GENETIC SEX: "A SYMBOLIC STRUGGLE AGAINST REALITY?"

-EXPLORING GENETIC AND GENOMIC KNOWLEDGE IN SEX DISCOURSES

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ABSTRACT

Genetic sex -the apparent fundamental biological cause of the two male and female human varieties- is a 20th century construct. Looking down the microscope, the stained chromosomes are concrete countable entities and lend themselves easily to genetic determinism. As the chromosome composition of a person is generally fixed at the time of conception, when a Y- or X-bearing sperm is united with the X-bearing egg, a person's genetic sex is taken as permanent and unchanging throughout their life. Drawing upon gender theory as well as science and technology studies this thesis explores how our particular construction of the concept of 'genetic sex' relies on four features of biological sex (binary, fixed, spanning nature, and found throughout the body) and in addition proposes one unique feature, inheritance.

The empirical research is based on an analysis of popular science books as well as two case studies of how genes relate to sex determination and development. The analysis of the metaphors used in these books and journal articles reveals how now, with genomic efforts to explore gene expression profiles, there is a shift away from seeing genes as having 'responsibilities' for determining phenotypes towards seeing them play a role along with other genes in genetic cascades where other factors such as timing can be incorporated. The analysis of genomic features such as imprinting and X-chromosome inactivation also provide evidence that such a change should be recognised. Rather than seeing sex in terms of fixed and static differences and similarities, current research offers new ways of conceptualising similarities and differences as dynamic and responsive to environment. This supports wider understandings of 'biology' as relying on the interactions between genetic processes, cellular environment, and tissue environment – in which the social physicality of bodies is important in forming and maintaining a person's biology and genetic processes. Yet as the historical analysis of the shift between the one sex to two sex model indicates, it remains to be seen whether the social sphere will respond by incorporating this new evidence into the tacit, everyday understandings of sex or seek to maintain the binary and fixed relationship(s) between men and women by governing them as males and females.

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This Phd is two hundred odd pages of paper and years of my life. Throughout its frustrations I have benefited from various officemates whom I've come to consider exceptional academics. For most in academia there are no clear boundary between work collages and friends, and I have come to value these individuals as friends. Part of this has been connected to the PFGS and I am indebted to the welcoming atmosphere which the annual colloquium offers to nervous presenters.

Early on in this PhD I decided not to deal directly with humans, for someone with a degree in biotechnology they were too messy and the ethics review too long. However recondition, acknowledgement and heartfelt thanks must also be given to the members of the intrsex activist groups who advise me on various presentations. Their willingness to engage with PhD students and researchers, as well as their personal stories has informed this thesis.

I would also like to thank those who read and commented so productively on various drafts including Bonnie, Conor, Claire, Lena, Mitchell and Desmond. I apologise if the 'clean' version is less amusing without the organism/orgasm and public/pubic 'typos'.

This thesis is dedicated to Jane Calvert –who is an inspiration and mentor to many a phd student!

CHAPTER ONE - INTRODUCTION

> What's the point of fighting for his right to have babies when he can't have babies?!
> It is symbolic of our struggle against oppression!
> …Symbolic of his struggle against reality.
>
> (Monty Python's Life of Brian 1979)

1.1 Original motivations and brief synopsis

The relationship between sex and gender has been debated by anthropologists, psychologists, biologists, sociologists and sexologists. Feminists in these fields have been successful in problematizing the gender-sex and social-natural binaries, and biological knowledge has played a critical role in their discussions. Elizabeth Grosz (1994) has challenged the notion of the male and female body as fixed and concrete substances, while Judith Butler (1990, 1993) and Anne Fausto-Sterling (2000) challenge sex as a natural category.

The issue of whether sex can be divided from gender has been explored by Judith Butler (1990), who has argued that immediately a child is born into the world it is already gendered, and similarly even before research is carried out the social environment of the research is gendered. Hence, no split can be drawn between sex, as a wholly scientific fact, and gender, as a culturally conceived actuality. So it would seem that sex is always gendered. Indeed, as this thesis explores the historical research surrounding the issues that our current society views as part of biological sex, the tight historical link between gender and sex will become clear.

The observation that humans exist in two distinct forms, male and female is critical to the idea of a fixed sex. Feminist deconstruction of this seemingly 'biological fact' has shown that the human body and its phenotype of sex are not static or fixed into two distinct classes of humans. Fausto-Sterling (2000) has detailed this extensively through her exploration of the construction of sex. She has shown how intersex genitals and gonads are read within cultural and social situations, and how sex-chromosomes are at times disregarded in favour of constructing a body that can function in the heterosexual sex act. Thus, the medical gaze observes and measures the genitals in relation to the

social expectations of reproduction and sexual life. This has led some feminists to question the very existence of binary sex model as a scientific reality**,** since what counts within the laboratory as male or female is tightly connected with what society holds as woman and man, with the result that sex itself is always a gendered category (Butler 1990). So, many feminists argue that the sex binary, which science claims to reveal, is the consequence of scientists imposing the gender binary upon their research (Butler 1990, 1993; Fausto-Sterling 2000), and that the sex/gender division is not, therefore, a feasible theoretical framework (Hood-Williams 1996).

As a scientist I was never concerned about what it meant to be 'female'. My interest was in looking at the working of cells, their activity and their life, and as such I didn't start my research from the viewpoint of feminist politics or the impact of gender on science. Instead I began from the starting point of questioning the impact of genetic and genomic knowledge and information as an empowering force for individuals and groups. From this initial question, and as my knowledge of gender studies grew, I directed my research to also include exploring genetic sex as ideology.

1.2 Research Questions

The over-arching aim of this thesis is to explore how genetic and genomic knowledge has impacted upon categories of biological sex, genetic sex and views of male and female.

The specific research questions addressed in this thesis are:

1) What role has scientific knowledge played in the way(s) in which biological sex has historically been constructed?
2) What are the main features of current Western view(s) of biological sex, particularly relating to 'genetic sex'?
3) How is 'genetic sex' communicated in popular science and what values and concepts are embedded in this communication?
4) What concepts, metaphors and values are used in the communication of genetic knowledge related to sex in scientific journal articles?
5) What impact does genomic knowledge have on features of genetic sex identified by question two?

The first question is explored by analysing the relevant historical and theoretical literature in Chapter Two, which also deals with question two. The third question is explored in Chapters Three and Four by analyzing the authors, book covers and narratives in three recently published popular science books. The fourth question is addressed by analysing 'professional' science communication contained within journal articles for two genes, SRY and DAX-1 (Chapters Five and Six). The final question is answered by exploring recent developments within the field of genomics including X-inactivation and imprinting (Chapter Eight).

1.3 Outline of thesis

The following chapter explores the historical foundation for our current way of thinking about sex. I draw upon the work of medical historians to show how sex differences have been conceived of in Western history. Thomas W. Laqueur (1990, 2003) suggested that during the 17th century there was a shift from a one-sex model where the male and female body were seen as variants on essentially the same (human) type, towards the current two-sex model, in which males and females were distinct different types, each with their sexually specific organs and functions. The historical exploration also illustrates that the concept of sex relies on a complex set of beliefs concerning a wide range of questions from reproduction through to sexuality. I use the concept of sex ideologies to encompass the wider set of knowledge (including sex models of the human body), scientific and non-scientific beliefs concerning sex and sexuality and the social and political institutions that govern such social and legal norms. Building upon Nelly Oudshoorn's (1994) description of how sex determination (genetics) became separated from sex development (endocrinology) the second section explores the recent developments in the formulation of 'genetic sex'. I argue that there are four aspects of biological sex that have become incorporated into our current understanding of 'genetic sex'. These include the idea of a fixed binary sex, which is seen through the human body and the male and female categories throughout nature. I then review how the idea of genetic sex as a fixed and static condition has played an important role in governing sports people along sexed lines.

The third and fourth chapters explore how issues around biological sex (male, female, genetic sex, 'sex-chromosomes') are communicated in the field of popular science through exploring three popular science books (*Y: The Descent of Men* by Steven Jones

(2002), *Adam's Curse* by Bryan Sykes (2003), and *The X in Sex* by David Bainbridge (2003)). Chapter Three draws on literature surrounding 'public understanding of science' to argue that popular science products are not clear educational or entertainment products, but rather play an important role as commercial 'fringe products'. Through exploring the background of the three authors it is apparent that there are significant differences, and that they approach popular science communication in differing ways. However the analysis of the book covers indicates that they draw on similar cultural symbols. These include religious, artistic, sporting, and physical references.

In Chapter Four the metaphors used by the three books to communicate genetics and sex are explored. Particular attention is paid to how the X- and Y- chromosomes are portrayed. This reveals a range of metaphors including those of war, marriage, divorce, politics, and transport. The analysis also indicates how the sex binary was naturalized and that the authors to varying degrees saw a natural connection between gender and biological sex. This chapter also indicates the extent that the four features of biological sex are present in popular science literature.

Chapter Five explores the case study of the TDF/SRY gene. This gene progressed through different identities, from being a simple inherited 'factor' linked to testis determination to being the 'master' switch of sex determination/development. SRY has gained publicity in the mass media, being characterised as the 'genetic switch' of sex determination. Chapter Six examines the second gene case study of DAX-1, which was linked to dose sensitivity. First suggested to be a female-determining gene, this gene underwent a surprising progression to becoming a 'pro-testis' gene, and was subsequently found to produce two alternative spliced forms. Both these case studies concentrate on the history of the genes, exploring how they were researched, as well as the metaphors, concepts and values that are embedded in the journal articles that describe then.

Chapter Seven sets the two gene case studies in the context of the work undertaken in the philosophy of biology regarding the various definitions and concepts of genes. It has been argued that much of the public's view of genes as having deterministic power stems from a fault within scientific communication or a failure of 'lay' audiences to understand the complexity of genetic causation. Lenny Moss (2003) argues that 'the

gene for' which is often seen in news articles proclaiming that scientists have found 'the latest gene' for cancer/obesity/homosexuality, stems from a conflation between gene D (a gene defined in terms of DNA) and a gene P (defined in relation to a phenotype). As this chapter will show, the two gene cases are more complicated and involve a variety of conflations and reductions including one between 'testis determination', 'male determination' and 'sex determination'. Finally this chapter will explore the current (as of 2005) view of sex determination and sex development to argue that these two research fields have become merged and this has had an impact on how 'biological sex' is conceived.

Chapter Eight will explore the potential impact of genomics on our current view of genetic sex. Building upon Butler's idea of gender performance this chapter will argue that the new field of genomics, while currently contained within the binary sex-gender framework, has the potential to transform genetic sex into a fluid or 'living' category.

Chapter Nine returns to reflect the five factors I outlined as being important to our view of biological sex, and reviewing the findings gathered in the preceding chapters I argue our idea of genetic sex should be viewed in terms of genomic living sex. To conclude, this chapter suggests future areas for study, including in-depth analysis of the institutional pressures, collaborations and conflicts which surround genetic 'sex' research, the norms and values held by the researchers in the laboratory, and increased research into the empowering and enslaving potential of personal 'sex' genetic knowledge.

CHAPTER TWO - SEX DIFFERENCES AND SIMILARITIES

God gave men beards for ornaments and to distinguish them from women
Carl Linnaeus (cited in Blunt 1971)

2.1 Introduction

The human genome project (HGP) attempted to sequence all the genes in the human genome and in the process raised old questions as to how a 'human' was defined within science and genetics. In this chapter, I will explore how western science has naturalised a view that there exist two types of humans, those that are male and those that are female. Until relatively recently, the idea of there being only two types or 'sexes' of humans was taken for granted as a natural fact. However, as anthropologists and science historians have shown, societies have not and do not necessarily see humans as divided into two separate kinds. While human bodies have undoubtedly changed very little in the time period covered by human history and do not physically change morphologies between cultures, there are a variety of different categories and ways of understanding these bodies depending on social, cultural and historical context. Thus the Native American 'Berdache' (Whitehead 1994) and the Indian Hijra (Reddy 2005) are considered by some academics to illustrate societies who have instituted three sexes (Herdt 1996).

The values used to define a human body as male or female depend firmly on these social, cultural and historical contexts. To a large extent the biological differences between male and female humans are now seen to stem from their chromosomes, as their 'genetic sex'. I am sure most readers, regardless of the level of their genetic knowledge, are aware that in humans, a male typically has a single X-chromosome and a Y-chromosome, while a female typically has two X-chromosomes. This difference in chromosomes has been seen as resulting in a difference in genes. The power of such 'differences' is illustrated in a commonly quoted statistic first mentioned in 2003 by Dr. David C. Page, a leading figure in genetic sex research. He was quoted in *The New York Times* as saying,

> (m)en and women differ by 1 to 2 percent of their genomes, which is the same as the difference between a man and a male chimpanzee or between a woman and a female chimpanzee. (Wade 2003)

He went on to explore the political and social connotations of such a difference,

> We all recite the mantra that we are 99 percent identical and take political comfort in it. But the reality is that the genetic difference between males and females absolutely dwarfs all other differences in the human genome.(Wade 2003)

Not only does Page seem to be arguing that a man is closer to a male chimpanzee, than he is to a woman, but that this difference between men and women has some political weight. However what Page is concerned with is not the active genetic processes which go on within cells but the differences in the genetic 'script' of DNA bases in the genomic sequence. This approach is clearly problematic. Such a view of genomic differences is rather like comparing the words 'cat' and 'rat' and concluding that they are 66.7 percent similar with no knowledge of how the letter c and r function within that word, or that word within the sentence. Indeed, in the case of comparing human to chimpanzee there has been renewed concern over what such percentages can reveal. Recent research on the chimpanzee 22 chromosome and the human counterpart chromosome 21 compared the expression patterns of genes and found that 20 percent of genes had different activity patterns (Watanabe et al. 2004). Thus, even if the DNA sequences in human and chimpanzees may be similar in sequence, they may work in strikingly different ways.

Chromosome and gene numbers have also been employed in support of the view that humans have a superior place in nature (Holmberg 2005). Initially humans were assumed to be more evolutionarily advanced with a superior number of genes, leading researchers to engage in what Tora Holmberg terms 'gene number fetishism'. As the HGP progressed it became clear that the human genome had considerably fewer genes than expected and researchers shifted towards describing human genes as 'working harder' or being more 'flexible' to maintain the superiority of humans. There was also a move in interest away "from structure to function to meaning" (Holmberg 2005, p.35), which was indicative of the shift from genetics to genomics. In this case numbers were used to create boundaries between animals and humans:

> When boundaries are drawn between humans and non-humans with the help of numbers, the certainty produced by absolute and percentage figures conceals that the categorization could be made in other ways. (Holmberg 2005, p.24)

Keeping Page's remarks in mind, it is clear that the use of percentages of difference between male and females creates similar obscurity. Indeed, I argue in Chapter Seven that with genomic understandings descriptions of biological sex can no longer rest on simple ideas of difference or similarity of sex-chromosomes or the difference in number of genes. Rather, within genomics it is the performance of genes, as well as non-genetic factors, that are important and this raises interesting questions about how gender interacts with and forms biological sex.

This chapter briefly explores the scientific views of the human body as sexed. Historians of science have explored this topic, including Anne Fausto-Sterling (2002), Alice Dreger (1998), Londa Schiebinger (1989, 1993, 2000, 2001), Thomas Laqueur (1990, 2003), and it was felt that this thesis should include a historical chapter to explore the recognition that our current view of binary sex, male and female, is not necessarily the only way humans can be conceived. The idea that sex was an ahistorical category was challenged by Michel Foucault (1980) in his introduction to the memoirs of Herculine Barbin and elsewhere, where he suggested that the pressure to conform to a 'two-sexed model' where only males and females were valid choices was specific to a historical moment and that at other times there had been an idea of a mixture of 'two-sexes in a single body'. Foucault goes on to argue that "(h)enceforth, everybody was to have one and only one-sex" (Foucault 1980, p.Viii). Inspiration for this chapter also comes from Thomas Laqueur's proposal that prior to the 18th century there was a 'one-sex' view of the human body (Laqueur 1990, 2003). While this chapter does not explore this shift in any great depth, Laqueur's work strongly suggests that sex does not actually have to be understood to be composed of separate kinds at all.

In the first half, I explore some of the historical developments within sex research, drawing out four key characteristics of our current dominant two-sexed view of biological sex. The first is that sex (at least in mammals) is binary; male or female. The second characteristic is that sex is fixed in humans. The third is that sex results in differences not only in the 'reproductive' organs, genitals and gonads, but that the differences between sexes can be found throughout the body. The fourth characteristic of biological sex which can be seen in this historical discussion is that it is assumed that

the categories of male and female can be applied in some meaningful way throughout nature. An additional feature, inheritance of sex, is suggested in the second section during the exploration of 'genetic sex'. The extent to which these five features are still influential within wider western society becomes apparent in the discussion of popular science covered in Chapters Three and Four.

This chapter has a number of caveats. First, it does not attempt a complete overview of the category of sex; rather it seeks to highlight some of the developments that have led to our current view of sex. Secondly, it should be clear that I do not attempt to introduce any novel historical work; there already exists a suitable body of historical work from which to draw (especially Schiebinger 1989, 1993, Oudshoorn 1994; Dreger 1998; Laqueur 1990, 2003 and Fausto-Sterling 2000). And finally, although the five factors I have mentioned may not be the most important factors throughout our currently dominant view of sex, I do wish to argue that they are the dominant factors with regard to the specific subcategory of biological sex, genetic sex.

In this chapter I wish to view sex within the framework of ideologies. There are a number of gender theorists who have made reference to gender ideology typically in reference to gender roles (Steward 2003; Frable 1989). However these authors fail to give a satisfactory description of how the framework of ideology is useful to their research. While ideology has been criticised as highly ambiguous I believe it brings some useful analytical tools to the argument of this chapter. In this regard I follow Christian Duncker (2006) who has argued that there should be a critical reflection on the ideology concept.

Willard Mullins (1972) has outlined four basic characteristics of ideology: it must have power over cognitions; it must be capable of guiding one's evaluations; it must provide guidance towards action; and it must be logically coherent (Duncker 2006). Thus, my use of the term ideology, rather than paradigm, seeks to emphasize the political and social purposes sex narratives and discourses serve, as well as referring to the explicit or implicit claim that such narratives or discourse are closer to 'real' truth. As Slavoj Zizek has remarked, ideologies seek to mask the "notion that reality itself is never fully constituted" (2005, p.86).

Taking the view that explanations and ideas of 'sex' are in fact ideologies has important conceptual consequences. Exploring how 'biological sex' and 'genetic sex' have contributed to an ideology opens up a multitude of questions, especially regarding what values and investments have been made in these explanations, rather than seeing the issue as one of 'truth' or 'accuracy'. In *Interrogating the Real,* Zizek notes,

> My point is that the way to recognize ideology at work is always through a denunciation of another ideology….Ideology is always a gesture of denouncing another position as being naïve ideology. (2005, p.64)

Certain authors have exemplified this turn through the denunciation of the dominant scientific view of sex differences as 'sexism'. Bonnie Spanier takes up the notion of ideologies, coming to the understanding that everyone has biased views, and noting the "cult of objectivity" which functions within science (Spanier 1995, p75).

From this discussion of the historical basis of sex as ideology, I move on, in the second half of the chapter, to exploring some of the forces that have shaped our current view of 'genetic sex'. While the idea of humans as two-sexed was well established by the 19th century, and researchers were quite certain that hormones played a key role in creating the two morphologies, there was still some debate regarding what was the essence of the difference. The discovery that male and female humans, like *Drosophila,* differed with regard to chromosomes suggested a 'genetic' difference, however it was not clear if this was due to a double dosage of X-chromosome or the presence of the Y-chromosome. This section will explore some of the research developments that led to the creation of 'genetic sex' as an established concept, before moving to explore the use of genetics as a social technology to govern human bodies within the wider society. Drawing upon the use of sex testing in the Olympic Games (1960s–present) I will show how this technology has been used to govern athletes along socially segregated lines. Science and technologies are marked by cultural and political ideologies and the social applications of 'sex testing' embody the beliefs inherent in sex ideologies. As will become clear, the development of the technology of 'genetic sex' allowed and justified the segregation of people into male or female, men or women.

2.2 Historical exploration of western sex

The dominant sex ideology, which is the basis of social and legal organisation in western society, holds that there are two, essentially fixed, separate sexes. As mentioned in the introduction, Laqueur (1990) has proposed that this view is in fact fairly recent, and that prior to the 18th century there was a one-sex model of the human body. This one-sex model drew upon a homological scheme which saw "men and women on a vertical, hierarchical axis, in which their bodies were seen as two comparable variations of one kind" (Harvey 2002, p.202). The humoral system, in which the body was composed of four humours in different quantities, offered a "flexible, physiological understanding of the body" where "differences of sex were differences of degree" (Harvey 2002, p.202). Laqueur has drawn on scientific and medical texts to argue that the shift to our current 'two-sex' model was motivated by a change in the Enlightenment political culture, rather than 'better' technology or increased knowledge (Laqueur 1990).

While there is wide acceptance of the one-sex/two-sex shift, its large-scale incorporation into gender history has been criticised by Janet Adelman on three main points (1999). Firstly, there has been a collapse of diverse models into a single theory. This is particularly problematic in reference to the Middle Ages in which there were widely diverse discourses and understandings of the human body (Cadden 1993). Secondly, Adelman questions whether the evidence on which the shift is based is actually representative of the various views of the body through the different time periods. Indeed, there is some discussion whether the homological scheme (in which womb=scrotum) on which the one-sex model relies was the dominant discourse within science and it has been argued that the references in scientific correspondence to a one-sex model were at most occasional (Schiebinger 1989). This is especially important as it would seem that those scientists commenting on the one-sex model were refuting it (i.e. Helkiah Crooke's *Mikrokosmographia* 1615) rather than arguing positively for its use or validity (Adelman 1999). The implication is that if researchers were arguing against a certain worldview then the worldview must be widely held, however this inference is debatable. Thirdly, the 'one-sex, two-sex model' may overemphasise change rather than capture the fluid nature of people's shared beliefs.

Picking up on Adelman's second point, that the one-sex model may not have been present as the dominant science discourse, there is also the concern that the model prioritises medical communication over other forms of knowledge and discourses which

the society would have drawn upon for views, explanations and descriptions of sex. Knowledge about bodies was, and is, not discovered in the fields of science and medicine and then communicated to other domains. Karen Harvey, in her account of erotic writings in the 18th century, remarks that "a feature which in science marks sexual difference took on quite a different meaning in erotica" and thus to speak of a single dominant model is problematic (Harvey 2002, p.216). As Harvey notes, "representations of sexual difference cannot be encapsulated in period-specific models" (Harvey 2002, p.219), and in her research she chooses to explore themes of 'sameness' and 'differences'. Hence this chapter follows Harvey's emphasis on 'sameness' or 'differences', but it will also view discussions of sex and sex differences within the framework of 'ideologies' rather than ideas of 'models' or 'themes'. The issue of seeing male and female as separate sexes thus becomes a political activity of prioritising certain biological and physical factors as being either different or similar.

The one-sex/two-sex dichotomy is problematic. The model is our interpretation of historical thoughts found in texts and diagrams that are coloured by our present values. As such my interest has been focused on how we, in our current cultural and social context, view historical categories, utilising them as a reflection for our contemporary categories and explanations. While I do not consider current evidence capable of conclusively arguing that prior to the 17th century the one-sex body was the dominant discourse, it does offer the interesting possibility that modern understandings of the human body could be supported within a 'one-sexed' view. This is especially interesting in light of the idea of a single 'human genome', and the view of the human body as default female which is propagated in three popular science books (see Chapters Three and Four).

The one-sex/two-sex model does provide this chapter with a useful historical framework within which to explore the question of how differences and similarities have been conceptualised. Laqueur (1990) draws upon a variety of different scientific research areas to illustrate how the one-sex model functioned, including descriptions of menstrual blood, lactation, gonads, semen, generation etc. Due to constraints of space the next section only explores the occurrence of the one-sex model within the technology of dissections before moving on to describe the shift towards the two-sex model.

2.2.1 Dissecting a one-sex body

Dissection of human bodies is likely to have been one of the first sites in which biological difference and similarity were explored. In the Middle Ages, medical knowledge regarding the body drew on a variety of ancient sources including Hippocrates, Aristotle and Soranus. In the 16th century, the translation of twenty-two texts of Galen, the Romeo-Greek physician (129-200 AD) opened up western dissection as a formal scientific activity. These became standard teaching texts and were illustrated by teaching sessions (Schiebinger 1989). In these practical demonstrations of the written texts, the surgeon, as unskilled labourer, carried out the dissections, while the physician as a learned man read aloud the Latin texts. In this division of labour, the surgeon's cuts were regulated to match what the text described and the sight of the audience was primed by what they expected to see (Schiebinger 1989).

Under such a gaze, the surgeon opened the female body to reveal the internal scrotum of a one-sexed model. Laqueur (1990) amongst others have argued that Galen's texts described the female and male reproductive organs as being the same except that as the female had less heat, her reproductive organs were internal. It may seem rather strange with our current views of male and female as being essentially different to think of the womb as an internal scrotum. However, what is emphasised by historians is that scientists did not fail to see reality. Rather, as Londa Schiebinger notes in her book, *The Mind has no Sex*, Renaissance scientists who saw the womb as an internal scrotum were not wrong or unobservant, but rather they were seeing the truth of their time (Schiebinger 1989).

During the 16th century, human dissections began not only to serve as 'real time' teaching, but they were also captured in illustrations. Andreas Vesalius (1514-1564) was one of the first to include illustrations of both male and female genitals in his general anatomical text, *De Corporis Humani Fabrica* (1543). He was also the first to break with the traditional split between the surgeon and physician and carry out the dissections and the oral descriptions to the audience. This convinced him that there were numerous errors in Galen's description (Saunders and O'Malley 1973). Vesalius in a later book, *Epitom*, points out the difference in curves and lines between the two sets of reproductive organs. However, in keeping with a one-sex view he saw these differences as only 'skin deep', and accompanied the male and female drawings with a single skeleton that he labelled 'human'. As Margrit Shildrick (1997) notes he also

used both male and female skeleton manikins interchangeably for 'dressing' the organs and the systems of nerves and muscles.

The 16th and 17th century illustrations of dissections are rather strange to our modern eyes. Typically, they are pictured as still living, opening and holding back parts of their own bodies. Laqueur argues that this was "a 'reality effect' [to] make pictures stand in for the bodies themselves and witness the truths of texts that viewers are invited to construe as only one remove from the cadaver itself" (Laqueur 1990,79).

A second notable feature of these illustrations is their reproduction of artistic works. Charles Estienne's *De dissectione partium corporis humani* (1545) illustrates this nicely:

> Estienne illustrated the female reproductive system and gravid uterus by borrowing poses from a series of erotic prints by Jacopo Caraglio that were based on drawings by the late Renaissance artists Perino del Vaga and Rosso Fiorentino. Entitled 'Loves of the Gods', this series illustrated the erotic dalliances of classical gods with varying degrees of explicitness. Many of Estienne's depictions of dissected female nudes quote from these provocative images. (…) the female figure's pose is the same, but in Estienne's illustration there is a somewhat clumsy woodblock insert showing the anatomy of the placenta. Estienne's anatomical female figures spread themselves suggestively out on plush pillows in bedrooms surrounded by thick drapes. The anatomy theatre and the bedroom often appear to be one and the same, conflated for the purposes of fantasy and edification. For male anatomists, the female's body, dead or alive, was shot through with erotic possibilities. (Glisson 2005)

Laqueur (1990) also reflects on this 'eroticisation' of the dissection models arguing that it was part of a representational strategy which "asserted male power to know the female body and hence to know and control a feminine Nature" (Laqueur 1990, p.73). However, eroticism is also seen in the inclusion of castrated models to illustrate the male dissected body:

> The male figures place the male audience in the position of visually consuming the male body as they would a woman's. This may explain why twelve out of the thirty-two male figures who have visible genitals have been castrated. Furthermore, intact penises and scrotums are extremely small, sometimes so slight as to be difficult to see. By removing them, a male viewer would not be confronted with the most mordant sign of male sexuality, yet its removal perhaps proved just as unsettling (…) and castration itself perhaps softened the possibility of male-to-male erotic interest. (Glisson 2005).

These two examples were discussed in the essay *Cutting It Both Ways: Dissection of the Male Anatomy as Castration*, which accompanied the Northwestern University exhibition, *The Anatomy of Gender: Arts of the Body in Early Modern Europe*. Taken together, it would seem that 16th century dissections were concerned with the eroticisation of both the female and male body. Dissections were not only carried out with an expectation of what the body would reveal – a one-sex view of reproductive organs -- but ideas of biological sex are also likely to have been conceptualised in ways dependent on the social norms and to have incorporated various bodies of knowledge and discourses, including, as the two quotes above indicate, erotic and sexual discourses.

Historians of science have made clear that at the time there were several contradictory theories in existence at the time, some based on the physical views of the body, while others were concerned with reproduction, which problematises the idea of a single 'dominant' ideology (Adleman 1999). While it is debatable to what extent a one-sex model was in existence, it is clear that prior to the 17th century, Galenic knowledge of the human body was not understood as 'two-sexed' in the way that this is currently understood in western society (Laqueur 2003). At the time the emphasis was placed upon the similarity between female and male reproductive parts (Schiebinger 1993) in contrast with the Renaissance researchers such as Antonius Pinaeus who compared penis and clitoris on the bases of differences in size, function and structure (Schleiner 2000).

2.2.2 Sexes as separate kinds

The view of the human body as 'one-sexed' recognised differences between males and females but attributed these differences in the bodies' organisation to the quantities of heat (males were hotter, females cooler). During the 17th century, with what is generally considered the emergence of modern science, the two-sex model began to dominate (Laqueur 1990). Physicians increasingly saw sex differences, not only in reproductive organs, but in the whole body including bones, hair, mouths, eyes, voices, blood vessels, sweat, and brains, to the extent that Jakob Ackemann called for the discovery of the "essential sex differences form which all others flow" (Schiebinger 1993, p.50). Londa Schiebinger has noted that the skeleton was thought of as the hardest part of the body and thus provided a 'ground plan' for the muscles, veins and nerves. Her research has traced how the illustrations of skeletons became segregated into male and female, in

line with the social structure of the time, which held men and women as essentially different.

In my earlier discussion of dissections of the human body, I briefly argued that illustrations of the dissected bodies incorporated other types of knowledge and context (i.e. eroticism). During the 18th century, scientific knowledge of the body was increasingly communicated to wider audiences through medical 'atlases'. Lorraine Daston and Peter Galison describe the primary function of standardising objects in visual form, and in addition,

> In addition to their primary function of standardizing objects in visual form, atlas pictures served other purposes in the natural sciences. In part, they served the cause of publicity for the scientific community, by preserving what is ephemeral and distributing what is rare or inaccessible to all who can purchase the volume, not just the lucky few who were in the right place and the right time with the right equipment. (Daston and Galison 1992, p.86)

This meant that scientific knowledge of the body became represented in books and in illustrations such as those already mentioned, which acted as transferable boundary objects between different audiences (Daston and Galison 1992). This relied not only on a social interest but also on technical developments that enabled skeletons and bodies to be illustrated. The standard methodology for drawing skeletons was set in 1734 by Bernhard Albinus, who used Leonardo Da Vinci's technique of drawing the skeleton from three different angles (front, side and back), and also broke way from using freehand to actual measurements (Schiebinger 1993). Albinus also developed a method for preserving the bodies. As these drawings could take up to three months, Albinus prepared the skeletons with water and vinegar so they would not lose moisture and change appearance (Schiebinger 1993). It is clear that this again shows the influence of a range of knowledge upon technological developments.

The selection of a suitable specimen to represent the different forms was also important. Albinus had been unable to find a suitable female model, although he did find the male form. The first female skeleton was drawn by a woman, Marie Genevieve-Charlotte Thiroux d'Arconville in 1759 (Schiebinger 1993). In comparison with her male skeleton it clearly showed that the female skull was smaller than the male and had a larger pelvis, which supported the prevailing sex ideology of the time, which held that the differences between females and males were based on their reproductive capacity

and mental capacity. A second female skeleton was drawn by the German anatomist Samuel Thomas Van Soemmerring and had been purposely selected as the body of a twenty year old woman who had a child. While Soemmerring had selected the body seeking to achieve a universal representation of the 'woman', the result was attacked for being inaccurate as it did not display a large difference when compared to the male skeleton (Schiebinger 1993).

The 18th century saw substantial changes in biological technology and it was able to answer the social call for justifying differing treatment of men and women on the basis of 'natural' sex differences. Laqueur has argued that there was a change in epistemology with metaphysics being replaced by biology, leading to "the categories of male and female as opposite and incommensurable biological sexes" (Laqueur 1990, p.153). The human body had become differentiated into two essentially different kinds, male and female. The shift, which began in the 17th century with the dissection of the genitals, was supported in the 18th century by the sexed skeletons, as the actual 'essence' of the human body.

This discussion of similarities and differences between female and male models for dissection and illustrations of skeletons brings critical issues for genomics. The question of who represents the 'universal' male, female and human is not a scientific issue, but requires social validation. As Daston and Galison remark,

> in order to decide whether an atlas picture is an accurate rendering of nature, the atlas maker must first decide what nature is. (Daston and Galison 1992, p.86)

They go on to highlight the difference between the "ideal" and the "characteristic" body. This difference is between the ideal image which renders

> not merely the typical but the perfect while the "characteristic" image locates the typical in the individual. Both ideal and characteristic images standardize the phenomena, and the fabrications of both insisted upon pictorial accuracy. (Daston and Galison 1992, p.88-89)

With regard to the 18th century and the sexing of reproduction, the woman's role in society was to bear children, and the perfect woman, and hence the ideal skeleton, was to emphasise this. According to Daston and Galison, the difference between the ideal and the typical pressed researchers such as Albinus to investigate typical skeletons, yet still hold the view of the ideal skeleton. As they note,

> Albinus believed that universals such as his perfect skeleton had equivalent ontological warrant to particulars, and that the universal might be represented in a particular picture, if not actually embodied in a particular skeleton. (Daston and Galison 1992, p.91)

This provides a cautious note for genomic research. The HGP relied on creating a similar representation of the 'perfect' human, which typified features of different humans. The assumption that there is no difference between the 'ideal' type and 'typical' case is problematic. I will explore some of these issues in Chapters five and six on the selection of natural variations for use in experiments, as well as how the sequencing of genes sets a certain DNA sequence as standard.

2.2.3 Male and female in Nature

So far I have explored how male and female were constructed as separate kinds with different 'skeleton' essences. As research progressed, an additional factor was introduced, the idea of unity throughout nature which lead to 'sex', 'male' and 'female' being applied to very different organisms (i.e. humans, flies, mice, birds etc).

The shift within science from exploring individual phenomena to seeing classes of exemplars occurred in the 18th century. Chunglin Kwa has argued that Alexander Von Humboldt taught his readers by means of painting how to appreciate the ecological unit of the natural landscape and it was this study of ecology that led to a view of nature as unified (Kwa 2004). Scientists saw a supernatural order in nature, a linear development from the simplest and earliest forms of life up to man, created according to God's plan (Gaissinovitch 1990). In 1735 Carl Linnaeus created a plant classification system based upon this social view. Researchers from around the globe were bringing back samples and seeking to organise these in line with nature and God's plan. Linnaeus's classification system sought to fulfil both a scientific need for a workable category of new specimens and samples, and a social need to explore God's plan. Schiebinger has termed this system 'Taxonomical Sexism', as it prioritises the male organs of plants over the female organs (Schiebinger 1999). The taxonomy was based solely on the number and arrangement of the reproductive organs; a plant's class was determined by its stamens (male organs), and its order by its pistils (female organs). Again, this is an illustration of how social and cultural sex ideologies influence scientific knowledge. This unity within nature allowed researchers to draw conclusions between different

species, and validated the use and extrapolation of animal studies to explore reproduction and sex.

The use of animals as 'experimental models' enabled researchers to explore the effects of castration in the late 18th and early 19th century. While undoubtedly castration had been used in the farming community and in the wider society (in religious establishments, for musical purposes, and as punishment) for centuries, it was not until 1849 that Arnold Berthold reported on the physiological and behavioural consequences of rooster castration. These experiments involved removing the gonads and transplanting them onto different parts of the body as well as transplanting ovaries into male birds and testes into female birds. Berthold concluded that since the severed testes were no longer connected to nerves they must affect behavioural and sexual characteristics by secreting a substance into the blood stream. Various experiments had indicated that in higher vertebrates the early embryo was morphologically female until the testes were formed and secreted substances which masculinized the embryo. The development of the female form was seen as passive, and the 'default' form of human development (Fausto-Sterling 2000).

Alice Dreger has argued that during this period, sex became seen as rooted within the gonads, and has terms it the 'Age of the Gonads' (Dreger 1998). As the female was seen as 'default', the processes of male development were defined as a movement away from the female basic body plan, and 'becoming a male' was reliant on the 'chemical messenger' produced by the testes, testosterone. The character of sex (masculinity and femininity) thus became seen as result of chemical 'messengers'. The scientific study of sex differentiation became defined in terms of the active physical processes leading to the formation of the testes (Fausto-Sterling 2000).

The perceived connection between males and the chemical role of testosterone in different species was exploited within medical treatment. In 1889 Charles Edouard Brown-Sequard (1817-1894) reported increasing his physical strength, mental abilities and appetite by self-injecting an extract derived from the testis of dogs and guinea pigs. By the end of the year more than 12,000 physicians were administering Brown-Sequard's fluids as a new 'Elixir of Life' (Shah, 2002. p437)

2.2.4 Sexed body

During the 19th century, genitals were seen as the 'essence' of sex. The testis was the root of masculinity in terms of physical strength, mental abilities, appetite and vigour, the ovary was the seat of femininity as defined by reproduction (Dreger 1998). Increasingly throughout the 19th century, it was argued that male and female bodies were perfectly formed for their roles within reproduction (Schiebinger 1987; Laqueur 1990). The male was the rational and active component, and his body and nature were created to provide for his family and to govern their actions. The female on the other hand was formed to conceive and bear children. This ideology of sex weaved together the liberal philosophical ideal that every person had a right to self-determination and should be treated equally, and the social principle that sought to maintain a segregated gender system (Laqueur 1990). This ideology rested on the idea that a person's sex, i.e. their body and constitution, was perfectly formed for their gender role within society. Thus, as a woman's role in society was as a mother, God had created her perfectly formed both in mind and body for motherhood. It could then be argued that women should be withheld from education and economic success since they were not suitable for that sphere (Schiebinger 1987).

In *The Descent of Man*, published in 1871, Charles Darwin proposed that male superiority had been originally produced by both sexual selection and natural selection and was only transmitted to the offspring of the same sex. There is not space in this thesis to explore the basis of the theory of evolution; however I will mention its impact upon one of Darwin's colleagues, Granville Stanley Hall. Hall undertook a number of studies to explore the differences between girls and boys and their mental concepts. In doing so, Hall developed Darwin's ideas so that what had traditionally been described as part of a divinely determined order of things, was now being explained scientifically as the agent of evolutionary purpose (Shields 1982). Darwin's work did not challenge the structure of social organisation, rather it changed the foundation of the argument by replacing the agent of 'God' with 'Nature'[1] as well as solidifying the view that the categories of male and female could be applied throughout nature.

[1] For an interesting rebuttal of Darwin view of male as superior to females see *The Sexes in Science and History, An Inquiry into the Dogma of Woman's Inferiority to Man,* by Eliza Burt Gamble 1919.

2.2.5 Summary

It is debatable whether prior to the 18th century there was a dominant discourse regarding sex, indeed it has been observed that by 1800 more than five hundred theories as to the cause of sex had been proposed (Maienschein 1984). So not only were there a number of differing and contradictory suggestions as to what caused sex, but the division between scientific and social knowledge of the human body was blurred. Yet by the end of the 19th century, with the consolidation and institutionalisation of science discourses, a dominant view was established. This view held that the human body was two sexed, male or female and that differences between the two sexes could be seen throughout the body. In addition the binary categories of male and female were found throughout nature. The role of sex narratives as ideology will become clearer in the next section where I explore the more recent history of sex, and genetic sex.

2.3 Genetic sex

Genetic sex, as defined by XX and XY-chromosomes, plays an important role in justifying the current view of humans as two-sexed. As noted in the early section the idea of humans as two-sexed was well established by the 20th century, and researchers were quite certain that hormones played a key role in creating the two morphologies (Dreger 1998; Oudshoorn 1994). There was still much discussion regarding what was the cause of the difference, as the 'essence' of sex. This section will give a brief history of the sex-chromosome and how 'genetic sex' became established as the sex determining factor(s) before moving to explore its use as a social technology used to govern human bodies within the wider society.

2.3.1 Searching for the sex determination factors

The discovery of genetic sex in mammals is relatively easy to outline. In 1891 a 'structure X' was observed in insects, which was linked to sex determination by Clarence Erwin McClung in 1902. In 1904 Edmund B. Wilson reported that some insects had smaller, differently shaped Y-chromosomes in addition to the X-chromosomes. A year later he karyotyped the male *Protenor belfragei* with 13 chromosomes (with one X) and the female with 14 (with two X). In 1909 he discovered the smaller Y-chromosome, and thus defined males, for this species, as having the genotype XY and females as XX. In 1917 it was reported that human cells contained X and Y-chromosomes. In 1923 Theophilus Painter, a well-known American zoologist,

stated that there were 24 pairs of chromosomes in human cells and that female mammals have an XX constitution whereas males have X and Y-chromosomes (Painter 1923). However taking this as a 'history' is problematic because it is based on the dates used to claim priorities in research 'discoveries' and does not take into account how these findings became recognised by the wider science community and incorporated into science narratives. This is especially important for 'genetic sex' as research was being conducted in different localities and published in different languages.

Jane Maienschein has suggested that early 20th century sex determination research occurred within three main themes; the externalist, internalist and hereditary approach. The externalist view of sex determination dominated from the 1880s to 1890's and was based on researching sex determination as caused by external factors which occurred during the organism's development. The internalist view, successfully pursued by German physiological or experimental embryology in the 1890s and 1900s, considered that sex determination occurred in the egg. This was superseded in 1905 by the hereditary approach, which considered sex to be determined by inherited factors.

Maienschein argues that none of these theories provided an adequate description, so that a "convergence of difference approaches provided a new approach, and by 1915 the result was a reshaped tradition of development study" (1984, p.458). During this time, Nelly Oudshoorn (1994) has argued, there was a dispute between genetics and endocrinology over sexual development. She notes how during the 1910s physiologists suggested that the determination of sexual characteristics was affected by environmental and physiological conditions during the development of the embryo. Geneticists suggested, however, that sex was irrevocably fixed at the conception by nuclear elements, the sex-chromosomes (Oudshoorn 1994, p.21). Oudshoorn concludes that the two research fields resolved the dispute by endocrinology limiting its study to sex differentiation (the biological process which the organism underwent to become a certain sex) and genetics limiting its focus to sex determination (the cause of the biological process).

Maienschein's and Oudshoorn's work provides a solid historical view for the period up till 1915 (after which Oudshoorn's research concentrates on endocrinology), however the idea of 'genetic sex' occurred slightly after these two accounts. To find this early history I briefly accessed the database JSTOR. It should be noted that JSTOR only

houses English language journals, and as a result this should be seen as a limited historical discussion. However the articles found from the 1920s and 1930s indicate that the research questions of which Maienschein and Oudshoorn speak were still fluid, and that the research split between sex development (endocrinology) and sex determination (genetics) was not resolved until as late as the 1940s.

The journal articles from the 1920s indicate that researchers were seeking a "single solution of universal application" to sex determination (Coulter 1925, p.226). It was widely accepted that sex in birds and mammals was determined at fertilization (Moore 1925), and the male XY elements and XX female elements were seen as having "a morphological association to chromosomes" (Moore 1925, p.177). Sex is recognized as having what researchers refer to as 'quantitative' and 'qualitative' aspects, and "the expression of latent possibilities of both sexes are often encountered in which elements of the two different sexes have developed simultaneously" (Moore 1925, p.178). The potential of each sex is taken to exist in the zygote, and the articles refer to 'zygote sex determination factors' which include both chromosomes and hormones.

The idea of a single solution to sex determination was based on the idea of a unity within nature, as indicated earlier in this chapter. Researchers used a variety of different organisms (*Drosophila*, moths, frogs, guppies, birds, freemartins [masculinised XX cows]) which they considered related in a hierarchical structure by evolution, and as such to share the same sex determination mechanism. Breeding experiments favoured the use of organisms with short generation times, clear sex differences and easily visualised cells and chromosomes, however each organism proved useful for specific types of experiments and the JSTOR articles indicate that the researchers sought to incorporate the results into a single sex determination description. During these early years the link between sex and karyotype began to be made, and while for some of the animals cytological studies were lacking, researchers sought to support claims that the results should be included based on the established view of evolutionary relations[2]. Similarly humans and *Drosophila* had both been shown to have sex-chromosomes and as such were accepted as sharing the same sex determination system.

There was agreement that the sex was determined at fertilization, however there was disagreement regarding whether this was due to the 'sex-chromosome machinery'

[2] One example is the discussion regarding whether the common frog was more closely related to *Necturus*, which had been shown to have sex-chromosomes, or to toads, which do not. (Lloyd 1929)

(quantitative) or metabolism differences in the egg (qualitative). Researchers who based their view of sex determination on birds argued that the "sex-chromosomes" were only one of many forces "operating to determine sex" (Coulter 1925, p.226) and that through changing the metabolism of the egg the environment could 'convert' the organism into an intersex or even the opposite sex. This research drew upon the gonad transplantation experiments in birds where they were able to create 'neutral' forms (Riddle 1924) and on the impact of changing the environment in experiments on frogs (Crew 1921). By 1925 it was agreed,

> In review it may again be stated that to the best of our knowledge sex determination occurs in the zygote: and as Lillie ('23) has stated we may make the "assumption that the zygotic sex-determining factors are also sex-differentiation factors….These factors are reinforced by early hormone production." There is a great deal of direct and indirect evidence that the sex-determining, as well as the sex-differentiating factors have a quantitative as well as a qualitative aspect and that the zygote contains the potentialities of both sexes; this is beautifully illustrated in sex intergrades or hermaphroditic forms. (Moore 1925, p.188)

In contrast to the qualitative factors, the 'quantitative' impact of the sex-chromosomes was stressed by Richard Goldschmidt and Calvin Bridges. Based on breeding different 'geographical races' of gipsy moths, Goldschmidt concluded that "the ultimate sex of every organism is here determined by two factors; (1) the relative dosage of the female- and male- determining subjects F and M (corresponding to X and A in *Drosophila*); and (2) by the genetic sex of the organism" (cited in Castle 1930, p.783).

Bridges based his view of sex determination on the model of *Drosophila*, and proposed what Castle considered "a 'sex factor theory' more than a 'sex-chromosomes theory', since sex (potentially quantitative but usually qualitative) is pictured as being influenced by factors upon all chromosomes" (Castle 1930, p.228). As the following quotation shows, human sex determination is closely linked to that in *Drosophila* as in both species, the XX karyotype is female and the XY is male:

> in *Drosophila* and man, and in mammals generally, the sex tendency of X is weak in comparison with that of the Y (and associated autosomes) so that an individual containing both is a male, XY. It takes a double dose of X (with a plus tendency) to offset the influence of the Y and associated autosomes (having a minus tendency). Normal females indeed contain no Y and are XX in formula, but Bridges has shown that XXY individuals can be produced under certain circumstances and they are also female in sex (egg producers). Hence 2X>Y, the net outcome of such a combination being female. (Castle 1930, p.788)

This initial analysis of the journal articles from the 1930s indicates that the different sex determination systems had not been separated and that there is an unspoken view of sex determination as being unified, as evidenced by the application of *Drosophila* research findings to the human system.

To do justice to this fascinating early period in genetics exceeds the space of this thesis however one more issue should be mentioned, the early suggestion that a single pair of genes may be the cause of sex:

> A further point emphasized by Winge is that his evidence supports the idea that sex determination is controlled by a single pair of genes – a dominant factor for maleness resident in the Y-chromosome and recessive factors for female present in the X-chromosome. He considers that if genes for maleness and femaleness were genetic complexes of many genes crossing over would take place and intersexes result. (Goodrich 1929, p.87-88)

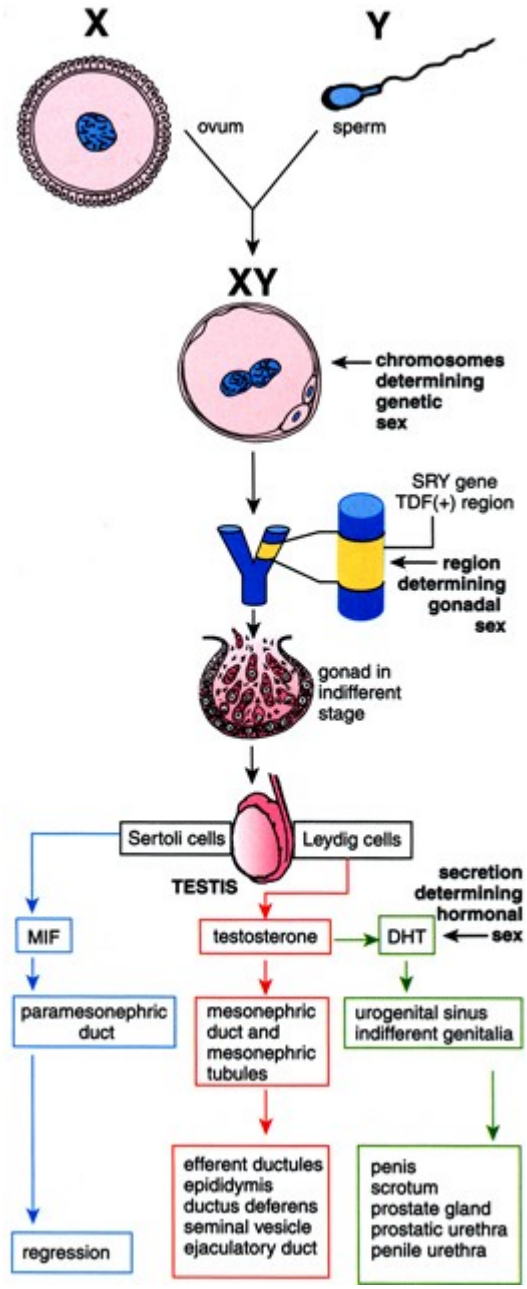
Øyvin Winge's proposal that there was a single 'testis determining factor' (TDF) located on the Y-chromosome will be further explored in Chapter Five. However it is important to note that the idea that sex was due to a single pair of genes was criticised by Thomas H. Morgan. During the 1930's Morgan voiced the opioin that sex linked characteristics were likely to be located on different chromosomes and separate from the genes required for sex determination (

The technological advances over the next 26 years enabled scientists increasingly to view the chromosomes more accurately by placing cells onto microscope slides. The standard textbook account held that there were 24 pairs of chromosomes. By 1956, it was obvious that the textbooks were wrong: there are in fact 23 pairs of chromosomes in human cells. The development of improved tissue culture techniques--introduction of colchicine to stop division in metaphase, and the use of hypotonic solution to improve the separation of chromosomes (purely serendipitous, a technician mistakenly made a 'wrong' concentration)--enabled the correct human chromosome count to be established in 1956 (Miller 2006).

When the 'standard' number of chromosomes was recognised as 23 pairs, many researchers who had found alternative numbers began to recognize that their techniques were not at fault, but their subjects might be. The first chromosomal abnormalities were detected in 1959 when researchers published the karyotype of a Down's syndrome

patient with 47 chromosomes (trisomy-21). In the same year Charles Ford and Kenneth Jones showed that individuals with Turner's syndrome had 45 chromosomes instead of the usual 46. As individuals with Turner's syndrome were viewed in the science community as being anatomically female, the gene which 'caused' maleness was take to be on the Y-chromosome and not due to the double dosage of X-chromosomes. This was supported by the finding that males with Kleinfelter's syndrome had 47 chromosomes (XXY) and that the double dosage of X-chromosome did not affect the person's male phenotype. Through this use of intersex conditions researchers found that the number of X-chromosomes did not seem to affect the phenotype of sex; rather it was the presence of the Y that determined the body's morphology (Fausto-Sterling 2000). Thus according to the standard view of sex determination male determination is active, requiring the Y chromosome (see Figure 2.1, a typical diagram of sex determination, it is the Y chromosome, and the SRY gene which determines sex and leads the gonad to differentiate into a testis).

Figure 2.1; Sex determination illustrated in a diagram taken from an undergraduate university course. When the egg (ovum) and an Y carrying sperm combined, and the SRY gene which is located on the Y chromosome will lead the gonad to differentiate into two types of cells which produce a range of hormones and produces the typical male phenotype.
http://anatomy.iupui.edu/courses/histo_D502/D502f04/lecture.f04/Malef04/ychromo.jpg



The idea of sex-chromosomes as an easily discoverable 'genetic sex' fitted neatly into the established endocrinological binary sex model where there were two opposite poles of morphologies (male and female). Within endocrinology, sex differentiation is viewed as an ongoing active process since 'sex hormones' are important throughout an organism's life, and are especially significant at two stages of development: in the early

embryo and at sexual puberty. This has allowed endocrinologists to conceptualize sex morphologies as linear, with the ideal female and male on opposite poles, and a range of morphologies in-between. In the case of geneticists those individuals viewed by the medical establishment as inhabiting the middle ground between the female and male poles could now be understood as the result of genetic mutations or a developmental abnormality (see Chapter Seven for a further discussion of how cases of 'sex-reversal' were interpreted within the binary model and used in the discovery of sex determination genes).

By the 1960s the two research fields, sex development and sex determination had been split. While sex development was seen as being influenced by the environment, sex determination in mammals was seen as genetic and fixed at conception. I argue in Chapter Eight that the view of 'genetic sex' as fixed is misleading as the 'genetics' of our bodies is constantly ongoing, every breath relies on changes in the genetic processes in our cells. However genetics is more commonly understood to relate to the 'inheritance' of traits and the case studies will reveal the complex interaction of inheritance and views of molecular genetic processes. In this regard the analysis of popular science books in Chapter Four indicated that the idea of sex determination as genetic has a wider connected to the idea that sex (and arguably gender) is inherited. This is the fifth factor I will argue is key to how genetic sex is understood (See Chapter Four).

2.3.2 Social use of sex genetics

There are a number of examples that indicate how scientific explications of the 'sex-chromosomes' have entered into social narratives of biological sex. These include the proposed link between the Y-chromosome and crime (Reid 1987), and the use of the 'Barr body' test to reveal the 'true' sex of people with intersex conditions (Miller 2006). However for this chapter, I have chosen to explore the use of 'sex-chromosomes' to replace gender verification in the 'sex tests' in the Olympic Games as this exemplifies how genetic sex has been constructed as a technology with political priorities.

During the 1950s the public grew suspicious of the lean, athletic bodies of female athletes in sports. In response a 'sex test' was instituted at the European Track and Field Championships in Budapest in 1966, which required participants to show their genitals and breasts to doctors (Fausto-Sterling 2000). In 1967 the International

Olympic Committee (IOC) decided that women athletes should undergo a similar test. The media termed these sex tests 'nude parades' and they provoked outrage. Understandably, there was soon a call for a more scientific test, and the officials implemented the 'Barr body test'.

The 'Barr body test' resulted from Murray Llewellyn Barr's discovery in 1948 that female cat cells had dark blobs that were a type of 'sexual chromatin' not found in male cat cells, and later identified as the remains of one of the X-chromosomes (Potter and Soltan 1997). The observation that in female cells the second X-chromosomes did not look like the other chromosomes indicated that they were unused by the cell, and hence were inactive. This solved a scientific puzzle, as a few years earlier it had been recognised that Down's syndrome was caused by an extra chromosome. The observation that the extra X-chromosome was inactive explained why it did not cause a major defect. Gradually the physical entity of the 'second' X-chromosome became termed the 'Barr Body'. This apparently static and inactive construct became the identifying determination of a genetic female, which lent 'sex' new scientific credibility and social legitimacy. Even before the 'Barr body' was clearly identified as related to the second X-chromosome it functioned as a 'good enough' test for sex, as it was

> embedded within a coherent system of scientific belief that sustained observational evidence about the Barr body, and scientific theories about sexual development in a mutually supportive relationship. (Miller 2006, p.462)

The use of the Barr Body test outside of the medical setting was facilitated by it being non-invasive, as it only involved taking cells from the female mouth and examining them under a microscope. This test within sports seemed to be legitimated by the discovery of Ewa Klobukowska, a Polish sprinter, who having passed the visual inspection of her body the year before failed the Barr test in 1968 (Elsas et al. 2000). However while the individuals detected were chromosomally males, many did not have the corresponding body type since they were androgen resistant and therefore unaffected by the strength-promoting qualities of testosterone, while other women who 'failed' the Barr body tests had variations of XY gonadal dysgenesis. The sex chromatin test would also not have identified men with XXY karyotype or Klinefelter's syndrome and they would be allowed to compete, although theoretically they would benefit from a larger quality of testosterone (Serrat and Herretos 1993). As more became known about the genetic foundation of these sex abnormalities it became

increasing clear that the test was not detecting those individuals who benefited from 'genetic maleness'.

In 1990 the International Amateur Athletic Federation (IAAF) held a Workshop on Methods of Femininity Verification. The workshop concluded that laboratory-based sex determination should be discontinued, a recommendation that was accepted shortly thereafter by the IAAF and subsequently by all but four of the international athletic federations (IAAF 1990). Under pressure IOC responded by replacing sex chromatin with DNA-based methods to detect Y chromosomal material, principally the SRY sex-determining locus on the Y-chromosome. This procedure was implemented at the 1992 winter games in Albertville (Serrat and Herreros 1993). However it was highly sensitive, which led to a high frequency of false positive results. But it has also come under criticism from scholars and activists including Myron Genel on the basis that it tested for the presence of a DNA sequence and as such was not a test for sex or gender (Genel 2000).

Social views of genetic information were also changing during the 1990s and in the 1996 Lillehammer Winter Olympics the local organisers decided that these tests should not be carried out. Reportedly the Norwegian government objected to foreign medical staff conducting the tests and the government sought to pass a law making such examinations illegal (Pittaway 1999). However the 1996 Summer Olympic Games in Atlanta included a comprehensive process for screening, confirmation of testing and counselling of individuals detected. At this time all the relevant professional societies had endorsed resolutions that called for elimination of sex/gender verification testing, including the American Medical Association, the American Academy of Paediatrics, the American College of Physicians, the American College of Obstetrics and Gynaecology, the Endocrine Society, the Lawson Wilkins Paediatric Endocrine Society, and the American Society of Human Genetics (Stephenson 1996).

