Part Two
Classifying Biological Entities: Epistemologies of Life

The polygenomic organism

John Dupré

Introduction: genomes and organisms

Criticisms of the excessive attention on the powers of genes, 'genocentrism', have been common for many years[1]. While genes, genomes, or more generally DNA are certainly seen as playing a fundamental and even unique role in the functioning of living things, it is increasingly understood that this role can only be properly appreciated when adequate attention is also paid to substances or structures in interaction with which, and only in interaction with which, DNA can exhibit its remarkable powers. Criticisms of genocentrism are sometimes understood as addressing the idea that the genome should be seen as the essence of an organism, the thing or feature that makes that organism what it is. But despite the general decline not only of this idea, but of essentialism in general,[2] the assumptions that there is a special relation between an organism and its distinctive genome, and that this is a one-to-one relation, remain largely intact.

The general idea just described might be understood as relating either to types of organisms or to individual organisms. The genome is related to types of organism by attempts to find within it the essence of a species or other biological kind. This is a natural, if perhaps naïve, interpretation of the idea of the species 'barcode', the use of particular bits of DNA sequence to define or identify species membership. But in this paper I am interested rather in the relation sometimes thought to hold between genomes of a certain type and an individual organism. This need not be an explicitly essentialist thesis, merely the simple factual belief that the cells that make up an organism all, as a matter of fact, have in common the inclusion of a genome, and the genomes in these cells are, barring the odd collision with a cosmic ray or other unusual accident, identical. It might as well be said right away that the organisms motivating this thesis are large multicellular organisms, and perhaps even primarily animals. I shall not be concerned, for instance, with the fungi that form networks of hyphae connecting the roots of plants, and are hosts to multiple distinct genomes apparently capable of moving around this network (Sanders, 2002). I should perhaps apologise for this narrow focus. Elsewhere I have criticized philosophers of

biology and others for a myopic focus on a quite unusual type of organism, the multicellular animal (O'Malley and Dupré, 2007). Nonetheless it is unsurprising that we should have a particular interest in the class of organisms to which we ourselves belong, and this is undoubtedly an interesting kind of organism. And in the end, if my argument is successful for multicellular animals it will apply all the more easily to other, less familiar, forms of life.

At any rate, it is an increasingly familiar idea that we, say, have such a characteristic genome in each cell of our body, and that this genome is something unique and distinctive to each of us. It is even more familiar that there is something, 'the human genome', which is common to all of us, although, in light of the first point, it will be clear that this is not exactly the same from one person to another. The first point is perhaps most familiar in the context of forensic genomics, in the realization that the tiniest piece of corporeal material that any of us leaves lying around can be unequivocally traced back to us as its certain source. At any rate, what I aim to demonstrate in this paper is that this assumption of individual genetic homogeneity is highly misleading, and indeed is symptomatic of a cluster of misunderstandings about the nature of the biological systems we denominate as organisms.

Organisms and clones

A clone, outside Star Wars style science fiction, is a group of cells originating from a particular ancestral cell through a series of cell divisions. The reason we suppose the cells in a human body to share the same genome is that we think of the human body as, in this sense, a clone: it consists of a very large group of cells derived by cell divisions from an originating zygote. A familiar complication is that if I have a monozygotic ('identical') twin, then my twin will be part of the same clone as myself. Although this is only an occasional problem for the human case, in other parts of biology it can be much more significant. Lots of organisms reproduce asexually and the very expression 'asexual reproduction' is close to an oxymoron if we associate biological individuals with clones. For asexual reproduction is basically no more than cell division, and cell division is the growth of a clone. If reproduction is the production of a new individual it cannot also be the growth of a pre-existing individual. Indeed what justifies taking the formation of a zygote as the initiation of a new organism, reproduction rather than growth, is that it is the beginning of a clone of distinctive cells with a novel genome formed through the well-known mixture between parts of the paternal and the maternal genomes.

