

# Male sex drive and the masculinization of the genome

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## Summary

Charles Darwin remarked that “males, with their superior strength, pugnacity, armaments, unwieldy passion and love songs, are almost always the more active and most often, the initiators of sexual interactions”.<sup>(1)</sup> Here, we propose that such male sex drive directly impacts the genome by leading to its progressive masculinization—genes that possess sex-specific effects on male fitness accumulate to a much greater extent and are generally more diverged.<sup>(2,3)</sup> The larger proportion of male versus female fitness modifiers in combination with stronger sexual selection may generate evolutionary signatures such as a greater sensitivity to male sterility<sup>(4)</sup> and a paucity of X-linked male-specific genes.<sup>(5–8)</sup> Male sex-drive theory complements the female-choice theory of sexual selection and allows for the genetic variation of costly sexual traits to be continuously replenished. *BioEssays* 27:518–525, 2005. © 2005 Wiley Periodicals, Inc.

## Introduction

Sexual dimorphism, i.e. phenotypic differences between male and female members of the same species, forms a major component of the total biological diversity found among sexual organisms. Morphological differences between males and females range from cryptic to explicit and cover a seemingly endless range of possibilities. Extreme sexual dimorphism, such as the length of the peacock's tail and coloration and brightness of its plumage, puzzled Charles Darwin as these traits on the surface appeared maladaptive and presumably could not have evolved by natural selection.<sup>(1)</sup> Noting that much of this dimorphism was due to larger differences among males, Darwin provided an explanation by invoking a special form of natural selection which he called sexual selection—secondary sexual traits showing exaggerated appearance in males are the result of female choice for choosing mates.<sup>(1,9)</sup> Darwin considered sexual selection important enough to give it a separate name and the evolution of male novelty has been the subject of intensive and prolonged study in evolutionary biology.<sup>(10)</sup>

In this paper, we highlight literature suggesting that a larger variance in male traits is observable not only at the level of morphology but also at the genic level, and that, among sexually reproducing species, the acquisition of new male characters and genes is a recurrent process precipitated by a male-driven force of evolutionary change. This process further masculinizes the genome by driving the rapid divergence of male-specific genes as well as differential patterns of male gene expression. As the flipside to female choice, we introduce the term, male sex drive, to encapsulate the general dominance of males over females in developing new strategies to mate and pass on offspring. The overall number of male-versus female-biased genes, the mutability and fitness differences between sexes, as well as the nature and propensity of sexual selection in males is addressed to explain the genetic basis of male sex drive. We conclude that a genome-wide pattern of masculinization is inevitable with indirect consequences at both molecular and organismic levels. The sensitivity of male sterility compared to female sterility in both natural populations and interspecific hybrids may be an indirect result of genomic masculinization. The observed paucity of X-linked male fertility genes may be a consequence of the evolution and selected enrichment of new male fitness modifiers or male-biased genes on the autosomes and, furthermore, the higher migration of retrogenes from the X chromosome to the autosomes could simply be the result of their preferential retention by stronger male sex drive in males. In addition, maladaptive male characters may arise and become immediately engaged in a cyclic process of sexual selection. The hypothesis that the animal genome is prone to ‘masculinization’, i.e. enrichment by an accumulating number of new and/or rapidly evolving male-biased genes or male fitness modifiers, is supported by a variety of genetic, molecular and fitness-related studies of male versus female function.

## A progressively masculinized genome

Just as males, on their surface, possess a greater collection of morphological and behavioural embroidery, genomes as a whole appear to be enriched in male genes. Moreover, recent findings show that, on average, these genes are more diverged between species. Below, we highlight studies with a special focus on *Drosophila* since this genus, by far, holds the most comprehensive sets of applicable data. The following evidence, which includes the larger presence of male-biased genes, the preferential production of male genes, and faster-

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male divergence, together, suggest that genomes from sexual taxa become masculinized over time.

#### *A larger repertoire of male sexual traits and genes*

In terms of their contribution towards reproduction, males and females are not equal. Males possess a broader spectrum of behavioural and other traits affecting reproductive fitness ranging from mate recognition and courting to mating and mate guarding after copulation. For example, males in different species are known to employ extreme acts such as self-sacrifice in order to procure copulation.<sup>(11)</sup> Accordingly, the diversity of traits affecting male fitness makes males a larger target for sexual selection.

