on '20 years of' - .

Buckley: That was it. Yes, well that would have given you a fair idea of the sorts of research we do. We've demonstrated you can dramatically improve their spoken language, social competence, memory function, literacy. 0.45.11

Twenty-five years ago we were not only laughed at, but I got hate-mail from professionals in the mid-80s when I said that kids with Down syndrome might be able to learn to read. 0.45.22

I mean, such was the blanket assumption: that their degree of disability – their degree of learning disability, mental retardation - whatever you choose to call it - was such they'd never learn to read or write. 0.45.36

The second poster there – the girl with the long hair and the glasses –

Holdsworth: Yes.

Buckley: - is my daughter.

Holdsworth: Oh yes?

Buckley: She is now 37. She was probably about thirty there in that picture. Now, [she] was adopted by us as a baby because she was living at a hospital I went to work in. 0.45.55

In 1969. Left by a family who didn't feel able to bring her up. She was left at five weeks old, which was not untypical in the 60s. 0.46.06

She was born in 1969. In this country at that stage a GP filled out a bit of paper based on his diagnosis, which described her as 'unfit to benefit from education'. Full stop. 0.46.19

We didn't have a law saying no child is ineducable until 1971. We started special schools in 1973, so by the time she was four the local health-run day-care centre changed its name from a 'junior training centre' to [...] 'school'. Didn't change anything that went on inside the school, at that point. 0.46.48

Up and down the country the law decreed now that every child was supposed to go to school. Children whose IQ was below 50, or expected to be, had been outside education. 0.47.03

So these kids with significant disabilities – suddenly schools had to be started for them. So that was the start of schools. At that stage we called them ESNS, and that stood for schools for children who are educationally sub-normal, brackets 'Severe'. So she had - 'severe subnormality' was the term. Living in a severe subnormality hospital. She moved to a school for children with severe subnormality. Their highest expectation, or they would have succeeded if she could learn how to pull her knickers up, basically. And I don't exaggerate. All the focus was on personal care skills for people like this. 0:47:50

So when we started in the 80s [...], we were looking more closely at what anybody else [understood] about development - why did they learn more slowly than a typical child? So we started looking at literacy. 0.48.06

We got an article in the Times Ed Supplement, I think it's January 1984.[344] I had children on the front page. It was the first time we presented a paper at a conference about the early

[344] Reference available?

reading work we were doing, whether we thought it might tell us something about their cognitive profile, which you can summarise as being visual learning, they're fluent in this. 0.48.30

Auditory processing's an issue, probably stemming from poor discrimination of speech, poor hearing from the outset. If you teach them visually with size of print you get dramatic effects. But we presented a paper at the British Psychological Society conference in the December. There were press there. [A journalist asked to do a feature, and we said] you can come and see the children for yourself [and meet some of the parents]. So we were on the front page. 0.48.58

Holdsworth: What year was that?

Buckley: '84. January '84, I think. January or February. I had head-teachers picking up the telephone saying how dare I peddle such nonsense, and how dare I raise such false expectations? 0.49.12

Put the phone down. Next person, who played a role in special schools, rang me up and said 'We've known this all along; you're not saying it's anything new'. To which I said 'OK, can I come and visit and see your school?' 0.49.21

My partner predicted that's what would happen. There'd be the people who felt threatened, pretending they knew already, and there'd be people who just don't believe you, of course. He predicted in advance the sort of reactions we were going to get. 0.49.36

We are still fighting battles with people like these. But why were we thinking about that and Roberta? Oh well, just because you led me into this about the research on development. 0.49.52

Holdsworth: I said: were there gaps?

Buckley: Absolutely. You know, we are almost always broke. Trying to persuade people to give money to do research into how – the four steps that might make a difference to their spoken language, their social confidence, their behaviour, their ability to read well, succeed in an inclusive community, is not nearly so effective as somebody who says they're going to deliver a pill to cure them. 0:50:23

So that's what the genetics is doing. People on that side of the fence give those sort of messages. We were in Denver last week, and another one of our children was with me and has a totally different career, and she was listening to all this. 0:50:38

It was quite interesting for her, because she's not immersed in this kind of debate, but she said something to me when we were discussing this and the fact that we were with a family foundation with a great deal of money available and now have a grand-daughter with Down Syndrome. 0:50:55

Holdsworth: I see.

Buckley: They have already spent quite a lot of money on the basic science, and bringing in people like, quote, 'the mother of a child with Down Syndrome'. They're all looking for this silver bullet. 0:51:07

My daughter said to me, in conversation, she said the trouble is, Mum, that what you learn requires some effort over reading. It's telling people what matters is how they interact with their child all day every day, and how their teachers interact with them. It is not a quick fix. 0:51:25

And she said that's probably what you need to get a hold of: what you're saying to people is you can produce considerable change, but they have to put some effort into it, as parents and educators and so on. It isn't going to be as easy as giving them a pill with their breakfast. 0:51:39

Holdsworth: Another point is that, supposing that somebody makes a ten-year prediction for a genetic silver bullet, it would still be wonderful if we achieved it in twenty years. But meanwhile, where have you been? 0:52:02

Buckley: Right. It's not going to affect children growing up now. Yes, it is missing the point that for any child best quality child care, support, education, is critical. 0:52:21

And a lot of the things we're looking at don't only relate to youngsters with Down syndrome: the kind of speech difficulties or language difficulties or literacy issues or movement difficulties they're seen in other groups of children anyway. 0:52:33

So, you know, even if you've got the magic bullet, and it improves the functioning of their nervous systems, somebody's still got to talk to them if they're going to talk effectively. So you're still going to have to teach them to read. And I don't think any of these people would suggest you're suddenly going to make them normal. Because they've such a profound disability. They have the extra chromosome in every cell, if you like. 0:53:01

So you might treat aspects of the development. Obviously, if we could make their nervous system – the basic transmission of information in their nervous system - to work better it would benefit everything which I mentioned, for sure. If you could do that successfully. That's the issue of course. But I think the messages are often over-simplified. 0:53:24

Holdsworth: What I find – if I might interject a comment. What's particularly interesting about what you're saying, among other things, is this: that some people might think, well, Down syndrome is a genetic disorder –

Buckley: Mm, hm.

Holdsworth: - the impact therefore of the genome in this case is relatively uncontroversial because the results are established. 0:54:08

Therefore, it's perhaps less interesting to investigate Down syndrome research, because there are many more questions that are open – or there are questions that are more open - in some other areas. And yet, of course, what you're strongly pointing out is that what's really interesting here is the developmental issue. 0:54:37

Really, it becomes a kind of – to use this term not in its genetic sense – a sort of 'locus' for the debate and for research about epigenetics and development. 0:54:58

Buckley: Yes, and of course, as I say, we run an enormous amount of training, and I always start by telling people we know quite a lot now about their developmental strengths (and weaknesses) which, to simplify, you could say is their visual learning. 0:55:15

They find it difficult to learn from listening. And of course you're expected to get your first language from just listening to it as a baby. 0.55.29

And then – and for a variety of reasons – hearing – some others we're not totally sure about in terms of auditory processing. They have short-term verbal memory delays. 0:55:42

But the root of that could be the same. If you don't hear clearly, and you don't discriminate speech sounds properly in the first year of life, it will affect – we would expect that to affect development of the working memory system: the immediate memory system we're using to listen to each other. 0:56:00

That holds speech so the brain can process it. That's what working memory's about. And the working memory model is you have two short-term stores: one for verbal information and one for visual information. The visual bit seems to work pretty well. And in fact if we train up the visual short-term memory it's even better. So remembering visual information – holding onto and processing visual information - works better for them than holding onto or processing verbal information. 0.56.31

Now if you think about that developmentally, you could say babies are supposed to just sit there and crack the code. You say 'Here comes Daddy', 'There's the cat'. They're supposed to pick it out from listening to language, used in a context related to [seeing what you mean]. If you don't hear it [...] properly, you don't get that. 0.56.52

If you think about the importance of language – you got up this morning, and you thought 'Oh, I'm going to do that interview today'. And what were you doing? You were talking to yourself in your head. 0:57:05

It was silent speech. The sooner you get a handle on language, it's the call the brain is waiting for, for thinking, remembering, reasoning, collecting knowledge. Children start off learning words for things. The size of our vocabulary reflects how much we know about one another. 0.57.25

And how much we communicate to other people. So, these are things with which you acquire vocabulary, things with which you acquire knowledge about the world. Then you can string that together, [and that allows you] to communicate. [...] It's vital for thinking, reasoning, remembering. Self-control, because you learn 'I need to do this and this and this before I can do the other'. 0:57:50

Behavioural control. You've a five-year-old who thinks if I run in the road I'll get knocked over, because they've been able to relate to the structure they've had earlier. If I get [knocked down no-one's going to] play with me again. 0:58:03

Self-control, control of behaviour, planning, organising. It's all silent speech in their head. [If a person hasn't acquired] either a sign language or a spoken language at three or four, it will affect all their mental development and their ability to do things, and a huge amount of plasticity

Holdsworth: And is sign-language a way forward? 0:58:22

Buckley: Yes. It could be. It can be a way forward for your typically deaf child. [Study of] the working memory system in the brain indicates that those of us who've got spoken language as a first language, which is what you're expecting to happen, spoken language, the code in that short-term memory bit in working memory is still phonological, it's a speech-pattern. 0:58:49

In the cortex the childhood memory system is still in its speech form [...] – the words are going round in their speech form. 0:59:00

If you were born very deaf, in a native signing home – so you've got both parents who sign as their first language – in working memory in children like that, the brain uses sign coding as a system. There's huge plasticity in the brain. Right? So in somebody who signs as their first language, properly, the area of the brain that's using a speech code for you and I uses a sign code. 0:59:27

So those people who learned sign as their first language: the bit of the brain that drives speech for you and I drives their hands. 0:59:34

There's huge plasticity after birth in terms of how brain functions. How pathways develop and connect. Everything you do of course is changing something in your head [...].Whether it's walking, talking or whatever. It's altering and leaving you specialisation of areas in the brain which people like Annette Karmiloff-Smith are experts in. 0:59:58

Because of course the brain imaging work is beginning to allow us to look at more of that. Including techniques for looking at speech discrimination in babies and so on, which will give us a much better handle on things which we can change after birth or are being affected. So, you know, we've got a fairly clear picture of where the biggest difficulties lead, and the knock-on effects those will have. 1:00:21

Holdsworth: Right.

Buckley: We go for long-term inclusion work. [...]. OK? We turn all this round and say, OK, not only do they have difficulty understanding and acquiring language. Clear speech is also a challenge. Most pupils have speech motor difficulties. There is a lot that they want to say that is not clear. You can look at the research on typical children that shows you they're tuning to the language they're listening to from the first days of life. They appear to discriminate sounds in any human language anybody's tried at three or four weeks. 1:00:57

Same children can't do it at twelve months. They currently no longer hear or discriminate sounds at twelve months they could do at three weeks. Because they haven't been exposed to that language. They don't hear Japanese or Chinese sounds, but they [may] get English or French spoken. Otherwise they won't be discriminating the sounds, basically. Because the brain's cues vary subtly, ready for talking. 1:01:30

Holdsworth: Right.

Buckley: So we, you know, we would turn that round and say, OK, we would be working at the speech discrimination. Some of the reasons they may have poor speech is they don't hear

the sounds, they don't discriminate them the words, and that would affect this working memory system. Which is having to listen to words and have to hear the difference between different similar words. And it would affect verbal information to produce those sounds. 1.02.00

We always keep our eye on the latest research on typically developing babies. Whatever area we're interested in, we want to know how much we know about how these things develop in typical children – how they're affected - and how we might apply that with what we know about children with Down syndrome. 1.02.18

And there is a huge amount of research that could be done, where we've now got the techniques to look in a more sophisticated way, [into the physical basis]. It's not yet been done in kids with Down syndrome. 1.02.30

[...]. As you know, there are huge changes developmentally after birth in the way the brain functions. Now of course it would be better to also fix that brain a bit if not after all this discussion, as I say, if somebody comes up with a drug that makes the synapses work better, and information gets transmitted better, we assume it will improve everything that we're doing. 1.03.18

It still doesn't mean, you know, we don't need the developmental bits. It goes right across the range. I mean, until recently people would have said very few teenagers learn to ride a two-wheeled bike because of their motor difficulties. Well, of course, you have people in the States now who reckon they can teach 60 to 70 per cent of people to ride bikes by just taking them to a summer camp, because they've worked out a technique for teaching them. And they come to us for some more money, if we can find it for them. 1.03.48

And they can gain from learning to ride a bike with their mates. Instead of writing them off because their motor skills are so delayed. You don't learn to ride a bike unless you have the opportunity to learn. But even though you may have balance issues and control issues, people are cracking it. And that may seem a bit like putting babies on treadmills to get them to walk earlier, but we can set up organised practice for walking. 1.04.13

Holdsworth: Right.

Buckley: So for getting money. I mean, I would have said ten years ago people were looking at the genes, but they weren't suggesting a cure's round the corner. 1.04.25

We are much more conscious now that we're competing in a market where their PR is better than ours.

Measurements of cognitive ability

Holdsworth: You mentioned IQ earlier. Are you satisfied with measurements of cognitive ability? 1.04.43

Buckley: 'No' is the short answer to that. We would never talk about a child's IQ as having any relevance for understanding how to shift their development forward, because what you need to know there is how well they already communicate, or read or run, and what's the next step to improve their communication or their reading or their running. Many of those things

may correlate with IQ. In other words, children who have better general nervous systems, probably, well - . 1.05.25

Let me back-track there. People get in a terrible muddle about all these things. General IQ measures may predict how well children might do, OK, so those who score higher on verbal reasoning or spatial reasoning tasks that you see in an IQ test may also be doing a bit better in some of the other areas of their development. So people still publish articles saying IQ predicts development: what they mean is they've got a correlation . 1.05.54

[*In this and subsequent passages, while speaking, Buckley is to be understood as illustrating certain points by pointing to an imaginary graph*.]

And so they may have somebody with – I mean, when there are a range of IQ scores, if we translate them into mental age *here* – right? – so mental age and non-verbal ability might go, I don't know, from, say, three to six, for the sake of argument – if we look at their reading ability, it may be *here* that actually the child with that non-verbal mental age of six is reading more like an eight- or nine-year-old. 1.06.20

But you've still got correlation. But that doesn't mean that their mental age scores predict their reading ages, or their language ages. Are you with me? 1.06.31

Holdsworth: I think so.

Buckley: [...] You might have mental ages that go from *here*, you know, three to six, from IQ tests, which you can read as a mental age, rather than an IQ. 1.06.53

And then you may have reading ages that do *this*: go from nine, you know, to five. Now if this child is *here* – right – if, then you'll get a high correlation if you try to correlate the two sets of scores. 1.07.10

Because they go up together, but actually what people then do is: 'OK, this is a mental age of six, so we'd expect that child only to read as a six-year-old'. And that's a complete mistake.

So for a lot of reasons IQ data's misunderstood. Researchers churn out loads of these correlations which they then talk about as one thing predicting the other, which drives me totally potty, because it's not a prediction. It doesn't predict how well they do at, you know at reading. 1.07.38

It's a correlation, you know? But papers are written where instead of using the words 'there is correlation', they talk about one measure predicting the other, which immediately sows the seed in people's minds of a causal link. 1.07.53

Holdsworth: Yes.

Buckley: Very misleading, often. The nearest we would get normally is: we might talk about their non-verbal reasoning ability, because IQs are nearly always a composite of the non-verbal reasoning and the verbal reasoning scale. 1.08.17

Nearly always. So we might talk about their non-verbal ability, because of mental age, and their verbal ability - particularly for research purposes, and particularly when we want to

point out to people they're doing a lot better than you would assume if you paid too much attention to that. 1.08.36

We definitely might be using the sorts of standard tests for research purposes because what they give you is some sort of ruler that you can repeat a year later. They are standardised; you do have norms, and if you repeatedly measure them on the same assessment you can see what's happening. 1.08.53

So for research purposes we might use them. For practical purposes - you're writing reports for children - never, unless we can use it positively to point out how sweeping it is. In this country, psychologists in education really would [want something better than][345] IQ tests now, but they still do in many other countries. The children earn their way to school on the basis of their IQ still in a lot of countries. 1.09.19

So it's quite important that we try to point out it's not very meaningful at all in predicting the academic or practical or social progress a child might make. 1.09.29

Holdsworth: I was interested by your paper on motor ability and motor control, and of course it struck me that in completely different contexts that's how we define intelligence. 1.10.00

[...]

Buckley: Motor skill is crucial. All the early cognitive tasks that psychologists use require motor skills to show that you understand which shape goes where, that you can stack things in the right order, that you can lift up a cap and look for something in the right place. 1.11.25

Which is why Piaget, of course, talked about early development as sensorimotor:[346] that you've got to have motor skills to explore your world, to understand what's going on, and then to move on to show you can solve problems [...]. Because if your motor skills don't keep up, you may be denied that learning opportunity. 1.11.47

So core motor skills will undoubtedly affect a child's cognitive development, and their social development, if we're not careful, because they don't move as early, so they can't follow Mum around the house, or go off with their brother and see what's happening. It can impact on social understanding, language learning and cognitive development if you don't move. 1.12.09.

The word 'retardation'

Holdsworth: Yes. A word about vocabulary. The word 'retardation': it still used?

Buckley: Well, it's been used until a couple of months back in the States, and it won't die that fast, I'm sure. 1.12.36

Holdsworth: Why did you say a couple of months, though?

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[345] Query here.

[346] Piaget, J. (1983): Handbook of child psychology, 1983.

Buckley: Because the big American Association for Mental Retardation, which is what it's called – American Association for Mental Retardation - has been huge, has published some of the most prestige research journals and stuck with it until a couple of months ago, and now it's dropping 'mental retardation' and replacing it with 'intellectual and developmental disability' - AAIDD.[347] 1.13.05

The rest of the world has tried to move to 'intellectual disability' over a period of eight, nine, ten years, I would say. In this country, we moved from 'sub-normality' to 'learning disability'. So we still talk about children with 'learning disability', instead of 'mental handicap' or 'mental retardation'. 1.13.32

So you've got the 'British Institute for Learning Disability' - BILD. We've still got 'Mencap', whose by-line is no longer - was it 'Society for mentally handicapped children? - I think it might be.[348] I'm not sure they've actually changed that. So it used to be 'mental handicap' in this country and 'mental retardation' in the States. People moved off 'mental handicap' some years ago here, predominantly, and replaced it with 'learning disability'. The trouble is, children with specific learning difficulties - kids like those with dyslexia. Which is why in the States they've opposed it, because their use of the term 'learning difficulty' means a child with specific disability against a background of normal IQ. So something like dyslexia. 1.14.29

Holdsworth: Yes.

Buckley: I don't like 'intellectual disability' in relation to kids with Down Syndrome, though quite obviously if you take the whole population of people with learning disability, if you [take] people with IQ [issues] – now, people with mild learning disability: you may just be talking about a cognitive or intellectual [delay]. In other aspects, they've just been slower learning. 1.14.58

Holdsworth: Yes.

Buckley: But you are mostly talking about intellectual disability, possibly. I still think that 'learning disability' is a nicer way to describe that [when you may be talking about] kids who just fell behind in school. So once you get to children like those with Down Syndrome, I prefer the term 'developmental disability', because it's affected all aspects of their development. 1.15.23

It's not *just* an intellectual delay. The Australians have been really heavy on intellectual disability: they've been really pushing that. But many people have felt it doesn't do justice, really. They don't just have an intellectual disability if they've Down syndrome. And that's true for many other disability conditions that are more significant. They carry with them often physical disabilities as well. 1.15.52

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[347] See also Footnote 4, above. The American Association on Intellectual and Developmental Disabilities. The former name was: The American Association on Mental Retardation. The Association's press release of 2 November 2006 on the change of name can be found at: http://www.aamr.org/About_AAIDD/name_change_PRdreen.htm (consulted 20 January 2008).

[348] The Mencap website apparently gives no expansion or explanation of the name of the organisation. The website is at http://www.mencap.org.uk/ (Consulted 24 September 2008).

I think the thing about 'learning' is it does put the emphasis on the fact people can change. 'Learning disability' highlights that we learn, and that's part of our development, and we might be able to change it. You'd say the same about the word 'development', but I'm not sure 'development' means that in common parlance for people. 1.16.11

For us 'development' means this huge developmental programme of change that goes on in children. But whether it really implies that to all people? Anyway, the Americans have gone for 'intellectual *and* developmental disability'. 1.16.25

That's a catch-all. And that's really only just changed. They are still called AAMR, but they've finally voted to change it. 1.16.33

Examination of the criteria 1.16.34

Holdsworth: You've been very generous with your time, but could we just spend a minute to look at this. (*Draws Buckley's attention to the draft Criterion Matrix*).

Buckley: Yes, do.

Criterion 1: '*Does the research cover all hominids or only* Homo sapiens*?*' 1.16.51

Holdsworth: 'Does the research cover all hominids or only *Homo sapiens*?' 1.17.12

Buckley: Well, OK. I don't think anybody – It - you're not 'hominids' – you go from people to mice. I don't think anybody's created a trisomic chimpanzee, though I might be wrong about that. I don't think so. So, it's not that it's just *Homo sapiens*, but it's – Oh, somebody will, won't they? Go up the scale? 1.17.40

Holdsworth: Or would we ever think of any way of determining whether Neanderthals had –

Buckley: Don't know.

Holdsworth: - genetic disorders?

Buckley: Yes, could do. People argue there are paintings around of people with Down syndrome and babies with Down syndrome that go back [a long time]. Some famous paintings.[349] But that's as near as that's got. 1.18.06

Again, for this first one, it's studied in people. There's a question-mark about other hominids. As I say, it's mice rather than primates.

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[349] See, for example: Levitas, A.S. and Reid, C.S. (2003) 'An angel with Down syndrome in a sixteenth century Flemish Nativity painting', *American Journal of Medical Genetics Part A*, Vol.116A, No.4, 1 Feb 2003, pp.399-405. This attracted a comment in: *Am J Med Genet A.*, 2004 Apr 15; 126A(2):220. A photographic reproduction of the painting is to be found in the following news report: 'Down Syndrome Through the Ages', *medGadget - Internet journal of emerging medical technologies*, Friday, 18 November 2005 at: http://medgadget.com/archives/2005/11/down_syndrome_t.html (Consulted 24 September 2008).

Criterion 2: '*Is behaviour studied in the ecological setting – or in the laboratory or clinic?*' 1.18.06

Holdsworth: Right. Now, is behaviour is behaviour studied, for your purposes, in the ecological setting or rather in the laboratory –

Buckley: Both.

Holdsworth: - or the clinic?

Buckley: Both. So there it would be both. Right? It would be both. 1.18.18

Criterion 3: '*Is the focus on species-typical traits or on individual differences?*' 1.18.32

Buckley: [*Now looking at the next question on the 'Criteria graphic'.*] The focus is on 'species-typical' traits, I would say. Though not exclusively. But there's been much more of a focus on how do people with Down syndrome differ from people with the right number of chromosomes. I think definitely 'species-specific'.

Criterion 4: '*Does the research typically draw on the findings of genomics?*' 1.19.14

Buckley: Again, you've got this divide. The genetics research draws on genomics without a doubt, but the behavioural research doesn't.

Holdsworth: So it's –.

Buckley: So it's definitely – I mean, there's lots and lots of genetics research drawing on genomics, so the answer's 'yes'.

Criterion 5: '*Is the research on genes or other DNA? If 'other': mtDNA or Y-chromosome?*' 1.19.38

Buckley: And it's both genes and other DNA. Yes. I would say, if that's - if I understand that right.

Holdsworth: Well, what I'm getting at here is – I keep coming back to the example of palaeoanthropology, and they study migrations in peoples based on mutations in non-recombining sequences of DNA.

Buckley: OK. No, I don't think are people doing that. 1.20.12

Holdsworth: Yes. Is there research on the DNA - ?

Buckley: Definitely doing that. No particular interest in the Y-chromosome, no.

One of the things I should tell you is some of the reasons for the interest of the geneticists in Down Syndrome is that they are at an increased risk of getting Alzheimer's – or thought to be. It's a bit controversial. OK? They seem to be at more risk of ending up with an Alzheimer's dementia, though some people argue it's a knock-on consequence of more rapid ageing: so by 50 they're more like a 70-year-old. So some people say the rates of

dementia at 50 – well, some people would say it's a 30-year shift – that their rates of dementia at 50 may be similar to the rest of the population at 80. 1.21.12

Which puts a slightly different shine on what you're looking at: if it's some sort of accelerated ageing, or if it's something specific to getting dementia. The brains have plaques and tangles in that look like Alzheimer's for the majority of people with Down syndrome, though they don't all get the symptoms, so that plaques and tangles on their own don't predict Alzheimer's. [...]. 1.21.35

The reason I'm telling you that is that's one of the reasons money pours into looking at Chromosome 21, hoping that it will tell us something about the causes of Alzheimer's-type dementia in the rest of us: that there's something on Chromosome 21 that might be relevant. 1.21.50

Similarly, half the children have structural cardiac defects at birth; so people interested in why children should be born with cardiac defects have also been interested in Chromosome 21.

People with Down syndrome are almost unheard of in terms of getting solid tumorous cancers. Solid tumours. 1.22.21

Holdsworth: Really?

Buckley: They also don't get their arteries clogged up. They've arteries like babies as old people. In other words, they don't get arterio-sclerotic disease. So there's some pluses as well as some minuses. So you can see, people interested in just some of those things are interested in what's happening on Chromosome 21. 1.22.43

So there's a lot of interest in the genetics of Chromosome 21 for a whole variety of reasons. Yes. Not just because of an interest in improving things for people with Down syndrome. 1.22.57

And some of those people might be doing – some of them will certainly be looking for individual differences in genetic material on Chromosome 21 that might explain why half of them have perfectly normal hearts and the other half don't. [...]. 1.23.22

Criterion 6. '*Is there research on the DNA of non-human/hominid species? If so, animals or plants?*'
1.23.24

Buckley: Now, on the DNA of non-human species, well yes, I've told you mice, but they've been artificially created to be models for trisomy 21, so I'm not sure whether that entirely links.

Holdsworth: Right, well, I've made a note of it anyway.

Buckley: Not plants. No. 1.23.48

Criterion 7: '*Is there research on other biomolecules? If so, proteins or other?*' 1.23.48

Buckley: And yes, there is research on the other biomolecules – on proteins – stuff that's coded. There's probably under the 'Other' as well, but I'm not necessarily a sufficient expert to tell you that. 1.24.02

It's probably yes to both, actually. Both proteins and others – biomolecules. Because these transmitter substances in the nervous system would be 'Others' - they're enzymes. So it's yes to both. 1.24.18

Criterion 8: '*Does the research use environmental markers?*' 1.24.19

Buckley: 'Does the research use environmental markers?' What does that mean?

Holdsworth: Well, for example, in biomolecular archaeology, the answer is an obvious yes. We're talking about human settlement sites, and things like that.

Buckley: So it's no, I think then. Although some people have looked at whether, if you keep your mice in rich circumstances, they do better. What a surprise! Children in rich circumstances may do better. But, I mean, 'no', I think really there. 1.25.04

Criterion 9: '*The main concern is phylogeny or ontogeny?*' 1.25.05

Holdsworth: There were some supplementaries. Fairly obvious. 'Emphasis rather on phylogeny or ontogeny?' Ontogeny.

Buckley: Yes.

Criterion 12: '*Is the research intended to have a clinical application?*' 1.25.27

Buckley: Well. Again, it depends what you mean, doesn't it? There's another whole piece of this. Well, first of all, of course, there's been quite a lot of work on their health-care needs. So they get their cardiac surgery, etc. They get their thyroids tested and get thyroxin, if they need it. And they get their hearing tested. So there's been a piece looking more closely at their health-care and medical needs, where obviously [there can be an] application. That obviously hasn't been linked to genetics. 1.26.03

Holdsworth: That doesn't matter. No.

Buckley: So there's obviously a clinical application for health-care. There's educational application from what we do. There's educational therapy. Now some people would put therapy under a broad clinical heading. But clearly there are educational and therapeutic possibilities. 1.26.26

Now, as I've told you already, the people who are studying the genes claim that there will be drug treatments, but nobody's anywhere near anything like that at the moment in my view. So there are no proven outcomes at all. 1.26.45

Holdsworth: But there are some disciplines in my list where the question doesn't arise at all.

Buckley: OK.

Holdsworth: Like archaeology.

Buckley: Yes.

Criterion 10: '*Does the research draw on fossil evidence?*' 1.26.59

Buckley: I don't think any body's got any fossil evidence that anybody's looking at. I think that's no. 1.27.03

Criterion 11: '*Is Newtonian mechanics relevant to the research?*' 1.27.04

Holdsworth: Now, why the next one? People interested in evolutionary biomechanics, and the reasons why humans evolved having a bipedal gait, are certainly interested in that. As a matter of fact, that is relevant to motor skills and - .