As I have noted, it is common to think of genomes as standing in one-to-one relations with organisms. My genome, for instance, is almost surely unique and it, or something very close to it, can be found in every cell in my body. Or so, anyhow, the standard story goes. The existence of clones that do not conform to the simple standard story provides an immediate and familiar complication for the uniqueness part of this relation. If I had a monozygotic ('identical') twin,

then there would be two organisms whose cells contained (almost) exactly the same genomes; we would both, since originating from the same lineage-founding zygote, be parts of the same clone. And lots of organisms reproduce asexually all or some of the time, so this difficulty is far from esoteric.

Some biologists, especially botanists, have bitten the bullet here. They distinguish ramets and genets, where the genet is the sum total of all the organisms in a clone, whereas the ramet is the more familiar individual (Harper, 1977). Thus a grove of trees propagated by root suckers, such as are commonly formed, for instance, by the quaking aspen (*Populus tremuloides*), in the deserts of the South West United States, is one genet but a large number of ramets. Along similar lines it has famously been suggested that among the largest organisms are fungi of the genus Armillaria, the familiar honey fungi (Smith *et al*., 1992). A famous example is an individual of the species *Armillaria ostoyae* in the Malheur National Forest in Oregon that was found to cover 8.9 km^2 (2,200 acres).[3] To the average mushroom collector a single mushroom is an organism, and it would be strange indeed to claim that two mushrooms collected miles apart were parts of the same organism. There is nothing wrong with the idea that for important theoretical purposes this counterintuitive conception may be the right one; there is also nothing wrong with the more familiar concept of a mushroom. The simple but important moral is just that we should be pluralistic about how we divide the biological world into individuals: different purposes may dictate different ways of carving things up.

It's pretty clear, however, that we cannot generally admit that parts of a clone are parts of the same individual. Whether or not there are technical contexts for which it is appropriate, I doubt whether there are many interesting purposes for which two monozygotic human twins should be counted as two halves of one organism. Or anyhow, there are certainly interesting purposes for which they must be counted as distinct organisms, including almost all the regular interests of human life. An obvious reason for this is that most of the career of my monozygotic twin (if I had one) would be quite distinct from my own. And for reasons some of which should become clearer in light of the discussion below of epigenetics, the characteristics of monozygotic twins tend to diverge increasingly as time passes. The careers of monozygotic twins may carry on independently from birth in complete ignorance of one another; but it is hardly plausible that if I were now to discover that I had a monozygotic twin, this would drastically change my sense of who I was (ie a spatially discontinuous rather than spatially connected entity). Some kind of continuing connection seems needed even to make sense of the idea that these could be parts of the same thing. Being parts of the same clone is at any rate not a sufficient condition for being parts of the same biological individual.

However, we should not immediately assume that the concept of a genet encompassing a large number of ramets is generally indefensible. A better conclusion to draw is that theoretical considerations are insufficient to determine unequivocally the boundaries of biological objects. Sometimes, perhaps always, this must be done relative to a purpose. There are many purposes for which we

distinguish human individuals and for the great majority of which it would make no sense to consider my twin and myself part of the same entity. My twin will not be liable to pay my debts or care for my children, for instance, if I should default on these responsibilities, though it is interesting in the latter case that standard techniques for determining that they are my children would not distinguish my paternity from my twin's. This may even point to an evolutionary perspective from which we are best treated as a single individual. And when it comes to the trees, this is surely the right way to go. For the purposes of some kinds of evolutionary theory the single genet may be the right individual to distinguish, but if one is interested in woodland ecology, what matters will be the number of ramets. If this seems an implausible move, this is presumably because of the seemingly self-evident individuality of many biological entities. I hope that some of the considerations that follow will help to make this individuality a lot less self-evident than it might appear at first sight. But whether or not the pluralism I have suggested for individual boundaries is defensible, the assumption of a one-to-one relation between genomes and organisms is not. I will explain the objections to this assumption in what I take to be an order of increasing fundamentality. At any rate, as the next section will demonstrate, the various phenomena of genetic mosaicism suffice to demonstrate that genotypes will not serve to demarcate the boundaries of biological individuals. Or in other words, genomic identity is not a necessary condition for being part of the same biological individual.