In terms of the relative number of loci, classic data from *Drosophila* isofemale lines argue for a larger fraction of male-biased genes. For example, homozygous chromosomal (autosomes) lines of *D. melanogaster* and *D. pseudoobscura* generate, on average, 17% sterility in males, 9.8% in females and 3.2% in both sexes.<sup>(4)</sup> In addition, because male-sterile mutability is roughly 15% that of lethality<sup>(12,13)</sup> and three-quarters of loci from each of the 5000 salivary-gland chromosome bands can produce inviability,<sup>(14)</sup> then more than 500 loci are capable of mutating to male sterility ( $0.15 \times 0.75 \times 5000 = 500$ ).<sup>(4)</sup> It was also found that one third of all temperature-sensitive lethal mutations produced male sterility at restrictive temperatures.<sup>(15)</sup> This suggests that one third of all loci required for normal development ( $0.33 \times 3750 = 1750$  genes) can produce male sterility.<sup>(4)</sup> Using more modern molecular approaches, Castrillon et al.<sup>(16)</sup> and Gonczy et al.<sup>(17)</sup> found that the majority of autosomal P-element introgressions show expression in the testis again emphasizing the abundance of male molecular targets, at least in the autosomes. In a more recent and comprehensive genetic analysis of male fertility in *Drosophila*, Wakimoto et al screened a large set of EMS-induced homozygote flies and estimated the size of the "male fertility genome" to be, at minimum, 500 loci.<sup>(18)</sup> The authors also find that male-sterile mutations are one-fifth as common as lethals, similar to previous estimates.<sup>(12,13)</sup> Table 1 summarizes a variety of studies that compare the distribution of

male fertility factors as well as sequence and gene expression differences. Overall, they suggest that male fertility genes are greater in number and are more highly diverged than corresponding female genes.

Expression data also support a masculinized genome. To estimate the relative number of transcripts expressed in various tissues, we conducted a global EST survey against the *D. melanogaster* genome (Table 2). All available *D. melanogaster* ESTs from the head, ovary and testis were matched against unique coding sequences from a recent fly annotation.<sup>(19)</sup> Our results indicate that a significantly large fraction of the genome is expressed in the testis and many of these are testis-specific (Table 2), supporting the contention that males have access to a larger number of genes (potential male-biased genes) that can modify their fitness. We note that these results should be viewed with caution. Different tissues contain different amounts of low abundant transcripts and these libraries have been generated using various procedures. In addition, the pool of collected ovary ESTs is much smaller. However, the ratio of total number of ESTs collected from the testis versus the ovary is far less than the ratio of testis-specific versus ovary-specific genes, as estimated from our analysis (2.6 versus 9.9,  $P=0.000$ ), indicating that male-specific germline factors are much more common than female-specific germline factors.

Genome-wide analyses comparing male- and female-biased levels of gene expression from microarrays have also identified a large male-biased fraction.<sup>(6,20,21)</sup> Recently, Parisi et al.<sup>(22)</sup> investigated the genomic basis of sexual dimorphism in *Drosophila melanogaster* using testis-, ovary- and somatic tissues and found that "the cells of the testis deploy a larger battery of specific genes than those of the ovary". Of course, more studies must be pursued in order to clearly assess the differences between male and female transcriptomes. For example, while male targets appear concentrated in the testis,<sup>(22)</sup> female targets of sexual selection may be dispersed throughout the organism, i.e. non-ovary tissues. In the future, similar studies using other organisms will certainly provide a more complete picture.

**Table 1.** Evidence in support of a relatively larger number of male-fitness modifier genes in *Drosophila*

Traits	Observation	Reference
Sexual behaviour and morphology	A larger repertoire of male traits	(29,58)
Estimated number of genes affecting male sterility	Roughly one-third of all genes	(4)
Sterility factors segregating in nature	17% (males) versus 10% (females)	(4)
Male sterile mutations	81% affect spermatogenesis of which 68% affect spermatid differentiation	(18)
Expression polymorphism in sex-biased genes	74% (testis) vs 41% (ovary)	(34)
Divergence in genes showing expression polymorphism:	0.180 (testis) versus 0.125 (ovary)	(34)
Hybrid sterility factors (chromosome segments):	23 times greater in males than females	(35)
Hybrid sterility factors (P-element transposition):	36% in males versus 7% in females	(36)
Rate of accumulation of hybrid sterility factors:	10 times greater in males than females	(37)