The arguments that were made against the need for physical testing were that athletic clothing could not 'hide' someone's sex, as well as the fact that athletes are required to give urine samples under direct supervision for doping purposes. In the 1999 meeting of the IOC's executive board, it was decided to discontinue the practice on a trial basis at the forthcoming summer Olympic Games in Sydney. As it stands now, intervention and evaluation of individual athletes is undertaken by appropriate medical personnel

only if a question has been raised regarding an athlete's biological sex identity (IAAF/IAF 1990). Peter Tallberg, chairman of the IOC's athletics commission,

> Testing of this nature is not a part of a proper, modern attitude to gender and equality in sport. Some individuals who have failed the examinations have not attempted to question the findings because of the acute embarrassment, even though they perhaps should have done. (Pittaway 1999)

This overview of the history of sex testing in the Olympic Games has the connection between the idea of genetic sex as an essential and deterministic property of the human genome/body and what I term the technology of genetic sex. This technology is partially a collection of different tools, karotyping, chromosome staining, DNA sequencing; tools which have been recruited from existent laboratory practise from different biological fields and morphed so that regular 'sex testing' of female athletes could be carried out through the technology of genetic sex. As Langdon Winner has argued, technologies can contain political properties in those cases where "the invention, design, or arrangement of a specific technical device or system becomes a way of settling an issue in the affairs of a particular community" (Winner 1980, p.22). Following Winner's concept of politics as "arrangements of power and authority in human associations as well as the activities that take place within these arrangements" (Winner 1980, p.22), the view of genetic sex as a political technology becomes clear. These arrangements of power are likely to relate not only to gender/sex but also to wider cultural and social structures such as cold war politics, national stereotypes especially that of 'Eastern European Women', drug testing and coverage of sport in the mass media, which opened up sport viewing to a general audience. While more research is needed to fully explore these features, it is interesting to note how national and international aspects have shaped sex testing. In the 1950s, at the start of the Cold war, athletes' bodies were seen as representatives of their nations, and some of the initial calls for 'sex testing' came from the assumption that Eastern European countries were likely to try to pass male athletes off as women and thus an international scheme for testing female athletes was needed. By the Lillehammer Olympics it would seem that there had been changes, both at the level of the tests being carried out by International medical staff and as a transformation from the athletes' genetic information as public to it being considered their own private information which they should not be forced to share. To see sex testing wholly in terms of enforcing gender and sex is to miss the wider motivations of inter/national politics and sports as a

political activity, which the technology of genetic sex was constructed to order and create trust in its activity.

As I will explore further in the final chapter, the perhaps unintended political consequences of the technology of genetic sex was the legitimisation and propagation of the segregation of male and females, men and women, as biological separate kinds. This separation of males and females in sport, as in many other areas, is unequal, as it is only female membership which is restricted through testing, and governed under the assumption that they must be protected as the 'weaker', less able bodied and less capable. However there are some logical inconsistencies within gender segregation in sports.

Men are generally seen as having a higher potential than women in sports, however for some activities this is questionable, yet sex segregation still takes place. At the 1992 Barcelona Olympics, Zhang Shan, a 24-year-old from Nanchong in Sichuan Province, represented China in the skeet shooting event, which included both men and women. Zhang caused a sensation by finishing first and becoming the first woman to win a mixed-sex shooting event. However after the Barcelona Games the International Shooting Union barred women from shooting against men which meant that Zhang could not defend her title (Olympic.org 2007). It becomes clear that women have been less present in sport for a number of reasons, not just biological differences. Alongside social changes, improved training and more girls becoming involved in sports, the observable differences between men and women athletes have narrowed and are likely to keep narrowing.

2.4 Conclusion

As Celia Roberts has remarked "bodies are produced through networks that fold and cut across science and other fields" (2002, p.21) and this chapter has explored some of the historical aspects of how sex, sex determination and genetic sex have been described. It is by no means exhaustive, but rather it sought to show both some of the scientific developments that led to our current view of genetic sex, as well as some of the social and cultural factors which add to the wider context of these developments.

The first section highlighted the shift from a one-sex model to a two-sex model. I noted that there were alternative views, and that it was problematic to talk of 'dominant' discourses as these prioritise medical knowledge over literature or other areas. As I showed in section 2.2, there was a wide variety of scientific developments from the 16th century onwards, all of which affected the way the body was viewed. The development of dissection technology allowed the body to be illustrated as sexed, and by the 18th century the illustrations in medical books were dominated by images of the male and female body as two-sexed. In keeping with the new sense of unity in nature, the scientific categories of the male and female formed during the 18th and 19th centuries came from comparing humans with animals. This involved a combination of the socially dominant view of human sex, and the study of animal endocrinology and genetics. Even before Darwin's suggestion that man was related through evolution to apes, scientists were making connections between the workings of different animals in generation and reproduction.

The second section explored the research that lead to genetic sex being accepted as deriving from a sex determination factor in the mammalian system. Researchers accepted that the 'primary' sex was fixed at fertilisation while seeking a single explanation of sex determination that held true for the variety of organisms that they studied. Chapter Five will expand further upon the search for the sex determining factor, however in this section I indicated how the karyotypes of human intersex conditions established the view of mammalian genetic sex as female being XX and male being XY. The idea of 'genetic sex' representing a person's true sex was exploited in the Olympics' use of 'Barr body testing' and other genetic tests to govern sport along segregated binary sex lines.

2.4.1 Sex as an ideology

Exploring how 'biological sex' and 'genetic sex' have contributed to ideology opens up a multitude of questions, especially regarding what values have been invested in these explanations. The proposal of the one-sex, two-sex shift would indicate that we should avoid thinking of scientific explanations of sex as having greater 'truth' or 'accuracy', but rather view them as successful or not within their historical and cultural context. As noted in the introduction, Mullins (1972) outlined four requirements of ideology. The first is that it must have power over cognitions. Thomas Kuhn (1962) stressed the power of scientific paradigms in structuring thought, and it is quite clear that many of

the features described in this chapter would be encompassed by an idea of a 'paradigm of binary sex'. However, in this thesis I will argue that the 'paradigm of binary sex' structures scientific research as well playing an important role in structuring political and cultural spheres. The use of ideology as a framework enables an exploration of how scientific views of sex structure political and cultural spheres and institutions.

The second factor which Mullins requires of ideology is that it is capable of guiding one's evaluations. The study of the view of sex in the human body has clearly shown how researchers throughout the ages have been guided by their ideological view of the world. Those researchers who expected to find the one-sex body, succeeded, and illustrated this within textbooks. However, with the change in political and social culture, researchers not only expected that the skeleton would reveal sex differences, but chose skeletons which would show the differences. The fact that certain methods and results were discarded because they did not reveal knowledge that fitted into the ideology supports Mullins' third factor of ideology, that it must guide actions. Finally Mullins argues that ideology must be logically coherent. In the case of sex, which is both a social and scientific category, this included being logical for scientists and for the general public. Indeed the shift to a two-sex model is likely to have been necessary to incorporate both the increasing knowledge of the human body and the social and reproductive roles which they were seen to have in their ideal form.

The proposal that descriptions involving sex should be viewed as ideological also opens up questions regarding feminists' descriptions of sex. The political project to split gender from sex in the 1970s was based on a natural boundary, leaving sex 'prior to gender' and as such the 'natural', transcultural and biological basis which was untouchable to change (Kraus 2001). While it is generally accepted that this split has been productive in the past, it has now come under criticism as it enforces a 'neutralization' of sex (Kraus 2001).

Judith Butler in *Bodies that Matter* (1993) has deconstructed this to some extent; however it is rather frustrating that much of the work is theoretical, relying on the reinterpretation of scientific studies, and what seems a haphazard gathering of examples which support the political project. Such arguments make heavy use of intersex conditions, arguing that they show Nature's plasticity, however this political project is currently being questioned by a number of intersex groups (i.e. Intersex Initiative, The

UK Intersex Association etc). I will explore this further in the final chapter; but at this stage it suffices to point out that the work within gender studies is in itself ideological. As Ruth Hubbard has noted, "every fact has a factor, a maker" (Hubbard 2001, p.159). She goes on to argue "integrating feminists politics into our science, we must insist on the political nature and content of science work and of the way science is taught and otherwise communicated to the public" (p.159). In regard to the possibility of creation of a 'feminist science' Helen Longino has called for researchers to redefine their relationship to the data,

> Instead of remaining passive with respect to the data and what the data suggest, we can acknowledge our ability to affect the course of knowledge, fashion or favour research programs that are consistent with the values and commitments we express in the rest of our lives. (2001, p.220)

There are clearly many models of feminist sciences, and it is only my intent here to argue that they, like the traditional sciences which they seek to deconstruct, are ideological. Views of sex and sex difference depend both on social and scientific perspectives. As a result one view of sex can not be said to be closer to 'truth', because what is considered to be 'sex' is defined in terms of the social world rather than the 'natural'. Sex and bodies have always been and still are seen from many angles. Thus, as sex is socially defined, biological views of sex are in constant flux. The idea of sex ideologies encompasses both the theoretical ideas of the world which people who support that ideology believe, but also the actions and institutions in which they become incorporated (as in sex testing in the Olympics).

It is clear that knowledge about the body was not simply produced within a laboratory and exported (Schiebinger 1999), but rather, as we now understand the practise of current science, there was a fluid interaction between society and science, as well as, between nature and culture. The next two chapters will explore the current portrayal of the X and Y-chromosomes in popular science. This analysis shows than many of the issues covered in this historical chapter, the erotic context of bodies used in science, the religious and social context of science knowledge, as well as the andocentric bias are visible within descriptions of genetic sex.

CHAPTER THREE - THE GENETIC PRODUCTS OF POPULAR SCIENCE

> What constitutes femaleness? It is my considered position that femaleness is conferred by the final pair of XX-chromosomes. Otherwise I don't know what it is.
>
> (Germaine Greer, AIS website 1999)

3.1 Introduction

While 'public understanding of science' (PUS) is a phrase which causes ripples of dread in many parts of the academic community, it arguably plays a critical role in many public science 'engagement' programs in the United Kingdom (Turney 2007). Public attitudes surveys such as the Eurobarometer indicate that trust in science has decreased in Europe and that there is low support for non-medical genetic research (Eurobarometer 2001). Governments have become concerned by this lack of support which jeopardises commercial interests in genetic research. PUS activity has been motivated by the suggestion that this decreasing support for science and its endeavours was due to a lack of understanding of the 'real' issues. In the United Kingdom organisations such as the Royal Society and the Festival of Science, have sought to encourage scientists to undertake public communication, illustrating how their research serves to benefit the public good and furthers society (Gascoigne and Metcalfe 1997). A visit to the science centre '@Bristol', "a unique destination, bringing science, nature and art to life", gives a picture of what goes on in a laboratory (http://www.at-bristol.org.uk/). In this picture science is exciting, world-changing and amazing. Not only does science produce the products and technologies on which our society is based, @Bristol highlights that it also enters our life in the forms of products and experiences which use science knowledge as both entertainment and education.

In the last three decades the publishing category of 'popular science' has grown in recognition and expanded in its media forms: from books, newspapers, magazines, television programs to whole channels and internet sites. The topics covered by this array of media range widely, including items on the environment (both human change and natural diversity), medicine (latest health advances as well as new understandings

of diseases), space exploration, and technological developments. Academic comments on popular science have given predominance to the items dealing with genetics for two main reasons. Firstly, there is a likelihood that genetic research may impact in some novel way on the human biological condition as well as certain social practices (e.g. criminal databases and parenthood tests, etc).

Secondly, the gene seems to have obtained an 'iconic' status (Nelkin and Lindee 1995). Donna Haraway (1997) has argued that there has been an objectification of the gene through its ascription of determinative power which has lead to gene fetishism. Similarly Bubela and Caulfield (2004) have argued that news coverage of genetics tends towards 'genohype', the hyping and selling of research claims. According to Abby Lippman (1993) there has also been a 'geneticisation' of social conditions and diseases with newspapers, television programmes and books playing an important role as channels of communication in this process (see also Geller et al. 2002).

While these are specific concerns related to communicating genetic knowledge, and will be explored in the next chapter, more fundamental to the issue of science communication are the assumptions on which the idea of 'public understanding of science' is based. The public is not one uniform group, but rather many diverse groups and subgroups of individuals. They are not 'blank slates' passively being educated about science, but rather people with various experiences and understandings of science (Michael 2002) who will have varying interest towards science-related activities. Finally it is important to note that different types of science communication conflict with each other and that people must make sense of this (Bucchi 2004).

According to Vasilia Christidou, Kostas Dimopoulos and Vasilis Kouladis (2004) communication directed to the general public should include two factors. The first issue is the understanding of the social practices and organisation of science and technology, including how scientists collect, interpret, and use data to direct their research and construct technological artifices. The second issue raised is that it is important to understand the values and assumptions that are inherent in the development of scientific and technological knowledge. Similarly it has been argued that the culture of science is important for audiences to understand how new scientific discoveries are made and that gaining an understanding of 'science culture' could help them place new findings in the

context of previously reported work (Kua et al. 2004). So, while newspapers have been found, on the whole, to accurately represent scientific findings (Geller et al 2002), they also

> (…) lack information and a suitable level of detail, assuming background knowledge that the reader is not likely to have or (...) not supplying the detail that will enable readers to make connections. (Kua et al. 2004, p.319)

Popular science books provide a possible method of increasing understanding of the daily scientific life, especially those books that seek to shed light on the 'inner workings' of science. In comparison to newspapers, popular science books have sufficient space to detail background knowledge, and can also outline the social situation of the scientists concerned and offer a wider view of the scientific fields and disputes.

The aim of PUS related activities is to increase trust and support for science activities, to which end they tend to present a picture of one united and dominant discourse. Felicity Mellor has argued that as popular science books do not respond to a specific controversy they constitute 'routine' boundary work for the demarcation of knowledge and expertise for professional goals:

> It is argued that by working at multiple boundaries, texts such as these are able to claim potentially contradictory attributes for science at the same time as sustaining its place at the top of a hierarchy of ways of knowing (Mellor 2003, p.509).

Typically the claims of science are viewed as free from commercial motivations. However in the United States there is a growing recognition that commercialisation is a major driving force in school education, especially as large corporations donate education material which counters environmentalism (Beder 1997). Of particular relevance to this thesis is the implication that science communication may be used to create a suitable market for related products. Research by the International Organization of Consumers Unions found that nearly 80 per cent of the sponsored educational materials it analysed,

> contained biased or incomplete information, promoting a viewpoint that favours consumption of the sponsor's product or service or a position that favours the company or its economic agenda. (Beder 1997)

It concluded that the commercialisation of education, arising from advertisements and sponsored educational material, posed a "significant and growing threat to the integrity of education in America" (Beder 1997).

There have also been efforts in the United States to entice mass media to carry popular science and health related information. 'Entertainment-education', as it is called is, defined as, "the use of entertainment media as a means of educating viewers about important health and social issues" (Kaiser Family Foundation 2006). While it is beyond the scope of this chapter to explore fully the extent to which educational and commercial purposes conflict within such products, it is important to recognise that these motivations, the educational and the commercial, both exist in popular science.

There has been little research into the quality and commercialisation of British material and nearly no research, either in the United States or the United Kingdom, as to the goal of market creation in the publishing of popular science books. Rather it is assumed that the authors of popular science are at the most motivated by earning money from the sales of the book (and any further publications), and gaining a reputation which will lead to further monies. Little discussion is raised regarding the role of these books in fuelling the consumption of spin-off products such as genetic testing products in Nutrigenomics or the use of DNA to trace ancient ancestors.

To explore how and what views of genetic sex and genetic sex difference are propagated in popular science I've chosen to look at three books from the 'popular science' category which deal with sex genetics: *Y: The Descent of Men* by Steven Jones (2002), *Adam's Curse* by Bryan Sykes (2003), and *The X in Sex* by David Bainbridge (2003). The three books chosen for this thesis were selected for their popularity in the dual sense of the term in that they are located within popular science and popularly read. The two selection criteria were that they concerned the X and Y-chromosomes and were recently published (within the last two years of the start of the thesis research) so that they could be expected to include the latest detailed explanations of genetic developments available to the public in book form.

As I have noted in the previous chapter, how sex and gender have been historically conceived of within society has been influenced and supported by science. It is clear that the creation of an ideology of genetic sex, which supports a binary view of

divisions between male and female, both in society and in science, is a fundamental part of our current social world. By exploring these popular science books I will shed some light on the current communication of genetic sex ideology.

The first half of this chapter explores the identity of the three authors. As I noted I did not base the selection on the authors but rather the book products. By exploring how the authors construct their identity as 'popular science authors' attention will be directed to the wider area of popular science as a status activity for scientists, the commercial value of the activity, as well as raising questions as to what type of author is interested in genetic sex.

The second half of this chapter explores the inclusion of social and cultural values in the 'packaging' of these books. The covers play an important role in catching the eye of casual browsers in bookshops and setting the readers' expectations regarding the content of the book. Rodger Bridgman (1996) has commented that there is a demand for science books to look like novels, supported in the case of these three books by their lack of diagrams and visual aids and the use of visual motifs in their covers. These draw upon a range of cultural and social topics including science, Darwinism, evolution, and Christianity as well as gender and sexuality. This discussion acts to sensitise both myself and the reader as to the range of latent cultural and social issues within the books.

3.2 Behind the curtain of popular science

Public science communication has been the traditional domain of the journalists who acted as both facilitators in a passive displacement of results and ideas from the expert specialists to the public and as gatekeepers and moderators for communication (Kelly 1998). However Media Studies and Science and Technology Studies (STS) have problematised the various concepts of 'the public', 'the media', and 'science' (Bucchi 2004). While much of the focus has been placed upon what the audience 'understands', this chapter explores the public image and persona of the popular science author.

3.2.1 Who are the authors, the 'senders' of science communication?

Traditionally popular science has been seen as a low status activity as it is unrelated to hands on research work.

> Essentially, popularization is not viewed as part of the knowledge production and validation process but as something external to research which can be left to non-scientists, failed scientists or ex-scientists as part of the general public relations effort of the research enterprise. (Richard Whitley cited in Shermer 2002, p.494)

In recent years the sales of popular science have blossomed with large sales and advances given to science writers (Shermer 2002). Carl Sagan claimed a US$2 million advance for 'Contact' in 1985, and Stephen Hawking's book *A Brief History of Time* spent a record 200 weeks on 'The Sunday Times' hardback bestseller list, with over 10 million copies sold worldwide (Shermer 2002 p.519). Clearly popularization of science is big business. However Sagan's scientific reputation and prestige may have suffered from his popular science success. He lends his name to the 'Sagan effect' commonly defined as:

> popularity and celebrity with the general public which was thought to be inversely proportional to the quality and quantity of "real" science being done. (Shermer 2002 p.492)

With this in mind it is rather surprising that scientists engage in popular science. In this section I explore the possible motivations of the three authors by exploring their academic and commercial background. Rather than exploring their own personal motivations, I wish to explore the public persona which the audience can access. To do so I have drawn on their public C.V.'s (located in November 2005 through a Google search) which provides insights into the type of identity the scientists respectively seek to portray to the 'public'.

David Bainbridge is a reproductive biologist who teaches veterinary students at the University of Cambridge. His staff page (http://www.pdn.cam.ac.uk/staff/bainbridge/) is clearly directed towards students at the university, detailing his teaching and research interests. His university page makes reference to his work with in "public understanding of science", both his popular science books and the talks which he delivers in schools. However he directs readers interested in his popular science work to another page; www.davidbainbridge.org. This page opens with:

> Hello. I am David Bainbridge and I write popular science books, usually about biology. My aim is to write books that can explain to anyone how we work. (http://www.pdn.cam.ac.uk/staff/bainbridge/)

This minimalist style is echoed in Bainbridge's main thesis regarding the simplicity of biology:

> Contrary to popular belief, science is essentially simple. Unlike most areas of human endeavour, our scientific knowledge has accumulated as a series of simple incremental steps. Because of this, it can all be explained as a simple story, so long as you leave out all the awful jargon. I used to work as a veterinary surgeon, and I soon realised that you can explain biology to anyone as long as you see it from their point of view. (http://www.pdn.cam.ac.uk/staff/bainbridge/)

Arguably scientists have traditionally refused to give up their viewpoint as experts, arguing that science can only be understood from a scientific point of view. By referring to scientific language in terms of 'jargon', Bainbridge seems to indicate that he is not seeking to be an 'expert'. Rather he emphasises the use of simple language that can be understood by everyone.

In contrast to Bainbridge's use of two web pages to separate university work from popular science, Steve Jones has only one page. His staff page is hosted on the University Collage London, (http://www.ucl.ac.uk/biology/academic-staff/jones/jones.htm) and contains both his academic-related work and his popular science. It is highly structured and places a marked empathise on Jones's relationship with the media. This is clearly apparent as it opens with a paragraph on his academic interests before moving on to his radio and television appearances.

> I have for several years been involved with the media, largely in presenting scientific work but also in a more general context. I have appeared on BBC Radio on more than two hundred occasions. I gave the 1991 Reith Lectures on "The Language of the Genes" and have since then written and presented a long-running Radio 3 series on science and the arts, "Blue Skies", and a six-part TV series on human genetics, "In the Blood", broadcast in 1996. I have also appeared in various other TV programmes, from Question Time to Late Review to Newsnight. In addition I have written extensively in the press on scientific issues and have a regular column in The Daily Telegraph – "View from the Lab". (http://www.ucl.ac.uk/biology/academic-staff/jones/jones.htm)

Public science communication can be seen as a 'fringe' activity, however Jones creates a trustworthy reputation by referring to the BBC and other reputable media including

political programmes. He then goes on to detail his 'outreach' work with schoolchildren,

> I have, I estimate, spoken directly to more than 100,000 school pupils during my career and am UCL's representative on the recently-established London Regional Science Centre, which aims to provide in-career training to science teachers.
> (http://www.ucl.ac.uk/biology/academic-staff/jones/jones.htm)

This outreach work to students is a strong motivation for many scientists who are concerned with the lack of 'future scientists' and thus 'outreach' work can be seen as an effort to recruit more 'bright minds' into the field. Popular science is encouraged by a variety of actors including an effort by company sponsored popular science prizes to attract more scientists to publish 'popular science' books. Jones webpage places the emphasis on the awards won (from media and other companies), not the number of copies sold:

> I won the Rhone-Poulenc book prize and the Yorkshire Post first book prize in 1994; and the BP Natural World Book Prize in 1999. In 1995 I was a member of the NCR Non-Fiction Book Prize judging panel, in 2000 the Guardian First Book Prize Panel and in 2001 the Samuel Johnson Book Prize Panel. I was awarded the Royal Society Faraday Medal for public understanding of science in 1997, the BP Natural World Book Prize in 2000 and the Institute of Biology Charter Medal in 2002. I am President of the Galton Institute.[3]
> (http://www.ucl.ac.uk/biology/ academic-staff/jones/jones.htm)

This emphasis on the recognition which the popular sciences books have attracted rather than the commercial success of the books is likely to be related to the peer recognition system within science.

The final paragraph of Jones' popular C.V. is related to his university positions. He notes that he has spent "much of my career at UCL" but has also had visiting posts at Harvard University, the University of Chicago, the University of California at Davis, University of Botswana, Fourah Bay College in Sierra Leone, and Flinders University in Adelaide. After this he lists his 'popular works'; *Genetics for beginners* (1991), *The Cambridge Encyclopaedia of Human Evolution* (1992), *The Language of the Genes* (1993 reprinted 9 times), *In The Blood* (1995 reprinted 7 times), *Almost like a Whale: The Origin of Species Updated* (1999), *Y: the Descent of Men* (2002). Finally his

[3] The Galton Institute is a charity which promotes "the public understanding of human heredity" (http://www.galtoninstitute.org.uk/).

webpage makes a simple reference to his academic work: "In addition I have published a hundred or so scientific papers in a variety of journals."

Jones does not draw upon his science publications to support his 'expertise', rather he draws first upon media (radio, TV and public lectures) and on his university positions. The lack of reference to his scientific papers indicates that his reputation is secured by the wider acceptance as an expert. Indeed, his status within PUS is strengthened by his inclusion as one of John Brockman's 'third culture intellectuals'. Brockman drew upon C. P. Snow's suggestion in 1959 that the clash between the two cultures of the literary intellectuals and scientists should be healed by a 'third culture' in which the communication gap between the two cultures should be bridged. In 1995 Brockman, who is a literary agent for science writers, published a book in which he argued that a third culture existed. Unlike in Snow's vision, however, the scientists were not communicating directly with literary intellectuals, but rather, "working scientists communicated directly with lay people, and the lay challenged them back….a peerage culture" (Kelly 1998, p.992). Brockman makes his view explicit, stating:

> literary intellectuals are not communicating with scientists. Scientists are communicating directly with the general public…Today, third-culture thinkers tend to avoid the middleman and endeavour to express their deepest thoughts in a manner accessible to the intelligent reading public. (http://www.edge.org/3rd_culture/ The edge 1991)

Brockman drew together 23 leading scientists as examples of 'third culture intellectuals[4]' but he also pursues this culture through his online magazine, *The Edge*. I will explore the idea of a 'third culture' further in the conclusion, however at this time it is sufficient to note that Jones was one of the scientists included by Brockman and that this rise of the scientist as a 'public intellectual' indicates a potential increase in the value of the field of popular science. In this regard Jones could be termed a 'professional popular scientist'. He clearly spends a predominant amount of time undertaking popular science activities, rather than teaching (unlike Bainbridge).

The final author, Bryan Sykes is listed as a professor of Human Genetics at Oxford University; however he does not have a staff page. Rather the Google search listed his

[4] The 23 scientists included were: Paul Davies, Richard Dawkins, Daniel C. Dennett, Niles Eldredge, J. Doyne Farmer, Murray Gell-Mann , Brian Goodwin, Stephen Jay Gould, Alan Guth, W. Daniel Hillis, Nicholas Humphrey, Steve Jones, Stuart Kauffman, Christopher Langton, Lynn Margulis, Marvin Minsky, Roger Penrose, Steven Pinker, Martin Rees, Roger Schank, Lee Smolin, Francisco Varela and George C. Williams. (Vesna 2001)

involvement with a company 'Oxford Ancestors', which he founded after the publication of *The Seven Daughters of Eve*. As the site notes:

> The Company was formally incorporated as a University of Oxford "spin-out" in March 2001 and operated, initially, from Littlemore, just south of Oxford. Over the next 12 months, following constant media attention, we were inundated with samples from people who wanted to know more about their own maternal ancestry and their place in the family tree of all humanity. Soon the number of samples became so large that we had to relocate to larger premises, based in Kidlington, just north of Oxford.
> (http://www.oxfordancestors.com/background.html)

The website portrays the company's formation as driven by the media attention and the demand from the popular science book readers for sequencing services. This company advertises itself as 'We bring ancestry to life' and the main page notes that,

> Oxford Ancestors is the world's leading provider of DNA-based services for use in personal ancestry research. Our services and products provide the scientific insight that allows you to explore and discover your own ancient genetic roots.
> (http://www.oxfordancestors.com/background.html)

Below is Sykes's entry in the 'who are we' page of the company website,

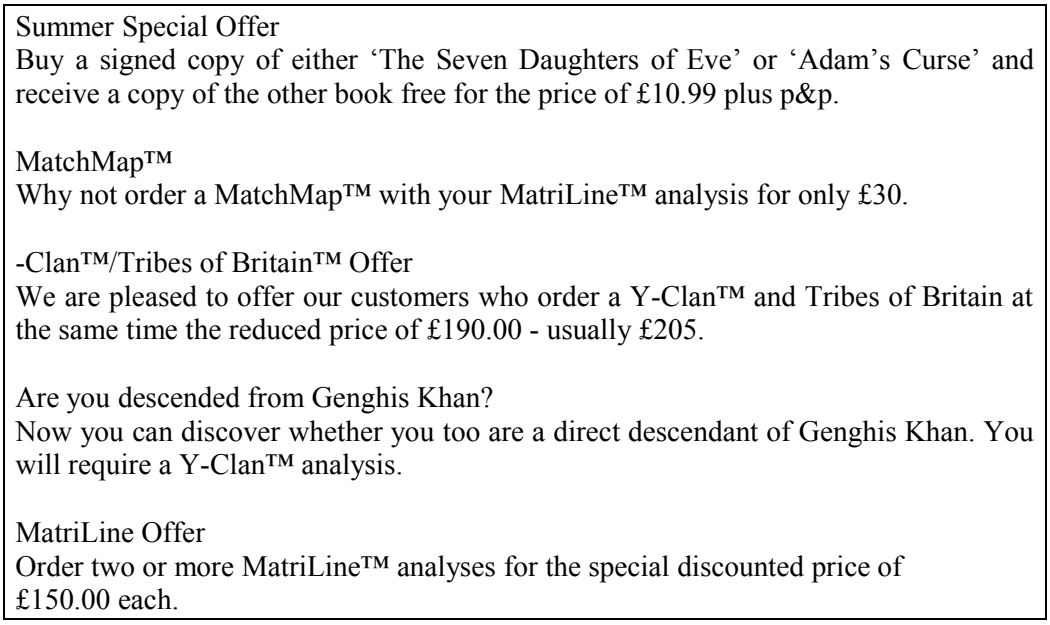
> Professor Bryan Sykes Chairman&Founder Tara 16126 T-C, 16292 C-T, 16294 C-T
> Interests: Croquet, Wine
> Bryan is the Founder of Oxford Ancestors and is a Professor of Human Genetics at the University of Oxford. His work in the field of mitochondrial DNA analysis allowed him and his co-workers to produce the most complete DNA family tree of our species yet constructed; the basis of our MatriLine™ service. Using his own surname, Bryan was the first to show the astonishingly close connection between surnames and Y-chromosomes, which became the basis for our Y-Line™ service. Bryan lives in Oxford and on the Isle of Skye.
> (http://www.oxfordancestors.com/the-team.html)

Though his academic title is used, in the main body of text there is a shift towards the use of his Christian/first name. This can be seen as an attempt to create a more personal relationship between Sykes and the reader, which is also indicated in the listing of 'personal interests'.

The company is clearly a 'spin-off' of his earlier popular science writing which analysed mitochondrial DNA (mDNA) to explore maternal inheritance. Indeed the tight connection between the popular science books and the products being sold by his

company is illustrated on the site, which during summer 2006 listed offers for the genetic tests and Sykes's books (see figure 3.1).

Figure 3.1. The 'Summer Special Offer' listed on Oxford ancestor's web page during the summer of 2005



Sykes could be thought of as a 'popular science entrepreneur', who has used his popular science as a vehicle for commercial successes. Indeed the company's Chief Executive, David Ashworth has made this clear,

> We have a very eminent Professor of Human Genetics, which is one of the keystones to the company's success. It's Bryan and his publishing which gives us gravitas and credibility that other companies don't have. (Holmes 2004)

It is clear the company has a well-established relationship with the media, and this has been exploited to create interest in their product, as Ashworth goes on to note,

> We can do fun things, like a Genghis Khan evening at a shish-kebab restaurant – Genghis Khan has more descendants than any other known person in history – and it pushed up all our sales because of the publicity. We could do interviews even with a paper like News of the World, and it generates interest! (Holmes 2004)

Ashworth argues that the company also has a beneficial impact upon genetics because prior to the company's formation, genetics had only been linked to negative issues.

> both Sykes and Ashworth have referred to their work, memorably, as 'DNA for fun'. 'It is. It's because, before us, the only thing DNA was associated with was bad news – GM foods, Dolly the sheep's ailments, guilt in rape or murder cases, pre-disposition to cancer – always negative. And for this? There's no bad news associated with knowing your ancient ancestral roots. It's only good. We are all from the same stock, and racial and ethnic discrimination between peoples means nothing.' Genetics can be very good news. (Holmes 2004)

Such uses of DNA have the potential to lead consumers to invest value in a fictional account of the life of their 'ancient ancestor'. On the back of the 2004 edition of *Adam's Curse*s Bryan Sykes is described by the *Sunday Telegraph* as "a specialist in deciphering the historians written in our genes" and on the inside cover Oxford Ancestors Ltd is described as giving "men and women the opportunity to find their place in the family tree of the entire human race through DNA based analysis and a chance to find their ancient ancestors" (Sykes 2004). It is questionable whether DNA tracing raises any novel issues when compared to 'traditional' family tracing based on written records.

The use of popular science and fringe products as 'good news genetics' may raise the scientific value of popular science in the eyes of scientists. Margaret Fahnestock (1986) argues that popular science books allow the circulation of positive images beneficial to scientists' interests in contrast to the alternative images produced in the news. Drawing upon Sykes's 'good news' genetic products it is possible that displaying genetic testing as a form of entertainment may support the normalisation of genetic information within public discourse as something harmless. This in turn may reduce the attention directed towards alternative views that see the use of genetic information in both medical research and social governance as problematic and potentially harmful.

It is clear from the discussions of the authors' identities that there are various motivations for pursuing a career within popular science and I suggest that there are three, if not more, possible characters. The first is based on Bainbridge as a part time 'new age' popular scientist who seeks to explain in uncomplicated terms using a simple story and who assumes the audience's 'point of view'. This contrasts with the second type as illustrated by Jones, who as an example of the original 'third culture intellectual' represents the full time 'expert popular scientist' and who is clearly accepted as a science 'expert' by the general public and the mass media. The third character suggested here is the 'popular scientist entrepreneur', based on Sykes, who seeks to

commercialise ‘fringe products’ related to popular science. As I noted these products have a potential to ‘normalise’ genetics products as harmless which may lead to the acceptance of their use in medical and governance contexts.

This discussion of the background of the authors has given an insight into three important factors. Firstly, traditionally PUS assumes that not only are popular science audiences homogenous, but that authors and those contributing to popular science are also homogenous. It is possible that if I had selected the authors as leading figures in the field, rather than the books as products, I would have developed an alternative view, in which the motivations and background were clearly homogenous. Instead this analysis has shown three differing identities: ‘new age’ popular scientist, professional popular scientist, and the popular scientist entrepreneur. Each of these authors is likely to have differing economic motivations and concerns based upon their backgrounds. Secondly, these authors create their ‘expertise’ in differing ways, drawing upon their university background, peer-recognition, PUS prizes, and media industry recognition etc. The ‘third culture’ supporters have argued that popular science provides a direct link between scientists and ‘lay audiences’, however the current success of popular science products rests on sufficient diversity of material available. Traditionally the scientific community has functioned as a ‘gate keeping’ facility as scientific standing and institutional acceptance has acted as a ‘quality’ control on popular science products, however as the market has grown in value the various non-academic actors such as editors and the publishing houses are likely to have gained influence.

Thirdly, the authors are all men. It has long been recognised that the popular view of ‘the scientist’ is predominantly male (i.e. Chambers 1983) but also science is portrayed as work which only men, with their rational and objective gaze, can pursue successfully (Wyer et al. 2001). As noted, I selected the books based on their popularity and success within the ‘popular science field’. However having recognised the sex bias I sought to identify popular science books authored by female scientists and there are surprisingly few, indeed Brockman included none within his twenty-third ‘third culture thinkers’. The lack of female participation within popular science is a concern, particularly in regard to the recruitment and retainment of young women to science. While it is recognised that there are fewer women within science how this impacts upon the apparent lack of female popular science writers needs to be explored further.

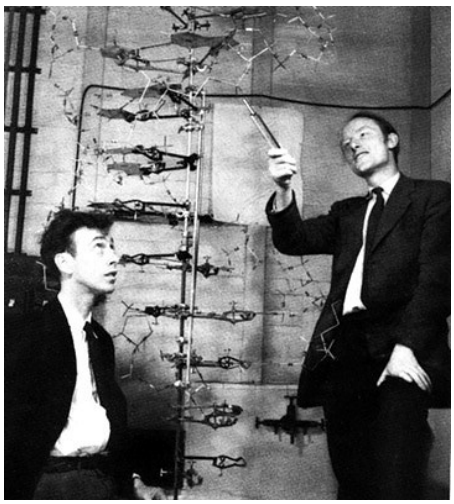
In this section I sought to slightly raise the curtain that separates the science writers from the audience of popular science. It is clear that there are a variety of different authors engaged in popular science, and that they undertake popularisation activities with different mindsets. They also construct themselves as 'experts' capable of writing popular science in different ways. There is little reason to think that one method is more 'effective' but rather the direct relationship between scientists and lay audience allows the heterogeneous audience to select from different products depending upon their personal background and interests. This direct relationship between scientists and the public may have also weakened the 'gate keeping' capacity of peer-review journals. Brockman has argued that this has given scientists themselves more power but it also removes the traditional source of credibility – peer review--which is not available to the consumer. This raises the question how the consumer selects between different popular science books.

In this next section I explore the presence of cultural values in the covers of the books. Book covers are important 'eye catchers' for people browsing in bookshops and thus the choice of images used to represent the content is important. The analysis focuses on the type of 'image' that the authors seek to create for their books and more specifically the portrayal of biology, genetics, gender and sex.

3.3 Visual Metaphors: Images of DNA, Genetics, X- and Y- chromosomes

One of the most famous visual metaphors in biology has been the molecular model built by James Watson and Francis Crick. This model was a valuable teaching tool in my undergraduate course, where we had to build the same model and measure the angles. Similarly in my Masters in Science and Technology course we explored the formation of molecular biology through the discovery of the structure of DNA. The photograph below has been widely used to illustrate Watson and Crick's discovery of the chemical model structure of DNA.

Figure 3.2. James Dewey Watson and Francis Harry Compton Crick Photographed by Anthony Barrington Brown 21 May 1953. (fr.encarta.msn.com)



Since this photograph was taken in 1953, DNA has been reified in a number of forms, most simply as two helical ribbons, and is used widely to symbolise genetics and DNA.

In this subchapter I will take apart the visual metaphors of three popular science books to see what type of visual images the authors have chosen to represent their claims and arguments. By unpacking the meaning contained within the visual metaphors, I will show that a link is drawn between the tiny molecules of DNA which the reader has no means to make sense of, and the human body, and that all the authors seek to show the reader a microscopic world through the written word.

My analysis of the visual images is based on semiotics and the work of Roland Barthes (1964), in which a distinction is made between two levels of meaning. The first is denotation or the first level of signification, drawing upon the obvious and readily understandable meaning, and not requiring specialised knowledge. At this level the photograph of Watson and Crick is easily understandable – the image is of two academics showing their model. The second level of meaning is that of the code or symbolic system that the reader is required to know to understand the image. This is called connotation and is one of the ways in which signs work on the second order of signification. At this level there is more uncertainty and flexibility in the meanings that are produced by the interaction of the object and its creator. At this level questions arise over the position of the men, their ethnicity, age and sex as well as the clothes they are wearing. So for example they are not wearing the typical white lab coats of wet-scientists but rather suits and ties. There is of course much more detail that could be discussed (medium, composition, placement and colour). However the focus of this chapter isn't the photograph of Watson and Crick but the three popular science books.

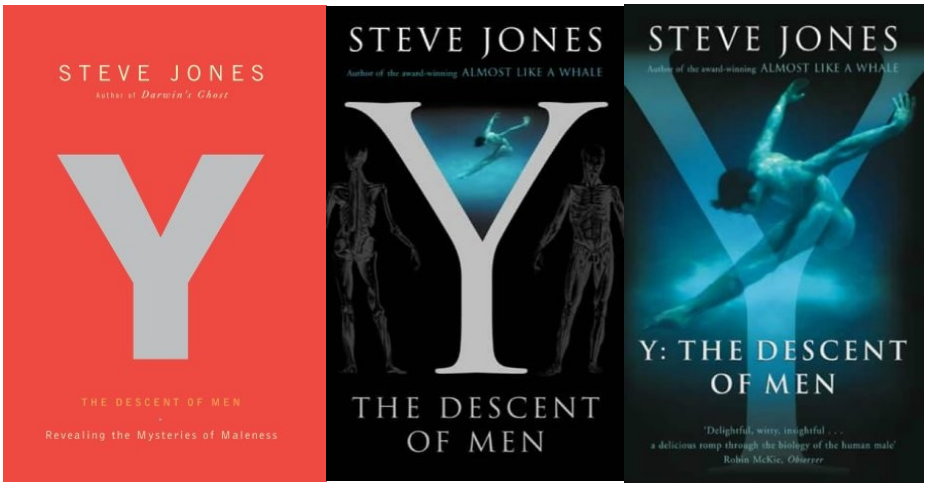
The images contained on the book covers are one of the ways in which potential readers make sense of the book. Indeed as a collection of symbols, images are "a means through which people clarify the world" (Buckley 1998, p.2). Symbols are, therefore, a means through which individuals grasp thoughts about products. As John Fiske (1982) explains, the meaning of any image depends on the dominant ideology within which the image locates the reader. Thus by exploring the images used, a clearer understanding can be given of the dominant ideology in which genetic sex as a concept finds itself.

The book cover is not only composed of symbolic images. Images themselves are anchored by the text that surrounds them, which in the case of the book covers is the titles and other additional text. This text names the book, cementing the images, and adds sound bites and recommendations. There is a clear symbiotic relationship between the title of the book and the images. While the book covers discussed here evolve through different editions, only in rare cases do their titles change (although an example will be given of this occurring). This connection between the title and image allows them to set expectations as to the book's content and while the titles of these popular science books are scientific, wider interest is established through the cover images. Thus the identity of the book is balanced as both a scientific work and as enjoyable reading. Now let me move on to the images of the book covers.

3.3.1 Y: The Descent of Men

Of the three books, Steve Jones' book, *Y: The Descent of Men* was the first to be published. It has appeared in three editions, first in the United States in hardback in September 2002, hardback in the United Kingdom in May 2003, and finally the paperback edition in August 2003. The three covers can be seen in Figure 3.3.

Figure 3.3. Hardback and paperback covers for *Y: The descent of men*.



There is a clear progression and redefinition from the first hardback edition to that of the final paperback edition. One of the subtlest changes is that in the edition published in the United States refers to Steve Jones as the 'author of *Darwin's Ghost*' while in the United Kingdom's edition he is described as 'author of the award winning *Almost like a Whale*'. The references are to the same book, which was published under a different title in the United States and in the United Kingdom. The British title of the book is a reference to Darwin's observation that a bear, swimming in a lake and catching insects in its mouth, might conceivably evolve over time into a creature 'almost like a whale'. On the other hand the United States' title, *Darwin's Ghost*, implies that Jones is Darwin's follower, clarified by the subtitle *Origin of the species updated*. What this case reflects is that book titles are chosen with reference to the specific audience and likely reflect the expected knowledge of their potential readership.

The title *Y: The Descent of Men* is a play on Charles Darwin's work, the *Descent of Man*. In Darwin's work the term 'man' refers to the human race. However Jones specifically refers his book to the descent of the human male by his use of the term 'men' and in the first American edition with the subtitle *Revealing the Mysteries of Maleness*. The title creates a clear link between Darwin's foundational work on natural selection and Jones' book on the Y-chromosome. As we will see, this connection between evolution and sex genetics is strengthened through the visual images.

The graphics of the book covers also show progress through the different editions. The first hardback book has a simple cover, with a red background and a grey capital Y in the centre. The 'Y' is the representation of a stylised Y-chromosome against a red background. The X and Y-chromosomes are unique in that they are referred to as

letters while the others in the mammalian genome are referred to by numbers. Even though the Y is coloured grey, not in a strongly contrasting shade such as black, the Y is a bold figure, and seems in a clear position of authority. This figure is the only explicit reference, visual or textual, to any feature of genes, chromosomes and genetics. The additional subtitle 'revealing the mysteries of maleness', which is at the foot of the Y, roots the figure of the Y as representing 'maleness', and for most browsers recalls the genetics behind 'maleness'.

In contrast to the first edition of the book, which is largely devoid of images, the second hardback cover keeps the large Y in its centre and has additional figures. On the right side there stands a muscular form of a man facing forward so one can see the genitals, while on the left side of the Y the form is reversed showing the rear view. These are reminiscent of science drawings found in physiology textbooks, particularly the nineteenth century anatomical illustrations, discussed in Chapter Two. The skeleton was seen as the basis of the human body and as such scientists illustrated it as sexed (female skeletons were drawn as having smaller skulls and larger pelvises). As I will show in the next chapter, this book seeks to root the difference between male and female in the genes and chromosomes.

There is the additional comment at the bottom of the cover; "Delightful, witty, insightful…a delicious romp through the biology of the human male', Robin McKie, Observer" (Jones 2003). It is clear from this that the book is partly at least entertainment. In this case one can see that newspapers and their journalists can also play a role in publicising popular science books through book reviews. The book cover's mention of the author as 'award winning' and the inclusion of newspaper reviews on the covers point to the connection the books have with the wider field of popular science, which connects to the discussion in the previous chapter regarding the authors' C.V.s.

In the cradle of the Y there is the image of a man with short brown hair and a muscular body, which is bent over with his arms at his back. In the paperback edition this diving figure is the main image superimposed over the Y. The use of this diving figure brings to mind grace and control: male power. As noted, the title of this book is a clear play on the nineteenth century publication of Darwin's *Descent of Man*, yet the paperback cover does not evoke images of dry academic scientific debates, but rather the diving figure

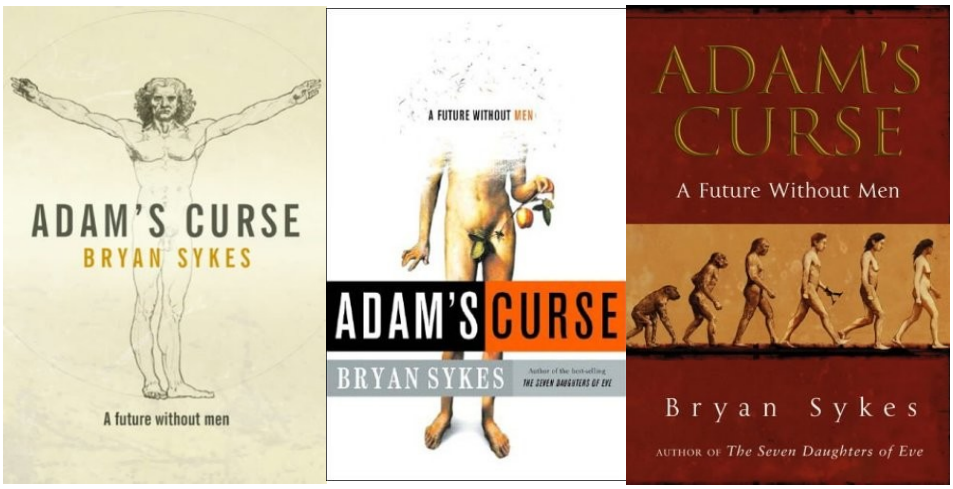
captures movement, flow, grace and masculine beauty. The male image has the traditional male possessions of strength and power channelled through the control of form and expression. This book is not about man's past evolutionary relationship to apes but about the transformation to the next, future, level. The use of the single visual image of 'Y' in the first edition singles to the buyer that the book contains the genetic explanation of maleness, while the cover of the later edition, with its added human figures, points to an increased complexity of meanings contained within the book. The later editions use a weaker image of the Y-chromosome (in blue) to contrast with the image of maleness contained within the human figure. In the later editions the symbol of the 'Y', as a cultural reference to the Y-chromosome, became less important while the male body was strengthened.

To summarise, the cover of Jones' books connect to the idea of popular science as a 'delightful romp' through biology. This book makes clear links to the wider field of science communication on its covers, and genetics remains stylised, inferred through the use of a 'Y'. In the third edition the scientific drawings of the subtly sexed human body were discarded in favour of a 'perfect' male body to represent male biology and science. (A fourth edition was published in 2005 and the images continue to evolve).

3.3.2 Adam's Curse

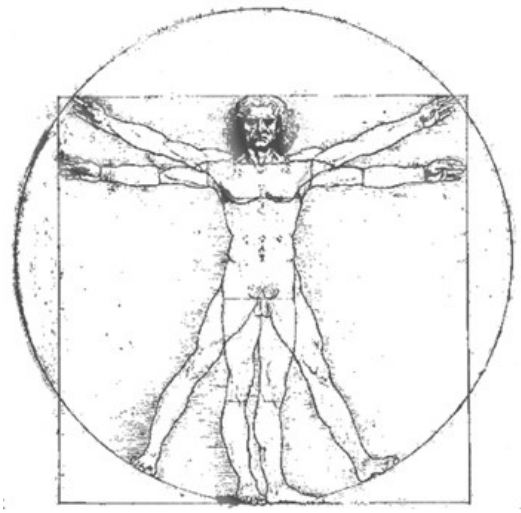
While *Y: The Descent of Men* conserved the images between different editions, *Adam's Curse* is an example of the much greater extent to which book covers can evolve from one edition to the next. The three covers from the 2003 and 2004 hardback editions and the 2004 paperback edition are shown in figure 3.4, and will be explored separately.

Figure 3.4. Hardback covers and paperback cover of *Adam's Curse*.



The first hardback cover is quite reminiscent of *Y: The Descent of Men*, as it also shows a figure of a man and brings to mind the Y by the body's position, (as the arms point to ten and two o'clock and the feet point to six). However, this book instead capitalizes on the established connotation of male perfection by using a reproduction of Leonardo Da Vinci's drawing, The Vitruvian Man.

Figure 3.5. The Vitruvian Man by Leonardo Da Vinci
www.ewh.ieee.org



The use of this image on the book cover creates a link to the status of Da Vinci as an iconic artist, scientist and genius. This then is the first order meaning which browsers in books shops are likely to be aware of.

This book cover also establishes a connotation to male perfection by using a reproduction of Da Vinci's drawing. The Vitruvian Man is based on the fifth century B.C.E. Greek sculptor Polykleitos's formulae for the perfect human proportions. Polykleitos "established the 'body' cannon,' a set of general rules that governed the production of art in the Greco-Roman world" (Lancaster 2003, p.122). Vitruvius, drawing upon this body cannon, maintained that when a correctly proportioned body was placed within a square, which in turn was placed within a circle in such a way that the corners of the square were just touching the arc of the circle, then the precise centre of both circle and square would be the belly button of the man (McEwen 2004). Da Vinci succeeded in creating a drawing of this figure by placing the centre, not on the belly button but on the penis, which could be drawn as flaccid or erect, allow the centre of the square and circle to be located on the same body part but in two different positions.

Comparing the original Da Vinci drawing with that of the book cover, one can see that the figure used on the book cover has been modified so it is composed of the arms touching the side of the circle, while the feet are those of the figure standing in the square. This introduces a second order meaning related to Vitruvius and his idea of a symmetry between the human body and the universe. The secondary meaning of this drawing is as an image representing the perfect body, which can only have perfect proportions in the male form.

Returning then to the book cover, the original drawing has been reproduced and modified to remove the double set of arms and legs. This gives the image value on two levels, that of the image and the artist. The first level is that of a male nude figure, standing with his arms stretched out in the form of a Y. This makes a clear link with the Y-chromosome. The man's feet are also in a Y shape, with his right foot pointing forward, and the left angled to his left. He is standing on the faint outline of a circle, which his fingers also touch. His body shape is athletic, reminiscent of the figure used in *Y: The Descent of Men.* However the face and longer hair give him the appearance of being older. Both of these figures are taken to represent male beauty and also

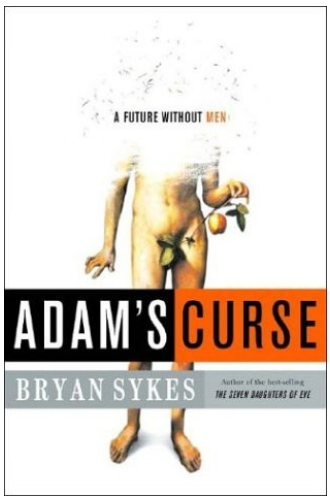
perfection and it is interesting to note that they share body type even when separated by hundreds of years.

The image is anchored by the script, which connects the man on the cover with the eye-catching phrase 'ADAM'S CURSE'. Indeed the title and author's name run on two lines as a type of fig leaf to cover the genitalia, which can be faintly seen through the lettering. Both these are in capitals and are strong features of the cover. A subtitle is placed under the feet of the figure and is in smaller front. The three items, the man, the book and the author, are connected through the use of colour. The background of the cover is a light brown colour, as would be expected of an old drawing. The use of the drawing rather than a photograph brings in the artist as well. A connection between author and artist is also established by the name of the author as the only other image with colour, a dark yellow. There thus is a linkage between Da Vinci, as a man of past science exploration and discovery, and Brian Sykes as the author of this book. Such attempts relate to the earlier decision regarding how authors position themselves and self-create their public image (see section 3.2)

In this edition of *Adam's Curse* there is the clear message that the book concerns the perfect man as represented by science. The critical role of the figure's penis in bringing together the two centres means that it would be impossible for the female body to be configured to these proportions. As shown in Chapter Two, through much of western history the human body was seen as perfect in its male form as it was further developed than the default female body. The use of the Vitruvian Man clearly reinforces the 'maleness' of the book's content. The text on the book cover is placed over the figure's genitals and the figure stands on the subtitle: 'A future without men'. Not only does this suggests that the future will not contain men, but the use of a drawing by a famous male artist carries the implication that the future will also be devoid of such geniuses.

Moving on to the second edition of the book, one sees a marked change in the types of images used from the 'perfect' man to the 'first' man. There is still a lone male figure on the cover; however this image refers to the Christian image of Adam.

Figure 3.6. The April 2004 hardback edition of *Adam's Curse*



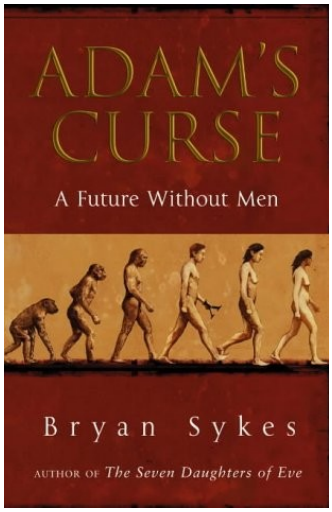
The male figure on the book cover is naked, lean, and lacking muscular tone. The face has been erased, with faint smudge marks left behind, and the subtitle is in capitals; 'A FUTURE WITHOUT MEN' which links to the men being erased. There is also a link between the colour of 'MEN' and the background block colour of 'CURSE'.

At the first level this edition of the book cover correlates Adam as the biblical character represented on the cover by the male figure (with its fig leaf over his genitals and an apple in his right hand) and the Adam mentioned in the title. As stated previously, the title is the label of the book's content, and as such the title sets the expectation that the book deals with the curse of Adam, which at a second level of analysis raises the question, 'Who is Adam, and what is his curse?'

Adam, as a biblical character has two levels. The first is Adam as the first human created by God. At this level Adam (man) is the human highest in creation, perfect. The second identity is Adam the sinner. Adam sinned because of Eve (woman) and the curse of the human species is seen to rest on her shoulders (Genesis Ch.1,26 – Ch.3,24, King James version). Sex, both the activity and the biological sex of the actors plays an important role in the idea of 'original sin' and the Genesis creation stories. The book cover brings attention to this by the placement of the genitals in the midsection of the cover, drawing the eye towards them. Close to the genitals 'Adam' holds the apple (from the tree of Knowledge of Good and Evil) which creates an association between the 'Adam's curse' in the title, and knowledge of the evolutionary 'curse' of sex and sexuality.

The final book cover for *Adam's Curse* is the paperback edition. When I discussed the importance of the visual images on the book covers it was mentioned they were important as 'eye catchers', and this is likely to be especially true for paperbacks, which are the majority of books in bookstores. Paperback books are directed towards a more general audience than hardbacks. This change in audience is reflected in the final book cover edition, which is somewhat drastic in comparison to the two earlier covers.

Figure 3.7. The September 2004 paperback edition of *Adam's Curse*.



The title and subtitle in this edition is placed predominantly at the top of the drawing and takes up nearly half of the top of the cover. There is an additional line below the author's name: "Author of the *Seven Daughters of Eve*". Clearly there has been a marked change in colours used in the cover to browns and yellows. Most of the cover is occupied by the title, which is in a yellow gold engraving, and the subtitle is placed directly below it. The bottom third of the page is taken over by a drawing of six stages of human evolution.

This drawing is based on Rudy Zallinger's drawing 'The March of Progress', published in *Early Man* by paleoanthropologist F. Clark Howell (1970). The original drawing shows the evolution of *Homo sapiens* as walking through time. In this drawing there

are six images of a figure walking from left to right. The first figure is similar to that found in the original drawing – an ape-like creature walking half bent and placing weight on its right arm. The second figure has less hair, is walking upright although still in a bent form and the right hand and right leg is forward in stride. The third figure is the next step of the walking figure (right leg forward) and has less hair and a more 'human' shaped face. In the fourth figure, which is clearly a man (less body hair, but with his head hair cut short and a somewhat muscular chest without breasts), he carries in his left hand a Y shaped object. He is in full stride with his left hand held vertical to his body. In comparison to the third Y carrying figure he has longer hair and his chest structure hangs lower. The final figure is that of a woman, slightly smaller, with full breasts and long hair that seems to be flowing behind her. To summarise, in the version used in this cover, the figures are not only becoming more 'human', with less hair and walking upright, but the last two seem to be 'female' with breasts and smaller stature. The message of this image is that the male human form is disappearing from evolution.

There are two issues with this representation of human evolution. The first issue is that there are arguments that males and females have different evolutions, and that there should be two evolutionary pictographs, one for the male and the other for the female, as they are thought of as undergoing somewhat separate selection forces. Indeed the reproductions of this drawing used in previous teaching material display only the form of the male human and this emphasis on the man as 'hunter' has lead to feminist debates about the fixation upon the male pre-human (Hager 1997). The second issue has to do with the time period covered by this drawing. As noted, the figures appear to be walking through 'evolution' but their strides differ. So figure one and two are pictured in a similar walking stride (both with weight placed on the left foot) but the phenotypic change between the two is more marked. Figure two strides into figure three, which is a whole step ahead with its weight about to be placed on the right leg. Figure four (modern man) is again a whole step away, however figure five represents only a slight movement forward (weight being lifted from the left leg). And in the final figure there has been little change in the position of the walking legs but a larger change in the physical appearance of the figure, which is in fact similar to the differences between one and two. Unlike the other editions this cover seeks to indicate evolutionary time.

