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PURGING THE GENOME WITH SEXUAL SELECTION: REDUCING MUTATION LOAD THROUGH SELECTION ON MALES

Michael C. Whitlock[1,2] and Aneil F. Agrawal[3,4]

[1]*Department of Zoology, University of British Columbia, Vancouver, BC V6T 1Z4 Canada*

[2]*E-mail: whitlock@zoology.ubc.ca*

[3]*Department of Ecology & Evolutionary Biology, University of Toronto, 25 Harbord St., Toronto, ON, Canada, M5S 3G5*

[4]*E-mail: a.agrawal@utoronto.ca*

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Healthy males are likely to have higher mating success than unhealthy males because of differential expression of condition-dependent traits such as mate searching intensity, fighting ability, display vigor, and some types of exaggerated morphological characters. We therefore expect that most new mutations that are deleterious for overall fitness may also be deleterious for male mating success. From this perspective, sexual selection is not limited to influencing those genes directly involved in exaggerated morphological traits but rather affects most, if not all, genes in the genome. If true, sexual selection can be an important force acting to reduce the frequency of deleterious mutations and, as a result, mutation load. We review the literature and find various forms of indirect evidence that sexual selection helps to eliminate deleterious mutations. However, direct evidence is scant, and there are almost no data available to address a key issue: is selection in males stronger than selection in females? In addition, the total effect of sexual selection on mutation load is complicated by possible increases in mutation rate that may be attributable to sexual selection. Finally, sexual selection affects population fitness not only through mutation load but also through sexual conflict, making it difficult to empirically measure how sexual selection affects load. Several lines of enquiry are suggested to better fill large gaps in our understanding of sexual selection and its effect on genetic load.

KEY WORDS: **Condition, male mating success, mean fitness, mutation load, sexual selection, vigor.**

Sexual selection is the selection that arises from differential mating success among living individuals. Although the study of sexual selection has focused on the evolution of showy secondary sexual traits such as the peacock's tail, other factors may contribute even more heavily to the mating success of an individual. For example, the overall health of a male may determine the energy with which he searches for and courts females, the strength and weight of a male may determine the outcome of interactions between rival suitors, and the vigor and condition of a male may directly affect his attractiveness to a potential mate (Andersson 1994). Although some of these effects may be mediated through effects on exaggerated morphological characteristics, the health and condition of a male has great potential also to directly affect his mating success.

Most genes in the genome likely contribute to the overall health of an individual (Houle 1991; Rowe and Houle 1996). If overall health affects mating success, then the majority of the genome is subject to some degree of sexual selection. Importantly, for this large class of genes, sexual selection will on average favor the same alleles that are favored by viability selection or selection on female fecundity.

Darwin recognized that most aspects of an organism's phenotype may help determine its mating success. In the *Origin* (1859), he said, "Amongst many animals, sexual selection will give its aid

to ordinary selection, by assuring to the most vigorous and best adapted males the greatest number of offspring." Later, Darwin wrote at greater length about sexual selection in *The Descent of Man* (1871). Starting a strong tradition that continues to this day, he recognized that the curious features of organisms that are only explained by sexual selection—such as the peacock's tail and the stag's horns—are the most interesting subjects for the study of sexual selection. However, most genes that are under sexual selection arguably do not directly affect elaborated morphological characteristics, but rather affect mating success through the health and condition of individuals.

In this perspective, we explore the population genetic consequences of genome-wide positive correlations between mating success and health. Sexual selection of this form can help purify the genome of deleterious mutations and facilitate adaptation generally. We review the evidence for genetic correlations between mating success and productivity, and we focus on the role of sexual selection in affecting the fate of deleterious mutations. We suggest that sexual selection can substantially reduce mutation load, although the total effect of sexual selection on mean fitness may be much smaller or in the opposite direction, because of sexual conflict.

Our argument is based on the idea that if a random mutation occurs it will tend to have a negative effect on male mating success as well as other aspects of fitness (e.g., viability, female fecundity). This logic follows from the premise that most mutations will be deleterious with respect to overall health/condition and that all major fitness components depend, at least in part, on overall condition (Houle 1991; Rowe and Houle 1996). Indeed, it has been argued that much variation in mating success results from variation in the ability to acquire resources, which should cause mating success to positively vary with other fitness components (Rowe and Houle 1996). We will argue below that for most loci selection should be in the same direction for both males and females. For some important loci, however, this assumption will clearly not hold. Some mutations will affect males and females in opposing ways; these sexually antagonistic alleles are important in creating intralocus sexual conflict (Arnqvist and Rowe 2005). More importantly, for this subset of loci, this antagonism between the sexes can create conditions for the maintenance of genetic polymorphism at high allele frequencies (Kidwell et al. 1977; Rice 1984). Consequently, loci with such alleles can disproportionately contribute to standing genetic variation for fitness components, even though they may represent a small fraction of the genome. In contrast, the magnitude of mutation load depends on new mutations (rather than alleles maintained by balancing selection), which are likely to be more consistent in their effects on different fitness components. Although our primary interest is in assessing the role of sexual selection in reducing mutation load, our perspective will necessarily include some discussion of sexual conflict. In experiments, sexual conflict may act to obscure the role of sexual selection in eradicating unconditionally deleterious alleles (Rowe and Day 2006).