**Table 2.** Functional chromosomal distribution of *Drosophila* genes using expressed sequence tags (ESTs)

	Tissue-expressed			Tissue-specific		
	Head	Ovary	Testis	Head	Ovary	Testis
Genes Hit	6551	2119	3610	1098	77	765
Autosomal	82%	82%	87%	82%	81%	85%
	5382 (5241)	1747 (1695)	3134 (2888)	895 (878)	62 (62)	648 (612)
X-linked	18%	18%	13%	18%	19%	15%
	1169 (1310)	372 (424)	476 (722)	203 (220)	15 (15)	117 (153)

ESTs derived from testis ( $n = 37,733$ ), ovary ( $n = 14,471$ ) and head (112,698) (BGDP) were blasted ( $P < 1E-200$ ) against a set of 20,622 *Drosophila* genes (Hild et al., 2003). Indicated is the number of genes expressed in the three chosen tissues. Those genes with ESTs expressed solely in one tissue are denoted as tissue-specific and are also not found in other libraries including embryo ( $n = 120,477$ ), larvae ( $n = 27,808$ ) and various cellular libraries ( $n = 34,985$ ). Expected numbers, based on the X chromosome harbouring one fifth of the total number of genes in *D. melanogaster*, are indicated in parentheses.

### New male genes

The testis appears to be especially well-suited for the evolution of new gene functions and uncovered de novo genes in *Drosophila* have, for the most part, been found to be testis specific. Such examples also provide a mechanism for possessing a larger repertoire of male genes. In one example, *Sdic*, a gene encoding a novel sperm-axoneme protein, was recently formed by the splicing of two neighbouring loci in the *D. melanogaster* lineage and not in any of its sibling species during the last three million years.<sup>(23,24)</sup> *jing-wei*<sup>(25)</sup> and *ocnus*<sup>(26)</sup> also encode newly evolved transcripts that are abundant in testis extracts. Comparative analyses at the genome-wide level are beginning to provide evidence that much de novo gene evolution is occurring among male-biased genes. These studies also have the added potential to identify a large number of newly evolved candidates. In a recent genomic comparison between two congeneric *Drosophila* taxa, it was found that genes with testis-derived ESTs in *D. melanogaster* are far less likely to have putative orthologs in the *D. pseudoobscura* draft sequence compared to *D. melanogaster* genes with ESTs from other libraries (Richards et al. 2004, In Press Genome Research). One-fifth of testis derived ESTs did not match any *D. pseudoobscura* sequence via TBLASTN hits, compared to approximately 13% of non-testis ESTs. Of course, many of these orphans may represent highly diverged gene sequences. Nonetheless, annotated protein-coding genes from *D. melanogaster* with ESTs derived from testis-specific libraries had a mean amino acid identity of 60%, much lower than the overall distribution's mode near 85% amino acid identity.

We would like to add that de novo male gene evolution not only includes the addition of new genes, but may also include the switching of sexually undifferentiated genes (or even female-biased genes) to male-biased expression. More research must be conducted to understand the prevalence of such switches (but see Ranz et al.<sup>(7)</sup> below).

### Faster male divergence

Molecular surveys also reveal a much larger variance in protein polymorphism and divergence as well as levels of gene expression among male-biased genes and orthologs. This generally higher evolutionary rate found among male genes has been previously termed the "faster-male hypothesis".<sup>(27)</sup> In *Drosophila*, some of the first evidence supporting faster-male evolution at the molecular level was observed using two-dimensional gel electrophoresis. Testis-expressed proteins exhibited higher levels of within species variation<sup>(28)</sup> as well as between species divergence<sup>(2)</sup> when compared to other tissues such as the ovary and brain. Later studies focused on gene coding sequences and found that sex-related genes, of which male genes form a large fraction, are more rapidly evolving than non-sex-biased genes.<sup>(29,30)</sup> In terms of specific function, accessory gland proteins have also been highlighted as a rapidly evolving class of genes in *Drosophila* possessing a high level of polymorphism<sup>(31)</sup> with a substantive fraction positively selected.<sup>(5)</sup> Since these early studies in *Drosophila*, literature from other organisms has also corroborated the faster-male hypothesis. Among primates, reproductive genes, the majority of which are male, are far more diverged than non-reproductive genes.<sup>(3)</sup> DNA sequence comparisons have shown the rapid evolution of mammalian sperm proteins<sup>(32)</sup> and the rapid evolution of sex- and reproduction-related genes in general.<sup>(29,33)</sup>