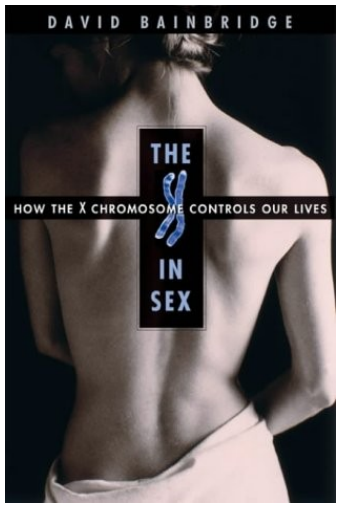
There is a clear evolution between the different editions of *Adam's Curse*. In the first edition the main reference is to male scientific exploration, while in the second there is

a clear religious connotation linking the curse of Adam with the curse of sex. It is only in the final cover that it becomes clear that Adam's curse is that of men, not disappearing as individuals, but rather turning into women. Within this sequence the image of the Y-chromosome is only seen in the Y shaped tool carried by the third figure. In this final edition the genetics of maleness is symbolised by the progression of the evolution of male figures walking across the book's cover. It is rather surprising that the book covers do not draw on social images of genetics to a greater extent. Rather the connection that the first cover makes (by the man standing in the shape of a Y) is lost in the second cover. In the last edition a single human body is shown, walking through evolution from a sexless ape, to a man, and finally evolving into a woman.

3.3.3 The X in Sex

Unlike the two other books so far discussed *The X in Sex* (Bainbridge 2003) is so recent that only one edition has been published. This book cover contrasts with the other two in that it is dominated by figures rather than text and also includes an image of a chromosome.

Figure 3.8. The March 2003 hardback cover of *The X in Sex* by David Bainbridge



The two figures on the cover are a photograph of the female body and a chromosome. The female figure is captured in black and white, standing with her back to the viewer. The body appears smooth and lean surrounded by a black background, which gives the

impression that the person is young. She is naked expect for a white cloth which is wrapped around her waist, revealingly slipping on her left hip. Her arms are down by her side; the left seems bent lower in front of her to hold her towel, while the right is bent slightly higher. Her hair is tucked in some way at the nape of her neck, and her head seems turned slightly to the left. This pose with its soft shadows and clothing are reminiscent of an artistic nude model and Renaissance paintings.

The first level of this image is clearly as a semi-naked female form which serves as an 'eye catcher' for browsers in books shops. However the photo of the female body seems to be indicating that there is something hidden: the image is interesting, as much for what it does not show as for what it does, and this raises the question why is the cover image of the woman's back and not front? It is possible that a photograph taken from the front would have been too sexualised, however in Chapter Two it was noted that in early illustrations the female body was used to represent 'Nature', which suggest that the figure is not representing specifically femaleness but rather 'Nature'. The text on the book cover anchors the images and supports this view as the subtitle mentions the X-chromosome and 'how it controls our life'. The initial idea that the female figure on the cover represents femaleness is connected to the male body's status as the typical 'human' body, while this use of the female body would suggest that in this case it is used to represent Nature, and the figure facing away from our gaze emphasises the hidden/unseen aspect of Nature.

Returning to the book cover, the author's name is spread across its top with the title running down the spine of the female body. In the subtitle, running at right angles to the main title, there is a second figure, that of an X-chromosome. The X is placed in the middle of the photo. The banding pattern both labels it as an X-chromosome to those who are familiar with karyotypes, but also shows it as a modified X-chromosome – one which has undergone scientist investigation to reveal its banding. The blue colour enhances the staining of the chromosome that is typically undertaken during karotyping and results in banding. The use of this stained image adds interest to an otherwise dreary X figure. However banding of the chromosome also draws attention to genetics, which in molecular terms draws upon karyotyping – being able to differentiate between chromosomes and observe changes in the chromosome. Thus it is not only a photo of an X-chromosome that might be found in anyone's body, but it is a photograph of a scientifically investigated object, stained and revealed in a way that the female figure on

the cover isn't. There is an implication that her body, indeed 'our' body, can be revealed through the staining and investigation of the chromosome.

3.3.4 Summary

This exploration of the visual images used in the book covers shows that various cultural and social factors are used to package popular science products. It is clear that these books evolved through their different editions and visual metaphors used to sell the books. This variety is likely due to the transformation as they pass from hardback to paperback, which indicates that the target audience changes as well. Popular science books are commercial products that must be 're-branded' to compete for attention in bookshops.

As noted in the first section, while the authors are all rather traditional scientists (Western, white and male) the authors' backgrounds and identities are quite diverse, as is their approach to popular science writing. This variety is also seen in the different images that are included on the book covers, including scientific drawings (Da Vinci and physiological drawings), religious figures (Adam), as well as representations of evolutionary theory (The March of Progress). It could similarly be argued that the authors and the book covers draw upon a fairly homogenous set of images drawn from the dominant culture of science as Christian, Western, white and male. which is likely a reflection of the current composition of high level science in the United Kingdom. However this study did not survey the full range of popular science books and there are examples, in particular the works of Anne Fausto-Sterling (1992) and Joan Roughgarden (2004), which would represent an alternative authorship.

These books have a striking similarity in that all the books at some stage used representations of bodies. While the images are of healthy bodies, predominantly male, only the X-chromosome is pictured as a chromosome and the Y is left as a letter, or body shape. One possibility for this difference is that the Y-chromosome looks misshaped compared to what we expect for a chromosome and it may be hard for people to recognize.

The connection between the chromosomes and the human body is clearest in those images where the body is formed to represent the chromosome –as in the human figure standing in a Y shape. This indicates that a connection is being drawn between knowledge of the chromosome and of our own biological being, however it also draws a

connection to our social being. Only the use of the skeletons in *Y the Descent of M*an's second edition visualises the biological body, as a 'human', objectified as scientific subjects. The other images of bodies, the naked back or the diver are not representations of 'female' and 'male', but photographs of people that we could come into contact with in our own social world. This raises some interesting issues as to what connection the authors wish to draw between the biological world and the social through the use of chromosomes, however this discussion requires some insights into the content of the books and as such will be taken up in the next chapter.

What is clear from this analysis of the book covers is that popular science as a commercial product is packaged within socially powerful concepts. The range of images that are used tends to represent the traditional view of sex, in which there is a clear cut division between male and female (e.g. Adam and Eve created separately). This raises the concern that the popular science books 'buy into' the dominant sex ideology to gain commercial success. However the book covers may use established representations of sex ideology while discussing reflexive views of science and knowledge production. Again this can only be fully explored in the next chapter.

3.4 Conclusion

As noted in the introduction, popular science has the potential to overcome many of the problems that traditional PUS supporters have encountered. However this chapter has shown that popular science communication is not purely a public education exercise, nor is it simply the production of a commercial product. The producers of the three books selected here have diverse identities and create their 'expertise' in various ways. I suggested that their C.V's indicated three different character types: new popular scientist, professional popular scientist, and the entrepreneur popular scientist. However, the use of visual images in the book covers indicates a similarity in how their popular science products are packaged for sale to the mass audience. As such the books have three aims: to sell copies, to educate and to have an impact on how people see the world and interact with it. It is critical to explore the values behind popular science and make them explicit, especially since, as explored in the preceding section of this chapter, the three books are advertised through scientific and religious metaphors.

Often the argument against bringing the media to task for sensationalist claims related to genetics is that they are commercial enterprises and it is only logical they will use stories to sell their products. However, as shown in this chapter, the field of popular science is itself a commercial industry, where authors create popular science books and these can help sell supplementary products such as Y-chromosome tracing. This discussion of the book covers has indicated that the books seek to entice buyers with a product which is represented by images they are familiar with and which not only draw upon science images (physiology drawings of skeletons and evolutionary images) but also from Christian creation stories, western art images, as well as photographs of (white) people. The use of photographs of living but unidentifiable people blurs the division between humans as biological creatures and humans as social persons and the analysis in the next chapter will expand upon this.

CHAPTER FOUR - SEX IDEOLOGY IN POPULAR SCIENCE

All animals are equal but some animals are more equal than others
(Animal Farm, George Orwell 1945)

4.1 Introduction

The popular science literary agent John Brockman (2001) has argued that we now have a 'third culture', in which scientists communicate directly with the general public (see Chapter Three). Traditionally, new scientific knowledge has been first published as 'scientific claims' within peer-reviewed journals, which allows them to be challenged by the wider scientific community (Merton 1942). Those claims that are accepted by the community are incorporated into science textbooks (Fleck 1935). This process, which allows the selection and development of 'scientific claims' to become 'scientific fact', has been challenged most recently by online non-peer review journals and also by the growth of popular science (Charney 2005).

In the last chapter I introduced three recently published popular science books that explored biological and genetic sex. I showed how these were not only educational products but also commercial ventures. By exploring the background of the authors it became clear that the three scientists engaged in popular science share a similar white male, western background, but construct their identities as experts in various ways. However, the analysis of the book covers indicated that the popular science products were packaged using similar cultural and scientific references.

The aim of this chapter is to explore the extent that the four features of biological sex (highlighted in Chapter Two) are found in popular science narratives, as well as investigating how the genetics of sex, sex determination, sex development, sex and gender relate to each other within popular science. To do so, the first section (4.2) explores how genetic sex is framed by analysing the metaphors used to describe the X and Y-chromosomes in the three books. In section 4.3 I show how these metaphors feed into three larger narratives: default female, active male and genetic war. In the

final section (4.4) I explore how these three narratives allow Sykes to propose a connection between sex genetics and the social world.

4.1.1 The metaphors and similes of DNA and genes

Metaphors and similes play an important role within science communication as 'teaching tools', and are particularly important to general readers of popular science books, as they explain and simplify complex scientific ideas by referring to behaviours or events they are familiar with (Wolfe 2001).

One of the earliest and most successful molecular metaphors was introduced by Erwin Schrodinger in 1946 when he spoke of the 'genetic code' in his book *What is Life?* Schrodinger used it both to describe the chromosomes and to identify their function and hence this was both a pedagogical and a theory-constructed metaphor (Knudesen 2005). This dual usage was strengthened in 1953 by Watson and Crick's DNA model, as the metaphor offered a framework for understanding the scientific theory as well as functioning as a 'promotional' metaphor in the reporting of the model in general science. Susanne Knudsen (2005) argues the discovery of 'messenger' RNA in 1961 and the 'cracking' of the DNA base to amino-acid code in 1966 firmly entrenched the computer program code metaphor. This metaphor incorporated the distinction between regulatory and structural proteins, but at the same time hid the complex interaction between genes and environmental factors (Nordgren 2003).

From the 1960s to the 1990s metaphors were introduced including a book of life, a map, a code and a blueprint. As Richard Strohman notes these all celebrate how the human genome 'programs' human beings (2001). Many of the more recent metaphors are marked by the initiation and implementation of the Human Genome Project. Leah Ceccarelli reviewed 75 articles about the metaphors and similes found in genomics:

> heirlooms, the motherlode, gems, low-hanging fruit, hieroglyphs, words, text, books in a library, an instruction book, a recipe, a blueprint, order forms, coded instructions for manufacture and operation, software code, building blocks, a toolbox, pieces of a kit, defective parts, workers dispatching order forms, slaves, immigrants, alien parasites, triggers, territory to be mapped, malfunctioning machines and life itsel. (Ceccarelli 2004, p.93).

The diversity of metaphors is especially important for external science communication as none alone captures all aspects of DNA. The popularisation of genetics is a complex

process, in which metaphors are likely to be multifaceted, and serve both to explain, and to suggest, new ways of understanding DNA and genes.

With the completion of the human genome project in 2003 there were increased calls for new metaphors to explain the complexity of the gene-protein-environment. As Strohman recounts,

> One scientist wrote: We need a new philosophy, or metaphor, or model for life. We thought the program was in the genes and now we see that it is in the cell as a whole and that the cell, through signalling pathways, is connected to larger wholes and to the external world. (Quoted in Nerlich and Hellsten 2004, p.257)

Drawing on an analysis of the texts of *Nature* and the *Guardian* Brigitte Nerlich and Iina Hellsten (2004) found that new metaphors included the human genome as an orchestra, a genome salad, a social collective and a miniature, cellular ecosystem. This indicates that the influence of post-genomics and proteomics are reflected in the choice of metaphors now used to describe the genomie (Nerlich and Hellsten 2004).

The types of metaphors used by researchers and writers not only indicate technological shifts – such as that from genetics to genomics, but can also indicate change within social and cultural understandings. By exploring the popular science communication, a clearer understanding is given of the types of metaphors and symbols that are used to describe biological sex, as well as indicating the dominant sex ideology which is propagated.

The impact of gendered metaphors in the descriptions of human bodies has been explored by Emily Martin (1987). Science descriptions in science journals and teaching texts are generally thought to be value neutral, seeking purely to describe the world as it is. However, as Emily Martin has shown, medical texts about menstruation and digestion also carry the common themes of sexism found outside of science. Bonnie Spanier has noted these as including items negatively associated with female activities, characteristics, or bodily functions. They incorporate an assumption of a natural order of centralised control and hierarchal relationships (Spanier 1995).

4.1.2 Re-importing popular science into the laboratory.

Science communication is currently seen as occurring in one direction only, however in this section I will argue that this is not an essential feature of popular science. On two

levels this is quite clear. The first is that 'tomorrow's scientists' are likely to read popular science and it can often be their earliest contact with the culture of science. The second point is related to the power of popular science metaphors to 're-infect' science and its workings. It is clear from the early chapters of this thesis that how society conceives of gender and sex impacts on how these topics are constructed within the laboratory. Popular science helps to form this social conception of gender and sex, which in turn provides a route for popular science to feed back into the laboratory. As these books are relatively recent, a re-infection from popular science into the science communication is unlikely as yet, however the metaphor of the 'selfish gene' first used by Richard Dawkins in *The Selfish Gene* (1976) provides an illustration.

Dawkins wrote *The Selfish Gene* with three different audiences; the general reader, the expert and the student in mind (1976). The success of the book rests on the perceived clarity of its 'selfish' metaphor. Studies have suggested that there are two types of metaphors, theory-constructive metaphors and pedagogical (Bacha 1980, p.185). Within science, theory-constructed metaphors tend to dominate as they generate and construct scientific hypotheses and theories (Keller 1995; Paton 1997). The more 'genuine' theory-constructive metaphors are critical to scientific thinking and if they were paraphrased would lose essential information (Boyd 1993). The second type, pedagological metaphors are used to describe concepts and being generally descriptive, it is generally unproblematic to paraphrase them. Pedagogical metaphors are particularly important to general readers of popular science books, as they explain and simplify complex scientific ideas by reference to behaviours or events the readers are familiar with. In the case of the 'selfish gene', the metaphor draws on a reference to the common behaviour of 'selfishness'. Indeed, from their first creation, new scientific metaphors undergo a process of clarification, which is repeated several times until the metaphor and the network of metaphors is considered officially, scientifically acceptable (Knudsen 2005).

Dawkins argues in the preface of the 1989 edition that metaphor of the selfish gene is a "new way of seeing" that "can in its own right make an original contribution to science" (p. ix). Indeed the metaphor of the 'selfish gene' has flourished beyond simple metaphoric use, and can be found in academic papers which refer to the 'selfish gene paradigm' (Balazs 2004) and the 'selfish gene network hypothesis' (Boldogköi 2004).

4.1.3 Methodology

The aim of this chapter is to explore the framing of biological and genetic sex in popular science. Often media studies are based on newspaper articles, which are a rich source and provide a large data set. However newspapers are often criticized as sensationalist, and as lacking in accuracy and depth due to limited space and time, and a conflicting commercial interest. Popular science books have sufficient space to explore issues in depth, as well as being written by authors who are able to dedicate much more time to research than newspaper journalists can. This study is not meant to be representative of the large field of popular science media, nor a complete survey of views related to genetic sex, rather it seeks to detail the range of frames and metaphors used by these three popular science books to describe issues around sex, sex determination and development as these are initiative of more general themes.

The first step in gathering the data for this chapter was selecting the popular science books as detailed in Chapter Three. The contents of the books were then analysed for metaphors in relation to the chromosomes, biological sex and gender. It should be noted that metaphors which themselves drew on gender roles and sexuality were not prioritised, rather all metaphors which were used to describe the scientific entities of chromosome, biological sex and gender were systematically noted. The metaphors were then grouped first within one particular text and then with reference to the others.

The content analysis of metaphors related to chromosomes is reported in section 4.2. Quotations have been selected to illustrate how the description of X and Y-chromosome draw upon references to the body, marriage and divorce, as well as political characters, pests and transport.

During the preliminary reading for metaphors a number of related metaphorical narratives were found which related not only to the chromosomes but also to the wider concept of biological and genetic sex. Section 4.3 is based on exploring what Paul Ricoeur has termed the ‘surplus of meaning’ and the wider frameworks of meaning of ideology (Freeden 2003). Under the heading ‘genetic sex’ this section explores the surplus meaning attached to the metaphors used between the chromosomes and sex. These are grouped as the ‘default female’, the ‘Y-chromosomes as bearer of maleness’ and the ‘genetic battle’.

In the final section 4.4, entitled 'social genetics', I focus on a predominant narrative used by Brian Sykes. The reason that I have chosen to include this is because the author seeks to extrapolate from genetic sex to explain cultural and political developments. This is particularly important as it was noted in Chapter Three that there exists the idea that popular scientists are the new public intellectuals who can provide the expert answers to social and cultural questions about human existence.

4.2 Metaphors and chromosomes

In this section I will explore the range of core metaphors used in the popular science books to describe chromosomes. I noted in Chapter Two that within these popular scientific discourses of biological sex the chromosomes are seen as fixed, and represented as a binary where each sex has separate genetic essences, which lead to differences rather than similarities. The analysis of the metaphors shows that the X and Y-chromosomes are conceived of as actual sex-chromosomes in that they are the site and cause of sex (4.2.1). The authors describe the X and Y-chromosomes as physical entities by drawing on characteristics of the body, including describing them in terms of 'health' and 'death' (4.2.2).

The evolutionary relationship between the two chromosomes is described using metaphors of marriage and divorce, indicating the extent to which the authors find gender metaphors useful. The chromosomes and the genome are also described in terms of political metaphors, including a great assembly of genes, princes, revolution, dictators, genetic wars, and peace treaties. Alongside these political metaphors the Y-chromosome is described in terms of being a pest or vermin. Not only do these metaphors indicate an (anti-male) gender bias but also the framework of 'control' and determination. How chromosome action and control is framed can be seen in the authors use of transport metaphors, in which the Y-chromosomes was described in terms of an active vehicle while the X-chromosomes is described as a static island.

4.2.1 Sex-chromosomes

In the popular science books the identities of the two chromosomes are unquestionably linked to sex and sexuality. This is made explicit by Bainbridge: "X and Y are seething

with latent sexuality. They really are, after all, sex-chromosomes" (2003, p.121). Identifying the X and Y-chromosomes as the sex-chromosomes is not unexpected, and reflects how they are portrayed in the media. However, it does indicate that the X and Y-chromosomes are viewed as tangible 'sex' chromosomes and not just biological markers of sex or 'carriers of sex genes'. In Chapter Two I mentioned how the X and Y-chromosomes have come to symbolise 'genetic sex' and their binary structure to support the deeply entrenched public view of sex as genetic. Further analysis revealed that the metaphors which were used to describe the chromosomes and the action of the chromosomes fell into five groups: those related to the physical body, marriage and divorce, political characters, pests/vermin and transport.

4.2.2 Body

The analysis of the visual symbols from the book covers indicated that the human body was central to the packaging of the popular science books. Indeed, the link between the biological body and the 'body' of the chromosome is for me one of the most interesting linguistic devices in the three popular science books. Bodily metaphors potentially link the microscopic chromosomes being described in the text and the biological body experienced by the reader.

In Chapter Three I discussed how only the X-chromosome was illustrated on the book cover while the Y-chromosome was illustrated by a Y symbol or a male body in the shape of a Y. I proposed that one reason for this was that a photographic representation of the Y-chromosome would not be seen as a chromosome, as it is recognisably smaller and of a different shape from the others. This difference between the X and Y-chromosomes is also reflected in the books written content where the X and Y-chromosomes are described as physical bodies. The X-chromosome is described as being alive, with the quality of being "healthy", a "full-sized, apparently normal chromosome" (Bainbridge 2003, p.61).

The idea of the X-chromosome as healthy contrasts with the Y-chromosome as a "tiny shrunken waif" (Bainbridge 2003, p.61) and the use of adjectives of death and decomposition.

> The human Y-chromosome is a **graveyard of rotting genes**, whose **corpses** are still sufficiently similar to active counterparts on the X-chromosome to be recognizable by their DNA sequence but whose **festering remains** contain the

> evidence of their own **demise -**here a few bases cut from a key section; there a spelling change that makes a nonsense of a once vital instruction. (emphasis added, Bainbridge 2003, p284)

Alongside the 'code' metaphors of genes and DNA (e.g. spelling change) Bainbridge creates a link between the Y-chromosome and the 'rotting' body of the person. In this way there is a connection drawn between the body as capable of biological death and the decay of the chromosome. The image of death and disease is also seen in the description of the Y-chromosome as a

> (…) **wasteland**, full of **junk fragments** of **damaged genes** interspersed with a few genes that have managed to cling on through the bad times. (emphasis added, Bainbridge 2003, p.60)

The X-chromosome is thus a healthy normal chromosome, and the Y-chromosome a decaying body, struggling to survive. This portrays the chromosomes as living entities, capable of being healthy and of dying and their genes as having the capacity to 'struggle' and 'cling on'.

The first issue that should be mentioned is that such descriptions reflect an evolutionary time scale. This draws upon the framework of evolution, illustrated on the cover of the third edition of *Adam's Curse* where human evolution was represented through changing bodies progressing from ape to man to woman (see section 3.3.2). The second issue that should be noted is that the books describe the X/Y-chromosomes as a general genetic entity but also specific X/Y-chromosomes possessed by a specific family and its members. As I will show in the final section the 'life' of the X or Y-chromosomes is measured as their presence in subsequent generations, as the passing on of the Y-chromosome from father to son is not seen as reproduction, but rather the passing on of what is portrayed as the same, identical chromosome (see section 4.3.2).

The use of these metaphors and adjectives related to biological bodies creates a strong sense that there is a link between the micro-level state of the X and Y-chromosome which the readers can not sense and macro-level biological bodies they are familiar with. In the covers of *Adam's Curse,* the X-chromosome and women are portrayed as healthy while the Y-chromosome and men decay. It is possible these metaphors are tapping into a wider framework of social and cultural change where men's power in the public and private sphere has decreased as a result of women's emancipation.

4.2.3 Marriage and divorce

In keeping with the idea of the X and Y-chromosomes as 'sex' chromosomes the authors use matrimonial metaphors in the three books. Bainbridge's book includes the subtitle "Drifting apart – the sad divorce of the X and Y" (2003, p.58). This group of metaphors draw on ideas of the chromosomes as being "an odd couple" (Bainbridge 2003, p.61) which had been in "a once happy marriage" (Sykes 2003, p.283). As already noted, in humans all chromosomes, except the 'sex-chromosomes', are considered to exist in duplicate; thus there are twenty-three pairs, labelled from one to twenty-three. Only the X and Y 'sex-chromosomes' are referred to as having been 'married' in the popular science books.

Recombination is a major theme in the

The metaphor of 'marriage' connects the chromosomes to the normality of heterosexuality. Until recently only a couple composed of a single male and a single female were allowed to marry and this has institutionalised heterosexuality in the religious and civil ceremonies of marriage. As such the metaphor of marriage is connected to the western concept of 'nuclear families', which are composed of two different but complementary units that unite to reproduce. In the popular science books marriage metaphors are used to describe recombination while divorce metaphors are used to describe the separation between the X and Y that occurred during the development of sexual replication:

> The couple first stopped dancing, and then they almost stopped communicating completely. They kept in touch by way of the non-sexlike region, but this was not really enough to stop them drifting apart. (Bainbridge 2003, p.58)

Bainbridge goes on to note,

> when couples look back over a divorce, it can be hard to remember exactly when different parts of the relationship started to change, and the same is true of the chromosomal divorce of the X and Y. (Bainbridge 2003, p.58)

The metaphor of marriage also connects biological sexual reproduction to human sexual expression. Evidence of this is seen in the use of adverbs related to sexual expression (embrace) to describing recombination: "the X and Y-chromosomes still embrace, if only very lightly, at their tips when the cells divide" (Sykes 2003, p.283). The idea of chromosomes embracing makes a connection with the human activity of embracing, as

connected with sexual reproduction. Thus the 'marriage' metaphor draws on the cultural perception of the state of marriage as the situation in which reproduction occurs. However now that the chromosomes have 'divorced' there is still 'embracing' but full recombination does not take place. As a result Sykes describes the separation of the X from the Y-chromosome as it having "no partner, nothing with which it can be matched" (Sykes 2003, p.29). In the next section I will discuss the significance of this idea of the Y-chromosome being 'unmatched'.

Social understandings of divorce often include conflict, and in the next section I will explore the narrative of a 'genetic war' between the male and the female, in which the conflict is not between the Y and X-chromosomes but between the Y-chromosome and mDNA. The popular science books are also portray female and male as 'opposite' sexes, which becomes linked to the characterisation of them as having opposite interests. Bainbridge portrays the X-chromosome as bringing the male and female together,

> (…) the X-chromosome has ingrained a delicious asymmetry between men and women, but a benign one in this case. It may be the Y-chromosome that makes the obvious difference between men and women, but it is the X that makes them **complementary rather than opposite**. It is the X that eventually **reunites** them. (emphasis added, Bainbridge 2003, p.170)

In Bainbridge's view it is the X-chromosome which reunites men and women, again drawing on the idea of husband and wife, man and woman as partners.

These uses of heterosexual matrimonial metaphors draw upon traditional gender roles where marriage is a positive union, and divorce is understood as "sad" (Bainbridge 2003, p.56) and to result in distance between two formerly united figures.

4.2.4 Political Characters

The analysis of metaphors used to describe chromosomes revealed a somewhat surprising finding that the popular books make use of political metaphors to describe chromosomes within the genome and the X and Y-chromosomes in particular. Nerlich and Hellsten (2004) have noted how the human genome has become described as an orchestra, a social collective and a miniature, cellular ecosystem. These metaphors stress the idea of harmony, working together, and balance, rather than the genome working as a computer program. Thus it would seem with the new metaphors of the genome as an 'orchestra' etc, new metaphors of control are possible and in the popular

science books these new control metaphors are linked to political systems. Jones is explicit in drawing a parallel between sex and politics, "Sex, like politics, depends on a hierarchy of command. Empires collapse and are superseded, and masculinity is much the same." (Jones 2002, p30). The analysis of political related metaphors form the books indicate the extent to which this idea of control in genetics dominates.

Sykes introduces the political metaphor in terms of the genome, stating; "(t)he inequalities between the sexes did not escape the notice of the Great Assembly of genes, the nuclear chromosomes" (Sykes 2003, p.239). This is very different from the idea of genes as bits of codes contained on chromosomes and indicates that Sykes is drawing on the new ideas of genomics. As well as reference to the 'great assembly', the books use political metaphors to explain the development from non-sexual to sexual reproduction. As noted in the previous section the authors described a divorce of the X and Y-chromosome, which is also described as a "genetic revolution" from which the X-chromosome has "emerged unscathed" and "flourish(ed)" (Bainbridge 2003, p.61). The political metaphors become apparent as Bainbridge goes on to describe it has having been left with "no effective opposition", which allowed it to "become our dictator" (Bainbridge 2003, p.62). In similarity to the metaphors of marriage, the reference to political systems is culturally connected, as in Western societies democracy and balance are positively valued.

There are also political references specific for the Y-chromosomes. Western political systems have been dominated by feudal patricidal systems and one of the clearest is found in Jones' book when he states that the Y-chromosome,

> has a single redeeming feature. To half of the human race the Y is the **prince of chromosomes**, for it gives the embryo a testis. There resides the **noblest** of all genes, the sine qua non of maleness. (emphasis added, Jones 2002, p.15)

Bainbridge sees it as "the essence of masculine" (Bainbridge 2003, p.150). As section 4.4 makes clear, Jones draws an explicit link between the Y-chromosome and social and cultural values such as power and money. However the prince does not rule by democracy, rather "half the population is a slave to its insistence presence" (Jones 2002, p.2), clearly indicating a strong sense of determination.

New metaphors related to genomics have been praised as they signal a move away from the deterministic metaphors of the 'genetic program'. However in these books the

introduction of new metaphors draws upon historically gendered political frameworks. The metaphors that are used to describe the issue of control and power in the genome are interesting in this regard. The idea of the genome being a 'great assembly' involves the recognition that each chromosome is found in the cell in two copies which 'balance' each other, that is for all but the 'sex' chromosomes in which the X is without 'effective opposition' and has become a 'dictator'. This draws upon the western value of democracy and balance within political systems, where dictatorship is a negative concept. In this view the sexual separation of the X and Y-chromosomes is seen as causing conflict and disharmony. Again this links into how the evolutionary interests of the female and male are conceptualised as a 'genetic war'.

4.2.5 Pests

The fourth group of metaphors which was found in the analysis of the popular science books was that of 'pests'. This group of metaphors was only used in negative terms to describe the Y-chromosome. In *Adam's Curse*, where the Y-chromosome is seen as a valuable fragment of junk, "intrinsically unstable" (Sykes 2003, p.3), "vermin" and a "super selfish chromosome" (Sykes 2003, p.204). Interestingly the 'pest' metaphors can also be seen in the description of males as parasites (see section 4.4.1). This group of metaphors clearly draws upon a wider evolutionary framework in which genetic investment in offspring is prioritised and gendered. As I will explore in the next section the interest of the human male often become reduced to that of the Y-chromosomes.

4.2.6 Transport

The fifth group of metaphors that was found related to the description of chromosomes as a type of transport to carry genes. The metaphors in this group emphasise the differences, rather than similarities between these two chromosomes.

Sykes characterises the Y-chromosomes as 'only' a type of transport,

> the Y-chromosome is really just a **vehicle to carry** the Sry gene –**a stunted, damaged, introverted shadow of its former self** that is so obsessed with controlling sex that it has become almost incapable of doing anything else. (emphasis added, Sykes 2003, p.60)

The idea of the Y-chromosome as a vehicle is connected to the view of the chromosomes within evolution as carrying traits through generations. Jones also makes

mention of Y-chromosome as a "vessel of manhood" (Jones 2002, p.2). These metaphors use the Y-chromosome to create a link between the SRY/Sry gene and 'manhood'. However the description of the Y-chromosome as a vehicle is not passive. Rather Bainbridge describes it as "the arbiter of sexuality" (2003, p.49) indicating it as an active force.

In contrast to the Y-chromosome there is "almost no limit to the sorts of genes that the X-chromosome can carry" (Bainbridge 2003, p.96). The ability to 'carry' genes in a 'healthy' way is considered to depend on the ability of the chromosomes to undergo recombination. In mammals all chromosomes, apart from the 'sex' chromosomes, are normally present as two copies which allow them to do this. The X-chromosome is able to recombine in females, but the Y-chromosome is unable to 'correct' mutations by recombination. Thus by pointing out that the X-chromosome is capable of carrying a wide variety of genes it emphasises that the Y-chromosome has become the 'vehicle' for the genes only useful in maleness. So while the Y-chromosome is a "single-issue chromosome" (Bainbridge 2003, p. 49) the X-chromosome is seen as "control(ling) our lives in thousands of different ways" (Bainbridge 2003, p.61), and so

> (t)he Y-chromosome may determine our sex, but the X determines whether we live at all. This is no longer just a matter of sex –it's a matter of survival (Bainbridge 2003, p.62).

Exploring bodily metaphors revealed that the Y-chromosome was defined in terms of a 'rotting' 'decaying' body and the X-chromosome is seen as 'healthy'. However, the chromosomes can also 'carry' or 'transport' diseases and the books note that the X-chromosome is particularly liable to 'carry' diseases. In *The X in Sex* one of its three chapters is dedicated to these diseases 'carried' by the X-chromosome. Bainbridge uses Duchenne muscular dystrophy to show the effect of mutations on the X-chromosome, stating,

> the disease is **passed** through the generation on a **rogue** X-chromosome, **carried silently** by double-X females and **afflicting poor** single-X males picked out by the hand of fate. Duchenne muscular dystrophy is yet another **ruinous** way in which a **damaged** X-chromosome can make boys' lives misery. (emphasis added, Bainbridge 2003, p.92).

Bainbridge describes the X-chromosome's diseases as "the curse of the lone X" (2003, p.89) because of their impact on males with one X-chromosome. As with the idea of

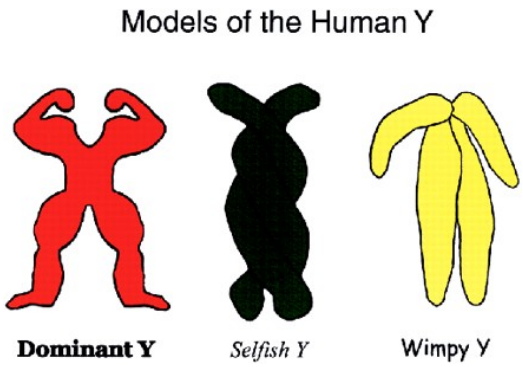
the Y-chromosome as a vehicle, the X-chromosome (or at least the genes on it) is portrayed as an active influence, yet silently carrying the afflicting condition. The idea of the chromosome acting as a 'carrier' has connections to the earlier roots of 'genetic inheritance' and the idea of properties being transported through generations. Bainbridge later goes on to stress a passiveness of the X-chromosome as being 'incapable of losing its genes to other chromosomes' and so they 'languish' on the 'stubborn chromosome island, unable to escape' (Bainbridge 2003, p.145). The idea of the X-chromosome being an island contrasts with that of the Y-chromosome being a vehicle: the X-chromosome is not carrying the genes anywhere.

The popular science books draw upon the idea of transporting genes through generations by their phrasing of the Y-chromosome as being a 'vessel' for masculinity. In the case of the books by Jones and Sykes this may serve to strengthen the readers' interest in their own 'genetic inheritance' and motivate them to have their Y-chromosome sequenced. The X-chromosome is referred to in different terms, as an 'island' which genes cannot 'leave'. The Y-chromosome is unique to males, while the X is shared by both men and women and is 'what unites humans'. This gives a gender bias in genetic 'inheritance' as males gain a connection to their fathers by sharing a Y-chromosome, but women gain a connection to only the female lines of their fathers and mothers. This role of the X-chromosome as sharing inheritance of both men and women is connected to the idea of the two chromosomes as the married pair that makes men and women 'complementary'.

4.2.7 Summary

In this section I have sought to explore, not only the metaphors that draw on gender and sex, but also how differences rather than similarities between the chromosomes are emphasised. There has been little analysis of these representations of the X and Y-chromosomes, however a notable exception is the work of Jennifer Graves. Graves has noted how there are three main concepts of the Y-chromosome illustrated in figure 4.1 (Graves 2000).

Figure 4.2. Graves' models of Y-chromosomes (Graves 2000)



The first is the dominant entity, "acting to determine a male, regardless of which other chromosomes are present" (Graves 2000, p.676). This is reflected in the political metaphors where the Y-chromosome was a 'prince' and an 'enslaver'. A second model is that of the Y as a selfish entity, which accumulates genes that are handy in a male and/or bad in a female. This model is seen in the use of metaphors of the parasite, the 'selfish chromosome'. Graves, herself, views the third model in which the Y-chromosome is a 'wimp' as more accurate. This she sees as,

> a pale shadow of its former self, having degraded to almost nothing. The genes that it contains are just relics of genes that were originally on an autosome and have been retained intact on the X-chromosome. (Graves 2000, p.676).

This view of the Y-chromosome was seen in the final metaphors of transport. What is apparent is that all three books characterise the Y-chromosome in these three ways, depending on the subject under discussion. In this regard the idea of the Y-chromosome as a Prince is not more accurate than seeing it as a 'vehicle'; rather these metaphors illustrate various facets.

It is clear that a range of metaphors are used in the books to describe and explain the various roles the chromosomes have. Figure 4.2 is a summary of the range of metaphors, showing the core grouping (i.e. matrimonial) and the specific metaphors related (marriage, divorce) and the type of biological activity the authors use these metaphors to describe (e.g., recombination and sexual reproduction) as well as the social connection which is drawn, that is the 'surplus meaning' which will be explored further in the next section.

Figure 4.2. Summary of chromosomes metaphors.

Core Metaphors	Metaphors	Biological	Social connection

		connection	
Body	Healthy	Genetic fitness	Positive
	Diseased	Genetic fitness	Negative
Matrimonial	Marriage	Recombination	Heterosexual as normal, loving, positive
	Divorce	Sexual reproduction	Failure -Negative
Political	Prince	Sex determination	Male, powerful, desirable (prince charming)
	Dictator	Genetic processes	Male, negative, evil, destructive.
	Genetic Revolution	Evolution of sexual reproduction	Drastic change -negative
Pests	Vermin/ parasite	Evolutionary interests	Negative
Transport	Island	Inheritance	Unconnected, stranded
	Vessel	Inheritance	A carrier made specifically for the task.

While this analysis indicated that the Y-chromosome is strongly perceived as connected with males, being amongst other things a 'vehicle' for manhood, the X-chromosome is not given such a role. As the next section will explore the X-chromosome is given no role in sex determination as it only causes biological sex by ensuring a lack of the Y-chromosome. Bainbridge on the other hand, argues that the X-chromosome is fundamental to every human, and that its action is as a 'dictator' for everyone, not just women. As such the characterisation of the X-chromosome involves both male and female. The impact of the X-chromosome is seen to construct an 'internal female' for men, and only when it is dealt with as a double pairing does it become considered as causing 'femaleness' in any unique way.

The analysis of these metaphors revealed the clear importance of heterosexuality to describe the relationship between the X and Y. The 'sex-chromosomes' are located within wider social understandings of gender and gender roles. This is clearest with regard to the idea of the chromosomes having been 'married', but it is also seen in the political metaphors where the X-chromosome is described as a 'dictator' while the Y-chromosome is a 'prince'. The X and Y-chromosomes are referred to in separate ways regarding the types of action the chromosomes carry out, where the X-chromosome is seen as an island while the Y-chromosome is seen as an active transporter of the 'maleness gene'.

4.3 Sex determination, sex development and war

Glifford Geertz (1973) has explored how ideologies are composed of 'ordered systems of complex cultural symbols'. Michael Freeden has noted that these symbols act as,

> representations of reality and provide the maps without which individuals and groups could not orientate themselves with respect to their society. (Freeden 2003, p.40)

Freeden (2003) has noted how ideologies are not only produced but also consumed and consumers of ideology may absorb the unconscious frameworks of understandings so that the ideology is undetectable and ingrained to the extent it becomes invisible. There is also 'surplus of meaning' which according to Paul Ricoeur enables alternative readings of the ideology. Many feminists have commented on the assumed natural state of heterosexuality, male superiority and dominance over females (Freeden 2003). This section seeks to explore the 'surplus of meaning' carried by the metaphors used in popular science descriptions of the X and Y-chromosome and biological sex.

Through analysing the metaphors in the popular science books it became apparent that the idea of biological sex as composed of two essentially separate fixed sexes fed into three larger narratives, briefly touched upon in the metaphor section. The first two deal with sex determination/development. It has been noted that sex determination has come to mean the determination and development of the male phenotype, leaving the female as the 'default' body development (Fausto-Sterling 2000). Thus in the first sub-section I explore how the books describe female development, and the relation which is proposed between the X-chromosome and the female ovary. In the second section I explore how the books describe male development and also the connection that is described between the Y-chromosome and the testis.

After detailing how the popular science books describe sex development and determination this section moves on to considered the narrative of a 'genetic war' between males and females. This relies on a reduction of the male and female to their genetic interests, where they are defined as producers of the egg and sperm. In this sub-section I will explore how the genetic essence of the male is seen as the Y-chromosome whereas in the case of the female it is mDNA.

4.3.1 Female sex development; the story of the default ovary.

In analysing the three popular science books it was found that the female was identified as 'default' on the basis of three factors: the lack of effect of the X-chromosome, the role of the ovary and the passivity of the egg. Bainbridge notes that the X-chromosome has an 'indirect and conditional' effect on sex, "(b)eing XX only makes you a woman in as far as it usually precludes you from having a Y" (Bainbridge 2003, p.27).

Within this view the XX pair is seen as doing nothing to 'make' a woman, except preventing 'you' from having a Y-chromosome. As has been detailed in Chapter Two male development is seen as stemming from the presence of the Y-chromosome. The Y-chromosome is connected with the development of the testis, which then produces hormones that lead to the male morphology. However the formation of the ovary was seen as a 'default' development of the early gonad. It is within this framework that Bainbridge uses the term Y-induced testis and XX-permitted ovary (Bainbridge 2003, p.33). Bainbridge's comments on the 'lack' of action by the ovary:

> The ovary really does not have to do anything at all to make the embryo become externally female (…) once more, the ovary is remarkable not for what it does, but for what it doesn't do. (Bainbridge 2003, p.30)

It is clear that the descriptions of the chromosomes and genes portrays them as having the power to 'make', or 'act', although in a sex specific approach. The question of why female development is 'passive' and the male has an active process is explored by Bainbridge. He explores these differences in the female and male processes, as he describes the difference between the passive default female and the active imposed male state:

> This may be why we maternally nurtured mammals have such an **active, strident process that turns us into males**….There was simply no pressure to design a fail-safe mechanism to make females, as the maternal environment was likely, if anything, to **push them towards femaleness anyway**. So while **maleness must be forcibly imposed on a baby, femaleness just happens**. (emphasis added, Bainbridge 2003, p.35)

The womb environment is seen as providing the justification for why 'nature' has not developed a mechanism for female development. Thus as it is the female sex that carries the baby in the womb, the womb's environment may 'push' all babies towards femaleness and so a genetic mechanism is needed to 'fight' against the environmental influences.

As I noted in the discussion of the metaphors used to describe the X-chromosomes, the single X-chromosome is shared by both sexes, and the metaphors reflect this. It is only the double X-chromosome pair that is uniquely related to femaleness. Bainbridge notes that women are "mixed creatures" (2003, p.130):

> The fact that all "normal" women are made up of a random mixture of two sorts of different cells, each using a different X-chromosome, is not just an interesting piece of biological trivia –it is something integral to our modern concept of femaleness. (Bainbridge 2003, p.148-9)

Later on Bainbridge again stresses this 'femaleness':

> women's bodies truly are mixed –in a very way that springs into relief whenever an X-chromosome is damaged. Each woman is one creature and yet two intermingled, as it were. (2003, p.151)

Bainbridge's use of the term 'creature' is interesting. The Oxford English dictionary notes that creature is often used to denote 'other than man' and as noted in Chapter Two, women have long been studied as 'the other' where the male has been taken as as the 'developed', 'perfect' standard. By using the term 'creature' Bainbridge, who himself is not a woman, creates distance between the observer and subject.

Bainbridge lays stress on the role of X-chromosome inactivation by stressing "… avoiding X-chromosome overdose lies at the heart of what it means to be female." (2003, p.143). In Chapter Eight I explore further the impact of genomic features on the idea of female and male categories. However, at this point it is sufficient to note that the X-chromosome is seen as passive with regard to sex and the ovary is default with regard to sex, the double dosage of the X-chromosome is seen to play an important and active role in femaleness.

Feminist critics of the default female paradigm have argued that it is only one way of portraying the biological processes, and that the passivity stems not from biology but from the gendered gaze of the researchers. Bainbridge comments on the contraction between the social advancement of women, and the biological retreat of the female in biology, which Bainbridge terms 'perverse':

> It certainly seems perverse that the latter half of the twentieth century, which brought unprecedented changes in the position of women in western society, also

> brought what appeared to be scientific confirmation that a woman was something akin to a "failed man". (2003, p.31).

As I argued in Chapter Two, the emphasising of similarities or differences between males and females is one of politics and is not based on greater scientific accuracy, but rather cultural and social values. The idea of a woman being seen as a 'failed man' is contrasted with Sykes's view that "men are basically genetically modified woman" (Sykes 2003, p.2). Banbridge makes reference to this as playing with words:

> So you can interpret the fact that humans are initially made female, but can be modified into males, however you like. It can mean that women are better or that men are better –it simply depends how you play with the words. Perhaps what all this is telling us is that the discovery of the mechanisms of sex determination has not altered the values we ascribe to the two sexes. (Bainbridge 2003, p.33)

The analysis of the narrative of the default female also revealed two interesting additions to the quite traditional view of the male as active and the female as passive. The first is that Jones describes man as "the diminished female" (title of preface, Jones 2002, p1-10). In this view there are not two separate sexes, rather we are all 'female' but that in men there is a battle against feminity. Thus it is women and female development that are seen as standard, yet this still fits into the dominant view of maleness as an active development away from the default female form.

The second addition to the 'traditional' narrative is the idea of a 'continuous spectrum of gender'. Feminist have long argued that the wide range of genders seen in human societies can not be easily placed upon two binary biological sexes and many have drawn upon the existence of 'intersex'. Bainbridge includes this:

> Human beings are not simply male or female (…) "intersexuality" is a fact of life, and not a particularly rare one either…The human sexes are not two opposites, or even two equivalents –the human sexes are many and varied, and while two predominate, the others form a continuous spectrum of gender that stretches between those two, and beyond them. (Bainbridge 2003, p.167)

However Bainbridge also includes a description of the division between sex and gender,

> In every human society men and women have had different roles, different destiny, and the same is true of the animals they herded or hunted. One thing is especially clear: males and females are more different than they really need to be simply to play their different roles in reproduction. Why do women look so different from men, think so differently to men? It is obvious that sexuality is

> not just restricted to the loins –it permeates the whole body. A young woman's hands are not like a young man's hand, but why, and how? Why should the sexes be so deliciously, unnecessarily different? (Bainbridge 2003, p.6)

Sykes also describes a concrete division between male and female:

> No matter how sex is decided, it always ends up the same. Females makes eggs and males make sperm. As we shall soon see, all manner of consequences spring from this one very simple distinction between males and females, between men and women. (Sykes 2003, p. 119)

This conception of females and males in terms of their reproductive cells is a critical part of evolutionary genetics, where sex stems from the specialisation of the sexed reproductive cells. However in sexual dimorphic animals such as humans the sex differences between the male and female are seen to encompass the whole body. Sykes goes on to portray male and female as completely separate:

> Yet, the simple distinction between male and female divides our species into two perennially polarized camps separated on either side of a great canyon from whose rim we signal to each other and struggle to hear, but which we can never cross. (Sykes 2003, p.2)

Throughout the book the evolutionary view of genetics is clear:

> two sexes caught in a dangerous genetic whirlpool, playing out in the flesh irreconcilable conflicts embedded deep within our genomes. (Sykes 2003, p.3)

By discussing gender roles as something that is in 'every human society' Bainbridge implies that they are a natural and an innate feature of human groups, and in doing so disregards the role which history and environment have played in creating the gender roles. This places gender roles as a natural part of human society, and links them with the biology of humans. This results in the question of sex differences and 'sexuality' being reduced to biological explanations.

4.3.2 Male sex development; Y-chromosome as bearer of maleness

In the exploration of the metaphors used to describe the Y-chromosome I noted how they could be easily placed within Graves's three models of Y-chromosomes. While the models give very different images of the chromosome, one thing remains unchallenged, the capacity of the Y-chromosome to make a human embryo develop as a male. The impact of this on ideas of sex determination and development was seen in

the previous sub-section where I noted how sex determination is seen as a capacity of the Y-chromosome, where the female is a default morphology of the human body.

It should be noted that the three popular science books are written by men, and as such the books are a connection between the gendered author and their biological subject, the Y-chromosome. This is the basis of one of the most surprising narratives the analysis revealed in the popular science books, the identification of the authors with their Y-chromosomes. Much of this analysis is based on *Adam's Curse,* which is written in the style of a personal exploration which focuses on tracing 'the original Mr Sykes' through Y-chromosome mapping. Regretfully due to space constraints I was not able to include *The Seven Daughters of Eve* (2001) as a comparison to how Sykes relates to X-chromosomes.

Sykes makes a clear connection between his Y-chromosome and the history of his family:

> to know that the Y-chromosome that I carry in all my cells had actually been there, in this place, in the fields beside the stream, was a completely different sensation. Now it felt as if I were experiencing the history of a real part of myself, a place where some of me had actually lived. And, of course, it had. (Sykes 2003, p.18)

Sykes not only creates a connection with 'his' chromosome, but as I noted in the analysis of the bodily metaphors also portrays it as having 'lived'. Sykes seems to be making a reference to the idea of organisms being 'carriers' for their genes, and I believe he is in fact seeking ownership/inclusion of his genetic history and identity. The wider context of 'Adam's Curse' is important to understanding the writing style. It is written in the form of a personal detective story, which is likely to invoke in the (male) reader a personal interest in their Y-chromosome and its 'history'. As I explored in Chapter Three, Sykes is a key figure in a spin off company which carries out mDNA and Y-chromosome tracing. The connection that Sykes is drawing to his Y-chromosome is fundamental to encouraging readers to explore the history of their own chromosomes as having relevance to them.

Sykes goes on to describe the Y-chromosome as the "genetic definition of masculinity" (Sykes 2003, p.176). The level of personification is strong, and Sykes maintains "the central character of such a powerful drama must have a face" (Sykes 2003, p.19):

> This is my Y-chromosome, the bearer of my maleness and the token passed unaltered down from a long line of fathers (…) I see it in my own father, as he leads his RAF squadron in the Second World War. I see it in my grandfather, fighting in the trenches and wounded in the battle of the Somme a generation earlier. (Sykes 2003, p.29).

Sykes characterizes the Y-chromosome as a token that carries maleness through fathers, drawing on the transport metaphors explored in the earlier section. There is also a clear connection between Sykes and his historical masculinity through their masculine actions (leading men, fighting and being wounded), however there is also a clear connection to wars as world-changing events. This is a typical romantic notion we all like to have of our forefathers. However, as Sykes goes on to state, it places the Y-chromosome in a special position with respect to all the other chromosomes as,

> It is only my Y-chromosome that now speaks with a single voice, one that has come to me from generations of men. It stands alone, a perfect copy of the chromosome that lived in my father, and in my father's father and in a thousand other of my paternal ancestors stretching back to thirteenth-century Yorkshire and way beyond, back through thousands upon thousands of men into the far distant past. (Sykes 2003, p.30).

This description raises three issues. The first is the apparent difference between the Y-chromosome as being a 'perfect copy' and being a 'decaying wreck'. This conflicting portrayal was introduced in the first section, which analysed the metaphors used to describe the Y-chromosome, and it as also touched upon in the previous chapter which explored the visual metaphors used in the popular science book covers. As mentioned previously the authors seek to emphasise different facets of the chromosomes at different times, and the Y-chromosome can be seen as a perfect copy in terms of the short time scale of inheritance between generations, but a 'decaying wreck' in terms of a extended time scale and non-sex genes.

The second issue is that the description of chromosomes as speaking, standing and living creates a link with people, as if the chromosome itself were human. This connects to the third feature, which is the Y-chromosome in terms of being inherited from his paternal ancestors. As I mentioned in the previous chapter this book is, at least practically, seeking to create a market for Y-chromosome tracing. As such this association between the Y-chromosome and the human readers is important to create interest in having their own Y-chromosome sequenced.

The connection between the chromosomes, genetics and people as social beings, capable of fulfilling gender roles (i.e. fighting men etc.) raises the question as to how the authors separate sex and gender. I argued in Chapters two and three that our current view of biological sex spans across nature, allowing researchers to draw parallels between how females and males of different species function and behave. However Jones seeks to argue that there is something special about humans in that,

> Animals have males, but only *Homo sapiens* have manhood. As a result, genes say a great deal about sex, but rather little about gender. (Jones 2002, p.8)

This clear distinction between gender as a socially constructed entity, and sex as a biologically constructed is reminiscent of certain arguments in feminism (see Chapter Two), however it had been argued that certain animals do exhibit gender roles, or at the very least specific sex roles (Roughgarden 2004) and indeed that genes play an important role in enabling the body to perform certain genders (See Chapter Eight).

It should also be noted that there is some difference between the authors in how they see the division between gender and sex in this regard. Sykes sees the Y-chromosome as being "the DNA that had made me a man" (Sykes 2003, p.19), reducing his gender expression to his genetic component. Not only is 'maleness' stripped of its cultural context, but the actions of historical men are reduced to their genetics as well, so that when Sykes looks down at his own chromosomes he notes,

> And at their centre, like a bloated maggot, more active than all the others, was the pale form of the Y-chromosome itself. It had no eyes and the frantic withering of its pallid, segmented body disrupted the choreography of the other chromosomes as they tried in vain to work the strings. The stage kept turning and when it had gone full circle the savage and dislocated play of life made sense. The long ships casting off into dark Atlantic waves, the cries of the murdered monks of Lindisfarne, the slaughterer on the shores of Morvern, the thunder of Mongol cavalry along frozen Russian rivers, the blood of defeated enemies and the screams of their women as they were led away to the Great Khan –all these were caused by the blind squirming of the Y-chromosome as it withered behind the scenery. (Sykes 2003, p. 190)

This creates the image of the Y-chromosome, in the 'centre' and more 'active' under the microscope than the other chromosomes and implies that it has played a more active role in the human evolution, although, as it is 'blind' it lacks the foresight to regard its actions. Finally genetics is believed to hold the key to understanding historical actions,

if one understands the actions of the Y-chromosome the whole of human history 'makes sense'.

4.3.3 The genetic war

During the discussion related to the marriage and divorce metaphors I noted that there is a strong narrative of conflict, a 'genetic war' between men and women. This relates to the point I mentioned in Chapter Two that our current ideology of sex holds that the two sexes, male and female are essentially different and that our idea of genetic sex reduced these essences to genetics, that is the X and Y-chromosomes. As this section will show this connects to the idea that sex, reduced to genetic sex is inherited.

It has already been mentioned that the female and male have been viewed as having different biological interests as a result of their differences in reproduction, and hence are in competition with each other within evolution. While in this view sex is determined by the size of reproductive cells produced, for the popular science authors there is some difference to what they take as the 'essence' of the two sexes. For all three authors the Y-chromosome stands as the essence of the male. Bainbridge sees the X-chromosome as the heart of femaleness, emphasises the difference between men and women in terms of the Y and X-chromosome and also the difference between having one or two X-chromosomes. However the two other authors argue that the X-chromosome has not aligned itself totally with the female because it is present in both sexes and it is the mitochondrial DNA which has become connected with female.

As indicated in the analysis of the metaphors in the first section the separation of the male and female is seen as occurring during the 'genetic revolution' of sexual reproduction. The war metaphors are clearly present in Sykes's discussion of the development of sexual reproduction. Again the political metaphors are used, with the term 'ancient peace treaty' and description of 'primeval cytoplasmic wars' and 'two camps with opposing genetic interests':

> (T)he terms of the ancient peace treaty drawn up by the nucleus to halt the primeval cytoplasmic wars had one fundamental flaw. In creating two sexes, this treaty **split every species into two camps** and gave them **opposing genetic interests** – and we live with the consequences every day. We, like all other sexual species, are **irreversibly segregated into male and female.** (emphasis added, Sykes 2003, p.118).

In Sykes's view the male and female are clearly segregated into two camps, and while conflict can create dynamic interactions, there is an underlying assumption that the genetic interests of male and female are fixed.

Sykes considers that the 'war' between the males and females has two 'fronts' based on the reproductive cells which define sex,

> In the **war zone that sex has created, there are two fronts**. The first is where the **perpetual skirmishes** of male and female are acted out; where the **strategies and tactics** of the members of each sex ultimately depend on whether they are the ones **to produce the eggs or the sperm**, but where each is ultimately dependent on the other. The second is the site of the more sinister and more single-minded **struggle** in which **two implacable genetic opponents, mitochondria and Y-chromosome**, fight it out. Each would happily eliminate the sex that did not serve its purpose – the sex on which the other depends to get it through to the next generation. (emphases added, Sykes 2003, p.120)

Sykes thus introduces the idea of a conflict between the Y as representing the male, and the mitochondrial DNA as representing the female. This rests on the idea of the female and male being similar to 'selfish' genes, in that they wish to only reproduce themselves.

In Sykes's view the female is essentially different because the mitochondrial DNA connects the female and her eggs as it is only passed down from mother to child. Sykes clearly states that the mDNA is "the essence of the feminine" (Sykes 2003, p.242), which is comparable to the Y-chromosome as the essence of the male. Many who are familiar with evolutionary theory will be aware that there is generally held to be a conflict between the male and female sexes over the genetic investment in offspring. One of the most perennial problems that theorists debate is how and why this division came about. In the mDNA, Sykes believes he has the explanation for what he terms the "universal division into two separate sexes" and he sees mDNA as "the guardian of the egg" and the Y as the broadcaster of sperm (Sykes 2003, p.274). The term 'guardian' is likely to refer to the small number, and hence valuable nature of the egg(s) and this contracts with the metaphor of 'broadcaster' which is used to convey the mass number of sperm. The metaphor of broadcaster also may indicate a difference in the conception of information as it relates to a presenter of information involved in mass communication. Taken within the context of sexual fitness, where it is the amount of

offspring produced which carry the genetic material the male is inherently 'more successful'.

Sykes maintains that the mDNA has a 'subtle plan' which not only gets rid of the Y-chromosome but which helps itself at the same time (Sykes 2003, p.273). Sykes again draws on the imagery of a political system noting,

> (i)t was mitochondria DNA which **ignited** the **genetic revolution**, and the Y-chromosome which has consolidated it. Their dual success is due to their total commitment to one sex or the other. (Sykes 2003, p.130)

Interestingly one can see the subtle remains of the conflict metaphors in the comparison between the Y-chromosome and the mDNA, in keeping with the idea of the mDNA and the Y-chromosome as combat armaments:

> The Y-chromosome, on the other hand, is a mess. While mitochondrial DNA is a model of **slimmed-down efficiency**, the Y-chromosome is a **genetic ruin**, **littered with molecular wreckage.** (Sykes 2003, p.282)

It is clear that two of the authors view male and females in terms of separate, violently competing camps with different genetic interests. This usage of metaphors was not as visible within Bainbridge's book which dealt with the X-chromosome. Quite possibly this is due to the differing readerships, as two of the books deal with the Y-chromosome and male development, their readership may be more predominantly male and hence conflict metaphors may seem more fitting.

4.3.4 Summary

It has been recognised that there is a heterosexist bias and a male gender bias in the discussion of research on homosexuality and sex determination, particularly in the vocabulary and use of metaphors (Petersen 1999, p.178). This bias was clearly seen in the analysis of the wider frameworks in these popular science books. The 'surplus of meaning' of the metaphors reveals the cultural and social assumptions concerning the differences between male and female, men and women. The metaphor of the 'default female' has lead to a wider metaphor family including the 'XX-permitted ovary' and the 'XY-induced testis'. The wider descriptions showed how the female development is seen as passive and default, while the male development is seen as active. Bainbridge justifies the view of the female development as not requiring a positive mechanism by

suggesting that the mammalian practise of carrying foetuses in a 'female' environment pushes both male and female towards femaleness. Thus the male foetuses must fight against this development. This clearly supported Spanier (1995) argument that the language used to describe the body is locked into gender stereotypes.