Genomic chimeras and mosaics

The general rubric of genomic mosaicism encompasses a cluster of phenomena. An extreme example, sometimes distinguished more technically as chimerism, is of organisms that have resulted form the fusion of two zygotes, or fertilised eggs, in utero. The consequence of this is that different parts of the organism will have different genomes – the organism is a mosaic of cells of the two different genomic types from which it originated. A tragic consequence of this has been the occasional cases of women who have been denied custody of their children on the basis of genetic tests that appeared to show that they and the child were not related. It has turned out that the explanation of this apparent contradiction of a connection of which the mother was in no doubt was that she was a genomic mosaic of this kind, and the cells tested to establish the parental relation were from a different origin from the gametes that gave rise to the child (Yu *et al.*, 2002). With the exception of a modest degree of chimerism found in some fraternal twins who have exchanged blood and blood cell precursors in utero and continue to have distinct genotypes in adult blood cells, such cases are generally assumed to be very rare in humans. However, chimeras do not necessarily experience any unusual symptoms, so the prevalence of full chimerism, chimerism derived from multiple zygotes, is not really known, and may be much higher than suspected.

Probably more common than chimerisms resulting from the fusion of two zygotes are those resulting from mutations at some early stage of cell division. One well-known example of this is XY Turner syndrome, in which the individual is a mixture of cells with the normal XY karyotype, the complement of sex chromosomes found in most males, and XO cells, in which there is no Y chromosome and only one X chromosome (Edwards, 1971). Turner syndrome is a condition of girls in which all the cells are XO (ie with one X chromosome missing, as opposed to the standard XX); people with XY Turner syndrome generally have normal male phenotypes, though a small percentage are female and a similar small percentage are intersexed. The large majority of fetuses with either condition are spontaneously aborted. The phenotype displayed by XY Turner cases is presumably dependent on exactly when in development the loss of the X chromosome occurs.

Chimerism is quite common in some other organisms. When cows have twins there is usually some degree of shared fetal circulation, and both twins become partially chimeric. This has been familiar from antiquity in the phenomenon of freemartinism, freemartins being the sterile female cattle that have been known since the 18th century invariably to have a male twin. This is the normal outcome for mixed sex bovine twins, with the female twin being masculinised by hormones deriving from the male twin.[4] This has occasionally been observed in other domesticated animals. Even more than for the human case, the prevalence of this, and other forms of chimerism, in nature is not known.

The chimeras mentioned so far are all naturally occurring phenomena. Much more attention has lately been attracted by the possibility of artificially producing chimeras in the laboratory. And unsurprisingly, the most attention had been focused on the possibility of producing chimeras, or hybrids, that are in part human. Recent controversy has focused on the ethical acceptability of generating hybrid embryos for research purposes by transplanting a human nucleus into the egg cell of an animal of another species, usually a cow.[5] Since all the nuclear DNA in such a hybrid is human, it can be argued that this is not a chimera at all, at least in the genetic sense under consideration. On the other hand such cells will contain non-human DNA in the mitochondria, the extranuclear structures in the cell that provide the energy for cellular processes.[6] No doubt the mixture of living material from humans and non-humans is disturbing to many whether or not the material in question is genetic, as is clear from controversy over the possibility of xenotransplantation, use of other animals to provide replacement organisms. But this will not be my concern in the present paper (though see Parry and Twine's papers in this volume).

Modern laboratories, at any rate, are well able to produce chimeric organisms. At the more exotic end of such products, and certainly chimeras, are such things as 'geeps', produced by fusing a sheep embryo with a goat embryo. The adults that develop from these fused embryos are visibly and bizarrely chimeric, having sheep wool on parts of their bodies and goat hair on others. Much more significant, however, are the transgenic organisms that have caused widespread public discomfort in the context of genetically modified (GM) foods (see Milne,

this volume). These are often seen as some kind of violation of the natural order, the mixing together of things that Nature or God intended to keep apart (see Barnes and Dupré, 2008). Whatever other objections there may be to the production of GM organisms, it will become increasingly clear that this is not one with which I am sympathetic: organisms do not naturally display the genetic purity that this concern seems to assume.