Moreover, recent gene expression studies support the rapid pace of male evolution. Using cDNA microarrays from a subset of the *D. melanogaster* genome, Ranz et al.<sup>(7)</sup> showed that sex-biased gene expression is a widespread phenomenon evolving very rapidly between sibling species of *Drosophila*. Approximately half the genes showed differences in expression between the sexes, and among these, a remarkably high fraction, ~83%, involved a gain, loss, increase, decrease or reversal of sex-biased expression between species. In an associated gene array study, it was also demonstrated that

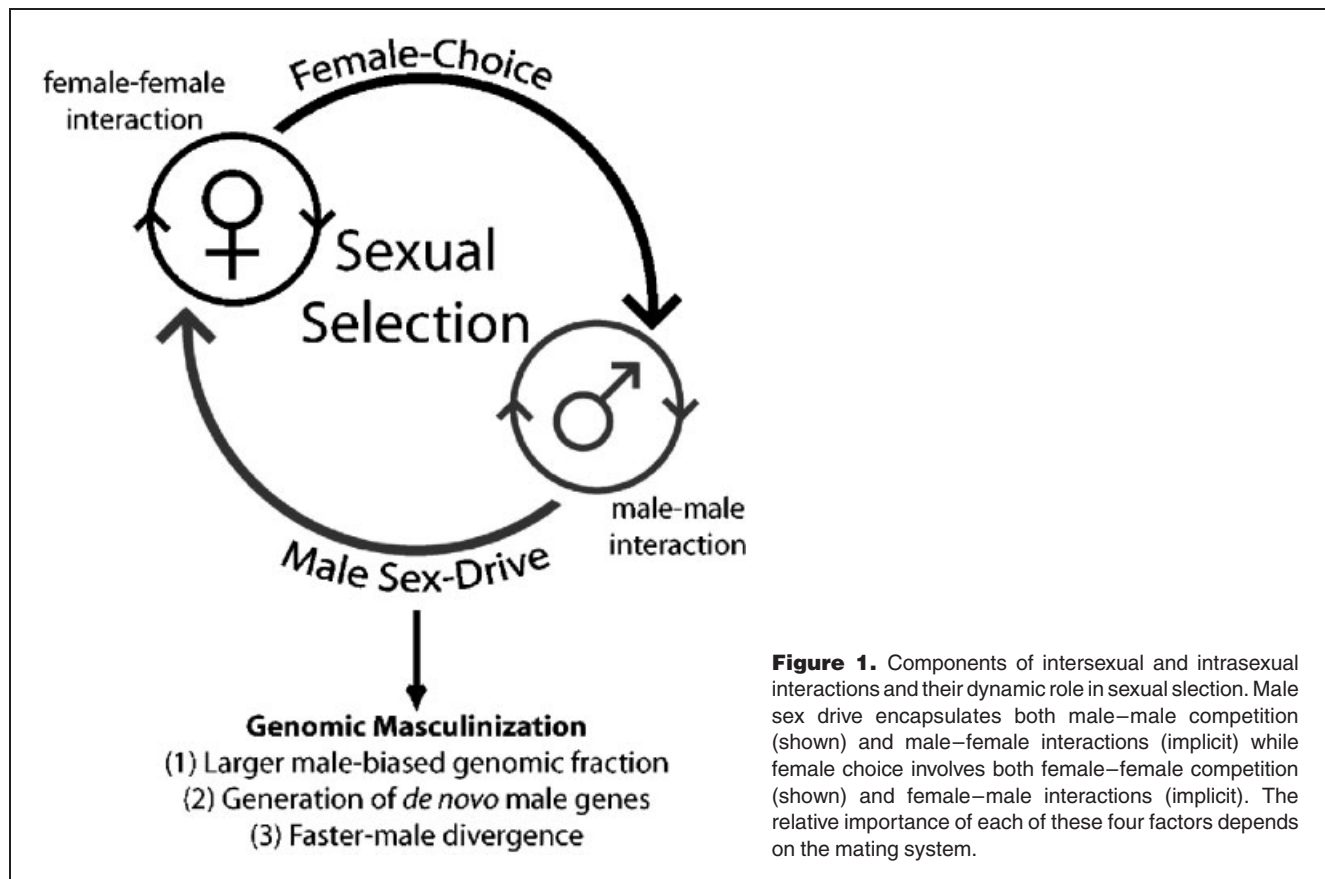
male-biased genes have higher level of gene expression polymorphism than both female-biased and sexually unbiased genes between natural populations of *D. melanogaster*,<sup>(34)</sup> thus connecting the long-term evolutionary dynamics of sex-biased genes to short-term within population variation. Therefore, the number of sexually dimorphic targets in the genome appears to be plentiful and the evolution of these targets occurs at a very rapid rate.