To be clear, we should describe what this review is not about. We do not discuss the evolution of showy sexual secondary characteristics or mating preferences, or the reasons behind them. Although we believe that a diversity of factors—for example good genes, sexual conflict, the runaway process—may play a role in the evolution of secondary traits, the mechanisms by which preferences evolve do not directly determine the mutational consequences of sexual selection. Although we argue that in many cases the individuals with "good gene" may have higher mating success, we do not address the issue of whether this correlation was instrumental in determining the evolution of mating preferences. For example, consider two alternative scenarios for the evolution of female mating behaviors. The so-called "good-genes" hypothesis for female preference postulates that females have evolved to prefer healthy males because their offspring will receive these good genes from their fathers (i.e., indirect benefits). In contrast, sexual conflict theory postulates that female behaviors evolve to minimize sexual interactions with males because of the direct costs of high mating rates (Arnqvist and Rowe 2005). Females tend to mate with healthy males, not because they actively prefer these males, but rather because females are better able to resist the advances of poor condition males than the more vigorous harassment by healthy ones. Although the underlying explanation for female mating behavior differs between these scenarios, the outcome is the same—healthy males have high mating success. We are concerned with the consequences, not the causes, of sexual selection affecting the genome as a whole.

Sexual Selection and Mutation Load

New mutations on average reduce the fitness of an individual (Lynch et al. 1999; Keightley and Eyre-Walker 2000; Keightley and Lynch 2003), and natural selection acts to remove those mutations from the population. However, selection does not immediately remove all deleterious alleles, so that some small frequency of deleterious mutations may exist at each locus. The mean fitness of the population is reduced as a result of these mutations, a reduction called the mutation load. Even though any specific deleterious allele is likely to be rare, most individuals will carry many deleterious alleles because there are so many loci at which mutations can occur.

Most of our theoretical understanding of mutation load uses logic originated by Haldane (1937). Haldane made several reasonable simplifying assumptions, such as random mating and large population size, and found that the frequency of a deleterious allele at an equilibrium between mutation increasing its frequency and selection removing it is approximately $q_{eq} = \mu / s$, where μ

is the mutation rate from good to bad alleles and s is the selection coefficient against the allele as a heterozygote. The reduction in the mean fitness of the population that results is equal to the frequency of the allele times its effects on absolute mean fitness, s_A, so that the mutation load caused by a locus is expected to be

$$L \approx 2s_A q_{eq} \approx 2s_A \mu / s,$$

assuming incomplete dominance with diploid individuals. Under the common assumption that the effects of a mutation on the population mean fitness are equal to its selection coefficient, $s_A = s$, and the load due to a locus simplifies to $L \approx 2\mu$.

Haldane showed that the mutation load can be surprisingly large when mutations across the entire genome are considered. Over the whole genome, the load is expected to be approximately $1 - e^{-U}$, where $U = \Sigma 2\mu$ is the number of new mutations per diploid individual. Under his assumptions, the average individual at mutation–selection balance is less than 60% as fit as expected in the absence of mutation when there is on average one deleterious mutation per genome per generation (Haldane 1937; Crow 1997). The potential for mutation to cause such dramatic reductions in mean fitness has caused biologists to propose that mutation load may contribute to population extinction (Lande 1994), the evolution of outcrossing (Charlesworth 1998), inbreeding depression (Charlesworth and Charlesworth 1999), the evolution of sexual versus asexual reproduction (Kondrashov 1982, 1988; Agrawal and Chasnov 2001; Keightley and Otto 2006), the evolution of specialization (Whitlock 1996), genome size evolution (Otto and Marks 1996), and human health problems (Crow 1997).