The chimeric organisms discussed so far in this section have been organisms originating to some degree from two distinct zygotes. (The exception is the XY Turner syndrome, which should strictly have been considered in the context of the following discussion.) Other cases relevant to the general topic of intraorganismic genomic diversity, but generally referred to by the term mosaicism rather than chimerism, exhibit genomic diversity but deriving from a single zygotic origin. Such mosaicism is undoubtedly very common. One extremely widespread instance is the mosaicism common to most or all female mammals that results from the expression of different X chromosomes in different somatic cells. In the human female, one of the X chromosomes is condensed into a cellular object referred to as the Barr body and is largely inert. Different parts of the body may have different X chromosomes inactive, implying that they have different active genotypes. This phenomenon will apply to most sexually reproducing organisms, though in some groups of organisms, for example birds, it is the male rather than the female that is liable to exhibit this kind of mosaicism.[7] The most familiar phenotypic consequence of this phenomenon is that exhibited by tortoiseshell or calico cats, in which the different coat colours reflect the inactivation of different X chromosomes. Although there are very rare cases of male calico cats, these appear to be the result of chromosomal anomaly (XXY karyotype), chimerism, or mosaicism in which the XXY karyotype appears as a mutation during development (Centerwall and Benirschke, 1973).

Returning to chimerism, mosaicism deriving from distinct zygotes, a quite different but very widespread variety is exhibited by females, including women, after they have borne children, and is the result of a small degree of genomic intermixing of the maternal and offspring genomes. Though scientists have been aware of this phenomenon for several decades it has recently been the focus of increased attention for several reasons. For example, recent work suggests that the transfer of maternal cells to the fetus may be important in training the latter's immune system (Mold *et al*., 2008). Another reason for increasing interest in this topic is the fact that it opens up the possibility of genetic testing of the fetus using only maternal blood, and thus avoiding the risks inherent in invasive techniques for fetal testing such as amniocentesis (Lo, 2000; Benn and Chapman, 2009). It should also be noted that maternal cells appear to persist in the offspring and vice versa long after birth, suggesting that we are all to some degree genomic mosaics incorporating elements from our mothers and, for women, our offspring.

One final cause of chimerism that must be mentioned is the artificial kind created by transplant medicine, including blood transfusions. Very likely this will continue to become more common as techniques of transplantation become

more refined and successful. A possibility increasingly under discussion is that this will eventually be extended, through the development of xenotransplantation, to include interspecific mosaicism. At any rate, any kind of transplantation, except that involving cells produced by the recipient himself or herself, will produce some genomic chimerism. So, in summary, both natural and artificial processes, but most commonly the former, generate significant degrees of chimerism in many, perhaps almost all, multicellular organisms including ourselves. The assumption that all the cells in a multicellular organism share the same genome is therefore seriously simplistic and, as mentioned above, conclusions drawn from this simplistic assumption, for example about the violation of Nature involved in producing artificial chimeras are, to the extent that they rely on this assumption, ungrounded.

Epigenetics

The topics of chimerism and mosaicism so far discussed address the extent to which the cells that make up a body are genomically uniform in the sense of containing the same DNA sequences. This discussion runs a risk of seeming to take for granted the widely held view that, given a certain common genome, understood as a genome with a particular sequence of nucleotides (the As Cs Gs and Ts familiar to everyone in representations of DNA sequence), the behaviour of other levels of biological organisation will be determined. Perhaps a more fundamental objection to the one genome one organism doctrine is that this common assumption is entirely misguided. The reason that the previous discussion may reinforce such an erroneous notion is that the comparisons and contrasts between genomes were implicitly assumed to be based entirely on sequence comparisons. But to know what influence a genome will actually have in a particular cellular context one requires a much more detailed and nuanced description of the genome than can be given merely by sequence. And once we move to that more sophisticated level of description it becomes clear that, even within the sequence-homogeneous cell lineages often thought to constitute a multicellular organism, there is a great deal of genomic diversity. These more sophisticated descriptions are sought within the burgeoning scientific field of epigenetics, or epigenomics.