The commonality of hybrid male over female sterility also supports a more rapid divergence and/or larger number of male genetic factors. Using chromosome segment introgressions between species, it was shown that male steriles appeared up to 23 times more frequently than female steriles.<sup>(35)</sup> In a similar introgression study, True and colleagues, using X-chromosomal P-element introgressions of *D. mauritiana* into a *D. simulans* background, found that only 7% of the homozygous autosomal sublines were female sterile whereas 36% showed male sterility.<sup>(36)</sup> More recently, using high density QTL mapping, Tao and Hartl<sup>(37)</sup> showed that there is at least a 10-fold greater accumulation of hybrid male-sterility factors than hybrid female-sterility or lethality factors. We expect that the number of loci that can mutate and interact to cause hybrid male sterility must be greater than the number estimated from within species since new male fitness

modifiers may become trapped by sexual selection over time thus enriching the genome with male-biased genes that may interact with each other in a non-additive manner. Nevertheless, the order of magnitude difference between incidences of hybrid male sterility versus hybrid female sterility in *Drosophila* strongly supports a masculinized genome.

### Sexual selection and male sex-driven evolution

So what drives such enormous diversity in males? In other words, what mechanism(s) generates the pattern of masculinization that we observe in sexual taxa such as *Drosophila*? Of course, Darwin's explanation for the large amount of male morphological diversity was sexual selection which could develop from either of two ways: 1) male–male competition or 2) female choice.<sup>(1)</sup> For years, researchers have focused on female-choice models of sexual selection. The main goal of this paper is to show that the countless examples of bizarre and radical male strategies that have evolved to procure mates at the behavioural, physiological and morphological levels have conspicuous parallels at the genomic level. We argue that genomic masculinization is so strong a pattern that we must assign a new term, “male sex drive”, to illustrate both its organismic and molecular natures that complements female choice (Fig. 1). The masculinization of the genome—de novo



**Figure 1.** Components of intersexual and intrasexual interactions and their dynamic role in sexual selection. Male sex drive encapsulates both male–male competition (shown) and male–female interactions (implicit) while female choice involves both female–female competition (shown) and female–male interactions (implicit). The relative importance of each of these four factors depends on the mating system.

and rapid divergence on the larger male-biased fraction of the genome—is part of a self-perpetuating selective process enveloping aspects of both intra- and intersexual competition.

In fact, recent studies of sexual dimorphism at the molecular level reveal that sexual selection is much more common than previously imagined. A growing body of data from a variety of organisms shows that sex and reproduction-related genes in general and particularly those expressed in males evolve under stronger sexual selection and evolve faster than other genes.<sup>(29,33)</sup> Understanding the genetic basis of sexual dimorphic characters is an emerging field and we encourage more researchers to study sex-dependent genotypic differences. Results such as those from the Ranz et al microarray analysis on whole adults from *Drosophila melanogaster* versus *D. simulans*<sup>(7)</sup> and the Parisi et al.<sup>(22)</sup> global transcriptome survey on germline versus somatic biased expression in *D. melanogaster* (see above) are exciting as they underscore the prevalence and rapid evolution of sexually dimorphic gene expression.

Naturally, we also need to consider alternative non-selective explanations for the rapid evolution of male genes. Higher divergence may be the result of higher neutral substitution rates caused by lower functional constraints. Yet numerous studies have demonstrated a selection-driven process of male-biased evolution among rapidly evolved genes.<sup>(3,33)</sup> Moreover, it would be very difficult to explain the preferential fixation of de novo male genes in the absence of strong selection.

### Implications of male sex-drive

While a larger repertoire and generally faster divergence of both ancestral and recently derived male genes demonstrate the genomic capacity of male sex drive, a number of indirect consequences are expected. Below, we address four implications of stronger male sex drive.