Various authors (e.g., Kodric-Brown and Brown 1987; Manning 1984; Koselag and Koselag 1993; Whitlock 2000; Agrawal 2001; Siller 2001; Lorch et al. 2003) have hypothesized that mutation load may be reduced by sexual selection because deleterious mutations may be reduced in frequency via selection on mating success, without the associated reduction in mean fitness caused by this selection. Selection on male mating success can reduce the frequency of deleterious alleles, but cannot affect the mean fitness of the population as long as females instead mate with other males. Agrawal (2001) and Siller (2001) suggested that this reduction in mutation load may give sexual populations a sufficient advantage over asexual populations (which of course do not experience sexual selection) such that sexual reproduction may be allowed to evolve and be maintained (see also Jaffe 2003).

Haldane implicitly assumed that selection against a deleterious allele was the same regardless of whether that allele occurred in a male or in a female. In reality, selection is likely to differ between the sexes, for example $s_f \neq s_m$ where s_f is the selection against the deleterious allele in females and s_m is the selection in males. Although viability selection may largely operate in a similar way for the two sexes (Chippindale et al. 2001), sexual selection is a powerful evolutionary force that, in most systems, primarily affects males. Most new mutations are likely to be deleterious in both sexes so we expect both s_f and s_m to be positive but of different magnitudes, often with $s_m > s_f$ (discussed below). When selection differs between the sexes, the equilibrium frequency of the deleterious allele depends on the average selection across the sexes, $s = (s_m + s_f)/2$,

$$q_{eq} = 2\mu/(s_m + s_f).$$

Although the equilibrium frequency of the deleterious allele depends on the average selection coefficient across the sexes, the impact of this allele on population mean fitness may depend primarily on how it affects females ($s_A \approx s_f$) because the number of offspring produced per generation depends largely on the number and fecundity of females. Such will be the case in situations in which we are interested in outcomes affected by population productivity (e.g., extinction risk, competitive exclusion between species, etc.). In such cases, we can express the mutation load as

$$L = 2s_f q_{eq} = 2\mu\left(\frac{s_f}{s}\right).$$

In this context, the load is reduced relative to Haldane's prediction of $L = 2\mu$ whenever the selection on females is weaker than the average strength of selection, s.

To assess the effect of sexual selection on mutation load, we may consider two types of comparisons. First, we may ask, in a sexual species with little sexual selection, what do we expect load to be relative to Haldane's prediction? Making this comparison, the selection against an allele in males would be only that causing differential survival, whereas in females selection will be a function of both differential survival and differential fecundity. If on average male survival and male mating success are affected in the same direction by mutations (which seems to be the case, see below), then without sexual selection s_m is smaller than it would be with sexual selection. As a result, Haldane's calculation assuming equal selection in both sexes will underestimate the true mutation load if applied to a bisexual species without sexual selection.

On the other hand, we may also wish to ask whether sexual selection can typically reduce load to a level lower that predicted by Haldane. Compared to Haldane's case when selection is equally strong in both sexes, load is reduced whenever selection is stronger on males than females ($s_m > s_f$). In essence, females enjoy the benefits of sharing a gene pool that is purified at the expense of stronger selection on males. For example, consider a situation in which there is on average one deleterious mutation per genome per generation ($U = 1$) and sexual selection causes selection to be twice as strong on these mutations when they occur in males relative to when they occur in females. Ignoring drift, the mean fitness of females at equilibrium with respect to

mutation load will be 40% higher than expected if selection was equal across the sexes (Agrawal 2001).

The arguments above are based on the idea that sexual selection makes selection in males stronger than selection in females ($s_m > s_f$). There is a second mechanism by which sexual selection can reduce mutation load: positive assortative mating. Either of the common modes of sexual selection (male–male competition or female choice) may indirectly cause positive assortative mating for fitness (Fawcett and Johnstone 2003). For example, males may always compete for females but those competitions may be more intense for access to high-quality females than for low-quality females such that only high-quality males are likely to win competitions for high-quality females. This would result in a positive correlation in fitness between mates. Regardless of how it occurs, assortative mating for fitness is important because it increases the variance in fitness (Fisher 1918), allowing selection to be more efficient. In simulations, Rice (1998) found substantial reductions in the mutation load if the number of deleterious alleles was even weakly correlated between mates.

Several empirical studies have found patterns suggestive of positive assortative mating for fitness. In a number of species where body size is likely to be positively correlated to fitness in both sexes, there is a positive correlation in body size between mates (e.g., Greenspan 1980; Hieber and Cohen 1983; Snead and Alcock 1985; McLain and Boromisa 1987; Brown 1990; Rowe and Arnqvist 1996; Bonduriansky and Brooks 1998). A study in sticklebacks found that high condition males were more strongly preferred by females in high condition than by females in low condition (Bakker et al. 1999). These studies suggest that the standard theoretical assumption of random mating is unlikely to be strictly true. However, we are still far from knowing whether there is a sufficiently strong correlation in genetic quality between parents (as required by theory) to have a substantial effect on mutation load. More theoretical and empirical work is needed, but we suspect assortative mating for fitness is likely to have only a weak-to-moderate effect on mutation load. Sexual selection is likely to be more important with respect to mutation load by making selection stronger on males than females ($s_m > s_f$). In the remainder of this article we consider the evidence for this idea.