In the popular science books the Y-chromosome is seen as 'bearing maleness'. In the two books which explore the Y-chromosome it is given complete deterministic power over sex determination. Sykes's connection with his own Y-chromosome indicated a clear reduction of his maleness to his chromosome. As I noted Sykes's company depends on successfully 'selling' the idea that tracing either the mDNA or Y-chromosome has some value. Sykes connects his own identity with that of the chromosomes and in doing so draws on stereotypic male gender roles and identity.

In the final section I explored how the authors describe the relationship between males and females. Bainbridge allows that there are other forms of sex, mentioning 'intersexuality'. However for the other two authors biological sex clearly consists of two separate 'camps', male and female. The use of conflict metaphors is rife to describe a 'genetic war', between the male and the female, the Y-chromosome and the mDNA, the sperm and the egg.

It is clear that Bainbridge takes a progressive view of sex, acknowledging fluidity and variations while Sykes takes a stronger, more deterministic view. In this next section I will explore Sykes's book in terms of the connections between, and the impact of sex genetics on, the relationship between men and women.

4.4 Genetics in the social world

This final section explores two examples from the popular science books which utilise genetics to explain social and historical developments. The split between sex and gender in the 1960s separated social gender from biological sex, enabling natural scientists to form theories regarding sex determination and development. The majority of the three popular science books concern themselves with sex genetics and so 'biological' differences between sexes, rather than social and cultural issues related to gender. However for some scientists the 'genetic war' between the sexes has had

obvious impacts on society, and this is reflected in Sykes's account of the Y-chromosome having resulted in the 'domestication' of women and colonisation.

4.4.1 Domestication of Women

The evolutionary relationship between males and females is generally considered in terms of sexual reproduction in which the two sexes have become specialised with different reproductive strategies. Sexual reproduction in mammals is linked to different reproductive obligations for the two sexes, as the female incubates and nurtures the developing embryo. Traditionally reproduction has been seen in terms of 'investment' with the male 'investing' his energy in creating many small gametes and having sex with as many females as possible, while the female 'invests' in one large egg. Jones emphasises the unequal 'reproductive investment' that males and females make in their offspring:

> (m)ales are, in many ways, parasites upon their partners. Their interests are to persuade the other party to invest in reproduction, while doing as little as they can themselves. (Jones 2002, p.19)

Sykes expands on this view, stating,

> women (…) are guardians of a rare and precious thing –an egg. Men are not in this happy position. They must seek out and find a female willing to accept their sperm. (Sykes 2003, p.122)

Sykes goes on to describe sexual selection in humans as 'supply and demand' (2003, p.122). The capitalist metaphor of inheritance, investment, indicates that something of value is 'put in' with the expectation of receiving something of greater value than that initially invested. As mammalian males produce many small reproductive cells each one is a low investment and their gain from a pregnancy is higher, because their investment was so low, than for a female who not only produces a large egg but also invests time and energy during 'incubation'. Not forgetting that this description is within a popular science book, Sykes's conflation between females/women, males/men naturalises the idea that men, as males, should wish to 'do as little as they can themselves' in terms of reproduction.

Sykes's concept of the relation between genes, chromosomes, members of biological sexes and people is highly problematic. Sykes creates the image of chromosomes and cells as having the capacity, for example, to care and be willing, "Y-chromosomes

really don't care whether the eggs are willing or not" (Sykes 2003, p. 235). These ascriptions of 'care' and 'willingness' to the Y-chromosomes and eggs as biological cells is somewhat strange. However by merging the biochemical level (genes, chromosomes, eggs, sperm) with the social world he is able to argue for a direct relationship between the Y-chromosome and men's and women's behaviour:

> (f)orced by the relentless ambition of the Y-chromosome to reproduce itself, women were reduced to a state of serial pregnancy, increasingly enslaved by dependence on men. (Sykes 2003, p.237)

He uses flamboyant language, arguing that "(t)he blind rage of the male, released from its chains, has slowly and deliberately enslaved the female" (Sykes 2003, p.235). In Sykes's account of human history, the actors are not human people, but genes and chromosomes which have 'agents' capable of violence and aggression.

> It is also an entirely new type of evolutionary mechanism: a selective advantage for a Y-chromosome obtained through the very system triggered by the chromosome itself through its agent testosterone –aggression, conquest, promiscuity and patriarchal succession. (Sykes 2003, p.187)

Gradually, Sykes argues, a social structure was set in place which conferred property, wealth and power upon the Y-chromosome:

> These concepts were property, wealth and power. They were entirely new and played straight into the hands of our old friend – the Y-chromosome – as a new and irresistible instrument for sexual selection. Now, at long last, there was an opportunity for a Y-chromosome that could get hold of these valuable assets to increase almost without limit; an opportunity to pursue their natural instinct for endless replication that had until then been contained. It was, in my view, men and through them the Y-chromosome that seized on this trio of property, wealth and power and pushed them to their present absolute prominence. (Sykes 2003, p.233)

Sykes provides a genetic explanation of patriarchal sexist society where Y-chromosomes, males and men have "gotten hold of" physical, social and economic factors, and which has led to women becoming "domesticated and imprisoned (by the Y-chromosome)" (Sykes 2003, p.237).

Sykes's explanation also provides a framework for exploring competition between different Y-chromosomes. Sykes argues, that certain Y-chromosomes 'succeed' in this system of patriarchal succession because they become linked to the wealth and statues

of the family name (Sykes 2003, p.182). In this case success is measured by the spread of the particular Y-chromosome.

> The inequalities between the sexes did not escape the notice of the Great Assembly of genes, the nuclear chromosomes. Indifferent to which sex transports them to the next generation, they began to savour the prospect of being carried along by wealthy men with their new opportunities for polygamy. The train of sexual selection was gathering speed, the boilers stoked by the energy and ambition of the Y-chromosome, the Great Assembly waving it off from the station. Just as power and wealth converged on fewer and fewer men, so their wealth became more and more necessary to the survival of the women, now utterly dependent and suppressed. (Sykes 2003, p.239)

Marian Lowe, a chemist, in 1978 noted that feminists may not have to take such arguments seriously as scientific theory, but that they should take heed of them as political theory (Lowe 1978). The idea that the social and cultural structures which 'enslave' women are the result of the Y-chromosome's genetic interests clearly provides justification for these structures to be seen as 'natural'.

I proposed in Chapter Two that descriptions of biological sex should be viewed as ideologies, with vested political aims. Sykes's descriptions of the 'enslavement of women' by the Y-chromosome and men seems to serve as a suitable illustration of this, with the reduction serving to naturalise, or even *pardon* past male domination. However Sykes description also serves to introduce the notion that there has been competition between Y-chromosomes. In Chapter Three I explored the background behind Sykes as a popular scientist and I noted how his PUS work was related to his involvement with the company Oxford Ancestors which offers Y-chromosome tracing. The story of the 'domestication' of women serves to prioritise the role of the male line (the Y-chromosome). This offers to the male readers a valuable context for their 'own' Y-chromosome and the hope of finding out how their own ancestors completed in this male dominated world. This is brought into focus in Sykes's description of the relationship between the Y-chromosome and colonisation, which is my final brief example of the expansion of genetic knowledge to the social world.

As I noted in the first example the metaphors are concentrated on the evolutionary aspects of the Y-chromosome and creates a link between genetic success and cultural success. While the major narrative is that of the relationship of Y-chromosomes to non-Y-chromosomes holders, Sykes also explores the conflict between different Y-

chromosomes. He does so by exploring how different Y-chromosomes have travelled around the world, through colonisation. He expresses the result in terms of genetic winners and losers.

> The genetic winners are the incoming Y-chromosomes; the clear losers are the Y-chromosomes of the original inhabitants or, in the case of the Afro-Caribbean and African Americans, exploited ethnic groups. (Sykes 2003, p. 149)

As with patriarchy, this type of genetic account allows colonization to be viewed as a consequence of the Y-chromosome, a form of genetic colonization. Social, cultural and religious factors, which in most historical accounts play a large role in explaining the motivation for colonization, are all under the power of the Y-chromosomes in the evolutionary story. This can be seen in how Sykes explains the 'Age of the Vikings':

> The Age of the Vikings has all the hallmarks of Adam's Curse: the insistent urge of men to mate with as many women as possible, and the intense rivalry among Y-chromosomes that ensues. As their first-born sons accumulate wealth enough to collect women at home, their unfortunate younger brothers, dispossessed of the means to attract a mate as surely as if they were peacocks with their tails trimmed, set off across the seas to look for sex on distant shores. (Sykes 2003, p.161-162)

Such descriptions could be seen as suffering from attempts to simply science for public consumption. However, similar, although less extreme, narratives can be found in scientific journal publications which draw upon mitochondrial DNA and the non-recombining portion of the Y-chromosome to explain human migration. As with Sykes, the conceptual paradigm is one of binary heterosexual relationships, a sample of one aspect is seen below:

> Contact between the forager and food-producing populations often involves hypergamy, in which forager females marry food-producing males and are assimilated into the expanding agricultural community. (Wilkins 2006, p.614).

Critically to Sykes's account of human history is that genetics and genetic information is given dominance over other factors. Sykes seeks to trace his family's name along with his Y-chromosome, and in these it is the genetic information which is held as 'true'. Sykes explains his concerns with tracing the Y-chromosome of a Scottish chieftain:

> My greater anxiety was that we might find that one or more of the five clan chiefs did *not* share the same Y-chromosome as the others. That would have to

> mean that their genealogies were wrong: that, somewhere on the lines between Somerled and themselves, so confidently traced in the Clan Donald histories, there was a mistake. (Sykes 2003, p.178).

Sykes goes on to note how if this had proved to be the case he would have kept the results confidential, and not included it in his book. Genetics is seen as unbiased, truthful, and *the* accurate account of genealogies and family histories. A similar portrayal is seen in the journal article where genetic data is prioritised in forming the framework into which other types of information can be incorporated:

> Taking full advantage of the information in the patterns of human genetic diversity will require the development of more complex and realist models. These models will have to incorporate geographic, linguistic, archaeological and ethnographic data. (Wilkins 2006, p.615)

While undoubtedly genetic data is an interesting new tool, the attempt to apply it to societies and periods which did not have access to its use is problematic. The interpretation of genetic samples carries underling assumptions of 'nuclear families', and patriarchal heterosexuality as the predominant organisational structure. Currently there is much concern that 'social' fathers may not be the 'biological' fathers of the children they consider their own and this issue would have been present in historical times as well. However it is assumed that maternal histories are accurate. The Biblical story of King Solomon's dilemma where two mothers claimed the same child, illustrates an example in which without state record-keeping questions of motherhood can also be raised. It is also clear that the migration of male 'genetic samples' may occur in many different situations and can not be taken as an indication of continued social and cultural contact. Rather than considering genetic tracing as the 'real' and 'accurate' trace of human migration, it would be more suitable to view it as one 'voice' in a complex story of human migration which also includes geographical, linguistic, archaeological and ethnographical voices.

4.5 Conclusion

The purpose of including the three popular science books was to explore how popular science framed and described sex. As this chapter showed, there is an unquestioned identity of the X and Y-chromosomes as 'sex-chromosomes' and the books describe there being essential differences between male and female as represented by the X and

Y-chromosome. The authors used a variety of core metaphors to describe the chromosomes, including physical reference to the body, marriage and divorce, political images and modes of transport. These different metaphors are employed to explain and describe the functioning of different features of the chromosomes. As the analysis showed, the description of the chromosomes through these metaphors reveals cultural stereotypes and a strong bias towards viewing the male as active and the female as passive.

With this in mind this chapter turned to analysing the frameworks of understanding within which the metaphors were located. These books' descriptions of sex determination and development followed the traditional view of the female as default (the XX-permitted ovary) and the male as active (Y-induced testis). The main feature which has been seen is the extent to which the idea of a 'genetic' war is present in the books. The use of conflict metaphors is apparent in the discussions of the X and Y-chromosome, as well as the descriptions of the male and female in terms of sex determination and development. This is seen to result in different genetic interests, which in the extreme descriptions of Sykes results in oppressive social structures and the 'imprisonment' of the female. In Chapter Two I argued that our concept of sex should be viewed as ideology, because it is deployed to produce social and institutional structures. I argued that in Sykes's case the effect of his reduction of social structures to the Y-chromosome created a suitable consumer product –Y-chromosome tracing.

With regard to the wider context of this thesis this chapter sought to provide an insight into the four factors I argued were key to our current understating of 'genetic sex'. In these three popular science books genetic sex is described as binary and fixed. There are a few, brief mentions of alternatives. The categories of male and female are portrayed as residing throughout nature, with the descriptions drawing upon a variety of organisms, some of which do not share sex determination systems. Sykes's book tightly connects nature to the narrative of genetic sex which naturalises social behaviour such as material greed, power and sexual oppression. Genetic sex is seen as impacting upon the whole body but also as leading to different reproductive motivation. In this case genetic sex is seen in terms of sexual selection and evolution. As I have shown, Sykes has expanded upon this to explain the structure of the social world, arguing that the Y-chromosome was at the heart of the 'enslavement' of women. This indicates that there is an additional factor important to our current understanding of genetic sex, that of it

being passed down from father to son and mother to daughter. These factors will be explored further in Chapter Nine. The next two chapters will explore the two case studies of SRY and DAX-1, two genes found to be important in sex determination.

CHAPTER FIVE - THE MOLECULAR SEX DETERMINING GENE

genetic male n,
1. An individual with one X-chromosome and one Y-chromosome, the normal male karyotype. 2. An individual whose cell nuclei do not contain Barr bodies. (The American Heritage® Medical Dictionary 2007)

"I'm penis ambient" (Eddy Izzard, Sexie 2000)

5.1 Introduction

This chapter explores the first gene case study; the SRY[5] gene. The search to find this 'gene for' sex spanned close to 65 years in which, I will argue, researchers undertook a process of scientific creation. In similarity with many, if not all, genes, the SRY gene was brought into existence through a process of negotiation between societal and scientific forces. While I do not argue against the existence of the DNA sequence found, the portrayal and characterisation of the gene was clearly shaped by social forces, as not only are scientists members of society who hold social goals and values, but they also exist within a social community of researchers. Nonetheless, with the announcement that the SRY gene had been located in 1990 it seemed as if the gene for sex had been defined. Its place as the 'master gene' for sex was further secured by the creation of an XX male transgenic mouse in 1991.

The SRY gene is not new to the feminist gaze. Judith Butler (1993) has used it as a brief example to show the continued existence of residual features of the 'default' female science paradigm. Joan Fujimura (2006) has also explored how SRY can be read in different ways from a variety of sociocultural perspectives. However in this chapter I have sought to provide a detailed history of the SRY, showing not only its relatively recent genetic identity, but also its 'pre-history' as the TDF.

The chapter has two aims. The first is to develop the feminist discussions by documenting how the SRY gene was clearly created to satisfy specific functions, set by the social ideology of binary sex and incorporated into the molecular search. Both the

[5] Genes found in the human are denoted by capitals (i.e. human SRY) while the corresponding mouse gene is denoted as Sry. The SRY/Sry stands for Sex region on the Y-chromosome.

SRY and DAX-1 case studies concentrate on the history of the genes from the journal articles, exploring how they were researched, as well as the metaphors and concepts connected to the genes. The second aim is to lay the foundation for discussions in Chapter Seven regarding the types of gene concepts used in the research as well as the development from genetics to genomics. These discussions have been kept separate not only due to space limits for this chapter but also to allow inclusion of the discussion of the second gene case study, DAX-1.

5.2 Analysis of the Medline record

This chapter gives a general background to the early research into the basis of sex determination. There was an early suggestion that there existed a 'testis determining factor' or the TDF, which later became known as the SRY gene. The search for the 'gene for' sex is an interesting case study because it highlights many issues with which current social and philosophical studies of genetics are concerned. Not only does it provide evidence for how different concepts of genes engage with each other, but also for how researchers both pursue and create research questions.

This case study is based upon journal articles and reviews found by searching Medline with the keywords 'testis determining factor + sex', and 'sex determining region + sex'. The search was conducted during November 2005 and for 'testis determining factor' gave 168 hits, and the search for 'sex determining region' gave over 990 articles. It should be noted that as with nearly all scientific productions, genetic discoveries are nonlinear and involve multiple groups. Indeed often many groups, with different research interests and questions, consider themselves to be working on the 'same' gene, and are collaborating and sharing techniques and biological samples while publishing in different journals. With this in mind the brief details of all papers (title, journal, type of article, authors) were collected. Articles in low impact journals were discarded as were those which concerned an alternative gene labelled Sry (Drosophila serendipity). This left a sample of 200 articles. Their abstracts were printed out and coded. Key phrase were highlighted (TDF, sex, development, determination, master, gene, factor, locus) as well their research findings and research methodology. From this collection articles which represented novel descriptions of the TDF, novel methodologies, and important findings (such as suggesting an identity for the TDF) were selected for further in-depth analysis.

5.2.1 Discovery of the sex determining gene

The Medline record of the TDF begins with an article in 1983 that explores the variation in tooth size in various human karyotypes (XX, XY, 45 X females, 47 XXY) (Micis et al. 1983). The paper, entitled 'A study of a 46,XX infertile man and his permanent tooth sizes', explored the case of a person who had been found to be a 46, XX male when seeking infertility treatment. Building upon research in the 1970s which indicated that genes on the Y-chromosome influenced tooth size in males (i.e. Alvesalo 1971), Micis et al. suggest that "the genes responsible for the testis-determining factor are present and that the genes influencing tooth size are absent in this patient" (1983, p.165). It is interesting to note that the genes are described as being involved in two different ways: genes 'influence' tooth size, while being 'responsible' for the TDF.

Three years later, in 1986, the TDF is mentioned in two articles published in *Science*. The publication of these articles in a high status journal indicates that the question of genetic 'sex determination' is of prominent research status. It is likely that the TDF gained such a high standing because of its primary relationship to 'sex' and 'the human condition', two topics which generally attract wide interest.

The first of these papers appeared in August 1986, entitled 'Chromosome Y-specific DNA is transferred to the short arm of X-chromosome in human XX males' (Andersson et al. 1986). As the title suggests, it reported the use of a DNA probe to detect Y-specific DNA in 'three XX males', to show that the Y DNA was located on the tip of the short arm of an X-chromosome. The article mentions maleness as being "probably due to the presence" of the "Y-encoded testis-determining factor (TDF)" (1986, p.786). This article also notes that XX males are probably due to the transference of Y-DNA to a paternal X-chromosome.

The second paper published in *Science* during this year an article was published entitled 'A pseudoautosomal gene in man' (Goodfellow et al., 1986). This article described a gene, MIC2, which the group saw as an important marker for the studies aimed at isolating TDF, which they termed "the sex-determining gene(s) TDF" (1986, p.740). It is clear that at this stage the research was focused on locating the TDF by limiting the area of the Y-chromosome in which the TDF resided. MIC2 was understood to

recombine with the TDF "at a frequency of 2 to 3 percent", and as the paper's abstract states was,

> the most proximal pseudoautosomal locus thus far described and as such is an important maker for use in studies directed towards the isolation of TDF. (Goodfellow 1986, p.740)

In 1987 the DNA sequence of the TDF was pursued further through the use of intersex conditions as reported in an article entitled, 'Localisation of Y-chromosome sequences in normal and 'XX' males'. The article was authored by seven researchers and published in the *Journal of Medical Genetics* (Buckle et al. 1987). It documented the mapping of three "unique sequences derived from the Y", and is presented as a further narrowing down of the location of the TDF (Buckle et al. 1987, p.197). As Chapter Seven will explore, positional information was given increasing value in the genome, and the TDF was understood to function as the gene for sex specifically dependent upon its location within the Y-chromosome in an area that did not recombine with the X-chromosome.

These genetic experiments are a marked departure from the research in the early 1980s (i.e. H-Y antigen and Snake DNA) where the concern was with similarities between different males in vertebrates (see Chapter Seven). Instead, they are based on using human intersex conditions as 'natural' experiments, to localise markers close to the TDF or, as the American group phrased it, 'a series of sex-reversed humans' (Buckle et al. 1987). As noted by Fausto-Sterling (2000) and Fujimura (2006) the conceptualisation of these individuals as 'sex-reversed' is problematic. At this time the research articles typically recount the standard endocrinological characterisation of the persons' bodies, while emphasising the gonadal tissue over other sex characteristics. Evidence which some physiologists and endocrinologists would have valued as indicating female anatomy and 'incomplete masculinization' were disregarded in genetic research. The lack of reference to hormone production and sperm production indicates that, for a geneticist, to be a male was to possess testes, but there was no requirement that they produce a certain level of hormones (perhaps because their body's morphology was thought of as adequate illustration of this).

In April 1987 *Nature* published an article with 'resounding proof' that the TDF was not the H-Y antigen (Simpson et al. 1987). Using a "series of sex-reversed humans" they created deletion maps for the Y-chromosome, which showed that the H-Y antigen was

on the long arm of the Y, while TDF was located on the short arm. This experiment is a clear illustration of the extent to which gene research at the time was a collaborative venture. The paper listed six authors from five different institutions. This cooperation between the different groups not only brought together a variety of different biological resources (H-Y blood, DNA probes and samples from 'sex-reversed' humans) but also accessed resources such as the pathology laboratory, expertise in immunohaematology, as well as a blood bank.

It is clear from this article that sex development and determination was conceived of in quite traditional terms. As the authors state in their abstract, "(e)mbryos with a Y-chromosome develop testes and become males whereas embryos lacking a Y-chromosome develop ovaries and become females" (Simpson et al. 1987, p.876). This view of sex development and determination is in keeping with the 'default female' view held by endocrinology and embryology (see Chapter Two and Four). Thus it is clear that even though this article is within the realm of molecular biology and genetics, the 'default female' paradigm has become incorporated.

This article also indicates that the TDF had begun to be conceived of as 'a master regulator of sex differentiation.' Bearing in mind that the researchers were seeking a gene that did not have a known protein product, it seems strange that they assumed that the gene was a 'regulator'. It is likely that this picks up on an earlier suggestion that the TDF was related to a sequence of receptive DNA sequence (GCGC) known as the Bmk Sequence (s found in snakes, which had been taken to be a single genetic switch. While I will discuss this further in Chapter Seven 'master regulators' were a common feature of developmental views of the embryo and how genetic pathways lead to the development of traits (i.e. eyes), and hence the search for a master regulator seemed logical.

A few months later a group working with David Page published an article entitled 'Exchange of terminal portions of X- Y- chromosomal short arms in human XX males' (Page et al. 1987a). This article investigated the hypothesis that XX males result from a transfer of a terminal portion of Yp to the X-chromosome and whether a terminal portion of Xp was lost in the process. The findings of this research paper are seen as the 'genetic proof' of the 1960's hypothesis of intersex conditions resulting from crossovers between the X and Y chromosomes during recombination. This was thought to imply,

> that the testis-determining factor gene (TDF) maps distally in the strictly sex-linked portion of Yp, near the pseudoautosomal domain. The XX males described here appear to result from single (and, at least in the second case, unequal) crossovers proximal to the pseudoautosomal region on Yp and proximal to or within the pseudoautosomal region on Xp. (Page et al. 1987a, p.437)

In this quote researchers speak of 'the testis-determining factor gene' as the TDF, which indicates that researchers are using both the concepts of the 'factor' from classical genetics and the gene from molecular genetics.

Around the same time, an article was published entitled 'A unique dicentric X;Y translocation with Xq and Yp breakpoints: cytogenetic and molecular studies' (Bernstein et al. 1987). The focus of this article is a 32-year-old woman who "presented with secondary amenorrhea and infertility" (p. 145). The authors describe her body as

> (of) normal height and her breasts were well developed, but she had streak gonads; there were no signs of virilization, and she showed no somatic stigmata of Turner syndrome. (Bernstein, et al. 1987, p.145)

The article goes on to indicate the acceptance of TDF being contained on the distal short arm of the Y-chromosome, which the woman does not possess:

> The Y-DNA studies of this female also revealed the absence of the distal short arm of the Y-chromosome, to which the testis-determining factor has previously been localized. (Bernstein et al. 1987, p.145)

The researchers link the woman's physical body (phenotype) with her DNA sequences, or rather her lack of Y DNA. Taken together these two articles

> reduced the region that must contain TDF to only 140,000 letters of the genetic code. This is not a trivial amount of DNA -140,000 letter are about equal to a hundred pages of a book -but on average would be expected to contain only one gene. (Cookson 1994, p.93)

William Cookson's comments indicate that the concept of gene 'size' was important in setting the expectation of what would be found. Indeed all of the articles so far have considered TDF as being one 'gene' (i.e. the testis-determining factor gene). But there were other suggestions. In 1987 Chapelle published a review entitled 'The Y-chromosomal and autosomal testis-determining genes' (De la Chapelle 1987). In this paper he notes that testicular differentiation in these "XX males is very likely induced

by the testis-determining factor, TDF, normally located on Yp" (De la Chapelle 1987, p.33). However, he takes a different tack by exploring the case of XX males who do not have Y-DNA "detectable by presently used methods". He notes:

> (t)he suggested conclusion is that an autosomal dominant testis-determining factor, TDFA, exists. TDFA shows somewhat variable expression in XX individuals often causing genital ambiguity or true hermaphrodism. TDFA has no phenotypic effect on XY individuals. It is argued that XX males without presently detectable Y-DNA are caused either by TDF or TDFA. (De la Chapelle 1987, p.33)

This area of research will be discussed in the next chapter, which explores a gene called DAX-1.

5.2.2 Proposing a gene, the ZFY

In December of 1987 a paper was published by nine authors including Page in which not only was a DNA sequence proposed, but also a likely gene product (Page et al. 1987b). The article, which appeared in *Cell*, was entitled 'The sex-determining region of the human Y-chromosome encodes a finger protein'. In similarity with past research scientists sought to narrow down the gene involved by using genetic samples from intersex individuals who either were or were not likely to have the gene based on their phenotype. The researchers detail how through "genetic deletion analysis" of "sex-reversed" individuals they identified a small portion of the Y-chromosome which they held was necessary and sufficient to induce testicular differentiation of the bipotential gonad. The researchers go on to describe this as,

> Walking 'right' from pDP307, we cross a Y-chromosomal breakpoint in female WHT1013, who has a reciprocal translocation between Y and autosome 22. Her chromosomal constitution can be described as 46, X t(Y;22) (p11.2,q11). At age 12, she was karyotyped because a gonadoblastoma had developed within her left gonad, which was "dysgenetic" (malformed and lacking in germ cells). Subsequently, a gonadoblastoma was detected in her right gonad, which was also dysgenetic. She was otherwise a phenotypically normal female. (Page 1987b, p.1094)

Clearly this description raises many issues, including the increased availability of medical records, closer links between genetic researchers and the human subject and their family, as well as views of 'normality', and the placement of secondary characteristics in views of 'phenotyically normal females'. However, it should be mentioned that in this quote 'WHT1013' is considered normal, yet no mention is made

of secondary sexual characteristics. This paper also makes a reference to the fathers of XX males, demonstrating that this research project has not only dealt with the individual but required the cooperation of families, which is an indication that the 'sex-reversed' subjects may be children or babies who have been clinically diagnosed.

The paper goes on to describe how the group cloned a segment of the Y-chromosome, which was thought to contain the TDF. After sequencing the segment they worked out the amino acid sequence and revealed that it would likely produce a protein with a certain folding structure known as a 'zink finger'. Hence the gene became known as the ZFY (Zinc Finger on the Y-chromosome). Cookson (1994) offers a clear description of zinc fingers as:

> proteins with finger-like protrusions containing Zinc. Zinc fingers can sit on DNA and control whether it is transcribed into RNA to make protein. (1994, p.94)

Cookson remarks that the ZFY was a 'very promising candidate' for the TDF. Indeed it seemed to offer a clear mechanism for action. We can infer the importance the authors gave to this article from the style of the paper, which contrasts with that used by earlier papers. It begins with a historical overview of the search for the "mechanism by which the sex of an individual is determined" (Page et al. 1987b, p.1091), noting Aristotle, Mendel, and the work on Drosophila and the H-Y antigen, and the Bkm DNA sequences. This introduction portrays the scientists as being engaged on a long and important journey, which has engaged thinkers throughout known history. Generally the opening of a research article serves to place the experiment within a research paradigm; however the opening of this article is notable because it signifies that this article is thought to be revolutionary. The introduction also makes clear mention of the role of autosomal genes in sex development.

In this paper the researchers use the term "the testis-determining factor gene (TDF), the master sex-determining locus" (Page et al. 1987b, p.1091). The view of TDF as 'master regulator' is strengthened later in the article through the bold statement; "(t)he mammalian Y-chromosome, by its presence or absence, constitutes a binary switch upon which hinge all sexually dimorphic characteristics" (Page et al. 1987b, p.1091). It would seem that the simple single switch which had been proposed in the late 1980s has expanded in importance. This switch is now seen to be one upon which "all sexually dimorphic characteristics" depend. This clearly evokes the 'default' female paradigm

explored in Chapter Two, as well as the idea that human sex exists naturally (and genetically) in only two forms.

The researchers also sought to provide evidence that the ZFY could be the TDF through showing that it spanned the evolutionarily diverse vertebrate sex determination systems. Thus in keeping with the earlier view that it would be useful to view the TDF within an evolutionary context, this research article describes the search for gene homologues across a wide range of mammals.

> (…) to this end, we prepared 'Noah's ark blots'. Onto these genomic DNA transfers "went one pair, male and female, of [many] beasts, clean and unclean, of birds and of [many things] that crawl on the ground, two by two" (Genesis 7,8-9), including humans, great apes (e.g. chimpanzee, gorilla), Old World monkeys (e.g., rhesus monkey), New World monkeys (e.g., owl monkey), rodents, rabbits, dogs, goats, horses, and cattle. (Page et al. 1987b, p.1095)

Quotations from Genesis are not normally found in research articles published in *Cell*. It does serve to lighten the research article, which may have been important as it is a topic that may interest people outside of the research area. Yet, this is a strong pointer towards the 'situated knowledge' aspect of this research as conducted within a predominantly Christian background. In Chapter Three I showed how Christian imagery played a large role on the covers of popular science books. The reference to Noah's ark is also important with regard to the idea of sex spanning through nature. Indeed the evolutionary importance of the TDF in sex determination systems is stated as "(t)he presence of similar sequences in birds suggests a possible role not only in the XX/XY sex determination system of mammals, but also in the ZZ/ZW system of birds" (Page et al. 1987, p.1091).

It is clear that the researchers to some extent presupposed the nature of the TDF gene by creating requirements that the gene must fulfil: it must only be present in the mammalian male, on the Y-chromosome, and it must have a semi-conserved evolutionary nature. In finishing the analysis of this article it is critical to return to the question of how the ZFY gene is characterised. As mentioned, this article characterises the TDF as 'testis-determining factor gene' and the 'master sex-determining locus' (Page et al 1987, p.1091) and ZFY as a 'master regulator' of sex determination. However it was seen to raise the question as to whether the process of sex determination

was cell-autonomous (each cell determined sex on its own) or whether signalising between cells played a role.

> Indeed, the results of mouse XX⇔XY aggregation chimera studies seem to exclude the possibility of cell-autonomous sex determination in all cell types. While our findings suggest that the first step in mammalian sex determination is cell-autonomous, subsequent steps need not be. (Page et al. 1987b, p.1100)

Thus, while the ZFY is considered a 'master' within the cell the article notes that this may not be the case within embryos and tissue. The article goes on to say, "(i)ndeed, it remains to be demonstrated that TDF is a single gene"(Page et al. 1987b, p.1100).

In some regards, scientific discoveries gain importance not because they solve questions, but rather because they raise new questions. One of the new questions raised was the relationship between testis formation and sperm production with reference to the TDF. In May the article entitled 'Y; autosome translocations and mosaicism in the aetiology of 45X maleness: assignment of fertility factor to distal Yq11' was published (Andersson et al. 1988). This article reported a study of three 45,X males with Y-DNA probes by Southern blotting and *in situ* hybridization. The authors note that "(t)he maleness in all cases was due to the effect of the testis determining factor, TDF" (Andersson et al. 1988, p.2). However this research also sought to link the phenotypical with the reproductive 'fertility' and the genotypical characteristics of the three subjects:

> Southern blotting studies with a panel of mapped Y-DNA probes showed that in all three individuals contiguous portions of the Y-chromosome including all of the short arm, the centromere, and part of the euchromatic portion of the long arm were present. The breakpoint was different in each case. The individual with the largest portion (intervals 1-6) is a fertile male belonging to a family in which the translocation is inherited in four generations. The second adult patient, who has intervals 1-5, is an azoospermic, sterile male. (Andersson et al. 1988, p.2 – see glossery for diagram of chromosome)

The paper goes on to detail the use of probes to track Y-derived DNA,

> these phenotypic findings suggest the existence of a gene involved in spermatogenesis in interval 6 in distal Yq11. The third case, a boy with penoscrotal hypospadias, has intervals 1-4B. In situ hybridization with the pseudoautosomal probe pDP230 and the Y-chromosome specific probe pDP105 showed that Y-derived DNA was translocated onto the short arm of a chromosome 15, 14, and 14, respectively. One of the patients was a mosaic for the 14p+ translocation chromosome. (Andersson et al. 1988, p.2)

It would seem that the search for the TDF has now developed into a search for genes on the Y-chromosome linked to spermatogenesis.

Up till now all the papers extracted through the Medline search have concerned humans. However in 1988 work was also progressing in the use of 'sex reversed mice (Sxr). These XX Sxr mice had a duplication of the Y chromosomal testis-determining factor which caused testis development. As one article noted,

> We believe the most likely explanation of our data is that the XXSxr genotype is not testis specific but also influences the epididymis directly. (Wilkinson et al. 1988, p.11)

Epididymis are tubes in the male reproductive system through which sperm travel (see glossery) The result of this XX Sxr experiment indicated that other genes, lower in the sex development cascade, could cause 'sex-reversal' and non-typical phenotypes.

5.2.3 ZFY not TDF

The first article found through Medline to raise doubts as to whether the ZFY was the TDF was published in Oct 1988. The article, 'Mammalian ZFY sequences exist in reptiles regardless of sex-determining mechanism' was published in *Science* (Bull et al. 1988). They showed that the ZFY "representing the putative testis-determining factor in mammals hybridized to both the DNA of reptiles with sex-chromosomes and to DNA of reptiles with temperature-dependent sex determination" (p. 567). This article's challenge to the candidacy of the ZFY as the TDF rests on the lack of an evolutionarily conserved gene in other sex determination systems,

> (f)or reptiles with XX/XY or ZZ/ZW systems, the absence of sex differences in hybridization patterns raises the question of whether the ZFY sequences reside on their sex-chromosomes. (Bull et al. 1988, p.567)

In December 1988 Page wrote an article entitled 'Is ZFY the sex-determining gene on the human Y-chromosome?'. As would be expected from the title, the article raises a number of the problems with ZFY being the TDF, in particular the presence of a similar gene on the X-chromosome;

> There is a closely related gene, ZFX, on the human X-chromosome. In most species of placental mammals, we detect two ZFY-related loci: one on the Y-chromosome and one on the X-chromosome. However, there are four ZFY-homologous loci in mouse: Zfy-1 and Zfy-2 map to the sex-determining region

> of the mouse Y-chromosome, Zfx is on the mouse X-chromosome, and a fourth locus is autosomal. (Page 1988, p.115)

In simple terms the human has two versions of the gene thought to be the TDF, one on the Y-chromosome (ZFY) and one on the X (ZFX). As mentioned this does not rule it out from being the TDF, as it could be dose specific (see glossary). In XX human females the second X-chromosome is generally inactivated and thus they would only have one active copy, while XY humans would have two active copies. It was possible that the male/female differences were caused by having one or two active copies of the gene producing a protein. However the difference in numbers of gene copies between animals did suggest it was not the TDF. As the TDF was considered to be a critical gene in development it was assumed that it would be highly conserved through evolution (i.e. between placental mammals). The finding that closely related organisms had differnet numbers of these gene in their genome made it unlikely that it played such a crital role in development.

The case of the mouse Zfy was explored further in an article published in *Science* by a group including Page in January 1989. The paper proposed that,

> Zfy-1 alone may suffice to determine maleness; Zfy-2 is dispensable, as it was deleted in an Sxr variant that retains sex-determining function but has lost other genes. (Mardon et al 1989, p.78)

A similar article (Nagamine et al. 1989) reported in the same issue of *Science* the successful isolation and mapping of the mouse complementary DNA sequence (mouse Y-finger). It was found to encode "a multiple, potential zinc-binding, finger protein homologous to the candidate human testis-determining factor gene" (Nagamine et al. 1989, p.80). In keeping with the earlier article which found four Zfy/x homologues, they found four similar sequences, two of which were mapped to the Y-chromosome. To summarise, as the mouse Y-finger sequences are duplicated several times in the mouse, but not in humans, doubt was raised as to whether the evolutionary function had been preserved.

In April 1989 researchers published an article in *Genetics* entitled, 'Localization of murine X and autosomal sequences homologous to the human Y located testis-determining region' (Mitchell et al. 1989). This article reported the ZFY as "recently a candidate gene for the primary testis-determining factor (TDF) encoding a zinc finger

protein (ZFY)" (Mitchell et al. 1989, p.803). In this article the researchers reported that in the mouse there was a 'highly homologous X-linked copy' of the ZFY. In fact they found that ZFY was more closely homologous to the mouse X and autosomal sequences than it is to either of the Y-linked loci. In addition, their findings suggested that the Zfy-2 was not necessary for male determination in mice.

The Medline search highlighted an interesting article from this time written by an anatomy professor, Ursula Mittwoch (1989), entitled, 'Sex differentiation in mammals and tempo of growth: probabilities vs. switches'. Up till now the articles had considered the TDF's significance to be one of 'switches'. As this article states the conventional model is one in which,

> a switch is envisaged to steer the indifferent gonad into the path of either testicular or ovarian development The immediate cause of the switch is thought to be the presence or absence of Sertoli cells, which in turn is controlled by the presence or absence of the testis-determining factor on the Y-chromosome (TDF in humans, Tdy in mice). (Mittwoch 1989, p. 455)

In this article the author draws upon embryology to explore the differences in growth rates of the XY/XX gonads and embryos, before the occurrence of the steps that were thought to determine sex differentiation. The abstract notes,

> Since the genetic constitution of the sex-chromosomes appears to manifest itself from the earliest embryonic stages onwards, the concept of indifferent gonads being switched into alternate pathways becomes inappropriate. (Mittwoch 1989, p.455)

The paper proposes a model where gonadal differentiation "depends on developmental thresholds" (Mittwoch 1989, p455). The standard view of sex differentiation held that sex was dependent on "the formation of Sertoli cells by a particular stage in time in a sufficiently developed gonad, failing which the gonad will enter the ovarian pathway" (Mittwoch 1989, p.455). TDF is seen to be a "principal factor enhancing the rate of gonadal growth" while "other factors which influence development rates can modulate the probability of a gonad becoming either a testis or an ovary"(Mittwoch 1989, p.455). This is a more holistic and balanced view of male and female development, typical of embryology where timing is critical.

As well as this broadening of the TDF into embryology in December 1989 another

research article was published that explored the differences in transcripts between tissue types. The article was entitled 'The putative testis-determining factor and related genes are expressed as discrete-sized transcripts in adult gonadal and somatic tissues' (Lau and Chan 1989). The abstract opens with the lines:

> The zinc-finger-Y (ZFY) gene is a candidate for the testis-determining-factor gene (TDF) on the human Y-chromosome and is postulated to initiate testis differentiation during embryogenesis. However, the present study indicates that the ZFY gene and its X homologue (ZFX) are differentially expressed in adult tissues. (Lau and Chan 1989, p.942)

The researchers found that the corresponding ZFY transcript encodes a protein with 801 amino acids. Their findings suggested that "the ZFY gene and its X homologue (ZFX) are differentially expressed in adult tissues", meaning that the ZFY still has the potential to be a candidate for the TDF as it has a "testis-specific transcription" (Lau and Chan 1989, p.942). As the paper goes on to note "(s)ignificantly, the 3-kb ZFY transcript was also detected in other mammalian adult testes" (Lau and Chan 1989, p.942) and the testis-specific transcription of the ZFY gene suggests that it serves a "conserved function" in the testis. While researches had set out to find a gene which was only used (and hence transcribed) in the testis, this article suggestions that the research has moved on to looking for 'testis-specific transcription' –up regulation or down regulation of translation -so the gene being used more or less in comparison to the levels its transcribed at in other non-reproductive tissues.

In December 1989 *Nature* ran a news item in the News and Views section 'Thumbs down for zinc finger' and an article from a group based in the United Kingdom which published findings that compromised the linkage between the TDF and the ZFY. The research article was entitled 'Genetic evidence that ZFY is not the testis-determining factor' (Palmer et al. 1989). This article "defined by analysis the genomes of XX males and XY females" and found 4 XX males who lacked ZFY, but did have a DNA from the Y-chromosome which was closer to the pseudoautosomal boundary (Palmer et al. 1989, p.937). The TDF is defined as "induc(ing) the undifferentiated gonads to form testes" (Palmer et al 1989, p.937), and makes no mention of sex determination but rather refers to the 'inducement' of the undifferentiated gonads to form testes by the Y-chromosome. The article goes on to list the

> many features indicating that it is TDF. For example, ZFY encodes a protein with many features of a transcription factor including a domain with multiple

> 'zinc-finger' motifs. Less consistent with ZFY being TDF, however, is the presence of a very similar gene, ZFX, on the X-chromosome, and the presence of a sequence related to ZFY on autosomes in marsupials. (Palmer et al. 1989, p.937).

The article reported the analysis of 'XX males lacking ZFY' and found that in these cases the 'male phenotype' could be "explained by a mutation in a gene 'downstream' of ZFY in the sex-determining hierarchy" (Palmer et al. 1989, p.937). In early 1990 this group also published research comparing the human ZFY and ZFX transcripts (comparison between the Y and X-chromosomes). This may indicate that in 1990 a new TDF requirement was added, that the TDF was only found in males (i.e. on the Y-chromosome).

However, an article in *Human Genetics* entitled 'Genotype-phenotype correlations in XX males and their bearing on current theories of sex determination' (Ferguson-Smith et al. 1990) indicated that there was still uncertainty surrounding the TDF. The authors use the term 'testis determining factors' in the plural, and their results "suggest that the ZFY locus is not essential for male differentiation and is not the primary testis determining factor" (p.198). They go on to note that:

> Male sex determination in sporadic, and familial Y-ve XX males and true hermaphrodites is likely to be the result of mutation in an X-linked TDF gene and its consequent escape from the constraints of X-inactivation. It seems premature to abandon the dosage model of sex determination on the recent evidence that ZFX does not show dosage compensation. (Ferguson-Smith et al. 990, p.198)

A paper published in March 1990 (Palmer et al. 1990) reports the isolation of cDNA[6] clones of the ZFY and its homologue ZFX. They found that the transcripts of these genes are very similar to each other and encode predicted proteins of equal size. Through the use of PCR (polymerase chain reaction) they 'demonstrate' that the expression of ZFY and ZFX occurs in a wide range of adult and foetal human tissues, and that in XX tissue the ZFX gene is also expressed (and so is not inactivated as is most of the second X chromosome which makes up the bar body). This lack of sex-chromosome specificity awarded a fatal blow to the ZFY/ZFX as a candidate for the TDF.

[6] Complementary DNA (cDNA) is DNA synthesized from a mature mRNA template. cDNA is often used to clone eukaryotic genes in prokaryotes.

5.2.3 'The search is on again'

As one review notes in its title, by 1990 '(t)he search for the mammalian testis-determining factor is on again' (Graves 1990), and it was not long before another 'candidate' was suggested. In July 1990 this candidate was proposed in the journal *Nature.* The identity of the TDF was discussed in three letters. Research letters are normally shorter and have a faster 'turn around time' than full length research articles indicating the fast moving pace of this research. The first letter was 'A gene from the human sex-determining region encodes a protein with homology to a conserved DNA-binding motif.' (Sinclair et al. 1990). The abstract opens with the bold statement:

> A search of a 35-kilobase region of the human Y-chromosome necessary for male sex determination has resulted in the identification of a new gene. (Sinclair et al. 1990, p.240)

The letter goes on:

> This gene is conserved and Y-specific among a wide range of mammals, and encodes a testis-specific transcript. It shares homology with the mating-type protein, Mc, from the fission yeast *Schizosaccharomyces pombe* and a conserved DNA-binding motif present in the nuclear high-mobility-group proteins HMG1 and HMG2. This gene has been termed SRY (for sex-determining region Y) and proposed to be a candidate for the elusive testis-determining gene, TDF. (Sinclair et al. 1990, p.240)

The SRY seems a perfect candidate for the TDF, since not only was it evolutionarily conserved, Y-specific among many mammals, and testis-specific but it also, in a strange twist of fate, shared homology with the Mc protein the 'mating type protein'.

The two other articles, ''A gene mapping to the sex-determining region of the mouse Y-chromosome is a member of a novel family of embryonically expressed genes' (Gubbay 1990) and 'Additional deletion in sex-determining region of human Y-chromosome resolves paradox of X,t(Y;22) female' (Page et al. 1990) offer additional support to the claim of the SRY being TDF. This is based on its expression in the developing embryo and the lack of the gene in 'sex-reversal' cases.

The overlap between research activities is illustrated by the publication of an article in October 1990. A German research group published an article in *Human Genetics* entitled 'A ZFY-negative 46,XX true hermaphrodite is positive for the Y pseudoautosomal boundary' (Jager, et al. 1990a). This article was important because it described a human subject who was considered male but did not have the ZFY gene

while having another part of the Y-chromosome. This Y-chromosome DNA was found to be closer to the part of the Y-chromosome that was known to regularly cross over. As the abstract notes, researchers had recently

> reported on seven 46,XX true hermaphrodites and one 45,X mixed gonadal dysgenesis case all presenting with testicular tissue in their gonads in the apparent absence of Y-specific DNA sequences. (Jager et al. 1990a, p.666)

A 'reanalysis' of these cases showed that they did lack the ZFY but that one "46 XX true hermaphrodite" had a DNA sequence which was known to be closer to the Y pseudoautosomal boundary. This case provided further evidence for assigning the TDF locus very close to the pseudoautosomal region on Yp.

While this chapter is primarily based on professional journal articles, I think it is also beneficial to include one article from the magazine *New Scientist* that appeared in early November of 1990. This article was by Mittwoch (1990), who had previously argued that the genetic pursuit of TDF was faulted as it discounted timing. In this article she notes how the current concept is based upon the idea of the single dominant male-determining gene, "whose presence or absence alone determines the sex of an individual" (Mittowch 1990, p.32). She argues that this concept is unlikely to be correct, and does not keep with what was known of embryonic endocrinology and tissue differentiation, which she described as being flexible in the early stages. Her scepticism is noted as she describes the TDF as "the hypothetical male-determining gene on the Y-chromosome" (Mittwoch 1990, p.33).

Mittwoch is one of the first to discuss the problems of 'determining' sex in intersex conditions. The article notes two reasons that a single gene could not be responsible for the TDF. Both of these rely on examples of intersex conditions and the article goes on to argue that the genetic experiments have failed to detail the conditions in their entirety. That is,

> The recent discovery of the SRY gene stems from the study of four patients with XX-chromosomes: three had testes but evidence of incomplete masculinisation, while one had ovotestes and was, therefore, a true hermaphrodite. These people were referred by different authors, as 'four XX males', 'three males and one intersex', 'four sex-reversed individuals'...these findings are compatible with the hypothesis that SRY plays an important role in the development of testis, but in view of the incomplete masculinisation of the patients, the gene cannot by itself direct the development of normal testes. (Mittwoch 1990, p.33)

The author's argument is that the genetic experimenters were misled into assuming that one gene could be responsible by taking testis development as the only factor that determined a male phenotype. In fact the research samples were from individuals who endocrinologists did not consider as true representatives of the male phenotype. The article suggests that true hermaphrodistism in humans is in fact strong evidence against "the view that the sex of an individual is determined by the presence or absence of a single 'testis-determining' gene" (Mittwoch 1990, p.33). Rather, differences in the growth rates of right and left gonads, population differences of intersex conditions and other reproductive characteristics indicates that sex development resembles 'multifactorial inheritance' rather than the relatively straight forward genetics of eye colour. The final argument of this article is that time and growth factors are the major factors determining maleness. From this perspective, the Y-chromosome is inherited as a unit, with an array of genes, to 'guarantee' that the developing gonad grows into a functioning testis, and as such "this arrangement simulates the pattern of Mendelian inheritance of a single dominant gene" ((Mittwoch 1990, p.33).

The 1990 November issue of *Nature* dealt extensively with the issue of TDF and male sex determination. Not only were three articles published, but the journal also included a news item entitled 'What makes a man a man?' by Anne McLaren. The news article offered a chronological review of the search for TDF, portraying it as a 'hunt' that has been both exciting and frustrating (McLaren 1990). As would be expected, the news article makes mention of the history of TDF from snakes, mouse, H-Y antigen to the ZFY, and in keeping with the default female view of binary sex notes that "(i)n mammals, once the gonad has been committed to form a testis, maleness follows" (McLaren 1990, p.216). While the hunt is potentially over, she notes that it could be "the beginning of the genetic analysis of mammalian sex determination" (McLaren 1990, p. 216). The article continues,

> Especially if TDF encodes a DNA-binding protein, we may be at the beginning of a gene-regulatory cascade at least as complex and as fascinating as those that are being unravelled in Drosophila and Caenorhabditis. (McLaren 1990, p.217)

McLaren also notes that there is the possibility that SRY and TDF are neighbouring genes and that conclusive proof is more likely to come from mouse than from human studies. The final note of the article is an afterthought:

> The Y-chromosome is the sole genetic contribution that fathers pass on only to their sons. The present prime candidate for the human Y-borne testis-determining gene shows strong homology to the yeast gene encoding the mating type protein Mc. It is an odd coincidence that 'Mc' in Gaelic denotes "son of". (McLaren 1990, p.217)

This news item indicates the wider interest in the hunt for the TDF. Thus the news item published the suggestion of the SRY to a wider audience than the scientific articles would have achieved on their own.

The first letter published in this issue of *Nature* is entitled, 'Genetic evidence equating SRY and the testis-determining factor' (Berta et al. 1990) which was a collaboration between the Human Molecular Genetics Laboratory in London and the Laboratoire d'Immunogenetique Humaine in the Institut Pasteur in France. This paper concentrated upon the identification of mutations in the SRY gene in 'sex-reversed XY females'. The basis for this research was the view that as TDF was "responsible for initiating male sex determination", and "(if) SRY is TDF, it would be predicted that some sex-reversed XY females, without Y-chromosome deletions, will have suffered mutations in SRY" (Berta et al. 1990, p.448). The paper goes on to describe the results of "tested human XY females and normal XY males for alterations in SRY using the single-strand conformation [SSCP] polymorphism assay and subsequent DNA sequencing" (Berta et al. 1990, p.448). The researchers found a 'de novo' mutation in the SRY gene of one XY female, however a second variant was found in the SRY gene of another XY female, which she shared with her 'normal father'. So while the 'de novo' mutation was compelling evidence that SRY is required for male sex determination, the article still noted the impact of "other genetic or environmental factors" (Berta et al. 1990, p.448). This paper also makes mention of the use of the earlier SSCP assay to compare DNA sequences for the SRY gene. The majority of XY females tested were 'normal', and the researchers conclude by noting that "ether the assay did not detect the band shift" or the mutation "fall(s) outside of the region tested", or "these individuals may have a mutation in another part of the sex-determining pathway" (Berta et al. 1990, p.448). This experiment shows the problem that faced the researchers in proving that the SRY gene is in fact the TDF, because at this early stage of DNA sequencing they could not be wholly sure what caused 'sex-reversal' in the naturally occurring human models.

The second research 'letter' is entitled 'Expression of a candidate sex-determining gene

during mouse testis differentiation' (Koopman et al. 1990). This article explored the tissue expression pattern of the mouse Tdf, finding that it was only expressed in the gonadal tissue. Throughout the articles in this edition sex is interchangeably defined in terms of 'testis', 'male' and 'sex' where sex determination 'hinged' on the testis determining gene as it 'initiates' male development while its 'absence' leads to ovaries and 'female characteristics'. The finding that the expression of the Tdf was confined to gonadal tissues preserved the special status which the gonads had historically been given as the location of sex and supported the idea that sex was determined in the gonads and developed throughout the body.

The final article to deal with the TDF in this issue of *Nature* was a case review by a German group, 'A human XY female with a frame shift mutation in the candidate testis-determining gene SRY' (Jager et al. 1990b). In this article the determination of sex is described in terms of a switch, as a 'primary decision'.

This article goes on to explore the "candidate gene for TDF, termed SRY, which is conserved and specific to the Y-chromosome in all mammals tested" (Jager et al. 1990b, p.452). The article notes that the 'corresponding gene' in the mouse has been deleted in XY mice to create female phenotypes. The rest of the article goes on to describe a case of a human XY who seems to have a whole Y-chromosome, but a mutation in the SRY gene.

> The four-nucleotide deletion occurs in a sequence of SRY encoding a conserved DNA-binding motif and results in a frame shift presumably leading to a non-functional protein. (Jager et al. 1990b, p.452)

The abstract concludes "(t)hese results provide strong evidence for SRY being TDF" (Jager et al. 1990b, p.452). However the case was still not completely solved, as the paper concludes with the paragraph,

> But another gene with the same embryonic expression pattern as SRY could be present in the Y-chromosome 35-kb region that is critical for human sex-determination. Until the existence of such an additional gene has been ruled out, mutations in SRY correlating with sex inversion do not strictly prove that SRY and the 'master' testis-determining locus are the same. (Jager et al. 1990, p.453)

In this November 1990 issue of *Nature* not only was the SRY gene proposed as determining testes, but also as determining sex (i.e. maleness). In March 1991 a review

article in the journal *Biology of Reproduction* asked in its title 'How many genes are involved?' (Bianchi 1991). The abstract goes on to note that the genetic mechanisms of sex determination in mammals "have not yet been clarified" (Bianchi 1991, p.393). It notes that it is now clear that the

> Y-linked zinc finger gene (...) is not the master gene triggering the cascade of events leading to sex determination. (Bianchi 1991, p.393).

The article goes on to note that in the region of interest a new gene has been found as a candidate for the "male-determining factor". The article later describes the experimental value of using samples from humans and laboratory mice as well as vole mice which have "done away with the SRY gene" (Bianchi 1991, p.393). These experiments showed that sex determination and development did not only rely on one gene but that

> testis development depends on the presence of a testis-determining factor gene functioning in cooperation with X-linked and autosomal genes (Bianchi 1991, p.393)

While the traditional view of the female had been that it was a 'default' development this article goes on to propose that ovary development may rely on 'alternative splicing':

> Ovary development would depend on the absence of the testis-determining factor and perhaps on an alternative splicing of the transcripts from autosomal and X-linked genes involved in sex determination (Bianchi 1991, p.393).

Genetic researchers agreed that the SRY/Sry possessed the genetic and biological properties expected of a Y-located testis-determining gene. These articles had exploited natural variations in sex phenotypes in humans (i.e. intersex conditions) and evolutionary links within and between organisms (e.g. drosophila, fish, snakes, birds, mice, etc). Yet this still did not seem to conclusively prove that the SRY gene was the TDF.

5.2.4 Randy: a genomic answer

In May 1991 an article was published in Nature entitled 'Male development of chromosomally female mice transgenic for Sry' (Koopman et al. 1991). The authors sought to test whether Sry was sufficient to induce testis differentiation by creating XX

transgenic mice which carried a copy of the Sry gene. This research was clearly located within the traditional research paradigm of sex determination where genes on the Y-chromosome are seen as having 'a critical role' and the differentiation of testes as 'the central event'. The article goes on to note that "all other differences between the sexes in eutherian mammals are secondary effects due to hormones or factors produced by the gonads" and explicitly states that "sex determination is equivalent to testis determination" (Koopman et al. 1991, p.117).

Out of the 93 mice born (49 males and 44 females), 5 were transgenic for Sry. Of these five, two were XY males but did not transmit the transgene, two were XX phenotypically female and one XX phenotypical male[7]. It is this last XX male, labelled m33.13, which was the main focus of the research paper.

Cookson describes this experiment as "the most satisfactory way possible" of determining if the Sry gene was the Tdf (Cookson 1994, p.94). Indeed, transgenic organisms were a traditional way of 'proving' the function of genes. The article reports that the creation of transgenic mice for Sry/SRY is the "best way to test the function of Sry/SRY and see if they develop as males" (Koopman et al. 1991, p.117). The researchers note that the "fragment containing Sry is sufficient to direct the formation of testis in XX transgenic embryos" and "give rise to full phenotypic sex-reversal in an XX transgenic adult" (Koopman et al. 1991, p.121). The results were not only described in the article, but as Cookson notes, photographs were also used and the results are,

> summarised by a pair of two mice holding on to a bar. The left-hand mouse was the possessor of an X and a Y-chromosome, the right owned two Xs and the transgenic Sry gene. Both mice sported a visible pair of testicles. Sry was indeed the sex-determining gene. (Cookson 1994, p.95).

Goodfellow, in his public lectures, relates how the first draft of the article was rejected because one of the *Nature* reviewers questioned whether an XX mouse with testicles was necessarily male (Cookson 1994). Additional proof of the status of the XX male

[7] The two other XX transgenic mice labelled m32.10 and m33.2, had external female phenotypes and were able to reproduce, yet carried copies of Sry. The researchers note this shows that f741 does not cause sex-reversal by its pure existence in the XX genome. They propose two probable explanations; first that the females are mosaic for the gene, and secondly that the expression of the transgene could be affected by the position at which it integrates. However, as m32.10 has transmitted the gene to female offspring this suggests that it is not a mosaic and the probability is that the gene has inserted in an area which is not transcribed.

was found by proving its 'masculinity' through mating behaviour. According to Cookson, the researchers pointed out that "not only did the transgenic mouse consider itself male, but that the female was obviously of the same opinion" (Cookson 1994, p.95) and the mouse became nicknamed 'Randy'. It was then that the paper was accepted. The outcome was that the TDF became viewed as sex determining, not simply because it led to the formation of the testes, but because it produced the 'male' physical phenotype and behavioural type.