Buckley: Well, it could be. Yes, it could be, though I don't know if anybody's come at it from that sort of direction.

General and concluding discussion 1.27.37

Holdsworth: Good, those were my questions. I could go on much longer discussing these topics with you.

Buckley: I don't know if that's given you enough information. Because in a – yes – in a sense, we feel a lot of the excitement about studying the genetics [...], if you like. 1.28.09

Holdsworth: Yes.

Buckley: I'm not sure if I should say this or not, but of course there's another area of our work, and that's around screening, and termination programmes. 1.28.19

You can identify the baby in utero by 12 weeks – possibly earlier. It's not usually done until 16 or 17 weeks. So on my black days I say to people the techniques for finding hormones for abnormal cells, etc., in a mother's blood, because they cross that through the placenta, are getting better. Right? 1.28.49

So on my bad days I say to people we won't have any children born with Down syndrome, before the geneticists come up with anything that will treat them, because the ability to identify them in utero are getting better. 1.29.09

It's a moving, moving figure that people who do decide to take the tests to find out – and that's not all parents – of those who get all the data, nine out of ten terminate. 1.29.26

Holdsworth: Is that in the UK or world-wide, or - ?

Buckley: Developed countries, where you can get the screening. The US. And the other educated, developed countries, such as in Europe. In the predominantly still very Catholic-dominated countries in South America you tend to get the rich and educated. The mass of the population wouldn't have access.

But there's a curious phenomenon afoot. Well, first of all, when the screening came in, and in this type of district they've been doing it at least 10 or 14 years – offering the test to everybody – the birth-rate in the UK was: roughly one in about 700 births was a baby with Down syndrome. Then it shifted to one in 1,000. 1.30.25

It didn't change as much as people anticipated, because not all babies are found on the screening, and not all babies – not everybody who chooses the screening [is leading to] termination. So it shifted the birth-rate from one in 600 to one in 1,000, and - . 1.30.41

Holdsworth: Over what time-span?

Buckley: Oh, quite quickly. Over a few years after the screening began to be rolled out. And there is a national register. It's St Bartholomew's Hospital that keep the register. We published in our journal their latest [data] a few months ago.[350] 1.31.01

So in the UK about 600 babies a year were born with Down syndrome: it changed to something like 900 babies, from 600 babies. However, they used to die early, which they don't do now, because of cardiac defects and pneumonia. 1.31.18

So we can do the surgery, and give antibiotics. Life-expectancy a few years ago was 20 to 30 – I mean, like, 20, 30 years ago. It's now 50 to 60. You see. Fewer babies born – likely to live to 50 or 60 – so the total population is still rising. Mothers in general now wait till they're thirty to have their first baby. 1.31.44

Average age for first baby's shifted about 10 years – to 29, instead of something like 20. And some Americans – Australians have just produced a study showing the known conceptions of children with Down syndrome is doing this [*Describes a rising curve*], because you're at greater risk as maternal age goes up. Right? 1.32.09

So conceptions – known conceptions have been doing this. [*Again describes a rising curve.*] So despite termination, birth rate's just levelled off. Also because a number of these older mothers won't choose to terminate. They leave it till their thirties, and then they need IVF to get pregnant, and they ain't going to terminate that baby after they've spent a lot of money on the way to get there. 1.32.29

So there are some very mad things going on, right? IVF without doubt is increasing the number of children born with Down syndrome. We see them all the time. And we see them with twins, triplets. We never saw this 15 years ago. 1.32.43

Holdsworth: I would have thought, if you have IVF - .

Buckley: You're at greater risk of an abnormal child. I can tell you that.

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[350] Citation needed.

Holdsworth: By definition, both of the twins or all three of the triplets - .

Buckley: No, not necessarily. They can be non-identical. If you think IVF - they implant two or three embryos. So you're more likely from IVF to have non-identical multiple births, from IVF, because they start more than one embryos. So we've triplets and twins - non-identical. We've identical sets of twins. I don't think anyone's got an identical set of triplets, that I know of, all with Down syndrome. 1.33.24

But the multiple birth thing also goes up with age. Risk of abnormality goes up with age. We are - I mean, everywhere we go [we see similar problems]. Triplets. IVF triplets. Little girl is fine. Little boy with Down syndrome. Boy with muscular dystrophy. 1.33.43

It doesn't bear thinking about, actually. All this money that's charged for IVF. And you cannot easily check the baby's chromosomes. [...]. [In the growing embryo.] Very difficult. They've just gone back to the human fertility people for permission to start screening embryos for certain things, but it's very difficult to do. 1.34.12

There is no doubt we're seeing more children. Right? So birth-rate's going up; some of these people will terminate, but there's a steady level of births that's not dropping. Even though we have screening and can terminate if we want to. 1.34.31

Holdsworth: Good heavens.

Buckley: Much to people's surprise. And the other thing, which is again probably something you probably don't want to know. The people who developed the screening - which at the moment is looking for markers, for hormones in the blood. You take the blood at about 12, about 14 weeks. OK? Those people [made an argument to] the government some years ago: look at the money you save if these babies aren't born. 1.34.59

Right? That was their paper. [It was published.][351] It made my blood boil. 'Look at the money we save if we don't have these children, don't have to bring them up'.

We get a request almost every week from a lawyer to be involved in a case of unlawful – no, wrongful birth. Now, you can screen. The mother who didn't get the screen data, or didn't understand it, and didn't choose termination when she might have done, sues the health authority. That's going on all over the country. 1.35.33

For wrongful birth. And compensation because she's got to bring this baby with Down syndrome up. I'd love to get my hands on how much that's costing the health service – all those settlements, because they always get something. So they fight all the way to court for the biggest settlement they'll get. And it is varied. I think there's been some effort to cap it at £45,000. But people don't want that. Depending on what went on and what cock-up there might have been over the screening information. You can see why doctors don't want to go into obstetrics. 1.36.07

So we've a whole industry now compensating people because they had a baby with Down syndrome. We've a whole industry keeping alive babies at 23, 24 weeks, who were born severely damaged 90 per cent of the time, costing the country a fortune. I mean, you know,

[351] Citation known?

society's totally mad. We're busy spending money terminating births with Down syndrome. These babies who are very low birth weight have multiple problems; they're often on respirators; they're tube-fed.[352] They go home – medically complex care required. 1.36.47

In all developed countries people are worried about these low birth weight babies. There's this whole new group of severely disabled children that we have to care for. [...]. And then we're busy at the other end, trying to terminate babies with Down syndrome who don't fall in that category of disability at all. Their quality of life is totally different. 1.37.09

So it's a totally mad world, all this science. From our perspective, totally mad. But because of the screening and termination, and people looking earlier and earlier to see if they can successfully identify, with a combination of detailed scans and blood tests, babies with Down Syndrome, I do think the people giving their money for the genetics research - . We're not going to have any babies born with Down syndrome before you find the cure for them. That's what we're doing, as a society. 1.37.38

It'll become less and less likely people will choose to have this baby, because the earlier you give the information the more likely they are to terminate. It's no joke being told to terminate at 18, 19, 20 weeks with a moving child inside you, which is what happens now. 1.37.52

You don't get the results until that point in your pregnancy. But if you can find that at 6 or 8 weeks when nobody even knows you're pregnant – if you can check the embryo at that stage – many people would terminate and start again, at that stage. 1.38.08

So those people are going to crack it before anybody finds a cure, a silver-bullet type of cure, studying that chromosome. Only, it's one reason why, if you like, at least one of the spin-offs of all the money going is we might know more about dementia and heart defects and things that are relevant to the whole population. 1.38.28

By knowing more about Chromosome 21. Or [...] why they don't get tumours. Why they don't get cancerous tumours, and why arteries don't clog up. So the genetics/biochemistry stuff may benefit the whole population more if people stuck to looking at those sorts of things and trying to understand them, [rather than] suggesting there's going to be a fix, a quick fix in their cognitive development. 1.38.59

Anyway, you've got more than enough from me, haven't you? And probably most of it not what you wanted! 1.39.03

Holdsworth: Not at all, that's all useful. Have you often had philosophers coming to ask for interviews?

Buckley: No. No. No. Probably not. I may not have addressed enough of the philosophical issues. In some ways, you know, as you will have gathered, I think in some ways the notion you

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[352] For an article on low birth weight infants, risk of disability, multiple births and assistive reproductive technology, see Schieve, Laura A. et al. (2002): 'Low and very low birth weight in infants conceived with use of assisted reproductive technology', *New England Journal of Medicine*, Vol.346, No.10, 7 March 2002, pp.731-737.

can understand their genetics has been negative. Because it creates false expectations.
1.39.32

Holdsworth: Well, Sue, thank you very much indeed.

Buckley: OK. Pleasure. 1.39.39

1.39.42

5. Research interview with Professor Ruth Mace – Edited Excerpts

Interviewed: Professor Ruth Mace, Professor of Anthropology, University College London (UCL).
Interviewer: Richard Holdsworth, PhD candidate, Economic and Social Research Council (ESRC) Centre for Genomics in Society, Egenis, University of Exeter.
Date and time of interview: Thursday, 15 March 2007, 11.30.
Place: Department of Anthropology, UCL, London.
Total length of the recording: 1 hour 20 minutes 1 second.

The interviewee's description of the research 0.05.40

Mace: Behavioural ecologists make a distinction between the proximate explanations of behaviour and the ultimate explanations of behaviour, in the sense that proximate are the sort of 'how' questions - of causation. Questions [like] whether or not something is nature or nurture, or what the genetic basis of it is, probably come into that category. And then you've got the 'why' questions, which include the phylogenetic history of the behaviour and the adaptive function of the behaviour – i.e., why did it evolve, how did it evolve? OK? That's what Tinbergen called his 'Four Why's', which are usually categorised into two different kinds of questions: the proximate questions and the ultimate questions.[353] And because behavioural ecologists have tended to focus on the ultimate questions more than the proximate questions, they're not – you know, they're interested in adaptive function, they're interested in the history of the behaviour - but that doesn't really require you to know, necessarily, that much about the genetics.

Holdsworth: Yes. 0.06.58

Mace: So that's why, you know, it's not really using this research explicitly for the most part, I would say. This isn't to say that we're not influenced by some of the lessons that are [there].

Holdsworth: Sorry, could you repeat – you said behavioural ecologists have been mainly concerned with the proximate - ? 0.07.20

Mace: The ultimate: i.e., how, how, how did, why did, you know, why, what is it, what is the adaptive advantage of behaving in this way – i.e., why is this behaviour being selected for? OK. You don't really need to know its genetic basis to answer that question. So even though it's an interest in how did behaviour evolve, you don't need to know much about genes to do that study. OK. So that's why it's kind of separate. 0.08.00

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[353] Tinbergen, N. (1963): 'On aims and methods of ethology', *Zeitschrift für Tierpsychologie*, Vol.20, 1963, pp.410-433. The Bard-Rockefeller Program, a collaboration between Bard College and The Rockefeller University, has made a pdf of this article available among its Class Notes at: http://www.rockefeller.edu/bard/pdfs/week_02_tinbergen_on_aims_and_methods_of_ethology_zft_1963.pdf (Consulted 7 August 2008).

Holdsworth: Yes. I see what you mean, but, for example, the idea that linguistic phylogenetic trees somehow fit genetic ones without being caused by them is a rather well accepted idea, and you build on that. 0.08.31

Mace. Yes, I'm just giving it to you very generally. Because there's lots of areas to my research. OK then, the cultural phylogeny. So geneticists have worked out, as you say, that you can use genes to make [estimates] about population history, and linguists have also been using language variation to look at population history, too. And we've been looking at language variation, and if you plug it into the same sorts of programs that really geneticists are using to build these trees - if you plug *language* variation, rather than *genetic* variation, into these programs, you can also build trees [of history]. And these seem to be very good models of population history. And they seem to work extremely well. I mean, the phylogeny-building programs are really designed to model the evolution of the species. 0.09.56

Holdsworth: Yes.

Mace: And if you look at the genetic variation within a species it's a bit of a mess, because you've got inter-breeding, obviously, between all these different groups, and the trees don't come out brilliantly. If you use *language*, they always seem to come out better than if you use genes - more tree-like. And I think the reason we think – well, the reason I think that's found, is because - you know, when you have a language - OK, so language is evolving in some ways a little bit - linguistic diversity is always a little bit similar to the way genetic diversity evolves. I mean, it's a neutral phrase, but when populations get separated their languages start to diverge; they start to get different. The longer they've been separated the more different they become, as with genetic diversity. OK? 0.10.57

Holdsworth: Yes.

Mace: But if you get migration between groups, then the genes get - obviously - very mixed up, but when you've got migration between groups, and you migrate into a new group, you bring your genes with you, but you probably don't bring your language with you, or at least your children will not speak your language. They'll speak the language of the group. So, I think that's why the integrity of the group is easier to maintain when you're looking at language than when you're looking at genetics. So we know that populations don't map out into nice genetic units very much at all: there might be certain markers in certain populations, but it is quite messy. Whereas with language it seems to lessen it. I think it's this process that - you know - language by definition has to be mutually intelligible for the members of your group, which therefore maintains the integrity of linguistic groups, which doesn't maintain the integrity of [genetic populations]. There's no reason why everyone has to have the same genes, but everyone living in that group does have to speak the same language, if they want to make themselves understood. 0.12.11

Holdsworth: Yes.

Mace: So the phylogenetic tree programs, which were built really for looking at species diversity, don't work very well within species or in genes, because the groups aren't different enough, but they do seem to work really well on languages. So people are now, including us, using language diversity to makes these trees of population history. 0.12.33

Holdsworth: Of course language is presumably the most important cultural marker, but you're interested in others as well. Could you give me some examples?

Mace: Well, I mean, one of the reasons we were interested in building trees is because we're interested in cultural evolution. And again, evolutionary biologists have come up with models where, if you know the tree - the historical tree - you can ask: is it co-evolving with another trait? OK, [you can ask this] every time we see the evolution of something like monogamy or polygyny, or some cultural trait we're interested in, or some behavioural trait we're interested in. So for example we did a study on matrilineal kinship versus patrilineal kinship in Africa. And is that co-evolving with cattle? So, we built a tree of the Bantu, which is – we were interested [in about 80 groups in Africa][354] using language, and then we mapped onto that tree which groups were matrilineal, which groups were patrilineal, which groups had cattle, and which groups didn't have cattle. And you can use these methods called 'phylogenetic comparative methods' which can tell you whether matriliny is – well, in this case we showed that patriliny and pastoralism – i.e., keeping cattle – were evolving together. So if a culture acquired cattle they were more likely to become patrilineal. 0.14.14

Holdsworth: And when you say 'evolving' you mean *culturally* evolving?

Mace: *Culturally* evolving. Yes. Now of course there might be genetic evolution in there too, because we also know that when you become a pastoralist you start evolving, for example, lactose tolerance. So you can use these methods to look at, you know, gene-culture co-evolution, or you can look at culture-culture co-evolution. So pastoralism and patrilineal kinship is cultural co-evolution. We've also used the technique to look at pastoralism and the lactose gene, and you can see that there there's gene-culture co-evolution: i.e., when groups acquire livestock they evolve the ability to digest lactose as an adult, which [indigenous human groups] can't do. This helps us to understand an aspect of the history of pastoralism. 0.15.14

Holdsworth: Yes.

Mace: What about Mark Thomas[355] and Dallas Swallow[356] over in genetics? They've done a lot more work on lactose tolerance.

Holdsworth: I saw the news last week in the media.

Mace: Oh, yes? They're often in the media. What was it last week? 0.15.37

Holdsworth: Well, it was more of this lactose [issue].[357]

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[354] Holden, Clare Janaki, and Mace, Ruth (2003): 'Spread of cattle led to the loss of matrilineal descent in Africa: a coevolutionary analysis', *Proc. R. Soc. Lond.* B (2003), 270, pp.2425-2433.

[355] Dr Mark Thomas, Senior Lecturer, Department of genetics, evolution and environment, UCL. A concise description of his research is at http://www.ucl.ac.uk/biology/academic-staff/thomas/thomas.htm (Consulted 31 July 2008).

[356] Professor Dallas Swallow, Professor of human genetics, Department of genetics, evolution and environment, UCL: http://www.ucl.ac.uk/biology/academic-staff/swallow/swallow.htm (Consulted 6 August 2008).

[357] BBC News report: 'Early man 'couldn't stomach milk'', 27 February 2007: http://news.bbc.co.uk/1/hi/health/6397001.stm (Consulted 6 August 2008). The report concerned the following publication. Ingram, C.J.; Elamin, M.F.; Mulcare, C.A.; Weale, M.E.; Tarekegn, A.; Raga, T.O.; Bekele, E., Elamin, F.M.; Thomas, M.G.; Bradman, N.; Swallow, D.M. (2007): 'A novel polymorphism

Mace: Yes. They've isolated specific genes now that cause this. When we did it we were just using, you know, physiological measures that people had made, like 'Can these people drink milk or not?' We didn't know what the gene was, but they've actually isolated the gene involved. 0.16.00

Holdsworth: Right. Just to take a step back, would you say that the discipline you're working in is 'human behavioural ecology', or would you give it another name?

Mace: I say it's 'human behavioural ecology', yes. I mean [some people] talked about 'cultural biology' [as if it's] kind of a subject, but, you know, that's not really using genes: it's using cultural data. But, I mean, the human behavioural ecologists don't really use genes, either. I mean, we're a completely evolutionary paradigm. We're testing for adaptation, and we're looking for the adaptive function of behaviour. So that's really a separate question from what genes programme. 0.16.40

Holdsworth: Right. Now, it's possible to have more than one idea of how adaptation, as they say, 'cashes out'. One popular measure is reproductive success. Would you align yourself with that, or do you think there are other measures of adaptation? What are the criteria for saying 'This is well adapted'? 0.17.18

Mace: Yes, it would be reproductive success. That's the first option – right? - natural selection. If you're talking about cultural evolution you might talk about an idea being good at making copies of itself - in other words, being influential at transmitting itself to others. But normally when we talk about 'adaptive' we do just mean it enhances your reproductive success, yes.

Holdsworth: But, for you, it could also mean the successful replication of an idea, some cultural pattern? 0.18.00

Mace: Well, it depends what you're talking about. If you're trying to understand the spread of a cultural idea, you know, it might spread because the individuals that had that idea left more descendants, and they also inherited the idea. That's the simplest explanation. Or it might spread because - you know, it's the whole meme debate. Some ideas have properties that are very good at spreading themselves, so even if they're not very good for your reproductive success, so long as they have properties which cause you to persuade other people to believe in them then they themselves will spread.

Holdsworth: I thought you introduced the word 'meme' with a certain amount of caution. 0.18.52

Mace: Well, I did really. I mean, most behavioural ecologists – I think what we tend to do is, sometimes we're measuring reproductive success, or sometimes we're measuring a currency that we think approximates to reproductive success. If you can't get data on reproductive success, though – yes, so it would be – [I can't think at the moment]. But for example, when we were interested in kinship systems, we proposed that - it's a slightly complicated argument - but if you've got cattle, it [enables] you. Pastoralists tend to be polygynous systems. In other words, individuals with lots of cattle can afford lots of wives

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associated with lactose tolerance in Africa: multiple causes for lactase persistence?', *Human Genetics*, Feb. 2007, Vol.120, No.6, pp.779-88.

– OK? - and the reason is, that it's a very good source of food. So, if you can marry a girl with a lot of cattle, you can have a lot of healthy children; there's going to be a lot of milk; it's much less hard work than farming. You know, it's a good deal all round. So if a man has lots of cattle, he can have very high reproductive success – because he can marry several wives, in fact, and that's often what you see in pastoralist societies. And because it so much favours your sons to have this cattle, then you get this kind of male-biased wealth inheritance. OK? So that's the explanation for why when societies gain cattle they become more patrilineal. 0.21.04

Holdsworth: Yes.

Mace: And then you can just test that and see whether it really happens, over evolutionary time. I mean, are societies that are adopting cattle becoming more patrilineal? And we find that they are. So you've built a model, and you make your prediction from it, and you test it using the data. So you don't really need to know about the –. It's an adaptive model in that we're saying, you know, there's a functional reason why this society switched from being matrilineal to being patrilineal, which is the reason I just gave you, and then you test it. So we're saying rather than cultural variation being random or whatever, it's actually to do with individuals trying to maximise their reproductive success. 0.21.52

Holdsworth: Yes.

Mace: So that would be an example of a behavioural ecological model.

General discussion of concepts and methods

Holdsworth: I was interested in the paper about the introduction of taps in Ethiopia and the effect on fertility and malnutrition in children. There, there was an obvious result in the area of reproductive success, in a sense, but it was also intermingled with an energetic calculus. 0.22.30

Mace: Yes, well that's another branch of my interests. That's kind of 'life-history theory'. Life-history theory is another branch of evolutionary ecology, really, or behavioural ecology – whatever you want to call it. Where it's to do with the timing of [life-history events]. You know, there's all these trade-offs. The energy that you put into parenting you can't put into [other things]. Do you have a few offspring in which you invest heavily, or more that you invest less heavily in. Do you spend time growing, or do you stop growing and start reproducing? Do you carry on reproducing, or do you stop reproducing and start looking after the children you already have? These are all life-history trade-offs, and people have worried about them across species: you know, why does one species have one life history and another species have another? [358] 0.23.23

Holdsworth: Is life-history theory well-developed? Is there now a large literature?

Mace: Yes. In animal behaviour and in human behaviour.

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[358] Mace, Ruth (2000): 'Evolutionary ecology of human life history', *Animal Behaviour*, Vol.59, No.1, January 2000, pp.1-10.

Holdsworth: Could you mention some other authors?

Mace: What, in the human side or animal?

Holdsworth: Human side. 0.23.53

Mace: Well, Kristen Hawkes in the States.[359] There are a few evolutionary anthropologists interested in life history and evolution. I mean, Stephen Stearns is a biologist who works on this.[360] He's in the States. Well, there are lots who are doing a bit on it, but - . So the whole question of how fast do you reproduce, or whatever, would be in that realm. And I guess that that paper was quite applied really, but what was evolutionary ecology about it really was that life-history theory predicts that there's this essential trade-off . So I think the development agency argued when they were putting the taps in that women would have to spend less energy on going and collecting water. Now if you're going to have more energy you might expect them to have healthier, fatter children. But that's only really one thing that could happen. The other thing that could happen, if you're trying to maximise your reproductive success, is not that you put more into each child, but you just have more children. 0.25.39

Holdsworth: And fatter ones?

Mace: Well, not necessarily fatter ones, because in fact what we found happened was that the women that weren't walking so far every day because of the taps were having children at [reduced] intervals. So they were just falling pregnant more quickly than they used to because they weren't so energetically stressed. 0.26.01

Holdsworth: Yes.

Mace: OK. So, in fact, infant mortality was going down, but also the birth rate was going up, and because there was no more food in the system, actually the family sizes were getting larger, and in fact malnutrition went up rather than down. So, it's a bit complicated, but it was a positive intervention, but of course if you think of it in terms of life-history trade-off, not all the results were obviously what you would expect, and I don't think the people putting in the taps thought that one outcome could be that children would get thinner. It's not an intuitively obvious one, but if you think of natural selection maximising your reproductive success, if life gets a bit easier, and you're not using any contraception, you can actually have more babies than you had before. And that can actually undermine the sort of improvements that you might see in other areas, because they're already very short of food. 0.27.06

Holdsworth: What I meant, of course, it was only a trivial interjection, but if the women were having fewer children then the children would be better nourished.

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[359] Kristen Hawkes, Distinguished Professor, Department of Anthropology, University of Utah: http://www.anthro.utah.edu/people/faculty/kristen-hawkes.html (Consulted 6 August 2008).

[360] See, for example (1) Stearns, S.C. (1977): 'The evolution of life history traits: a critique of the theory and a review of the data', Annual review of ecology and systematic, Vol.8, November 1977, pp.145-171, and (2) Stearns, S.C. (1989): 'Trade-offs in life-history evolution', *Functional ecology*, Vol.3, No.3, 1989, pp.259-268.

Mace: Well, exactly. So if there was a contraception available, then I think the overall benefit could be realised, if they could keep to the same number of children.

Holdsworth: A very interesting example of what happens when you make a technological intervention. You must bring not only taps but also birth control.

Mace: Well, exactly. So you're not always getting exactly what you would expect coming out the other end. You have these knock-on effects. And thinking of it in the life-history way, we predicted that would happen, and we were right, but the development people didn't really want to hear about that. They just assumed it would be an all-round benefit, and it was a benefit in a sense. Everyone welcomed it, but, you know, there was this unforeseen consequence: that they were getting pregnant even faster than they had been before.

Holdsworth: To take a different kind of cultural marker, I think something you've written mentions - is it basket-weaving methods? 0.28.25

Mace: Yes, that's not my work - just citing someone else's - but they were arguing – that's going back to the phylogenetics - rather than just using language you can use some other traits as well. I mean, archaeologists have always done this. They've found bits of pots and said, well, these pots look like this and the pots don't look like that, so we think this is a different population from the ones here. I mean, I think language is a much better marker if you've got it, you know. But obviously archaeologists have to use whatever they can find. 0.29.01

Holdsworth: Was that basket-weaving in the aesthetic sense or some functional one?

Mace: I can't quite remember. They were just trying to measure all these traits of the baskets, and trying to work out if they could make trees out of the basket similarities in the same way we'd been making trees out of language similarity.

Holdsworth: I saw one possible criticism of the cultural phylogenetic tree approach. Somebody said it works if you can assume that the culture is transmitted longitudinally, vertically. It works less well if you have to take into account that it went horizontally. 0.29.44

Mace: Yes. That's true. Well, the question is what history are you trying to study. It may be a cultural history. Some groups almost get swallowed up by other groups: i.e., they gain their language, and then that group is almost lost. It's almost submerged into the other group. So if what you're interested in is the cultural history, you know, it might not be the genetic history, but it might still be quite a good model of the cultural history, if you see what I mean. But they might not be exactly the same, because it is possible that certain groups just get, kind of, run over almost by other groups and end up speaking their language. And once they're speaking their language they lose their own cultural identity altogether and just become part of this wider group. But the tree-building programs are based on the idea of vertical transmission, so it's true that they don't work too well if there's too much horizontal transmission. 0.31.19

Holdsworth: What about the phenomenon, which I believe is established, that there is a steady loss of languages, a steady loss of language diversity in the world? But do we want to say the same thing about cultural diversity, using other markers? 0.31.39

Mace: Well, it depends if we believe that genetic diversity and language diversity are prone to similar things like barriers – populations being separated. It doesn't matter if they were separated by mountain ranges or rivers or distance or what have you, those kinds of things can cause separation. 0.32.05

Holdsworth: Yes. Wasn't it in an article that you co-authored in *Nature* that there was a very good diagram about barriers.

Mace: Yes, exactly. I mean, we don't know the exact causes, but it's evidence that there are ecological processes involved. So if you look at species diversity in North America like we did in that article, you know, you get certain patterns. So, [in] certain parts of North America, especially towards further south, or on the coast, they've got very high species diversity. These are areas where ecologically there's tons of diversity. Then you go up to the north, and species diversity goes right down. 0.32.44

Holdsworth: Yes.

Mace: You get big ranges and big areas. OK? That's a well-known [phenomenon]. Ecologists have noticed that rule for ever. We know the tropics are incredibly diverse, and the northern climes are much less diverse. And interestingly enough if you plot linguistic diversity you get exactly the same thing. So in the tropics you've got very small areas, and there you can go over the hill and there's another language being spoken, and you go over the next couple of valleys, and there's another language being spoken. Whereas you go north, and there's this huge language area where people are migrating large distances. So you do get this latitudinal gradient. This is looking at native American languages - obviously, not now – it's all English now apart from a few pockets – but pre-colonisation there was indeed this latitudinal gradient, which is suggestive that there are some parallels between processes that give rise to species diversity and processes that give rise to diversity in [...] linguistic groups. And exactly what they are I don't think we really know, but it does suggest that similar processes are going on. Barriers to gene flow, for example, could cause species to diverge, we think, and obviously in modern times it's just so much easier to travel or to transmit ideas across [barriers]. Migration basically means that those barriers are being broken down, so it's not really surprising that we're losing both linguistic and cultural diversity now, because the diversity arises when groups get separated, and they start going off in different directions. And when they're not separated then you're going to get more socialisation. 0.34.39

Holdsworth: Yes.

Mace: So we think that, like, 10,000 years ago there were, you know, ten thousand languages or whatever, and then it's gone down to six thousand, and, you know, it'll probably end up going down to two or three languages if we carry on at the rate we're going! Because you know there's a kind of global reason why it's useful to speak English, or in parts of the world where it's useful to speak Chinese - and maybe Spanish in parts of the world, you know, Arabic, Russian - and that'll probably be it. Because it's all changed. But when you were living in a small group that was just farming a particular area and had largely hostile relationships with neighbouring groups it was completely different. So linguistic diversity has definitely gone down. Once agriculture started actually we started getting much bigger language groups as well. So people think the peak of linguistic diversity was back when we were all hunter-gatherers, and it's been going down since then. And then globalisation – recent globalisation – is probably speeding it up even faster. 0.35.47

Holdsworth: How old is life-history theory? When did it get going?