A good way of approaching the subject matter of epigenetics is to reflect on the question why, if indeed all our cells do have the same genome, they nevertheless do a variety of very different things. It is of course very familiar that not all the cells in a complex organism do the same things – they are differentiated into skin cells, liver cells, nerve cells, and so on. Part of the explanation for this is that the genome itself is modified during development, a process studied under the rubric of epigenetics or epigenomics.[8] The best-known such modification is methylation, in which a cytosine molecule in the DNA sequence is converted to 5-methyl-cytosine, a small chemical addition to one of the nucleotides, or bases, that makeup the DNA molecule. This has the effect of blocking transcription

of the DNA sequence at particular sites in the genome. Other epigenetic modifications affect the protein core, or histones, which form part of the structure of the chromosome, and also influence whether particular lengths of DNA are transcribed into RNA. It is sometimes supposed that these are not 'real', or anyhow significant, alterations of the genome, perhaps because we still describe the genome sequence in the same way, referring to either cytosine or 5-methylcytosine by the letter C. But all this really shows is that the standard four letter representation of genomic sequence is an abstraction. As a matter of fact there are about 20 nucleotides that can occur in DNA sequences, and it is only our choice of representation that maintains the illusion that some chemically fixed entity, the genome, can be found in all our cells. If we were to change the representation to a more fine-grained description of chemical composition, we would find a much greater genomic diversity than is disclosed by the more abstract and familiar four letter code.

It is true that part of the value of the abstraction that treats the genome as consisting of only four nucleotides is that this does represent a very stable underlying structure. This has provided extremely useful applications that use stable genome sequence to compare or identify organisms, applications ranging from phylogenetic analysis to forensic DNA fingerprinting. Phylogenetic analysis, the investigation of evolutionary relations between kinds of organisms, here depends on the stability of genomes as they are transmitted down the generations, and DNA fingerprinting depends on the admittedly much shorter term stability of genome sequence within the life of the individual. Methylation, on the other hand, is reversible and often reversed. However over-emphasis on this stable core can be one of the most fundamental sources of misunderstanding in theoretical biology.

Such misunderstanding is sometimes expressed in the so-called Central Dogma of Molecular Biology.[9] This is generally interpreted as stating that information flows from DNA to RNA to proteins, but never in the reverse direction. I don't wish to get involved in exegesis of what important truth may be alluded to with this slogan, and still less into the vexed interpretation of the biological meaning of 'information' (Maynard Smith, 2000; Griffiths, 2001). What is no longer disputable is that causal interaction goes both in the preferred direction of the Central Dogma, and in the reverse direction. Epigenetic changes to the genome are induced by chemical interactions with the surrounding cell (typically with RNA and protein molecules). A reason why this is so important is that it points to a mechanism whereby even very distant events can eventually have an impact on the genome and its functioning. The classic demonstration of this is the work of Michael Meaney and colleagues, on ways in which maternal care can modify the development of cognitive abilities in baby rats, something which has been shown to be mediated by methylation of genomes in brain cells (Champagne and Meaney, 2006). The most recent work by this group has provided compelling reason to extrapolate these results to humans (McGowan *et al.*, 2009). Whether epigenetic research shows that genomes are diverse throughout the animal body of course depends on one's definition of 'genome'

and one's criterion for counting two as the same. It needs just to be noted that if we choose a definition that, *pace* the points made in earlier sections, counts every cell as having the same genome, we will be overlooking differences that make a great difference to what the cell actually does.

Symbiosis and metaorganisms

In this section I want to make a more radical suggestion. So far I have considered the diversity of human (or other animal) cells that may be found in an individual organism; and the phenomena I have described are generally familiar ones to molecular biologists. In this section I shall propose that there are good reasons to deny the almost universal assumption that all the cells in an individual must belong to the same species. This may seem no more than tautological: if a species is a kind of organism then how can an organism incorporate parts or members of different species? The resolution of this paradox is to realise that very general terms in biology such as species or organism do not have univocal definitions: in different contexts these terms can be used in different ways. For the case of species, this is quite widely agreed among philosophers of biology today (see, eg Dupré, 2002, chs. 3, 4.) I am also inclined to argue something similar for organisms. Very roughly, I want to suggest that the organisms that are parts of evolutionary lineages are not the same things as the organisms that interact functionally with their biological and non-biological surroundings. The latter, which I take to be more fundamental, are composed of a variety of the former, which are the more traditionally conceived organisms. But before explaining this idea in more detail I need to say a bit more about the facts on which it is based. I shall introduce these with specific reference first to the human.