As I noted, although m33.13 was not the only mouse to be born, 'he' was the only mouse to be referred to using human subjective personal pronouns. m33.13 is referred to as 'he', while 'his' XX female littermate is referred to as 'it'. He is also characterised as normal, both in behaviour as "his copulatory behaviour is normal, mating four times in six days" (Koopman et al. 1991, p.119), and physically:

> the only difference between m33.13 and a normal XY sibling was the size of the testis: m33.13 had a testis weight of 17mg (in the range expect for an XX Sxr male), as opposed to 76 mg for an XY control littermate (…) Internal examination of m33.13 revealed a normal male reproductive tract with no signs of hermaphroditism. (Koopman et al. 1991, p.119)

As I will explore in the next chapter, this experiment was not without critics, including some who asked whether a male with smaller than normal testes should be considered male, and whether males need be capable of reproducing. However what was accepted was that if there was one gene that could 'switch' on the male development pathway then it was the SRY gene.

5.3 Summary

In this chapter I have sought to detail the history of the SRY gene from its first suggestion as a testis-determining factor through its location in 1990 and the confirmation of its capacity to create an XX male transgenic mouse. I have based this history on journal articles found by searching in Medline. These articles have been analysed both as historical data points to mark progress as 'historical discoveries' and through the content analysis of high status articles. This gives a particular version of the discovery of the SRY gene that is not concerned with the factual activity of the researchers, but rather with the communication of experiments and results. This version

of events seeks, in part, to tell the story of the SRY gene as it would be visible to a curious general science researcher who seeks to ‘read up on’ the history of the ‘gene for’ sex.

To summarise, in the early stages of research there was not just one paradigm being pursued, but rather many hypothetical views were taken regarding sex determination. During the 1980s the development of DNA probes and greater understanding of intersex conditions led to a number of suggestions for the identity of the TDF. However researchers increasingly viewed the TDF as a ‘master’ gene of sex determination and used human cases of ‘sex-reversal’ to narrow down the gene’s location on the Y-chromosome. Additionally, the research paradigm clearly was based on the assumption that the male development was active while the female was a ‘default’ genetic program and that one ‘master’ gene could switch the developmental program towards both physical and behavioural maleness. This accumulated in the use of transgenic mice to ‘prove’ that the SRY gene was both a Mendelian factor for sex determination and a genetic master gene in control of sex development.

CHAPTER SIX -THE DOSE-SENSITIVE SEX -DETERMINING GENE

"I'm a lady don't you know?"
(Little Britain)

6.1 Introduction

This chapter explores the second gene case study; the DAX-1 gene. This gene was discovered in 1994 and increasingly became viewed as a dose sensitive gene (DSS) involved in female mammalian sex development. This chapter will explore how sex determination and sex development are now conceived after the discovery of the SRY gene as the 'master' gene, as well as investigate why this gene was first described as a 'female' gene.

The search for DSS/DAX-1 is similar to that of TDF/SRY in two ways. It was based on a research paradigm which hypothesised its existence, in this case as a dose sensitive site (DSS), prior to the identification of any related DNA. Also the research was based on intersex conditions with ill-defined phenotypes. However it is also different in occurring after the SRY had been crowned the 'master gene' of sex determination and within the knowledge of the wider genomic context. As noted in Chapter Five and as will be explored further in this chapter, throughout the 1980s and 90s a few researchers did not follow the standard 'male active development' view of sex determination and sex development. These researchers considered the process of sex development to be multi-factorial, including time and gene dosages. The impact of such genomic factors became increasingly incorporated in the construction of DSS/DAX-1.

DSS/DAX-1 is an interesting case study for a number of reasons. Firstly, it has not been widely explored in sociological literature, a notable exception being Joan Fujimura (2006). Secondly, in the early stages DSS was implicated in female ovary development, which challenged the predominant view of the SRY as a 'master gene'. As will become clear, it was assumed that DSS played a role within the SRY-embedded descriptions of sex determination and development, presupposing binary descriptions in which the master gene was a 'genetic' switch between two contrasting and conflicting genetic

pathways. This 'locking in' of the research paradigm led researchers to view other sex genes that caused phenotypic differences as 'female determining genes' that complemented the 'male determining gene'. Thus DAX-1 is an excellent case study to explore constraints which researchers placed upon sex genes after the discovery of SRY, and how sex genetics was explained within a binary concept of sex.

There are two main aims of this chapter. The first is to explore how research into genetic sex determination developed after the definition of SRY as the 'sex gene'. I will show that as DAX-1 became accepted as a sex determining gene (DSS), pressure was placed upon the SRY construction to incorporate an explanation of how the 'master gene' could still play a primary role in sex determination. This in turn necessitated a wider understanding of sex determination as well as a deeper understanding of the relationship between genetic determination of sex and hormonally driven development of sex. The second aim is to highlight the introduction of new metaphors and changing concepts of sex determination and development, beyond those of genetic programs, and including ideas of cooperation and genetic cascades. This chapter, together with that of the SRY gene will lay the foundation for the more detailed analysis of the philosophical and sociological issues in Chapter Seven.

6.2 Analysis of Medline record for DAX-1

This case study, like that of the SRY, is based upon a search of Medline using the keywords 'dose sex determining gene', 'DAX-1', 'NROB1A' and 'sex'. The final search was conducted on the 1st of November 2005 and revealed 120 articles. These provide historical data points, from which the most relevant and important (characterized by the impact factor of the journal) were selected. In keeping with the SRY case study, the aim is to provide the image of DAX-1's history from the viewpoint of an educated science reader of science journals. The analysis of the early history of the DSS and DAX-1 also incorporates some additional articles found by searching Medline with the keywords 'DSS' and 'sex' as well as any earlier work that the authors themselves have drawn upon in their articles to create a history of DSS/DAX-1.

This history was somewhat difficult to construct. Certain issues, such as new metaphors, were introduced and proposed in review articles and it was difficult to

ascertain when they were accepted within the wider community. This reinforces the fact that scientific knowledge does not progress smoothly. For simplicity, I have chosen to introduce the developments when they are first mentioned. It should also be noted that I will not focus on deconstructing the metaphors, but rather leave this to the next chapter.

6.2.1 DSS, ACH and DAX-1 (1994-1998)

Genes are generally considered as DNA sequences which work by either being in the genome and so functioning to produce the trait or by being absence and not producing the trait, however there are types of genes which produce traits depending at the level of their transcription product. These so called dose sensitive genes have a relatively long history within genetics. As early as 1921 researchers found that in *Drosophila* sex was determined by the balance between X-chromosomes and autosomes, irrespective of the Y (Bridges 1921, 1925). By the very end of the 1970's the importance of dose sensitive genes was being explored in a number of different organisms. One of these was *Caenorhabditis elegans*, which researchers reported in 1979 as having 'dose-sensitive sites':

> There exist on the *C. elegans* X-chromosome at least three (and perhaps many more) dose-sensitive sites that act cumulatively in determining sex. (Madl and Herman 1979, p.393).

As I mentioned in Chapter Two, researchers established that the mammalian sex determination system was based on the Y-chromosome, and for mainstream researchers this ruled out dose sensitive sex genes playing a role in human sex determination. However, in the same year as the *C. elegans* paper appeared is the first suggestion that I can find that humans could have dose sensitive genes related to sex. This article reported a family in which 46 XY 'gonadal dysgenesis' (phenotypic females with rudimentary streak gonads) was inherited in an X-linked manner:

> Evidence is presented for the existence of a gene, probably on the X-chromosome, which prevents testis differentiation when present in 46,XY human embryos. Affected 46,XY women are not completely normal because of premature ovarian involution, as a result of which they have "streak gonads" similar to those of 45,X women. (German et al.1978, p.53)

This and other cases (Bernstein et al. 1980; Scherer et al. 1989) indicated to early researchers that a mechanism similar to dose sensitive genes could possibly be

functioning in mammals[8]. It was mentioned in the preceding chapter that in 1987 Chapelle proposed an autosomal dominant testis-determining factor, TDFA.

> TDFA shows somewhat variable expression in XX individuals often causing genital ambiguity or true hermaphrodism. TDFA has no phenotypic effect on XY individuals. It is argued that XX males without presently detectable Y-DNA are caused either by TDF or TDFA. (Chapelle 1987, p.33)

In 1991 the testis-determining factor (TDF) was found, by the creation of a transgenic XX male mouse, to be the SRY gene. Researchers concluded that the mammalian sex system functioned based on the SRY action as a genetic 'switch'. However in the following years papers were published proposing that other genes could be involved in sex determination (Ogata et al. 1992; Fechner et al. 1993; Bardoni et al. 1993). Significant increases in the sensitivity of technology indicted that some 'sex-reversal cases' (XX phenotypic males) did not possess any Y material. This led researchers to believe that this particular intersex condition, Adrenal Hypoplasia Congenital (AHC) later became known as adrenal congenital hypoplasia (ACH), was caused by a gene found on the X-chromosome. The search was on to find this 'dose sensitive sex gene' responsible for 'dose sensitive sex-reversal' (DSS).

DAX-1 is first mentioned in the Medline search in the December 1994 edition of *Nature* which published two articles[9]. While the articles have different lead authors, Françoise Muscatelli and Elena Zanaria, the research groups overlap, indicating that these papers were joint collaborations. Both groups describe using probes to isolate DSS as 'the gene responsible for' AHC (Zanaria et al. 1994).

The link between DSS and AHC is, in a certain respect, reminiscent of the identification of the TDF as the DNA sequence SRY. However, DAX-1 stemmed from a merging of two traits, that of the phenotype of dose sensitive sex reversal and a disease trait, AHC. Sex linked disease phenotypes had been widely used in classical genetics since researchers could use them to deduce which genes 'resided' on which chromosomes, but also were a useful tool for deducing gene orders. In fact one of the articles notes "the following gene order has been deduced: Xpter-ACH-GKD-DMD-cen" (Muscatelli

[8] It should be noted that there were also a number of alternative ideas of how mammalian sex determination occurred including the proposal of a ovary-inducing molecule (Wachtel 1983) as well as the possibility that there were two differential sex-determining pathways, one inducing the ovary, the other the testis (Eicher and Washburn 1986)

[9] Fujimura (2006) has suggested that the first mention of a X linked sex gene occurred in August 1994 when Bardoni published an article in Nature Genetics .

et al. 1994, p.672). This is a reference to the structural order of the DNA sequence in terms of Xpter (a known location on the X-chromosome), ACH (adrenal congenital hypoplasia), GKD (Complex Glycerol Kinase Deficiency), DMC (Duchenne Muscular Dystrophy) and cen (the centromer of the chromosome). This link between physical maps of 'disease phenotypes' and DNA sequences is further spelled out when the paper describes how DAX-1 had been isolated,

> An AHC critical region of 200-500 kilobases has been defined by physical mapping and partially overlaps with a 160-kilobase dosage-sensitive sex (DSS) reversal critical region. The DAX-1 (DSS-AHC critical region on the X, gene 1) gene was isolated and found to encode a new member of the nuclear hormone receptor family. (Muscatelli et al. 1994, p.672).

The label 'DSS-AHC critical region on the X, gene 1' ties both dose sensitive sex-reversal (DSS) and adrenal hypoplasia congenita (AHC). It is likely the researchers designated this gene sequence gene-1 because it was possible that there were more than one DAX gene. AHC not only provided researchers with a defined phenotype, but it also seems to have provided a medical justification. A review of the articles from 1995 illustrated that DAX-1 was seen as offering "exciting experimental possibilities" to develop a "rapid diagnostic approach" for AHC (Guo et al. 1995, p.324). AHC was described as a "medical emergency" in which a "specific diagnosis" "permits anticipatory management" and "prenatal counselling for parents of the affected child and other members of their families" (Guo et al. 1995, p.324)

The second article published in this edition of *Nature* explored the question of what type of protein product was encoded by the new gene. Zanaria et al's use of terms such as 'encode' to describe DNA indicates that the researchers are drawing upon ideas of genes as information and genetic programs.

> DAX-1 encodes a new member of the nuclear hormone receptor superfamily displaying a novel DNA-binding domain. The DAX-1 product acts as a dominant negative regulator of transcription mediated by the retinoic acid receptor. (Zanaria et al. 1994, p.635)

Researchers had found that DAX-1 'encoded' a nuclear hormone receptor, a member of the 'ligand-activated transcription factor' family. These transcription factors require a ligand, in this case a hormone, to carry out their function of regulating gene expression. This was understood to occur in a two step process: first the protein receptor is

'activated' through the binding of the hormone, and then the receptor binds to the DNA and thereby regulates transcription.

These first two articles which introduced DAX-1 to the wider research community not only suggested a linkage between DSS and a gene on the X-chromosome, but by identifying the potential product of DAX-1 as a nuclear hormone receptor provided a possible mechanism for how cells could respond to the wider genomic environment. Nuclear hormones are considered modulators of chromatin organization, in that they regulate the expression of genes and are now known to be involved in a range of diverse biological characteristic of cells such as reproduction, differentiation, development, metabolism and homeostasis. This provided researchers with a potential mechanism by which the 'genetic program' of sex determination could be connect and respond to wider environment. The connection and capacity to respond to the wider environment was important in terms of the 'Randy' experiment indicated in the preceding chapter. Researchers increasingly saw the process of sex determination as connected to both development of a physical sexed morphology and a heterosexual sexuality.

The connection between sex determination and sex is seen in the use of terms such as 'bedfellows' and 'affair' in the title of a review from 1995 in *Trends in Genetic:;* 'New bedfellows in the mammalian sex-determination affair' (Capel 1995). The inclusion and interesting the other 'bedfellows' of Sry would seem to indicate a more complex picture of sex determination. However in the journal articles from 1995 sex determination is still portrayed within quite traditional terms of classical genetics. The SRY was portrayed as *the* sex determining gene with 'sex-reversal' sometimes due to allelic variation.

In the environment of the laboratory researchers were able to breed strains of mice that showed allelic variations. By proposing this type of variation within the mouse model they bypassed the problematic proposition that men exhibited allelic variations of the SRY gene (see Chapter Seven for further discussion). There are a number of interesting issues covered by the journal articles, however due to limits of space I will only explore three of these; the incorporation of a genomic perspective, DSS and DAX-1.

Genomics is difficult to define (see Chapter One), however it typically includes the interaction between DNA sequences and the genomic environment as well as the

relationship between genes and their wider cellular environment. The articles from 1995 demonstrate how genomic factors are becoming apparent and included in these descriptions based not only on new experiments but also the reinterpretation of the 'Randy' experiments. As I showed in Chapter Five, 'Randy' was taken somewhat uncritically as a male and the SRY gene as 'the' sex determining gene. However, the review in 1995 noted,

> the function of Sry is strongly dependent on the level of gene expression in transgenics and deletion mutants. Only about 30% of XX transgenics carrying Sry actually exhibit sex-reversal, and this has been assumed to mean that the timing or level of expression is critical and dependent on the integration site of the gene. (Capel 1995, p.161)

It is clear that there is a growing recognition that gene 'function' depends upon genomic features that could vary considerably between transgenic individuals such as their site of integration. While the low result of 'sex-reversal' is not something unique to the Sry gene[10], the 'Randy' experiment made visible the connection between the SRY gene and genomic geography.

It was noted in the SRY case study that researchers had explored XX/XY cell aggregates and proposed that cell signalling and dose sensitivity possibly played a role in sex determination. Researchers wondered if sex was determined in every cell separately or if it was determined in certain cells and communicated by some means such as cell signalling. The *Trends in Genetics* review mentions this genomic context of genes, indicating that a gene, SOX9, seems to be expressed in a separate cell type in response to the SRY signal in another cell type:

> The only cell type of the developing testis in which the Y-chromosome is required is the Sertoli cell. This must mean that other cell types are recruited into the testis pathway by signals from the pre-Sertoli cell that arises as a result of Sry expression. (Capel 1995, p.162)

The idea that the Y-chromosome (SRY) is only 'required' in one cell type, and that cell-signalling 'recruits' others into the male pathway is "based on the dynamic nature of induction and response during embryogenesis" (p.162). This connection with embryology is also seen in new metaphors being used in the descriptions of sex

[10] The integration site of transgenes was well established to be an important factor in phenotypic expression in all organisms from bacteria to humans.

determination and development including the idea of recruitment and 'development programs'.

> The recruitment of the whole organism on to the development program is accomplished by the export of the hormones produced by the developing testis (Capel 1995, p.162).

The traditional computer program metaphor of genetics is still apparent, however, the introduction of the metaphor of the whole organism being 'recruited' seems to indicate analysis related to sex development and endocrinology. It should be noted that this description is specific to the male, as an active recruitment away from the 'default' female pathway. The new metaphors, in particular the use of 'recruitment', allows a wider number of genes to be involved and it also enables researchers to include indirect genetic factors including genes dosages, inactivation and timing.

Having discussed the genomic descriptions that the Medline record indicated from 1995, I will now move on to the descriptions concerning the DSS. Researchers saw the existence of two separate genetic pathways, male and female but that these were 'competing' and DSS was clearly part of the female pathway. In this quotation DSS is clearly considered female because of two 'facts':

> Two facts imply that this gene lies in the competing female pathway of development: (1) unlike SOX, an increased dose of DSS leads to sex-reversal from male to female; and (2) the absence of DSS is compatible with the male phenotype. (Capel 1995, p.162).

DSS is not thought of as a female SRY – rather researchers suggest that it lies on the female pathway. Two active copies of DSS are seen to override the function of SRY and its role is to inhibit male sex determination. Researchers propose that "SRY may trigger male sex determination by repressing or functionally antagonizing the product of this gene" (Capel 1995, p.161). It would seem that DSS became linked to female development because it seemed to works against the male pathway – not because it actively promoted the female pathway as a female SRY. Indeed the idea of binary sex was still prevalent in the general science community regarding sex genetics, illustrated by the title of a news item, 'Snaring the genes that divide the sexes for mammals' which was published in the September issue of *Science (*Marx 1995).

At this time the DSS was still unidentified and both DAM genes and DAX-1 were thought of as representing DSS candidate genes (Zanaria et al. 1995). Indeed in 1995, only a year after DAX-1 was discovered, not much was understood about the gene and its role within 'primary sex' was not clear. As a review noted, this was probably due to the lack of clarity surrounding "the interrelationship of the pituitary gland, hypothalamus, adrenal glands and gonads during development" (Capel 1995, p.162). However, even at this stage DAX-1 is not seen as a female SRY, but rather is seen as important in the wider formation of the female endocrinological system. This system includes the adrenal glands, two structures in the brain (the pituitary gland and hypothalamus), as well as the gonads, and is sometimes described as the hypothalamic-pituitary-adrenal/gonadal axis. Researchers thought it likely that DAX-1 was involved at 'multiple levels':

> The expression of DAX-1 in these tissues indicates the involvement of DAX-1 in the development of the reproductive system at multiple levels within the hypothalamic-pituitary-adrenal/gonadal axis. (Guo et al. 1995, p.8)

Also connected to this idea of a reproductive axis was the idea that SF-1 and DAX-1 should be viewed as "components of a cascade required for development of steroidogenic tissues" (Guo et al. 1995, p.8). In the past the main metaphor had been 'the testis determination pathway' and the focus had been placed upon a single gene acting as switch. Researchers were increasingly describing this pathway as a 'cascade' in which a multitude of genes were involved.

Why did DSS and DAX-1 not pose more of a challenge to the view of the SRY as a 'master' sex-determining gene? From the Medline record it is apparent that these two genes were being proposed as genetic features of a different system. DAX-1 was proposed as having an evolutionary link to an ancestral, X-chromosome-based, dosage-dependent, sex-determining mechanism. One review article which later commented on the DSS noted how it was thought to be a "residual mechanism' of an 'X-linked dosage mechanism" that would, according to researchers, normally be 'masked' in humans by X inactivation (Capel 1998).

I noted in Chapter Two how our current view of biological sex is characterized as something apparent throughout nature. Marsupial sex determination was seen to constitute a more 'primitive' system and by inference the SRY system was more

'developed', 'stringent' and tightly controlled. As I'm sure the reader recognizes, the idea of 'primitiveness' is problematic, however it also has the additional impact of degrading the DAX-1's role as part of the 'primitive' system so that it does not present a challenge to the SRY gene.

In 1996 the genomic sequence of the human (Guo et al. 1996) and mouse DAX-1 gene were published. The human sequence set a standard for the 'normal' DNA sequence. This was useful in defining diseased phenotypes and during this year there were also numerous identifications of mutations in DAX-1. As the sequencing article noted it was hoped that "single-strand conformational polymorphism analysis" would be useful in "linkage analysis" in families (Guo et al. 1996, p.2481). The sequence of the mouse DAX-1 gene (termed Ache) was also important because it was found to have a 75% overall nucleotide sequence homology to its human homologue). This allowed mice to be used as the main animal model for AHC and hypogonadotropic hypogonadism, again reaffirming the connection between the diseases and DAX-1, as well as the role of DAX-1 in adrenal development and activation of the hypothalamic pituitary-gonadal axis.

The sequencing of the DAX-1 gene also allowed researchers to explore the gene expression profiles. Using the mouse model, researchers detected messenger RNA of DAX-1 in the central nervous system, pituitary, lung, heart, spleen, kidney, and thymus, as well as adrenal and testis, indicating that DAX-1 was important outside of tissues thought of as being involved in sex determination and development (Bae et al. 1996). The importance of the transgenic mice was noted in the final line of the abstract:

> Future studies using mouse models of altered DAX-1 expression will be critical in defining the role of this factor in tissue- and development-specific gene regulation. (Bae et a*l.* 1996, p.3921)

DAX-1 was seen as causing complex endocrine phenotypes (Ikeda et al. 1996) and became further linked to the identity of 'female gene'. In an article published in *Nature Genetics* from April 1996, researchers explored the expression of Dax-1 in the ovary of mice, noting:

> Expression was detected in the first stages of gonadal and adrenal differentiation and in the developing hypothalamus. Moreover, Dax1 expression is down-regulated coincident with overt differentiation in the testis, but persists in the developing ovary. (Swain et al. 1996, p.404)

Later in the year researchers demonstrated that DAX-1 and SF-1 were expressed and regulated in Sertoli cells of rat testes during spermatogenesis, the first indication that this gene was involved in testis formation (Tamai et al. 1996). There was an increasing emphasis upon the temporal nature of gene expression, supported by the metaphor of 'cascades' used to describe gonad differentiation in the first line of the abstract as "dependent upon a cascade of molecular and morphological events" (Majdic and Saunders 1996, 3586). This metaphor incorporated the increased understandings that DAX-1 and SF-1 had different patterns of expression, and therefore DAX-1 may "play a separate or complementary role to that of SF-1 in the modulation of testicular gene expression and differentiation" (Majdic and Saunders 1996, 3586). The idea of 'modulation' of tissue formation seems to indicate a new way of thinking of how genes interact to form tissues. The idea of 'cascades' relies on interlinking gene pathways. In another article the authors go on to explain:

> This down-regulation requires transcription and de novo protein synthesis. Taken together, these data indicate that DAX-1 expression in Sertoli cells may influence the development of spermatogenic cells in response to steroid and pituitary hormones. (Tamai et al. 1996, p.1561)

This quotation, hesitant as it is, indicates that researchers thought DAX-1 might serve a role in the male phenotype. This role was not as a switch or as a gene involved in developing 'primary sex', but rather as a gene that responds to hormones secreted in the blood at later stages of development.

In 1997 the research articles found by Medline covered an increasing range of subjects including intersexuality in pigs (Lahbib-Mansais et al. 1997), ontogenesis of steroidogenic tissue (Morohashi 1997), and evolution of sex determination in mammals (Pask et al. 1997). During this year there were further developments within the research relating to reproductive axis and organ formation as well as the metaphors used to describe the action of genes. DAX-1 was seen as connected to female development through its association with ovary development for two reasons: expression was "down-regulated" in the "differentiating testis", and mutations in DAX-1 in humans showed that "this gene is not necessary for testis development" (Swain and Lovell-Badge 1997, p.46).

> The properties of the DAX-1 gene suggest that it is important in ovary determination and might therefore be antagonistic to the action of the Sry gene (Swain and Lovell-Badge 1997, p.46).

The use of the term 'antagonistic' to explore the relationship between DAX-1 and Sry indicates the strength of the idea of opposite sexes.

In these opening years DAX-1 became increasingly seen as an important 'female' gene. In the years after the Randy experiments DAX-1 was identified through the convergence of the quests for DSS and ACH, and it was understood to possibly be a dose sensitive gene and responsible for a 'lethal' intersex condition. Unlike the SRY gene its function was not considered only to be linked to one tissue, but rather to apply within a wider range of tissues including those within the 'reproductive axis'. The descriptions of sex determination and development began to introduce new metaphors such as 'recruitment', 'permit', and 'cascades' and include a wider range of tissues, not just that of the gonads. One example of the change incorporating a wider set of tissues as well as shifting from seeing sex as determined at a single time period is seen in an article entitled, 'Active hypothalamic-pituitary-gonadal axis in an infant with X-linked adrenal hypoplasia congenita.' The child's genome reveals that

> the DAX-1 mutation does allow a normal reproductive axis at birth. We speculate that some time between infancy and puberty this mutation in the DAX-1 gene leads to an inability to activate the reproductive axis from its childhood suppression; thus puberty will not develop in this infant. (Takahashi et al. 1997, p. 485).

This article indicates that a wider view is being taken of sex determination linked to how it is developed. Sex determination was seen as the determination of the child's potential to mature into a male or female, however this potential is suppressed until puberty. This indicates a change from seeing sex as purely determined by the presence or absence of the testis, towards seeing sex as a feature of the body which changes with time and development.

6.3.2 The rise and fall of the female sex determining gene (1998-2002)

During 1998 the research progressed rapidly into both DAX-1 and DSS genes. Researchers began to explore the effect of mutations in Dax-1 on subjects who did not

show signs of 'sex-reversal'. An article published in *Nature*, entitled 'Dax1 antagonizes Sry action in mammalian sex determination', reported that

> XY mice carrying extra copies of mouse Dax1 as a transgene show delayed testis development when the gene is expressed at high levels, but do not normally show sex-reversal. (Swain et al. 1998, p.761)

In this article DAX-1 is clearly seen as responsible for DSS:

> These results show that DAX-1 is largely, if not solely, responsible for dosage-sensitive sex-reversal and provide a model for early events in mammalian sex determination, when precise levels and timing of gene expression are critical. (Swain et al. 1998, p.761)

I have mentioned how timing was thought of as critical to the functioning of the SRY gene. Now it would seem that the research paradigm was beginning to integrate the factors both of time and of dosage. An article in May of the same year, entitled 'Nuclear receptor DAX-1 recruits nuclear receptor corepressor N-CoR to steroidogenic factor 1', strengthens this view (Crawford et al. 1998). The article uses metaphors of 'recruitment' and ideas of 'interaction' between various genetic elements including DAX-1, N-CoR, SF-1, RevErb, and SMRT.

There was also increased interest in the gene product of DAX-1. The quote below shows the importance of this product in creating a property of the gene:

> Therefore, DAX-1 can serve as an adapter molecule that recruits nuclear receptor corepressors to DNA-bound nuclear receptors like SF-1, thereby extending the range of corepressor action. (Crawford et al. 1998, p.2949)

Similar terms are used in the article, 'Wilms' tumor 1 and Dax-1 modulate the orphan nuclear receptor SF-1 in sex-specific gene expression', which uses the phrases 'associate', 'synergize', 'antagonizes synergy', 'oppose':

> Additionally, the X-linked, candidate dosage-sensitive sex-reversal gene, Dax-1, antagonizes synergy between SF-1 and WT1, most likely through a direct interaction with SF-1. We propose that WT1 and Dax-1 functionally oppose each other in testis development by modulating SF-1-mediated transactivation. (Nachtigal et al. 1998, p.445)

This description should be viewed within the context of DAX-1 being conceptualized as a 'female' gene, which opposes and replaces the male pathway. The extent to which DAX-1 was seen as a female gene is seen in a review from September published in

Bioessays, entitled 'Mammalian sex determination: joining pieces of the genetic puzzle'. The author relates how recent experiments by Swain et al. (1998)

> basically confirm the previously proposed hypothesis that SRY acts by inhibiting the action of DSS/DAX1, which is a repressor of genes of the male pathway. (Jimenez and Burgos 1998, p.696-9)

In a review entitled, '*Mammalian sex determination; from gonads to brain'*, there is mention of a 'regulatory cascade hypothesis for mammalian sex determination'. In this system the pathways are regulated through more than one switch:

> [that] SRY represses a negative regulator of male development, was recently supported by observation of mice that expressed a DAX1 transgene and developed as XY sex-reversed females. (Vilain and McCabe 1998, p.74)

DAX-1 is linked with female development, not because its product was involved in actively developing the female phenotype, but rather because it is a 'negative regulator' of the potential for male development, which when mutated in a XY human genome created 'sex-reversed females'.

Researchers were also exploring the possibility that other genes could function as a DSS and took a wider view of the potential for multiple genes to play a considerable role in sex determination and development. The wider role of different tissues other than the gonads was explored:

> the role of some sex-determining genes, such as DAX1 and SF1, in the development of the entire reproductive axis, a functionally integrated endocrine axis, leads to a new concept. Normal sexual development may result from the functional and developmental integration of a number of different genes that play roles in sex determination, sex differentiation, and sexual behaviour. (Vilain and McCabe 1998, p.74)

It would seem that DAX-1 has become accepted as a 'sex-determining gene' and this is the earliest reference I have found in which SRY or DAX-1 researchers propose that a connection exists between sex determination, sex differentiation and sexual behaviour. Clearly from the experiments with Randy there was the assumption that 'sex' involved all three. However, the quotation here indicates that researchers were now thinking of sex in terms not of being defined by a testis or a particular tissue, but rather as a functionally integrated system. This indicates the extent to which the holistic view of the development of the human body was taking hold.

At the end of 1998, in December, *Nature Genetics* published an article entitled 'Role of Ahch in gonadal development and gametogenesis' (Yu et al. 1998). In this article Ahch (the mouse version of the DAX-1 gene) is presented, not as a gene playing a role in the female pathway, but rather as 'an ovarian determining gene'. In fact I have not found another reference to DAX-1 as an ovary determining gene prior to this article. The designation of this gene as 'an ovarian determining gene' gives the gene a valued status, similar to the TDF/SRY. However the article seems to set this gene up to knock it down:

> although Ahch [the mouse homolog of human DAX-1] has been postulated to function as an ovarian determining gene, the loss of Ahch function in females does not affect ovarian development or fertility. Ahch is instead essential for the maintenance of spermatogenesis. (Yu et al. 1998, p.353)

The article goes on to say:

> Lack of Ahch causes progressive degeneration of the testicular germinal epithelium independent of abnormalities in gonadotropin and testosterone production and results in male sterility. Ahch is thus not an ovarian determining gene, but rather has a critical role in spermatogenis. (Yu et al. 1998, p.353)

The findings being reported in this article suggest that the lack of Ahch, and thus DAX-1, results in male sterility. Male sterility had been an issue in the Randy experiment where it was the ownership of testes and male reproductive behaviour that had been used to argue that Randy was male. In this article Ahch/DAX-1 is seen as having a 'critical role' in maintaining the male pathway in the human body. The idea of a gene being necessary for maintaining sex is in keeping with viewing the male body as the active development away from the female default system. Yet the male phenotype is being further refined to incorporate the prerequisite for reproduction. Thus the testes not only must produce 'male' hormones but also male reproductive cells. It is not enough to be born male (with testes); the male body must also be capable of reproducing as an adult.

Researchers were increasingly reporting the interaction of DAX-1 with other genes (including SRY, SOX9, Midkine CYP17). One example of this was a paper published in *Mechanism of Development,* which compared the expression profile of SRY and DAX-1. The article reports:

> low-level DAX1 expression predates peak SRY expression by at least 10 days, and persists in Sertoli cells throughout the entire sex determination period. In dosage sensitive sex-reversal, the anti-testis properties of DAX1 over-expression could act prior to the peak effects of SRY and continue during the period of SOX9 expression. (Hanley 2000, p.403)

While DAX-1 was not considered critical to spermatogenesis, it was understood that its product would be likely to have different impacts depending on the stage of development. This interest in expression profiles led another research group to explore large-scale screening. In an article, simply entitled '*Large-scale screen for genes involved in gonad development',* the researchers found 72 genes which, "may play a role in gonad or sex duct development and /or sex determination" (Wertz and Herrmann 2000, p.51).

That as many as 72 genes were involved in gonad development was not a surprise. It had been long assumed that the 'genetic program' of sex development and determination was complex. In this mass screening there was no detail regarding the level of involvement. Rather it is interesting to note the change in research methods, from a focus on the static image of genes being present or not, towards exploring the expression within space and time. The reader would be correct in noting this development as in line with the birth of 'proteomics' which explores the products of genes.

As well as this large scale project, there was continued growth in research which related to DAX1 – not only the sex determination work which held DAX1 and SRY at its centre, but also expression profiles of other genes (i.e. WNT-1), of the enocrinological glands, biochemical research, endocrinological research and modelling. This variety of research topics is likely to have been one of the reasons why in 2000 DAX-1 underwent a re-naming, noted as the orphan receptor DAX-1 (NROB1) (Zhang, et al. 2000) to create a separation between the DNA sequence now being referred to as NROB1 and the 'gene' product DAX-1. This is in keeping with the growing genomic importance of the role of messenger RNA's and proteins (Morohashi et al. 2000). It is clear that at this stage DAX-1 is starting to be constructed away from association with disease conditions and dose sex sensitivity, and relocated within the family of genes which code for nuclear receptors.

In 2001 researchers found that DAX-1 also impacted the transcription of WNT-4. In 1999 this gene had been the focus of news reports that researchers had found a 'female' gene. Indeed the New Scientist published an article entitled, '*There's more to being a woman than not being a man*' stating "…scientists have now found a gene that needs to be switched on for female sexual organs to develop normally" (Knight 1999). In 2001 the relationship between DAX-1 and WNT-4 became clearer and researchers noted that DAX-1 up-regulated WNT-4 signalling. The researchers describe this as follows:

> Wnt-4, a member of the Wnt family of locally acting secreted growth factors, is the first signalling molecule shown to influence the sex-determination cascade. In mice, a targeted deletion of Wnt-4 causes the masculinization of XX pups. Therefore, WNT-4, the human homologue of murine Wnt-4, is a strong candidate gene for sex-reversal phenotypes in humans. (Jordan et al. 2001, p.1102).

The idea of 'masculinization' in this context shows the extent to which the binary idea of sex is still present in the research. The research articles describe only one sex-determination cascade, but with two possible pathways. While the pathways share genes this is not portrayed as overlapping between male and female development, but rather these shared genes are seen as providing non-specialised roles. Male and female development are portrayed as being in conflict based on the action of the specialised genes (i.e. WNT-4 and DAX-1) playing both a role in female development and the prevention of testis formation.

> Thus WNT-4, a novel sex-determining gene, and DAX-1 play a concerted role in both the control of female development and the prevention of testis formation. (Jordan et al. 2001, p.1102)

Till this point sex determination had been viewed as having two active pathways –one male the other female. SRY was the genetic switch at the top, the deciding factor to cell 'fate'. DAX-1 was a negative repressor of SRY. As the researchers note, 'These observations suggest that mammalian sex determination is sensitive to dosage, at multiple steps in its pathway (Jordan et al. 2001, p.1102). With the discovery that WNT-4 was a signalling molecule researchers began to glimpse at how 'cell fate' is influenced by the neighbouring cells. Researchers also became increasingly concerned with the development of the testis not only in terms of the Sertoli cells but the requirement for DAX-1 in other somatic cells for normal testicular development (Jeffs 2001).

In December 2001 the final nail in the coffin of DAX-1 as a 'female' gene came in the form of an article entitled 'RY interacts with and negatively regulates androgen receptor transcriptional activity'. The abstract summarises the findings of the study as

> indicat[ing] that interactions between the AR, SRY, and DAX1 contribute to normal male development and function and suggest a general role for protein-protein interactions between HMG [high mobility group] box protein and steroid hormone receptor in regulating tissue-specific gene expression. (Yuan et al. 2001, p.4647)

The old metaphor of the 'genetic program' was based on the idea of genes 'interacting' in a hierarchal manner and while the program could respond to earlier outputs researchers incorporated new metaphors of the interactions between genes as 'contributing' to sex development, and involving interactions at the level of gene products. The research articles show how the research was increasingly being explored in terms of a richer molecular biology, encompassing the relation between genes, their products and their context in the living cell.

6.3.3 Dynamic patterns of gene expression (2002-2003)

Researchers increasingly researched DAX-1 or rather NROB1, in terms of being a 'male' gene required for 'normal male development' and there was an increased research into non-genetic features involved in DAX-1 such as the timing of gene expression. In an article from April 2002 researchers published the first *in vivo* study of the regulation of DAX-1 expression, in which they stated that "The expression of the gene in the gonad follows a dynamic pattern in time and place in the embryo and the adult" (Hoyle et al. 2002, p.747).

While this may indicate that the roles of genes in sex determination and development are being viewed as active, it should be noted, however, that this is in reference to the male development. The following quote shows how NROB1 was 'active in maintenance' in the male:

> Ironically, NROB1 (formerly DAX1), once presented as the paradigm of genes responsible for ovarian development and function, is probably one of these male fertility factors and is active in the maintenance of spermatogenesis. (Vaiman 2002, p.224).

Another article shows that DAX-1 has a 'crucial role' in 'regulation' (March 2003 *Development*):

> we conclude that Dax1 plays a crucial role in testis differentiation by regulating the development of peritubular myoid cells and the formation of intact testis cords. (Meeks 2003a, p.1029)

Researchers were increasingly concerned with the functioning of NROB1 in terms of producing a protein product. DAX-1 was found to 'shuttle' between the cytoplasm and the nucleus with, "particular relevance for the modulation of androgen-dependent gene transcription in the male reproductive system" (Holter et al. 2002, p.515).

In May *Nature Genetics* published the final confirmation in a paper simply entitled 'Dax1 is required for testis determination' and the abstract is equally simple, two sentences long:

> The orphan nuclear receptor, Dax1, was originally proposed to act as an 'anti-testis' factor. We find, however, that NrOb1 (also called Dax1 and Ahch, which encodes Dax1) is in fact required for testis differentiation. (Meeks et al. 2003b, p.32)

This article is one of the few crucial dates that can be marked in the history of DAX-1's 'discovery', and as such I will explore it in detail[11].

In the article the researchers note that DAX-1 was initially proposed as a 'dosage-sensitive ovarian determining gene'. However, experiments with mice had shown that mutations in NrOb1 did not prevent ovarian development. For the researchers this raised a question as to how NROB1 should be conceived, as a 'pro-testis' or an 'anti-testis' gene. In the next section I will explore further the link between seeing an 'ovarian determining gene' and describing its action as 'anti-testis'. In regard to the intent of the researchers they summarized it as follows:

> We tested whether NrOb1 is a 'pro-testis' or an 'anti-testis' gene by crossing NrOb1-deleted mice to *Mus domesticus poschiavnus*, a strain known to be susceptible to XY sex-reversal because of an altered Sry allele. (Meeks et al. 2003b, p.32)

As with Randy this is a form of genomic testing, creating living experiments as opposed to observation of natural phenotypes. Also, as with Randy, the researchers use

[11] (The paper is available through Nature's website: http://www.nature.com/ng/journal/v34/n1/full/ng1141.html.)

photographs to demonstrate the 'truth' of the results. In the SRY experiment the lab animals were illustrated by two mice, Randy and one of 'his' female litter mates. Both were hanging from sticks showing their genitals, the reproductive tracts and histology of ovaries. In this article, which explored DAX-1, there are three mice hanging in a similar way.

In this experiment, unlike the creation of the transgenic Sry mouse, all the animals are reported un-named but labelled in relation to their genomic state (see figure 6.1). The two controls are an XY positive – a 'natural' male of the strain known to be susceptible to XY sex-reversal and another labelled XX –female. The final mouse has a mutation in its DAX-1 gene (Nrob1-/Y XY positive) and is intended to show whether DAX-1 is a 'pro-testis' or 'anti-testis' gene. The first row of the photos shows the complete living organism, the phenotype of the body and the external reproductive organs. As the caption notes the mutant mouse has external genitalia that 'were identical to those of XX siblings'.

The second row of pictures – labelled d, e and f show the reproductive organs, extracted from the context of the whole body and lying on blue tissue. At this level the effect of DAX-1 is taken as "completely sex-reversed". The third row of pictures explores a third level, that of the cells of the gonads. At this level it is noted mutant mice "showed follicles with irregular boarders and multiple oocytes but no corpus luteum." (Meeks et al. 2003b, p.32)

Figure 6.1. Reporting of Dax-1 in Nature (Meeks et al. 2003b, p.33)

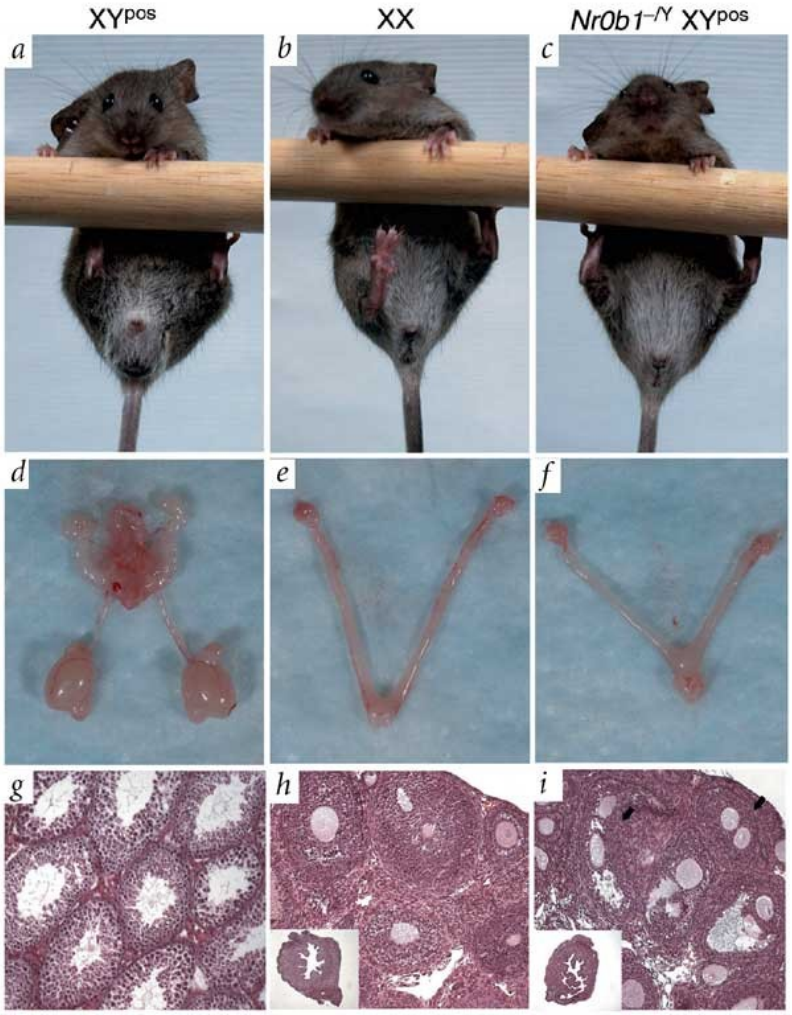


Figure 1. XYposNr0b1-/Y mice were indistinguishable from XX mice. a–c, External genitalia of XYpos Nr0b1-/Y mice at 7 wk (c) were identical to those of XX siblings (b). d–f, Reproductive tracts of XYpos Nr0b1-/Y mice at 7 wk were completely sex-reversed. g–i, Gonadal histology of ovaries from XYpos Nr0b1-/Y mice showed follicles with irregular borders and multiple oocytes (arrows, i) but no corpus luteum.

The corpus luteum is essential for establishing and maintaining pregnancy in females. In the ovary, the corpus luteum secretes estrogens and progesterone, which are steroid hormones responsible for the thickening of the endometrium and its development and maintenance, respectively. The article concludes that these results,

> indicate that Dax1 deficiency disrupts the developmental events that occur between expression of Sry and Sox9. (Meeks et al. 2003b, p.32)

Rather than DAX-1 switching on or off Sry, Dax-1 deficiency 'disrupts' the chain of developmental events. The disruption of these events leads the body to progress down the 'default female pathway'. Sex development had been seen as a somewhat fluid process, however the term 'developmental events' gives the reader an idea of stages of development. This fits well with how genes are thought of as acting and the article goes on to note:

> Dax1 is required at several points in embryonic testis development. We conclude that the effects of Dax1 are highly dosage sensitive. Transgenic over-expression of Dax1 causes varying degrees of gonadal dysgenesis and male-to-female sex-reversal at the highest dose, perhaps by inhibiting key pathways mediated by steroidogenic factors 1 (...) suggesting that Sry and Dax1 are both required for normal testis determination. (Meeks et al. 2003b, p.32)

The use of the term 'required' fits with the traditional idea of sex determination genes as being necessary and sufficient for activating male determination. Again there is an emphasis on time and dosage sensitivity, however according to Meeks et al (2003) both Sry and Dax1 are required for normal testis determination. It is an open question whether 'normal testis determination' is required for the male phenotype to be attributed to a mouse (or human).

A second issue this article explores is the extent to which the gonads with the mutation developed as ovaries (as illustrated in the figure 6.1). This clearly shows the extent to which DAX-1 is seen as a second sex determination gene, contrary to the traditional view. Again the three vertical rows relate to the three different mice –XY, XX and mutant. The five horizontal rows are stained to show up different features of specialized gonad cells (the numbers at the right hand side relate to the day on which the staining was done, e.g. 13.5 is midday on day 13). The final row is taken up by a graph that shows the level of Sry expression in the male control and the mutant. The last figure, labelled q, shows the pathway that the researchers are proposing.

Figure 6.2. Reporting of cellular data related to Dax-1 in *Nature* (Meeks et al. 2003b, p.32)

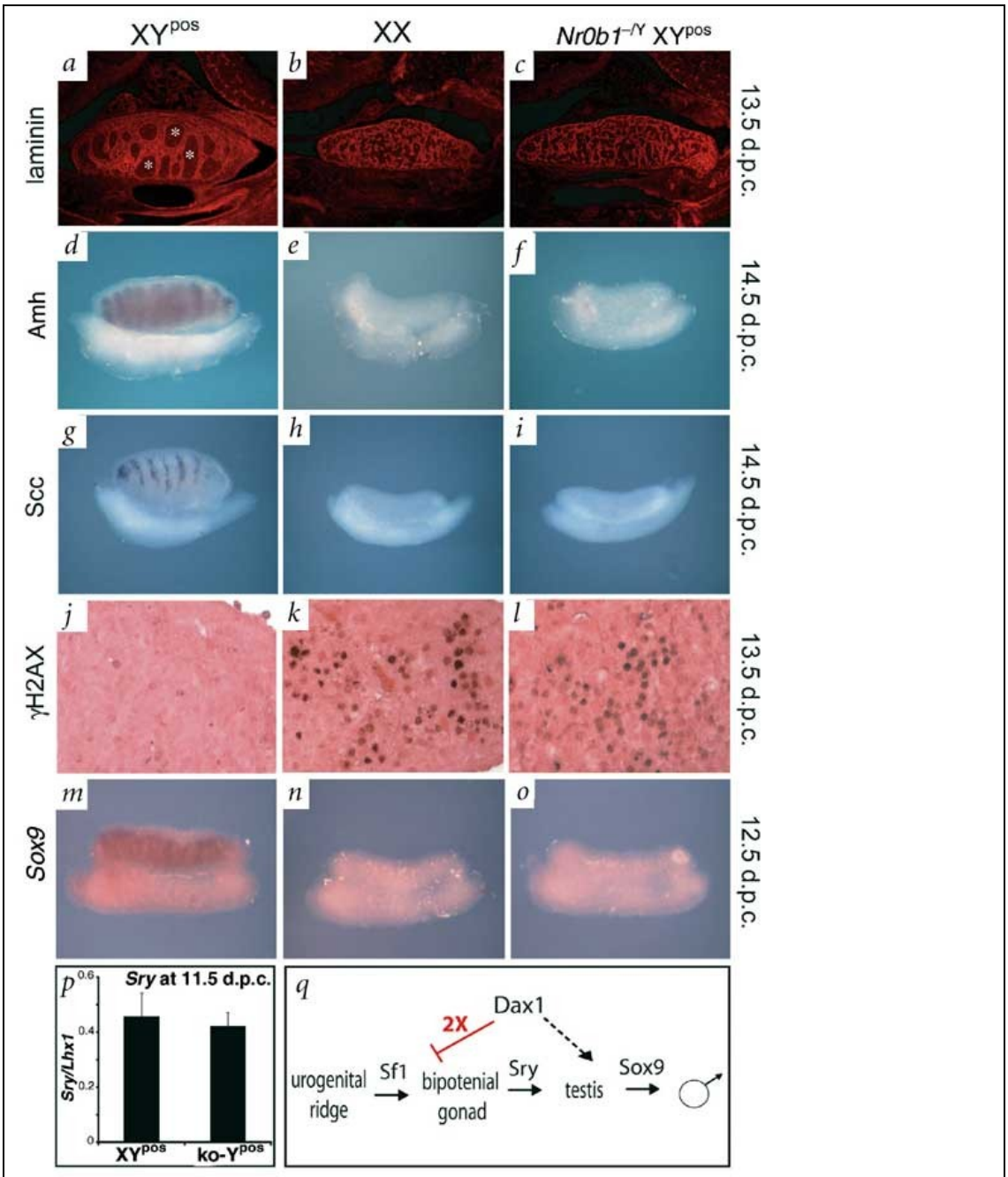


Figure 2. XYposNr0b1-/Y gonads developed as ovaries. No testis cords (asterisks) were identifiable by laminin staining (1,200; Sigma) in gonads of XYpos Nr0b1-/Y mice at 13.5 d.p.c. (a–c), and no Sertoli or Leydig cells were present (d–i) at 14.5 d.p.c. In the absence of testis determination, germ cells (stained with an antibody against H2AX, 1,100; Upstate Biotechnology) entered meiosis at 13.5 d.p.c. in gonads of XX Nr0b1-/Y and XYpos Nr0b1-/Y mice (j–l). Expression of Sox9 was absent in gonads of XX Nr0b1+/+ and XYpos Nr0b1-/Y mice at 12.5 d.p.c. by in situ hybridization (m–o). Sry expression was equivalent between XYpos Nr0b1-/Y (ko Ypos) and XYpos gonads at 11.5 d.p.c. (primer sequences for Sry and Lhx1 are described in ref. 11; (p). This suggests that Dax1 is required to maintain or induce Sry-mediated testis development (q).

The caption notes the ‘absence of testis determination’ again referring to the view of the ‘default female’. Similar is the linear view of male determination seen in figure q. One of the strongest characteristics of the SRY gene has been that it is a ‘genetic switch’ for sex determination. In 2003 a review article was published entitled ‘Battle of the sexes:

new insights into genetic pathways of gonad development' (Jameson et al. 2003). The first line of the abstract opens:

> Sex determination is governed by a series of genetic switches that influence cell fate and differentiation during critical periods of gonadal development. (Jameson et al. 2003, p.51).

This article shows how both the multiple genes involved and time have been incorporated into the paradigm of sex determination and development.

Interestingly in September 2003 an article was published in *Molecular Genetics and Metabolism,* which noted that phenotypes of patients and animal models are complex and not always in agreement, while cell lines have proved difficult to interpret (Clipsham et al. 2003). With these restrictions the article stresses study of a number of genes as 'network partners' in development of the hypothalamic-pituitary-adrenal/gonadal' axis (HPAG) and a 'network analysis'. This raises a question as to the link between phenotypes and genotypes, which will be explored in the next chapter.

6.2.4 Not one, but two genes (2004-2005)

This chapter has shown how DAX-1 research has progressed through new metaphors and ways of seeing the gene's function. These changes came from the incorporation of more than one sex determining gene, and questions of gene dosages and timing. In this last section the issue of timing is revisited.

In April 2004 an article appeared entitled, 'Sex determination: a 'window' of DAX1 activity' reporting that DAX-1 functions as a 'pro-testis' gene and,

> [t]herefore, perhaps DAX1/Dax1 acts within a 'window' of activity, outside of which testis formation does not occur. Here, we discuss the function and possible mechanisms of DAX1 action in male gonadogenesis. (Ludbrook and Harley 2004, p.116)

The idea of DAX-1 working within a 'window of opportunity' exemplifies the idea of 'developmental events' mentioned earlier.

Researchers were also exploring the activity of DAX-1 in wider tissue systems. They suggested that it may have a broader function as a negative co-regulator of oestrogen

receptor, liver receptor homologue-1, androgen receptor and progesterone receptor, each by distinct repression mechanisms.

A surprise was in store in December 2004 when researchers found that the mRNA from the DNA sequence of DAX-1 was alternatively cut to produce two different forms of protein. As an article in *Genetic Metabolism* reported:

> We confirmed the presence of an alternatively spliced form of NR0B1, which we will refer to as NR0B1A, by reverse transcriptase-polymerase chain reaction (RT-PCR), and will refer to the deduced protein isoform as DAX1A. Sequencing of the NR0B1A cDNA revealed slight differences from the recently described splice form, DAX1alpha. (Ho et al. 2004, p.330)

The researchers detail the differences between the two forms and note that NR0B1A is detected in a number of tissues including the adrenal gland, testis, ovary, and pancreas. As the authors noted, the finding that the DNA sequence identified as DAX-1 was in fact two genes – as it gave two gene products – necessitated reinterpretation of many previous experiments involving expression and knockout of NROB1 and DAX1[12].

The connection that DAX-1 had in the beginning of its history with disease is also present in research in 2004. In December 2004 an article in the *Journal of Paediatric Surgery* explored the transplantation of cells from adrenal glands. It was noted that "ex vivo gene transfer followed by adrenal cortical cell transplantation may lead to curative therapy for patients with adrenal insufficiency" (Dunn et al. 2004, p.1856)

DAX-1 was also increasingly seen in the context of a whole host of genes including Sox8, Sf1, Gata4, Wt1, Fog2 and Sox9. The main developments were related to increasing in vivo understanding of the interaction between DAX1 and SF1. While researchers had explored the interactions *in vitro*, the article 'Nuclear receptors Sf1 and Dax1 function cooperatively to mediate somatic cell differentiation during testis development' reported that *in vivo* studies indicated that:

> although Sf1 and Dax1 function as transcriptional antagonists for many target genes in vitro, they act independently or in cooperation in vivo during male gonadal development. (Parks et al. 2005, p.2415)

[12] As noted in Chapter Two genes can be defined in different ways, based on DNA sequence, mRNA product or on the basis of its protein product. There are cases where the same DNA sequence can produce different mRNAs and thus different protein products. See Chapter Seven for further discussion.

In keeping with the idea of a 'genetic cascade' researchers also found the differentiation of Sertoli cells as depending on the coordinated expression of Dax2, Sry and another gene, Tda1 (Bouma et al. 2004) Thus the metaphors of 'coordination' and 'cooperation' between genes and gene projects had begun to take a leading role.

The final article I will explore in this chapter is from September 2005, published in *Molecular Genetics and Metabolism*. It illustrates quite clearly the long road that DAX-1 had travelled, from its start as DSS, moving through disease conditions and finally being referred to as NROB1. The article notes how the NROB1's protein, DAX-1 is

> responsible for the establishment and maintenance of the steroidogenic axis of development, and that there were alternative spliced variations in humans which had a role in maintenance of embryonic stem cell pluripotency. (Ho et al. 2004, p.330)

The research focus has moved towards molecular cellular biology, exploring the establishment and maintenance of cellular processes. At this level of molecular biology the researchers are concerned with the 'steroidogenic axis of development' indicating the integration of genetics with endocrinology and embryology. Finally it would seem that genetic sex determination and endocrinological sex development as research areas had merged once again.

6.3 Conclusion

Once the SRY gene had been identified as the TDF there was a clear assumption of the mammalian sex determination pathway being governed by a 'master gene' which was the only gene 'necessary and sufficient' for sex determination. While the mechanism of the SRY and the sex determination pathway were still unknown, when DAX-1 was discovered it was announced to be a female gene. The discovery of this gene increased interest in the genomic and non-genetic factors which possibly had roles in mammalian sex determination, especially with regard to the DSS. Research into the DSS was framed within traditional genetics seeking to determine the locus of DSS. When DAX-1 became accepted as a sex determining gene, pressure was placed upon the SRY construction to incorporate an explanation of how the 'master gene' could still play a primary role in sex determination. This in turn necessitated a wider understanding of sex determination as well as a deeper understanding of the relationship between genetic

determination of sex and hormonally mediated sex development. In the next chapter I will explore what can be learned from the case studies of the SRY and DAX-1 gene in terms of gene concepts and the metaphors used.

CHAPTER SEVEN - ANALYSING GENETIC SEX

> "Anyone who believes that the laws of physics are mere social conventions is invited to try transgressing those conventions from the windows of my apartment. (I live on the twenty-first floor)."
>
> (Alan Sokal 1996, p.62)

7.1 Introduction

The idea of researchers 'discovering' a gene portrays them as involved in a quest to unlock nature's secrets (Petersen 2001). The rhetoric used in these discourses frames the activity of researchers, whether wet-lab scientists or bioinformaticians, as 21st century detectives and explorers. As Ron Curtis has argued, this serves to represent science and scientific discovery as 'Baconian', emphasising cooperation between researchers and the conquering of nature rather than presenting science as a competitive, even adversarial process (Curtis 1994). These representations of science characterize genetic research as linear, as if researchers hypothesise the existence of a gene and then seek to locate it within the genome. However, as the two previous gene case studies illustrated, genetic research often involves both cooperation and conflict between researchers and their various ideas of what the gene is and how it functions. The two case studies also indicated that the research target evolves and develops as the research progresses.

Research on the two genes, SRY and DAX-1, has also been recently explored by Joan Fujimura (2006). Her analysis centres on what she terms the socialmaterial nature of sex/gender, offering alternative readings of the research data. This chapter will add to Fujimura's and other feminists' discussions by setting the two gene case studies in the wider context of the work undertaken in the philosophy and history of biology regarding gene concepts. The portrayal of the ZFY/TDF as the 'gene for sex' has been criticised by Judith Butler (1990) who has argued that the search for the gene for sex was inherently constrained by the binary paradigm, and gendered from the start. While Chapters Five and Six indicated this indeed was the case, spending time exploring the wider context of genetic research, including that of gene concepts, will add richness to this account and set the stage for the discussion in Chapter Nine regarding the five factors of biological sex which I argued were key to our current concept of genetic sex.

7.2 What are genes?

One of the main issues regarding genes is the question of what they are, unit of inheritance or of development, material object or information. This chapter makes clear that gene concepts are historically and culturally located, with a surprising variety in their form and causal powers, as well as encompassing various relationships to inheritance.