Mace: Life-history theory? Gosh, I should know that. Evolutionary biologists coined the term, and behaviour people. That's the other side of my research. I don't know when it went back to. I mean, most of these things go back to Darwin, but he probably didn't use the phrase. 0.36.24

Holdsworth: No, I mean in a self-conscious way. When did people start talking about 'life-history theory'?

Mace: Good question. I don't know when they actually did.

Holdsworth: Was it you?

Mace: No, no. I mean. I personally don't know whether Darwin talks about 'life history'. I don't think he did. I'm sure he gave examples relating to it, but - . 0.37.04

Holdsworth: What about human behavioural ecology? You mentioned Tinbergen.

Mace: Yes, he was probably - . I mean, he got the Nobel Prize – also in honour of Konrad Lorenz - in - was it the 60s, or early 70s?[361] They founded the field of animal behaviour, and they actually got the Nobel Prize for medicine, because there was no Nobel prize for zoology or whatever. 0.37.42

Holdsworth: Yes.

Mace: Because they founded this. They really started the whole thing in evolution of behaviour.

Holdsworth: They called themselves 'ethologists', didn't they?

Mace: Yes, I suppose they did. That's just the study of behaviour. And then I guess the term 'behavioural ecology' – I mean, Krebs and Davies wrote that book in – when did they write their introduction to behavioural ecology? 0.38.06

Holdsworth: I would have said in the 1970s.

Mace: Well, it would have been seventy - late 70s, I would say.[362] I think that was the first big [publication]. And then people just started. I mean there were the sociobiologists, who were kind of applying the same ideas in anthropology. 0.38.35

Holdsworth: Do we have to draw a line between 'human behavioural ecology' and 'sociobiology'? And 'evolutionary psychology', while we're about it?

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[361] The winners of the 1973 Nobel Prize in medicine were Karl von Frisch, Konrad Lorenz and Nikolaas Tinbergen.

[362] Krebs, J.R., and Davies, N.B., eds. (1978): Behavioural Ecology: An Evolutionary Approach, Blackwell, Oxford, 1978.

Mace: Yes, well, some people talk about 'the three schools of thought'. So what was originally just broadly called 'sociobiology', which was a sort of catch-all term for the evolution of human social behaviour - people now talk about 'evolutionary psychology', 'human behavioural ecology' and 'gene-culture co-evolution' as the three schools of thought, that I see as kind of having arisen out of sociobiology. OK? So everyone used to be lumped together as 'sociobiologists', and people don't use that term much any more at all, but it's not really that the evolutionary project has disappeared: it's just that it's 'reproduced', really. I mean, there's the evolutionary psychologists; there's the human behavioural ecologists, which is where I probably put myself, - .

Holdsworth: It's branched.

Mace: It's branched. Yes. And there are some differences between those three branches, really.

Holdsworth: But of course sociobiology - .

Mace: There's a book called 'Sense and nonsense' by Laland and Brown that maps all that out for you[363] and puts in the detail. It's a good book. 0.40.04

Holdsworth: Edward Wilson's conception of sociobiology in 1975 was pretty strongly genetically based.

Mace: Yes, well, you see, I [would call] it a red herring, whether - . Because, you see, let's not get back into nature-nurture because it's so boring. Because everything is both. Everything is both. Genes expect to be in a certain environment. If you don't put them in the environment they expect to be in, you get weird organisms. 0.41.00

Holdsworth: Yes.

Mace: The environment that you're in is going to have an influence on how you're going to develop, and your genes are going to have an influence on how you develop, and some things are going to be at one end of the spectrum, and some things are going to be at the other end of the spectrum, and some things are going to be in the middle, but exactly where they are – you know, it depends on how variable your environment is for a start! So it's actually a bit of a sterile debate. But whether or not behaviour is adaptive is a separate question from whether or not it's nature or nurture. 0.41.42

Holdsworth: Yes, I agree.

Mace: I think, you know, Wilson was trying to say, 'Look, behaviour evolved, we have to think of it as something that evolved; our brains are organs like our intestines or anything else: they've evolved to do the job'. And our behaviour, as Tinbergen and Lorenz and all that said, our behaviour is not immune from evolutionary study. Our behaviour is subject to natural selection just like our bones are and our muscles are, and our skulls are, and our breeding seasons and everything else, you know. So, he may have done it, you know, being a sort of early person, I think. You know that his book 'Sociobiology' was mostly about animal behaviour. 0.42.30

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[363] Laland, Kevin N., and Brown, Gillian R. (2002): Sense and nonsense: evolutionary perspectives on human behaviour, OUP, Oxford, 2002.

Holdsworth: True.

Mace: The last chapter was the only one about human behaviour. And that just kind of sparked everyone off, but I think he's been proved right. He said all these other disciplines like economics, psychology, anthropology should all become branches of evolutionary biology. And of course that pissed everybody off, and everybody's hackles rose, and they all started attacking him, but had he put it slightly more diplomatically, he's been proved right, in that there is now a field called 'evolutionary psychology'; there is a field called 'evolutionary economics'; there is a field called 'evolutionary anthropology', and those fields are all doing really well and coming up with all sorts of interesting insights. 0.43.14

Holdsworth: Do you also call yourself an 'evolutionary anthropologist'?

Mace: I guess I do. I'm not quite sure what that phrase means. I think that's what I am, yes. That's a kind of catch-all. 0.43.24

Holdsworth: Right. Good. Then you said there was a third school of thought: 'gene-culture co-evolution'.

Mace: Yes. You see, behavioural ecologists don't worry too much about mechanisms of transmission, typically. I mean, as it happens I'm quite interested in mechanisms of transmission, but you don't need to. We are arguing that you don't necessarily need to know about them to work out what is the adaptive solution. You don't really need to know where they got this idea from or whatever. Whereas the gene-culture people are saying, well, there are two inheritance routes you have to worry about: the genetic one and the cultural one. It's a very theoretical subject. As you know, it's a lot mathematical models. It's arisen really out of population genetics and population [genetic modelling]. They use population genetic modelling, but instead of just modelling alleles they say you have to model the spread of cultural variants, because they can spread in a non-Mendelian way. 0.44.36

Holdsworth: Right.

Mace: You know, your genetic parents are your parents: there's nothing you can do about that. But your cultural parents might be your friends or your age-mates or influential people on TV or your teachers or people you admire because they're prestigious in society, and they argue that these transmission processes can lead to the evolution of slightly strange variants. 0.45.10

Holdsworth: Excuse me, could you cite some names in that field?

Mace: Boyd and Richerson.[364] They're the [prime examples], and still the most prolific, or their students. But they're kind of teaming up with the evolutionary economists[365] now, who are also, you know, doing very similar models. It's a very mathematical field. It's quite hard to

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[364] Richerson, P.J., and Boyd, R. (2005): Not by genes alone: how culture transformed human evolution, University of Chicago Press, Chicago, 2005.

[365] For evolutionary economics, see, for example, Hodgson, Geoffrey M. (2002): 'Darwinism in economics: from analogy to ontology', *Journal of evolutionary economics*, 12, 2002, pp.259–281.

do empirical work on cultural change. I mean, we're trying to with the phylogenetic stuff, but - most of the work in this field has been mathematical models of what can happen in theory, and they're actually quite hard to assess.

Holdsworth: Any names in evolutionary economics?

Mace: Sam Bowles,[366] Herb Gintis.[367] And they often write papers. A lot of papers by Gintis, Bowles, Boyd and Richerson are all about evolutionary [economics] and altruism, which are very fashionable at the moment. 0.46.12

Holdsworth: Altruism? Yes.

Mace: It's a huge field. It's actually a thriving field. It's really growing. I was actually just in Bath yesterday doing something for the ESRC Festival of Science. It was about evolutionary approaches to social science, and I only had, like, half – well, twenty-five minutes to talk. I was just trying to review the whole field, and it was impossible going in twenty-five minutes. It was interesting to see. I think a lot of social scientists don't really know what's going on in the field. They might have a gut reaction against it or whatever, but they won't actually know the field very well. 0.47.00

Holdsworth: In evolutionary psychology there's a tendency to caricature the attitude of social scientists under the – what is it? – 'the standard social science model'.

Mace: Yes. Also, within the evolutionary sciences we have a tendency to caricature the evolutionary psychologists as well, because they have a - . Yes, well, 'the standard social science model'. Yes. Actually I haven't heard that phrase for a while. You're absolutely right. I can't quite remember what the standard social science model was, whether it was just that everything's complicated.

Holdsworth: Well, it would reject any form of genetic influence.

Mace: It rejects any genetic influence at all.

Holdsworth: And indeed, as portrayed, it rejects an evolutionary picture. 0.47.44

Mace: Well, I think the social sciences are opening up, actually. Not all of them. You know, but I think there is change in the air.

Holdsworth: Yes. Well, it's the purpose of my research to explore divergence in approach. It goes in the same direction really, because when people were happy to talk about the nature-nurture problem, you know, implicitly they were talking as if there were only two camps. But when you look into what's really happening you find that there's a range of disciplines each with their own focus, their own concepts, their own models, their own methods.

Mace: Oh, absolutely.

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[366] Website of Sam Bowles at the Santa Fe Institute: http://www.santafe.edu/~bowles/ . (Consulted 5 August 2008).
[367] Website of Herb Gintis at the University of Massachusetts Amherst: http://people.umass.edu/gintis/ (Consulted 5 August 2008).

Holdsworth: And so that's a way out of the trap. 0.48.35

Examination of the criteria

Criterion 1: *'Does the research cover all hominids or only Homo sapiens?'* 0.49.50

Holdsworth: Well, first of all: 'Does the research cover all hominids or only *Homo sapiens*?'

Mace: Mostly *Homo sapiens*, but behavioural ecology can cover anything, from a *Drosophila* to a - you know. 0.50.10

Holdsworth: Yes, other species come later.

Mace: I think it's the fact that they're all dead. So if you were interested in something like - . Some people talk about 'human evolutionary ecology'. You really must read *Sense and nonsense*, you'll love it. I think you'd better read that, because it will actually make everything I've said today much clearer in terms of how all these different behavioural parameters fit together. [I think that will be] worth your reading. 0.50.54

Holdsworth: Good.

Mace: [If you're interested in] something like age at first reproduction , or age at menopause or something, it's more 'life history' than behaviour. So human evolutionary ecology is slightly broader. It might include, you know, the evolution of menopause, but then one of the hypotheses for the evolution of menopause is the 'Grandmother hypothesis' – i.e., grandmothering as an adaptation to stopping reproduction in yourself, but looking after your daughter, helping your daughter reproduce. 0.51.32

Holdsworth: Yes.

Mace: So it has a behavioural dimension, but human 'evolutionary' ecology is just slightly broader than 'behavioural' because 'behaviour', you know, might just imply a slightly narrower focus. So I guess if we're doing just 'behavioural' then we're mainly doing *Homo sapiens*, because it's the only extant species, whereas if you were doing human 'evolutionary' ecology - I mean, people have written papers on, you know, 'Did *Homo erectus* have menopause'[368] and this kind of thing. I suppose. I would tick mainly the first one: *Homo sapiens*. 0.52.05

Criterion 2: *'Is behaviour studied in the ecological setting – or in the laboratory or clinic?'*

Holdsworth: Right. And then: 'Is behaviour in this discipline studied mainly in the ecological setting?

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[368] See (1) O'Connell, J.F.; Hawkes, K., and Blurton Jones, N.G. (1999): 'Grandmothering and the evolution of *Homo erectus*', *Journal of Human Evolution*, Vol.36, No.5, May 1999, pp.461-485, and (2) Aiello, Leslie C., and Key, Cathy (2002): 'Energetic consequences of being a *Homo erectus* female', *American journal of human biology*, Vol.14, No.5, 2002, pp. 551-565.

Mace: Yes, that's the defining feature, really, I would say.

Holdsworth: Yes. I thought I was on safe ground with that one. 0.52.16

Mace: Yes. I'll show you something. There's a lecture I gave. You know, I started out with my three schools of thought, and I said that it is now getting even more complicated. 0.53.26

Holdsworth: Oh good!

Mace: There are millions of them! And (*Gesturing towards the papers on her desk.*) there's even more than that! You know, these are only some of the ones that I'm interested in. But that was the kind of overview lecture about the three schools of thought in human behavioural – in human evolutionary studies. 0.53.43

Holdsworth: So this basic schema of the three schools of thought - .

Mace: I'm now saying it's got more complicated than that.

Holdsworth: Yes, but that was you, was it?
0.53.52

Mace: No, not really – I would say, lots of people. That's widely accepted in the field now. It's not just me. I mean, read *Sense and Nonsense* on that. They talk about that as well. I think they may have four, rather than three. 0.54.04

Criterion 3: *'Is the focus on species-typical traits or on individual differences?'* 0.54.28

Holdsworth: Now, 'Is the focus on species-typical traits or on individual differences?'

Mace: I would say it was on individual differences.

Holdsworth: Really? 0.54.40

Mace: Yes. Well, it's actually on both. If you're interested in 'How did menopause evolve?', then obviously that's a species-typical trait, but you might [approach it by asking], as we do [when we are dealing with] traditional populations with high mortality, are children with grandmothers more likely to survive than children without grandmothers? OK, that might be the kind of analysis that you would do. 0.55.14

Holdsworth: I think that counts as species-typical rather than individual.

Mace: Oh, I see.

Holdsworth: If you said to yourself, which grandmothers are most successful? Take a typical Ethiopian community. What kind of grandmother is the most adaptive? Of course it doesn't make sense, but [focusing on] the structure of your question: why are some better than others, why are some richer than others, fatter than others, have more children than others?

Mace: Yes.

Holdsworth: That sort of thing. That's the differences between individuals.

Mace: That's the kind of thing we do. No, we do a lot of that, because you're looking at variation in behaviour to see what works. Is there a fitness advantage to having a grandmother? You compare children who do have grandmothers and don't have grandmothers, and you see which ones are more likely to die. 0.56.25

Holdsworth: Ah yes, that's a clear example.

Mace: Yes. I mean, we have a slight problem doing human behavioural ecology which the animal behavioural ecologists can obviously do experiments. They can experimentally manipulate things, which we can't do. So you have to look for, as it were, natural experiments. So that question about the grandmothers: if you use a natural population, you can actually look. You know, just by chance half of them will have grandmothers; half of them won't.

Holdsworth: Yes.

Mace: [So you can see] the variation there. Or with the water pump. That was a natural experiment. Some villages had taps put in them; some villages didn't, and we could compare. 0.57.08

Holdsworth: Yes, because it doesn't make sense there - am I [getting this] right? - to say it's a species-typical trait to have a tap in your village. You're examining precisely the differences between the situation where you do have the tap or you don't have a tap.

Mace: Yes. We're getting data from individuals. So I'd say I think we do study individual variation. There's not much you can do by comparison across species, because there's only one species of humans. There are comparisons with other apes. 0.58.02

Holdsworth: But for example, lower down my list I've got 'evolutionary biomechanics'.

Mace: OK.

Holdsworth: So: a species-typical trait for our species is upright bipedal gait.

Mace: Yes. OK. Yes. (*Meditatively repeating the question*:) 'Is the focus on species-typical traits or on individual differences?'

Holdsworth: I mean, neither of these concepts is actually unproblematic. I'm looking at whether it tips one way or the other.

Mace: Yes. My research is on individual differences, because, you know, you're also looking at how people in one ecological setting might behave differently from people in another ecological setting. So, you know, whereas an evolutionary psychologist might be interested in a mental module as a human universal, a behavioural ecologist is kind of interested in positing why some people are doing something different than others. 0.59.08

Holdsworth: I think that's a clincher, actually. Yes.

Criterion 4 (1st part): *'Does the research typically draw on the findings of genomics?'* 0.59.14
[Criterion 5: *'Is the research on genes or other DNA? If 'other': mtDNA or Y-chromosome?'*]

Holdsworth: 'Does the research typically draw on the findings of genomics?'

Mace: I would say no.

Holdsworth: Right. Fair enough. So we can skip the next [criterion].

Mace: I'm not saying that we're not completely uninfluenced by genetic research. It's interesting to know about, but I wouldn't say that we need to - I mean, Darwin didn't even know about genes. 0.59.52

(Note: *Having apparently dealt with Criterion 4 at this point, Criterion 5 was deemed no longer pertinent, and the interview then moved on to a brief consideration of Criteria 6 and 7. However, after that, it returned after that to the themes of Criterion 4 and, indirectly, Criterion 5.*)

Criterion 6: *'Is there research on the DNA of non-human/hominid species? If so, animals or plants?'* 1.00.00

Holdsworth: 'Is there research on the DNA of non-human species?'

Mace: No.

Criterion 7: *'Is there research on other bio-molecules? If so, proteins or other?'* 1.00.13

Holdsworth: 'Is there research on other biomolecules?' No – or is there?

Mace: There doesn't need to be, no. I mean if you talk to an archaeologist. Well, that's different, you see. There you are, you've got biomolecular archaeology on your list.

Criterion 4 (2nd part): *'Does the research typically draw on the findings of genomics?'* 1.00.56

Mace: The other thing that's going on, as I'm sure you're aware, is this. Actually, I'll backtrack slightly. If you're interested in the mating system of some group or other, which is the kind of thing anthropologists and behavioural ecologists are interested in, obviously if we could get everyone's DNA, we would learn an awful lot about their mating system. We would learn, how monogamous are people, how polygynous are they? You know, who wins? Do children tend to be all from the same father, or do they tend to be actually all from different fathers, or what? 1.01.39

Holdsworth: Yes.

Mace: And, of course, the ethical hurdles of doing that kind of research are practically insurmountable. So we would love to have DNA, but basically you're hanging yourself if

you say you're going to do something like that. It's got worse and worse, and you're getting these ethics panels. It's becoming - . I just had a huge grant come down for no reason whatsoever, because I wanted to ask women about their contraceptive history. It's just not something that I've ever had any problem with before. But, you know, ethics panels are esoteric. And f someone on the panel – you know, they have lay members on them - and if someone thought it's not really acceptable to ask Ethiopian women about their contraceptive history there's not much you can do about it. So that was a bit weird. But, you know, people have tried to work out how much paternity uncertainty there is, and things like that. So we could use DNA data to help answer certain questions. On the whole we don't, because that data isn't –. I mean, I think it's crazy. So, for example, it would be possible to take a British sample, and say, OK, the proportion of UK children fathered outside wedlock is *x*. 1.03.08

Holdsworth: Yes.

Mace: [There must be scores of genetic databases that would be able to answer that question tomorrow]. You know, try and get that through an ethics panel : you will have a headache. And it is a little bit ridiculous, I have to say, because I think people are quite interested in that result. Obviously, you have to scrupulously maintain the anonymity of any sample that you use, but at the population level, I don't think that's a controversial question, to be honest. But I think this must be part of your work. In a way, you know, the ethical climate round anything to do with DNA has gone completely bonkers. I mean, in parts of the world it's basically closed down any kind of anthropological genetic research work whatsoever. 1.03.54

Holdsworth: Yes.

Mace: [...] So, [there are things] I would love to know. Like we've done this long-term study in The Gambia; we've done this long-term study in Ethiopia, and I would love to have everyone's DNA and be able to say who's actually related to who. And it would tell me an awful lot about the social system and the mating system and everything else, and everyone's reproductive success, but because I'm dealing with humans I can't do that. I mean, Mark Thomas gets things off humans. He asks questions about population history; he doesn't ask questions about paternity uncertainty, all that kind of thing. 1.04.46

Holdsworth: What sort does he ask, sorry?

Mace: Well, you know, he gets Y-chromosomes and says right, that means that the Vikings did this and that and the other. 1.04.54

Holdsworth: Yes.

Mace: But if you wanted to use it to ask anthropological questions about mating systems and all this sort of stuff, and paternity - . I mean, bird behavioural ecologists use it all the time. They collect DNA from chicks, and they say 'Oh, right, in this pair extra-pair copulation's going on here, and actually the female mated partially with her mate, but she's also got two from the next door, you know, great tits or whatever it is what they're studying,[369] and

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[369] For instance, see: Norris, K.J., and Blakey, J.K. (2008): 'Evidence for cuckoldry in the Great Tit *Parus major*', Ibis, Vol. 131, No. 3, 2008, pp.436 – 442.

they've done tons of studies like that which have told us about mating systems or, you know, polyandrous dunnocks[370] tend to have two partners and one of them is more genetically successful than the other. Now, we can ask people in [surveys] – you get data all the time about who are your children, blah, blah, blah. But you wouldn't be allowed, I think. I mean, I don't know. 1.05.53

Holdsworth: Up to now, as a matter of the history of the discipline, it has not been a part.

Mace: No. Just because - for ethical reasons. But it would be a useful tool, if we could use it. Just because the animal behavioural ecologists have made extensive use of genetics. I mean someone's doing it: some of the evolutionary economists now. You can still do it in behavioural genetics, obviously. And some of the evolutionary economists are now interested in different genes that give you different responses in economic games.[371] But in an anthropological context I just don't think you would ever get – at the moment – you would not get permission to do this. So people don't, and it isn't because they don't want to know. It's because they don't want a stink. An ethics committee sank a huge three-year grant that I should have got. And I wasn't doing anything that was remotely controversial except, you know, DNA! For some reason, DNA was very, very controversial. And you could imagine that if your anonymity was not respected - . 1.07.19

Holdsworth: And you didn't want to collect DNA; you wanted to use databases? 1.07.22

Mace: Oh, well, I mean I would love to know the DNA of everyone in my sample that I've got other data on. I would love to know that, because then I would know – for example, in the grandmothers research, I would really know who was related to who. You know, if I knew that for everybody, that would be a brilliant resource, and it would tell me an awful lot about all the relatedness of everybody in the field. So it would be useful to know it. But we just have to use completely indirect [methods]. So we just say 'This is your aunt; this is your father; this is your grandmother'. OK, that a measure of relatedness, of who's related to who. It would be nice to know if we'd got it right. But I've never asked to check that data, because I know I would never be allowed to. 1.08.07

Holdsworth: That's very interesting. 1.08.11

Mace: Whereas if you are studying – you know, people who are studying animals get that data all the time. Whereas you go to any clinic in London and get a paternity test done one way or another you would be able to do it. But in an anthropological context I don't think anyone is doing it. We'd all love to have that information. But, you know, it's invasive. It's private. So you wouldn't be - . I mean, I would like to use databases that ask general questions like what is the paternity uncertainty in this population. That would be very interesting to use a general database to ask that question. I don't think there's any ethical consideration there, but ethics committees would think would think that there are various [issues]. On an individual level it would also be very interesting to have that data, but it is very personal data that you would never be allowed to collect. 1.09.13

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[370] For instance, see: Burke, T., Davies, N.B.; Bruford, M.W., and Hatchwell, B.J. (1989): 'Parental care and mating behaviour of polyandrous dunnocks *Prunella modularis* related to paternity by DNA fingerprinting', Letter, *Nature* 338, 16 March 1989, pp. 249 – 251.

[371] Citation?

Holdsworth: There was a study recently reported on the radio which showed that a surprising proportion of people in Yorkshire had a black ancestor.[372] And the people who took part in the study had agreed to take part in the study, but they didn't agree to the release of [all] the information. The key information was that it was associated with a particular surname. And they hadn't given permission for the researchers to release the name.

Mace: Well, I think you can see you don't want individuals to be identified from your research, and obviously the surname would be the give-away. So you know, I think you have to maintain the basic principle that you can maintain anonymity, and if you can't then you - it would be very difficult to do the research. 1.10.13

Holdsworth: Yes.

Mace: But this is a bit of a red herring in a way, but if you could do paternity testing, for some questions in human behavioural ecology that would be very interesting, but because it's personal information that they're very unlikely to get, I'm not aware of anyone using that kind of information.

Holdsworth: But to turn it round another way what you're saying is that conceptually the subject is open to the adduction of DNA evidence. 1.10.49

Mace: It's a different kind of [genetic evidence] than before. We're not interested in whether genes can cause behaviour, but because genes can act as a marker of relatedness in a community, then that would be very useful to have. But I'm not aware of any anthropological study that has that data. So someone like Mark Thomas has got DNA from individuals, but he doesn't know the relationship between those individuals. He just knows that, OK, this is an Ethiopian who is living on this plateau here, whose ancestors were also Ethiopians, and therefore this is an Ethiopian Y-chromosome from this region. I mean, he's looking at it at that level, whereas I'm looking at databases of individuals who are reproducing and everything like that. I would love it if someone could tell me, yes, that one's definitely that one's son, and that one's definitely that one's mother, and those two are related at this level. That would be very, very useful information, but we just have to estimate it from what people tell us, which bears a strong relationship to the truth, but it's not the full picture. You know, if we could check it with DNA that would be very useful. It would be a useful tool, but the - . 1.12.06

Holdsworth: I was just going to say – there is a theoretical connection. I mean, you're not operating in a closed environment.

Mace: No.

Holdsworth: The link could be made, conceptually.

Mace: Oh absolutely, yes. No, paternity uncertainty is a very important concept in behavioural ecology. If we could measure it, that would be very nice. 1.12.24

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[372] BBC news report: 'Yorkshire clan linked to Africa', 24 January 2007: http://news.bbc.co.uk/2/hi/science/nature/6293333.stm (Consulted 31 July 2008). The report referred to the following research article: King, Turi; Jobling, Mark, et al. (2007): 'Africans in Yorkshire? The deepest-rooting clade of the Y phylogeny within an English genealogy', *European Journal of Human Genetics*, 1 March 2007, Vol. 15, pp.288 – 293. For an interview with Jobling here, see Annex 00, pp.00-00.

Holdsworth: I suppose also – well, many people certainly bandy about the expression 'the extended family'. There must be contexts where it would be interesting to test that and to find out to what extent, in different places and at different times, the extended family was actually [real].

Mace: Absolutely. 1.12.42

Criterion 8: *'Does the research use environmental markers?'* 1.12.51

Holdsworth: 'Does the research use environmental markers?'

Mace: What's that?

Holdsworth: Yes, in the sense that you would - the whole question of adaptation is in relation to features of the environment. 1.13.05

Mace: I suppose so, yes.

Criterion 9: *'The main concern is phylogeny or ontogeny?'* 1.13.15

Holdsworth: 'The main concern is phylogeny or ontogeny?' I don't know to what extent that is relevant to your research.

Mace: Well those would both be. I would say the *main* concern is adaptive function. But, you know, people are interested in phylogeny, and they are interested in ontogeny. You might have to expand your number of questions! Or, you know, 'Which of the following are people interested in? - Rank them in order', or something like that, because I wouldn't say that - . I mean, some behavioural ecologists are not interested in phylogeny or ontogeny. I happen to be quite interested in phylogeny. But I'm really interested in population history, which is – I mean, I'm interested in cultural phylogeny. 1.14.14

Holdsworth: But if we're talking about ontogeny in terms of what happens within a single generation - .

Mace: Well, I'm certainly interested in the development of behaviour. Phylogeny is evolutionary history. And they're both separate questions from 'What is its function?' - which is what human behavioural ecologists are primarily, mainly concerned with.

Holdsworth: Yes, well it's a bit of each.

Mace: Or neither, really. I would say the main concern was neither of those. The main concern was the adaptive function. You don't need to know the phylogeny or the ontogeny to know that. 1.15.05

Holdsworth: Right. OK. Fair enough. Thank you. That's your reply.

Criterion 12: *'Is the research intended to have a clinical application?'*

Holdsworth: 'Is the research intended to have a clinical application?' 1.15.13

Mace: It's not intended to. I mean, I think it can. You know, there's this kind of branch of evolutionary medicine where people are trying to say that evolutionary principles can [be relevant]. So I wouldn't - . I would say 'no' to that, for the most part. 1.15.33

Holdsworth: I mean that's a question for people in behavioural pharmacogenomics.

Mace: Yes, OK. 1.15.40

Criterion 10: *'Does the research draw on fossil evidence?'*

Holdsworth: 'Does the research draw on fossil evidence?'

Mace: Not very much.

Criterion 11: *'Is Newtonian mechanics relevant to the research?'*

Holdsworth: 'Relevance of Newtonian mechanics?'

Mace: No.

Criterion 13: '*Does the research use cultural markers, e.g., surnames?'*

Holdsworth: And, 'Does the research use cultural markers?'

Mace: Yes. 1.16.04

General and concluding discussion

Holdsworth: Are there any questions you would have liked to have seen on that list?

Mace: Well, I think 'adaptive function' is something on which you could expand.

Holdsworth: 'Adaptive function'. I'll have a think about that.