A functioning human organism is a symbiotic system containing a multitude of microbial cells – bacteria, archaea, and fungi – without which the whole would be seriously dysfunctional and ultimately non-viable. Most of these reside in the gut, but they are also found on the skin, and in all body cavities. In fact about 90 per cent of the cells that make up the human body belong to such microbial symbionts and, owing to their great diversity, they contribute something like 99 per cent of the genes in the human body. It was once common to think of these as little more than parasites, or at best opportunistic residents of the various vacant niches provided by the surfaces and cavities of the body. However it has become clear that, on the contrary, these symbionts are essential for the proper functioning of the human body. This has been recognized in a major project being led by the U.S. National Institutes of Helath, that aims to map the whole set of genes in a human, the Human Microbiome Project.[10]

The role of microbes in digestion is most familiar and is now even exploited by advertisers of yoghurt. But even more interesting are their roles in development and in the immune system. In organisms in which it is possible to do the relevant experiments it has turned out that genes are activated in human cells

by symbiotic microbes, and vice versa (Rawls *et al*., 2004). Hence the genomes of the human cells and the symbiotic microbes are mutually dependent. And it seems plausible that the complex microbial communities that line the surfaces of the human organism are the first lines of defence in keeping out unwanted microbes.[11] Since the immune system is often defined as the system that distinguishes self from non-self, this role makes it particularly difficult to characterize our symbiotic partners as entirely distinct from ourselves. Finally, it is worth recalling that we are not much tempted to think of the mitochondria that provide the basic power supply for all our cellular processes as distinct from ourselves. Yet these are generally agreed to be long captive bacteria that have lost the ability to survive outside the cell.

These phenomena are far from being unique to the human case, and arguably similar symbiotic arrangements apply to all multicellular animals. In the case of plants, the mediation of the metabolic relations between the plant roots and the surrounding soil is accomplished by extremely complex microbial systems involving consortia of bacteria as well as fungi whose webs pass in and out of the roots, and which are suspected of transferring nutrients between diverse members of the plant community, suggesting a much larger symbiotic system (Hart *et al*., 2003).

My colleague Maureen O'Malley and I (Dupré and O'Malley, 2009) have suggested that the most fundamental way to think of living things is as the intersection of lineages and metabolism. The point we are making is that, contrary to the idea that is fundamental to the one genome one organism idea, the biological entities that form reproducing and evolving lineages are not the same as the entities that function as wholes in wider biological contexts. Functional biological wholes, the entities that we primarily think of as organisms, are in fact cooperating assemblies of a wide variety of lineage-forming entities. In the human case, as well as what we more traditionally think of as human cell lineages, these wider wholes include a great variety of external and internal symbionts. An interesting corollary of this perspective is that although we do not wish to downplay the importance of competition in the evolution of complex systems, the role of cooperation in forming the competing wholes has been greatly underestimated. And there is a clear tendency in evolutionary history for entities that once competed to form larger aggregates that now cooperate.

Conclusion

It should be clear that there is a continuity between the phenomena I described under the heading of chimerism and mosaicism and those discussed in the preceding section. Living systems, I am arguing, are extremely diverse and opportunistic compilations of elements from many distinct sources. These include components drawn from what are normally considered members of the same species, as illustrated by many of the cases of chimerism, but also, and more fundamentally, by the collaborations between organisms of quite different

species, or lineages, which have been the topic of the preceding section. All of these cases contradict the common if seldom articulated assumption of one genome, one organism.

One plausible hypothesis about the attraction of the one genome one organism assumption is that it represents an answer to the question, what is the *right* way of dividing biological reality into organisms. But, as I have argued throughout this essay, there is no unequivocal answer to this question. From the complex collaborations between the diverse elements in a cell, themselves forming in some cases (such as mitochondria) distinct lineages, through the intricate collaborations in multispecies microbial communities, to the even more complex cooperations that comprise multicellular organisms, biological entities consists of disparate elements working together. Different questions about, or interests in, this hierarchy of cooperative and competitive processes will require different distinctions and different boundaries defining individual entities. As with the more familiar question about species, in which it is quite widely agreed that different criteria of division will be needed to address different questions, so it is, I have argued with individuals. This is one of the more surprising conclusions that have emerged from the revolution in biological understanding that is gestured at by the rubric, genomics.