The term gene was introduced in 1909 by Wilhelm Johannsen, three years after William Bateson suggested genetics as the name for the study of hereditary phenomena (Keller 2002). According to Jean Gayon (2000) prior to this the study of heredity was within a 'biometric' stage, where heredity was seen as a force of measurable magnitude, especially by physicians and breeders. The study of heredity included both the conservation of traits across generations as well as their appearance in the developing organism (Keller 2002). The rediscovery of Mendel's breeding experiments in 1900 ushered in the Mendelian era of classical genetics in which the loose concept of 'inheritance factors', became termed genes: units passed down from parent to offspring, as stable entities, capable of self-replication, and located at designated positions on the chromosome (Waters 1994). Researchers used pedigrees and breeding experiments to explore the inheritance of dominant or recessive traits such as white or red eyes in *Drosophila*. The Mendelian gene concept is typically viewed as offering a deterministic account where there is a 'one to one' relationship of genotype (genes) to phenotype (physical trait). However, Kenneth Waters argues that Mendelian researchers were well aware that there was actually a 'many to many' relationship between genotype and phenotype. For example it was established that eye colour in *Drosophila* was affected by mutations at many different loci (Waters 1994). Waters describes the research as being concerned with "character differences, not characters, and what explained them were differences in genes, not the genes themselves" (Waters 1994, p. 172).

Evelyn Fox Keller in her book *Making Sense of Life* (2002) argues that during these early years the study of heritance split into two separate studies, genetics (transmission/inheritance) and embryology (development). The study of genetics then progresses through three key periods: classical genetics (1930-1960), early molecular biology (1960-1980) and post-recombinant DNA developmental molecular biology (1980-2000). Each of these three stages has framed the problem of development in

novel ways, and Keller argues that much of the theoretical work involved in constructing explanations of development from genetic data was based in linguistics, drawing upon multiple meanings, ambiguity, and the introduction of novel metaphors (Keller 2002, p.117).

The idea of gene action dominated during the first stage of classical genetics as a framework for understanding development. By 1960 the early molecular phase was ushered in by an increased understanding of the material nature of genes allowing for the idea of molecular genes as a specific segment of DNA. The hypothesis that one gene coded for one protein seemed to provide a clear one to one relationship between genes and proteins as biological building blocks. In this second stage of gene research ideas of a 'genetic program' led to a 'gene centred' approach that privileged genes by virtue of a direct causal relationship between presence of the gene in the genome and an organism's expression of a trait (Keller 2002). In the third stage, post-recombinant DNA developmental molecular biology, Keller argues that the notion of positional information has been given increased importance.

The current portrayal of the TDF/SRY as the gene 'for' sex rests on this idea of genes as sufficient causes of phenotypic traits. Moss has argued that the idea of 'genes for' phenotypic traits stems from a conflation between two distinct gene concepts, reflecting opposed traditions of embryological thought. The gene P stems from the preformationist school and has evolved into the concept of a gene as a statistically useful predictor of phenotypes, a concept that distances itself from the molecular nature of the DNA elements which are the underlying causes of these patterns of inheritance (Moss 2003). The gene D, from the epigenetic school, relates to the idea of a gene as a DNA sequence, where there is a one to one relation between the gene and the 'molecular norm of reaction' (Moss 2003).

Karola Stotz et al (2004) have explored how scientists themselves conceive of genes, indicating that different fields have various views of what constitutes a gene. As Chapter Two has described, the use of genetics to explore sex (sex differences, sex development and sex determination) has involved researchers in a variety of different fields and one would expect, in view of Stotz et al's work, that each field held differing views concerning genes. Even within the different fields of biological science the exact definition of a 'gene' remains loose and fluid. Rafi Falk argues that this 'slippage'

between different gene concepts has been useful in allowing research flexibility (Falk 2000; Rheinberger 2000). However it has also been argued that the conflation of the various different gene concepts into a single 'informational gene' has lead to confusion (Falk 2000; Moss 2003; Stolz et al 2004).

This chapter places genetic sex, and the two gene cases studie within the work of the philosophy of biology, feminist studies and science studies. As such it is not primarily concerned with the philosophical *truth* of gene causation; rather it aims to explore how researchers within sex genetics have communicated and conceptualised the two genes in relation to wider research. The analysis of the metaphors used to report the research findings will show three features of the research paradigm. The first is that the research moved between different conceptions of the research goal (to find the gene responsible for testis formation, sex differentiation, sex determination and male determination). The second feature is that researchers included views and explanations of sex related to both the inheritance and development of male/female sex drawing upon conceptions of sex from various other disciplines (i.e. embryology, endocrinology, cellular biology, and medicine). The third feature is that the research into the two sex genes was clearly in contact with social and cultural views, and these influences were important in how the genes' action was portrayed.

7.3 Mendelian inheritance factors

As indicated in Chapter Two in the early 1900s researchers were unsure whether sex was in fact an inherited trait or not. At the time heredity was seen as a force (Moss 2003) and researchers began to suggest that sex was a trait, inherited according to Mendelian laws. As Jane Maienschein has detailed, researchers conducted large scale breeding experiments (insects, frogs, and birds) as well as using royal genealogies and birth records to study how sex was inherited (Maienschein 1984). Not only did these experiments aim to detail sex linked inheritance and the sex ratio (and to find proof of the expected 3,1 or 1,2,1 ratio) but researchers also sought to influence the ratios by changing the environment or, as in Richard Goldschmidt's case, to examine the breeding of different geographical races of gypsy moths which resulted in a range of intersex types (see Chapter Two).

In these early years the Mendelian theory of heredity was widely criticised and it was only with the publication of Morgan's *The Mechanism of Mendelian Heredity* in 1915 that classical genetics came to dominate the study of heritance (Allen 1974). I noted in Chapters Two and Five that in the early years of the 20th century mammalian and avian sex determination and development was seen as determined by the presence of the testes. As a result researchers interested in sex prioritised the inheritance factors that were linked to testis formation. In 1927 the Danish geneticist Øyvin Winge proposed that there existed a 'testis determining factor' on the Y-chromosome, which was linked to the development of the male phenotype. Winge's work was based on population pedigrees, which were common tools not only for studying the nature of heredity, but for inferring the genetic structures of individuals (Gayon 2000). While the physical nature of the material inherited through breeding was not known, researchers such as Winge used breeding experiments to explore their transmission through generations. Winge's used guppy populations and their pedigrees to explore the correlation of inheritance of the TDF with the fish's colour using similar experiments to Mendel's (Winge 1927). Articles from this time reported Winge's research as concerned with characters that were dominant or recessive, and the guppies as being mutants who's mutations could be "autosomal mutant characters" (Demerec 1928). This language is typical of references to the elusive gene of the pre 1940s, which

> was not sequenced, its structure was unknown (and generally thought to be protein), and the mechanisms accounting for genetic change (mutation, recombination) were unexplained. (Gilbert 2000, p.179)

Keller has shown how this period of genetic research relied on the term 'gene' having a "latent ambiguity" which allowed a "black-boxing of its uncertainty" at the same time as providing a explanatory framework to make sense of their day-to-day work (Keller 2002, p.132). As Chapter Five showed, the term 'testis determining factor' was fluid in two ways. First, the term was used interchangeably with the terms 'sex determining factor' and 'male determining factor' showing the lack of clarity regarding how 'sex' was being defined. Second, till the mid 1980s researchers were well aware of the uncertainty regarding what the genetic factor was. These two issues raise questions regarding how they perceived the action of the TDF. Keller has argued that the general notion of gene action allowed the observations of intergenerational transformation (development) and transgenerational transmission to reframe thier two research questions as one.

> Gene action is a shorthand expression for this way of thinking: it represents development as proceeding along chains of reactions that start with fertilization (the event that triggers the onset of gene action) and culminate in the production of an organism seen as an effective summation of the end products of the activity of all its genes (Keller 2002, p.128).

In the case of sex there was a separation between the questions of sex determination and sex development. Researchers viewed the female body as 'default' with the gonads being naturally female but pushed by male hormones into the alternate male pathway. As noted in Chapter Two, endocrinology played an important part in setting up the view that sex development began with the formation of the testes, and this became incorporated into the genetic research paradigm with the search for the 'determining factor' of the testes. By the 1950s the Y-chromosome was seen as 'responsible' for sex determination both as the inherited unit and as the developmental unit. Gradually these two actions became increasingly viewed as specifically the role of the TDF. However the TDF continued to be elusive, and researchers at the time were unsure of what type of entity the TDF was – whether it was a gene, genes or simply some other type of factor linked to the Y-chromosome.

While the Y-chromosome was accepted as the critical factor within sex determination, during this early period there were two suggestions as to the biological product that caused maleness, which did not prioritise the testes but rather used the general term 'sex determination factor'. One of these was the H-Y male-specific antigen. The H-Y antigen is a histocompatibility antigen which plays a role in allowing the immune system to distinguish the body's 'own' cells from foreign cells, as illustrated by experiments of graft rejection in mice (Eichwald and Silmser 1955). In 1975 the H-Y antigen was proposed as a possible candidate for sex determination (Wachtel et al. 1975), as it was known to be exclusively male, with its gene being located on the Y-chromosome. As the antigen was contained on the cell wall this raised the possibility that it was involved in a cell-signalling mechanism similar to those understood to be important for tissue differentiation. The proposal of the H-Y antigen being the TDF was also supported by the idea that it was also connected to male to female trans-sexuality and homosexuality (Enclander-Golden et al. 1980; Blanchard and Klassen 1997; Blanchard 2001). However, the location of the H-Y antigen gene was yet to be established as residing on the male specific region of the Y-chromosome.

A second proposal as to the sex determining factor was made by two researchers, Lalji Singh and Kenneth W. Jones, who were conducting research into the sex determination of snakes. William Cookson in his book *The Gene Hunters* proposed that Jones and Singh's work in the late 1970s and early 1980s focused on snakes because of the karyotypic differences seen in the species. Some snakes have chromosomes, commonly refereed to as W and Z, which function in a similar way to the mammalian X and Y. Other snakes do not have sex-chromosomes but do have sex determining genes on other chromosomes. Jones and Singh attempted to isolate the DNA sequence from the snake W chromosome to compare it to the mammalian sex determining DNA. In 1981 they found that a highly conserved, repetitive DNA sequence, sex specific in snakes was also found on the mouse Y-chromosome. These were repetitive GATA sequences which became known as Bkm DNA sequence (Singh 1972; Singh et al. 1981; Jones and Singh 1981; Jones and Singh 1982). The fact that these sequences were present in many copies on the sex-chromosomes of some vertebrates supported the idea that they may have a possible role in sex determination (Epplen et al. 1983).

The idea of sex being determined by a non-coding sequence of DNA is interesting in relation to the obsession with genes (protein coding sequences) as the causally significant entities. In 1985 an article was published which advocated that mammals, *Drosophila*, *C. elegans* and snakes shared a similar genetic regulatory mechanism, perhaps the Bmk sequences (Chandra 1985). This mechanism was thought to be based on a non-coding sequence, a sequence which did not result in a sex-determining protein. In the mammalian sex determination system this non-coding sequence was thought to be located on the Y-chromosome and determine sex by its absence or presence in the genome. In the dosage sensitive systems of *Drosophila* and *C. elegans* the sequence was thought to function in a sex determining manner by the "copy number or accessibility to regulator molecules" being different between sexes (Chandra 1985, p.1165).

These two alternative suggestions as to the mechanism by which sex was determined (rather than a TDF gene) reflected the idea of underlying unity in both body and nature. The suggestion of the H-Y antigen as the sex determining factor supported the view that sex spans throughout the body, and while the testes may play a leading role in forming the body, molecular sex differences marked each cell. The exploration of evolutionarily conserved sex determination mechanisms such as the Bmk sequence indicated the

strong sense that there was a 'unity in nature' with regard to sex and sex determination systems. While the sequence was found to be barely represented on the human Y-chromosome, which cast doubt on it having a role in mammalian sex determination (Kiel-Metzger et al. 1985), the Bkm DNA proposal led to the idea that a single switch determined the difference between males and females (Cookson 1994), an idea that came to dominate the search for the TDF.

Central to the research into the TDF in the 1980s and 90s was the use of intersex conditions. It should be recognised that researchers were also using intersex conditions to explore genes on the Y-chromosome which were not involved in sex determination/developmental pathways. These genes were important in the phenotypes of height, bone density, and tooth size[13]. As Chapter Five showed, it was this research which expanded in the latter half of the 1980's to using intersex conditions to narrow down the location of the TDF. Winge's early work was never referred to in the Medline articles; however the use of the word 'factor', rather than gene, indicates to me that it was not entirely forgotten. The TDF has a far longer history than is normally recognised and this incorporates a much wider research context, including views of sex within endocrinology, and concepts of gene action, inheritance and evolutionary relations. Keeping this in mind the next section will move on to exploring the research which 'discovered' the TDF and DAX-1, paying particular attention to the wider developments and understandings of genes.

7.4 Molecular sex genes

The 'molecular' phase of genetic research was initiated by the 'discovery' of the structure of DNA in 1953 (Watson and Crick 1953). The structure of DNA gave rise to the idea that there was a one to one relationship between the gene (DNA sequence) and protein (amino acid sequence). This, Rheinberger argues, brought about molecular genetics which "transformed its boundary object, the gene, into a material, physicochemical entity" which was given "informational qualities" (Rheinberger 2000, p.221). The particular view of genes located at definable positions on the chromosomes led researchers to use linkage and physical mapping as a research technology to locate the two genes. This discussion highlights that as with other genes, the technology used

[13] It is somewhat surprising that that genes related to tooth size are found on the Y-chromosome. In fact the Y and X-chromosomes encode different versions of a tooth protein, providing forensic scientists with a method of sexing severely disfigured bodies (Sivagami et al. 2000).

to ‘locate’ the genes led to the view that there was an actual physical DNA sequence identifiable as a gene ‘for’ the specific phenotype of interest.

7.4.1 Locating the molecular gene

The technology which is used to locate an item not only determines how you find it but it also defines what you are capable of finding. The impact of molecular biology in genetics opened up new research technologies including new techniques of ‘mapping’. The Mendelian method of mapping was based on linkage maps. These maps are constructed by comparing the frequency of recombination events or ‘crossovers’ between characteristics (phenotypes) in relation to specific ‘genetic markers’ which serve as ‘landmarks’ on the chromosome in question (for details see Hall 2003). These maps were applicable to all of the chromosomes except the Y-chromosome, which could only be partially mapped as part of it, the male specific region, does not normally recombine with the X-chromosome.

As I indicated in Chapter Six, a linkage map for the X-chromosome was produced and this provides a suitable example to show how linkage maps were created. For the X-chromosome disease conditions allowed a gene order to be deduced. For example, researchers might write: ‘Xpter-ACH-GKD-DMD-cen’ (See Chapter Six). Xpter is a known landmark on the X-chromosome, and this landmark, ACH (adrenal congenital hypoplasia), GKD (Complex Glycerol Kinase Deficiency), DMC (Duchenne Muscular Dystrophy) and cen (the centromer of the chromosome) are claimed to be ordered as shown. As Edward Hall has shown these linkage maps created a bridge between the genotype and phenotype:

> The internal spatialising of the genetic sequences and the production of a framework of gene location also makes it possible for the connection between genotype and phenotype to be concretised – if the (relative) location of a gene sequence is determined, then it’s ‘casual relationship’ to a bodily characteristic can be more easily ‘pinned down’. (Hall 2003, p.153)

Linkage maps are based on pedigrees, the inheritance of characteristics from parents and comparisons with siblings, and the relevant concept of genetics is “purely one of inheritance” (Hall 2003, p.153). However as I have already mentioned they were not successful with regard to the TDF, since it resides in an area of the Y-chromosome which has a very low recombination rate with the X-chromosome. Due to the way in which intersex conditions were ‘corrected’ as medical emergencies during the 1970-80s

it is also likely that genetic researchers would have been unable to identify the few individuals who did have a chromosome which had resulted from such a recombination event. Additionally it is now known that the genes Y-chromosomes carried were mostly related to reproduction, thus resulting in reduced reproduction for those carrying phenotypic variations.

Many of the articles explored in Chapter Five reported using intersex conditions to 'narrow down' the location of the TDF and trying to find the 'genes responsible for the testis determining factor'. Linkage mapping was further developed by Goodfellow et al's suggestion in 1986 that the gene, MIC2, could serve as an important marker for the studies aimed at isolating TDF (see 5.3). A year later, in 1987, using a version of linkage maps (deletion maps) researchers ruled out the H-Y antigen being the TDF because it was located on a different part of the Y-chromosome from the area understood to be sex determining (Simpson et al. 1987).

This research was based on tracing the inheritance of chromosomes through families, allowing researches to compare DNA samples from family members with 'normal' phenotypes (fathers; XY males and mothers; XX females) against those with alternative phenotypes (i.e. XX males). The social and medical changes in how intersex conditions were managed are likely to have been fundamental in allowing researchers to have access to genetic samples and family histories. The importance of these transgenerational relationships can be seen in a paper from 1987 where the researchers report following the inheritance of a pseudoautosomal restriction fragment length polymorphism in two XX-male families. It describes the results of one such investigation noted as 'the family of XX male LGL163':

> The father is heterozygous: his 1.4- and 2.0-kilobase (kb) fragments must be on his Y-chromosome, because that allele is present in the grandfather but not the grandmother. The XX male inherited his father's Y allele. Densitometry reveals that the XX male has one copy of the XX-kb allele. This must be from the mother, because she is homozygous for that allele. Thus, at MIC2, XX male LGL163 inherited his father's Y allele but not his father's X allele. (Page et al. 1987b, p.437)

The research article incorporates a variety of evidence and research data both traditional and new. This is seen in the main figure in the article, which includes pedigrees with the traditional Mendelian figures (squares representing males, circles representing females, filled squares representing XX males). Under the pedigree the result of a

hybridisation is shown, so that "each autoradiogram lane corresponds to the individual above that lane in the pedigree" (Page et al. 1987, p.438). The figure connects Mendelian traits with DNA fragments, and shows individuals such as the male grandparent, represented in the pedigree by an unfilled square, with a LGL12 X fragment of 3.3. KB and a LGL163 Y fragment at 2.0 kb. This figure indicates that at the time it was important to portray different types of evidence as supporting one another and fitting together with different techniques as illuminating different facets of the problem. I noted in Chapter Five (5.3) how this paper 'proved' that XX males were the result of crossover events, and it is clear that the researchers were still using traditional terms such as 'alleles' and reporting data within pedigrees. This brings us to the question of how they were conceptualising the genes in terms of their action.

7.4.2 Gene action: master regulators, switches and pathways

Keller has shown how the idea of a 'genetic program' suggests a plan or procedure, a schedule, a set of instructions and a 'genetic blueprint' which relates gene action as "genetic control, genetic regulation, genetic switches, genetic activation" (Keller 2002, p.136). As already mentioned the idea of a single 'genetic switch' stemmed from the proposal that Bmk sequences were sex determining. As this idea grew, the TDF came to be seen as a 'master' gene of sex determination.

The metaphor of 'master genes' has come under heavy criticism by feminists, mostly due to the concept of control and of a hierarchical structure of power. Bonnie Spanier has noted how genes within molecular biology are prioritised over other cellular components, controlling and determining proteins: "in this framework, genes are at the pinnacle of the complex process of regulation of life in cells" (Spanier 1995, p.85). Spanier argues that the researchers saw a hierarchy in genes, with certain genes such as those termed 'housekeeping genes' having a lesser role. It could be argued that these genes are in fact the most fundamental as their role is related to maintenance to the cell's life. Spanier also suggests that scientists no longer use terms such as "master" and "slave" (Spanier 1995, p.87), I think the two case studies have shown that at least with respect to sex determination these terms are still in use.

The idea of 'master genes' had a long history in embryology and development, stretching back to the 1970s. Michel Morange has argued that in the 1970s and early 1980s research within embryology converged with research on *Drosophila*, and

suggested that development was due to the action of a limited number of genes controlling the "activity of a battery of structural genes" (Morange 2000, p.199). In 1984 two research groups showed that a set of genes produced proteins with a particular DNA-binding structure, which was known to allow proteins to regulate the expression of other genes by binding to their promoters (Morange 2000). This lead the researchers to argue that the MyoD gene was a developmental regulatory gene.

As I noted, according to Cookson (1994) the idea of the TDF being a 'master gene' was related to the research into the Bmk sequences in snakes that had proposed a single 'genetic switch'. The Bmk sequence was not thought of as a molecular gene, in that it did not represent a DNA sequence which would result in a structural protein. As such it was seen as acting as a 'switch' by the simple effect (though with unknown mechanism) of its presence in the genome, much as researchers in the early 1920s had been willing to accept the Y-chromosome as 'determining sex' with no concept of how it might function as such.

The TDF was first termed 'a master regulator of sex differentiation' in the research article published in the April 1987 edition of *Nature,* which published the 'resounding proof' that the TDF was not the H-Y antigen (Simpson et al. 1987). I noted in the earlier section how this paper was based on linkage maps, which do not suggest the type of gene action only the inheritance of the sequence and phenotype in question. This raises the question, why did researchers at the time suggest that that the TDF was a 'master regulator' if they were trying to locate the cause of a phenotype without a clear idea that a gene (as defined as encoded in a DNA sequence) was involved?

Spanier has noted how 'differentiation' (the process in which cells become more specialised in embryonic development) became the research topic of molecular biology. The indication being made by Simpson et al, is that the TDF is connected to the differentiation of cells within the gonad, hence the characterisation of the TDF as the 'master regulator of differentiation'. As Spanier notes, this builds upon the idea that differentiation reaches further back to cellular events:

> The controlling gene exerts a primary influence by determining the course of development, while the other genes involved in the "myriad molecular consequences" that constitutes the actual process of differentiation are clearly secondary. (Spanier 1995, p.87)

In the case of the TDF, the gene was seen as acting as a genetic switch which placed it in a position of authority as necessary and sufficient to result in the male phenotype as defined by possessing testes. However rather than this placement stemming from a sexist view of sex determination, I would argue that it was in keeping with the view of genetic pathways held by researchers at the time. The idea of a 'master gene' was tightly connected to the view of how genetic pathways functioned in development. By 1987, when the ZFY was proposed to be the TDF, 'master regulators' were understood to function as genetic switches in complex genetic developmental pathways where they controlled or determined phenotypes. These constructions of control and power were not unique to sex and sex determination. The popular science books analysed in Chapter Three and Four indicated that genetics was thought of in terms of political structures of governance with one clear 'leader' (dictators and princes etc). The dominant image of genetic processes was that they functioned as tightly controlled hierarchies. With the suggestion that the DAX-1 was a 'female' gene researchers discuss two pathways, with two master genes:

> Mice and humans start out having both male and female reproductive systems, and both have master genes that guide their development. In females, the gene is called Dax-1; in males, it's SRY, a gene on the Y-chromosome. (Cromie 1999 available online)

DAX-1 was proposed as a female gene because it seemed to have 'anti-testis' properties during sex determination (testis formation). While the idea of DAX-1 as a 'master' gene for the female determination pathway challenged the research superiority of the SRY gene and male development, it replicated the view of genetic pathways requiring a master controller and the view of power in hierarchical terms.

To summarise, the idea of the TDF serving as the single genetic switch between the male and female genetic developmental pathways offered researchers a method for locating a DNA sequence through physical mapping, without requiring that it was a single gene (DNA coding sequence) which resulted in a protein product. This lack of certainty as to what type of DNA sequence would be found may indicate 'gene slippage' which Falk has argued can be conducive to successful genetic research. As already noted the TDF was referred to in a number of different ways: possible candidate for sex determination (1975): the genes responsible for the testis-determining factor (1983): sex-determining gene(s) (1986): master regulator of sex differentiation: testis-

determining factor gene (TDF) (1987): the master sex-determining locus (1987): primary testis-determining factor (TDF) (1989); testis-determining factors (1990); testis-determining gene (1990); testis-determining factor gene (1991); and sex-determining gene (1994). Even after the TDF was 'identified' as the SRY DNA sequence it was still referred to in different ways depending on the article's content. The reason for this is that the identity of a gene is not fixed merely by researchers having located it, as the next section will show.

7.4.3 Molecular gene –creating a gene's identity

Physical mapping expands upon linkage mapping which provided the "framework of the landscape" (Hall 2003, p.154) and enabled researchers to identify the gene sequence with accuracy and then sequence the base pairs which make up that sequence. Researchers using physical mapping assumed that the gene exists in a physical location and as such could be identifiable with a definable stretch of DNA. The stretch of DNA is seen to have 'informational' qualities, which the researchers refer to in terms of the gene incorporating a code.

In the case of the TDF physical mapping was first used in a research article from 1987, which Fujimura (2006) has argued was critical in setting the research paradigm of sex determining genes. David Page and his co-workers used genetic samples from persons with intersex conditions to narrow down the location of the TDF on the Y-chromosome. In the paper the researchers assume a naive position regarding the identity of the gene in question, stating:

> we set out to characterise TDF with an approach that does not presuppose the nature of the gene or gene product. Despite our ignorance of the biochemical and cellular events regulated by TDF, we felt it possible to clone the TDF gene by precise determination of its chromosomal location. (Page et al. 1987, p.1094)

Unlike linkage maps, which relied on creating a link between two characteristics of phenotypes, "(p)hysical maps of the genes represent the 'actual' or 'precise', as opposed to relative, locations of gene DNA sequences along the chromosome" (Hall 2003, p.154). In the case of DAX-1 this linkage was immediate since, as mentioned in Chapter Six DAX-1's acronym tied together two phenotypes, 'dose sensitive sex-reversal' (DSS) and the disease condition 'adrenal congenital hypoplasia' (AHC), to a specific DNA sequence termed the 'critical region' . In the case of the TDF the

connection between gene and physical DNA occurred slightly later in its history, when it was proposed to be the ZFY. At this time there was a conflation between the 'factor' and the 'gene', although there was a still question whether the factor was a single gene (Page 1987).

The TDF construction underwent a number of changes before its identity was established as the SRY. As research progressed the term 'regulator', which related to sex development, was dropped and the TDF came to be referred to simply as the 'master sex gene'. This indicates that the two research topics of sex determination and sex development were becoming increasingly interlinked. The question of what determined that an embryo would develop as a male or female was no longer separate from how it developed, and what genes were involved. When, in 1990, the TDF became located by physical mapping as the SRY gene, there was a shift away from these pathway and hierarchy metaphors towards ideas of 'cascades'. Increasingly as research progressed the articles explored in the two case studies used the expression 'the sex-determining hierarchy' to describe their research interest. However, before I move on to exploring this move towards genomic metaphors I will explore the role that 'sex-reversal' played in narrowing down the TDF and DAX-1 and how this influenced the way in which the genes were conceived.

7.4.3 Sex-reversal

It should be clear that people with non-typical sex phenotypes and genotypes have been fundamental to researchers interested in sex genes. People with 'alternative' sex phenotypes have been referred to in many ways including hermaphrodites, sex-reversed (Simpson et al. 1987), and X-Y interchange males (Pritchard et al. 1987).

The idea of 'sex-reversal' hinges on the idea of a body having a true sex, a sex in which all the different sex factors (chromosomes, genital, gonads, secondary sexual characteristics) are congruent. In this view sex is determined at fertilisation by the chromosomes, and developed by the hormones so that the body has one sex, male or female. Within the medical management of intersex conditions, revealing the 'true sex' has been the main concern of the doctors involved (Dreger 1998). Historians of medicine have indicated that this may be motivated by a fear that the person may engage in homosexual actives without knowing it (Dreger 1998). Within genetic laboratories the concepts of true sex and sex-reversal have been slightly different. As

explored in Chapter Two researchers were able to create what they saw as a 'neutral' type of bird which did not show male or female secondary characteristics by transplanting gonads. In the early 1900s researchers sought to achieve similar results through breeding and changing the environment (i.e. Goldschmidt's experiments with gypsy moths). Genetic sex, or the sex-specific karyotype, was the first criterion used to serve as the essential indicator of the body's 'true sex', and the analysis of the popular science books in Chapter Three and Four has shown that the 'sex' chromosomes are now seen as indicating what sex a person *should* be, or what 'nature' intended the body to be. This discourse has, for me, a distastefully moral flavour, prioritising nature as revealed by science as the authority on how humans should live.

The construction of sex-reversal was not only critical to the linkage and physical mapping of the TDF, but also for providing a mechanism by which to identify the TDF as the SRY DNA sequence. As I explored in Chapters Five and Six, researchers sought to create a sex-reversed mouse as the ultimate proof of the SRY's capacity to create the male phenotype. However in this case sex-reversal was not just a physical phenotype but also a sexual phenotype – the journal editors also required that the XX animal behaved as if it considered itself male and it did so successfully to earn the nickname Randy (see Chapter Five). Once the account of the animal's sexual behaviour was included in the article alongside photographs of its genitals, the SRY gene could be accepted as the only gene necessary and sufficient to create a male from a XX female.

The importance of the sex-reversal paradigm is also clear in the case of DSS/DAX-1. Before the identification of the SRY researchers had considered that the intersex conditions with chromosome 'abnormalities' (XY females and XX males) were due to a single gene. After Randy had 'proved' that the SRY gene was sufficient for male development it became clear that there were cases which were not caused by this gene. As I detailed in Chapter Six, these cases were believed to be caused by 'dose sensitive sex-reversal' genes, thought to be on the X-chromosome. However unlike the case of the TDF/SRY identification, the X-chromosome had been mapped quite successfully by linkage and physical mapping and DAX-1 was identified almost immediately. The researchers proposed that this sex-reversal was dose sensitive (DSS) and involved an 'anti-testis' gene which, as it worked against male development, was seen as a female gene. This model of sex-reversal led to an emphasis on the idea that there was overlap

between the male and female pathways, which supported the view that rather than a single linear pathway the metaphor of cascades of genes was more appropriate.

In both the case of TDF and DAX-1 the research was based on the use of sex-reversal to locate the DNA sequences. Once the locations of the genes were known they could be sequenced, the amino acid product deduced and its biochemical action inferred. This then allowed researchers to explore how the gene was expressed in different tissues at different times which added complexity to the identity of these genes and their roles within sex.

7.5 Genomic sex genes

The field of genomics seems to offer an alternative to the deterministic and reductionist view of biology that has, arguably, played a major role in genetics in the 1980s and 90s. The definition of genomics is problematic, nearly as much as defining what a gene is. What most agree upon is that it includes what is normally referred to as the "complete set of genes in an organism". It is typically described in terms of maps and blueprint metaphors, and draws on images both of genome-as-code and genome-as-text (Ceccarelli 2004, p.92) as well as newer suggestions such as the genome as a jazz score and genomics as quilting (Porta 2003). In addition to this, genomics includes a wider set of factors, including non-protein gene products, temporal sequence, and imprinting and X-chromosome inactivation, which will be explored in Chapter Eight.

It has been argued that genomic concepts of genes signal a change towards less deterministic and reductionistic ideas of genes themselves. Unlike molecular genetics which portrayed genes as actors, genes now tend to be viewed as 'activated', as processes rather than substances (Keller 1994). Partly this comes about from a greater understanding of what genes do. As Gayon states, "the better our causal accounts of what genes are and do, the less these entities are likely to be interpreted as 'agents'" (2000, p.295). In the next section I will explore the impact of genomics on the concept of sex determining genes, including new metaphors and changes in the DAX-1's identity.

7.5.1 The genomic phenotype of sex

It will be clear to the reader that the dominant view within mammalian genetics sex has been to define sex in terms of the male body: possessing testes, and male sexual behaviour. Even in the case of DAX-1, sex genes were defined by their 'responsibility' for creating and causing the differentiation of cells in a single organ, the gonad. In the early stages it was considered female precisely because it did not seem to have a role in the male pathway. However I would argue, based on the two case studies, that there has been a change towards exploring the 'reproductive axis' and the interrelationship of the pituitary gland, hypothalamus, adrenal glands and gonads during development. In an article entitled 'Mammalian sex determination: from gonads to brain' researchers state:

> A regulatory cascade hypothesis for mammalian sex determination, proposing that SRY represses a negative regulator of male development, was recently supported by observation of mice that expressed a DAX1 transgene and developed as XY sex-reversed females. The role of some sex-determining genes, such as DAX1 and SF1, in the development of the entire reproductive axis, a functionally integrated endocrine axis, leads to a new concept. Normal sexual development may result from the functional and developmental integration of a number of different genes that play roles in sex determination, sexual differentiation, and sexual behaviour. (Vilain and McCabe 1998, p.74)

Also called the hypothalamic-pituitary-adrenal/gonadal axis the reproductive axis includes the adrenal glands, two structures in the brain (the pituitary gland and hypothalamus), as well as the gonads. As the case study of DAX-1 showed, as early as 1995 researchers were aware that DAX-1 was involved at multiple levels in this system (Guo et al. 1995, p.8). This change also introduced new metaphors which will be explored in section 7.5.2.

This change in research interest raises questions regarding how the genes were defined in terms of phenotype. The case studies showed how at the start they were located based on phenotypes (TDF, DSS and ACH). As more became known about the action(s) that their gene products had in the cell, the idea of these genes having a single 'role' or 'responsibility' with regard to sex (determination and development) became problematic. It becomes impossible to define what the SRY or DAX-1 does in terms of a single function because any role occurs within a wider genomic context as well as a larger system. This becomes clear in the case of WNT-4 which impacts on both kidney formation and sex development. In Chapter Nine I will suggest that genes can not be identified either in terms of phenotypes or of DNA sequences but rather, following Keller, genes are seen as processes occurring within a genomic space. In the rest of this

section I will explore the developments of genomic metaphors in regard to the two case studies and ideas of genomic time and control.

7.5.2 Genomic metaphors

Following Keller's research it is clear that shifts in metaphors can indicate a shift in underlying concepts, and the impact of genomics on the two genes, SRY and DAX-1 was seen in the introduction of new metaphors. During the hunt for the TDF and DSS researchers had used the metaphor of pathways. However as more was known about these genes a new idea was developed, that of the reproductive axis. The change in focus from defining sex in terms of the testes towards the entire reproductive axis also brought new metaphors, specifically of genetic cascades. Brigitte Nerlich and Iina Hellsten (2004) have explored how within genomic accounts researchers tend to draw on established genetic models but to qualify the genomic accounts with additional descriptions. While researchers continued to use the metaphor of a genetic switch, it was increasingly accompanied by the description of a gene 'cascade' to which genes were 'recruited'. The metaphor of recruitment had been used previously, but related to the role of hormones secreted into the blood by the gonads and 'recruiting' the body into male development (see Chapter Six). However as research progressed it was the genes and their products which were seen as doing the recruitment that determined the 'cell's fate'. This became increasingly important in the description of genes which were sensitive to dosage at multiple steps in the pathway (Jordan et al. 2001, p.1102)

As research progressed researchers became aware that DAX-1 was required in the male phenotype at a later stage of sex determination. This press release offers an interesting description:

> The sex of newborns is **dictated** by the X and Y-chromosomes – girls are XX whereas boys are XY. However, new research from Northwestern University has shown that normal testis formation **depends** on two genes -- the so-called male-determining SRY gene, found on the Y-chromosome 10 years ago, and a gene called Dax1 on the **X (female)** chromosome. (emphasis added, Crown 2003; available online)

As research advanced it became clear that DAX-1 was critical to the 'maintenance' of the male testis. The idea of there being two separate gene pathways was further complicated by the discovery that Wnt-4, which had been conceived of as a female gene, was also required for male sexual development (Jeays-Ward et al. 2004), which

emphasised that the two 'pathways' were interlinked and likely to use some of the same genes at different times.

These developments raised three issues. The first was the continued emphasis that a clear division between sex development and sex determination was impossible, as sex was not determined at a single time point in development but rather required the body to be 'maintained' as a certain sex. Genes were important not only as inherited units and in terms of development of organs but also in maintaining these organs as living collections of cells and in developing these organs during the life cycle (for example the production of sex cells in puberty). The research record detailed in Chapter Six showed how researchers moved towards describing a reproductive axis, and that DAX-1 and SF-1 came to be seen as components of the cascade required for the development of these steroidogenic tissues.

The cascade metaphor incorporated a number of non-gene components, and DAX-1 was also increasingly seen in the context of a whole host of genes including Sox8, Sf1, Gata4, Wt1, Fog2 and Sox9. The idea arose of a "functional network of transcription factors" important in embryonic development, and genes were described as acting independently, yet in 'cooperation' with each other, in 'coordinated expression' (Clipsham et al. 2004). The case studies indicate that there was a development from seeing sex in terms of a tissue type (gonads) towards systems, specifically the hypothalamic-pituitary-axis, and researchers characterise the SRY and DAX-1 as "network partners" in its development (Clipsham and McCabe 2003.)

To summarise, the metaphor of 'cascades' incorporated three issues. Firstly, the idea of 'cascades' also allows the possibly of interlinking gene pathways, as well as emphasising the effect of one gene on a number of different pathways depending on time and tissue. Secondly, the descriptions of 'cascades' not only include genes, but articles also described gonad differentiation as dependent upon a cascade of molecular and morphological events (Majdic and Saunders 1996). Thirdly, this not only offers new ways of understanding the issue of control in genetic processes, but also raises the factor of timing. Rather than a straightforward binary view of genetic control, where the switch is on if the genome contains the DNA sequence or off if it does not, the articles emphasise 'governing' and 'influencing' what was now seen as not one, but a

series of genetic switches (Jameson et al. 2003). These three issues were incorporated into the expression profiles of the genes.

7.5.3 Expression identity

I have noted that the movement to a more genomic understanding of phenotypes complicates a direct relationship between the presence of a gene (DNA sequence) and the physical effect. The limited success of the experiment to create XX transgenic male mice showed that it is not enough for the genome to contain a specific DNA sequence, but rather that the development of a phenotype is also related to the location of the sequence in the genome and that the sequence is incorporated into the cell's genetic processes.

One way of determining if a DNA sequence is used by the cell is to explore the expression of the gene. Expression maps trace the presence of mRNA and, as Hall (2003) notes, rely on the chemical link between a gene sequence and the change/action of a protein. Expression studies became increasingly used in the study of the two genes allowing researchers to focus on identifying the range of mRNA being expressed. As noted in Chapter Six, in 2000 a large-scale screening experiment found 72 genes which researchers thought might be involved or 'play a role in' the genetic mammalian sex determination pathway (Wertz and Herrmann 2000, p.51). Other researchers were concerned with exploring how multiple gene expression patterns interacted, particularly during XX and XY mouse fetal gonad development (e.g., Bouma et al. 2004). It is likely that much of this shift was enabled by advancements in technology, particular microarray technology, which was noted to "provide greater insights into the steps necessary to elicit a functionally competent tissue", which would "allow for a more complete description of gonad differentiation and development" (Small et al. 2005, p. 492). These advances allowed researchers to pursue their interest in the genetic processes that lead to sex development, and this indicates that researchers were no longer drawing a division between genetic sex determination and endocrinological sex development but rather placing both within the wider context of gonad development.

The impact of molecular biology was also seen in the renaming of the DAX-1 gene to NROB1. Its renaming removed its connection to the two phenotypes, replacing them with a connection to the large gene family to which it was it was related. While DAX-1 was then used to refer to the protein product of the gene, the rest of this thesis will

continue to use the first name given, DAX-1. Researchers then became aware that NROB1 produced two alternatively spliced mRNAs, which potentially meant that what had been considered one gene should, on the basis of its expression, be considered two different genes. DAX-1 had been constructed as a dose sensitive gene: the amount of its product was critical to how it functioned in the cell and the phenotype. Now there was a recognition that the molecular function of the two gene products was likely to be more complex.

7.5.4 Genomic time

In the 1960s investigations regarding genetic sex were based on stained slivers of dead cells, showing the sex-chromosomes. These investigations were static and taken to represent a non-changing aspect of the body under investigation. In this section I wish to briefly introduce the notion of genomic time, the recognition that the cells in our bodies are constantly changing and that this relies on genetic processes occurring at a rate we find difficult to comprehend (this will be further explored in the next chapter). The two genes, SRY and DAX-1, illustrate the importance of understanding that time is essential for understanding genomic processes.

Increasingly the genetic switches were portrayed as influencing the cell at critical times in development, reinforcing the view that sex determination was not a single event, but rather constantly ongoing throughout sex development. As early as 1989 it had been suggested that timing in the form of the tempo of growth was important (e.g., Mittwoch 1989). By 2003 SRY was seen as working within 'critical periods of gonadal development' (Jameson et al. 2003). In April 2004 an article appeared entitled, 'Sex determination: a 'window' of DAX1 activity', which proposed that

> perhaps DAX1/Dax1 acts within a 'window' of activity, outside of which testis formation does not occur. Here, we discuss the function and possible mechanisms of DAX1 action in male gonadogenesis". (Ludbrook and Harley 2004, p.116)

The idea of DAX-1 working within a 'window of opportunity' relies on the idea of 'developmental events'. As mentioned, the metaphor of genetic cascades opened up new ways of conceiving of control. However, coupled to this is the change in research expectation and, as the next chapter will explore, a new interest in female development.

7.6 Conclusion

The question of how feminists should deal with the materiality of the body and biological knowledge is problematic. One could argue that descriptions of sex are inherently ideological and framed by social goals and expectations, and as feminists have recognised their own readings are similarly affected. Alternative readings of research data, while important for showing the limitations of existing research paradigms, are located within their own ideological framework. What is clear is that any attempt to interact with scientific claims, specifically developments in genetics, should be based on an understanding of the wider issues. According to Fujimura, Butler and Fausto-Sterling, the search for a 'male gene' began with the research of Page who, in their view, coined the term TDF. However the history that I have detailed begins earlier and argues that the use of the term 'factor' was in keeping with the understandings of genetics and endocrinology in the 1920s when it was first suggested. By the 1960s (male) sex determination was seen as connected to the Y-chromosome, and as the status of the TDF grew, so did the reduction of the Y-chromosome to the TDF. Finally in the 1970s and 1980s the TDF had assumed the traditional 'responsibility' of the Y-chromosome as sex/testis determining. The Bmk sequence indicated that it was likely to function as a genetic switch which, by its presence, determined maleness and in its 'off' position produced the female.

The dominant ideology of sex holds that sex should naturally be a single definable phenotype, with the different factors of sex (chromosomes, gonads, genitalia, secondary sexual characteristics) congruent. The idea that there was a single genetic cause of sex enabled researchers to pursue linkage and physical mapping. Feminists have somewhat misleadingly raised concerns as to the TDF being portrayed as the master regulator of sex determination/differentiation, as this conception was reasonable considering both the view of sex and the genetic research paradigm in which the researchers were located. In this regard the TDF was not unique, but rather the assumption of hierarchical power relationships was inherent to genetic research itself and at times political metaphors were actively used in popular science communication (see Chapter Four).

A second concern for feminists is the linkage between the SRY gene, sex development and sexual behaviour. I noted in Chapter Five that this connection stemmed not from

the researchers themselves but rather arose from the reviewers questioning whether a morphologically male mouse (possessing testes) should in fact be considered male. The test devised was a display of heterosexual behaviour, again connecting the organs of sex determination (testis and penis) and sexual development (acting as a male). It is impossible to know if the researches intended to create male heterosexuality along with male morphology, however it is clear this became a subsequent requirement of the experiment being considered successful. There are a number of problems with the experiment including the application of an innate biologically determined sexuality to laboratory animals, and the implicit idea of a binary sexuality (male or not male behaviour). .

It is clear that researchers used a variety of different ways of thinking about genes through the two case studies. It is possible this involved conflating different gene concepts, 'slippage' between concepts, or was a feature of the methodology. An alternative methodology could have been used in this dissertation by following specific research groups and explore how their discourses developed. However the strength of my analysis is that I gained insight into how the research into the genes developed, regardless of the interests and concepts of the different groups.

The replacement of 'pathways' by 'cascades' and 'networks' indicates the wider shift towards genomics as well as the wider interest in molecular biology. While these research articles still initially describe the SRY or the Y-chromosome as sex determining, other factors are not only acknowledged, but the main research interest seems to be directed towards sex development. The reformation of sex determination and development should be recognised as destroying the idea of genetic sex (XX or XY) as in representing the genetic processes that are involved in sex determination/development. The next chapter will explore this further, drawing upon examples from genomics to show how a new concept, that of living genomic sex, could be formed.

CHAPTER EIGHT - BEYOND XX AND XY: LIVING GENOMIC SEX

> "The eye of the scientist, like that of everyone else, is a trained eye that has learned to see. The act of looking, and what is sought, affects what nature discloses."
>
> (Roger Lancaster 2003, p.76)

8.1 Introduction

Anne Fausto-Sterling in her book, *Sexing the Body* (2000) argues that organisms, as objects of study, are actually moving targets, from fertilization until death, thereby stressing the idea of an organism's life cycle. The view of the body as an active process is widespread in the discussions of the paradigm shift from studying single genes in genetics to studying genetic networks in genomics (Moss 2003). The previous chapters have explored the range of metaphors and gene concepts used both in popular science books and in journal articles to describe features of genetic sex, sex determination and sex development. In this chapter attention is directed towards the paradigm shift from genes to genomics involving a change from the capacity to look at fixed, static objects to that of being able to watch living biological samples. The previous chapter touched upon this issue in its exploration of expression maps and the shift towards including the ideas of genetic cascades and recruitment. This chapter, through its exploration of X-chromosome inactivation and imprinting, illustrates two more examples of the shift from static genetics to dynamic genomics influencing the descriptions of these biological mechanisms.

This chapter will follow Fausto-Sterling's lead in recognizing that live organisms are active processes. By exploring the new position of genes within these active processes it will become clear that this research is still located within a fixed binary view of sex. First this chapter explores the idea that humans are female by default. As discussed in Chapter Seven, this view allowed researchers to locate a gene that seemed to switch the default pathway to male. It has since been shown that the early embryonic gonad is not female but rather bi-potential. By briefly exploring the views on the starting point of sex determination and development I will again stress that sex descriptions are located and utilised for wider social aims. The chapter then moves on to explore the portrayal

of X-chromosome inactivation and imprinting, which is clearly locked within the 'sex binary'. This discussion will provide a clearer understanding of how the current scientific evidence complicates a view of binary fixed genetic sex and will propose a new mindset for feminist study –the idea of a living genomic sex which will be explored in the next chapter.

8.2 Nipples and the default female

Alfred Jost, a French developmental endocrinologist, reflecting in 1960 on the past research describing the male's struggle against the internal 'default female', stated "becoming a male is a prolonged, uneasy and risky adventure: it is a kind of struggle against inherent trends towards femaleness" (quoted by Fausto-Sterling, 2000, p.199). As I explored in Chapter Two, throughout history scientists have had different views as to when sex was determined. However by the 20th century it was established within endocrinology that the female form was the default morphology, which male hormones 'masculinised'. This paradigm was supported by genetic research which saw the early human embryo and its gonads as morphologically female and as requiring a genetic switch to activate testis formation which then produces masculinising hormones.

There is evidence that this view of the 'default' nature of the female directed genetic research away from certain questions. As described above, the TDF/SRY gene was tracked down over a seventy-year period, yet it was not until 1998 that the first gene required for female development was discovered, by accident. *New Scientist* reported the discovery with a news article entitled *There's more to being a woman than not being a man* and detailed how a well characterised gene, Wnt-4, was found to play a previously unacknowledged role in the development of the female morphology. The experiment, reported first in *Nature* (Vainio et al. 1999), consisted of breeding mice with a defect in Wnt-4, which was known to produce a protein important in the development of the foetal kidney. As expected the mutant mice of both sexes did not develop kidneys and died soon after birth from toxins in their blood. However, the female mutant mice also had differences in their reproductive system, as the Müllerian duct (precursor to uterus and vagina) lay dormant, and the sperm-carrying Wolffian duct matured instead. This discovery emphasised that the early embryo has both male and female pre-structures (the early Müllerian and Wolffian reproductive ducts) and that

development of male or female morphology requires, in both sexes, active degeneration of one or other of these structures (Knower et al. 2003).

One of the most important effects of this discovery of a gene required for female development was, as Eric Vilain stated in the *New Scientist* "(a) shift from being obsessed with the testis to becoming more interested in the ovary" (Knight 1999). Ovarian hormones also began to be seen as playing "an important role in development of the female brain". As the article 'The female phenotype : Nature's default?' states:

> The existence of an active ovarian influence on female development (which supplements passive feminization via the absence of testosterone) changes our assumptions and ideas about sexual differentiation and has important theoretical and scientific implications for the study of behavioural similarities and differences between the sexes, and their neural substrates. (Fitch et al. 1998, p. 212)

As the research focus changed, it revealed a greater complexity in sex genetics, emphasising that sex genes were not bound to the sex-chromosomes. As one scientific review article states in the abstract:

> (s)ince other genes, such as Wnt-4 and DAX-1, are necessary for the initiation of the female pathway in sex determination, female development cannot be considered a default process. (Sinisi 2003, p.23).

However the portrayal of the genetic sex determination processes, especially in the mass media, followed the model of conflict seen in the popular science books (see Chapters Three and Four).

> It looks like a battle occurs between the male and the female gene," McMahon says. "The winner determines sex." Wnt-4 is a leading general on the female side. When it functions normally, the gene suppresses the male sex system by preventing production of the hormone testosterone. At the same time, Wnt-4 initiates development of the Müllerian duct, which gives rise to the oviduct, uterus, and upper vagina. Apparently, the gene also plays a role in egg development; biologists aren't totally sure how this occurs. (Cromie 1999 online)

In Chapter Four I explored how within the popular science books the portrayals of an active conflict between males and females in evolutionary competition, and McMahon's comments seem to suggest that this is also seen as resulting in male and female genes.

I also noted in Chapter Four that the popular science books portrayed humans as being default female, and men having an 'internal female'. A modern example of Alfred Jost's comments regarding the 'default female' (see Chapter Two) is taken from an article entitled, "Soya is making our kids 'gay'":

> In fetal development, the default is being female. All humans (even in old age) tend toward femininity. The main thing that keeps men from diverging into the female pattern is testosterone, and testosterone is suppressed by an excess of estrogen. (Ruze 2006, available online)

The idea of people being biologically 'proto-females' has been used in fields such as psychology to support views of homosexuality as biological.

> What is the evidence that life begins for all of us as proto-females? We all have nipples, that's the evidence. As Leyner and Goldberg put it, "During development, the embryo follows a female template until about six weeks, when the male sex-chromosome kicks in for a male embryo." But before the end of the sixth week, a pair of sweat glands on the chest has already begun to differentiate as nipples. All infants are therefore born with nipples and some breast tissue. As they approach puberty, the female hormones that course through the bloodstream of girls reshape their body in womanly ways, including the development of their breasts. Males are left with vestigial nipples, a reminder that life begins for all of us as proto-females, and some of us are fated to become more masculinized than others. Undermasculinized men usually become gays. (Berman 2003, available online)

In the preceding chapter I suggested that sex determination and sex development as research topics have merged once again. It is clear that in the past the idea of the human form as default female has played a role within medical views of homosexuality, and it is likely that the findings that the early embryonic gonad is bi-potent with regard to its identity as an ovary or testis will be invested with a similar political motivation. As explored in Chapter Four, the idea that "humans are initially made female, but can be modified into males" (Bainbridge 2003, p.33) is still present in popular science, perhaps because it serves to represent the idea that 'we all begin in a shared form' and thus supports the idea of 'we're all human'. It is likely that the dominant political force will be able to set the agenda on how such knowledge is framed.

The genetic research on the development of the ovary has opened up questions regarding how female humans differ in their genetic processes from male humans. The realization that the embryo is not set as default to become female, but that the embryo is

bi-potent and active biological processes are ongoing in both the male and female form, means that sex is not located in a single gene. Thus, slowly the genetic view on sex has given way to the genomic understanding of sex as a morphology that relies on a network of genes, which are located across the genome (see Chapter Seven). However it would seem that the gaze of the researchers is still locked into a binary state.

8.3 Methylation

The basic difference in DNA sequences between the genomes of human females and human males is relatively easy to establish. I noted in Chapter Two that Dr David Page remarked that the genetic differences between man and a male chimpanzee as less than between a man and a woman (see Chapter Two). Therefore, genetic difference cannot be reduced to the presence or absence of a gene; rather, it is how genes are used by a cell that has a larger significance.

One of the most important impacts of the change from genetics to genomics has been the growing recognition that genetic processes can be regulated through other processes not dependent on base changes of the DNA (e.g. mutations). One such process is epigenetic regulation and inheritance, defined as the transmission of information from one generation to the next or during the organism's development through fertilization and cell division and not contained or 'encoded' within the holy grail of nucleotide bases of an organism's DNA or RNA. Most of the research has concentrated on a system called methylation marking, where the presence of methyl (CH3) groups on some cytosines are transmitted through one cell generation to the next. This is a type of chemical tip-ex or white out, where the cell modifies the backbone of the DNA so the cellular systems do not 'read' the gene, which renders those genes in the cell inactive. The methylation marking system is relevant for sex development in two important ways. First, methylation plays a major role in the inactivation of the second X-chromosome in female mammals. Second, methylation is associated with the 'imprinting' of certain genes, which refers to a kind of parent-specific methylation, where the cell selectively, and not randomly, uses genes that are inherited either from the mother or the father. The rest of this chapter will detail how research on methylation is harnessed to support the binary sex model and the view of genetic sex as fixed and static. It will be suggested that methylation challenges the binary model of sex and supports the idea of genetic sex as a dynamic process.

8.3.1 X-inactivation: From genetic sex to genetic processes

X-chromosome inactivation has become the cornerstone that supports a dichotomous, genetic notion of sex, even if inactivation could be understood in genomic terms to challenge the binary sex model. The test that was once used in the Olympic Games to detect the presence of the second, inactive X-chromosome to differentiate between females and males has shaped the notion of a biologically inactive female (see Chapter Two). Yet, it is questionable to what extent science supports the view that the extra X-chromosome is something non-functioning and redundant. Prestigious science journals, such as *Nature*, portray X-inactivation using metaphors, such as "Shutting up the X" or "A gene that gags the X-chromosome keeps females alive", that lend support to the binary sex-model (Clarke 2001). The popular and scientific media coverage of X-chromosome inactivation had a penchant for using verbs and nouns associated with sound, such as 'shutting up', 'a molecular gagging order', 'muffles', and 'silence', to describe the research, expanding the metaphor of DNA as information to the area of oral communication. Verbs such as silencing and gagging indicate a situation where genes are either 'silenced' or 'vocal' and either 'passive' or 'active'.

However, these metaphors do not do proper justice to the processes involved in the inactivation of the second X-chromosome. It is now known that the X-chromosome is inactivated into Barr Bodies at the 64 cell stage of the human female foetus (See chapter two for explanation of Barr Bodies). Evidence from mouse studies has shown that the first step of X-chromosome inactivation is the methylation (i.e. tip-ex/white-out) of most of its genes, through the production of RNA from a gene named Xist. The second step is the modification of the histones (e.g. structural proteins in the chromosome backbone one), which causes the X-chromosome to condense. Within 1 to 2 cell cycles most of the genes on the X-chromosome are silenced. The new found importance given to RNA in this mechanism is typical of the change from genetics to genomics. Genes can no longer be viewed as complete and self-standing DNA sequences or the first step of the linear track assumed by the so-called 'central dogma of molecular biology', which understands a one-way causal sequence from DNA to RNA to proteins. Instead, DNA is increasingly analysed within an interactive structural cellular network, in which factors such as chromosomal RNAs play an important part. Metaphors, such as gagging, which connote abrupt events, do not do justice to this interactive and processional nature of inactivation.

Furthermore, current research has revealed that the X-chromosome is not simply 'gagged' but that 19 percent or one fifth of the second X-chromosome is active (Graves 2000). Thus, the genetic difference created by the inactivation of the X-chromosome is not one of different gene products, but one of different levels of the product, as the genes that remain active in the second X-chromosome result in double dosage of those gene products. Currently these genes are called 'escapees', which brings into mind improper and unnecessary entities. However, the importance of these active genes is illustrated by Turner's syndrome, which afflicts women who lack the double dosage of these genes and who have short stature, lack some factors connected with reproduction, as well as lacking some spatial ability, which is attributed to the non-dominant (usually the right) cerebral hemisphere (Netley and Rovet 1992). Turner's syndrome illustrates that parts of the second X-chromosome remain active and that the active parts of it are not irrelevant left-overs but play an important role in the development and functioning of the organism.

Moreover, there are similarities between the second X-chromosome and the Y-chromosome. Researchers generally believe that 19 of the genes that 'escape' inactivation on the second X-chromosome have a related DNA sequence on the Y-chromosome. Also, while the male Y-chromosome has been historically characterized as active, parts of the Y-chromosome are also inactivated. Some of the same genes, such as synaptobrevin-like 1 gene, on the second X-chromosome, which are subject to X-chromosome inactivation are also silenced on the Y-chromosome in XY cells (Matarazzo et al. 2002). So, the same process of silencing or inactivation happens on the Y-chromosome, drawing attention to the way in which the X and Y-chromosomes may be different at the karyotype level, yet share similar processes and genes.

All in all, in the current science, X-chromosome inactivation seems to neatly conform to the old idea of female as the default developmental pathway and metaphors, such as 'muffling', reinforce the old idea of femininity as something passive and voiceless and masculinity as active and vocal. Similarly, the notion of silencing or gagging gives the impression of an 'event', consolidating the idea of sex determination as a decisive happening. However, what is radical about the research on methylation and X-chromosome inactivation is that it draws attention to its processual nature. So, sex determination is not an event but a process of sexing the early embryo. What is more,

both the X and the Y-chromosome go through the process of methylation and this process is never complete but results in some of the genes on the chromosome remaining active while others are inactivated. However, the idea of inactivation or sexing as a precarious and always incomplete process that affects both the X and the Y-chromosomes gets lost in explaining it in historically and culturally loaded terms of silencing the X or the woman.

8.3.2 Battle of the Sexes

Another process of methylation with gendered implication is imprinting, a kind of parent-specific methylation. This process is often described in terms of a 'genetic battle' between the sexes using vocabulary that resembles John Gray's (1992) popular self-help relationship bestseller, *Men Are From Mars And Women Are From Venus*.

When an embryo forms, it receives half of its chromosomes from the female and half from the male, and is thus diploid. The embryo has two copies of every gene on the non-sex-chromosomes. Which copy is used by the cell appears random; however this is not the case with imprinted genes. When the chromosomes are being packaged into sperm or egg cells the cellular machinery covers over certain genes with a chemical modification of the DNA backbone which 'hides' that gene from the cellular mechanism. This process called imprinting accounts for the fact that in some cases the cell uses specific genes because they are inherited either paternally or maternally.