Mace: I would have thought that evolutionary biomechanics might be interested in the adaptive function of biology. There are other disciplines you can add to your list as well. 1.17.00

Holdsworth: Thank you, yes?

Mace: If you're interested in the behavioural sciences.

Holdsworth: I mean, I started with a list of over fifty

Mace: Oh, you've sharpened down.

Holdsworth: This is supposed to be the interview list. But which did you have in mind?

Mace: Well, no, you might want to talk to an evolutionary psychologist. Well, I think they don't use genes. I mean, they don't use genes any more directly than I do, I guess. 1.17.27

Holdsworth: Anyone else?

Mace: People like Mark Thomas. He's a molecular anthropologist, I would say. There are all these people out at the Max Planck Institute doing all kinds of things on molecular anthropology as well, like, you know, the DNA of Neanderthals. I don't know if you've got those kind of people. ?[373] 1.18.08

Holdsworth: Right. That was very helpful for me. Thank you very much.

Mace: Do read *Sense and Nonsense*. 1.20.01

[373] Mace was referring to Prof. Dr. Svante Pääbo, Director, and other workers at the Department of Genetics, Max Planck Institute for Evolutionary Anthropology, Leipzig. Website: http://email.eva.mpg.de/~paabo/ (Consulted 1 August 2008).

6. Research interview with Professor Peter McGuffin – Edited Excerpts

Interviewed: Professor Peter McGuffin, Professor of Psychiatric Genetics and Dean of the Institute of Psychiatry at the Maudsley, London.
Interviewer: Richard Holdsworth, PhD candidate, Economic and Social Research Council (ESRC) Centre for Genomics in Society, Egenis, University of Exeter.
Date and time of interview: Friday, 16 March 2007, 14.00.
Place: Institute of Psychiatry, London.
Total length of the recording: 51 minutes 28 seconds.

The interviewee's description of the research

Holdsworth: I had put you down, as it were, as a researcher in behavioural genetics, although I might have also put you down as a researcher in psychiatric genetics, I imagine. 0.04.00

McGuffin: Yes.

Holdsworth: So could I begin by just asking you where you position yourself, and to describe a little bit your type of research.

McGuffin: I describe myself as a researcher in normal and abnormal behaviour. Mostly, because I'm a psychiatrist, I'm interested in abnormal behaviour, but I don't think you can actually study one without the other.

Holdsworth: Yes.

McGuffin: So - and I think this is a view commonly held among psychiatrists, not just biological psychiatrists, but most psychiatrists these days – that there's for all practical purposes a continuum between normal and abnormal behaviour. There's not a clear-cut distinction between them. And to some extent the dividing line is a bit arbitrary at times.

Holdsworth: Yes? And does that condition your approach to the genetic dimension of the enquiry? 0.05.02

McGuffin: Yes, yes.

Holdsworth: Could you give me an example of a behaviour that might be called a disorder but which shades off into - .

McGuffin: Yes. A very good example is depression. So there are very few among us who haven't had a day or two of feeling low, but for most people it doesn't interfere much with their lives, and they recover spontaneously. Then there are people at the other end of the spectrum who are absolutely devastated by depression with all the associated symptoms of sleep disturbance, weight-loss and all the rest of it, who have their lives seriously disrupted by it and require treatment – sometimes in-patient treatment. Then in the middle [you've got] people who have depressive symptoms that are sufficiently impairing for them to consult their GP or some other professional, but they don't actually come to the attention of psychiatrists. Well, as I say, while people have attempted to make a clear-cut distinction

between depressive disorder and depressive symptoms and normal low mood, they've been hard-pressed to make any clear-cut distinction, so one seems to shade into the other.

Holdsworth: Right. 0.06.19

McGuffin: So at the extremes it's clear-cut what's completely normal and healthy and what's depressed, but there's a lot of grey area in the middle.

Holdsworth: Yes. I saw a book in the display-cabinet downstairs. I think it said: 'Does schizophrenia exist?' Is that a good question?

McGuffin: Yes, it's a question with lots of shades of meaning, I think, because clearly, descriptively schizophrenia exists, and actually probably causes – well, it used to, anyway, result in more occupancy of hospital beds than any other disorder.

Holdsworth: Right.

McGuffin: But the question is: is it one disorder or is it a grouping of dimensions? The question is, is it – another question arises is: is it absolutely distinct from what are called 'mood disorders'? Or are there some over-lapping phenomena – aetiological factors, for example bipolar disorder? Most of the current evidence is suggesting that yes, indeed, there are over-lapping aetiologies.

Holdsworth: Depression and bipolar disorder you would call 'mood disorders'? 0.07.26

McGuffin: Yes.

Holdsworth: If one takes the expression 'behavioural genetics', at a quick count how many sort of sub-areas of that could one distinguish?

McGuffin: There are two pretty big sub-areas. One is behavioural genetics in the traditional sense that deals with behaviour in a quantitative sort of way. And the main tools are statistics. Then there's behavioural genetics that's much more biological, where the focus is on finding genes and discovering what they do - at the molecular level. So, traditionally, I think behavioural genetics has been very much on the quantitative side. And to some extent that's why there has come up something of a split between people who call themselves 'behavioural geneticists' and people who call themselves 'psychiatric geneticists'. Because psychiatric geneticists by and large tend to be more interested in the hard-core biology, if you like. So there's a society called the International Society of Psychiatric Genetics. And much of the stuff that you'll see presented at meetings is about finding genes, doing functional genomics, looking at the biology of what actually happens when where there's a variation in a particular gene or set of genes. Whereas if you go along to the Behavior Genetics Association's meeting you'll find the people describing structural equations, models and various fancy stats approaches. 0.09.30

Holdsworth: Right. But what about thematic distinctions between people who are studying cognitive ability, the dimensions of personality, or indeed single-gene disorders?

McGuffin: Yes. Well, there are thematic distinctions, you're quite correct. But it depends where you position yourself, or whether you need to position yourself at all. I position myself pretty much across the spectrum, which is why I started off saying I work on normal and

abnormal behaviour. I'm just helping Robert Plomin edit the latest edition of his book. I'm co-editor and have been for the last couple of editions. And that book is called 'Behavioural genetics' and it covers everything. I'm also an editor of another book, called 'Psychiatric genetics', where the focus is very much on disorders, so the scrutiny is on disorders. But we have to have some discussion in there of things like cognitive ability and personality even in a book that deals mainly with disorders, because for reasons I've said I don't think you can have a complete discussion of disorders without a context of the genetics of normal behaviour. 0.11.06

Holdsworth: Right. Quantitative genetics infers the existence of genes from the statistical analysis.

McGuffin: Yes.

Holdsworth: And that's been going on for a good long time.

McGuffin: Yes.

Holdsworth: And precedes even the existence of molecular genetics.

McGuffin: Precedes even the existence of Mendelian genetics. So you could say the first person to systematically attempt to do quantitative genetics was Francis Galton, back in the late eighteen hundreds, 1860s. But of course you could go back further than that, and you could say that physicians – doctors interested in behaviour observed a long, long time ago that what used to be called insanity quite often ran in families. So that was a crude observation, but it was an observation nevertheless. And an important one. And you can even find instances, if you go eight miles down the road to the Bethlehem Royal Hospital, which is one of our associated hospitals, to their museum, you can pick up case-notes from the early 1800s, where there's a section in the front of the case-notes where the admitting doctor had to record of a patient: whether hereditary? There's a little question there: 'Whether hereditary?'

Holdsworth: Oh! Right. And the methods of molecular research – linkage studies and association studies – they precede the full sequencing of the human genome.

McGuffin: Yes. By quite a way, actually.

Holdsworth: What got that started? 0.13.00

McGuffin: What got it started? The first observation of linkage is usually attributed to Morgan, who was a fruit-fly geneticist who spotted that some traits were linked in fruit-flies. Of course, Mendel hadn't seen that, and he formed his Law of Independent Assortment. Morgan and his followers found that that law wasn't always followed, and they made the inference that these traits were linked. Chromosomes were discovered, and the physical basis for linkage in other organisms was discovered. Methods for studying it in human beings were devised. So, one of the earlier methods was that of Lionel Penrose, who was actually a psychiatrist, but probably more famous for being a geneticist who proposed the first sib-pair linkage test. And there were various, well, really likelihood-based methods for

inferring it in humans. And the big breakthrough was Newton Morton's devising the LOD score method in a landmark paper in 1955.[374] 0.14.14

Holdsworth: Right.

McGuffin: Those people got into genetic analysis in a big way with physical traits, looking at – firstly, Mendelian disorders, and then looking at markers like blood-groups – later on, the HLA system. And in my own case, I got interested in the HLA system in the mid-1970s, when I'd just graduated from medical school and was working in cardiology, and everyone was becoming terribly [interested in HLA]. The HLA system is the major histocompatibility system in man.

Holdsworth: Yes.
0.14.54

McGuffin: Now known to be carried on a complex of genes on the short arm of Chromosome 6. We didn't know that in the early 1970s. But anyway it turns out that variants in the HLA system are associated with susceptibility to various common diseases, various types of arthritis, and Type 1 diabetes, and so on. Anyway, to cut a long story short, I got involved in the study of HLA and coronary heart disease, which turned out to be completely negative, but it got me turned on to the idea that you might be able to find genetic markers associated with common traits, so I did a study on schizophrenia, and I thought we'd found something on HLA and schizophrenia. That was an association study. And then was awarded a fellowship by the MRC to do what was one of the first linkage studies in schizophrenia. So I managed to get very good, generous help from a couple of really top labs: Hilliard Festenstein's very good HLA lab at the London Hospital,[375] and then there was a group at the Galton Lab at University College. There was somebody called Peter Cook[376] who ran the marker lab, and these were mainly markers – pre-DNA markers – markers based on electrophoresing proteins, really. How you can, you know, separate out various alleles by just separating the proteins on electrophoretic gels. And similarly, red cell blood types behave in a Mendelian fashion and can be used as genetic markers. So my PhD thesis was based on about 30 different marker types, which was the most you could do in those days. I calculated that you could cover about six per cent of the genome. So my magnificent PhD thesis, excluding a schizophrenia gene, essentially from six per cent of the genome!

Holdsworth: But the completion of the Human Genome Project has had two – at least two beneficial effects from the point of view of this type of research. First of all, there's the existence of the sequencing data itself. And also it's improved the technology. 0.17.37

McGuffin: Yes. Well, the technology really started improving in leaps and bounds from the 1980s onwards. So, first of all, a type of marker called Restriction Fragment Length Polymorphisms were discovered, so that round about the end of the 80s we could really cover almost 100 per cent of the genome for linkage. So, for linkage you only need a few hundred

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[374] Morton, Newton. E (1955): 'Sequential tests for the detection of linkage', *Am J Hum Genet*, 1955, 7:277-318. See also Morton, Newton. E (1995): 'LODs past and present', *Genetics*, 140: 7-12 (May, 1995).
[375] Demant, P. (1989): 'Hilliard Festenstein', *International Journal of Immunogenetics*, Vol. 16, No. 4-5, pp. 255-256, and David, Chella S. (1990): 'In memoriam' [Hilliard Festenstein], *Immunogenetics*, Vol. 31, No. 2, March 1990, pp. 63-64.
[376] Mentioned in Morton (1995), p.8.

markers to cover the genome. Then all the gaps were filled in with the new generation of markers called microsatellites, which mainly consist of dinucleotide repeats. 0.18.15

Holdsworth: When was this?

McGuffin: Well, CA repeats[377] came in in a big way really towards the end of the 80s, early 90s. So, I can't remember the exact date now, but the Généthon from Paris - there's a lab in Paris, Généthon - published their microsatellite-based map in early 1990s.[378] So that really made it possible to, for sure, map any disease as Mendelian - or any non-Mendelian disease, [where there's a genome-large effect].

Holdsworth: And then of course there's been the rise of bioinformatics

McGuffin: Yes. So I was just sketching - what I can just say: even before 2001, which people usually mark as the time (you know, when *Nature*[379]and *Science*[380] published genome sequences and so on, at least partial genome sequences – partially annotated genome sequences – in the same week), so before all that we [had access to] all these other quite important discoveries: RFLPs, microsatellites and all that.
0.19.36

Holdsworth: Right. Could I just ask you, for you – I know you've approached this subject in a short article in *Science* in 2001[381] - you've got a certain conception of what you could mean by 'behavioural genomics' as opposed to 'behavioural genetics' in your own field. Could you just say a word about that? 0.20.02

McGuffin: OK, well I think it's a kind of slippery term really, 'behavioural genomics', but when I use it - or when colleagues I work with like Robert Plomin, on whose last book I am a co-author, use it - I think we're talking about – in addition to doing the traditional bottom-up approach, where you start off with the gene, study its sequence and structure, study the gene products, and then study the possible effects of the gene from that sort-of bottom-up route – you start with a whole organism – it might be man; it might be fruit-fly; it might be a rodent – and you study the behaviour of the organism, and you study the component traits of behaviour, some of which might be models for parts of disease like depression (you can never model depression completely in the animal, but you can model components of it) and then looking further down to then see what genes might be involved, and then see what pathways might be involved. So it's not so you don't do the bottom-up approach, but it's actually taking the whole-organism approach at the same time. And the attraction of taking the whole-organism approach is that you can then, not just study the consequences of

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[377] 'CA repeats': the type of microsatellite comprising dinucleotide repeats of the motif 'CA' . See Brown, T.A. (2007): Genomes 3, Garland Science Publishing, New York and London, p. 218.

[378] Gyapay, Gabor; Morissette, Jean; Vignal, Alain; Dib, Colette; Fizames, Cécile; Millasseau, Philippe; Marc, Sophie; Bernardi, Giorgio; Lathrop, Mark, and Weissenbach, Jean (1994): 'The 1993−94 Généthon human genetic linkage map', Nature Genetics, 7, 1994, 246-339.

[379] Lander, E.S., et al. (2001): 'Initial sequencing and analysis of the human genome', Nature, Vol. 409, pp. 860-921, 15 February 2001.

[380] Venter, J.C. et al. (2001): 'The sequence of the human genome', *Science*, Vol. 291, No. 5507, 1304-1351, 16 February 2001.

[381] McGuffin, Peter; Riley, Brien, and Plomin, Robert (2001): 'Genomics and behavior: Toward behavioral genomics', *Science*, Vol. 291, No. 5507, 16 February 2001, pp. 1232-1249.

anomalies in metabolic pathways, but you can actually study gene-environment interactions. So the centre that I'm still working in, but I was directing until I became Dean here three months ago, was called the MRC Social, Genetic and Developmental Psychiatry Centre, and the whole aim of that is really behavioural genomics. It's to put together social and other environmental factors and genetics in the development of psychiatric disorders. 0.21.56

Holdsworth: It sounds different from the approach, for example – if I've understood it at all correctly – of the Genes to Cognition programme. 0.22.16

McGuffin: Yes, it is different. I mean – I'm on the steering group of the Genes to Cognition programme.[382] It's a very interesting programme. I think they do have some elements of the top-down as well, because they are certainly modelling lots of stuff in animal models. 0.22.31

Holdsworth: Yes.

McGuffin: But it's true that a lot of what they do is looking at, in great detail, at pathways, particularly in their case what goes on at NMDA receptors, and all the complicated stuff that goes on in the post-synaptic density, which is the bit inside the cell that's attached to the NMDA receptor. So yes, I suppose that is a bit more, kind of, bottom-up, because it's setting up pathways and seeing what the consequences are. 0.23.02

Examination of the criteria

Holdsworth: Now, in order to give some structure to my discrimination, if that's the right word, between different research disciplines, I've made a list of criteria which, if I may, I'd like to talk through with you.

McGuffin: OK. 0.23.28

Criterion 1: *'Does the research cover all hominids or only Homo sapiens?'* 0.24.02

Holdsworth: So the first question is: 'Does the research cover all hominids or only *Homo sapiens*?'

McGuffin: Well, my own research doesn't deal with any other hominids.

Holdsworth: No. So that's an easy one. You see, [there] are other disciplines that I'm taking into consideration, where I'm interviewing other researchers.

McGuffin: Right.

Criterion 2: '*Is behaviour studied in the ecological setting – or in the laboratory or clinic?'*

[382] For a description of the Genes to Cognition (G2C) neuroscience research programme, see: http://www.genes2cognition.org/ (Consulted: 24 June 2008).

Holdsworth: And the next one: 'Is behaviour studied in the ecological setting, as opposed to laboratory, clinic, etc.?'

McGuffin: Well, it is to some extent. So that a lot of my research has been, for example, looking at naturally occurring hazards, such as unpleasant life-events, and how they impinge upon people to make them depressed or not, and the extent to which those sort of naturally-occurring hazards interact, or co-act with genetic predisposition. So in that sense, if you call it 'ecological', yes, I think it is. 0.25.19

Holdsworth: It is. Yes. But it's also studied in the laboratory –

McGuffin: And the clinic. Yes. 0.25.35

Criterion 3: *'Is the focus on species-typical traits or on individual differences?'*

Holdsworth: Now, behavioural genetics is sometimes spoken of as the study of individual differences.

McGuffin: Mm.

Holdsworth: So hence the next question: 'Is the focus on species-typical traits or on individual differences?'

McGuffin: Yes, my own research is very much on individual differences.

Holdsworth: I was just wondering, when I was reading the chapter on the G2C programme in the fat book you co-edited on *Behavioural genetics in the post-genomic era*,[383] whether there was a distinction there, and that type of research is really looking at the genetic – if you like - infrastructure of everybody. 0.26.29

McGuffin: I suppose it is, yes. But the only research I've personally been involved with that's to do with cognition *has* been to do with individual differences: so, for example, [a study with] Robert Plomin on ways of looking at what genetic differences there may be between individuals who are one extreme on the distribution of IQ with individuals who are slap-bang in the middle range or sometimes individuals who are at the low end. So that's an example of where the individual difference approach is. 0.27.06

Holdsworth: It's a point that interests me: obviously, there's a lot of research effort going into individual differences in IQ.

McGuffin: Mm.

Holdsworth: Or 'g', as one might call it. What about research into intelligence as something that the whole species has? 0.27.34

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[383] Plomin, Robert; DeFries, John C.; Craig, Ian W., and McGuffin, Peter (2003): Behavioral genetics in the postgenomic era, Washington, 2003, pp. 123-138, Chapter 8 by Grant, Seth G.N.: 'An integrative neuroscience program linking mouse genes to cognition and disease'.

McGuffin: It would require a different type of experiment! Ha, ha.

Holdsworth: Ha, ha. But can you think of any research discipline that's doing it?

McGuffin: Well, yes, there are – there are geneticists who are interested in differences between genomes, and quite a lot of bioinformatics experts who are interested in differences between genomes, and you could argue that that's how you might find the genes – quote – 'for' speech and human-style cognition. By comparing humans with –

Holdsworth: Chimpanzees.

McGuffin: Yes, chimpanzees.

Holdsworth: But the names of any particular researchers don't occur to you?

McGuffin: No, it's not really my area.[384]
0.28.30

Criterion 4: *'Does the research typically draw on the findings of genomics?'*

Holdsworth: 'Does the research typically draw on the findings of genomics?'

McGuffin: Yes.

Criterion 5: *'Is the research on genes or other DNA? If 'other': mtDNA or Y-chromosome?'*

Holdsworth: And here we move on to the next question: Does that mean human nuclear genes?

McGuffin: Yes.

Holdsworth: In some other disciplines, it might mean mitochondrial DNA.

McGuffin: Yes, well, we have done some work on mitochondrial DNA. 0.29.00

Holdsworth: In what connection?

McGuffin: Well, just looking at mitochondrial DNA in schizophrenics compared with controls. So in one of our early linkage studies - actually, not the very early one, but one in the 1990s - we had quite a lot of what appeared to be maternal transmission. There are lots of explanations of maternal transmission other than mitochondrial DNA, but it did make some mitochondrial DNA experts interested in what we were doing. And it also made us interested in it, too. Yes, essentially we looked at the mitochondrial DNA of schizophrenics, and we found actually differences compared with controls. We haven't

[384] A survey article that argues for the potential importance of animal models in the study of human cognition, concentrating on mouse and *Drosophila melanogaster*, is Morley, Katherine I., and Montgomery, Grant W. (2001): 'The genetics of cognitive processes: candidate genes in humans and animals', *Behavior Genetics*, Vol. 31, No. 6, November 2001, pp. 511-531. This article was published in the special issue of *BG* mentioned here in footnote 21 below.

followed that up because he differences weren't all that striking, but the findings are still there and need to be looked at again by someone.[385]
0.30.01

Holdsworth: Right. That's interesting. The question is here because for some of these other disciplines, like biomolecular archaeology, it's a question of tracing patterns of migration and human settlement, and using the Y-chromosome.

McGuffin: Sure. And, yes, using the Y-chromosome. I've not done any Y-chromosome stuff. 0.30.25

Criterion 6: '*Is there research on the DNA of non-human/hominid species? If so, animals or plants?*'

Holdsworth: 'Is there research on the DNA of non-human species?'

McGuffin: Yes, there is. Yes.

Holdsworth: Mice, for example?

McGuffin: Mice. Mainly mice in our centre, but we collaborate with other groups who use rats. 0.30.48

Criterion 7: *'Is there research on other biomolecules? If so, proteins or other?'*

Holdsworth: 'Is there research on other biomolecules?'

McGuffin: Yes, particularly in recent areas, we've got into pharmacogenetics. And we have a big pharmacogenetics study on the go, looking at the effects of anti-depressants. And so we're working with proteomics experts. 0.31.20

Holdsworth: And other biomolecules?

McGuffin: No, not really, no. That's mainly it: proteins. 0.31.33

Criterion 8: *'Does the research use environmental markers?'*

Holdsworth: 'Does the research use environmental markers?'

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[385] Marchbanks, R.M.; Ryan, Margaret; Day, I.N.M.; Owen, M.; McGuffin, P., and Whatley, S.A. (2003): 'A mitochondrial DNA sequence variant associated with schizophrenia and oxidative stress', *Schizophrenia Research*, Vol. 65, No. 1, 2003, pp.33-38. This article is cited in, among others, Bandelt, Hans-Jürgen; Yao, Yong-Gang, and Kivisild, Toomas (2005): 'Mitochondrial genes and schizophrenia', *Schizophrenia Research*, Vol. 72, Nos. 2-3, January 2005, pp.267-269.

McGuffin: Yes, very much. Depends what you mean by 'markers'. Certainly uses environmental measures.

Holdsworth: Could you give me an example?

McGuffin: Well, I mentioned earlier life events and depression, but we also have an interest in early childhood trauma. And we have an interest in physical environmental measures, like smoking in pregnancy.

Holdsworth: Dietary questions?

McGuffin: Dietary, yes, we haven't – at least, I haven't done much about diet, but I have done a little bit. And certainly when I was starting out and had my interest in HLA, one can make a nice story about food allergy and mental illness. In fact, all - everything I did on that turned out to be negative.

Holdsworth: Right.

McGuffin: I was quite interested at one stage in looking at food antibodies in schizophrenia. There's [another] story linking – associating, rather, schizophrenia with coeliac disease, which is a disorder where you get – essentially - atrophy of the gut's lining, and it seems to be related to allergy to certain foods, particularly foods that contain gluten. People with coeliac disease make antibodies against gluten. So I did a study looking at antibodies against gluten and its effects, and we didn't find any!

Holdsworth: Right. What about things like housing conditions?

McGuffin: Yes, OK. I suppose that's back to ecological measures again. Yes, certainly: housing conditions, deprivation, living in an area where most people don't have a car. We certainly use those types of measures. And there's no doubt they have a small but significant effect in some behaviours - particularly anti-social behaviours. 0.34.00

Holdsworth: Really?

McGuffin: Well, by 'effect' I mean there's an association.

Holdsworth: OK, can you give me an example?

McGuffin: Oh, yes. I supervised an MSc when I was in Cardiff looking at ecological indices of deprivation.[386] These are things like the Jarman Index and the Townsend index which are based on things like measures of where you live, how many people have a car, how many people are unemployed and that sort of stuff. So there are interesting indices that people have made: public health doctors and GPs. And the study showed there was a substantial influence of those measures on behaviour, particularly anti-social types of measures, conduct disorders and so on. Subsequently, I later supervised a PhD thesis on anti-social behaviours in children and adolescents, where we found much the same thing: that measures of deprivation have a small but significant effect that you couldn't throw out of

[386] Koppel, Siân and McGuffin, Peter (1999): 'Socio-economic factors that predict psychiatric admissions at a local level', *Psychological Medicine*, Vol. 29, No. 5, September 1999, pp. 1235-1241.

your model when you're trying to explain individual differences in the severity of a disorder.[387] 0.35.28

Holdsworth: Right. And what about the workplace environment? Has that been taken into account? 0.35.34

McGuffin: It hasn't been taken into account much in my own research except in a very broad way: so, for example, looking at socio-economic status. No. So that's not looking at workplace environment as such, but it's actually looking at, you know, where people come in socio-economic bands. Which we actually found, in adults with depression, despite what some other people have found, didn't have any influence. 0.36.03

Holdsworth: Right. Interaction with technology?

McGuffin: Let me think. Don't think I've done anything on that. 0.36.15

Criterion 9: *'The main concern is phylogeny or ontogeny?'*

Holdsworth: Is the main concern phylogeny or ontogeny?

McGuffin: Ha, ha! Ontogeny.

Criterion 12:[388] *'Is the research intended to have a clinical application?'*

Holdsworth: 'Is the research intended to have a clinical application?'

McGuffin: Yes, it's - it's intended to have a clinical relevance, if not an application. So, an application - application is difficult. There are some people who view the sort of research I do as terribly applied, but those are people who do extraordinarily basic research on molecules or organisms or, you know, cells in vitro and nothing else. My more clinical colleagues regard me as a basic scientist, so I've got stuck in the middle. Well, yes, of course, most of my research has been funded by the Medical Research Council, so it has medical, clinical applicability in the broader sense. 0.37.24

Criterion 10: *'Does the research draw on fossil evidence?'*

Holdsworth: Right. Here's a good one. I've blocked this in as 'No' already. 'Does the research draw on fossil evidence?'

McGuffin: No.

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[387] Thapar, Anita and McGuffin, Peter (1996): 'A Twin Study of Antisocial and Neurotic Symptoms in Childhood', *Psychological Medicine*, Vol. 26, No. 6, November 1996, pp. 1111-1118.

[388] The numbering of the Criteria has been held constant across the whole series of interviews for convenience of reference, although the order in which they were taken sometimes varied, as here.

Holdsworth: Of course, it's applicable in other cases.

McGuffin: Yes.

Criterion 11: *'Is Newtonian mechanics relevant to the research?'*

Holdsworth: And similarly this question: 'The relevance of Newtonian mechanics?'

McGuffin: Oh, that's everywhere. But not particularly, no.

Holdsworth: Interesting question when you're discussing evolutionary biomechanics.

McGuffin: Yes. 0.38.01

Holdsworth: And upright bipedal gait and so on.

Criterion 13: *'Does the research use cultural markers, e.g., surnames?'*

Holdsworth: And the last question in the list: 'Does the research use cultural markers?'

McGuffin: Hm. Maybe you could give me an example of what you mean by a cultural marker?

Holdsworth: Well, in anthropology it would be things like certain types of ritual or ceremony.

McGuffin: Well, in that case, no. 0.38.45

General and concluding discussion

Holdsworth: Thank you. Can you think of any questions I didn't ask on this list?

McGuffin: No. Pretty comprehensive. 0.39.03

Holdsworth: In something that Plomin wrote, he said that

> Despite the slow progress to date in finding genes associated with general cognitive ability, as well as other complex traits, I am confident that the pace of QTL discovery will pick up as the Human Genome Project continues to shower the field with new information and technologies.[389]

Would you share this confidence?

McGuffin: Yes, absolutely. The pace of change and development in technology is absolutely breath-taking. So, we're just about to embark on a study of depression using the new Affymetrix 500k chip, which has dropped in price dramatically. So you can look at 500,000

[389] Plomin, DeFries, Craig and McGuffin (2003), p.196.

SNPs in one, you know, in one experiment quite quickly, and they've just brought out a million k chip – a million chip, a million-SNP chip - 1,000k, and I think it's not going to be too long before we can see pretty rapid whole-genome sequencing, you know, being feasible and affordable on a large-scale. So I think that we're going to discover [less] of those genes that have a small effect on behaviour. You know, at the moment the level of resolution with linkage is pretty poor: you can only pick up genes with comparatively big effects. It's much better with association, particularly if you've got a very [large] grid of markers, but with the ability to sequence whole genomes affordably, I think you'll be able to detect more of the genes effectively.[390]
0.41.19

Holdsworth: That's quite a confident prediction.

McGuffin: Yes! Well, I'm not saying when! But - well, ten years ago I was confidently saying we'll soon be able to do whole-genome scans in association, and lots of people said that was nonsense. Lots of people say they agreed with me, because I wasn't the only one saying it by any means! And now you can. 0.41.55

Holdsworth: Is a QTL a purely inferred entity?