#### *Higher sensitivity of spermatogenesis*

The higher incidence of male sterility over female sterility and of hybrid male sterility over hybrid inviability has been argued to be the result of a greater susceptibility to developmental perturbation in spermatogenesis.<sup>(27)</sup> Much of this may have to do with the instability caused by the rapid divergence of male factors as well as the recruitment of new spermatogenic genes. The early condensation of the X chromosome during spermatogenesis may also be a destabilizing factor as the X chromosome is not a suitable location for postmeiotic genes affecting spermatogenesis.<sup>(38)</sup> Sexual conflict and evolution of meiotic-drive genes on the sex chromosome can also make spermatogenesis more sensitive to perturbation.<sup>(6,37)</sup>

In *Drosophila melanogaster*, spermatogenesis shows an enhanced sensitivity to such genetic changes as translocations, deletions and insertions that involve the X chromosome.<sup>(39)</sup> Males carrying a reciprocal translocation between

the X chromosome and an autosome T(X:A) are known to be sterile yet females that are heterozygous or homozygous for a T(X:A) are fertile. The conclusion drawn from these observations is that spermatogenesis, and not oogenesis, requires synchronous decondensation and condensation events between the X and autosomal chromosomes. Interestingly, the type of sterility involved with this translocation is spermiogenic, similar to the sterility phenotypes found in F<sub>1</sub> hybrids of closely related species.<sup>(40)</sup> It was also shown that X-chromosomal duplications have a much more severe effect on male than female sterility.<sup>(4)</sup>

These chromosome-dependent explanations of a higher sensitivity of spermatogenesis may result from male sex drive. Although earlier comparisons that have tested the faster-X hypothesis do not find a difference in divergence between the X chromosome and autosomes,<sup>(41–43)</sup> it has recently been shown that, if genes are grouped according to functional class, significantly higher divergence rates may be seen, for example, among sperm-specific mammalian proteins.<sup>(44)</sup> Important to this discussion is the fact that the majority of male-biased genes are concentrated in the testis while female-biased genes appear to have a wider tissue distribution.<sup>(22)</sup> Therefore, the faster divergence of male genes on the unmasked hemizygous X chromosome, as well as their narrow tissue distribution relative to female-biased genes, may both factor into the prominence of male sterility. This may also explain the much weaker pattern of the prevalence of hybrid sterility over hybrid inviability in taxa with female heterogamy.<sup>(27)</sup>

#### *Deficiency of male fertility genes on the X chromosome*

Performing a global microarray analysis of gonadal versus non-gonadal tissues of *Drosophila melanogaster*, Parisi et al.<sup>(6)</sup> reported a paucity of male-biased genes and an excess of female-biased genes on the X chromosome. They found that 45% of X-linked genes were expressed preferentially in testis whereby the average proportion for autosomal genes was 57%. Further, by comparing the *Drosophila* genome against the mosquito, *Anopheles gambiae*, they found that only a handful (5%) of *Drosophila* genes with male-biased expression have retained X-linkage in *Anopheles*. In contrast, about 10% of *Drosophila* female-biased genes maintained X-linkage in *Anopheles*. These authors conclude that the X chromosome has become ‘demasculinized’ due to the transfer of X-linked male-function (male-biased) genes to the autosomes and this has occurred, because of the hemizygous expression of genes affecting male function. The authors invoke sexual antagonism,<sup>(45)</sup> i.e. that genes that are beneficial to males but detrimental to females will be better off being on the more male-friendly environment, the autosomes. Ranz et al.<sup>(7)</sup> too found fewer male-biased genes but more female-biased genes on the X chromosome. Another explanation offered is the condensation of the X chromosome and silencing of X-

linked genes during male meiosis.<sup>(46)</sup> Our systematic comparison of ESTs between *D. melanogaster* and *D. pseudoobscura* demonstrate that, unlike genes expressed in the head and ovary, testis-expressed and testis-specific genes are underrepresented on the X chromosome (Table 2).

Recent studies in other organisms appear to uphold the contention that male genes that are more likely to be targets of sexual selection are preferentially found on the autosomes. For example, sperm-enriched transcripts were too found to be rare on the worm X chromosome.<sup>(47)</sup> In contrast, at first glance, mammals appear to have an overrepresentation of spermatogenic genes on the X chromosome.<sup>(48)</sup> However, on closer inspection, these X-linked loci are expressed in early-stage spermatogonial cells.<sup>(49)</sup> Late spermatogenic genes—those genes that may directly be involved in the fine tuning of sexual selection processes—are significantly underrepresented on the X chromosome.