The main framework for understanding the evolution of this cellular mechanism is the 'genetic conflict theory', which relies heavily on the binary sex model. The following statement by Dr. Shirley Tilghman, the researcher who first discovered an imprinted mammalian gene, explains the general idea of the theory: "This is an arms race where the weapons in the race are genes, where the protagonists are the parents, and where the battlefield is the placenta and the uterus" (Potier 2002, available on-line). The imprinted mammalian gene discovered in 1999 by Tilghman fits into this gendered assumption, as it produces the protein insulin-like growth factor II, a growth-stimulating hormone that plays an important role in embryonic growth. Researchers first discovered imprinting in insect genetics, but in mammalian genetics it was quickly translated into supporting the culturally laden assumption that a mother wishes for the offspring to be small to minimize her burden, while the father wants a large offspring to maximise the potential of his genes to survive. The spread of this theory into the mass media can be seen in the BBC's online news article *Gene battle may cause small*

babies' (BBC 2002). This article first discussed the health application of screening mothers, and then developed the gene conflict view, stating that

> (t)he more babies a woman has, the more chance there is that her genes will pass on to a further generation. However, having a baby places immense stresses on the body, and in times of poorer nutrition and health, having a bigger baby might reduce a woman's chance of surviving to give birth to many more. So, in theory, it would be advantageous to have higher numbers of slightly smaller babies. Equally, if a man was having babies with a number of different partners, it would be better for him to have as large a baby as possible with each. This means that the man and woman are in unknowing competition for the survival of their genetic code. (BBC 2002, available online)

The article goes on to describe a gene called IGF that comes from the father, terming it his 'weapon' in boosting the size of his infant. The heavily gendered presumptions underpinning the language of such reports are quite clear and gloss over the location of this gene on chromosome 11. This means that both sexes carry the gene, and if both copies were active it would result in an over-expression and potentially offspring too large to give birth to, while if both of the copies were inactive the under-expression would effect the formation of a healthy baby.

A second example of the genetic battle comes from behavioural genetics and research on 'nurturing genes'. The first report of the gene for this behavioural trait was announced 1996 under the title *The Nature of Nurture* as a "genetic switch for nurturing behaviour in mice" (Crown, 1996 available online). This article emphasized that what had been found was a 'genetic switch' for a hormonal pathway that is important to mother-offspring bonding and not a gene for nurturing. However, in 1999 it was reported, under the title, "Second 'Good Mother' Gene Found", "that males appear to have the upper hand when sexes battle over how much time to spend with the babies" (Fox 1999, available online). This story concerned the imprinted gene PEG 3 (paternally expressed gene 3) on chromosome 19. Genetically modified mother mice without PEG 3 do not exhibit nurturing behaviour, and their pups normally die. In 2001 Randy Jirtle and Susan Murphy, researchers in the Duke University Cancer Centre, reported in an issue of *Genomics*, that the related gene in humans is paternally imprinted as seen in mice. On the face of it, this seems to reveal that imprinting has an important role in behavioural expression, and thus have important implications for the biology of gender roles; however, some have argued that the imprinting mutation results in autistic behaviour which would then account for the observed lack of nurturing behaviour

(Hurst et al. 2000). The idea that the imprinting of nurturing genes reflects conflicts between the sexes has also come under criticism as a recent article points out that the 'nurturing gene' effects not the offspring but the grand-offspring and "grand-offspring are equally related to their maternal grandmother and to their maternal grandfather" (Hurst et al. 2000, p.116). So there is no evolutionary reason to expect "differential expression of paternally and maternally inherited genes that affect the fitness of grand-offspring through maternal care behaviour" (Hurst et al. 2000, p.116). As the authors of this article argue, other issues must be drawn on to explain imprinting of genes that influence maternal care.

The findings of both these examples related to the size of offspring and the idea of nurturing having a genetic cause are clearly politically and emotionally powerful. The 'genetic conflict theory' views the genetic battle as having evolved to control sex-specific gene expression in early embryos, and some researchers have expanded its impact to later developmental stages where the offspring is still reliant on parental protection.

What the story about imprinting tells us is how new biological knowledge easily gets interpreted in terms of old social tropes, such as the "battle between the sexes". The idea that paternal imprinting aims to render the foetus large or female foetuses nurturing is culturally appealing, because it conforms to a cultural idea of 'what men want' as well as the populist idea of genetics and evolution in terms of 'selfish' genes propagated by Richard Dawkins. However, the recognition that different tissues have different imprinting patters indicates that an alternative view is possible. It may be that certain tissues require one copy, while others require the amount of product produced by two copies. Thus the function of imprinting is to insure that only one copy of such genes is active in most tissues, while allowing other tissues the ability to use two copies as these tissues requires a higher level of the gene's product. This would lead to a picture a mutually beneficial outcome for both paternal and maternal points of view. Furthermore, what is interesting about imprinting is that it, again, highlights that DNA sequences only tell us part of the story, as cells may not use all genes and that the usage of genes may vary between different tissues and during the organism's life-cycle. Thus, the truly novel idea of viewing the meaning and role of genes not as parts of a stand-alone blueprint but as part of genetic and cellular processes gets lost in the rather stale stories about sex wars and weaponry.

8.4 From genetic sex to living sex

In the end, it seems that new genomic knowledge that might challenge old notions of sex determination gets interpreted within old social discourses underpinned by the binary sex model. Maybe what is needed are new metaphors to replace the old existing ones, such as switching on and off and silencing or battle between the sexes. It has been suggested that rather than describe DNA in terms of blueprint we should think of it as a 'jazz score', which rather than determine performance leaves plenty of room for playing or jamming the score differently in different contexts (Porta 2003).

The concept of a fixed and static genetic sex is also challenged by the simple observation that a cell does not use all the genes in its genomes at once, but rather the organism uses different genes at different times in its life cycle and depending on its environment. The point may be illustrated by considering those XX individuals who have the SRY (which is typically found on the Y-chromosome) on one of their X-chromosomes. Because the genes required for the typical male phenotype are not on the Y-chromosome, this gene is able to activate typical male genetic processes and a male phenotype results. A notion of genetic sex as related to the genetic process would understand the situation as the person being a genetic male, since his genetic processes are that of a typical male while his karyotype is non-typical male. Clearly, the concept of genetic sex is tightly linked within both society and science to the karyotype. While the validity of the sex karyotype has been challenged in the Olympic games, the analysis of the popular science books illustrated that it still underpins the tacit common sense understanding of binary sex within society and science as indicated by the success of popular science books advocating a tight connection between chromosomes and sex, and one would expect it to be resistant to change. However, the concept of a living genomic sex may be useful, where the stress is placed upon the genetic processes of the body.

CHAPTER NINE - THE FACT OF GENETIC SEX

> "The appearance of scientific facts as discovered things is itself a social construction, a made thing."
>
> (Ludwik Fleck 1979)

9.1 Introduction

Genetic sex, the apparent fundamental biological cause of the two male and female human varieties, is a 20th century construct. Looking down the microscope, the stained chromosomes are concrete countable entities and lend themselves easily to genetic determinism. As the chromosome composition of a human is generally understood as fixed at the time of conception, when a Y or X bearing sperm is united with the X bearing egg, a human's genetic sex is taken as permanent and unchanging throughout their life.

This thesis has sought to examine the concept of genetic sex, not to deny the existence of chromosomes associated with male and female sex determination and development in mammals, but to raise questions as to how these are understood and conceived of in terms of genes, genetics and social concepts. This chapter returns to the research questions proposed in the first chapter, paying particular attention to the five features I argued were key to how genetic sex is understood in our current society. The final section examines the research limitations of this study as well as indicating some further research questions which have been raised but that I have not attempted to answer here.

Main conclusions

What role has scientific knowledge played in how biological sex has historically been constructed?

Sex, as separate from gender, is often thought of as the 'physical' sex of the body as indicated by the body's morphological structures, genitals, gonads, secondary sex characteristics as well as chromosomes and hormones. I use the general term 'biological sex' when referring to this composite view of sex. 'Biological sex' is a historically and socially contingent concept which spans a wide range of research questions, from evolution and reproduction through to sexuality. The theoretical discussion in Chapter Two identified that for many historians the proposal of a one

sex /two sex shift occurring during the 18th century is an important framework for understanding the role which science has played in constructing, posing and researching questions related to biological sex. This model, proposed by Thomas Laqueur (1990) drew on the work of Londa L. Schiebinger who had shown that prior to the 18th century the dissections and reporting of human skeletons was not seen as sexed/gendered (for a detailed description see Chapter Two). Within a two sex model the body has a single unified 'true sex', and in cases of babies born with 'ambiguous genitals' scientific examination can reveal this true sex (Kessler 1998). According to Laqueur (1990) the shift towards the current two sex model was not brought about by changes in scientific knowledge, but rather by the wider social, cultural and political shifts which necessitated new scientific justifications for holding that men and woman were different. I have reviewed some of the changes which occurred to show that while science and technology may not have led the changes, scientific developments clearly helped to enable this shift.

I have some reservations regarding the proposal of a one sex /two sex shift. As noted in Chapter Two, I am unconvinced that there exists a suitable 'data trace' to fully explore the role(s) of science and technology in the ways in which sex and gender have historically been conceptualised. The data trace which is available relates to discourses tightly linked to a particular strand of medical practice carried out by learned physicians (descriptions of medical dissections etc). Since it is quite possible, and I would argue quite likely, that the majority of daily 'medical' practice incorporated other unwritten scientific practices and discourses, the lack of balance within historical traces of these other knowledge(s) may offer misleading conclusions as to how sex was viewed in science and other spheres of society.

The one sex/two sex shift is often used to support the view that the materiality of the body can be understood in different ways, and that scientific knowledge should not be taken for granted as advancing understandings. In my view scientific research has the potential to offer new understandings of the world and our biology, and in doing so may make possible a variety of new interpretations. Thus, as can be seen in the historical discussions of biological sex, science and scientific knowledge offered insights which have been used to emphases similarities or differences rather than to offer revolutionary new truths about the body (Harvey 2002). These perceived similarities and differences between bodies are deployed in support of particular narratives of how women and men

act and relate in current social structures. I proposed earlier in this thesis that these narratives could be best understood in terms of 'ideology'.

9.2.2 Sex 'ideology'

Ideology has been used by feminists to highlight the way in which gender is constructed and used in society. Bonnie Spanier has defined gender ideology as,

> a set of predominating beliefs specific to this moment in Western culture, in which male and female are considered a fundamental complementary pair of polar opposites. In this framework, male and female are inherently different from each other, with maleness assumed to be superior and associated with the natural controller, the action initiator, the "brains", as compared to the female as weaker, more passive, inferior. (Spanier 1995, p.3)

Unlike Spanier I would argue that there is not one predominant set of beliefs, but rather several competing systems of understandings, discourses, structures and views which people draw upon to order their daily lives. In this thesis I have used the term 'sex ideologies' to encompass the wider set of knowledge (including sex models of the human body), scientific and non-scientific beliefs which are used when the concept of 'biological sex' is invoked. In line with this I argue that in our current society there exists ideological diversity which allows the possibility to shift between disparate interpretations of the world and to refashion these interpretations.

The idea of sex ideologies, as artefacts of science, connects with broader discussions regarding the role(s) and function(s) of scientific knowledge and technology in the structure of societies. One example is John Dupré's notion of scientism, the "exaggerated and often distorted conception of what science can be expected to do or to explain for us" (2001, p.1). Science could be thought of as today's religion, offering both an explanation of how the world is and also, apparently following from this, normative directions as to how to live. As discussed in relation to the analysis of the popular science books, descriptions of biological sex do offer such politicised explanations to consumers of science culture.

Scientific knowledge not only offers explanations of how the world is, but also forms the basis for applied action, in the form of products and technologies. In this regard scientific knowledge has been central in creating what I have termed the *technology of*

genetic sex (Barr body testing and later the SRY gene) which was and still is used not only to order humans along sexed lines, but also to justify such ordering. Fiona Miller has explored this in terms of the use and acceptance of the Barr body in the 1950s as a marker for sex for intersex conditions. Miller (2006) argues that this was seen as a '*good enough'* tool and it was accepted because it supported rather than contradicted social views at the time. The observation that biochemical differences can be found between 'normal' male and female humans has been taken as justification for ordering them differently in social contexts, especially in those spheres which make use of some features of their physical bodies as illustrated in the discussion of the sexing of female athletes in the Olympic Games.

The question arises as to what extent can the political patterns of power embedded within genetic sex technology be challenged? Langdon Winner has noted that political qualities are embedded within technologies in the cases where "intractable properties of certain kinds of technology are strongly, perhaps unavoidably, linked to particular institutionalized patterns of power and authority" (Winner 1985, p.38). The current concept of sex is institutionalised within a number of patterns of power and authority based on the physical features of sex (gonads, chromosomes, hormones, etc). In theory these different characteristics produce a single unified biological sex, in which genetic sex is the fundamental 'essence' of sex. A number of authors have shown that genetic sex technologies do not take priority in deciding which sex the person or being is, but rather the decision is contextually based (Fausto-Sterling 2000; Kessler 1998). Challenges to this contextual basis are rare, however they do exist.

As many readers will be aware, in most Western legal systems there is a requirement that a person be registered as male or female and a person is not able to change sex unless medically diagnosed with certain conditions. However in 2002 Alex MacFarlane won the battle to gain an Australian passport which did not register sex as male or female, instead recognizing Alex's karyotype as XXY and sex state as being un-determined, not being male or female (Butler 2003). Alex argued that it was impossible to choose to be male or female, and to do so would be committing fraud. Rather than Alex's claim being a drastic challenge to the institutional structure that rests on the idea of a binary 'true sex', I would argue that it was accepted because it was supported by what is seen as a fairly rare karyotype variation. The flexibility of the binary institutional structure is seen also in the case of the Olympic Games where there is still

a fundamental separation between male and female athletes but where the institutional structures have adapted to include people with intersex conditions and transgender histories.

To summarise in relation to the first research question, it is clear that scientific knowledge is unlikely to have played a major role in *motivating* the historical shift from a one-sex understanding of the human body towards our current fixed binary model, if such a shift indeed occurred. However it is clear that within the 20th century scientific knowledge has been activated in support of social arguments regarding biological sex as well as being fundamental in the development of the technology of genetic sex, the essential justification and explanation of the binary fixed separation between male and female. Challenges to binary fixed institutional structures have been particularly successful in creating flexibility for what are seen as a relatively small number of cases (perhaps as they are seen as exceptions to the 'rule' of nature). However, the dominant sex ideology of there being a biological truth behind the binary, fixed and heterosexual power dynamic resists change.

What are the main features of Western view(s) of biological sex and 'genetic sex'?

Spanier's (1995) definition of gender ideology mentioned above introduced a fairly typical view of biological sex; where male and female are polar opposites in terms of gender roles and complement each other within reproduction. Much has been written criticising conceptions of biological sex particularly related to the concepts hetronormativity (Rubin 1975) and the heterosexual matrix and its role in structuring the performance of identities (Butler 1990). One of the main problems is that the sexual power structure of heterosexuality relies on the idea of sex differences between the female and male to structure desire and sexuality. While I am aware of such debates, my primary aim was not to argue 'how the world/nature really is', but instead to characterise how researchers conceived, structured and framed concepts such as biological and genetic sex.

It has been fruitful to structure this thesis's analysis around five features related to the characterisation of biological sex in the mammalian system, without worrying whether these features are real or not. It should be noted that these features are interlinked with each other. The first two features have already been mentioned; biological sex is seen as a binary category (male or female) which is fixed and unchanging. The third feature

is that sex is seen to 'mark' the whole body, not just the genitals and reproductive organs. Fourth, sex is seen as a meaningful category which applies throughout nature. The final feature, the inheritance of sex, was suggested by the early history of 'genetic sex'. To suggest these five features as being key to how sex is conceptualised is not revolutionary, indeed they have been the basis of much of the criticism that gender studies and feminist biologists have directed towards the concept of sex. Within the context of this thesis they have been useful for organising historical and contemporary developments and exploring the topics discussed in the popular science and journal articles. As will be shown in addressing the major research questions, the five features are not static constructs but rather have diverse meanings as well as being arranged in various forms to produce different narratives depending on sex ideologies.

9.2.4 How is 'genetic sex' communicated in popular science and what values and concepts are embedded?

'Genetic sex' is communicated in a wide range of popular science mediums including news articles and television documentaries as well as popular books. Some work has already been carried out related to the gendered use of metaphors to portray sex-based differences within popular science articles (Petersen 1999). However, little work has been done regarding popular science books and it was decided that for this thesis these would offer the greatest potential to access detailed 'lay' communication regarding 'genetic sex'. It was not the intent to present a comprehensive sample of the popular science field, but rather to highlight the range of values and concepts which were connected to 'genetic sex' within popular science. For this purpose it was felt that the analysis of three recently published popular science books was sufficient; *Y: The Descent of Men* by Steven Jones, *Adam's Curse* by Bryan Sykes, and *The X in Sex* by David Bainbridge.

Though the third research question of this thesis was directed towards exploring the concepts and values related to 'genetic sex', it is important to acknowledge that the type of values embedded in the books relate not only to biological/genetic sex, but also to the wider portrayal of science and genetics. As Felicity Mellor has explored, scientists conduct popular science as routine boundary work and "by working at multiple boundaries, texts such as these are able to claim potentially contradictory attributes for science at the same time as sustaining its place at the top of a hierarchy of ways of knowing" (2003, p.509). As would thus perhaps be expected, the books portrayed

scientific knowledge in a wholly positive light, with no discussion regarding its construction, while describing the scientists as undertaking a value-free exploration into nature. The books presented the opportunity for a type of 'good news' communication (see 3.2), where genetic knowledge could be linked to positive events to counter the more common role of genetic knowledge within news articles concerning disease and crime.

The main motivation for scientists writing popular science books is often seen as 'education' to increase public support for their work, as advocated under the 'deficit' model of public understanding of science. Initially it was assumed that the three popular science books analysed in this thesis were part of this movement, however it was found that a subtle shift has occurred. One of the clearest indications that the books were not seeking to educate the reader was their lack of visual diagrams. While one of the books did have six simple figures, in general all the editions were remarkable for their lack of diagrams, and this may stem from the publishing requirement for the books to look like novels (see Chapter Three). However the lack of diagrams also indicates a shift away from seeking to educate readers of the facts of science towards using a narrative story to describe and explain the subject matter. This is supported by Bainbridge's online webpages in which he notes, "My aim is to write books that can explain to anyone how we work" (Bainbridge .org).

This suggests a shift from the traditional goal of educating and explaining how nature works towards explaining how scientists and science work. The wider context of this shift is the failings of the deficit model to cope with the countless scientific news stories ranging across 'mad cows', bird flu, cloning, GM food etc. These stories have cast doubt on the capacity of science to adequately answer questions and concerns as well as seemingly lowering trust in the activities of scientists. Within this context the three popular science books are 'good news' communications, clearly aligned with and feeding into the tacit understandings general readers are likely to hold regarding sex, gender and sexuality.

Returning to the values expressed in the popular science books it is clear that the image of science being advertised is positive, however the analysis indicated that science was also portrayed against a Western Christian background. The covers include religious, artistic, athletic, and physical references which were predominantly drawn from

Western culture, including Christian creation myths, art images, and the idea of the male form as perfection. These visual images were complimented by written metaphors that related to war, marriage, divorce, politics, and transport. Apart from this standardisation of science as western and drawing upon a Christian history, the use of social concepts to explain and describe science allows for an overlap between questions of biological science and what could be seen as the area of social sciences, clearly seen in the lack of a distinction between gender and sex.

In regard to the concept of sex and gender, feminists have argued that a clear distinction can not be drawn between sex and gender (e.g. Hood-Williams 1996 see 1.2); however, the division is still seen as useful in general discussions. Yet within the popular science books the authors use sex terms (male and female) interchangeably with terms of gender (man and woman), often shifting between talking of biological bodies and social beings. The following quote shows not only how the authors shift between talking of biological bodies and social beings, but that the relationship between the two is seen as deterministic, with the social being an end product of biology. (The author is discussing the research to locate the SRY gene and the use of people with a particular intersex condition).

> [B]ut the fact remained that they did have a large chunk of y-chromosome – including a double helping of its long arm –and yet they were still women. That suggested that the sex gene could not be on the Y-chromosome's long arm. If it had been located there, these patients would not have been women, they would have been men instead. (Sykes 2003, p.63)

In general it would seem that the main interest for researchers was, as a BBC online newsarticle phrased it, what "made a male a man" (BBC 2001). Researchers were interested in the workings of social gendered beings, not just the biological formation of body morphologies. Alongside the interchangeable use of the terms 'female', 'woman', 'male' and 'man' which blur the boundaries between the social and scientific world, the descriptions of chromosomes, the Y-chromosome in particular, were linked to social, gendered symbols and values. This association between genetics and social gender discourses enables a connection to the wider social world and gives genetic knowledge relevance to the reader's life. While the blurring between social beings and biological bodies could be seen as stemming from a desire to support sexist descriptions of the differences between men and women as biological, I suggest that it should be seen in the context of the wider drive for scientific research to have relevance to the public who

are now primed to expect that it is relevant in some way to their life (e.g. cure diseases, solve starvation, create money, etc.). This is particularly significant as the popular science books were not only educational and entertainment products, but also served an important role in creating a market for commercial 'fringe products' (i.e. mDNA and Y-chromosome tracing). Regardless of the motivations for explaining genetic and biological features through social concepts and values, it must be noted that it may result in the reader prioritising biological explanations over social explanations.

It is clear that all three popular science books propagated narratives based on the idea of human bodies possessing a single unified 'true sex', being male or female. The authors expand from this biological basis to explain social divisions between men and women. Having explored the wider context of the concepts and values which the popular science books contained I will now move on to explore the five specific features I noted were key to how genetic sex is conceptualised.

9.2.5 The five features of 'genetic sex' in popular science

I have mentioned two features of biological sex which are invariably linked in current Western concepts, its fixed and its binary nature. There are a variety of binaries connected to the two sex model of biological sex: two separate genders, two separate body morphologies and two separate reproductive strategies. These binaries are considered to be maintained throughout the body's life as sex is genetically determined at conception and is fixed at that time. The popular science books offered descriptions which were in keeping with this standard view, where the male and female were seen as complementary opponents. While this could be seen as a rather contradictory view, it entails the two sexes being complementary in the action of sex but opponents in evolutionary terms. The idea of 'complementary opponents' is reflected in the metaphors used to describe the 'sex-chromosomes' as married and divorced, as well as the books' discussions of the natural 'fit' between men and women in current society.

The modern fixed binary sex concept is generally assumed not to offer overlap or flexibility between the two forms, but in the popular science books there is an overlap and flexibility between the two sexes. This overlap relies on the view of the default human morphology being female, and male development being an active struggle against this form. This view draws upon an endocrinological view of sex development where the early embryo is viewed as female and it is the presence of the SRY which activates the gonads to become testes which in turn secrete the male hormones needed

to push the embryo towards masculine development. While this is a fairly typical view, the popular science books indicate that the 'push' towards maleness is seen as required through the man's life.

> Men themselves evolve towards their wives as they age. The enzyme that transforms their prime hormone into oestrogen increase in activity with the years –which is why the ancient seem almost neuter, with a voice that turns again towards childish treble as the woman within at last makes her presence felt. (Jones 2002, p.76)

The body's biological morphology is thus not portrayed in the popular science books as fixed in the traditional sense but rather the books incorporated flexibility of the endocrinological changes which occur throughout the body as it ages and progresses throughout the lifecycles. While this flexibility is based on the biological-endocrinological working of the body, the Y-chromosome is seen to take part in this 'work': The Y-chromosome works hard to prevent men from turning into women (Sykes 2003, p.73).

This shift from seeing differences between the sexes (genders) as due to one sex possessing a genetic entity while the other does not, to the genetic units in the male 'working hard' throughout life, is similar to a change in rhetoric which occurred during the human genome project. Tora Holmberg (2005) has detailed how once researchers became aware that the human genome could not be maintained as more developed due to numbers of genes, researchers shifted towards arguing that human genes 'worked harder'.

The idea of male genes/chromosomes as working hard contrasts with the portrayal of the female genome which is described in two ways. One author, Bainbridge, describes females not through a unique working genetic unit, but rather by the internal conflict caused by possessing two X-chromosomes and thus two dosages of certain gene products (see Chapter Four). This internal conflict is resolved by X inactivation and silencing, again emphasising the female as embodying a lack of action and work. Another view is offered by Sykes who focuses upon the evolutionary genetic units. In his view the X-chromosome does not function as the genetic unit of the female as it is shared/inherited between and passed on by both male and female parents. Rather it is the mitochondrial DNA (mDNA) which is evolutionarily unique to the female (in that it is passed on only by the mother). However as the mDNA is also present in both males

and females and as such it can be used to define the female evolutionary being, but not the living female in the same way as the male can be defined as the living owner of the Y-chromosome. In both cases the narrative of the female clearly suffers from a lack of a distinctive genetic entity, which results in her failing to offer anything with which to counter the historical socio-evolutionary stories told by Sykes in which the powerful Y-chromosome shapes and defines human history through sex and aggression.

The third key feature to our view of biological sex is that it is seen throughout the body. In the popular science books the X and Y-chromosomes are not just biological markers which play an important role within specific tissues, but rather they are *actual* sex-chromosomes (see Chapter Four). Each of our cells holds these sex-chromosomes, and this strengthens the expectation that genetic sex is seen throughout the body. Bainbridge in particular makes reference to sex as resulting in differences in the hands of men and women, implying that for sexually dimorphic animals there must be a 'reason' or 'function' behind the differences, rather than emphasising the similarities between hands in general. The differing genetic essence of the male and female (lack of Y-chromosome, double dosages of X) are seen to result in clear sexual dimorphism which not only effects body morphology related to reproduction but also gender roles. Jones develops this in his discussions related to sex differences in brain structures, including crime, homosexuality etc. Sykes focus his attention on the role of sex in creating social structures, describing how the Y-chromosome has led to the 'domestication of women' and colonization.

The fourth feature is the idea that sex as a category can be meaningfully applied throughout nature. Animals are frequently used in the laboratory as metaphors and models of the biological body (Birke 1994). As Lynda Birke notes, since animal nature is assumed to be innate, animals can offer access to nature without the contamination of culture (1994). As Bonnie Spanier has argued, the findings from animals are often applied to humans without qualification:

> Scientists frequently make leaps between (nonhuman) animal research (for example, research on reproductive behaviour such as lordosis [mounting] in rats) and implications for humans, to the advantage of the predominant theories. Or with more subtlety, studies of rats, primates, and humans are cited *without* qualifying statements. (Spanier 195, p.73)

Anne Fausto-Sterling (2000) also offers an analysis of this use of animals within biological sex research in her book *Sexing the Body: Gender Politics and the Construction of Sexuality*. The chapter entitled 'A rodent's tail' explores how the laboratory rat has been constructed as a sexed object to represent the mammalian sex system and highlights how mammalian sexual expression relies on a complex biological and social context. Donna Haraway (1989) has explored the science of primatology, showing how there is a tendency to masculinize narratives related to reproductive behaviour in primates, while female primatologists focus on communication behavior. However of more relevance here is Haraway's (1997) use of the oncomouse, the first patented animal, as a cyber-invention, which brings to mind similarities with Randy, the XX transgenic mouse, which will be discussed further later in this chapter.

It is little surprise then that the popular science books show a similar use of animals as models for explaining sex. Sykes includes a Chapter entitled "Sex tips from fish", illustrating an alternative sex determination system, but in which he applies the shared categories of male and female as defined by the size of their gametes. The idea of a genetic sex which spans sex determination systems is seen in Sykes's descriptions of the honey-bee where he draws a clear parallel based on chromosomes:

> They have two sets of chromosomes, just as we do. They, like us, are diploid. Just like us, they inherit one set of chromosomes from their mother, the queen and one from their father, a drone. (Sykes 2003, p.78)

Sykes stresses the shared diploidness and sexed inheritance regardless of the fact that bees do not share the same sex determinism mechanism with humans. However this emphasis on the similarity in the workings of chromosomes between honey-bees and humans expands as Sykes 'naturalises' social and historical organization of humans as animals. This connects to the fifth factor I argued was key to our current view of genetic sex, that sex is inherited. The discussion regarding the three popular science books illustrated how the Y-chromosome was portrayed as 'handed down' from father to son. This supports the proportion that a son is more like his father than his mother, giving a genetic basis for understanding the shared sex and assumed shared sexuality. However connected with the idea of sex as inherited from parents is the requirement that the offspring have the potential capacity to also pass on their sex.

As the history of the two gene case studies showed the capacity to reproduce was an unspoken requirement of being male or female. Research attention was directed towards creating the sexed morphology (sexed gonads and genitalia) and once this was archived the requirement that 'Randy' could perform as a male was tested. The mouse's lack of viable sperm was not seen as a sufficient reason for it not to be considered male. Randy looked and behaved as a male and so was accepted as a male. The construction of the SRY as 'the master sex determination gene' was an attempt at pin-pointing the essential cause of sex, however this has failed. As with the shift from seeing the womb as an internal scrotum in the 18th century, the act of looking is primed in regard to expectations and anticipated (See Chapter Two). As finer tools became available, researchers deepen the levels of genetic analysis and explored gene expression to be explored over time. However rather than revealing fundamental or essential quality, researchers became aware that it was the connection and interplay between different biological characteristics (cellular morphology of the gonads, reproductive organs, hormones, external genitalia etc) which leads to a body which is social recognised and accepted as male, female or intersex.

The discussion as to whether Randy should be considered a male as he was infertile tap into a very strong social anxiety related to infertility and not being a 'real' man or woman. However such anxieties are stronger for those with intersex conditions. Within science binary sex and heterosexuality have long been accepted as the natural and correct determination and development of mammalian sex, with alternative physical and behavioural phenotypes being portrayed as 'mutations' and 'variations'. The expectation that genetic sex is 'naturally' binary and fixed in humans is highly apparent in the two case studies where differences rather than similarities were emphasised.

An alternative reading of genetic sex may lead one to view intersex conditions as natural variations. This decreases the perceived importance of the Y-chromosome for male development and has lead to the suggestion by Professor Jennifer Graves that the Y-chromosome may degenerate. This is supported by the existence of two species of field mice which have completely done away with SRY and the Y-chromosome, where the sex-determining genes are on a transposition. Graves has publicized the view that certain intersex conditions could be seen as part of human evolution, as the Y-chromosome disintegrates leaving humans to "separate into two different species" and that intersex individuals were potentially the "saviours of humankind" (ipdxWIRE

Intersex News 2003, available online). Intersex activists groups came out in force against being labelled 'a new species', arguing:

> We feel that the socially stigmatizing implication of suggesting that intersex people would become a "new species" outweighs any scientific merit this argument might have. (ipdxWIRE Intersex News 2003, available online)

It could be agued that this conflict is between the scientific concept of sex and sexual reproduction and the socially functioning concept of sex (being a woman or a man). There would seem to exist a notion of sex as 'natural' and biological. Graves' comments confirm that being capable of reproducing is critical to being considered as possessing a sex. Thus genetic sex is both the cause of sex, and the outcome of being able to reproduce. The capacity to reproduce validates any sexual form being seen as 'natural'. Intersex cases provide a rich building ground for an alternative views of gender, however historically the medical emphasis has been placed on denial, normaliztion and inclusion within the binary model. As noted, current research stresses the connection and interplay between different biological characteristics to form a body which is social recognised and accepted as male, female or intersex. This was my major concern when presenting the findings from this thesis, to convey that variations from the 'normal' sex determination and development of sex are likely to occur in us all and that there does not exist a single male or female as they are ideal types.

Within the popular science books the link between reproduction and sex is not only a shared biological relationship, but also social. Within Sykes's evolutionary narrative the idea of inheritance is key; however, it is questionable what is in fact being inherited. It is clear that not only is the Y-chromosome or the mDNA being passed down but also the sexual characteristics and their evolutionary benefits and those of associated traits.

> The Age of the Vikings has all the hallmarks of Adam's Curse: the insistent urge of men to mate with as many women as possible, and the intense rivalry among Y-chromosomes that ensues. (Sykes 2003, p.161)

As this quote indicates, behaviour and biological sex are reduced to genetics and inheritance of social systems through family ties; upbringing is not mentioned. As a result our current binary sex system which has become institutionalised is seen as a natural result of the evolutionary differences between males and females, and to reflect the division within nature in a neutral way.

The reader of the three popular science books is encouraged to perceive a tighter connection between the same-sexed parent and offspring (i.e. between females to female offspring and males to male offspring). This linkage creates interest for the reader in their own historical family which I would suggest has a more economic incentive. As I noted in Chapter Three, companies have been set up to trace the mDNA and Y-chromosome and the books play an important role in creating an economic market for such tracing.

To summarise in relation to the second and third research questions, the accounts of biological sex and genetic sex in the three popular science books indicate that there are variations to the established view of biological and genetic sex as fixed and binary. The construction of biological and genetic sex as fixed depends on context, and these books offered explanations in which biological and genetic sex was changeable, potentially even fluid. However they drew on a hidden narrative of the body having a 'true' sex which was changeable in terms of the male body aging and turning to female. The concept of binary sex, composed of males and females, was for certain research questions based on gamete size, for others similarities in chromosomal genetic sex. The acceptance that the logic of sex and binary sexual reproduction spans throughout nature has lead researchers to drawing on very different systems to justify both binary sex differences in terms of physical morphologies, and also binary gender roles.

9.2.6 What metaphors and values are used in scientific journal articles to communicate genetic sex?

As Evelyn Fox Keller (1992) has discussed, the practice of science takes place within the context of a shared language which involves membership within a conceptual universe. These scientific ideas and concepts become stabilized in the use of similes and metaphors. The analysis of the two case studies illustrated the extent to which the concepts and values of a binary and fixed genetic sex are contextually based within sex determination research (full analysis is reported in Chapters Five, Sex, and Seven). In this section I will explore how genetic sex has developed and, with particular reference to the five key features, the changes in concepts and values within the research.

Research into sex determination was based on the view that sex was found throughout nature. On this basis, animals as representatives of nature could be taken into the laboratory and experimented with. Not only were animals such as fish, moths, birds, and

snakes useful as 'natural models' of evolutionarily related sex determination systems, they were also experimental tools for surgical interventions (removing or transplanting gonads) and breeding experiments (in particular the creation of 'intersex' moths). As the different sex determination mechanisms became segregated, the cause within chromosomal based systems became constructed as either dosages of X-chromosome or, as in the mammalian case, the 'testis determining factor' (TDF). The chromosome theory of biological sex dictating that the sex of a person was only dependent on the presence of the Y-chromosome and the early genetic research into the identity of the TDF relied on exploring similarities and differences between male organisms of differing types (i.e. snakes, birds and mammals). As technology developed the emphasis shifted towards narrowing down and locating the genetic entity which caused sex determination through analysing the DNA related to the Y-chromosomes in humans with intersex conditions.

The dominance of the fixed and binary view of sex determination resulted in researchers hunting for the gene *necessary and sufficient* to determine maleness in the mammalian system. During the 1970s and 1980s there were a number of suggestions as to the identity of the TDF, including the H-Y antigen. Genes increasingly became seen as unified biological agents and causal principles in themselves (Waldby 2001) and the TDF increasingly became seen as a single DNA gene, defined not by the function of its product but by its presence in the genome of people who had intersex conditions. The first such sequence, ZFY, proved not to be the TDF; however it did introduce the notion of a single 'master' gene for sex determination and the second suggestion, the SRY, was placed within this discourse. To prove that the SRY was in fact the TDF, researchers created Randy, a mouse produced from a fertilized female egg which was injected with the DNA sequence SRY. As the discoverer of the SRY and the creator of Randy stated, "SRY is the only gene you need on the Y-chromosome to develop testes and become male" (Andrew Sinclair quoted in Beale 2001). However sex determination was not only about creating a male morphology (possessing a penis), but as the testing of Randy's sexual behaviour, showed the importance the scientists attached to aligning sexual physiology and sexual behaviour in the service of a unified concept of sex. *Nature*'s editors made the explicit requirement that if the SRY was the TDF then the 'XX +SRY mouse' must perform as a social/sexual male (see Chapter Seven). However, while sex and gender had become linked, Randy was accepted as male while being infertile.

The predominant metaphor related to sex determination is that of the 'master gene'. The use of the 'master' metaphor in the headline reporting of the SRY brought to the fore the patriarchal construction of sex as it was based on locating the genetic cause of the male form, disregarding the female form as a passive development and determination. The differentiation in the 1970s between the terms sex and gender had done little to challenge this assumption, focusing gender studies on the construction of gender, rather than sex. However in the last two decades the study of sex and sex differences has been revisited by feminists, leading some to conclude that

> valid and demonstrable claims cannot be made about sex-determination, but rather that cultural assumptions regarding the relative status of men and women and the binary relation of gender itself frame and focus the research. (Butler 1990, p.109)

After the discovery of the SRY criticism of binary sex increased, drawing predominantly on intersex cases. Thus Fausto-Sterling (1993) suggested to a science audience that there existed as many as five sexes including males, females, herms (hermpaphrodites), merms (male pseudohermaphrodites), ferms (female pseudohermaphrodites). This expansion of the two sexes to five failed to break from basing sex on phenotypic aspects of the body (i.e. ovaries or testes) and it was not pursued. Within science journals non-binary sex explanations remained unwelcome (Spanier 1995) and the analysis of the two case studies found that the majority of the 'high status' articles described sex as fixed and binary, determined by genetic sex at conception.

To fully understand the research into sex determination it is important to recognise that the research was not only located within a gendered framework but also within the broader paradigm of molecular genetics. Chapter Seven explored how the two gene case studies exhibited typical features of this wider context, especially when researchers reported on the materiality, functionality and their apparent hierarchal relationship of the genes to other cellular components. Within embryology and developmental molecular genetics, the concept of 'master genes' was an accepted structure for understanding how linear gene pathways were structured and controlled. Feminists have focused on the SRY as *the* sex determining gene. However, when researchers became interested in DAX-1 within the context of sex determination and development it was considered a possible female 'master' gene. It is possible that this labelling raised

the status of the gene which the researchers were concerned with, and thus raised their own status within the research community although further research would be needed to confirm this.

The discovery of DAX-1 as an important sex determining gene did challenge the view of binary genetic sex. The realisation that some 'sex-reversal' cases were not caused by mutations or translocations of the SRY raised the possibility that the X-chromosome may play an active role in the sex determination system. The idea of the DAX-1 acting as a master gene for female sex determination would seem to have challenged the idea of the SRY as the master gene for sex as a whole. However its role within sex determination was aligned with dose sensitive genes, which were characterised as left over from the more primitive female sex determination system in which X-chromosome dosage determines sex (as in some insects).

The traditional way of thinking about binary genetic determination systems had been on the absence or presence of a specific gene. However as the link between DAX-1 and dose sensitive genes increased it became clear that the female morphology was the result of an active genetic developmental pathway, with its own 'switch'. Potentially this supported the view that while sex determination was binary, it was composed of two active and separate gene pathways, one for the female and one for the male. However researchers were aware that there was overlap between the genes involved in the two pathways, and DAX-1 became characterised as a master sex determining gene for its anti-male rather than pro-female qualities. Thus DAX-1 as a switch was not a female on-switch but rather a male off-switch. This once again defined the female sex determination pathway in opposition to the male. As evidence grew that DAX-1 was not in fact anti-male but required for testis development this view of two separate hierarchal gene pathways was challenged and DAX-1 incorporated into the male gene pathway as a regulator of SRY. The researchers moved towards considering the differentiation of cell types in tissues and sought to understand how the gonad formed into a *functioning* testis, that is one that produced testosterone, as indicated by genital formation and sperm, rather than simply an external gonad. While the SRY gene could produce Randy, researchers became interested in the wider context of the genes which maintained the male reproductive phenotype. The requirements of the male sex determination pathways are not only that they produce a male by sight and sexual behaviour but also by reproductive function.

The view of a fixed binary genetic sex also relies on a particular characterisation of genetic control. As I noted, the concept of master genes of regulation in development was a dominant paradigm and should not be considered unique to sex determination. However the case studies showed that initially the researchers did hold a deterministic view of the relation between the traits they were interested in and the DNA sequences they were trying to locate. However the wider research field of molecular genetics was increasingly adopting a more context based view of gene action, and thus as the research progressed genes in general lost their absolute control. As the case studies showed, the traditional concept of 'gene control' had been one in which the gene had a 'responsibility' for a trait, and this shifted towards the gene 'playing a role in' trait formation and even having a indirect role, as a 'recruiter' to genetic cascades. Thus in the later articles, where it was clear that the SRY in a XX genome did not produce a reproductive male, SRY was seen as working within a window of opportunity and working within the wider sex determining genetic cascade. Genetic sex in this view was still fixed. However it did not occur at one specific time point (i.e. conception), but rather the products of different genes were required at different time periods.

As sex determination research expanded to include a wider set of genes, so too did the number of locations and contexts in which the genes were active. One experiment reported that as many as 120 genes are likely to interact with each other in producing sex morphologies in the mouse embryo. This, coupled with the shift towards sex genes being described as working within a temporal window of opportunity and the wider tissue context of the 'reproductive axis'; have reunited the research topics of sex determination and sex development.

To summarise, the five features of genetic sex have not disappeared but mutated. The logic of heterosexual biological sex is clearly assumed to span the sexually reproducing natural world, and has proven fundamental to research on sex determination and sex development. While early researchers sought to draw similarities and differences between types of animals, modern research has been based on drawing evolutionary narratives particularly related to social structure and the disappearing male/ Y-chromosome. Sex determination is still seen as binary, but with two active pathways that share the majority of their genes. Sex determination is still seen as fixed, but fixed at different time periods, and with the possibility for revisiting the fixing. The sex

determination pathway has shifted away from its traditional emphasis on the formation of the testis to the wider body. Sex determination and sex development as research topics have merged to include the development of the reproductive axis, which includes gonads and brain structures, linking sex determination with endocrinological development. This potentially creates a powerful explanation of how, through genetic sex, sex differences in the gondads, genital, and brain (i.e. reproductive axis) are the product of evolutionary genetic specialisation.

What is the impact of genomic knowledge on the features of genetic sex?

While there is confusion as to how genomics as a research field is defined, it is generally agreed that it combines techniques from genetics, molecular biology and bioinformatics, transforming a traditionally one dimensional study of single genes into a multi-dimensional study of genetic processes paying particular attention to issues of time and space. The concept of genetic sex, which currently supports a fixed two sexed view of the human body, could be threatened by genomics and to explore this possibility Chapter Eight paid particular attention to the genomic processes of imprinting and the silencing of the second X-chromosome in the female genome. It was found that while genomics does offer evidence as to the complexity of sex differences, the results are conceptualised within the traditional binary sex model. However, as with the two gene case studies, genomics challenges the traditional concept of a fixed and binary genetic sex on a number of levels.

Firstly, genetic sex (XX, XY) was conceptualised in relation to the difference between the male genome as defined by the presence of the Y-chromosome and the female as the absence of the Y-chromosome. The shift from defining genetic sex in terms of the Y-chromosome to the SRY gene also supports this view of sex difference. However at the genomic level there seems very little difference between female and male humans, at most 20-30 genes of the Y-chromosome (of which most are 'housekeeping genes') and a few double dosage genes on the X-chromosome. Though it may be true that the Y-chromosome has key genes in spermatogenesis, the genes which function in making the human foetuses into a phenotypic male seem to be located on the non-sex-chromosomes. Sex difference in genomic terms includes factors such as the genetic composition, the transcription of genes, and the biochemical pathways.

Secondly, while genetic sex is considered determined at conception, taking genomics into account sex determination and sex development cannot be separated. As the studies showed, sex is not decided at a single time point, but rather it is an ongoing process which the body performs. Genomics stresses that genes are not functioning in a local nuclear environment but in a genomic one, so it is no surprise that sex-determining genes seem to be spread over other chromosomes (i.e. 9p24, 9q33, 11p15, 17q25). Rather than the traditional concept of a genetic pathway, the later research articles describe sex in terms of genetic networks. Thus the SRY gene, or any other gene, should not be taken in isolation but rather as a unit which functions within a complex, multidimensional developmental cascade. This moves away from the Mendelian genetic approach, which defines genes in terms of phenotype traits, and moves towards a position in which a phenotype is a result of many genes as well as environmental factors.

Thirdly, moving towards a concept of living genetic sex follows Fausto-Sterling's call to recognize that nature and nurture cannot be separated. Within genomics, genetic processes cannot be separated from the cellular environment in which they occur, nor can they be separated from the local (tissue) and global (body) environment in which they occur. The genetic mechanisms and knowledge explored in Chapter Eight suggests that the concept of genetic sex should be seen in terms of a lived process and life cycle, where different genes are expressed at various levels interacting with the cellular and outer environment.

9.2.9 Conclusions

Chapter Seven opened with a quote by Alan Sokal in which he challenged social constructivists to test gravity by walking out of his window. During my PhD I have often felt like posing a similar challenge to fellow PhD students who discount biological/genetic sex as purely an illusionary feature of human bodies. However as this chapter's opening quote by Fleck indicates, quite rightly, many feminists have quite rightly challenged concepts including sex, gender, biological sex, and sex differences as well as highlighting how scientific facts are co-constructed by the social word. However the extreme social constructivist view in which it is denied that natural selection and sexual reproduction have created two sex forms of the human species, hinders the discussion of why the social world should reflect the structures of both the 'natural' and the 'biological' world.

I have argued that the two research questions of sex determination and sex development have once again merged, and so too have sex and gender. The concept of 'genetic sex' could be placed within the performance of doing sex, to show how genetic processes facilitate and enable the body in its 'doing' of gender. Butler's theory of gender performativity holds that gender and sex are fluid and variable over time and place. A person's every day surroundings and activities shape their expression of sexuality and gender, and biology cannot be divorced from this play. This thesis has taken the stand that genetic processes are an important actor within gender performativity, one which denies the passivity of the body. In Butler's later book, *Bodies that Matter* (1993), she argues that sex is a social and cultural norm, which is expressed on the surface of the body. This thesis has shown that the apparently fixed nature of sex biology is part of the scientific cultural norm, forming genetic sex as an inner, core identity of fixed sex-chromosomes. The new genomic approach to genetic sex holds potential to recast sex in terms of genetic processes, which are deeper than the skin of gender performance, reaching, connecting and moulding both body and culture. Butler has noted that

> (g)ender ought not to be conceived merely as the cultural inscription of meaning on a pre-given sex (a juridical conception); gender must also designate the very apparatus of production whereby the sexes themselves are established. (Butler 1990, p.7)

In Butler's view, sex/gender should be conceptualized in terms of 'doing' gender. Within the field of endocrinology, sex is viewed as relatively fluid and capable of being seen in as involved in the body's biological performance of sex. This contrasts, however, with the current view of 'genetic sex' as fixed, a view based on the idea that 'sex' is an adult phenotype determined by an underlying genotype.

Greater acknowledgment of the fluid and dynamic nature of genetic processes would allow sufficient flexibility to recognise that a person's sex is not an inert mark on their birth certificate, but a composite of self-identity and changing biology that is constantly used when applying for jobs, going to the public toilet and taking medicine. Instead of forcing congruency between the four commonly assumed properties of sex -gonads, genitals, chromosomes and brain- a deeper understanding should be developed of how they relate and form under influence from each other, e.g. through the influence of hormones on the brain. Such an idea would also incorporate the biological changes that take place during sexual maturation, pregnancy, transgender surgery, menopause, etc.

This holds the potential to recast sex and the body from objects of study into actors, and to transform the sex-chromosomes from static sex markers into parts of the genome which, as dynamic genetic entities, interact with the physical body through biological processes.

Throughout researching this thesis I have considered how to incorporate the idea of genetic sex as fluid and dynamic into current social and cultural concepts. The concept of a living genetic sex, based on genetic processes occurring in the human body throughout its life cycle would diminish the idea that a child is sexed in the same way as an adult, as well as restoring the link between genetic processes and the environment in which they occur. With the developments in the Olympics it is clear that the era of genetic testing to prove femaleness is at an end. The proposal approved this year, 2004, by the IOC executive board, allows athletes who have undergone a sex change and undergone two year postoperative hormone therapy to compete in their chosen gender. Being born female or male no longer governs one's identity, and equally as biological cyborgs we do mutate our sexual biology from the seemingly slight changes through contraception pills to severe surgical operations, and these in turn influence our genetic processes.

9.3 Research Limitations and further research

A number of research limitations and further areas of interest have already been highlighted at suitable points in this thesis. However in this final section I will address three main limitations of this thesis.

The first limitation is related to the trade off between scope and depth. This is always an issue when undertaking research and a balance must be struck as directed by the research questions. In this case rather than taking a detailed look at a specific period this thesis has explored the history of biological sex and 'genetic sex' over 100 years. This was not the initial intention, rather the gene case studies were chosen with the rather naive assumption that their 'history' was less than 20 years long. As a result a level of specificity has been lost and questions have become apparent that that have not been addressed here. In relation to the historical basis of 'genetic sex' these include questions related to:

1. The connection and relationship between research into sex determination in the United states and Europe in the early 1900s
2. The construction of the 'intersex' moth and other 'neutral' animals
3. The division between different sex determination systems
4. An analysis of the original Danish articles in which the TDF was proposed.

The second concern is related to the lack of 'first hand' accounts of the research procedure. This focus would have been interesting, but I felt it was not necessary within this limited project to interview the researchers involved. In this regard this thesis was directed to the narratives that the researchers themselves produced. Also, the selection of popular science books was not based on a comprehensive survey, and it would be useful to deepen the analysis by exploring books written by a wider range of authors. I have noted in Chapter Three that all three authors are male white scientists who are tacitly identified as heterosexual. This research could be broadened to include recently published books by scientists who do not fit this traditional background (i.e. Joan Roughgarden and Bruce Bagemihl) as well as examining popular books within gender studies (e.g. Anne Fausto-Sterling's work). Building upon the research presented here it is now possible to further develop a network analysis of the research actors' locations and positions. Suggestions for future areas of study include in-depth analysis of the institutional pressures, collaborations and conflicts which surround genetic sex research, the norms and values held by the researchers in the laboratory, and increased research into the empowering and enslaving potential of personal sex genetic knowledge.

The final concern relates to the value of this thesis outside of the academy. Initially it was hoped to have greater involvement of people with intersex conditions, particularly in relation to their experience of the research environment. However due to problematic access it was felt that a focus on scientific communication would be more useful. While I still consider it important to explore people's experience of being involved within the research context, by donating biological samples etc, at the end of this thesis I recognise that academic projects such as PhDs have little to offer by way of 'empowerment' or regaining 'ownership' over research paradigms for patients, unless this is specifically addressed. However as is clearly shown by the work of academic 'intersex' activists such as Alice Dreger, there is a number of activities and ways in which academics can become involved and be of use to those who come into contact with research.

GLOSSARY

Unless stated otherwise the terms in this glossary are taken from the Genetics Education Centre, University of Kansas Medical Centre (http://www.kumc.edu/gec/glossnew.html**).**

Allele: An alternative form of a gene; any one of several mutational forms of a gene.

Amino acid sequence: The linear order of the amino acids in a protein or peptide.

Amplification: Any process by which specific DNA sequences are replicated disproportionately greater than their representation in the parent molecules.

Autosome: A nuclear chromosome other than the X- and Y-chromosomes.

Barr body: The condensed single X-chromosome seen in the nuclei of somatic cells of female mammals. base pair a pair of hydrogen-bonded nitrogenous bases (one purine and one pyrimidine) that join the component strands of the DNA double helix.

Base sequence: A partnership of organic bases found in DNA and RNA; adenine forms a base pair with thymine (or uracil) and guanine with cytosine in a double-stranded nucleic acid molecule.

[Bmk Sequence: Bkm (banded krait minor satellite) was a repetive sequence of DNA which was frist discovered in the banded krit snake.]

Carrier: An individual heterozygous for a single recessive gene.

cDNA: Complementary DNA produced from a RNA template by the action of RNA-dependent DNA polymerase.

Centromere: A region of a chromosome to which spindle traction fibers attach during mitosis and meiosis; the position of the centromere determines whether the chromosome is considered an acrocentric, metacentric or telomeric chromosome.

Chromosome: In the eukaryotic nucleus, one of the threadlike structures consisting of chromatin and carry genetic information arranged in a linear sequence.

Chromosome banding: A technique for staining chromosomes so that bands appear in a unique pattern particular to the chromosome.

Clone: Genetically engineered replicas of DNA sequences.

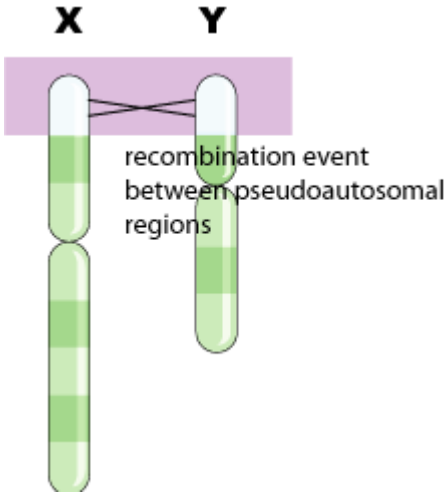
Cloned DNA: Any DNA fragment that passively replicates in the host organism after it has been joined to a cloning vector.

Codon: A sequence of three nucleotides in mRNA that specifies an amino acid.

Cosmids: Plasmid vectors designed for cloning large fragments of eukaryotic DNA; the vector is a plasmid into which phage lambda cohesive end sites have been inserted.

Crossovers -- the exchange of genetic material between two paired chromosome during meiosis.

Figure 4.1. Recombination between the X and Y chromosome in the human (from **www.scq.ubc.ca/?p=491**



Cystic fibrosis: An autosomal recessive genetic condition of the exocrine glands, which causes the body to produce excessively thick, sticky mucus that clogs the lungs and pancreas, interfering with breathing and digestion.

Deletion: The loss of a segment of the genetic material from a chromosome.

Deletion maps: The use of overlapping deletions to localize the position of an unknown gene on a chromosome or linkage map.

Dose specific genes: genes which produce affects dependent on how many copies of the gene are present in the cell.

DNA hybridization: A technique for selectively binding specific segments of single-stranded (ss) DNA or RNA by base pairing to complementary sequences on ssDNA molecules that are trapped on a nitrocellulose filter.

DNA probe: Any biochemical used to identify or isolate a gene, a gene product, or a protein.

DNA sequencing: "Plus and minus" or "primed synthesis" method, developed by Sanger, DNA is synthesized in vitro in such a way that it is radioactively labeled and the reaction terminates specifically at the position corresponding to a given base; the "chemical" method, ssDNA is subjected to several chemical cleavage protocols that selectively make breaks on one side of a particular base.

Dominant: Alleles that determine the phenotype displayed in a heterozygote with another (recessive) allele.

Down syndrome: A type of mental deficiency due to trisomy (three copies) of autosome 21, a translocation of 21 or mosaicism.

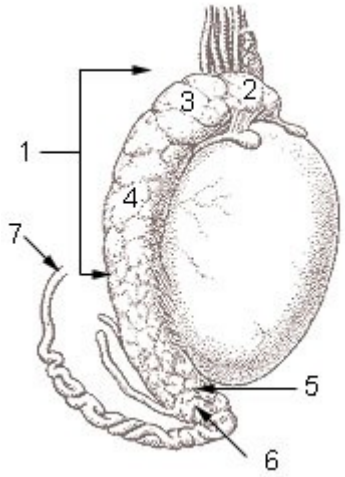
Duchenne/Becker muscular dystrophy: The most common and severe form of muscular dystrophy; transmitted as an X-linked trait. X-linked recessive. Symptoms include onset at 2-5 years with difficulty with gait and stairs, enlarged calf muscles, progression to wheelchair by adolescence, shortened life span.

Endonuclease: An enzyme that breaks the internal phosphodiester bonds in a DNA molecule.

Euchromatin: The chromatin that shows the staining behavior characteristic of the majority of the chromosomal complement.

Exons: Portion of a gene included in the transcript of a gene and survives processing of the RNA in the cell nucleus to become part of a spliced messenger of a structural RNA in the cell cytoplasm; an exon specifies the amino acid sequence of a portion of the complete polypeptide.

[Epididymi:
http://training.seer.cancer.gov/ss_module11_testis/unit02_sec01_anatomy.html



1: Epididymis
2: Head of epididymis
3: Lobules of epididymis
4: Body of epididymis
5: Tail of epididymis
6: Duct of epididymis
7: Deferent duct (ductus deferens or vas deferens)]

FISH: Florescent in situ hybridization: a technique for uniquely identifying whole chromosomes or parts of chromosomes using florescent tagged DNA.

5' - end : The end of a polynucleotide with a free (or phosphorylated or capped) 5' - hydroxyl group; transcription/translation begins at this end.

Fragile-X syndrome: X-linked trait; the second most common identifiable cause of genetic mental deficiency.

Gamete: An haploid cell.gel electrophoresis the process by which nucleic acids (DNA or RNA) or proteins are separated by size according to movement of the charged molecules in an electrical field.

Gene: A hereditary unit that occupies a certain position on a chromosome; a unit that has one or more specific effects on the phenotype, and can mutate to various allelic forms. [note this is a standard definition based on the classical genetic view of a gene]

Gene amplification: Any process by which specific DNA sequences are replicated disproportionately greater than their representation in the parent molecules; during development, some genes become amplified in specific tissues.

Gene map: the linear arrangement of mutable sites on a chromosome as deduced from genetic recombination experiments.

Gene therapy: Addition of a functional gene or group of genes to a cell by gene insertion to correct an hereditary disease.

Genetic linkage map: A chromosome map showing the relative positions of the known genes on the chromosomes of a given species.

Genetic variation: A phenotypic variance of a trait in a population attributed to genetic heterogeneity.

Genome: All of the genes carried by a single gamete; the DNA content of an individual, which includes all 44 autosomes, 2 sex chromosomes, and the mitochondrial DNA.

Genotype: Genetic constitution of an organism.

Germ cell: A sex cell or gamete (egg or spermatozoan).Haldane equation Haldane's law: the generalization that if first generation hybrids are produced between two species, but one sex is absent, rare, or sterile, that sex is the heterogamic sex.

Heterozygote: Having two alleles that are different for a given gene.

Hemophilia: A sex-linked disease in humans in which the blood-clotting process is defective.

Heterogeneity: The production of identical or similar phenotypes by different genetic mechanisms.

HGP: Human Genome Project.

Homologous chromosomes: Chromosomes that pair during meiosis; each homologue is a duplicate of one chromosome from each parent.

Homozygote: Having identical alleles at one or more loci in homologous chromosome segments.

Housekeeping genes: Those genes expressed in all cells because they provide functions needed for sustenance of all cell types.

Hybridization: The pairing of a single-stranded, labeled probe (usually DNA) to its complementary sequence.

Imprinting: A chemical modification of a gene allele which can be used to identify maternal or paternal origin of chromosome.