McGuffin: Their existence is inferred, but, I mean, you can measure effects of QTLs on quantitative traits, quite literally. There are lots of examples of - .

Holdsworth: Yes, could you give me an example? 0.42.20

McGuffin: OK. Well, the earliest examples were on the tomato. That was probably one of the first breakthroughs in QTL mapping. So, you know, there are various quantitative things you can measure in a tomato, from its size to its redness to its *pH*, and there's been quite good success in finding QTLs. Interestingly, in plant genetics, what tends to happen is that there appear to be a few QTLs with quite big effects, and then a larger number of QTLs with smaller effects, and so on. And probably the same thing will turn out with most human traits, which is - . 0.43.06

Holdsworth: But is a QTL a complex of genes?[391]

McGuffin: No, the concept of a QTL is a gene that – it's a single gene that has a small but measurable effect on a quantitative trait.

Holdsworth: Right. And in the behavioural genetics literature I came across a paper which said that there ought to be, but at the time there wasn't, more interaction between the discipline of behavioural genetics and cognitive neuroscience.[392] Was that a fair comment?

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[390] See Plomin, Robert; Hill, Linzy; Craig, Ian W.; McGuffin, Peter; Purcell, Shaun; Sham, Pak; Lubinski, David; Thompson, Lee A.; Fisher, Paul J.; Turic, Dragana, and Owen, Michael J. (2001): 'A genome-wide scan of 1842 DNA markers for allelic associations with general cognitive ability: a five-stage design using DNA pooling and extreme selected groups', *Behavior Genetics*, Vol. 31, No. 6, November 2001, pp. 497-509. This article was published in the special issue of *BG* mentioned here in footnote 21 below.

[391] Clark, William R., and Grunstein, Michael (2000): Are we hardwired? – The role of genes in human behaviour, OUP, Oxford, 2000, refers (p.257) to "behaviour-associated gene complexes (QTL)".

[392] "As yet an unfortunate gap exists between behavior genetics and cognitive neuroscience. Behavior genetics, through its sophisticated statistical modelling in twin and family studies, focuses mainly on

McGuffin: I suppose it is. The trouble is that what we need in genetics a lot of the time is accurate and repeatable information on a very large number of subjects, and the sorts of things that turn on cognitive neuroscience experts are doing small, precise studies on, you know, groups of individuals. 0.44.25

Holdsworth: Yes.

McGuffin: And very often cognitive neuroscientists are more interested in species-typical behaviours rather than individual differences.

Holdsworth: Right. Because they want to find out, for example, a place in the cortex which is doing a particular information-processing task.

McGuffin: Yes.

Holdsworth: For all of us.

McGuffin: Yes. For all of us.

Holdsworth: So that wouldn't be helpful? 0.44.51

McGuffin: Well, it would be. I mean, we have people who work in the MRC SGDP[393] Centre who are normally speaking – could be classed as cognitive neuroscientists - people like Francesca Happé.[394] Now, she's interested in individual differences in traits that may be associated with the autism spectrum. Her [work is involved in] putting forward theories such as 'weak central coherence'.[395] 'Weak central coherence', I understand, is when individuals are very good at having an eye for detail, and attention for detail, but aren't particularly good at seeing the overall big picture, which is said to characterise people within the autism spectrum, because often they're very, very good at, you know, proof-reading, for example, but not very good at extracting the overall meaning of the paragraph that they've just proof-read. You can treat that as a quantitative trait. And you could do twin-studies on it, as she and Robert Plomin are doing.[396] Or map the genes, if you're confident that [that place is helpful]. 0.46.29

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individual differences in cognitive ability. Cognitive neuroscience tends to focus on species universals in specific cognitive operations, isolated by clever experimental design, and located in the time and (brain)space by modern imaging techniques. Both parties could gain from a complementary approach." de Geus, Eco J.C.; Wright, Margaret J. Wright; Martin, Nicholas G., and Boomsma, Dorret I. (2001): 'Genetics of brain function and cognition', Editorial, *Behavior Genetics*, Vol. 31, No. 6, November 2001, p. 493. This editorial introduced an issue of *Behavior Genetics* devoted to studies on the genetics of cognition.

[393] Social, Genetic and Developmental Psychiatry Centre.

[394] Dr Francesca G. Happé, Reader in Cognitive Neuroscience.

[395] Booth, R., Charlton, R., Hughes, C. & Happé, F. (2003) Disentangling weak coherence and executive dysfunction: Planning drawing in Autism and ADHD. Philosophical Transactions of the Royal Society (Special Issue: 'Autism: Mind and Brain'), 358 (1430), 387-392.

[396] See, for instance, Happé, Francesca; Ronald, Angelica, and Plomin, Robert (2006): 'Time to give up on a single explanation for autism', *Nature Neuroscience*, Vol.9, No.10., October 2006, pp.1218-1220, and Ronald, Angelica; Happé, Francesca, and Plomin, Robert (2006): 'The genetic relationship between individual differences in social and nonsocial behaviours characteristic of autism', *Developmental Science*, Vol.8, No.5, 2005, pp.444-458.

Holdsworth: Right. Well, from the point of view of people who are interested in the philosophy of mind, an interesting feature, obviously, of cognitive neuroscience is that it's putting things on a material footing, and that seems to open the door to a form of genetic analysis.

McGuffin: Yes.

Holdsworth: Going back to QTLs, could you explain a phrase that I've come across in the literature that I didn't quite understand: 'breaking the 1% QTL barrier'.[397] 0.47.03

McGuffin: Ah, this is one of Robert's, yes, the idea being that many of the QTLs that exist may contribute a very small amount of variance, and if it's as little as 1% it may be very, very difficult to detect, because you might have enormous fluctuation round it or very dense groups of markers, or both.

Holdsworth: So, what's the way out of this?

McGuffin: Well, you know, it's having your million-SNP chip or, better still, sequencing the entire genome of lots of individuals. 0.47.46

Holdsworth: Right. Well, thank you, we've gone through the questions I wanted to put to you. If I could just come back to this question of – can be tedious, but – the question of nomenclature. Do you think one ought to be strict in one's rules for using the expression 'behavioural genomics', and do you have a strong view on the subject? 0.48.16

McGuffin: Well, although I and my colleagues – particularly Robert Plomin – probably use the term more than anyone else, and we use it in what we think is a fairly restrictive way, we don't have a copyright on it. Ha, ha!

Holdsworth: Ha, ha! No, but as I said, my practice in my research has been to use it in a very - in a deliberately as broad as possible a way.

McGuffin: Mm, mm.

Holdsworth: Do you quarrel with that?

McGuffin: Well, I won't get very hot under the collar about it!

Holdsworth: But you don't think any crucial issues are involved? 0.49.03

McGuffin: No, I mean we've defined it in that particular way, with the emphasis on the top-down meeting the bottom-up, but one could use it in a much more general sense.

Holdsworth: Right. Well, thank you very much.

McGuffin: Good. And good luck with your research.

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[397] For instance, Plomin, DeFries, Craig and McGuffin (2003), p.196, and Craig, I., and Plomin, R. (2006): 'Quantitative trait loci for IQ and other complex traits: single-nucleotide polymorphism genotyping using pooled DNA and microarrays', *Genes, Brain and Behavior*, 2006, 5 (Suppl. 1), pp.32–37.

Holdsworth: Thank you. [...] But as you can imagine it is both fascinating and bewildering.

McGuffin: Yes.

Holdsworth: The variety of information!

McGuffin: There's a lot of jargon to get hold of – get your head around. Not just behavioural genomics, but all the other terminology.

Holdsworth: One of the interesting things is the name of a discipline. The rules for naming disciplines – they're not laid down anywhere. It can be the name of an approach, or a name that somebody once put up on a brass plate. [...]

McGuffin: Well, it's sometimes interesting being studied! The problem is, someone wrote a paper on the use of metaphor in behavioural genetics, and they took lots of examples from a paper of mine, and I regret I'd never thought about it actually – I'd been using lots of metaphors![398] [...]

0.51.04

[398] Nordgren, A. (2003): 'Metaphors in behavioral genetics', *Theoretical Medicine*, Vol. 24, 2003, pp. 59–77.

7. Research interview with Professor Mark Jobling – Edited Excerpts

Interviewed: Professor Mark A. Jobling, Wellcome Trust Senior Research Fellow in Basic Biomedical Science, Professor of Genetics, Department of Genetics, University of Leicester.
Interviewer: Richard Holdsworth, PhD candidate, Economic and Social Research Council (ESRC) Centre for Genomics in Society, Egenis, University of Exeter.
Date and time of interview: Monday, 4 June 2007, 14.00.
Place: Department of Genetics, Adrian Building, University of Leicester, Leicester.
Total length of the recording: 1 hour 11 minutes 41 seconds.

0.00.16

Holdsworth: (*Showing Jobling his copy of* Human Evolutionary Genetics.[399]). The reason I particularly wanted to see you: such an interesting and invaluable tool.

Jobling: But I only wrote a third of it. (*Laughter.*) So I'll do my best. 0.00.42

[...]

0.01.15

Holdsworth: The book is called *Human Evolutionary Genetics*. The first thing I wanted to ask you was whether that was just an appropriate title for a book, or whether you consider that to be the name of a subject.

Jobling: Well, it certainly is an appropriate title for a book, and it mirrors the title of another book, called 'Human Molecular Genetics'. Do I think it's a subject? Well, it seems to be sort of becoming a subject in that you now see advertisements for, you know, a 'post-doc in human evolutionary genetics', which you didn't use to see. So I think it's pretty much becoming a subject, I would say. It's distinct from human genetics in general because of its evolutionary perspective. In a sense I take the Dobzhansky view that nothing in biology makes sense without evolution. And so it seems to me that evolution – an evolutionary aspect – is a given of any biological subject, so it seems almost unnecessary to have the 'evolutionary' bit in the title in a way, but operationally it really is becoming a subject, I think. 0.02.39

Holdsworth: And from the way you're talking, you'd like it to be. You think it's a good idea.

Jobling: Yes, I do think it's a good idea, yes, because much of human genetics is extremely medically focused on specific issues – sometimes extremely rare diseases, which are of course interesting, but I think that in order to understand diseases, for example, you need to have an evolutionary perspective. It's the frequencies of alleles that determine susceptibility to disease. And resistance to disease has an evolutionary framework behind it of population history and selection. 0.03.16

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[399] Jobling, Mark A.; Hurles, Matthew, and Tyler-Smith, Chris (2004): Human evolutionary genetics – origins, peoples and disease, Abingdon, 2004.

The interviewee's description of the research 0.06.54

Holdsworth: Good. Well, could we just go back to the idea of a discipline of human evolutionary genetics, and could you describe for me how you see it? 0.07.11

Jobling: Well, in part it has to do with our history as a species, how we came to be – how the human species, however you define it, came to be - anatomically and behaviourally modern humans, and how we are related to other species - in particular the great apes, who are reasonably close in relation to us, and how we differ from them. And then it has to do with how our species came to be distributed around the world, and what the differences in genetic diversity are, if any, between us – between different populations. And it has to do with the genetic explanations for phenotypic differences. There clearly seem to be differences – differences in appearance, in particular in susceptibility to disease - between different populations. And then it has to do with the distribution of disease alleles within the population: diseases themselves, and what the evolutionary explanation for those disease distributions is. And within that there are various issues like the issue of population admixture: you know, there have been populations that have been separated for a thousand generations essentially that are now coming back together again; how one can recognise that moment and what its implications are. And again, within that, the consideration of the impact of various changes in human behaviour and lifestyle which have occurred in the past – a good example is the agricultural revolution, which clearly has had an enormous impact on us as a species, the census size of our species, the diseases to which we have been exposed, the distribution of alleles that are associated with cultural changes. And then I would take it right up to issues that would affect individuals. 0.09.26

Holdsworth: Yes?

Jobling: So, for example, if you are arrested by the police in this country for almost anything you have a DNA sample taken from you whether you like it or not, and you go into a database. So there is an evolutionary context to that: to understand the distribution of the alleles present within donors' DNA profiles that the police have obtained and how they differ between populations and sub-populations. So I would take it seriously as a subject, and I think that's why it's interesting to teach to undergraduates. It goes right from the origins of our own species or even the divergence with chimps, and the chimp-human common ancestor, right up to issues that are very current and have social implications [of their own]. 0.10.18

Holdsworth: Right. And, briefly, what are some of the key methods of human evolutionary genetics? 0.10.30

Jobling: Well, the raw material, if you like, is DNA diversity. So you need to be able to tell the difference between different individuals at the DNA level. You need to be able to sample individuals and to define groups of individuals that you might call populations, and then you need to be able to analyse their DNA and detect differences and then interpret those differences. And to interpret those differences the methodology is the statistical methods of inference that you can use. 0.11.04

Holdsworth: Yes.

Jobling: From comparing one group of people to another group of people at DNA level you can say something about the relationship between them in a meaningful way. So essentially you've got DNA technology. You have sampling, DNA technology and then statistical methodologies to say what the differences you see actually mean. There also some more medically important issues like phenotypic testing. If you're interested in disease alleles, you need to know when someone has a disease and when they don't. That can be surprisingly difficult to know when you come to think about complex diseases. And it can be surprisingly difficult because of heterogeneity – in other words, you get the same manifestation with maybe not the same [genetic basis]. 0.12.00

Holdsworth: The evolutionary perspective really draws the boundary, in the sense that clinically-orientated research in medical genetics doesn't have this evolutionary focus.

Jobling: No, but some people think that it should, particularly a guy called Randolph Nesse, who founded the field of evolutionary medicine as he calls it, and he's a medic – a proper medic – but he strongly believes that evolutionary thinking should be part of medical school training for people.[400] So taking an evolutionary perspective to medicine in general he believes is essential for fully developing a someone who's training to be a doctor.0.12.49

Holdsworth: Yes. Do you agree with that?

Jobling: Well, yes, I tend to agree with it. I don't know whether - he is a bit of a voice in the wilderness, I think, because medical students are too busy memorising all the bones in the hand to worry too much about evolution. 0.13.10

Examination of the criteria 0.13.31

Holdsworth: Thank you. (*Holdsworth draws Jobling's attention to the sheet of paper displaying the Criterion Matrix*). Could we perhaps have a look at this schema of criteria, because some of the general issues will come up as we go through it? 0.13.42

Criterion 1: '*Does the research cover all hominids or only Homo sapiens?'* 0.14.53

Holdsworth: 'Does the research cover all hominids or only *Homo sapiens*?'

Jobling: Well, human evolutionary genetics covers other hominids – lots of hominids.

Holdsworth: Yes. Are there boundaries? We're going to come on to other species later in the interview. 0.15.14

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[400] Professor Randolph M. Nesse, M.D, The University of Michigan, at http://www-personal.umich.edu/~nesse/ (Consulted 11 August 2008). See Nesse, Randolph M., and Williams, George C. (1998): 'Evolution and the origins of disease', *Scientific American*, November 1998, pp.86-93. Ness and Williams were the authors of *Why We Get Sick: The New Science of Darwinian Medicine*, 1994. See also (1) Trevathan, Wenda R; Smith, E.O., and McKenna, James, eds. (2007): *Evolutionary medicine and health – new perspectives*, OUP, New York, 2007, and (2) Stearns, Stephen C., and Koella, Jacob C., ed. (2008) *Evolution in Health and Disease*, OUP, New York, 2nd edition, 2008. For Stearns as a leading author in the field of life-history theory, see the interview here with Ruth Mace, above.

Jobling: Are there boundaries within human evolutionary genetics? Not really, because I mean the taxonomy of hominids is always controversial and frequently changing. So I don't think you can rule any hominids out of human evolutionary genetics. Most of them are under debate. There's still a question mark over whether Neanderthal contributed genes to our gene pool of modern *sapiens*. And I think you can't rule out any other hominids, and they're all of interest.

Holdsworth: How should we characterise the distinction between 'hominid' and 'hominin'?

Jobling: I can't remember. You can refer to our glossary item on the subject, which may even be wrong. I mean, it's quite difficult actually to pin down even quite reputable biological anthropologists on such things. Put me down as uncertain.

Criterion 2: *'Is behaviour studied in the ecological setting – or in the laboratory or clinic?'* 0.16.18

Holdsworth: The next question: in this discipline, 'Is behaviour studied in the ecological setting?' 0.16.22

Jobling: So you mean people in their own environments, as opposed to DNA in laboratories?

Holdsworth: Or behavioural testing in laboratories.

Jobling: Well, almost exclusively it's DNA analysis in laboratories, but there is a clinical aspect. So, for example, in lactose persistence, ideally people will be tested for lactose persistence in a direct way, but often that's not the case. I'd say, more often than not, behaviour was not studied in the ecological setting. 0.17.04

Holdsworth: And yet it's designed to elucidate behaviour in the environment.

Jobling: Well, it depends what you mean by 'behaviour', doesn't it? I mean, clearly, if you're interested in, for example, whether microcephalin haplotypes affect IQ, then you need to ask certain questions. There's a gene called microcephalin, and a certain haplotype comes with high frequency in some populations relatively recently.[401] It's expressed in the brain, and if you knock out the gene you get a small brain. But quite what it does normally we don't know. It spread very fast, very recently. And it's brain-expressed, so people were interested in whether it had some influence, and if carrying that haplotype made a difference to some easily measurable aspects of behaviour, and so they did an IQ test, and it doesn't. So there are those kinds of things. It's difficult. I can come up with more examples. Skin colour, for example. 0.18.11

Holdsworth: Skin colour?

Jobling: Yes. Pigmentation studies do measure skin colour. [You can't do it without.] If you are saying behavioural – behaviourally related research within human evolutionary genetics,

[401] For an account, inter alia, of the controversy that has surrounded some aspects of microcephalin research, see the article in Wikipedia, 'Microcephalin': http://en.wikipedia.org/wiki/Microcephalin (Consulted 12 August 2008). For an example of the literature, see: Evans, Patrick D.; Anderson, Jeffrey R.; Vallender, Eric J.; Choi, Sun Shim, and Lahn, Bruce T. (2004): 'Reconstructing the evolutionary history of *microcephalin*, a gene controlling human brain size', *Human Molecular Genetics*, Vol.13, No 11, 2004, pp.1139-1145.

then, yes, there is an ecological [aspect]. It depends again whether you mean something like an IQ test, or a skin-reflectance test. Does that count as an ecological setting or is it just the laboratory? 0.18.46

Holdsworth: It's interesting what you're saying, because, looking at your book and other literature, one thinks about the accounts that are now given of prehistoric migrations, for example. You've already mentioned the investigation of the Neolithic revolution. All these things seem to be very closely concerned with the ecological setting of the humans concerned. 0.19.21

Jobling: They are, but we're interested there, in the case of the Neolithic revolution, in a past ecology. We can't revisit the times of the Palaeolithic[402] and say what was the ecological setting at the time. So it's inferred from modern populations. So that's, in a sense, the problem with the subject: that you need to sample modern populations and infer something about the past. That process of inference is controversial and difficult. It doesn't matter whether you are a farmer now, or a City worker, or a lay-about or whatever you might be, to what your ancestors were doing ten thousand years ago. So we just sample, in a sense, in a behavioural, ignorant way: we just take people and then we classify them in some way - [I suppose, Romanians or Basques] or something like that, which again has its problems - and then we try and infer something about people who lived in the past from the DNA that their modern descendants carry. 0.20.37

Holdsworth: There's also contemporary evidence in the soil or in food residues.

Jobling: Yes, yes. There is.

Holdsworth: That seems to me to imply an ecological setting.

Jobling: That's archaeology, though, isn't it? And, I mean, I think archaeology helps people who study human evolutionary genetics, but it can't be said to be part of human evolutionary genetics. It's another discipline that illuminates the question that we all might be interested in, whether we are archaeologists or prehistorians or linguists or whatever, so that you can make some kind of synthesis based on this, but I think nonetheless they are different things. So if you look at the human evolutionary genetics 'thing', that's about inheritance, really. It's about inheritance in a certain way. So it's a, you know, slightly odd word to see there: an 'ecological' setting. 0.21.45

Holdsworth: That's interesting.

Jobling: I'm not an anthropologist, and some anthropologists talk about ecology a lot, and some of them don't seem to be very interested. So there seems to be a school that sees ecology as being something to do with non-human species. Humans are somehow set aside. But there are anthropologists who see humans as very much in an ecological setting. There's a journal called *Molecular Ecology*, and that's an interesting journal because it never, never, never has any articles about human beings: always about pine trees or starfish or beetles or anything else but humans, as if humans are somehow apart - they don't have anything that could be called 'molecular ecology'. 0.22.37

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[402] Clarification sought.

Criterion 3: *'Is the focus on species-typical traits or on individual differences?'* 0.22.40

Holdsworth: Well, let's see how far we get with the next one: 'Is the focus on species-typical traits or on individual differences?' Does the question make sense in this context? 0.22.51

Jobling: It does make sense, and I would say definitely both. Because we are both interested in what makes humans different from, for example, chimpanzees, and we are very much interested in what makes one human or one human population different in some respects from others. 0.23.10

Holdsworth: And what makes one individual different.

Jobling: What makes one individual different.

Holdsworth: That's species, population and individual. 0.23.23

Jobling: Yes.

Holdsworth: Do you find it comfortable to deal with the idea of 'species-typical' traits?

Jobling: Yes, I think so.

Holdsworth: Off the top of your head, could you think of some examples which fit in?

Jobling: Of human species-typical traits? Well, capacity for a complex language. 0.24.03

Holdsworth: Yes. Bipedal locomotion?

Jobling: Yes, though I suppose birds do that. Depends how tightly you want to draw your kind of region of comparison. Yes, quite a lot of things.

Holdsworth: But one of the questions which isn't on the list but I wanted to ask you is - you've mentioned already behaviour. Earlier in the conversation you said 'anatomically modern humans', 'behaviourally modern humans'. Is that the same thing? 0.25.03

Jobling: No, not at all. And, I mean, it's, again, not a subject for geneticists, in a sense. It's a subject for palaeontologists. Because it's clear that you see evidence of anatomical modernity earlier than you see evidence of behavioural modernity. And behavioural modernity is associated with things like burial practices, making tools, certain [things] like the use of ochre in graves, the production of sort of art, and evidence of certain kinds of living, in the past. So you have anatomical modernity and then later on you see these things cropping up, and the problem always of course is one of dating these things and also the survival of the evidence. With human fossils and evidence of past human behaviour the evidence is extremely scarce. There just isn't very much of it. And so it's very much influenced by individual finds. Many of those are very controversial, because people disagree about what some of those things are. So there does appear to be a time-difference between being anatomically modern and behaviourally modern. But how real that is, I'm not entirely sure. I think it could be to an extent artefactual, based on dating problems and just general scarcity of evidence. But I'm not an expert on that. 0.26.36

Holdsworth: Some of the traits that you mentioned are ones which people cite when they're trying to discriminate – if that's the right word – between *Homo sapiens* and Neanderthals.

Jobling: But Neanderthals buried their dead. I mean, clearly Neanderthals were - are anatomically distinct from *sapiens*. So you have that distinction. I think when people look on the lineage what they see is the lineage, which is anatomically similar to us, and [they'd assume] that these people may have been our ancestors, and then they look at behavioural modernity among [them]. So it doesn't mean to say that other anatomically distinct humans didn't have behaviours that we would regard as typical of, you know, humans. So, tool-making and the use of beads and things like that. There is evidence that Neanderthals did that.[403] 0.27.40

Holdsworth: There's some controversy about whether in fact they copied *Homo sapiens*.

Jobling: Yes. I think 'Who knows?' is the answer to that. Because, again, the evidence is so thin that you can build a career on a fragment of skull. There's a strong pressure for people in the field to come up with something rather surprising or interesting rather than something rather humdrum or similar to what somebody else found. That's one of the problems in palaeontology, I think. 0.28.09

Holdsworth: Right.

Jobling: Well, in all science, there's a positive pressure on people to come up with something interesting. The answers aren't always necessarily interesting or novel, and so that can be a bad thing. 0.28.25

0.29.14

Holdsworth: How strict do you think one ought to be, or can be in - over the use of the term 'behaviour'?

Jobling: Well, I don't know that I've ever thought about how strict one ought to be about it.0.29.36

Holdsworth: I mean, is farming a behaviour?

Jobling: Yes. I would say that it is. I mean, we tend to talk about 'cultural practices'. For example in our book, but those are 'behaviours' in a sense. I've never felt at all strongly you that should draw distinctions between what is a behaviour and what isn't. I know that's because of my background. I've never studied behavioural genetics, for example, or psychology. People in this department work on behaviour in flies - fruit flies. They work on circadian rhythms, and aggression, and things like that. So they have proper terminology, and they will probably use the word 'behaviour' in a very clear and precise way, but I guess that I use it in rather an imprecise way. 0.30.31

Holdsworth: Well, as I said, my approach is pluralist. It's merely an attempt to find out how people are using it. You can imagine that some people who are in another field, when they think of behaviour they might think 'Oh: extroversion/introversion, neurosis or gender orientation'.

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[403] Jobling et al. (2004), pp.247-248.

Jobling: Well, I suppose I'm rather generalist in that case. And I would say that things that people do are behaviour. That would cover you know painting, farming, killing other people, sailing across the sea. 0.31.09

Holdsworth: Technology?

Jobling: Yes, an element of technology. Religion.

Holdsworth: Right. That is certainly a cultural practice that is associated with AMH.

Jobling: Apparently. 0.31.30

Criterion 4: '*Does the research typically draw on the findings of genomics?*'

Holdsworth: Right. 'Does the research typically draw on the findings of genomics?' 0.31.38

Jobling: Yes. Much more so now than it did in the past, but very much so now, yes.

Holdsworth: Would you like to expand on that?

Jobling: Well, I think that, in the past, studies of DNA – the parts you need for human evolutionary genetics - were very much small-scale studies, because of the technology. So we would tend to study a very small bit of the genome – one that was of interest for some reason or another, and what's happened since that time is that pretty much the whole genome has been sequenced, and so now we have the raw material there to discover variation across the entire genome rather than in a little bit of it, and to sort of explore hypotheses about patterns of variation of one piece of DNA compared to the other, for example. So it's now, you know, possible to do that on a very large scale. The technology was there to sequence the genome - that's been done. But now the technology [exists] to analyse variation in very many segments of the genome simultaneously. 0.32.53

Holdsworth: Using bioinformatics tools?

Jobling: Well - or using a technology like SNP typing. In the past we would type, say, 20 or 30 SNPs in the β-globin gene. But now you can type a million SNPs across the whole genome, including the β-globin ones, if you want. So what you have is a very rich context in which to look at variation in one place that you might be interested in: you have the context of all the rest. Or you can look, simply for its own sake, at genome-wide variation. And what you get away from is locus-specific effects. Any one bit of the genome is a, is a specific locus - for example, of the β-globin gene. And that will have experienced locus-specific effects due to selection, for example in relation to malaria.[404] 0.33.51

Holdsworth: Can you give me an example that elucidates the phrase 'locus-specific effects'?

[404] See the review article: Williams, Thomas N. (2006): 'Red blood cell defects and malaria', *Molecular & Biochemical Parasitology*, 149, 2006, pp.121–127.

Jobling: Well, a good example would be if you took the lactose gene, and you used that as a marker to investigate human population relationships, you would come up with a picture which reflects - not how people migrated and how generally similar or dissimilar they are - but you would come up with a picture which reflects very strong selection for lactose persistence with the practice of agriculture and milk-drinking.[405] So you would find great similarities between populations which are generally rather dissimilar, because what you are seeing is the strong force of positive selection in maintaining that allele at a high frequency in populations that are otherwise rather distantly related, simply because they happened to drink milk. 0.34.52

Holdsworth: I see, yes.

Jobling: So that would be a locus-specific effect. Similarly, malaria resistance: you would look at the sickle-cell gene, sickle-cell variant, and you would see [if you typed that marker], you'd see great similarities in populations that had been exposed to malaria. So if you were then to type the whole genome in some general way, you'd see a much more - if you like - an average and a more reliable picture of similarities between populations, or dissimilarities between populations, because selection is locus-specific. It's interested in a little bit of DNA which does a particular job. For example, it's interested in a bit of DNA that stops lactase being switched off after weaning, or the bit of DNA that disrupts β-globin, which means that malarial parasites can't get into the red blood cells. But the rest of the genome is going its own sweet way. It will be evolving not under a specific selective force. There may be lots of other, different ones, acting elsewhere. But on the whole it's just providing a reasonably neutral - if you like - picture of the relationships between different populations. 0.36.14

Holdsworth: Right.