Returning finally to the distinctively human, the capacities that most clearly demarcate humans from other organisms – language, culture – are the capacities that derive from our increasing participation in ever more complex social wholes. A further extension of the argument sketched in the preceding paragraph would see this as the next stage in the hierarchy of collaboration and perhaps, as has often been speculated, genuinely marking the human as a novel evolutionary innovation. Rather less speculatively, it is arguably a striking irony that the often remarked centrality of individualism in the last 200 years of social theory has perhaps been the greatest obstacle to seeing the profoundly social, or anyhow cooperative, nature of life more generally.

Acknowledgement

I gratefully acknowledge support from the Economic and Social Research Council (ESRC) and the Arts and Humanities Research Council (AHRC). The research in this paper was part of the programme of the ESRC Centre for Genomics in Society (Egenis).

Notes

1 For a recent example, see Barnes and Dupré 2008.
2 At any rate among philosophers concerned with the details of scientific belief. Essentialism has had something of a resurgence among more abstractly inclined metaphysicians (Ellis, 2001; Devitt, 2008).

3 See http://www.scientificamerican.com/article.cfm?id=strange-but-true-largest-organism-is-fungus (Accessed 2 Nov 2000).
4 Exactly to what extent this is the normal outcome remains as with so many phenomena in this area somewhat unclear, however (Zhang *et al*., 1994).
5 Although research involving hybrid embryos is generally thought unacceptable unless there are clear potential medical benefits, opinion in the UK is quite finely divided on this topic (Jones, 2009).
6 As a matter of fact the mitochondria are now known to be descendants of bacteria that long ago became symbiotically linked to the cells of all eukaryotes, or 'higher' organisms. This may suggest a further sense in which we are all chimeric, a suggestion I shall elaborate shortly.
7 Curiously, however, it appears that birds find less need to compensate for the overexpression of genes on the chromosome of which one sex has two (in birds the male has two Z chromosomes). So this kind of mosaicism will be less common, or may not occur at all (Marshall Graves and Disteche, 2007).
8 It appears that the phenomenon in question may not be fully explicable at all, however, as gene expression is also importantly affected by random processes, or noise (Raser and O'Shea, 2005). But there is also growing evidence that noise of this kind may be adaptive, and hence this effect may have been subject to natural selection (Maamar *et al*., 2007).
9 This phrase was introduced originally by Francis Crick, and I have no wish to accuse Crick himself of misunderstanding. Indeed the use of the word 'dogma' suggests a degree of irony.
10 See http://nihroadmap.nih.gov/hmp/. (Accessed 28 Oct 2009).
11 More traditional views of the limits of the human organism might make it seem strange that a strong correlate of infection with the hospital superbug, *Clostridium difficile*is exposure to powerful courses of antibiotics, though this correlation is not quite as pervasive as was earlier thought (Dial *et al*., 2008).

References

Barnes, B. and J. Dupré, (2008), *Genomes and What to Make of Them*, Chicago: University of Chicago Press.

Benn, P.A. and A.R. Chapman, (2009), 'Practical and ethical considerations of noninvasive prenatal diagnosis', *JAMA*, 301(20): 2154–2156.

Centerwall, W.R. and K. Benirschke, (1973), 'Male tortoiseshell and calico (T – C) cats', *The Journal of Heredity*, 64: 272–278.

Champagne, F.A. and M.J. Meaney, (2006), 'Stress during gestation alters postpartum maternal care and the development of the offspring in a rodent model', *Biological Psychiatry*, 59: 1227–1235.

Devitt, M., (2008), 'Resurrecting biological essentialism', *Philosophy of Science*, 75: 344–382.

Dial, S., A. Kezouh, A. Dascal, A. Barkun and S. Suissa, (2008), 'Patterns of antibiotic use and risk of hospital admission because of Clostridium difficile infection', *CMAJ*, 179(8): 767–772.