Incomplete penetrance: The gene for a condition is present, but not obviously expressed in all individuals in a family with the gene.

In situ hybridization: Hybridization of a labeled probe to its complementary sequence within intact, banded chromosomes.

Introns: A segment of DNA (between exons) that is transcribed into nuclear RNA, but are removed in the subsequent processing into mRNA.

Klinefelter syndrome: An endocrine condition caused by a an extra X-chromosome (47,XXY); characterized by the lack of normal sexual development and testosterone, leading to infertility and adjustment problems if not detected and treated early.

Karyotype: A set of photographed, banded chromosomes arranged in order from largest to smallest.

Linkage: The greater association in inheritance of two or more nonallelic genes than is to be expected from independent assortment; genes are linked because they reside on the same chromosome.

Linkage: Analysis of pedigree the tracking of a gene through a family by following the inheritance of a (closely associated) gene or trait and a DNA marker.

Meiosis: The doubling of gametic chromosome number.

Methylation: Addition of a methyl group (-CH3) to DNA or RNA.

Missense mutation: A change in the base sequence of a gene that alters or eliminates a protein.

Mitochondrial DNA: The mitochondrial genome consists of a circular DNA duplex, with 5 to 10 copies per organelle.

Mitosis: Nuclear division.

mRNA: Messenger RNA; an RNA molecular that functions during translation to specify the sequence of amino acids in a nascent polypeptide.

Multifactorial: A characteristic influenced in its expression by many factors, both genetic and environmental.

Mutation: Process by which genes undergo a structural change.

Nonsense mutation: A mutation in which a codon is changed to a stop codon, resulting in a truncated protein product.

Northern analysis: A technique for transferring electrophoretically resolved RNA segments from an agarose gel to a nitrocellulose filter paper sheet via capillary action.

Nucleotide: One of the monomeric units from which DNA or RNA polymers are constructed; consists of a purine or pyrimidine base, a pentose sugar and a phosphoric acid group.

[Nuclear hormones: Nuclear hormone receptor proteins form a class of ligand activated proteins that, when bound to specific sequences of DNA serve as on-off switches for transcription within the cell nucleus. These switches control the development and differentiation of skin, bone and behavioral centers in the brain, as well as the continual regulation of reproductive tissues.]

[Orphan receptor: Orphan receptors are apparent receptors that have a similar structure to other identified receptors but whose ligand (chemical molecule which the receptor needs to work) have not yet been identified. If a ligand for an orphan receptor is later discovered, the receptor is referred as "adopted orphan receptor".]

PCR: Polymerase chain reaction; a technique for copying the complementary strands of a target DNA molecule simultaneously for a series of cycles until the desired amount is obtained.

Phenotype: Observable characteristics of an organism produced by the organism's genotype interacting with the environment.

Physical map: Map where the distance between markers is the actual distance, such as the number of base pairs.

PKU: Phenylketonuria, an enzyme deficiency condition characterized by the inability to convert one amino acid, phenylalanine, to another, tyrosine, resulting in mental deficiency. plasmid double-stranded, circular, bacterial DNA into which a fragment of DNA from another organism can be inserted.

Pleiotropy: The phenomenon of variable phenotypes for a number of distinct and seemingly unrelated phenotypic effects.

Polymerase: Any enzyme that catalyzes the formation of DNA or RNA from deoxyribonucleotides or ribonucleotides.

Predisposition: To have a tendency or inclination towards something in advance.

Presymptomatic diagnosis: Diagnosis of a genetic condition before the appearance of symptoms.

Primer : Nucleotides used in the polymerase chain reaction to initiate DNA synthesis at a particular location.

Probability: The long term frequency of an event relative to all alternative events, and usually expressed as decimal fraction.

Probe: Single-stranded DNA labeled with radioactive isotopes or tagged in other ways for ease in identification.

Recessive: A gene that is phenotypically manifest in the homozygous state but is masked in the presence of a dominant allele.

Recombination: The natural process of breaking and rejoining DNA strands to produce new combinations of genes and, thus, generate genetic variation. Gene crossover during meiosis.

Repeat sequences: The length of a nucleotide sequence that is repeated in a tandem cluster.

RFLP: Restriction fragment length polymorphism; variations occurring within a species in the length of DNA fragments generated by a species endonuclease.

Ribosomal protein: One of the ribonucleoprotein particles that are the sites of translation.

Sex determination: The mechanism in a given species by which sex is determined; in many species sex is determined at fertilization by the nature of the sperm that fertilizes the egg.

Sickle cell anemia: An hereditary, chronic form of hemolytic anemia characterized by breakdown of the red blood cells; red blood cells undergo a reversible alteration in shape when the oxygen tension of the plasma falls slightly and a sickle-like shape forms.

Somatic cell hybrid: Hybrid cell line derived from two different species; contains a complete chromosomal complement of one species and a partial chromosomal complement of the other; human/hamster hybrids grow and divide, losing human chromosomes with each generation until they finally stabilize, the hybrid cell line established is then utilized to detect the presence of genes on the remaining human chromosome.

Somatic mutation: A mutation occurring in any cell that is not destined to become a germ cell; if the mutant cell continues to divide, the individual will come to contain a patch of tissue of genotype different from the cells of the rest of the body.

Southern blotting: A technique for transferring electrophoretically resolved DNA segments from an agarose gel to a nitrocellulose filter paper sheet via capillary action; the DNA segment of interest is probed with a radioactive, complementary nucleic acid, and its position is determined by autoradiography.

Syndrome: A recognizable pattern or group of multiple signs, symptoms or malformations that characterize a particular condition; syndromes are thought to arise from a common origin and result from more than one developmental error during fetal growth.

3' - end: The end of a polynucleotide with a free (or phosphorylated) 3' - hydroxyl group.

Trait: Any detectable phenotypic property of an organism.

Transferase: Enzymes that catalyze the transfer of functional groups between donor and acceptor molecules.

Transcription: The formation of an RNA molecule upon a DNA template by complementary base pairing.

Translation: The formation of a polypeptide chain in the specific amino acid sequence directed by the genetic information carried by mRNA.

Translocation: A chromosome aberration which results in a change in position of a chromosomal segment within the genome, but does not change the total number of genes present.

Triplet code: A code in which a given amino acid is specified by a set of three nucleotides.

Transgenic organism: One into which a cloned genetic material has been experimentally transferred, a subset of these foreign gene express themselves in their offspring.Turner syndrome a chromosomal condition in females (usually 45,XO) due to monosomy of the X- chromosome; characterized by short stature, failure to develop secondary sex characteristics, and infertility.

Vector: A self-replicating DNA molecule that transfers a DNA segment between host cells.

Western blotting analysis: A technique used to identify a specific protein; the probe is a radioactively labeled antibody raised against the protein in question.

X-inactivation: The repression of one of the two X-chromosomes in the somatic cells of females as a method of dosage compensation; at an early embryonic stage in the normal female, one of the two X-chromosomes undergoes inactivation, apparently at random, from this point on all descendent cells will have the same X-chromosome inactivated as the cell from which they arose, thus a female is a mosaic composed of two types of cells, one which expresses only the paternal X-chromosome, and another which expresses only the maternal X-chromosome.

XYY syndrome: Genetic condition in males with extra Y chromosome (in 1 in 1000 male births). Symptoms: tall stature (over 6'), may including sterility, developmental delay, learning problems.

YAC: Yeast artificial chromosome; a linear vector into which a large fragment of DNA can be inserted; the development of YAC's in 1987 has increased the number of nucleotides which can be cloned.

Zoo blot: Northern analysis of mRNA from different organisms.

BIBLIOGRAPHY

Adleman, J (1999) 'Making Defect Perfection: Shakespeare and the One-Sex Model' in Viviana Comensoli and Anne Russell (Eds) *Enacting Gender on the English Renaissance*, Urbana: University of Illinois Press

Allen, MR (1991) 'The "third culture" and Disciplinary science' *The edge* Online at http://wwwctheorynet/articlesaspx?id=357 [Accessed 2 January 2007]

Allen, G (1974) 'Opposition to the Mendelian-Chromosome Theory: The physiological and developmental genetics of Richard Goldschmidt' *J Hist Biol* 7; 49–92

Alvesalo, L (1971) 'The influence of sex-chromosome genes on tooth size in man' *Proc Finn Dent Soc* 67; 3-54

Andersson, M et al (1986) 'Chromosome Y-specific DNA is transferred to the short arm of X chromosome in human XX males' *Science* 33, 4765; 786-8

Andersson, M et al (1988) 'Y;autosome translocations and mosaicism in the aetiology of 45,X maleness: assignment of fertility factor to distal Yq11' *Hum Genet* 79, 1; 2-7

Associated Press (1996) 'Scientists Discover Genetic Switch For Nurturing Behaviour in Mice' Boston USA

Bache, C M. (1980) 'Towards a Unified Theory of Metaphor' *The Journal of Aesthetics and Art Criticism*, 39, 2: 185-193

Bagemihl, B (1999) *Biological Exuberance, Animal Homosexuality and Natural Diversity* Profile Books Ltd

Bae, DS et al (1996) 'Characterization of the mouse DAX-1 gene reveals evolutionary conservation of a unique amino-terminal motif and widespread expression in mouse tissue' *Endocrinology,* 137, 9; 3921-7

Bainbridge, D (2004) *The X in Sex How the X-Chromosome Controls Our Lives* London: Harvard University Press

Balazs, A (2004) 'What does a molecule want? The myth of the self-replicating molecule comments on the "selfish-gene" paradigm' *Biosystems*, 73, 1; 1-11

Barthes, R (1964) *Elements of Semiology* Hill and Wang, New York

Bardoni, B et al (1993) 'Functional disomy of Xp22-pter in three males carrying a portion of Xp translocated to Yq' *Hum Mol Genet,* 91; 333-338

BBC (2002) 'Gene battle may cause small babies' 28 June BBC Online Health Available on line http://newsbbccouk/1/hi/health/2072597stm [Accessed 2 January 2007]

BBC (2001) 'What makes? Made a male a man' 1 May BBC Online at http://newsbbccouk/1/hi/health/1306869stm [Accessed 2 January 2007]

Berta, P et al (1990) 'Genetic evidence equating SRY and the testis-determining factor' *Nature, 348*; 448-50 Online at http://wwwnaturecom/nature/journal/v348/n6300 /abs/348448a0html [Accessed 2 January 2007]

Beale, B (2001) 'The Sexes; New insights into the X and the Y chromosomes' *The Scientist* , 15, 15; 18

Beder, S (1997) *Influencing future decision makers,* Australian Broadcasting Corporation, Online at from http://wwwabcnetau/science/slab/beder/storyhtm [Accessed2 January 2007] Based on a chapter in *Global Spin: The Corporate Assault on Environmentalism* Scribe, Melbourne 1997

Bernstein, R et al (1980) 'Female phenotype and multiple abnormalities in sibs with a Y chromosome and partial X chromosome duplication: H-Y antigen and Xg blood group findings' J *Med Genet,* 17; 291-300

Bernstein, R et al (1987) 'A unique dicentric X;Y translocation with Xq and Yp breakpoints: cytogenetic and molecular studies' *American Journal of Human Genetics,* 41, 2; 145-56

Berman, LA (2003) [Book review] *The Puzzle: Exploring the Evolutionary Puzzle of Male Homosexuality* Online at http://wwwnarthcom/docs/berman2html [Accessed 2 January 2007]

Berta, P et al (1990) 'Genetic evidence equating SRY and the testis-determining factor' *Nature*, 348, 6300; 448-50

Bridgman, R (2002) [Book review] *Y: The descent of men* by Steve Jones, *New Scientist* 2369 Available from http://wwwnewscientistcom/channel/life/mg17623695800, [Accessed January 2007]

Bianchi, NO (1991) 'Sex determination in mammals. How many genes are involved?' *Biology of Reproduction*, 44, 3; 393-7

Birke, L (1986) *Women, Feminism and Biology* Brighton: Wheatsheaf Books Ltd

Blanchard, R (2001) 'Fraternal Birth Order and the Maternal Immune Hypothesis of Male Homosexuality' *Hormones and Behaviour*, 40, 2; 105-114

Blanchard, R and Klassen, P (1997) 'H-Y Antigen and Homosexuality in Men' *Journal of Theoretical Biology*, 185, 3;373-378

Bloom, FE (2001) 'What does it all mean to you?' *The Journal of Neuroscience,* 2121;8304-8305

Blunt, W (1971) *The complete Naturalist: A Life of Linnaeus,* London: William Collins Songs

Boldogköi, Z (2004) 'Gene Network Polymorphism Is the Raw Material of Natural Selection: The Selfish Gene Network Hypothesis' *Journal of Molecular Evolution,* 59, 3; 340-357

Bouma, GJ et al (2004) 'Using real time RT-PCR analysis to determine multiple gene expression patterns during XX and XY mouse fetal gonad development' *Gene Expression Patterns*, 51;141-149

Bouma, GJ et al (2005) 'Gonadal sex reversal in mutant Dax1 XY mice: a failure to upregulate Sox9 in pre-Sertoli cells' *Development* ,132; 3045-3054

Boyd, M (1993) 'Metaphor and Theory Change' In A Ortony ed *Metaphor and Thought*, 2nd edn, pp 481-533 Cambridge: Cambridge University Press

Bradbury, JT et al (1956) 'Chromatin test in Klinefelters syndrome' *J clin Endocr*, 16; 689

Brockman, J (2001) 'The third Culture' *The edge* Available from http://wwwedgeorg_ /_3rd_culture/ [Accessed 1 May 2007]

Bridges, CB (1921) 'Triploid Intersexes in Drosophila melanogaster' *Science,* 54; 252-254

Bridges, CB (1925) 'Sex in Relation to Chromosomes and Genes' *America Nat*, 56; 127-137

Bubela, TM and Caulfield, TA (2004) 'Do the print media "hype" genetic research? A comparison of newspaper stories and peer-reviewed research papers' *CMAJ,* 170; 99

Bucchi, M (2004) 'Can genetics help us rethink communication? Public communication of science as a double helix' *New Genetics and Society,* 23, 3; 269-283

Buckley, AD (1998) 'Daring Us to Laugh: Creativity and Power in Northern Irish Symbols' in AD Buckley Ed *Symbols in Northern Ireland Belfast* Institute of Irish Studies: Queens University of Belfast

Buckle, VJ et al (1987) 'Localisation of Y-chromosome sequences in normal and XX males' *Journal of Medical Genetics,* 244; 197-203

Bull, JJ et al (1988) 'Mammalian ZFY sequences exist in reptiles regardless of sex-determining mechanism' *Science,* 28; 242, 4878, 567-9

Butler, J (1990) *Gender Trouble Feminism and the Subversion of Identity* London: Routledge

Butler, J (1993) *Bodies that Mater: On the Discursive Limits of sex* New York: Routledge

Butler, J (2003) 'X Marks the Spot for Intersex Alex' *The Western Australian,* 11 January Online at from http://wwwtgcrossroadsorg/news/?aid=597 [Accessed 01 May 2007]

Clipsham, R and McCabe, ERB (2003) 'DAX1 and its network partners: Exploring complexity in development' *Mol Genet Metab,* 80; 81–120

Clipsham, R et al (2004) 'Nr0b1 and its network partners are expressed early in murine embryos prior to steroidogenic axis organogenesis' *Gene Expr Patterns,*4; 3–14

Capel, B (1995) 'New bedfellows in the mammalian sex-determination affair' *Trends in Genetics,* 11, 5, 161-163

Capel, B (1998) 'Sex in the 90s: SRY and the switch to the male pathway' *Annu Rev Physiol*, 60, 497–523

Carrel L, et al (1999) 'A first-generation X-inactivation profile of the human X chromosome' *Proc Natl Acad Sci,* 96, 25; 14440-14444

Castle, WE (1930) 'The Quantitative Theory of Sex and the Genetic Character of Haploid Males' *Proceedings of the National Academy of Sciences of the United States of America,* 16, 12; 783-791.

Ceccarelli, L (2004) 'Neither Confusing Cacophony nor Culinary Complements: A Case Study of Mixed Metaphors for Genomic Science' *Written Communication*, 21, 1, 92-105

Charney, D (2005) 'Lone Geniuses in Popular Science: The devaluation of Scientific Consensus' *Written Communication,* 20, 3; 215-241

Chandra, HS (1985) 'Sex Determination: A Hypothesis Based on Noncoding DNA' *PNAS,* 82, 4; 1165-1169

Christidou, V et al (2004) 'Constructing social representations of science and technology: the role of metaphors in the press and the popular scientific magazines' *Public Understanding of Science*, 13, 4; 347

Clarke, T (2001) 'Shutting up the X' *Nature Science Update* 23 July Online at http://wwwnaturecom/news/indexhtml [Accessed 01 May 2007]

Cookson, W (1994) *The Gene Hunters: Adventures in the Genome Jungle* London: Aurum Press

Corbett v Corbett (1970), Probate, Divorce and Admiralty Division, United Kingdom Online at from Press for Change http://wwwpfcorguk/node/319 [Accessed 1 January 2007]

Coulter, M.C. (1925) A Distortion of the 3:1 Ration" *Bot. Gaz*, 79, 2; 226-228

Cromie, WJ (1996) 'The Nature of Nurture' *Harvard Gazette* October 31 Online at http://wwwhnoharvardedu/gazette/(1996)'/1031/TheNatureofNurthtml [Accessed01 May (2007) ']

Cromie, WJ (1999) 'Key Gene Found for Female Development *Harvard Gazette,* Availableonline http://wwwhnoharvardedu/gazette/1999/0211/femaledevelhtml [Accessed01 May (2007) ']

Crawford, PA et al (1998) 'Nuclear receptor DAX-1 recruits nuclear receptor corepressor N-CoR to steroidogenic factor 1' *Molecular and Cellular Biology,* 18, 5; 2949-56

Crew, FAE (1921) 'Sex-reversal in frogs and toads. a review of the recorded cases of abnormality of the reproductive system and an account of a breeding experiment' *Journal of Genetics* xi, 2; 141

Crooke, H (1615) *Mikrokosmographia a description of the body of man* London: Printed by William Iaggard dwelling in Barbican

Crown, E (2003) 'Two genes--Dax 1 and Sry--required for testis formation' Northwestern Press release, Public release date: 8-Apr-2003 Online at http://wwweurekalertorg/pub_releases/2003-04/nu-tg-040803php [Accessed 1 January 2007]

Curtis, R (1994) 'Narrative form and normative force: Baconian story-telling in popular science' *Social Studies of Science* 24; 419-461

Daston, L and Galison, P (1992) 'The Image of Objectivity' *Representations*, 40; 81-128

Dawkins, R (1976) *The Selfish Gene* New York: Oxford University Press

De la Chapelle, A (1986) 'The use and misuse of sex chromatin screening for "gender verification" of female athletes' *JAMA*, 256; 1920-1923

De la Chapelle, A (1987) 'The Y-chromosomal and autosomal testis-determining genes' *Development*, 101, Suppl; 33-8

Demerec, M (1928) A possible explanations for Winges findings in lebistes reticulates' *The American Naturalist*, 62, 678; 90-94

Dozier, B (2005) 'Beards, Breasts and Bodies; Doing sex in a gendered world' *Gender and society,* 19, 3; 297-316

Dreger, AD (1998) *Hermaphrodites and the Medical Invention of Sex* Cambridge: Harvard UP

Duncker, C (2006) *Kritische Reflexionen des Ideologiebegriffes*, London: Turnshare

Dupré, J (2001) *Human Nature and the Limits of Science*, Oxford University Press

Dunn, JCY et al (2004) 'Adrenal Cortical Cell Transplantation' *Journal of Pediatric Surgery,* 3912; 1856-1858

Elsas, LJ et al (2000) 'Gender verification of female athletes' *Genetics in Medicine*, 24; 249-254

Eichwald, E and Silmser, CR (1955) 'Communication' *Transplant Bull* 2; 148–149

Enclander-Golden, P et al (1980) 'H-Y antigen in transsexuality' *Lancet*, ii, 1137-1138

Epplen, JT et al (1983) 'On evolutionarily conserved simple repetitive DNA sequences: Do sex-specific satellite components serve any sequence dependent function' *Differentiation,* 23 Suppl; 60–63

Eurobarometer (2001), 'Eurobarometer 55.2: Europeans, science and technology', on line at at: http://europa.eu.int/comm/dg10/epo/eb/eb55/eb552_sctech.html. [Accessed 1 January 2007]

Fahnestock, J (1986) 'Accommodating Science: The Rhetorical Life of Scientific Facts' *Written Communication* 3; 275-96

Falk, R (2000) 'The Gene: A Concept in Tension' In Beurton, P/Falk, R/Rheinberger, H-J, Eds *The Concept of the Gene in Development and Evolution* Cambridge: Cambridge University Press

Fausto-Sterling, A. (1993) The five sexes: Why male and female are not enough. *The Sciences*, 33, 2; 20-25.

Fausto-Sterling, A (2000) *Sexing the Body: gender politics and the construction of sexuality* New York: Basic Books

Fechner, PY et al (1993) 'Report of a kindred with X-linked or autosomal dominant sex-limited 45, XY partial gonadal dysgenesis' *J Clin Endocrinol Metab,* 76; 1248-1253

Ferguson-Smith, MA (1998) 'Gender verification and the place of XY females in sport' (pp355-365)In: Harris W, Williams C, Stanish W, Micheli L, eds *Oxford Textbook of Sports Medicine* Oxford, England: Oxford University Press

Ferguson-Smith MA et al (1990) 'Genotype-phenotype correlations in XX males and their bearing on current theories of sex determination' *Human Genetics*, 84, 2; 198-202

Fiske, J (1982) *Introduction to Communication Studies*, London: Methuen

Flannery, MC (2001) 'Quilting: A Feminist Metaphor for Scientific Inquiry' *Qualitative Inquiry*, 7, 5; 628-645

Fleck, L (1935) *Genesis and Development of a Scientific Fact* Trenn TJ and Merton RK Ed, Chicago: Univ of Chicago

Foster J W et al (1992) 'Evolution of sex determination and the Y chromosome: SRY-related sequences in marsupials' *Nature* 359; 531-533

Foucault, M (1980) *Herculine Barbin* New York: Pantheon

Fox, M (1999) 'Second good mother gene found' *Reuters* (9 April) Online at http://wwwfwworg/famnews/0408chtm [Accessed 1 January 2007]

Frable, DE (1989) 'Sex typing and gender ideology: two facets of the individuals gender psychology that go together' *J Pers Soc Psychol*, 56, 1; 95-108

Fitch, RH et al (1998) 'The female phenotype : Natures default?' *Developmental neuropsychology*, 14, 2-3; 175-441

Freeden, M (2003) *Ideology: A very short introduction* Oxford University press

French, R (1999) *Dissection and Vivisection in the European Renaissance* Aldershot, UK: Ashgate

Fujimura, JH (2006) 'Sex Genes: A Critical Sociomaterial Approach to the Politics and Molecular Genetics of Sex Determination' *Signs: Journal of Women in Culture and Society,* 32; 49–82

Gaissinovitch, AE (1990) 'CF Wolff on variability and heredity' *History and Philosophy of the Life Sciences* 12; 179–201

Gascoigne, TH and Metcalfe, JE (1997) 'Incentives and impediments to scientists communicating through the media' *Science Communication*, 10, 3; 265-82

Gayon, J (2000) 'The human genome project: Archeology and Prospected, Cognitive and Practical: A commentary on "is there and Organism in this Text?"' In *Controlling our Destinies: Historical, Philosophical, Ethical, and Theological Perspective on the Human Genome Project* Notre Damn in: University of Notre Damn Press

Gayon, J (2000) 'From Measurement to Organization: A philosphyical scheme for the History of the concept of Heredity' In Beurton, P/Falk, R/Rheinberger, H-J, eds *The Concept of the Gene in Development and Evolution* Cambridge: Cambridge University Press

Geertz C, (1973) Interpretation of Cultures, New York: Basic Books Classics

Geller, G et at (2002) 'The media and public reaction to genetic research' *JAMA,* 287; 773 Available online http://jama.ama-assn.org/cgi/content/full/287/6/773 [Accessed 1 January 2007]

Gendel, M (2000) 'Gender Verification No More?' MD Medscape Womens Health, 2, 3; 53 Online at http://wwwmedscapecom/viewarticle/408918 [Accessed 1 January 2007]

German, J et al (1978) 'Genetically determined sex-reversal in 46, CY humans' *Science,* 2002; 53-56

Goodrich, HB (1929) 'Mendelian Inheritance in Fish' *Quart Rev Biol* 4; 8

Gieryn TF (1983) 'Boundary-work and the demarcation of science and non-science: strains and interests in professional ideologies of scientists' *American Sociology Reivew*, 48, 6; 781-795

Glisson, J (2005) 'Cutting It Both Ways: Dissection of the Male Anatomy as Castration' *The Anatomy of Gender: Arts of the Body in Early Modern Europe* Online at http://anatomyofgendernorthwesternedu/glisson01html [Accessed 1 January 2007]

Gilbert, SF (2000) 'Genes classical and genes developmental': The different uses of the gene in evolutionary syntheses' In Beurton, P, Falk, R, Rheinberger, H-J, Eds *The Concept of the Gene in Development and Evolution* Cambridge: Cambridge University Press

Goodfellow, PJ et al (1986) A pseudoautosomal gene in man *Science*, 234, 4777; 740-3

Graves, J (2000) 'Human Y Chromosome, Sex Determination, and Spermatogenesis –A Feminist View' *Biology of Reproduction*, 63, 3; 668-676

Graves, J (1990) 'The search for the mammalian testis-determining factor is on again Reproduction' *Fertility, & Development* , 2, 2; 199-204

Gray J.(1992) *Men Are From Mars And Women Are From Venus*, New York: Harper Collins

Greer, G (1999) communication cited on the AIS website http://wwwmedhelporg/www/ais/debates/letters/FATHERHTM [Accessed 1 January 2007]

Griffiths, R (1991) 'The isolation of conserved DNA sequences related to the human sex-determining region Y gene from the lesser black-backed gull Larus fuscus' *Proceedings Biological Sciences/The Royal Society*, 244, 1310; 123-8

Grosz, E (1994) *Volatile Bodies: Toward a Corporeal Feminism Theories of Representation & Difference* Bloomington/Indianopolis, Indiana University Press

Guo, W et al (1995a) 'Expression of DAX-1, the gene responsible for X-linked adrenal hypoplasia congenita and hypogonadotropic hypogonadism, in the hypothalamic-pituitary-adrenal/gonadal axis' *Biochem Mol Med*, 56, 1; 8-13

Guo, W et al (1995b) 'Diagnosis of X-linked adrenal hypoplasia congenita by mutation analysis of the DAX1 gene' *JAMA*, 274; 324-330

Guo, W et al (1996) 'Genomic sequence of the DAX1 gene: an orphan nuclear receptor responsible for X-linked adrenal hypoplasia congenita and hypogonadotropic hypogonadism' *Journal of Clinical Endocrinology & Metabolism*, 81, 7; 2481-6

Gubbay, J et al (1990) 'A gene mapping to the sex-determining region of the mouse Y chromosome is a member of a novel family of embryonically expressed genes' *Nature* 346; 245-250

Hager LD (1997) *Women in Human Evolution* Routledge Press

Haraway, D (1997) *Modest witness@second-millenniumfemaleman©-meets-oncomouse™: Feminism and technoscience* New York and London: Routledge

Harvey, E (1992) *Ventriloquized Voices: Feminist theory and English Renaissance texts* London Routledge

Harvey, K (2002) 'The Substance of Sexual Difference: Change and Persistence in Representations of the Body in Eighteenth–Century England' *Gender & History* 14, 2; 202

Hanley, NA et al (2000) 'SRY, SOX9, and DAX1 expression patterns during human sex determination and gonadal development' *Mechanisms of Development*, 91, 1; 403-407

Hall, E (2003) 'Reading maps of the genes: interpreting the spatiality of genetic knowledge' *Health and Place* 9, 2; 151-161

Herdt, G (1996) *Third Sex, Third Gender: Beyond Sexual Dimorphism in Culture and History*

Hindess, B (1996) ' *Discourses of Power From Hobbes to Foucault* Oxford, Blackwell

Hird, M (2002) 'Unidentified Pleasures: Gender Identity and its Failure' *Body & Society* 82; 39-54

Ho, J et al (2004) 'NR0B1A: an alternatively spliced form of NR0B1' *Mol Genet Metab*, 83, 4, 330-6

Holmberg, T (2005) 'Questioning the Number of the Beast: Constructions of Humanness in a Human Genome project HGP narrative' *Science as Culture*, 14, 1; 23-37

Holmes, C (2004) 'David Ashworth, Oxford Ancestors A company by popular demand? *OxSex Newsletter* October Online at http://wwwscience-enterpriseoxacuk/html/DavidAshworthasp [Accessed 1 January 2007]

Holter, E et al (2002) 'Inhibition of androgen receptor AR function by the reproductive orphan nuclear receptor DAX-1' *Molecular Endocrinology*, 16, 3; 515-28

Hood-Williams, J (1996) 'Goodbye to sex and gender' *The sociological Review*, 44, 1; 1-16

Hoyle, C et al (2002) 'Dax1 expression is dependent on steroidogenic factor 1 in the developing gonad' *Molecular Endocrinology*, 16, 4; 747-56

Hubbard, R (2001) 'Science, Facts and Feminism' In *Women, Science and Technology*, Mary Wyer et al eds., New York: Routledge, 2001

Hurst, LD et al (2000) 'Peg3 and the Conflict Hypothesis' *Science*, 287, 5456; 1167 Online at http://wwwsciencemagorg/cgi/content/full/287/5456/1167a [Accessed 1 January 2007]

IAAF (1990) '*Reports on Approved Methods of Femininity Verification'* November, Monte Carlo

ipdxWIRE Intersex News (2003) '*Intersex People As "Saviours of Humankind"?'* Sep 3 Available online from http://wwwintersexinitiativeorg/news/000044html [Accessed 1 January 2007]

Ikeda, Y et al (1996) 'Steroidogenic factor 1 and Dax-1 colocalize in multiple cell lineages: potential links in endocrine development' *Molecular Endocrinology*, 10, 10; 1261-72

Imperato-McGinley J et al (1979) 'Male pseudohermaphroditism secondary to 17 beta-hydroxysteroid dehydrogenase deficiency: a gender role change with puberty' *Journal of Clinical Endocrinology and Metabolism* 49; 391-395

Jablonka, E and Lamb, MJ (1998) 'Bridges between Development and Evolution' *Biology and Philosophy*, 13; 119-124

Jager, RJ et al (1990a) 'A ZFY-negative 46,XX true hermaphrodite is positive for the Y pseudoautosomal boundary' *Human Genetics*, 85, 6; 666-8

Jager, RJ et al (1990b) 'A Human XY female with a frame shift mutation in the candidate testis-determining gene SRY' *Nature*, 348, 6300; 452-454

Jameson, JL et al (2003) 'Battle of the sexes: new insights into genetic pathways of gonadal development' *Trans Am Clin Climatol Assoc*, 114; 51-63 (discussion 64-5)

Jeays-Ward, K et al (2004) 'Wnt4 is required for proper male as well as female sexual development' *Developmental Biology* 2762; 431-440

Jeffs, B et al (2001) 'Sertoli cell-specific rescue of fertility, but not testicular pathology, in Dax1 Ahch-deficient male mice' *Endocrinology,* 1426; 2481-2488

Jimenez, R and Burgos, M (1998) 'Mammalian sex determination: joining pieces of the genetic puzzle' *Bioessays*, 20, 9; 696-709

Johannsen, W (1991) 'The Genotype conception of Heredity' *The American Naturalist*, 45, 531; 129-159

Johnson, B (2001) 'Renaissance Body Matters: Judith Butler and the Sex that is One' *International Journal of Sexuality and Gender Studies*, 1, 2; 77-94

Jones, KW and Singh, L (1981) 'Conserved repeated DNA sequences in vertebrate sex chromosomes' Hum Genet, 58; 46-53

Jones, KW and Singh, L (1982) 'Conserved sex-associated repeated DNA in vertebrates' (pp 135-154) In *Genome Evolution* Eds G Dover and R Flavell Londonn: Academic Press

Jones, KW et al (1987) 'Rapidly evolving Bkm DNA is associated with hypervariable domains' *Chromosomes Today,* 9; 22-29

Jones, S (2002) *Y: The Decent of Men* London: A Little, Brown Book

Jordan, BK et al (2001) 'Up-regulation of WNT-4 signalling and dosage-sensitive sex reversal in humans' *Am J Hum Genet*, 68, 5; 1102-9

Kessler, SJ (1998) *Lessons from the Intersexed* New Brunswick, NJ: Rutgers University Press

Kelly, K (1998) 'The Third Culture' *Science*, 289, 5353; 992-993

Keller, F (1995) *Refiguring Life: metaphors of twentieth century biology*. New York: Columbia University Press.

Keller, F (2000) *The Century of the Gene*. Cambridge, Mass.: Harvard University Press

Keller, F (2002) *Making sense of life; Explaining biological development with models, metaphors and machines* Cambridge MA: Harvard University Press

Kaiser Family Foundation (2006) online at http://www.kff.org/entmedia/7047.cfm [Accessed 1 January 2007]

Kiel-Metzger, K et al (1985) 'Evidence that the human Y chromosome does not contain clustered DNA sequences Bkm associated with heterogametic sex determination in other vertebrates' *N Engl J Med,* 313; 242–245

Kincaid, H (1990) 'Molecular Biology and the Unity of Science' *Philosophy of Science*, 57; 575-593

Knight, J (1999) 'There's more to being a woman than not being a man' *New Scientist Magazine*, 2172, 161; 9

Knower, K et al (2003) 'Turning on the male --SRY, SOX9 and sex determination in mammals' *Cytogenetic and genome research*, 101, 3-4; 185-98

Knudsen, S (2003) 'Scientific metaphors going public' *Journal of Pragmatics*, 35, 8; 1247-1263

Knudsen, S (2005) 'Communicating novel and conventional scientific metaphors : a study of the development of the metaphor of genetic code' *Public Understanding of Science,* 14, 4; 373-392

Koopman, P et al (1990) 'Expression of a candidate sex-determining gene during mouse testis differentaition' *Nature*, 348, 6300, 450-452

Koopman, P et al (1991) 'Male development of chromosomally female mice transgenic for Sry' *Nature,* 9, 351, 6322;117-21

Kraus, C (2000) 'Naked Sex in Exile: On the Paradox of the "Sex Question" in Feminism and in Science' *NWSA Journal* 12, 3; 151-176

Kua, E et al (2004) 'Science in the news: a study of reporting genomics public' *Understandings of Science*, 13; 309-322

Kwa, C. (2005) Alexander von Humboldt's Invention of the. Natural Landscape. *The European Legacy* 10; 149-162.

Kuhn, T (1962/1970) *The Structure of Scientific Revolutions*, Chicago: University of Chicago Press

Lahbib-Mansais, Y et al (1997) 'Mapping in pig of genes involved in sexual differentiation: AMH, WT1, FTZF1, SOX2, SOX9, AHC and placental and embryonic CYP19' *Cytogenetics & Cell Genetics*, 76, 1-2; 109-14

Lalli, E et al (1997) 'Transcriptional silencing domain in DAX-1 whose mutation causes adrenal hypoplasia congenita' *Molecular Endocrinology*, 11, 13; 1950-1960

Lancaster, RN (2003) *The trouble with nature, sex in science and popular culture* London: Univeristy of California Press

Laqueur, T (1990) *Making Sex: Body and Gender from the Greeks to Freud* London: Harvard University Press

Laqueur, TW (2003) 'Sex in the Flesh' *Isis*, 94; 300-306

Lau, YF and Chan, KM (1989) 'The putative testis-determining factor and related genes are expressed as discrete-sized transcripts in adult gonadal and somatic tissues' *American Journal of Human Genetics*, 45, 6; 942-952

Laughon, A and Scott, MP (1984) 'The sequence of a Drosophila segmentation gene: Protein structure homology with DNA binding proteins' *Nature* 310; 25-31

Lee, JT (2003) 'Molecular Links between X-Inactivation and Autosomal Imprinting: X-inactivation as a Driving Force for Evolution of Imprinting' *Current Biology,* 13, 6; R242-R254

Longino, HE (2001) *Can There Be a Feminist Science?* In Women, Science and Technology, Mary Wyer et al eds., New York: Routledge, 2001

Lippman, A (1993) 'Prenatal genetic testing and geneticisation : Mother matters for all' *Fetal Diag Therap,* 8 suppl 1; 175-188

Littleton v Prange (1999) 288th Judicial District Court Bexar County Texas October 27 USA Online at http://wwwpfcorguk/node/370 [Accessed 1 January 2007]

Longman, J (2004) 'DRUG TESTING; East German Steroids Toll: "They Killed Heidi"' New York Times (26 January_ Section D Online at http://querynytimescom/gst/fullpagehtml?sec=health&res=9C01E3D91738F935A15752C0A9629C8B63 [Accessed 1 January 2007]

Lloyd, HJ (1929) 'Hermaphroditism in the Common Frog Rana temporaria' *The American Naturalist*, 63, 685; 130-138

Ludbrook, LM and Harley, VR (2004) 'Sex determination: a window of DAX1 activity' *Trends Endocrinol Metab* 153; 116-21

Lyon, M (1963) 'Lyonisation of the X-chromosome' *The Lancet* II; 1120-1120

MacNamee, E (2004) ' Girls and Boys' *Law and Critique*, 15; 25-43

Maienschein, J (1984) 'What Determines Sex? A Study of Converging Approaches' Isis, 75, 3; 456-480

Majdic, G and Saunders, PT (1996) 'Differential patterns of expression of DAX-1 and steroidogenic factor-1 SF-1 in the fetal rat testis' *Endocrinology*, 137, 8; 3586-3589

Madl, JE and Herman, RK (1979) 'Polyploids and sex determination in Caenorhabditis elegans' *Genetics,* 93; 393–402

Mardon G et al (1989) 'Duplication, deletion, and polymorphism in the sex-determining region of the mouse Y chromosome' *Science*, 243, 4887; 78-80

Martin E (1987) *The Woman in the Body: A Cultural Analysis of Reproduction* Boston: Beacon Press English edition, Open University Press

Matarazzo, MR et al (2002) 'Allelic inactivation of the pseudoautosomal gene SYBL1 is controlled by epigenetic mechanisms common to the X and Y chromosomes' *Hum Mol Genet*, 11, 25; 3191-3198

Marx, J (1995) 'Snaring the genes that divide the sexes for mammals' *Science*, 269, 5232; 1824-5

McEwen, IK (2004) *Vitruvius: Writing the Body of Architecture*; MIT Press

McLaren, A (1990) 'What Makes a Man a Man?' 19 July November *Nature*, 216-217

Meeks, JJ et al (2003a) 'Dax1 regulates testis cord organization during gonadal differentiation' *Development* 130; 1029-1036

Meeks, JJ et al (2003b) 'Dax 1 is required for testis determination' *Nature Genetics* 34; 32-33 Online at
http://wwwnaturecom/ng/journal/v34/n1/full/ng1141html [Accessed 1 January 2007]

Mellor, F (2003) 'Between Fact and Fiction Demarcating Science from Non-Science in Popular Physics Books' *Social Studies of Science*, 33, 4; 509-538

Merton, RJ (1942) 'Science and Democracy Social Structure' pp 604-15 in *Social Theory and social structure*. New York: Free Press

Micis, S et al (1983) 'A study of a 46,XX infertile man and his permanent tooth sizes' *International Journal of Fertility* 28, 3; 165-8

Michael, M (2002) 'Comprehension, Apprehension, Prehension: Heterogeneity and the Public' *Understanding of Science, Science, Technology, & Human Values ,* 27, 3; 357-378

Miller, FA (2006) 'Your true and proper gender: the Barr body as a good enough science of sex' S*tudies of History and Philosophy of Biological and Biomedical Science*, 37; 459-483

Mitchell, M et al (1989) 'Localization of murine X and autosomal sequences homologous to the human Y located testis-determining region' *Genetics,* 21, 4; 803-9

Mittwoch, U (1989) 'Sex differentiation in mammals and tempo of growth: probabilities vs switches' *Journal of Theoretical Biology* 137, 4, 445-55

Mittwoch, U (1990) 'One gene may not make a man' *New Scientist* 128, 1742

Moore, M (1996) 'Meanings of sex difference in the Middle Ages: Medicine, Science and Culture' *Configurations* 4, 2; 241-243

Moore, CR (1925) 'Sex Determination and Sex Differentiation' *The American Naturalist,* 59, 661; 177-189.

Morange, M (2000) 'The developmental gene concept: History and limits' In Rheinberger H-J Eds*The Concept of the Gene in Development and Evolution Historical and Epistemological Perspectives* Cambridge University Press, Cambridge, 193-215

Morohashi, K (1997) 'The ontogenesis of the steroidogenic tissue' *Genes to cells*, 2, 2; 95-106

Morohashi, K et al (2000) 'Adrenocortical and gonadal differentiation regulated by transcription factors, Ad4BP/SF-1 NR5A1 and Dax-I NROB1' *Endocrine Research* 26, 4; 953

Moss, L (2002) *What Genes Cant Do* Cambridge, MA, MIT Press

Mullins, WA (1972) 'On the concept of Ideology in Political Sciences' *The American political Science Review*, 66, 2; 498-510

Murphy, DG et al (1993) 'X-chromosome effects on female brain: a magnetic resonance imaging study of Turners syndrome' *Lancet,* 342; 8881

Murphy, SK and Jirtle, RL (2003) 'Imprinting evolution and the price of silence' *BioEssays* 25; 557-588

Muscatelli, F et al (1994) 'Mutations in the DAX-1 gene give rise to both X-linked adrenal hypoplasia congenita and hypogonadotropic hypogonadism' *Nature* 372; 672-676

Nachtigal, MW et al (1998) 'Wilms tumor 1 and Dax-1 modulate the orphan nuclear receptor SF-1 in sex-specific gene expression' *Cell* 93, 3; 445-54

Nagamine, CM et al (1989) 'Chromosome mapping and expression of a putative testis-determining gene in mouse' *Science* 243, 4887, 80-3

Nelkin, D and Lindee, S (1995) 'The DNA mystique: the gene as a cultural icon' WH Freeman, New York

Nerlich, B and Hellsten, I (2004) 'Genomics: shifts in metaphorical landscape between 2000 and 2003' *New Genetics and Society*, 23, 3; 255-268

Netley, C and Rovet, J (1982) 'Atypical hemispheric lateralization in Turners syndrome subjects' *Cortex* 18, 3; 377-84

Nordgren, A (2003) 'Metaphors in behavioural genetics' *Theoretical Medicine,* 24, 1; 59-77

Ogata, T et al (1992) 'Sex reversal in a child with a 46, X, Yp+karyotype: support for the existence of a genes, located in distal Xp, involved in testis formaiton' *J Med Genet* 29; 226-230

Olympic.org (2007). Spotlight on Shan Zhang! online at http://en.olympic.cn/athletes/athletes_news/2007-03-26/1085915.html

Oudshoorn, N (1994) *Beyond the Natural Body; an archaeology of sex hormones* London: Routledge

Page, DC et al (1987a) 'Exchange of terminal portions of X- and Y-chromosomal short arms in human XX males' *Nature,* 328; 437-440

Page, DC et al (1987b) 'The sex-determining region of the human Y chromosome encodes a finger protein' *Cell*, 516; 1091-1104

Page, DC (1988) 'Is ZFY the sex-determining gene on the human Y chromosome' *Series B: Biological Sciences,* 322, 1208; 155-157

Page, DC et al (1990) 'Additional deletion in sex-determining region of human Y chromosome resolves paradox of X,tY;22 female' *Nature* 346; 245-250

Painter, TS (1923) 'Studies in mammalian spermatogeniesis II The spermatogenesis of man' *JExpSool*, 37; 291-321

Palmer, MS et al (1989) 'Genetic evidence that ZFY is not the testis-determining factor' *Nature* 342; 937-939

Palmer, MS et al (1990) 'Comparison of human ZFY and ZFX transcripts' *Proceedings of the National Academy of Sciences of the United States of America* 875; 1681-5

Paton, R (1997) 'The organisations of hereditary information' *Biosystems* 40; 245–255

Parks, SY et al (2005) 'Nuclear receptors Sf1 and Dax1 function cooperatively to mediate somatic cell differentiation during testis development' *Development* 132, 10; 2415-2423

Pask, A et al (1997) 'The candidate sex-reversal is autosomal in marsupials: implications for the evolution of sex determination in mammals' *Genomics* 413; 422-426

Petersen, A (1999) 'The portrayal of research into genetic-based differences of sex and sexual orientation: a study of "popular" science journals, 1980 to 1997' *Journal of Communication Inquiry*, 23, 2; 163-182

Petersen, A (2001) ' Biofantasies: genetics and medicine in the printed news media *Social Science and Medicine* 52; 1255-1268

Pittaway, B (1999) 'Olympic bosses suspend sex tests' *The Express* Saturday 10th July Online at http://wwwpfcorguk/node/857 [Accessed 1 January 2007]

Porta, M (2003) 'The genome sequence is a jazz score' *International Journal of Epidemiology*, 32; 29-31

Potier, B (2002) 'Genetic arms race described' *Harvard Gazette* March 21 Online at *http://wwwhnoharvardedu/gazette/(2002) '/0321/12-tilghmanhtml* [Accessed 1 January 2007]

Polanco, JC and Koopman, P (2006) 'Sry and the hesitant beginnings of male development' *Developmental Biology,* 302, 1; 13-24

Potter, P and Soltan, H (1997) 'Murray Llewellyn Barr, O C 20 June 1908-4 May 1995' *Biographical Memoirs of Fellows of the Royal Society*, 43, 32-46

Pritchard, CA et al (1987) 'Isolation of a sequence which maps close to the human sex determining gene' *Nucleic Acids Res,* 15, 15; 6159-69

Ray-Chaudhuri, SP et al (1971) 'Evolution of sex chromosomes and formation of W-chromatin in snakes' *Chromosoma Berl,* 33; 239-251

Ray-Chaudhuri, SP and Singh, L (1972) 'DNA replication pattern in sex chromosome of snakes' *Nucleus Calcutta,* 15; 200-210

Reddy, G (2005) 'With Respect to Sex: Negotiating Hijra Identity in South India' in *Worlds of Desire: The Chicago Series on Sexuality, Gender, and Culture* New York: University of Chicago Press

Reid, IS (1987) 'Science, politics, and race' In Harding, Sandra and Jean F OBarr eds *Sex and scientific inquiry* New York: University of Chicago Press

Roberts, C (2000) 'Sex Hormones as Biocultural Actors: Rethinking biology, sexual difference and health' In JM Ussher ed, *Women's Health: An International Reader* Routledge

Roberts, C (2002) 'A matter of embodied fact': sex hormones and the history of bodies' Feminist Theory, 3, 1; 7-26

Roughgarden, J (2004) *Evolutions Rainbow: Diversity, Gender, and Sexuality in Nature and People* Berkeley: University of California Press

Rheinberger, H-J (2000) 'Gene Concepts: Fragments from the Perspective of Molecular Biology', in Peter Beurton, Raphael Falk, and Hans-Joerg Rheinberger eds, *The*

Concept of the Gene in Development and Evolution New York: Cambridge University Press

Rice, WR (1996) 'Evolution of the Y sex chromosome in animals' *Bio Science,* 46; 331-343

Riddle, O (1924) 'A hitherto unknown function of the thymus' *Amer. Jour. Physiol*. 68; 180

Ruze, J (2006) 'Soya is making our kids gay Worldnet Daily (December 12) Online at http://worldnetdailycom/news/articleasp?ARTICLE_ID=53327 [Accessed 1 January 2007]

Rubin, G (1975) "The Traffic in Women: Notes on the Political Economy of Sex" in *Towards and Anthropology of Women*, ed Rayna Reiter, New York; Monthly Review Press

De Saunders, JB and OMally, CD (1973) *The illustrations from the works of Andreas Vesalius of Brussels : with annotations and translations, a discussion of the plates and their background, authorship and influence, and a biographical sketch of Vesalius* New York : Dover Publications Inc

Scherer, G et al (1989) 'Duplication of an Xp segment that includes the XfX locus causes sex inversion in man' *Hum Genet* 81; 291-294

Schleiner, W (2000) 'Early Modern Controversies about the One-Sex Model, *Renaissance Quarterly*, 53; 180-91

Schiebinger, L (1987) 'Skeletons in the Closet; The first illustrations of the female skeleton in Eighteenth-Century Anatomy' In Schiebinger, L Ed, *The Making of the Modern Body, Sexuality and Society in the Nineteenth Century* London: University of California Press

Schiebinger, L (1989) *The Mind Has No Sex? Women in the Origins of Modern Science* Cambridge: Harvard University Press

Schiebinger, L (1993) *Natures Body: Gender in the Making of Modern Science,* Boston: Beacon Press

Schiebinger L, (1999) 'Why mammals are called mammals: Gender politics in eighteenth-century natural history' *American Historical Review* 98; 382-411

Schiebinger L, (2000) *Feminism and the Body* Ed L Schiebinger London: Oxford University Press

Schiebinger L (2001) *Feminism in Twentieth-Century Science, Technology, and Medicine* Ed A Creager, E Lunbeck, and L Schiebinger New York: University of Chicago Press

Serrat, A and de Herreros, AG (1993) 'Determination of genetic sex by PCR amplification of Y-chromosome-specific sequences' *Lancet* , 341; 1593-1594

Shah, J (2002) ‘Erectile Dysfuncion through the ages, *BJU International,* 90; 433-441

Shapin, S (1982) ‘History of science and its sociological reconstructions’ *Hist Sci,* 20; 157-211

Shermer, MB (2002) ‘Stephen Jay Gould as Historian of scince and Scientific Historian, Popular Scientist and Scientific Popularizer’ *Social Studies of Science,* 32, 4; 489-524

Shields, SA (1982) ‘The Variability Hypothesis: The History of a Biological Model of Sex Differences in Intelligence’ *SIGNS* 7,4; 769-797

Shildrick, M (1997) *Leaky Bodies and Boundaries Feminism, Post-modernism and Bioethics* London: Routledge

Small, CL et al (2005) ‘Profiling gene expression during the differentiation and development of the murine embryonic gonad’ *Biology of Reproduction,* 722; 492-501
Simpson, E et al (1987) ‘Separation of the genetic loci for the H-Y antigen and for testis determination on human Y chromosome’ *Nature,* 326, 6116; 876-878

Simpson, JL et al (1993) ‘Gender verification in competitive sports’ *Sports Med*, 16; 305-315

Sinclair, A et al (1990) ‘A gene from the human sex-determining region encodes a protein with homology to a conserved DNA-binding motif’ *Nature,* 346; 240-245

Singh, L et al (1981) ‘Conserved sex chromosome-associated nucleotide sequences in eukaryotes’ *Cold Spring Harbor Symp Quant Biol*, 45; 805-813

Singh, L (1972) ‘Evolution of karyotypes in snakes’ *Chromosoma Berl*, 38; 185-236

Singh, L and Jones, KW (1982) ‘Sex reversal Sxr in the mouse Mus musculus is caused by a recurrent non-reciprocal cross-over involving the X and an aberrant Y chromosome’ *Cell* , 28; 205-216

Singh, L and Jones, KW (1986) Bkm sequences are polymorphic in humans and are clustered in pericentric regions of various acrocentric chromosomes including the Y *Hum Genet*, 73; 304-308

Sinisi, AD et al (2003) ‘Sexual Differentiation’ *Journal of Endocrinolgical Investigation* 263, Suppl; 23-8

Spanier, BB (1995) ‘*Im/partial Science: Gender Ideology in Molecular Biology* Bloomington, IN: Indiana University Press Spanier,

Stephenson, J (1996) ‘Female Olympians sex tests outmoded *JAMA* 276, 3; 177-178

Stewart, J (2003) ‘The mommy track: the consequences of gender ideology and aspirations on age at first motherhood’ *Journal of Sociology and Social Welfare*, 30, 2; 3-30

Stotz, K et al (2004) 'How scientists conceptualise genes: An empirical study' *Studies in History & Philosophy of Biological and Biomedical Sciences*, 35; 647-673

Strohman, R (2001) 'Human Genome Project in Crisis: Where is the program of life?' California Monthly (4) Online at http://wwwbiotech-infonet/Strohman_March09pdf [Accessed 1 January 2007]

Sturgi, P and Allum, N (2004) ' Science in society: re-evaluating the deficit model of public attitudes' *Public understanding Sci*, 13; 55-74

Sivagami, A et al (2000) 'A simple and cost-effective method for preparing DNA from the hard tooth tissue, and its use in polymerase chain reaction amplification of amelogenin gene segment for sex determination in an Indian population' *Forensic Science International,* 110, 2; 107-115

Swain, A et al (1996) 'Mouse Dax1 expression is consistent with a role in sex determination as well as in adrenal and hypothalamus function' *Nature Genetics* 124; 404-409

Swain, A and Lovell-Badge, R (1997) 'A molecular approach to sex determination in mammals' *RActa Paediatr Suppl*, 423; 46-9

Swain A et al (1998) ' Dax1 antagonizes Sry action in mammalian sex determination' *Nature* 391, 6669; 761-767

Sykes, B (2003) *Adams Curse: A future without men* London: Bantam press

Takahashi, T et al (1997) 'Active hypothalamic-pituitary-gonadal axis in an infant with X-linked adrenal hypoplasia congenita' *Journal of Pediatrics* 1303; 485-488

Tamai, KT et al (1996) 'Hormonal and developmental regulation of DAX-1 expression in Sertoli cells' *Molecular Endocrinology* 1012; 1561-1569

Tiersch, TR et al (1991) 'Studies on the phylogenetic conservation of the SRY gene' *Human Genetics* 875; 571-573

Turney, J (2007) Wellcome Trust's Understanding and engagement website http://wwwwellcomeacuk/doc_WTD004756html [Accessed 1 January 2007]

Wade, N (2003) 'Y Chromosome Depends on Itself to Survive' *The New York Times* June 19:1 Online at http://querynytimescom/gst/fullpagehtml?res=9804EFD 81138F93AA25755C0A9659C8B63&sec=health&pagewanted=print [Accessed 1 January 2007]

Watanabe, H et al (2004) 'DNA sequence and comparative analysis of chimpanzee chromosome 22' *Nature* 429; 382-388

Wachtel, SS et al (1975) 'Possible role for H--Y antigen in the primary determination of sex' *Nature*; 257, 5523; 235-236

Waldby, C (2001) 'Code Unknown: Histories of the Gene' *Social Studies of Science*, 31, 5; 779-791

Waters, KC (1994) ‘Genes Made Molecular’ *Philosophy of Science*, 61; 163-85

Watson, JD and Crick, FHC (1953) ‘A Structure for Deoxyribose Nucleic Acid’ *Nature* 3, 171; 737-738

Wertz, K and Herrmann, BG (2000) ‘Large-scale screen for genes involved in gonad development’ *Mech Dev,* 981-2; 51-70

Webster, A (2005) ‘Social science and a post-genomic future: alternative readings of genomic agency’ *New Genetics & Society*, 24, 2; 227-238

Wilkins JF (2006) ‘Unraveling male and female histories from human genetic data’ *Current Opinion in Genetics & Development* 16, 6; 611-617

Wilkinson, L et al (1998) ‘Ultrastructural abnormalities of epididymal tissues in XXSxr pseudomale sex-reversed mice’ *Archives of Andrology,* 201; 11-20

Winge, Ø (1927) ‘The location of eighteen genes in Lebistes reticulatus’ *I Genet* 18; 1-43

Winge, Ø (1932) ‘The nature of sex chromosomes’ *Proc 6th Int Congr Genet*, 1; 343-355

Wittig, M (1992) *The Straight Mind* Boston, Beacon Press

Winner, L (1986) *The Whale and the Reactor: A Search for Limits in an Age of High Technology* Chicago: The University of Chicago Press

Whitehead, H (1981) *The bow and the burden strap: a new look at institutionalized homosexuality in Native North America* In "Sexual meanings: the cultural construction of gender and sexuality", (eds) SB Ortner & H Whitehead New York: Cambridge University Pp 80-115

Wolfe, CR (2001) ‘Plant a Tree in Cyberspace: Metaphor and Analogy as Design Elements in Web-Based Learning Environments’ *CyberPsychology & Behaviour*, 4, 1; 67 -76

Yu, RN et al (1998) ‘Role of Ahch in gonadal development and gametogenesis’ *Nature genetics* 20, 4; 353-7

United Kingdom Passport Service (2004) United Kingdom Passport Application Online at https://wwwpassportgovuk/Epa1d/indexaspx?c=1 [Accessed 1 January 2007]

Zanaria, E et al (1994) ‘An unusual member of the nuclear hormone receptor superfamily responsible for X-linked adrenal hypoplasia congenita’ *Nature* 372, 6507; 635-641

Zanaria, E et al (1995) ‘Xp duplications and sex reversal’ *Philosophical Transactions of the Royal Society of London - Series B: Biological Sciences* 350, 1333; 291-296

Zhang, H et al (2000) 'DAX-1 functions as an LXXLL-containing corepressor for activated estrogen receptors' *Journal of Biological Chemistry* 275, 51; 39855-39859

Slavok, Z (2005) *Interrogating the real* London: Continuum

Vainio, S et al (1999) 'Female development in mammals is regulated by Wnt-4 signalling' *Nature* 397; 405-409

Vaiman, D (2002) 'Fertility, sex determination, and the X chromosome' *Cytogenet Genome Res*, 991, 4; 224-8

Vesalius, A (1543) *De Corporis Humani Fabrica* Images can be viewed online http://wwwnlmnihgov/exhibition/historicalanatomies/vesalius_homehtml [Accessed 1 January 2007]

Vesna, V (2001) 'Toward a Third Culture: Being In Between' *Leonardo* 34, 2; 121-125 Online at http://musejhuedu/journals/leonardo/v034/342vesnahtml [Accessed 1 January 2007]

Von Staden, H (1995) 'Anatomy as Rhetoric: Galen on Dissection and Persuasion' *The Journal of the History of Medicine and Allied Sciences* 50; 47-66

Vidal, C (2005) 'Brain, Sex and Ideology' *Diogenes* 208; 127-133

Vilain, E and McCabe, ER (1998) 'Mammalian sex determination; from gonads to brain' *Molecular genetic & metabolism* 652; 74-84

Yuan, X et al (2001) 'SRY Interacts with and Negatively Regulates Androgen Receptor Transcriptional Activity' *Biol Chem*, 276, 49; 46647-46654

Xu, J et al (2002) 'Sex differences in sex chromosome gene expression in mouse brain' *Hum Mol Genet* 1112; 1409-1419