Jobling: So we are right now able to have a genome-wide rather than a locus-specific picture, because of the advances in [sequencing] being there and the technology being there to analyse variation. And what's going to happen soon is that we'll be able to completely [re-sequence] human genomes, relatively cheaply. And that will make a big difference, because instead of looking at specific sites of variation you might be able to take someone's genome and just throughput the whole thing. And the Holy Grail that people talk about is the 'thousand-dollar genome'. So you could take someone's genome and sequence the whole shebang, instead of looking at little bits of variation. 0.37.00

Criterion 5: '*Is the research on genes or other DNA? If 'other': mtDNA or Y-chromosome?*'0.37.02

Holdsworth: Right. Good. Now what about 'genes' or 'non-recombinant sequences': mitochondrial DNA and Y-chromosome? 0.37.23

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[405] For lactase persistence, see Jobling et al. (2004), pp. 414-421. See also the article already cited in Annex 0 to the present, the Edited Excerpts of the interview with Professor Ruth Mace, Footnote 5 on p.5: Ingram, C.J.; Elamin, M.F.; Mulcare, C.A.; Weale, M.E.; Tarekegn, A.; Raga, T.O.; Bekele, E., Elamin, F.M.; Thomas, M.G.; Bradman, N.; Swallow, D.M. (2007): 'A novel polymorphism associated with lactose tolerance in Africa: multiple causes for lactase persistence?', *Human Genetics*, Feb. 2007, Vol.120, No.6, pp.779-88.

Jobling: Yes, well we're interested in all of those things, you know, definitely. So, mitochondrial DNA and Y-chromosomes are interesting because they escape recombination and don't get reshuffled every generation. That means that they're relatively straightforward-to-interpret patterns of diversity. You see modern individuals in terms of how they came to be that way – their ancestry – you don't have them reshuffling in each generation. But they are only two loci – genetic locuses. Mitochondrial DNA and the Y: those are just two pictures, if you like, of the evolutionary process. And it's very much only part of the story. 0.38.13

Holdsworth: And how can this be filled out with autosomal DNA?

Jobling: Well, any segment of DNA that doesn't undergo recombination has its own history, because it comes down – it coalesces back at some point to a single ancestor. Those ancestors didn't all live in the same place, and they didn't all live at the same time. So, to provide a rich picture of human history through DNA you need to look at a lot of them – to look at their history. Because if you look at – if you take one at random, you will find, for example, that it may have a relatively recent origin in Asia. If you look at another, you might find it has a very ancient origin in Africa. If you look at a third one - . 0.39.00

Holdsworth: Could you give an example?

Jobling: Not specifically, no. I can't. But, because each segment of DNA has its own evolutionary history, each one has its own past. I mean, each one has its own place of origin. So, if you look at just one, that's fine, that's the history of that piece of DNA, but to what extent it reflects the history of our species may be another matter. So you need to look at a lot, and that means Y-chromosomes and mitochondrial DNA on their own are just two pictures of the evolutionary process. OK, they may happen to represent the species picture as well, but they may not. I mean, it's striking. If you look at humans, chimps, gorillas and orangutans, then we have a phylo- , an accepted phylogeny for the relationship between those species, but orangutans and the rest are – orangutans are a sister clade of the rest, and the gorillas are a sister clade of chimps and humans, but if you take any piece of DNA it can give you a different tree. It can give you a tree that shows that gorillas are the most ancient [branch]. And then come orangs and then humans and chimps. 0.40.19

Holdsworth: Right.

Jobling: Or you can even get ones that place humans as the most ancient. From one sequence. And that's fine, but what you need to do is look at a lot of them, and then you get a true picture – or a truer picture. 0.40.37

Holdsworth: Right. [You may have seen] this article by these researchers from the University of Arizona that was published in *Nature Reviews Genetics* last September?[406] (*Holdsworth shows Jobling the article*). It seemed to be a criticism of relying on mtDNA and Y-chromosome. 0.41.39

Jobling: Well yes, well absolutely, yes. I think it's fair to criticise. Indeed what we're doing at the moment - I've been traditionally a Y-chromosome researcher in my own research -

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[406] Garrigan, Daniel, and Hammer, Michael F. (2006): 'Reconstructing human origins in the genomic era', *Nature Reviews Genetics*, Vol.7, September 2006, pp.669-680. I am grateful to Maureen O'Malley of Egenis for bringing this paper to my attention.

although we continue to use it, we're moving towards using the output of the HapMap Project.[407] That's the genome-wide project which looks at haplotype structure of the whole genome, and what it allows you to do is identify regions of DNA within the autosomes that have never historically undergone any recombination. They're like little 'Y-chromosomes' embedded in the autosomal DNA. So they haven't had recombination, but they have had a history. You can then use those as you might use a Y-chromosome. You can build a tree and so on and so forth. 0.42.30

Holdsworth: So what you're saying is that the – in inverted commas, because it sounds funny to say it – the 'traditional' mtDNA and Y-chromosome approaches are only as good as they are, and not better. They can be supplemented by evidence from the autosomal DNA, which is possible now because of the high-powered systems for investigating it. It would not have been possible a few years ago. 0.43.02

Jobling: Yes. And because of the HapMap project, which certainly wouldn't have been possible a few years ago because it required the analysis of, I think, about 3.1 million markers – about 3.1 million SNPs - for a population. That's been extremely helpful, because we didn't have to do any work: it's all available. Just with a genome browser you can – you can actually take down that data and use it and find these bits of DNA. 0.43.27

Holdsworth: And have we already seen, so to speak, 'corrections' of the picture that was emerging? Or do you expect us to?

Jobling: Well, I don't think we are, no. So I think that – I think it unlikely that the generally-held view that there was an African origin for modern humans is going to be overturned by the new genetic methods. 0.44.01

Holdsworth: You think that's unlikely.

Jobling: I think that very unlikely. What seems to be happening is that most – if we look at these little bits of DNA within the genome that are non-recombining – that have not recombined in the past - the majority of them are of African origin. Which is kind of what we expected. So I think we're getting a richer picture by having more markers and more systems to look at, but I don't think it's likely to overturn the general view that is held at the moment. 0.44.34

Holdsworth: And it's certainly not going to – well, perhaps putting words in your mouth - but it's not going to eliminate the validity of mitochondrial DNA and Y-chromosome research?

Jobling: No. I mean, both mitochondrial DNA and Y-chromosomes have the trees – the phylogenies have African roots, for example. And I think those both do reflect the species history. They needn't necessarily have done so, but they did. 0.45.05

Holdsworth: There's some question about time-depth.

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[407] The International HapMap Project. Website: http://www.hapmap.org/ (consulted 14 January 2008). See also: Thorisson, Gudmundur A.; Smith, Albert V.; Krishnan, Lalitha, and Stein, Lincoln D. (2005): 'The International HapMap Project Web site', *Genome Research*, 2005, Vol. 15, pp.1592-1593.

Jobling: Yes. That's a difficult one. I mean, mitochondrial DNA and Y-chromosomes have a low effective population size, as we say. So for every one Y-chromosome in a global population there are four copies of chromosome 1, for example. And that means that there are just fewer of them out there, and that the time at which they will coalesce to a common ancestor is proportional in number. That's the time we expect them to coalesce to the common ancestor. And so when we look at mitochondrial and Y-chromosome ancestry for time-depth it's very shallow. That doesn't necessarily reflect the species time-depth. [It's variable]. It may do, but it's unlikely. I mean, it depends what estimates you use, but one estimate of Y-chromosome time-depth is about 60,000 years. That clearly can't be the species time-depth. That's too young, based on palaeontological evidence. 0.46.13

Holdsworth: Which would be between 150 and 200,000 years.

Jobling: Something like that. Whereas autosomal markers we expect to, on average, to coalesce to something around about four times as old as the Y-chromosome and mitochondrial, which may actually pre-date the species origin. There are autosomal sequences with coalescence times of about 800,000 years, or even older. 0.46.46

Holdsworth: Simply because - .

Jobling: [...] A species is not descended from one individual, but from a group.

Holdsworth: Yes.

Jobling: So before you can try and reach the event of a speciation, you've got a group of individuals who contain diversity themselves. To go back to the time of the speciation, you sample everybody, look at the histories of their people's DNA. Some of them will go back quite a long way. A pair of chromosomes - a pair of individuals in the population will themselves have a coalescence time that might be hundreds of thousands of years. And if those lineages survive them through the speciation event to modern times, and you now look at the time-depth, you're going to find that ancient time-depth that was already separating those lineages, plus the time that's elapsed since speciation - which is, say 200,000 years. So you can find sequences which have – which are really ancient in their time-depth. On average, they will be younger than the species, but it is possible to find lineages which have very, very old genetic histories. 0.47.55

Holdsworth: Earlier, when you talked about HapMap and finding autosomal sequences that in their history have not in fact been subject to recombination, is there a special term for that? 0.48.11

Jobling: Well, there isn't an accepted term. They're sometimes called 'haplotype blocks'. That's how they're normally referred to.[408] 0.48.21

Criterion 6: *'Is there research on the DNA of non-human/hominid species? If so, animals or plants?'* 0.48.40

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[408] Gabriel, Stacey B. et al. (2002): 'The Structure of Haplotype Blocks in the Human Genome', *Science*, 21 June 2002, Vol. 296, No. 5576, pp. 2225 – 2229.

Holdsworth: 'Is there research on the DNA of non-human/hominid species?'

Jobling: Yes. There's the subject of comparative genomics. Comparative genomics seeks to illuminate the genetics of one species by looking at the genomes of other species. 0.49.02

Holdsworth: Right.

Jobling: One aspect is comparing human genomes with those of chimps and bonobos and gorillas and so on. We can learn quite a lot about patterns of diversity in our own genomes by looking at – by using as a reference point genomes of other species. So we can understand, for example, that there are differences between the human and the chimp genome. And the question is: did those differences arise from the lineage that led to chimps or the lineage that led to humans? So now the macaque genome – the rhesus macaque genome- is published, so it provides a reference-point, which we can compare humans and chimps from each other, but then also with an out-group: the rhesus macaque. And you can say, OK, well, chimps and rhesus macaques have the same DNA base at this position; humans have a different one; so it's a human-specific change. And you may find that rhesus macaques and humans have the same base at this position; chimps have a different one; so it's a chimp-specific change. That's quite useful – to be able to know, of the many differences between humans and chimps, which ones have occurred on our lineage, and which ones occurred on theirs, for example. So it's then interesting to compare human diversity with the diversity among different chimps, different gorillas, different orangutans, that have different histories and different behaviours. 0.50.31

Holdsworth: Sorry, when you say 'among different' - different *populations*?

Jobling: Yes. Or a group. There's a study done, for example, of Y-chromosome diversity in chimpanzees, or in gorillas, and you see very different patterns than you see in humans, which reflect their different histories. Then moving away from primates, then, a lot of studies have been done of diversity of species that are commensal, or humans have been associated with: so, for example, JC polyoma virus or *Helicobacter pylori*. JC polyoma is a virus. I don't even know what it does to you, but a lot of people carry it around. And you can look at the diversity of its DNA sequence to provide another picture of human migration and contact. 0.51.24

Holdsworth: Is that mentioned in your book?[409]

Jobling: Yes, I think so. More recently, people have looked at *Helicobacter pylori* strains and how they vary in different human populations, to give an indication of how long that bacterium's been associated with humans and whether it provides a picture of diversity similar to that of human being genes diversity. And then there are domesticated animals and plants that a lot of people have looked at to see evidence of how agricultural practices were adopted, and when they were adopted, by looking at the genomes of maize or rice or wheat, or cows or sheep or goats or any of these. 0.52.17

Criterion 7: *'Is there research on other bio-molecules? If so, proteins or other?'* 0.52.18

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[409] Jobling et al. (2004), p.369.

Holdsworth: Right. And is there research on other biomolecules apart from DNA?

Jobling Well, genetics is essentially about DNA. So it's very DNA-centric. The question that you might ask is, OK, there's a change in the DNA, but does it have a functional effect – what is the functional [consequence]? And that could involve studies of protein, or studies at the RNA level to ask what differences there are. But I think it's very much DNA-centred. 0.52.59

Criterion 8: *'Does the research use environmental markers?'* 0.53.05

Holdsworth: 'Does the research use environmental markers?'

Jobling: What do you mean by 'environmental markers'?

Holdsworth: Well, in an interview with a biomolecular archaeologist there wouldn't be much problem, because the DNA is found in some – the bones or whatever - are found in some environmental matrix. So – something like that.

Jobling: Well, in that sense, yes. I mean, if you were studying ancient behaviour - .

Holdsworth: Settlement sites.

Jobling: Yes. Mostly, environmental objects are people. So all you do is sample people, in some sense. So we don't, in our work, use environmental markers, I'd say. But in terms of studies of Neanderthal bones – well, OK, yes. 0.54.08

Holdsworth: And then, the whole concept of phylogeography implies some spatial location.

Jobling: Yes, you have a box in the freezer with a hundred tubes in, and the box is called, for example, 'Basques'. I've got several of those. And so in some sense you regard those people as the Basques. So that locates them geographically and culturally, and it tells you what language they speak. And you, well, organise them and file them in a filing-cabinet or something which has a sheet, or set of sheets, that refers to those samples, and you have a consent form for each one of those people, and they self-define as 'Basques'. They give their first language as Basque, and they tell you that they were born in such a village or such a place, and that their father was born in the same [place] – with mother and grandmother, grandfather both sides, and that's your environmental marker. 0.55.06

Holdsworth: Yes.

Jobling: That allows you to place a person, in some sense, in a place or a population, but you don't necessarily have to go there, of course, but you have information which allows you to say, OK, this box of DNA samples is a distinct set.

Holdsworth: I mean, once you know that this box came from the Basque land, south of the Pyrenees, or north of the Pyrenees, you might have some inference to draw.

Jobling: Right. Indeed. Yes. 0.55.34

Criterion 9: *'The main concern is phylogeny or ontogeny?'* 0.55.35

Holdsworth: 'The main concern is phylogeny or ontogeny?' 0.55.41

Jobling: Well, I'd say the main concern is phylogeny, of those two.

Holdsworth: Yes. Not much more to add.

Jobling: No, not really. 0.56.05

Criterion 10: *'Does the research draw on fossil evidence?'* 0.56.05

Holdsworth: 'Does the research draw on fossil evidence?'

Jobling: Yes. Certainly. Strongly. And I think that it's as we say in our book: there are different records of the past. The genetic record is one, and that's what is our focus, but there are the other records. The palaeontological record is another very important one. We want to know to what extent the genetic record is giving a similar picture to the other kinds of records: the archaeological record, the palaeoclimatological record, the fossil record.

Holdsworth: Yes, you go into climate quite a bit in your book.

Jobling: Yes, I think it's pretty important. 0.56.53

Criterion 11: *'Is Newtonian mechanics relevant to the research?'* 0.56.55

Holdsworth: The next criterion is 'relevance to Newtonian mechanics'. That was for the evolutionary biomechanics people. There, the forces of nature act – natural selection acts in a very direct way. 0.57.12

Jobling: So I'd say - I would have said no to that.

Criterion 13:[410] *'Does the research use cultural markers, e.g., surnames?'* 0.57.24

Holdsworth: 'Does the research use cultural markers?' And I took an example from one of your own.

Jobling: Yes, it does. We use surnames, in some of our research.[411] There are studies that use language, studies that use religion, also, as a way of sub-dividing populations. And studies which use lifestyle, so, in the sense of nomadic or sedentary, or farming or hunter-gathering, or something like that. Milk-drinkers and non-milk drinkers. 0.58.02

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[410] The order of the criteria was changed on this occasion.

[411] See, for example: Kingl, Turi E.; Jobling, Mark A. et al. (2007): 'Africans in Yorkshire? The deepest-rooting clade of the Y phylogeny within an English genealogy', *European Journal of Human Genetics*, Vol. 15, 2007, pp.288–293.

Holdsworth: Any particular thoughts on that criterion? How surnames are important?

Jobling: Well surnames is a rather specialised branch, but I think it's interesting, because it in principle allows you access to the past in a way that you can't get with other things, because surnames are heritable cultural markers. And you can put them together with a heritable genetic marker and start to find out what patterns of those heritable genetic markers were like in the past, and how much they've changed in the last few hundred years. It will only work in a society where you have heritable patrilineals, though - which is most. But the time-depths vary a lot. [It's rather limited, generally.] The other ways of sub-dividing have their disadvantages as well. Language is often used, but language can change pretty rapidly. OK, we know about some of the language changes that have occurred. We know that Hungarians, not that long ago - about a thousand years ago - spoke an Indo-European language, and now they speak a Finno-Ugric, a Uralic language. 0.59.25

Holdsworth: As recent as that, was it?

Jobling: Mm. So if you look at the genetics of Hungarians, to my knowledge there's no evidence that would cluster them with other Uralic speakers. And then Turks speak a Turkic language. But again, fifteen hundred years ago they didn't speak a Turkic language. And then we classify the people of Iberia. We have the Basques and then everyone else, but it's a subject of great debate as to what the languages were like before the Roman Empire. The Romans were very good at lots of things, but one of them was spreading [Latin] everywhere. So we see the influence of that here. Virtually, English is a sort of bastard language made up of all sorts of different things, whereas some languages are very clearly the way they are because of the Romans, and Romanian is one of them. 1.00.21

Holdsworth: Right, yes.

Jobling: So languages can change pretty fast. So as a cultural marker that can be a problem. Religion: I don't think I have much comment on that. Never use that as a divisor. Some people do, though – certainly people who are interested in the history of Jewish populations do. And, you know, there are papers about the genetics of Samaritans and all sorts of people. And Buddhists in Ladakh, and people like that, looking at some aspect of their genetics.

Holdsworth: Yes. Sometimes interesting because they have – not them, particularly, but in some groups – have dietary practices. 1.01.08

Jobling: They do. They also often have odd disease spectra. It seems to me that what the cultural things do is simply lead to a certain amount of population isolation, small effective population size. Religions tend to exclude people who aren't in the religions, so by definition they lead to small effective population size. And then you've got an isolate, and in that isolate you can have high frequencies of disease. So Ashkenazi Jews are a good example, because they do have quite a lot of otherwise rather rare diseases: Tay-Sachs disease, for example.[412] 1.01.52

Criterion 12: *'Is the research intended to have a clinical application?'* 1.01.55

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[412] Jobling et al (2004), p.392.

Holdsworth: 'Is the research intended to have a clinical application?'

Jobling: It certainly has a clinical interest. I think it would be too strong to say that it has a clinical application. But it is interested in the history of human populations and all genetic causes of disease - or all genetic influences on disease - that come to be distributed in populations because of our evolutionary history. Some through neutral processes like drift, and some through non-neutral processes like selection or migration. So a general understanding of those things, I think, is important if you want to - for example - learn about the genes that influence Type 2 diabetes susceptibility. 1.02.47

Holdsworth: Right. So medicine could perhaps find information of interest coming out of human evolutionary genetics?

Jobling: Yes. Definitely. 1.03.01

Criterion 14: *'Does the research offer other economic or social benefits?'* 1.03.02

Holdsworth: And what about other economic or social benefits, such as agriculture?

Jobling: Well, economic and social benefits of the *subject*, evolutionary genetics, or human evolutionary genetics?

Holdsworth: Yes. I'm not doing a kind of utility audit. But it's interesting to know whether people are aiming for – if their methods and objectives are in any way related to [utility].

Jobling: Well, I don't see there's a strong aim to have economic or social benefits. I think that one thing our field does do that's socially beneficial is that it's a good field to engage the public. It contributes towards public understanding of science, because everyone has a natural interest in their own origins, or nearly everyone does. If there's a subject [with an] interest in human origins, it's usually of interest to people, generally speaking. 1.04.01

General and concluding discussion 1.04.25

Holdsworth: Finally, just to go back, if we may just for a second, to the Neolithic revolution. In the book, one of your colleagues made the point that there is this apparent time-lapse. Why do people – why does our species, having been around for maybe 150,000 years or more, suddenly take to farming?

Jobling I don't know the answer to that!

Holdsworth: But is there any conceptual way to, sort of, capture these delayed-action phenomena? 1.05.07

Jobling I don't know. I think it's very difficult for us to think about it. I mean, what could the modern time-frame or stand-point tell us - where everything changes so fast? In prehistory, there are these enormous periods of stasis where absolutely nothing happens. Some of these stone tool technologies went on for thousands and thousands and thousands of years and didn't change one iota, as far as we can see. To the modern person, I think it's really

inconceivable why things were like that to us, literally, because of the way our lives are driven by change all the time now. It's very difficult. So I really don't have an answer to the question why it took people such a long time to come to agriculture. Especially, with the benefit of hindsight, it looks such an obvious thing to do! 1.05.51

Holdsworth: But I come back to the concept we discussed earlier of the 'species-typical'. What people would be tempted to say is that it was absolutely species-typical now that we eat food that was the product of farming. There are other things in the pipeline. Take urbanisation. I've read that, about now, about half the population of the world lives in towns. That proportion will certainly rise, and one day it will appear to be species-typical to live in a town. I suppose that we just have to accept that these things are happening, but probing back into your own researches and thoughts you haven't got any particular model to apply?

Jobling: No, I haven't. Well, maybe I should do, but - . I think there were conditional changes – in climate and so on - that coincided with the birth of agriculture, that might have contributed to it. But I don't think we can be certain about that.[413] 1.07.12

Holdsworth: Well, I think we've covered the main points. From my point of view we could go on for a long time. It's very interesting. Thank you very much.

Jobling: OK. Not at all. Good. 1.11.35

[413] Jobling et al. (2004), Chapter 10, 'Agricultural expansion', pp.299-338.

8. Research interview with Professor Susan Lindsay – Edited Excerpts

Interviewed: Professor Susan Lindsay, Professor of Human Developmental Genetics, Institute of Human Genetics, University of Newcastle upon Tyne.
Interviewer: Richard Holdsworth, PhD candidate in the Economic and Social Research Council (ESRC) Centre for Genomics in Society, Egenis, University of Exeter .
Date and time of interview: Wednesday, 20 June 2007 15.00.
Place: Institute of Human Genetics, University of Newcastle upon Tyne.
Total length of the recording: 1 hour 20 minutes 24 seconds.

0.00.00
[...]

The interviewee's description of the research 0.06.25

Holdsworth: Well, let's plunge into the first question: human developmental genetics, and what sort of thing you're doing. I have of course looked at your website and some of your publications. So I've got a general idea, but perhaps in your own words you'd like to define your field.

Lindsay: Certainly. We are principally looking at the patterns of gene expression during development: so when and where genes are active or activated – turned on and then turned off, if they are, or maintained, and how that relates to the development of individual tissues or particular structures as the embryo develops, and my particular areas in the brain and looking at gene expression in the brain with an interest in, at the moment, producing an atlas and a gene expression map of the human embryonic brain. 0.07.50

Holdsworth: Right.

Lindsay: So one first thing is that: definition of embryo and foetus? I work on post-implantation development. Because 'human embryo' has come to mean pre-14 days, when human embryonic stem cells are developed. I do not work on human embryonic stem cells. That's pre-implantation.
0.08.26

Holdsworth: Yes, I see.

Lindsay: I work post-implantation. And I work from the time when - . The Central Nervous System starts as a tube, basically. It starts as a flat field, that rolls up.

Holdsworth: The neuroepithelial - .

Lindsay: Neuroepithelial, exactly. It rolls up, and it closes at both ends. And I work from about three and a half weeks of human development, at which point we have a fully closed tube. 0.08.54

And then after that the major regions of the brain are developed through the rest of the embryonic period to about eight weeks. And then in the foetal period there's obviously a huge growth and further differentiation and development of the fine detail of all of the different brain regions, particularly in humans, cerebral cortex. 0.09.24

Holdsworth: Really?

Lindsay: Yes. So we do some work in foetal stages, but it's mostly in embryonic. So it's mostly in that three and a half to eight weeks of development. 0.09.36

Holdsworth: And you use some quite novel methods - 3D modelling.

Lindsay: The 3D modelling is novel. The generation of gene expression data – finding out when a gene is active or inactive - is using very traditional methods. Immunocytochemistry, looking at proteins – that's something that's been done for a long time. What we do most of is looking at messenger RNA. 0.10.03

[...] 0.10.18

So, messenger RNA is more difficult to look at, because everywhere - on our fingers, all over our skin, we have enzymes which break down RNA, and they're very resistant to all sorts of things that we might usually use to get rid of them. So the tissue has to be treated in quite careful and specific ways in order to preserve that messenger RNA. 0.10.48

Which is why the collection that we have here, which is part of a national collection held here and at the Institute of Child Health in London, that's one of the reasons why it's a valuable resource. 0.11.08

Holdsworth: It's a kind of reference resource? 0.11.10

Lindsay: It's a resource for people to obtain material, but also as we get results we're sticking them into a database.

Holdsworth: I see.

Lindsay: And then we try and grow that database. I hope. That's one of the ideas: to build it into a reference database for gene expression patterns. 0.11.26

Holdsworth: Right. Yes, I noted the National Collection of Human Embryonic and Foetal tissue. And 'Large-scale gene expression studies and analyses'.

Lindsay: Right. Well, 'large-scale' means lots of different things to different people. 0.11.40

Because with genomics you – if you were using micro-arrays and looking at all of the human genome on an Affymetrix chip or on other kinds of microarrays – these techniques are ones where we're looking at all human gene sequences. 0.12.14

Lindsay: That's one definition of large scale – you're looking at all of the genome. But in doing that you don't have any information about the – detailed information - about the spatial expression patterns: where, precisely, the gene is expressed. 0.12.34

Can I show you a section? It's not going to interfere [with your recording]?

Holdsworth: No, do. So now we're going to look at something on the screen. 0.12.52

Lindsay: I have just given a talk where I went through quite a lot of this, so by chance I have quite a lot of the information ready. 0.13.09

One of the things I wanted to show you was this section.[414] I'll make this bigger. Yes. 0.13.27

OK. So these are the two techniques. This is the immunocytochemistry, looking for protein, and you can see this is a tissue section with the developing head at the top. And the embryo's curved round, so this is head and this is spinal cord; these are developing eyes, and you can see the signal in brown. 0.13.50

Holdsworth: That reminds me of the 3D images on your website. 0.13.55

Lindsay: Yes, but the 3D images are built up section by section from this kind of data. But you can see from here – and here's the gene expression pattern here for this particular gene. This was RNA in situ hybridisation. You get a very distinct and clear idea of where the gene is precisely expressed. 0.14.24

Holdsworth: Right. Could you just explain that one a bit more?

Lindsay: So, instead of protein this is messenger RNA. And it happens that the staining gives a purple stain rather than a brown one, which is just to do with the chemicals. But this is showing where the mRNA for this particular gene is, and you can see it's in a very confined place. 0.14.49

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[414] For a description of the techniques used in this research see the following article (with illustrations): Kerwin, Janet; Lindsay, Susan, et al. (2004): '3 dimensional modelling of early human brain development using optical projection tomography', BMC Neuroscience, 2004, Vol.5, No. 27. See also here Footnote 4, below.

This is an Affymetrix chip here. So you could - and we have been trying – you can get a detailed idea of localisation by cutting out the tissue area that you're interested in and generating RNA and then putting that RNA on a chip. 0.15.15

So the detailed spatial information which in situ hybridisation and immunocytochemistry give you - people are reconstructing by very precise microdissection. And then you can see that in this area that you've microdissected, and then screen the 20-odd thousand or however many sequences there are on an Affymetrix chip, I can say that in this region here are all the genes that are expressed. 0.15.55

Whereas, what we're doing at the moment is one gene at a time, which is going to take us an enormously long time. However, we're not looking at all the genes in human- mouse developmental groups are doing all of the genes through particular stages of development, or adult brains for example. We're not going to do that with humans. 0.16.14

Holdsworth: So ISH is 'in situ hybridisation'.

Lindsay: Yes.

Holdsworth: And ICT?

Lindsay: Immunocytochemistry. Protein and RNA, basically. 0.16.25

Holdsworth: But what I haven't grasped yet is the ISH image that we're looking at - how is that created?

Lindsay: OK. Sorry. Both of these images are - in both cases what we have is an embryo embedded in a block of paraffin wax. And then very thin sections cut through the embryo, and then these sections mounted onto glass slides. And so what this is, is a section through an embryo. 0.17.06

And if I reduce that you can see that - . If you go to the website that you've obviously looked at already for this one here. On this particular one. [What have I got?] What we have - let me see – yes. What I'm looking for is the – here, yes. This is a real section – a physical section through the embryo. 0.17.49

The black block. And this has just been stained with a stain that identifies cell structure. What's called a histological stain. It's not a particular gene, it's just showing cells. And this is a view of the painted 3D model. But as you move through the structure you can see - look, this is the forebrain, this is the developing eye, this is the mid-brain, developing cerebellum, into the hind-brain and down into the spinal cord. That's the heart, and that's the liver. 0.18.27

So you can see that, as you move down - here we're into, just moved from the mid-brain into the forebrain, and you see you've got that kind of squashed circle here,

and then you've got a bit of the hind-brain, and this is the developing ear, which is what this yellow is, and then you see you come across the spinal cord which is here, and these little blue structures are called the dorsal ganglia. There's that – which one goes in there. So this is the real section, and this is the digital section. 0.19.03

Holdsworth: Right. 0.19.04

Lindsay: And one of the first things we did was we wondered what can we see in these models? These models are generated from intact specimens using a method called Optical Projection Tomography.[415] And then the real principle of the method, or the real beauty of the idea is that you've got a three-dimensional, digital model that you can section in any plane, and you can compare the sections in one plane to another. 0.19.41

Because, as you can see, the developing brain has a lot of bending and folding, and the shape changes quite dramatically. 0.19.54

Holdsworth: Yes, that is dramatic.