Sexual Selection and Drift Load

Sexual selection may also affect the drift load, that is, the reduction in mean fitness caused by fixation of deleterious mutations via genetic drift. Drift load is the cause of mutation meltdown, hypothesized to increase the extinction probability of small populations (Lynch et al. 1995). Whitlock (2000) showed that, all else being equal, sexual selection could substantially reduce the rate of fixation of deleterious mutations, if as assumed above mutations that negatively affect population mean fitness also have negative effects on male mating success. The basic principle is the same as with mutation load: selection on mating success will increase the total strength of selection against the new deleterious allele, but the effects of the selection on mating success need not affect the mean fitness of the population if the allele ends up fixing by drift.

However, two factors reduce the importance of sexual selection for reducing drift load. First, sexual selection results in greater variance among males in reproductive success, which in turn reduces the effective population size of the species. Lower effective size leads to lower efficacy of selection in removing deleterious alleles, resulting in a counterbalancing effect that acts to increase drift load with sexual selection. The balance of the effective size effect and the strengthened selection effect is not yet known. Second, sexual selection sometimes acts in a density-dependent way, where small populations may have less competition among males than larger populations (Kokko and Rankin 2006). As a result, sexual selection may be less effective precisely when drift load matters most, in small populations. On the other hand, some sexually selected traits, such as mate-search ability, are under stronger selection in low-density populations (Kokko and Rankin 2006); selection mediated through these types of traits would be stronger in low-density populations. The only study that has measured sexual selection on deleterious alleles at different densities found no clear effect of density on the strength of sexual selection; selection was stronger at high density for some mutations but stronger at low density for other mutations (Sharp and Agrawal 2008). We do not yet know enough about the total effect of sexual selection on the genetic dynamics of small populations, although the topic deserves further empirical study.

Sexual Selection and Male-Biased Mutation Rates

We have emphasized the beneficial role that males have for the selective purging of deleterious mutations. However, males may also be the primary source for mutations. In a number of taxa, mutation rates are higher in males than females (Li et al. 2002; Ellegren 2007; Hedrick 2007; Bachtrog 2008). A major reason for this pattern is likely the increased number of germ-line cell divisions in the production of sperm relative to eggs (Haldane 1947), although other factors are also involved (Ellegren 2007). The excess of germ-line divisions in males is necessary to produce a large number of sperm. Thus, sexual selection may be viewed as the source of many mutations to the extent that sexual selection drives the evolution of high sperm numbers.

However, a bias in mutation rates between the sexes is not sufficient to indicate higher mutation load caused by sexual selection; load will be proportional to the overall sex-averaged rate of mutation in a species. Although there is evidence from vertebrate species that mutation rates are higher in males than females and

that this is associated with sexual selection (Bartosch-Härlid et al. 2003), there is little evidence that sex-averaged mutation rates are elevated in species with more sexual selection. In comparisons between sexuals and asexuals (Normark et al. 2003) or between outcrossers and selfers (Wright et al. 2002; Cutter and Payseur 2003; Artieri et al. 2008), there is little evidence for changes in mutation rates. In fact, in passerine birds, there is some evidence that the elevation in bias associated with sexual selection is caused by a reduction in female mutation rates as well as an increase in males (Bartosch-Härlid et al. 2003). More work is needed to compare the mutation rates of different types of species, for example, comparing synonymous substitution rates between species with greater or lesser degrees of sexual selection.

Some papers arguing that sexual selection reduces the load of sexual populations relative to asexual populations ignore the possibility of additional mutations contributed by males due to biased mutation rates (Agrawal 2001; Siller 2001; but see Redfield 1994). Assuming multiplicative selection, sexual selection will reduce mutation load only when the increase in mutation rate from sexual selection is less than the selection bias. If we assume that mutation rates in females are not directly or indirectly affected by sexual selection, the required condition is that $\mu_m/\mu_f < s_m/s_f$. Estimates for μ_m/μ_f in birds and mammals fall in the range of 3–10 (Hedrick 2007). Unfortunately, we do not have estimates of the ratio for selection coefficients from these (or almost any) taxa, and estimates of μ_m/μ_f are lacking for most taxa. Moreover, it is worth noting that with respect to the evolution of sex, birds and mammals are particularly uninteresting groups as there seem to be strong constraints against transitions to asexual reproduction.