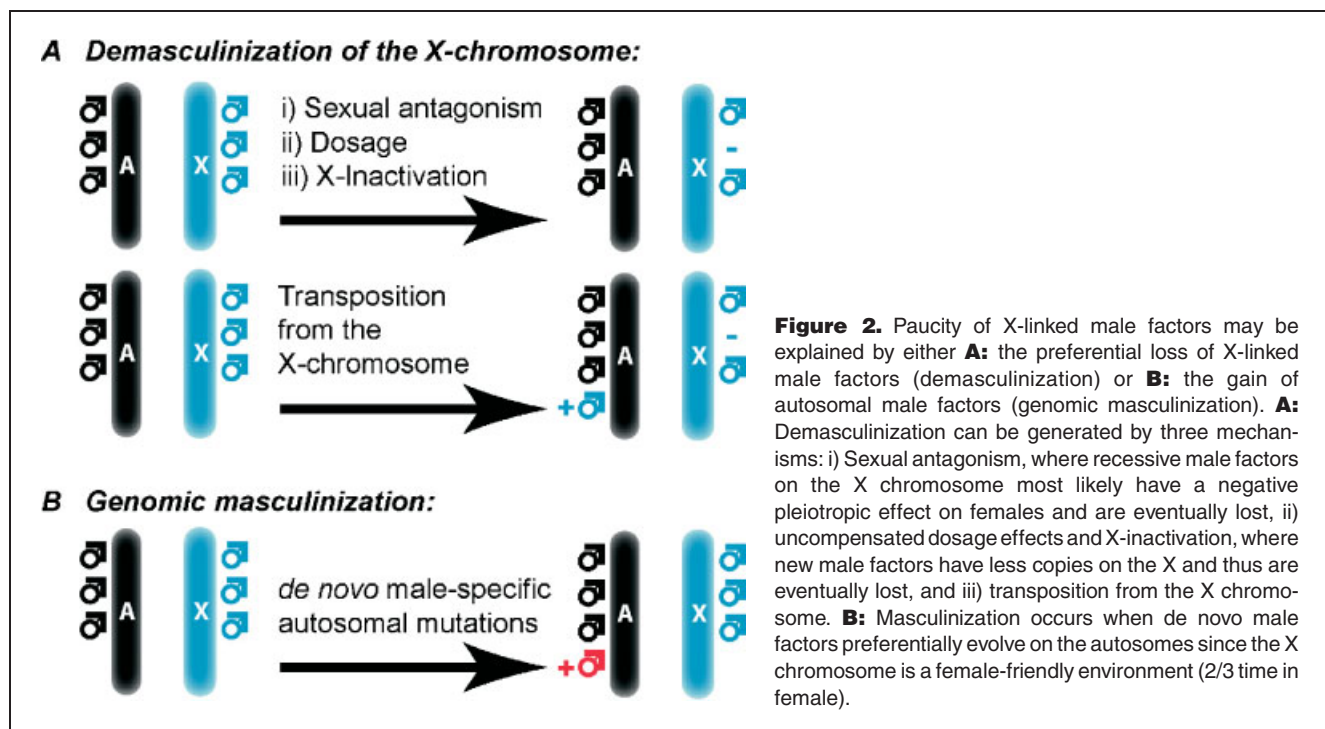
While some authors have argued that the lack of spermatogenic genes on the X chromosome may be due to X-specific inactivation during male meiosis,<sup>(38,49)</sup> somatic male-specific genes that are not affected by chromosome-specific X-inactivation are also underrepresented on the X chromosome. Swanson et al.<sup>(5)</sup> screened over 200 expressed sequence tags (ESTs) from male accessory glands in *D. simulans* and observed a highly significant underrepresentation of accessory gland-derived ESTs on the X chromosome. Accessory gland proteins (ACPs) assist sperm in female insemination and many have been demonstrated to be under strong

selective forces.<sup>(5)</sup> Their autosomal location makes sense in view of their post-spermatogenic role. However, fly ACPs are somatically expressed and the X chromosome is not inactivated in the soma.

The male sex drive hypothesis predicts a higher autosomal fraction of male-biased genes without invoking X-inactivation. The difference in the proportion of male genes between autosomes and X chromosomes may simply be the result of a mutation-selection enrichment of male-biased genes on the autosomes. Such new male genes and new male-fitness modifiers are expected to evolve relatively rapidly as a result of sexual selection. As a result, many more genes on the autosomes are available to mutate to produce sex specific male functions compared to available loci on the X chromosome. In retrospect, this would have the effect of the X chromosome expressing fewer than expected and the autosomes more than expected male-biased genes as shown by microarray and EST datasets<sup>(5–7)</sup> (Fig. 2) across flies, worms and mammals.