Lindsay: And so it's very difficult to navigate yourself and work out where you are, when it may be that actually over quite large regions it's just a series of circles. And it's the relationship between the different structures that helps you to know where you are. 0.20.15

Holdsworth: Right. What are you looking for – the pattern of differentiation?

Lindsay: Well, what we see here with these sections is very clear, and then what we do is - we can paint on the anatomy; so we compare these real sections with model sections. 0.20.36

But then, also onto the model, we map gene expression patterns. So the other one that's here, say, is this one. I think. Good. OK. So this is protein. This is the immunocytochemistry. And here what we would do is we would threshold out - we would differentiate between that brown signal and the blue and identify all of that as protein expression - and then map that detail onto the model to really build up three-dimensional layer, or three-dimensional domain. 0.21.22

And what that then lets you do is to see what that pattern is in three dimensions, because then you can identify the - the course of nerve track or the expression which might stop at the end of a particular structure. 0.21.43

This particular one is outlining new neurons and developing axon tracks, which is in fact everywhere, which is why we use it as an example. But with something more

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[415] OPT.

specific you might well feel that yes, you're seeing expression here in the forebrain, but when you move into the mid-brain the expression stops or the pattern changes. 0.22.08

Holdsworth: What do you mean, 'You're seeing expression?'

Lindsay: I mean that I'm seeing a brown pattern here while I might see a dark blue, a dark – yes, a purple pattern that would be in situ hybridisation. 0.22.19

Holdsworth: I see.

Lindsay: So what that in situ hybridisation is - I just put that down. So here - that section here - that's a physical section that we have hybridised. A short bit of DNA that matches the RNA of a specific gene. 0.22.47

Holdsworth: Right.

Lindsay: So it's finding RNA from a specific gene. And that particular gene happens to be expressed in a very specific place. 0.22.57

Holdsworth: It's finding it and localising it.

Lindsay: Yes. 0.23.00

Holdsworth: It's identifying it and localising it.

Lindsay: Yes. And sticking to it. Because it's the linking of DNA and RNA. The whole idea of the Double Helix is that the bases pair with each other. 0.23.18

Holdsworth: Yes.

Lindsay: So if you have a complementary sequence they will identify and stick together. That's what that means basically. 0.23.28

Holdsworth: Right. Well, thank you.

Lindsay: We can see that little purple stain there. And so even though – even if we did dissect this out and hybridise this and got a somewhat clearer idea of localisation, what that wouldn't do: if we look at this under the microscope at higher power we would actually be able to see the particular cells that this gene is expressed in. 0.23.55

And so we'd get very detailed expression information. You could do that against an Affymetrix chip, but dissection of individual cells is a very long and laborious process, apart from anything else would need a huge number of Affymetrix chips. It's still going to be true that going back to sections and using the microscope and

seeing things at high power is still going to give a lot of information about gene expression patterns. 0.24.28

Holdsworth: Right. Would it be possible to print that out?

Lindsay: Yes, I think so. If I can do that. 0.24.39

[*Conversation is interrupted as the printer is set to work.*]

0.26.35

Holdsworth: So, you're concerned with the expression of the genes concerned in the development of neurons?

Lindsay: And other brain regions. Because it's not only the neurons that are important in shaping the brain and also in the function of the developing brain. 0.27.01

We're really concerned with expression of a whole variety of different genes during brain development, and our selection of the genes partly depends on - are they genes underlying particular genetic disorders. 0.27.20

Holdsworth: Right. 0.27.21

Lindsay: So there's a relevance to humans, or human beings, but in order to understand those we need also to need to know about patterns of key developmental genes. 0.27.32

We know from mouse and other species that there are certain families of genes that are very important in the development of not only the brain, but all sorts of different organs, and quite often it's the same genes in different organs or different members of the same gene families. There are key gene families you can identify. 0.27.56

Holdsworth: You mentioned just now the use of 'traditional' methods, but surely this is all quite a young field. 0.28.07

Lindsay: Genetics is. The study of the human brain and looking in this kind of sectioning, and looking at it – no, I think that would have a history of probably just over a century. 0.28.30

But not the molecular side. Not the mRNA.

Holdsworth: No.

Lindsay: The proteins and looking in detail at brain development using different stains – the histology stains – and then different antibodies if they were available. So the antibodies also they're - they're obviously later, too, but - . 0.28.50

Holdsworth: But the bringing together of the old neurological preoccupations with the DNA - . 0.29.02

Lindsay: Yes. And the 3D modelling. Certainly. And putting those – making that digital, and being able to look at it in the detail that we're looking at, then yes, that is. I suppose when we - . 0.29.14

Holdsworth: What sort of time frame?

Lindsay: Really digital modelling? Well, successful digital modelling is probably about five years. And the molecular side of things and the in situ hybridisation – that's been probably for - late '80s, something like that? So maybe – yes - 25 years for the molecular side, being able to look at mRNA. 0.29.52

Holdsworth: Right. Only in the last five years that - . Surely the developments in the last five years have enormously increased the power of your research methods.

Lindsay: That's true. Yes. Because prior to that the methods for generating 3D models were very labour intensive.. So, for example simply drawing round images of sections and then making them in wax and sticking all the wax bits together. So there've been, people have been generating 3D reconstructions also for a while, but obviously at the end it's a solid wax block. You can't section it again. 0.30.41

Holdsworth: No, no.

Lindsay: It's that - . And we and others have been trying methods for capturing images of whole sections, putting those images together, and then digitally sectioning those images. 0.30.58

But you introduce a lot of artefacts when you section. 0.31.02

Holdsworth: Do you? What sort of thing do you mean?

Lindsay: That the section can expand or contract, or the sections are of different sizes, or you might tear things, or you get holes, or dirt. And when you put all of that together, it looks very nice in the plane in which you section, but then when you section in a different plane it can be fuzzy, or the structure is distorted. 0.31.32

Now, people have been working in order to overcome these things, and have now – there are methods now for doing that - but the beauty of the OPT is, it's from an intact specimen, and you get 3D models very quickly.[416] 0.31.51

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[416] "Optical projection tomography (OPT) microscopy is a new technique which allows the 3D imaging of biological specimen over 1 cm across. It was initially developed with the hope of enabling accurate measurement of 3D shapes. However, it has proven to be a fast method for scanning the 3D distributions of gene expression patterns during embryo development. In particular it has two important advantages over confocal microscopy: it can image much larger specimen, and it can image non-fluorescent specimen. This

Holdsworth: Right.

Lindsay: And for mouse you can have 3D models which also contain gene expression. 0.31.58

Because human is bigger, and we don't have so many specimens, we haven't done what are called 'whole mount' experiments, where you take a whole sample and ask about the gene expression pattern directly in that whole sample. 0.32.15

So when we section, depending on the size of the embryo and the organ of interest, let's say we might generate, through the brain, 500 slides. Now we're going to be able to look at gene expression patterns from many genes on those 500 slides. Whereas if you use a whole-mount you've got – you know, one sample, and you're maybe only going to see expression from one or two genes. 0.32.39

Holdsworth: A gene expression pattern is the pattern that is revealed when genes are being expressed in particular cells. 0.32.47

Lindsay: Yes. Sorry, all gene expression pattern means is to define the regions, or cells, where a gene is either off or on. 0.33.00

Holdsworth: Right.

Lindsay: So, here's another example. Where again the expression is in purple, so again, here is the section, and you can see this is mapping into this – this is a 3D model. And here - we've expression here, so the gene is on here. It's off here. It's on here. So that's the pattern. I can see that it is expressed in this bit of tissue because I can see the purple stain. 0.33.29

Holdsworth: When it's dark - ?

Lindsay: It's on. And when it's light it's off. And when it's like that – you have to make a decision. 0.33.40

Holdsworth: Good heavens.

Lindsay: So you can see it isn't – . So say here. Is that on? Is it off? Is it [less]? It's very, very clear in areas where the expression is strong. And it gets increasingly difficult, or can do, to distinguish expression from background. 0.34.05

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means that BCIP/NBT in-situs or LacZ staining can be mapped in 3D." From the OPT homepage of the MRC Human Genetics Unit, Edinburgh, UK: http://genex.hgu.mrc.ac.uk/OPT_Microscopy/optwebsite/frontpage/index.htm (Consulted 9 October 2008).

And that's where doing things over and over again, seeing a pattern that's there in lots of sections, is very important. 0.34.12

Holdsworth: Which is amazing. Just for the record, we're looking at the slide headed 'Gene expression signals are maps to the OPT models'. I see.

Lindsay: Yes.

Holdsworth: Now, obviously in some sense neuronal and other brain structures are a prerequisite for explaining behaviour, but is there any direct sense in which your research is looking at the development of behaviour? 0.34.43

Lindsay: I think the honest and real answer to that is no, because we're looking at a much earlier stage than that. Because, for example, this is going to be the cerebral cortex, where you - . What I was going to say –. It may be that other people that you talk to would argue about this, but I would imagine –. That's going to be the cerebral cortex – and that's where, as you develop into an adult, all the different sulci and gyri – they are a picture of the adult - we're getting to the adult brain! 0.35.23

So usually the map that people have of functions of the brain - the cerebral cortex is really showing, and that's where all our thinking power comes from. But I don't know how much of behaviour – certainly in lower animals too, but primates, behaviour would also be to do with reflex actions. 0.35.51

Holdsworth: Oh I see.

Lindsay: And so how much of our behaviour would also be in our cerebellum, affecting how we move? And there may be lots of other places. 0.36.03

Holdsworth: In cognitive neuroscience people are looking at real-time imaging of the brain in action. I mean, that's certainly an investigation of behaviour. 0.36.16

Lindsay: Yes.

Holdsworth: Clearly, there's no doubt about it.

Lindsay: Yes. My hesitation was whether they were only looking at the cerebral cortex and other areas of the forebrain. 0.36.27

Or whether you might also say or argue that other areas of the brain that were more to do with control of motor – like the cerebellum – control of our movement might also be involved in behaviour. I don't know the answer to that question. I don't know the answer to that. 0.36.53

If we just think of the cerebral cortex, this is what this is going to develop into, but you can see there's very little there. We're at a very, very early stage. So there isn't anything at the time, and this is near the end of embryonic development. There isn't

anything here that is directly going to - or that you could directly study behaviour. 0.37.20

What's happening here is that the cells are dividing. They're proliferating in the layer that then will produce all the neurons that will go to make the cerebral cortex. 0.37.32

Holdsworth: Right.

Lindsay: If there was a malfunction in one of these genes that was then important for a particular layer of neurons or a particular type of neuron that then at a later stage would be involved in particular behaviours, it might well be that going back and looking at the expression at these early stages and asking -as people are - . About what controls proliferation, what controls the cell division in different regions and in general, would be important. 0.38.07

But it would be, if you were building an argument or finding out it would be a kind of bottom layer of the argument. 0.38.16

And you'd need lots of other information to link that cell proliferation, for example, to a change in behaviour. 0.38.25

Holdsworth: But let me put the question in a different way. If somebody came to you and said, when it comes to the development of the brain – the human brain – the DNA provides the 'blueprint' -

Lindsay: Mm. hm.

Holdsworth: - you would argue with that? 0.38.55

Lindsay: No. The DNA does provide the blueprint. 0.39.00

Holdsworth: Mm.

Lindsay: But what we're looking at is how that blueprint is expressed at the very early stages when the brain is - . I have to keep thinking of different words for meaning 'development'. Developing the developing brain! So the DNA is underlying this and can select choices about which genes are switched on or not in particular cells or particular places. 0.39.47

Holdsworth: Yes.

Lindsay: Switching on - that happens at DNA level.

Holdsworth: Right.

Lindsay: OK?

Holdsworth: But what releases the switching on and the switching off? Surely a multiplicity of causes. 0.40.01

Lindsay: Of factors. Yes. Including proteins and - . I mean, that multiplicity of factors is not known in full or anywhere near, because what you study or what you think is – I could say for one gene which is switched on here maybe there may be another transcript, another factor that affects its – how it's regulated, how it's controlled. 0.40.35

Holdsworth: Right.

Lindsay: But what you do is you simply move the decisions further back in development in a way because you keep coming to the question, well, OK, what switched that gene on or what caused that? 0.40.52

Holdsworth: Right.

0.40.52 [*Brief telephone interruption.*] 0.41.16

Lindsay: I'm not sure if that answers your question, because some of the things that start off development are to do with the position of fertilisation, and there are already protein and RNA in the egg. And there's a kind of a cascade of things that happen, so that by this time there are differences in these transcription factors, or these factors that regulate other genes. 0.41.44

It's those that are then switching on or switching off genes, not usually as single factors, but as groups of factors. 0.41.53

Holdsworth: They could be signals coming from other cells?

Lindsay: Yes. In fact there will be signals from other cells, signals from within the cell, signals to do with - . And the signals from other cells will be of proteins, the equivalent of hormones - signalling molecules. 0.42.13

Holdsworth: When people suggest that there are genes for behaviour, how could that work, then? I mean, that - . At what point - ? That would be part of the ontogeny of the organism. That would mean the expression of genes in early development. 0.42.54

Lindsay: Well, there are genes that are involved in getting a structure to its adult form, and then there are genes – which may be the same ones or may be different ones – but there are genes that are involved in that adult structure functioning. 0.43.11

Holdsworth: Right, I see what you mean.

Lindsay: And so the genes that we need to develop the brain may not be the same genes, or may only be some of the genes we need to think.

Holdsworth: Right, but for example – and it's an open question, but I mean some people are interested in the idea of genes for personality traits like extroversion, something like that. I mean, I wonder at what point in this whole process one would expect these genes to express themselves, and would your techniques provide evidence one way or another? 0.43.52

Lindsay: Not at the stages we're looking at. So unless the - . I think you would need to look much later in development. It might well be that there's – that there are some of the same genes. And it might well be that what you do is say that - . You were mentioning MRI? 0.44.20

Holdsworth: Yes, yes.

Lindsay: And functional MRI?

Holdsworth: Yes.

Lindsay: Where you can see how people react to different images or tasks or whatever. And one of the interesting things I was hearing at the meeting I was at was that people have looked at individuals with Turner's Syndrome which is 45, X. They lack an entire X-chromosome. And have shown that – or have preliminary evidence that – these women have less ability to detect expressions of fear. If they're shown a whole range of pictures - that they don't recognise fear in the images that they're being shown. 0.45.16

Holdsworth: Right.

Lindsay: That would suggest that there might be a gene or genes , or an interplay of genes on the X-chromosome, that would have an effect on the area in the brain that is to do with fear recognition and possibly feelings of fear, although obviously that's not something that's been worked on. 0.45.38

So at that level you could then say, OK, let's look at the development of that particular region of the brain and take it back through its development and see what genes are important, but that's really what I meant about it being – providing almost the substrate or the basis for your argument rather than being able to ask questions directly. 0.46.04

Because the other thing you could do is these kinds of experiments in other animals and then ask, OK, we think this gene varies in a particular way when a mouse behaves in one way or another. Is that a gene that's expressed in the right place in humans? 0.46.27

Holdsworth: I see.

Lindsay: You might then ask those kinds of questions. 0.46.32

Holdsworth: Right.

Examination of the criteria 0.46.35

Criterion 1: '*Does the research cover all hominids or only* Homo sapiens*?*' 0.46.48

Holdsworth: So the first question was 'Does the research cover all hominids or only *Homo sapiens?*'

Lindsay: Only *Homo sapiens*. 0.47.01

Criterion 2: '*Is behaviour studied in the ecological setting – or in the laboratory or clinic?*' 0.47.02

Holdsworth: 'Is behaviour studied in the ecological setting?'

Lindsay: No. Nor in the laboratory, or clinic. Because behaviour as such is not - we're not studying.

Holdsworth: No. Fair enough. 0.47.22

Criterion 3: '*Is the focus on species-typical traits or on individual differences?*' 0.47.23

Holdsworth: Is the focus on species-typical traits or individual differences?

Lindsay: If we were - . It would be species-typical. So if we were then taking information from another stage in development in human life-span or from other animals we would go looking for something that's generally true in humans. 0.47.46

Holdsworth: Right.

Lindsay: We wouldn't be looking - . There may well be differences – individual to individual, or embryo to embryo - but we wouldn't have sufficient numbers there be able to pull those out. 0.48.00

Criterion 4: '*Does the research typically draw on the findings of genomics?*' 0.48.21

Holdsworth: So back to the series: 'Does the research typically draw on the findings of genomics?'

Lindsay: Yes, because that's where we find the information about genes - particularly the gene sequences, yes. 0.48.34

Criterion 5: '*Is the research on genes or other DNA? If 'other': mtDNA or Y-chromosome?*' 0.48.34

Holdsworth: And another question – are we talking about genes and/or - .

Lindsay: We are not really looking at mitochondrial DNA. So there are genes in human nuclear DNA. Y-chromosome? We might do, we haven't as yet. We have certainly looked at a number of genes on the X-chromosome. And that's because a number of those underlie different mental retardation syndromes. 0.49.10

Criterion 6. '*Is there research on the DNA of non-human/hominid species? If so, animals or plants?*' 0.49.10

Holdsworth: Right. Is there research on the DNA of non-human species?

Lindsay: Not directly within my group, but yes. There is a lot of mouse developmental genetics. Yes. Mouse, zebra fish, in terms of the brain chick is a widely used experimental model, and also - . 0.49.38

Holdsworth: Chicken chicks?

Lindsay: Chicken chicks, yes. And rat often people use. 0.49.46

Holdsworth: Mm, hm. Plants perhaps not relevant here.

Lindsay: No. 0.49.52

Criterion 7: '*Is there research on other biomolecules? If so, proteins or other?*' 0.50.54

Holdsworth: Is there research on other biomolecules?

Lindsay: Yes. Proteins and now other kinds of – there's now non-coding RNA. 0.50.09

Holdsworth: Non-coding RNA.

Lindsay: And that's very recent in terms of recognising this as an area of importance for regulating gene expression. 0.50.25

So there's a point of turning a gene on and off, that's at the DNA level, but then fine-tuning or fine-controlling that – the RNA, and turning the RNA into protein - that can be done by non-coding RNAs, and in fact the turning the gene on and off at the DNA level, we're finding it's being done by RNAs as well as by proteins. 0.50.58

Holdsworth: Right. That is interesting.

Lindsay: Have you heard of micro-RNAs? So these are whole sets of RNAs that people are just discovering, and they are proving to be really - . 0.51.11

Holdsworth: 'Micro'-RNAs.

Lindsay: 'Micro'-RNAs. And these are non-coding RNAs, but they regulate specifically the activation of genes. I don't know if they regulate turning some genes off, they may do, I just don't know. 0.51.32

Criterion 8: '*Does the research use environmental markers?*' 0.51.32

Holdsworth: Right. Now does the research use environmental markers? I don't see that as being relevant.

Lindsay: No we don't. We would certainly like to be able. I'm sure we will in the future try and look at gene-environment interaction, but it is difficult to do that. 0.51.57

Holdsworth: How could that conceivably emerge in your area? 0.52.05

Lindsay: I think we would need to generate - if we were doing it in human - cell lines – from particular areas of the brain say, and then we could ask whether exposing these cell lines to particular changes in glucose, or oxygen - or you could ask about –

Holdsworth: I see, yes.

Lindsay: - these kind of environmental factors. I suppose then you could ask about pesticides, or things that you might worry would have toxic effects during development. 0.52.43

Holdsworth: Right.

Criterion 9: '*The main concern is phylogeny or ontogeny?*' 0.52.45

Holdsworth: On the next page, 'Is the main concern phylogeny or ontogeny?'

Lindsay: Ontogeny.

Holdsworth: That's clear.

Criterion 10: '*Does the research draw on fossil evidence?*' 0.53.0

Lindsay: And we don't draw on fossil evidence! A fossil in situ hybridisation – I mean, yes! Maybe. Maybe one day! 0.53.10

Criterion 11: '*Is Newtonian mechanics relevant to the research?*' 0.53.13

Lindsay: Newtonian mechanics. Well, that's a possible yes.

If we had a way – and we don't do this, but one of the things that's obviously very interesting, is what regulates or shapes growth. And from the brain perspective the starting – or the point where we start looking at is a tube. And that tube then bends at specific places, and also structures grow out of it. 0.53.56

Holdsworth: Right.

Lindsay: So these lateral ventricles, so these structures here – this is kind of the remains of the tube where it's been bent, and these lateral ventricles that are going to, in human, expand enormously – actually to grow right up and cover the whole of the rest of the brain basically, apart from the cerebellum – apart from this bit right at the back. 0.54.18

I'm sure that that the forces – that there will be forces of just physically pushing out and expanding – and that the role of pressure will make a difference in how rapidly – and maybe the shape – that these lateral ventricles expand. 0.54.45

And we know that's true, because if with some disorders where the skull - because usually the skull in humans – well, the skull - there's room for expansion. Because after babies are born, the skull still keeps expanding, which allows the brain to expand. 0.55.02

So if you have a situation where the skull fuses early, there isn't any further, I mean, the brain stops growing. 0.55.12

And so there is an interplay between - .

Holdsworth: Is that something that happens?

Lindsay: Yes. So there are disorders where the brain sutures fuse, and then the - . 0.55.24

Holdsworth: Could you mention the name of such a disorder?

Lindsay: Craniosynostosis. And there are a number of these. And the effect on brain development is that usually and unfortunately the patients are mentally retarded. So the brain doesn't develop properly. So the mechanical and physical forces are important. 0.55.52

And there may well also be an evolutionary dimension. In the sense there must have been a period when it was – when obviously the brain expanded, but there must also have been a mechanism to allow the skull to expand as well. 0.57.09

Now in fact in human I think a lot of human characteristics it's now recognised particularly in the head and the face are – it's as if we're not – neonatology? Neo- ?

Holdsworth: Neoteny.

Lindsay: Neoteny – that's the word. Yes. So it may be that – well, presumably in chimps also the skulls, the sutures don't fuse. So maybe they just didn't fuse for a longer and longer period in development, which then allowed the brain to expand. 0.57.44

Holdsworth: Right.

Lindsay: Yes. So I'll stop talking about that, since that's well off my area of expertise. I'm at the hand-waving stage! 0.57.50

Criterion 13: '*Does the research use cultural markers, e.g., surnames?*' 0.57.52

Holdsworth: Well, I don't know about the next one: 'Does the research use cultural markers?'

Lindsay: No.

Criterion 12: '*Is the research intended to have a clinical application?*' 0.58.22

Holdsworth: 'Is the research intended to have a clinical application?'

Lindsay: In the very long term, it is. One would expect that the expression patterns that we see might help to inform the mechanisms behind different aspects of brain development, but it's not directly clinical. 0.58.47

Holdsworth: But you are already contributing to the understanding of disorders.

Lindsay: Yes. We are looking directly at genes that are mutated in human disorders. Yes. 0.59.04

Criterion 14: '*Does the research offer economic or social benefits?*' 0.59.06

Holdsworth: 'Other economic or social benefits?' I'm not doing an audit here, but it's interesting.

Lindsay: Social benefits I think would be at the training level. So the three-dimensional models and the expression patterns and the capturing of expertise within the database or within the anatomy painting – all of that is to do - we do use on an ad hoc basis for training people, and you can – we would hope to do more of that. I think training and, yes, capturing expertise, would be the benefits. 0.59.52

General and concluding discussion 0.59.53

Holdsworth: Right. We're running out of time. Just to go back to the question I was asking you about behavioural genetics. In that context people often speak of the concept of the QTL. Is that pertinent to your work? 1.00.12

Lindsay: Quantitative Trait Loci.

Holdsworth: Yes.

Lindsay: Yes – or 'locus'. It may be that as we have more sophisticated ways of measuring expression patterns that we might be able to look at 'quantitative' because at the moment this is not really quantitative. 1.00.50

Holdsworth: It's either 'on' or 'off'?

Lindsay: No, the genes are quantitative. You can see a very nice gradient here. And you can see different levels - . The genes have very specific quantitative differences, cell to cell. What's difficult is for us to measure those reproducibly and accurately. So I would be quite happy saying on this slide the expression pattern – the expression of this gene is high in this area and low in that area. 1.01.21

But if I look from section to section, or I look from embryo to embryo, if I could measure that and say there were - I don't know – 10,000 copies of RNA of this specific gene in these cells. Because of experimental variation I couldn't be sure that that there were 10,000 copies of the mRNA here. I couldn't be sure that the measurements which generated these figures were meaningful. 1.01.51

Holdsworth: Is that an in-principle impossibility, or something which, with time and further investigation could be resolved? 1.01.56

Lindsay: I think that with time it might be. Because I think one thing that would help would be if we could look at the expression of a known marker on the same section, so you had a reference, a standard that you could compare it to. 1.02.13

It may also be that if you did do individual dissections of cells, and individual dissections of eggs, small groups of cells, then you could also get standards that you could superimpose on these kinds of images. 1.02.29

So I think that's a technological development, rather than an impossibility. But that is a digression. When people talk about Quantitative Trait Loci, often what they're measuring are the differences among instanced individuals. 1.02.52

Holdsworth: Yes.

Lindsay: They're looking for tall people or small people – those are the quantitative traits. Whereas this is measuring differences within an individual. And it may be that, part of the difficulty is being able to look at sufficient numbers of these individuals to draw any sensible scientific conclusion. 1.03.15

Holdsworth: Right. Thank you.

Lindsay: I don't know whether we'll be able to do that. 1.03.21

Holdsworth: We've dealt with evolution. That sounds a bold claim, doesn't it!

Lindsay: Yes! In those five minutes – yes! 1.03.35

Holdsworth: You do work on the development and function of the motor system.

Lindsay: Yes. 1.03.42

Holdsworth: Could you just say a word about what you're doing?

Lindsay: OK. Well that is a direct link with particular disorders. So patients who have cerebral palsy have either – it's not clear – there's not a single genetic insult, so there's not a single gene that's mutated and leads to cerebral palsy. So it's a complicated, or complex disorder. 1.04.11

And it can have environmental as well as - purely environmental, or environmental plus genetic causes. 1.04.23

Holdsworth: What sort of environmental cause are we talking about?

Lindsay: If there's hypoxia at the time of birth – so there's a – the baby doesn't have enough oxygen during birth. Then that can lead to cerebral palsy. Or if there's a bleed in the brain, again that cuts off oxygen supply to a particular region of the brain. And the – So it's not a straightforward - . It's definitely not a Mendelian genetic disorder. It's a complex of causes. But what happens – or the particular problem – the motor cortex and the particular nerve tracks that controls motor – our ability to move - are affected. 1.05.22

And that system seems to be particularly sensitive to the insults that cause cerebral palsy. And so what we're looking at are what – I mean, very straightforwardly in terms of gene expression – as you can see here – here – there aren't any sulci and gyri. There aren't very many features at these early stages. 1.05.42

Holdsworth: Right.

Lindsay: And in fact there aren't very many features on this developing cerebral cortex until quite late in development. About six months of development and further on. 1.05.57

Holdsworth: Right.

Lindsay: And so it's not – if you look at that - . Where on an adult brain - . Here. (*Looks at a paper*). So this is rat, and this is [...] in a human. Where in an adult brain you can say, OK, I recognise this sulcus here, and this is the central sulcus, and so I know that the motor cortex is here, and I know the somatosensory cortex is here. So if I'm looking for some problem or want to look at gene expression, - and it's something to do with motor cortex - I know I'm to look here. 01.06.34

Holdsworth: Mm, hm.