Sexual Selection Throughout the Genome

CAN MOST VARIATION IN MATING SUCCESS BE EXPLAINED BY FACTORS OTHER THAN EMBELLISHED MORPHOLOGICAL TRAITS?

A large amount of thought and effort has gone into understanding the evolution of flashy morphological traits whose primary function is to increase mating success (e.g., peacock tails, stag antlers), but exaggerated morphological characters are not the only determinants of mating success. Other types of traits, many of which are likely to be strongly condition dependent (e.g., mate searching intensity, fighting ability, display effort), are also critically important to mating success.

Successful mating requires several steps (Andersson 1994). A male must search for and find a female, he may have to gain access to her by circumventing or besting other males, he must court her or coerce her into mating, and he may have to defend her against other males after mating or have his sperm compete against others'. If a male is sick, he is less likely to perform all the functions above. As a result, a mutation that interferes with the general health of an individual is likely to result directly in lower mating success.

Although the sexual selection literature has focused on the variable success of males during encounters, we do not know to what extent that variable mating success depends on variable success in finding females. As the comedian Woody Allen said, "80% of success is showing up." Although this is unlikely to be quantitatively precise, potentially a missed source of variation in mating success among animals is due to variable search effort, which is likely to be condition dependent.

If males are of low quality, they on average would be expected to have fewer resources available for prolonged courtship or competition for females. Most studies of morphological traits make no measure of courtship intensity, but many of the studies that do measure courtship intensity find it to be an important contributor to success. For example, time at the lek is a strong determinant of mating success in many species (Fiske et al. 1998), and male dung beetles of low condition (by experimental nutritional stress) courted females less often than their well-nourished counterparts (Kotiaho 2002; see also Mappes et al. 1996; Jennions and Backwell 1998; Judge et al. 2008). Alatalo et al. (1998) proposed that females are more likely to encounter healthy males who move around more. In general, courtship intensity and effort expended searching for females is likely to depend on condition. In addition, direct competition between males seems to favor healthy males. Contests between males typically test strength and/or endurance, which are typically viewed as related to condition (Andersson 1994; Wiley and Poston 1996). Indeed, there are numerous examples that behaviors related to obtaining mates are energetically costly (reviewed in Halliday 1987; Briffa and Sneddon 2007).

Body size may be a good indicator of nonsexual fitness components, as body size is usually correlated with female fecundity and survivorship (Kingsolver and Pfennig 2004). Body size is also often correlated with male mating success, both male–male competition and mate choice (Andersson 1994; Kingsolver and Pfennig 2004). Body size is often factored out of analyses of sexual selection, but variation in body size may play a strong role in the determining overall variation in mating success that can be associated with overall health.

A large fraction of the variation in mating success is not explained by morphological secondary sexual characteristics. In field studies of sexual selection applying the Lande and Arnold (1983) approach to the measurement of selection, typically the model describing variation in fitness has an r^2 that is usually between 10% and 30% (e.g., Conner 1988; Moore 1990; Bertin and Cézilly 2003). This means that about 70–90% of variation in the observed mating success is not explained by the secondary sexual traits measured and may be in part due to general condition. This

is clearly an imperfect measure of the effect of vigor for several reasons. First, because of measurement error for fitness and the resulting attenuation, it is likely that the traits actually explain somewhat more of the variation in mating success. Second, not every secondary sexual characteristic is measured in these studies, so other traits may explain more variation. Finally, there are other reasons for the remaining variation in mating success besides search ability and vigor. Still, a great deal of variation in mating success left unexplained by major morphological secondary sexual characteristics.

Moreover, some of the variation in mating success explained by secondary sexual characteristics may be due to variation in condition. Morphological sexual characteristics are often positively correlated with condition, although not always (see reviews in Price et al. 1993; Rowe and Houle 1996; Cotton et al. 2004). This positive correlation has been shown observationally on unmanipulated animals, as well as experimentally through modification of diet or disease. Most of these studies have focused on traits involved in female choice, but traits used in intrasexual interaction also display condition dependence (e.g., Mateos and Carranza 1996; López et al. 2004). In some cases, factors that affect sperm competition (such as testes size [Schulte-Hostedde et al. 2005] or sperm velocity [Urbach et al. 2007]) have been shown to be correlated with condition. As a result, even much of the variation in mating success attributed to sexually selected morphological traits may also reflect variation in genetic quality of the males that carry them. Jennions et al. (2001), in a meta-analysis of a wide variety of animal species, found that on average the phenotypic variation in sexually selected characteristics is positively correlated with longevity or survival.