#### *Retrotransposition of genes from the X chromosome to autosomes*

In mammals, Emerson et al.<sup>(8)</sup> found that a significantly higher number of functional retrogenes have moved from the X chromosome to the autosomes than in the reverse direction in both mouse and human. This pattern is also observed in *Drosophila*.<sup>(50)</sup> In both cases, they show that a significant proportion of the transposed genes are expressed in the



testis. At first glance, this differential movement of genes from the mammalian X chromosome provides a mechanistic explanation for the paucity of spermatogenic genes on the X chromosome of worms,<sup>(47)</sup> *Drosophila*<sup>(6,7)</sup> and mammals.<sup>(49)</sup>

Similar to the previous section, there is a simpler and more logical explanation for the excess of X-chromosome to autosome retrotranspositions that does not assume that the X chromosome is a non-preferred site for spermatogenic genes. Even if the rate of retrogene movement is equal in both directions, stronger selection on male sexual genes and traits<sup>(29)</sup> would result in the selective retention of a larger number of retrogenes moving from the X to autosomes than those moving in the opposite direction—this pattern should occur since we assume that a higher proportion of transposed genes from the X chromosome are, or may become, preferentially involved in affecting sexual function<sup>(51)</sup> and hence may be under stronger sexual selection. A growing number of examples of testis-specific retrogenes that were originally X-linked and now are autosomal, are observed in mammals (see ref. 12–23 in Ref. 51). This observation is also strongly observed in *Drosophila*.<sup>(50)</sup> In addition, unbiased gene transpositions most likely result in a higher probability of lethality and may rarely fix. The newly transposed retrogenes on the autosomes would provide additional copies of the parental genes from the X chromosome, which may lead to higher levels of gene expression. Sex-biased gene transpositions from the autosomes to the X chromosomes do not have this advantage. New retrogenes would also provide raw material (duplicate copies) for the evolution of new gene functions.

**Maintenance of genetic variation in costly male traits**  
Since continuous female choice would lead to an eventual loss of genetic variation in male sexual traits, it has been suggested that the “Lek paradox” may result, i.e. why females keep exercising choice in mate selection when there is nothing to gain from this behaviour.<sup>(52)</sup> Rowe and Houle<sup>(53)</sup> introduced the gene recapture hypothesis to solve the Lek paradox by proposing that a condition-dependent expression of costly sexual male traits would involve a large number of genes in the genome and thus would provide an inexhaustible source of genetic variation in sexual traits.

The male sex drive hypothesis would effectively and unconditionally solve the problem of the maintenance of genetic variation, not only for costly visible sexual traits but for all sexual traits—visible and cryptic. This is because the male's drive to secure mates and reproduce would lead to recapture mutations that affect any male trait involved, directly or indirectly, in sex- and reproduction-related function. Under the male sex drive hypothesis, the loss of genetic variation in sexual traits by selection and drift would be more than compensated by a continuous input of mutations (new genes) and selection. Thus male sex drive is a more general hypo-

thesis than the gene capture hypothesis proposed to solve the problem of costly sexual traits.<sup>(54)</sup>

### Conclusions

A variety of sources suggest that the number of loci available to affect male function including fertility are larger than those affecting female function. The recruitment and accumulation of new male-fitness modifiers through strong male sex drive leads to a gradual enrichment or ‘masculinization’ of the genome by male-biased genes. Genomic masculinization via the rapid evolution of male genes is not limited to sequence divergence (i.e. faster-male evolution) and differential expression levels but also extends to loss and gain of function as well as the creation of new male-specific genes. Stronger sexual selection through higher variation in gene expression is seen here as the driving mechanism for the differential accumulation/excess of autosomal male-biased genes. This explanation provides a different perspective on the cause of the unbalanced chromosomal distribution among male- and female-biased genes than those previously offered<sup>(6,8,55,56)</sup> as well as the higher sensitivity of spermatogenesis. Furthermore, the consequences of male sex drive are not only seen in the overall number, distribution and divergence of male-biased elements, but also in the overall sexual dimorphism of the species.

Darwin proposed sexual selection as a special mechanism to explain exaggerated secondary sexual male traits. Sexual selection differs from natural selection in that it is a cyclic process that takes place continuously every generation in all sexually reproducing organisms and in all environments—constant or variable. Furthermore, sexual selection is a combined process involving female choice and male sex drive (Fig. 1) and initiates after viability selection is completed. Thus, it has the potential to make significant readjustments to the outcome of viability selection. Recent molecular studies extend the role of sexual selection, particularly male sex drive, and reinforce the idea that it is a powerful force of evolutionary change—explicit or cryptic.<sup>(2,29,57)</sup> Looking back to Darwin's treatment of sexual selection, the peacock's tail appears to have been only the tip of the iceberg.

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