Lindsay: If you imagine that this is a smooth embryonic or foetal cerebral cortex you don't know where to look. You don't know whether they're developing in proportion, so that the motor cortex is still sort of in the middle, or whether in fact some areas develop first, and then there's a lot of growth, or – so, what we were looking for, and are still looking for, are genes that are expressed differentially between the back and the front and the middle, so: can we see regional expression of development of the cortex? 1.07.13

And then also to see whether we can identify some genes that we might say 'OK, this gene is important in motor cortex at later times', can we kind of follow its expression pattern back in time, and so we can say this bit *is* the motor cortex, and therefore what other things are happening at that time – where is it connected to, has it got its - is it sending out its axon, has it got its axon, so we would - we would kind of know where we were. 1.07.45

That's a crucial and a very difficult thing to do with human brains is: knowing where you are. 1.07.54

Holdsworth: Right. 1.07.55

Lindsay: Because in mouse what you could do is you could say, OK, this bit's motor cortex, is connected to this axon track, and so if I put a dye in, I can follow this axon track back to where it connects. 1.08.12

Holdsworth: Right. 1.08.12

Lindsay: In human, the scale of the brain is too big, really, to do that. It's just that – again, with the dyes that we have, we can't do that. Maybe in time we will. 1.08.27

Also, with human obviously - well, with mouse what you can do is you can mark particular cells genetically in transgenic mice, and then follow those cells through development. We can't do that with human. 1.08.45

So there's different - . You can follow the lineage of a particular cell in mouse, or group of cells, and in humans we have to deduce things, or try and work things out by other means. 1.09.00

Holdsworth: Further knowledge in the area of the motor cortex and so on will contribute to our understanding of behaviour – behavioural ontogeny? 1.09.14

Lindsay: Yes, it will, because I'm sure motor cortex as well as the frontal, and the, the sort of 'thinking' cortex, I'm sure that, under control, that must – the control of our movements, and the connection between control of our movements and the thinking part of the brain must have – must be important in behaviour, because a lot of behaviour involves moving our bodies. 1.09.49

Holdsworth: And another important thing is sensation.

Lindsay: Yes.

Holdsworth: Perception. Is this part – at the moment part of your [work]? 1.10.00

Lindsay: [*Pointing to a diagram*] Well, the somatosensory cortex sits just on the other side of that line! I mean, there is so little known about gene expression patterns in the developing brain, or gene expression in the developing brain, and relating that to the development of particular areas of the brain in human. 1.10.25

There is a lot of work in mouse. There is a fair amount of work in monkey, and it depends how well the results translate from monkey to man. Some of the results from mouse will translate into human, but much of what you might – particularly for behaviour - that you might be interested in, you wouldn't be able to look at in mouse, and that's one argument why people look in monkey. 1.10.55

Holdsworth: Have you or other workers in your field been involved in the 'Genes to cognition' programme?

Lindsay: I haven't. 1.11.05

Holdsworth: Is there a natural link, or channel of communication? That's what I'm getting at. An affinity.

Lindsay: I think the channel would be - would actually be from the – from disorders where behaviour or cognition's affected, I suppose like mental retardation, mental disability. That often affects cognition in a really global way. 1.11.50

But we are looking at a whole range of different genes that underlie – or, when they're mutated, when they're faulty - they underlie a whole range of different disorders that involve mental retardation. 1.12.05

And I can imagine - and this is the hope - that when you put all of that data together you might begin to see patterns of particular places – I think, particular places that are susceptible – say - at particular times in development. 1.12.26

Holdsworth: Oh, yes. 1.12.28

Lindsay: Places where things are proliferating, particularly for particular pathways, say, or types of gene- actually, it looks as if all sorts of different genes if they're damaged can cause mental retardation. 1.12.46

So that of itself tells you that things are very complicated, and if you damage - in a whole variety of ways - you're going to cause mental retardation. 1.13.01

And it may – where I could imagine – actually, I *have* been involved. I'm just thinking about – one, sort of - what I was going to say was, what I could imagine, is that, as the tools for discriminating the behavioural phenotype get finer, and get refined, then you could ask more specific questions about gene expression. 1.13.33

And I – there was a family where we were involved in the mapping where the gene was to be found. And then another group discovered what the gene was, and then we were involved in going back and looking at expression patterns. 1.13.54

But one of the things that the – we wanted to do was then to look in that family, and see whether you could - you could more finely say what - what aspects of cognition were affected. 1.14.10

Holdsworth: Right. 1.14.12

Lindsay: Now often with X-linked disorders the males are very badly affected, but the carrier females are not, and so you can't – you really can't say very much if somebody is very badly affected, but if you're affected to a lesser extent then you can ask if it's their spatial awareness, is it their maths ability, is it their speech - what aspect of their ability – their cognition is affected. 1.14.44

And you could say that, I mean, that whole area is getting more sophisticated in a way as well, and that might give us some specific things to look for. 1.14.57

Holdsworth: Mm, hm. Is there a field of the energetics of gene expression? 1.15.08

Lindsay: There might – the differing amounts of energy that are needed for cells to function, or to -?

Holdsworth: Yes, and -

Lindsay: Or the energy cost of gene expression? 1.15.22

Holdsworth: That's right. A quotation I came across was that in protein synthesis, ribosomes assemble on the mRNA - . Ah, I'm looking at the wrong quote. I've lost the quote. How annoying. That the proteins fold in the most energetically optimal way. 1.15.50

Lindsay: I think there's a drive towards systems biology and to try and integrate information from lots of different specialities or disciplines. 1.16.13

But also to – if you're looking at a particular tissue or – say, heart or brain - to try and not simply look at one small bit or one small cell set, or indeed one approach to a problem, but to try and add your information to other people's information that makes more of a whole, and I could imagine that energy requirements –. 1.16.41

I mean, there is 'metabolomics', which must also be to do with the kinds of enzymes that are there for efficient or less efficient use of – or generation of energy. 1.16.54

So I can see that that might be, or is likely to be something in the future, but it's not something that I have any knowledge of. 1.17.05

Holdsworth: Right. Well, thank you very much. My final question would be: is there some natural positioning of your discipline vis-à-vis others. Do you have natural 'neighbours' in the conceptual map of this area? 1.17.23

Lindsay: I think the – I personally have come from human genetics. – and human molecular genetics. So I think our – because we are interested in what's important in humans I think clinical genetics – medical genetics – so that these are our natural neighbours. 1.17.53

Holdsworth: Sorry – human genetics and medical genetics?

Lindsay: Yes. They're to do with patients. 1.17.58

Holdsworth: Yes.

Lindsay: I think our – then there are disciplines that we need because – because of the information we're generating, so the imaging and bioinformatics and these computer- or software-based physical sciences. We need these because – in order to analyse our data. So those are not biological neighbours, but they're neighbours of – to do with handling the data that we have. 1.18.36

Holdsworth: Right. The OPT technique. Who developed that?

Lindsay: That was actually a biologist who was interested in limb growth and wanted a technique that would allow him to follow limb growth. But he was working in Edinburgh in the MRC human genetics unit with a group where there was already a very strong collaboration between a computing group and a developmental biology group. 1.19.12

And so he was able to grow out of that and to try this - or generate this Optical Projection Tomography technique. 1.19.24

Holdsworth: Mm, hm. I'd like to go on, but I've taken more than my share of your time already. I apologise for that. 1.19.31

Lindsay: No problem.

1.19.43

Holdsworth: Well, it's very, very kind of you. Thank you very much.

1.20.24

9. Research interview with Professor Robin Crompton – Edited Excerpts

Interviewed: Professor Robin Huw Crompton, Primate Evolution and Morphology Group (PREMOG), Department of Human Anatomy & Cell Biology, School of Biomedical Sciences, University of Liverpool.
Interviewer: Richard Holdsworth, PhD candidate in the Economic and Social Research Council (ESRC) Centre for Genomics in Society, Egenis, University of Exeter.
Date and time of interview: Wednesday, 11 July 2007, 11.00 (UK time).
Place: Liverpool and Neuhäusgen, Luxembourg. Skype conversation linking Professor Crompton in Liverpool and the interviewer in Luxembourg (Recorded on DS-2300 DVR and also on Powergramo software).
Total length of the recording: 28 minutes 34 seconds (Powergramo). Timings in the transcript relate to the WAV file created from the Powergramo recording.

The interviewee's description of the research 0.02.04

Crompton: Well, very briefly, I'm interested in the evolution of our locomotor system - that is, walking and other ways of moving around for our immediate relatives. And I'm interested in this from the fieldwork aspect, and also laboratory studies of biomechanics and locomotion.

General discussion of concepts and methods

Holdsworth: Right, thank you. I've seen that evolutionary biomechanics is often talked about as a way of explaining the form and function of organisms. What do you think of that description? 0.02.48

Crompton: That's fair enough. I'm not sure that every kind of biomechanics researcher would use the same way. My meaning of biomechanics is quite specific and concentrated, and that's not always the case. People tend to sometimes use the word biomechanics interchangeably with 'function' which I don't think is appropriate. It's not exactly the same thing

Holdsworth: That's interesting. A point which has occurred to me in my reading is that the term 'function' is often used rather vaguely, and in evolutionary biomechanics, and in some other areas it could be replaced by the term 'work'. 0.03.37

Crompton: Well, when I use the term 'work' I'm using it very specifically. In fact, you can't see it, but I'm just writing a talker for a paper I'm giving next Monday, and there we do use the term 'work' in its Newtonian sense, purely. In the sense of Newtonian mechanics. And I'm not sure that a lot of people who use the word 'biomechanics' are all that familiar in my field with Newtonian mechanics. I'm not

a physicist, I'm an anthropologist, but at least I've learnt enough to be able to, I hope, use words in an appropriate sort of way.

Holdsworth: Yes, but that's interesting because you couldn't use the term 'work' to cover every meaning of the term 'function'.

Crompton: No, certainly not.

Holdsworth: You couldn't use it to cover every meaning of the term 'behaviour'.

Crompton: No.

Holdsworth: But in specific cases it may be the appropriate term to use.

Crompton: Yes, absolutely. I mean, for example, this paper I'm about to give, this is actually on prosimians, comparing the work done in crossing between two trees by leaping across to the work done against gravity if you climb down the tree, cross the ground and go up the next tree. So, that's a very specific use of 'work'. 0.05.23

Holdsworth: In what species is that?

Crompton: Oh, about five different species, actually. I started off working with prosimian primates – like bush-babies and lemurs and things like that – and I still do. But I also look at human evolution. We've just had a paper in - well, a couple of papers - one in *Science* looking at work, to some extent, in orangutans, and so on. So these are terms which I use on a daily basis, but not necessarily just about humans.[417] 0.05.59

Holdsworth: Right. I've often been struck by the way that authors avoid using the term 'work'. You probably won't want to comment negatively on somebody else's book, but just to take one example that struck me coming from the outside. This year I read the book by Chris Stringer and Peter Andrews called *The complete world of human evolution*, and nowhere do they mention the term, or the concept 'work'.[418] I found that strange.

Crompton: They come from a very different tradition than I come from.

Holdsworth: How would you describe that?

Crompton: Well, Peter Andrews in particular is quite an old-fashioned comparative anatomist. Both of them are really concerned with relationships amongst animals,

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[417] Thorpe, S.K.S., Holder, R.L. and Crompton, R.H. (2007): 'Origin of Human Bipedalism as an Adaptation for Locomotion on Flexible Branches', Science, Vol.316, 1 June 2007, pp.1328-1331. See also: Begun, D.R., Richmond, B.G. and Strait, D.S. (2007): 'Comment on "Origin of Human Bipedalism as an Adaptation for Locomotion on Flexible Branches"', Science, Vol.318, 16 November, p.1066d.

[418] Stringer, Chris and Andrews, Peter (2005): The complete world of human evolution, London, 2005.

not function at all. It's not their strong point. What they actually do these days is phylogenetics and systematics. Function is not their area of research at all. They're concerned with phylogenetics, systematics, relationships - establishing relationships amongst fossil species and things like that. 0.07.31

Holdsworth: Right. In the theories of human behaviour that come one's way looking at the literature on – how shall I put it? – the 'biologicisation' of the study of human behaviour, there is a lot of attention paid to what you might call the 'propagation calculus', the chances of successful reproduction, the spread of the genes.

Crompton: Yes.

Holdsworth: There's comparatively little on the bioenergetic calculus – energy conversion. 0.08.09

Crompton: Not that many people in my field have adopted a biomechanical or energetic perspective, so that, yes, it's unusual.

Holdsworth: When you say 'in your field', do you mean anthropology in general?

Crompton: I mean anthropology. Yes, sorry – my broader field in biological anthropology as a whole.

Holdsworth: I was particularly struck by your paper on 'The role of load-carrying in the evolution of modern body proportions' with Wang.[419] And the inferences from the skeleto-muscular data about an organism to its behaviour in the sense of tool utilisation or tool transport. Have you done much study on tool utilisation? 0.09.16

Crompton: Tool utilisation - no I haven't. I've actually done a little bit of work with a colleague on the Acheulean industry and really looking at form and the scaling of form in handaxes in Africa. So I've done a little bit of archaeology, but not a lot.

Holdsworth: I'd like to follow that up. Who's the co-author?

Crompton: John Gowlett.[420]

Holdsworth: Thank you. Your article on 'bent-hip, bent-knee' walking in humans is another case in point. You talk about the 'metabolic costs'.

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[419] Wang, W.-J. and Crompton, R.H. (2004): 'The role of load-carrying in the evolution of modern body proportions', *Journal of Anatomy*, Vol. 204, No. 5, May 2004, pp. 417–430.

[420] Professor John A.J. Gowlett, Professor of Archaeology and Evolutionary Anthropology, School of Archaeology, Classics and Egyptology (SACE), University of Liverpool. See the following articles: Crompton RH, Gowlett JAJ (1993) Allometry and multidimensional form in Acheulean bifaces from Kilombe, Kenya. *J. Hum. Evol.* 25, 175–199, and Gowlett JAJ, Crompton RH (1994) Kariandusi: Acheulean morphology and the question of allometry. *Afr. Archaeol. Rev.* 12, 1–40.

Crompton: Yes.

Holdsworth: Is this another case where you're rather unusual in adopting this approach? 0.10.15

Crompton: Yes. My 1998 paper – this is the 1998 paper I presume you're talking about[421] - that one actually wasn't able to even predict metabolic cost. That was just an estimate from mechanical cost. These days what we're doing - we had a paper with Bill Sellers in *J. Royal Soc. Interface* - we're actually using a different kind of dynamic modelling with which we can actually predict metabolic cost, and actually we've done it for walking, and now for running. So we can actually verify. We can actually do studies, model human walking and running and compare predicted costs to experimental costs measured in the lab. So things have moved on an awful lot since that 1998 paper. 0.11.03

Holdsworth: Actually I was thinking of the paper with Carey in 2005.[422] 0.11.07

Crompton: Oh right, OK. Well that was the follow-up to the 1998 paper. Because the first reaction to the 1998 paper was to say: 'Oh, it's just a computer model, what's it go to do with reality?' Tanya Carey did a PhD with me in which we actually measured the costs of 'bent-hip, bent-knee' walking in humans – which was obviously the closest we could get.

Holdsworth: Right. Looking ahead, do you see an even bigger contribution from your perspective to anthropology in the future?

Crompton: Well, I hope so! Ha, ha! I've got a few years left before I start to take retirement! Yes, well the next big exercise is to – well, there's two things – one is to move on to looking at the evolution of running in a similar sort of way. So that's probably for the next five years or so. That's one direction we'll be going in. Also, looking at the costs of moving on compliant supports. You know, I think [the evolution of upright bipedal walking was in] arboreal contexts in the trees. So it's obviously relevant to look at compliant supports. If our ancestors started upright bipedal walking in the trees, not on the ground - which is what I think - then we started doing it in a context of moving around on bendy branches. So if you tread on a branch, then you are actually imparting energy to the branch. If it's a small branch - small-diameter branch - then the branch can bend, and you're losing energy. And

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[421] Crompton, R.H. , Li, Y. , Wang, W., Günther M. and Savage, R., (1998): 'The mechanical effectiveness of erect and 'bent-knee, bent-hip' bipedal walking in *Australopithecus afarensis*,' Journal of Human Evolution 35: 55-74.

[422] Carey, T.S. and Crompton, R.H. (2005): 'The metabolic costs of 'Bent-Hip, Bent-knee' walking in humans' Journal of Human Evolution 48: 25-44.

unless the rebound happens within your walk cycle, you lose the energy.[423] So that's one of the things we need to look at. 0.13.05

Holdsworth: Right. So you've described research on posture and gait. Have you done work on the biomechanics of the hand?

Crompton: No. Other people have done a bit. We're studying the foot in quite a lot of detail, but the hand, no, we won't. Can't cover everything, and it's, you know - got other things to do.

Holdsworth: Of course. But can you mention any other researchers who are working on it?

Crompton: Yes. There's a group in Arizona. Mary Marzke. Do you know of her?[424] And she's got or had some students, one of whom is now working at – whose name escapes me, I'm afraid – the George Washington University in Washington. So Marzke's group – they have done a little bit of biomechanics of the hand.[425] 0.14.19

Examination of the criteria

(*Holdsworth begins to take Crompton through the Criteria Graphic.*)

Holdsworth: The general idea behind this is that - is to disclose – presuming it exists – the diversity between different disciplines, by using these criteria.

Crompton: Yes. 0.14.45

Criterion 1: '*Does the research cover all hominids or only Homo sapiens?'*

Holdsworth: Does the research cover all hominids or only *Homo sapiens*?

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[423] See: (1) Thorpe, S.K.S., Crompton, R.H. and R. McN. Alexander (2007): 'Orangutans utilise compliant branches to lower the energetic cost of locomotion', Biology Letters doi:10.1098/rsbl.2007.0049, and (2) Thorpe et al. (2007), op. cit.

[424] Professor Mary Marzke, Professor Emerita, School of Human Evolution and Social Change, Arizona State University.

[425] Professor Marzke contributed to the April 2008 issue of Journal of Anatomy (see also footnote 12 below). In that issue, she was a co-author of the review article: Tocheri, Matthew W.; Orr, Caley M.; Jacofsky, Marc C., and Marzke, Mary W. (2008): 'The evolutionary history of the hominin hand since the last common ancestor of *Pan* and *Homo*', Journal of Anatomy, Vol. 212, No.4 (April 2008), pp. 544-562. Professor Marzke's other recent publications include: (1) Marzke, M.W., Shrewsbury, M. S., & Horner, K.E. (2007). Middle phalanx skeletal morphology in the hand: Can it predict flexor tendon size and attachments? *American Journal of Physical Anthropology, 134*(2), 141-51, and (2) Marzke, M.W. (2005). Who made stone tools? In V. Roux and B. Brill (Eds.), *Stone knapping: The necessary preconditions for a uniquely hominin behaviour.* Cambridge: McDonald Institute for Archaeological Research.

Crompton: My research?

Holdsworth: Yes.

Crompton: Yes. All. Other hominids, yes, obviously.

Criterion 2: *'Is behaviour studied in the ecological setting – or in the laboratory or clinic?'*

Holdsworth: Now, is behaviour studied in the ecological setting? 0.15.02

Crompton: 'Yes', I suppose, is the answer to that. For example, quite a lot of our – the work about the origins of human upright walking has been informed by studies of orangutans in Sumatra. We had a paper in *Science* at the beginning of this month which is actually looking into that.[426]

Holdsworth: Yes, I saw the reports of that.

Crompton: Yes. OK. So 'yes' is the answer to that.

Criterion 3: *'Is the focus on species-typical traits or on individual differences?'*

Holdsworth: Now, is the focus on species-typical traits or on individual differences?

Crompton: Species-typical, I'm sure. Largely. Yes.

Criterion 4: *'Does the research typically draw on the findings of genomics?'*, and
Criterion 5: *'Is the research on genes or other DNA? If 'other': mtDNA or Y-chromosome?'*

Holdsworth: Does the research typically draw on the findings of genomics?

Crompton: I'm not sure if you asked me to define genomics I'd be able to help. To the best of my understanding of it: slightly. But I'm really not sure that I know what genomics actually is. 0.16.07

Holdsworth: Well, if we were talking to somebody in behavioural genetics they might be talking about genes, but people in palaeoanthropology are tracing lineages in mitochondrial DNA or on the Y-chromosome.

Crompton: OK, if we're talking at that level, I suppose the answer is yes, inasmuch as for example I've just been writing a big review of the hominoid - I mean, the ape and

[426] Thorpe et al. (2007), op. cit.

human - locomotive system, and obviously the recent information on genetic separation dates of humans and chimpanzees is relevant to that, and it's mentioned in the paper, but that's about as far as I take it.

Holdsworth: When and where will that be published?

Crompton: Well, it's coming out in *Journal of Anatomy*, but when, sorry, I'm not sure, but it's the end of this year.[427] 0.17.06

Holdsworth: *Journal of anatomy*.

Crompton: Yes, there is a special issue on human evolution and modelling the last common ancestor of humans and chimpanzees, edited by Bernard Wood[428] and Sarah Elton.[429] And it's supposed to be coming out later this year in *Journal of Anatomy*.[430]

Holdsworth: Is Bernard Wood an American?

Crompton: No, he's not. British. He's now at George Washington University, but he is actually British.

Holdsworth: He is the person who brought out a big book on anthropology.[431]

Crompton: I don't know. He may well have done. 0.18.02

Criterion 6: *'Is there research on the DNA of non-human/hominid species? If so, animals or plants?'*

Holdsworth: Is there research on the DNA of non-human species?

Crompton: Do I do any? No.

Criterion 7: *'Is there research on other biomolecules? If so, proteins or other?'*

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[427] In the event, the relevant issue of *Journal of Anatomy* was the one that appeared in April 2008. For an introduction to that issue, see: Wood, Bernard, and Elton, Sarah (2008): 'Symposium on 'Human evolution: ancestors and relatives'', Editorial introduction, *J. of Anatomy*, Vol. 212, No.4 (April 2008), pp. 335-336.
[428] Bernard Wood is Henry R. Luce Professor of Human Origins at George Washington University, Washington DC.
[429] Dr Sarah Elton is Lecturer in Anatomy and a member of the Functional Morphology and Evolution Research Unit at the Hull York Medical School (HYMS).
[430] Crompton, R.H.; Vereecke, E.E., and Thorpe, S.K.S. (2008): 'Locomotion and posture from the common hominoid ancestor to fully modern hominins, with special reference to the last common panin/hominin ancestor', *Journal of Anatomy*, Vol. 212, No.4 (April 2008), pp. 501-543.
[431] Miller, Barbara D., Wood, Bernard, Balkansky, Andrew, Mercader, Julio and Panger, Melissa (2006): Anthropology, Pearson, Boston.

Holdsworth: Is there research on other biomolecules?

Crompton: No.

Criterion 8: *'Does the research use environmental markers?'*

Holdsworth: Does the research use environmental markers?

Crompton: What do you mean by an 'environmental marker'?

Holdsworth: Well, habitat sites, tools.

Crompton: Yes is the answer to that. Yes.

Holdsworth: Any particular examples you want to give? For example, fossilised footprints.

Crompton: Yes, because we are working currently on the Laetoli footprints and trying to reverse engineer them and work out what the gait was from the footprints. So that's a major current project I've got on at the present moment. 0.19.00

Holdsworth: Has that produced a publication yet?

Crompton: No, not yet. It's only a year old.

Criterion 9: *'The main concern is phylogeny or ontogeny?'*

Holdsworth: The main concern: is it phylogeny or ontogeny?

Crompton: Neither. Sorry!

Holdsworth: No?

Crompton: It's function. I'm interested in function. I'm not interested in relationships, and I'm not really interested in development. I mean, I obviously have to deal with them, but I'd rather do it from a safe distance. So neither, I'm afraid.

Criterion 10: *'Does the research draw on fossil evidence?'*

Holdsworth: Does the research draw on fossil evidence?

Crompton: Absolutely. Yes.

Criterion 11: *'Is Newtonian mechanics relevant to the research?'*

Holdsworth: The next criterion is the relevance of Newtonian mechanics.

Crompton: Highly relevant. Crucial.

Holdsworth: That was put in after I discussed with another person in evolutionary biomechanics: John Hutchinson of the Royal Veterinary College. 0.20.04

Crompton: Oh yes. He's holding a symposium at the Natural History Museum in Easter of next year. I'm talking at it. So, yes, I do know him.

Criterion 12: *'Is the research intended to have a clinical application?'*

Holdsworth: Is the research intended to have a clinical application?

Crompton: I'm not interested in the clinical application, to be honest, but yes, it would – it is likely to. If it has a clinical application, that's fine, but I really regard myself as a pure scientist.

Criterion 13: *'Does the research use cultural markers, e.g., surnames?'*

Holdsworth: Does the research use cultural markers?

Crompton: Probably no.

Criterion 14: *'Does the research offer other economic or social benefits?'*

Holdsworth: Are there other economic or social benefits? 0.20.54

Crompton: Quite positively. All the work that we do on the foot, for example, is highly relevant to, well, to orthopaedics, to sport science, design of shoes – running shoes – that sort of thing. 0.21.06

Holdsworth: Right. I'm not doing a kind of social utility audit. It's just I'm interested to know the things that are favourable to your kind of research, or the things that give them a boost, whether there are fashions, or trends or funding issues.

Crompton: Yes, obviously, I mean, every time you write a grant application to the national grant agencies we have to have a section 'applicability' and benefit to the country – that sort of thing. 0.21.41

General and concluding discussion

Holdsworth: What is meant in your article with Carey – going back to general questions – what's meant by the expression 'positive work'? 0.22.21

Crompton: Well, 'positive' work is essentially work output. You're working against the substrate, for example when you're walking. You're doing external work.[432]

Holdsworth: Right.

Crompton: If you're walking downhill, you're doing negative work walking against gravity. In the specific context of that paper, because if you walk around with bent hips and bent knees your quadriceps muscle, for example, has to do negative work. It has to work to extend the knee, but it is actually itself being stretched by the force of gravity pressing on it from above, which tends to stretch it. So work is being done - negative work is being done - by the outside against you. That is one of the things that cause a rise in core-body cost - energy cost. That's what that discussion was about in that paper. 0.23.42

Holdsworth: Yes, there was a table about the effect of posture on oxygen consumption and heart-rate.

Crompton: Yes, that's right.

Holdsworth: Is that 'negative work'?

Crompton: It's related to it, yes, because if energy is not being output but is being stored in muscle it's going to increase the core body temperature, because the only way it can be dissipated is as heat. 0.24.15

Holdsworth: Right.

Crompton: Because if you're not doing positive work then the energy has to be dissipated as heat: there's no two ways about it. 0.24.26

Holdsworth: Right. I'd like to read you a brief quotation from a book by Paul Brand on the mechanics of the hand.

Crompton: Mm, hm.

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[432] See also: Wang W., Crompton, R.H., Wood, C.G., Li, Y. and Günther, M.M. (1998): 'The concept of positive and negative signs for work, power and energy and their special meaning in biomechanics', The Engineering of Sport 2, Hakke, S. (ed.). London: Blackwell pp. 225-232.

Holdsworth: "The hand is for work. Too often muscle balance is thought of as if flexor strength had to balance extensors. In fact the major use of muscles is to oppose external loads."[433]

Crompton: It's true up to a point, if that's what you are asking. 0.25.04

Holdsworth: Yes, but is it an entry-point for making inferences about things like tool-use and so on?

Crompton: I don't think I'd get into that. I don't think I know enough about the hand.

Holdsworth: OK. Can you refer me to any further literature on some of the points that we've discussed, other than - .

Crompton: Yes, you probably should look - because there's also a little bit about the Laetoli footprints in it - so you might want to look at our paper - 'Sellers et al' – in *Journal of the Royal Society Interface*. If you hang on a minute I can tell you when. Yes, so it's *J. Roy. Soc. Interface*. That's 2005, Volume 2.[434]

Holdsworth: Yes. 0.26.28

Crompton: So it's a paper by Sellers et al., which is the cover. It's actually the cover image. But that one you should have a look at, because that's much more up to date stuff than some things we've been talking about earlier.

Holdsworth: Right. And, finally have you come into contact with interest from philosophers of science or sociologists of science in your area of work before? 0.26.58

Crompton: No. Don't think so. Not really. Not real ones. Ha, ha! People who fancy themselves, perhaps as, but - .

Holdsworth: Well, for you are there any natural points of contact with fields like those? 0.27.16

Crompton: No, I don't think so. No.

Holdsworth: Right, well that's a very frank answer. Ha, ha!

Crompton: Ha, ha! Sorry! It's not that I'm not interested, you know, full stop, but I can only be interested in so many things – ha, ha! – at a time. I feel rather like Sherlock

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[433] Brand, Paul W. (1985): *Clinical Mechanics of the Hand*, St. Louis, 1985, p.50.

[434] Sellers, W.I., Cain, G., Wang, W.J. and Crompton, R.H. (2005): 'Stride lengths, speed and energy costs in walking of Australopithecus afarensis: using evolutionary robotics to predict locomotion of early human ancestors', *Royal Society Interface 2*: 431-442.

Holmes: I've only got a certain amount of storage capacity in my brain, and so I have to make decisions to be relatively ignorant about certain topics, and I think this would be one of them that I would be relatively ignorant of. 0.27.52

Holdsworth: Anyway, thank you for your frankness. One final point. You mentioned that – I hope you don't mind my asking – you mentioned you were going to be out of access to Internet for two months. 0.28.05

Crompton: Yes. Well, not all the time, but pretty much - I think so - because I'm going to South Africa. I've got a conference, and I am going to do some fieldwork. This is actually related to the foot. We're looking at the foot pressure in people who all their lives have never worn shoes.

Holdsworth: I hope it goes well. Thank you very much for your help.

Crompton: OK. You're welcome. Bye-bye.

Holdsworth: Bye. 0.28.34

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