Although we have focused on animals, it seems reasonable to expect that mating success is also condition dependent in plants (Skogsmyr and Lankinen 2002). Plants grown in good environments tend to have greater total biomass with larger floral displays than plants grown in poor environments (e.g., Campbell and Halama 1993; Parsons et al. 1995; Heer and Korner 2002). Plants with larger floral displays tend to attract more pollinators (Ohashi and Yahara 2001) and thus are likely to have higher siring success (e.g., Conner et al. 1996). In some wind-pollinated species, size may be directly related to male mating success because pollen can travel further distances when dispersed from a higher point (e.g., Handel 1976). Moreover, larger individuals likely produce and disperse more pollen into the air stream. Deleterious alleles that reduce a plant's ability to take up and/or process nutrients from the soil or efficiently collect sunlight and convert it into energy would thus be expected to reduce its growth, its floral display, and/or pollen production and thus its mating success. Unfortunately, we are not aware of any studies that directly measure how specific deleterious mutations in plants affect male fitness relative to their effects on female fitness.

To summarize, there are various forms of evidence that individuals of high condition have greater mating success than individuals of low condition. In his classic book, Andersson (1994) listed five mechanisms of sexual selection: scramble competition, endurance rivalry, contest competition, mate choice, and sperm competition. As discussed above and by Andersson, the first three clearly have a strong connection to condition. Mate choice can be linked to condition if choice is directly based on condition-dependent traits (Cotton et al. 2004) or if females set up situations that test the condition of the males they encounter (Wiley and Poston 1996). Finally, there is evidence that even sperm competition is condition dependent to some extent (Halliday 1987; Simmons and Kotiaho 2002; Amitin and Pitnick 2007; McGraw et al. 2007). Although it is clear that condition may affect mating success through a variety of mechanisms, it has been difficult to quantify how much of the total variation in mating success can be attributed to condition.

We have been using the word "condition" in this article as a synonym for "health," but in practice it is difficult to define and measure. There have been several proposals for measures of condition (e.g., percent fat content), and they all have difficulties (Jakob et al. 1996; Tomkins et al. 2004; Lailvaux and Irschick 2006; Irschick et al. 2007). It is likely that there is no simple measure of condition that is suitable for all organisms. Similarly, the other variables we refer to above, such as body size and courtship intensity, are not necessarily positively correlated with health or nonsexual fitness, although such links have been demonstrated in many species. As a result, although it seems intuitive that measures of health such as the ratio of body mass to length, body size, and courtship intensity are likely to be positively related to condition, these studies do not conclusively support the idea that mating success is correlated with health and condition unless the link to fitness has been confirmed.

SEXUAL SELECTION ON DELETERIOUS ALLELES

The most direct test of whether sexual selection can affect randomly chosen loci is to measure mating success among males with different genotypes at various loci. Classical studies on visible markers often found reductions in mating success in males carrying visible mutations (e.g., Merrell 1949, 1965; reviewed in Grossfield 1975), but these early studies did not typically measure effects on female fecundity of the same genotypes. All of the published studies on the relative effects of individual mutations on male mating success and female fecundity have used a single species, *Drosophila melanogaster* (Whitlock and Bourguet 2000; Stewart et al. 2005; Pischedda and Chippindale 2005; Sharp and Agrawal 2008, D. Houle, pers. comm.). Whitlock and Bourguet examined four mutations that significantly reduce productivity (a combined measure of egg to adult survivorship and female fecundity). Three of these four alleles also had strong reductions

in male mating success, whereas the fourth had no significant effect. Unfortunately, the experiments reported in Whitlock and Bourguet (2000) cannot be used to cleanly separate male and female fitness effects of the mutations, because the "productivity" measure they used is not only affected by female fecundity and survivorship, but also by male survivorship.

Sharp and Agrawal (2008) examined seven deleterious dominant visible marker mutations that significantly decreased total female fitness, and of these four also exhibited significantly stronger reductions in male fitness than female fitness (N. P. Sharp and A. F. Agrawal, unpubl. data). (Selection was not significantly different for two of the seven alleles although the point estimates were stronger in females than males.) In contrast, one allele that reduced female fitness (*U*) showed a significant increase in male mating success and therefore demonstrated the pattern defined by sexual conflict. Three other studies have each measured the effects of sexual selection on a single deleterious allele, and all found that sexual selection increased the effects of purifying selection against deleterious alleles (Stewart et al. 2005; Pischedda and Chippindale 2005; D. Houle, pers. comm.). In total, 14 deleterious alleles have been investigated in this way, and 10 also reduce male mating success. Unfortunately most of these studies do not allow a comparison between the total selection coefficient in females and males, as required by the theoretical analysis.