Dupré, J., (2002), *Humans and Other Animals*, Oxford: Oxford University Press.

Dupré, J. and M.A. O'Malley, (2009), 'Varieties of living things: Life at the intersection of lineage and metabolism', *Philosophy and Theory in Biology* http://www.philosophyandtheoryinbiology.org/

Edwards, O.M., (1971), 'Masculinized Turner's syndrome XY-XO mosaicism', *Proceedings of the Royal Society of Medicine*, 64(3): 300–301.

Ellis, B., (2001), *Scientific Essentialism*, Cambridge: Cambridge University Press.

Griffiths, P., (2001), 'Genetic information: A metaphor in search of a theory', *Philosophy of Science*, 68: 394–412.

Harper, J.L., (1977), *Population Biology of Plants*, London: Academic Press.

Hart, M.H., R.J. Reader and J.N. Klironomos, (2003), 'Plant coexistence mediated by arbuscular mycorrhizal fungi', *Trends in Ecology & Evolution*, 18: 418–423.

Jones, D.A., (2009), 'What does the British public think about human–animal hybrid embryos?' *Journal of Medical Ethics*, 35: 168–170.

Kripke, S., (1980), *Naming and Necessity*, Cambridge, MA.: Harvard University Press.

Lo, Y.M.D., (2000), 'Fetal DNA in maternal plasma: Biology and diagnostic applications', *Clinical Chemistry*, 46: 1903–1906.

Maamar, H., A. Raj and D. Dubnau, (2007), 'Noise in gene expression determines cell fate in Bacillus subtilis.' *Science*, 317: 526–529.

Marshall Graves, J.A. and C.M. Disteche, (2007), 'Does gene dosage really matter?' *Journal of Biology*, 6(1): 1.

McGowan, P.O., A. Sasaki, A.C. D'Alessio, S. Dymov, B. Labonté, M. Szyf, G. Turecki and M.J. Meaney, (2009), 'Epigenetic regulation of the glucocorticoid receptor in human brain associates with childhood abuse.' *Nature Neuroscience*, 12: 342–348.

Maynard Smith, J., (2000), 'The concept of information in biology', *Philosophy of Science*, 67: 177–194.

Mold, J.E., J. Michaëlsson, T.D. Burt, M.O. Muench, K.P. Beckerman, M.P. Busch, T.-H. Lee, D.F. Nixon and J.M. McCune, (2008), 'Maternal alloantigens promote the development of tolerogenic fetal regulatory T cells in utero, *Science*, 322: 1562–1565.

O'Malley, M.A. and J. Dupré, (2007), 'Size doesn't matter: Towards a more inclusive philosophy of biology', *Biology and Philosophy*, 22, 2007: 155–191.

Raser, J.M. and E.K. O'Shea, (2005), 'Noise in gene expression: Origins, consequences, and control'. *Science*, 309: 2010–2013.

Rawls, J.F., B.S. Samuel and J.I. Gordon, (2004), 'Gnotobiotic zebrafish reveal evolutionarily conserved responses to the gut microbiota'. *PNAS*, 101(13): 4596–4601.

Sanders, I.R., (2002), 'Ecology and evolution of multigenomic Arbuscular mycorrhizal fungi' *The American Naturalist*, 160: S128–S141.

Smith, M.L., J.N. Bruhn and J.B. Anderson, (1992) 'The fungus Armillaria bulbosa is among the largest and oldest living organisms', *Nature*, 356: 428–431.

Yu, N., M.S. Kruskall, J.J. Yunis, H.M. Knoll, L. Uhl, S. Alosco, M. Ohashi, O. Clavijo, Z. Husain, E.J. Yunis, J.J. Yunis and E.J. Yunis, (2002), 'Disputed maternity leading to identification of tetragametic chimerism', *The New England Journal of Medicine*, 346: 1545–1552.

Zhang, T., L.C. Buoen, B.E. Seguin, G.R. Ruth and A.F. Weber, (1994), 'Diagnosis of freemartinism in cattle: the need for clinical and cytogenic evaluation', *Journal of the American Veterinary Medicine Association*, 204(10): 1672–1675.