A related experiment was performed by Radwan (2004). Populations of bulb mites were exposed to mutation via ionizing radiation, and as a result the viability of the mites decreased. These mutated populations were then exposed to one generation of sexual selection or, alternatively, relaxed sexual selection. The sexually selected treatment had embryo viability that was over 80% higher than the treatment without sexual selection.

Beyond these direct measures, there are other approaches that may shed some light on how sexual selection affects the majority of the genome. Unfortunately, all of these other approaches have confounding factors that make it difficult to ascertain unambiguously the effects of sexual selection on genetic load. Given the paucity of direct data, we review some of the indirect measures here: adaptation under experimental manipulation of sexual selection and correlations between fitness components in observational studies.

FITNESS CHANGES WITH AND WITHOUT SEXUAL SELECTION

To measure the change in mutation load that may result from sexual selection, one could measure the change in fitness of populations that experience sexual selection compared to those in which the opportunity for sexual selection has been experimentally removed. If sexual selection typically acts against deleterious alleles, mutation load is expected to increase (and fitness to decline) when sexual selection is experimentally removed. Unfortunately, the manipulation of sexual selection not only affects selection on deleterious mutations but also changes the opportunity for sexual conflict, which can also affect the mean fitness of populations (Chapman et al. 1995; Pitnick and García-González 2002; Rowe and Day 2006; Prasad et al. 2007). Interlocus sexual conflict occurs when phenotypes that engender higher reproductive success to the males possessing them directly reduce the fitness of the females with whom these males interact (e.g., male harassment of females). Intralocus sexual conflict occurs whenever an allele that is favored when found in one sex is disfavored when found in another sex. When populations are released from sexual conflict by experimentally removing sexual selection, female fitness is expected to increase. The net effect on mean fitness of removing sexual selection will depend on all three of factors: mutation load, intralocus sexual conflict, and interlocus sexual conflict. It is difficult to guess a priori which factor will dominate.

These types of experimental evolution studies have produced mixed results. Although some early *Drosophila* studies found that populations experiencing sexual selection improved with respect to some fitness components (Partridge 1980; Promislow et al. 1998), recent studies using more complete measures of fitness have found other results. Holland and Rice (1999) found that females from lines maintained with enforced monogamy (and thus little scope for sexual selection) had lower fecundity than females from lines experiencing sexual selection (i.e., the polygamy treatment) when both types of females were housed with males from the ancestral stock. However, when females were housed with males from their own respective lines, females from the monogamous lines had a higher reproductive rate than females from lines with sexual selection. These results demonstrate that measures of female fitness can be highly sensitive to the males used in the assay, as expected if both mutation load and sexual conflict are important. Similar results were found by Crudgington et al. (2005). Most other experiments have focused on fitness assays in which females are housed with males from their own lines or treatments, which should fully capture the negative effects of sexual selection caused by sexual conflict. Martin and Hosken (2003) found no difference in female reproductive rate between lines with and without sexual selection in the dung fly, *Sepsis cynipsea*. A study with the bulb mite *Rhizoglyphus robini* (Tilszer et al. 2006) found no difference in fecundity between females from lines with and without sexual selection when all females were housed with males from lines without sexual selection. However, females from lines without sexual selection had reduced fecundity relative to females from the other treatment when all females were housed with males from lines with sexual selection—a result suggestive of sexual conflict. In a different bulb mite experiment, Radwan et al. (2004) experimentally eliminated natural selection (using the "middle class neighborhood" approach [Shabalina et al. 1997]) and

compared the fitness of lines with and without sexual selection. They observed ~15% decline in fecundity after 11 generations, which the authors attributed to the accumulation of deleterious mutations. However, there was no difference between lines with and without sexual selection (although the scope for sexual selection in this experiment was somewhat limited).

It is difficult to draw any strong conclusions from these results other than, collectively, these studies do not appear to provide much support for the idea that sexual selection improves mean fitness. However, this may be because negative effects of sexual selection arising from sexual conflict mask the positive effects of sexual selection on mutation load. Although we cannot infer much about the magnitude of the effect of sexual selection on mutation load from this class of studies, it is tempting to conclude that the net effect of sexual selection on mean fitness is unlikely to be positive on average (i.e., the negative effects of sexual conflict balance or overwhelm positive effects on mutation load). However, such a conclusion would be premature at this point. Most of these experimental evolution studies continued for only a few dozen generations, and these "short-term" results will be very sensitive to the nature of standing genetic variation and may not reflect what would happen in the long term. A few dozen generations is certainly not long enough for mutation load to reach a new equilibrium. The genes controlling sexual antagonism are expected to be segregating at high frequencies and may be of larger effect, so they can respond more quickly to selection. In other words, such studies may be biased toward observing the detrimental effects of sexual antagonism/conflict over the positive effects of sexual selection on mutation load.

This can be illustrated with a simple example. Imagine there are $l = 2 \times 10^4$ loci each experiencing a deleterious mutation rate of $\mu = 2 \times 10^{-5}$, giving a diploid genome-wide rate of deleterious mutation of $U = 2l\mu = 0.8$. Assuming that selection against the deleterious allele at each locus is $s_f = 0.005$ in females and $s_m = s_f$ in males, the equilibrium frequency of the deleterious allele at each of these loci is $q_{eq} = 0.0027$ (i.e., quite rare). In addition, imagine there are eight X-linked loci under sexual antagonism (sex chromosomes are expected to be enriched for sexually antagonistic variation [Rice 1984]). At each of these eight loci allele "two" is deleterious in females but favored in males such that the fitness of females are $w_{f11} = 1$, $w_{f12} = 1 - h\,t_f$, and $w_{f22} = 1 - t_f$ and in males $w_{m1} = 1$, $w_{m2} = 1 + t_m$. With $h = 0.3$, $t_f = t_m = 0.1$, the equilibrium frequency of the female-deleterious allele is 0.42 (i.e., quite common). If the experimental removal of sexual selection makes selection in males negligible ($s_m \approx t_m \approx 0$), then after 25 generations of this treatment the mean fitness of females from the perspective of mutation load is 6% lower than in the control treatment with sexual selection. With respect to the sexually antagonistic loci, the mean fitness of females from the population without sexual selection is 13% higher than the control. Considering both factors together the mean total fitness of the females from the population without sexual selection is ~6% higher than the control. However, after 10,000 generations, the effects of mutation load swamp out those of antagonism such that the mean fitness of the females from the population without sexual selection is ~56% lower than the control. On the other hand, new alleles that are weakly favored in females (but strongly selected against in males) will ultimately fix in monogamous treatments, but these will not be represented in standing variation, thereby also requiring longer-term evolution. This numerical example shows that short-term changes to mean female fitness caused by the removal of sexual selection cannot be used to infer the magnitude, or even the direction, of the net effect of sexual selection in the long term.

Experiments that focus on adaptation to a new environment create conditions in which sexual selection and increased efficacy of natural selection should both act rapidly. There are only a few experiments like this, and some find more rapid adaptation with sexual selection (Fricke and Arnqvist 2007) whereas others do not (Holland 2002; Rundle et al. 2006). The role of sexual selection on adaptation is complex, as shown by the recent review by Candolin and Heuschele (2008).

A related type of experiment has been conducted which looks at the relationship between sexual selection and fitness in the other direction. Dolgin et al. (2006) measured male mating success in lines of flies that had been adapted to different chronic temperatures. On average, males had higher mating success when tested in their adaptive environment. Local adaptation was correlated with male mating success, but in this case the chain of causality was reversed.

CORRELATION BETWEEN MALE MATING SUCCESS AND OTHER FITNESS COMPONENTS

The experiments described in the last section, manipulating the degree of sexual selection and looking at the effects on mean fitness, have appropriately looked at many components of fitness, and most included adult female fecundity. However, female fecundity is a trait that is most likely to express negative genetic correlations with male mating success in standing variation because of sexually antagonistic selection (e.g., Chippindale et al. 2001; Fedorka and Mousseau 2004; Brommer et al. 2007; Foerster et al. 2007). In contrast, Czesak and Fox (2003) have observed positive genetic correlations between male and female fecundity in seed beetles. Because correlations in fitness components are usually measured on standing genetic variation, results comparing adult fitness components may be dominated by the genetic polymorphisms expected with sexually antagonistic selection. In principle, we would prefer to measure genetic correlations based on only new mutational variation, to understand the potential for mating success to affect genetic load.

Failing that, to look for the effects of sexual selection on mutation load alone, it may be more powerful to look for correlations between male mating success and other fitness components that are less likely to be affected by sexually antagonistic alleles, such as juvenile survival. A large number of studies have compared paternal mating success with their offspring's survival as juveniles (see review by Møller and Alatalo 1999). Although many studies find no strong correlation between the male mating success and offspring viability and some find a negative correlation, the majority of studies find a positive correlation. For example, male peafowl with more elaborate tails produce offspring that grow faster and are more likely to survive (Petrie 1994). However, the amount of variation in offspring survival explained on average by male trait values is only a few percent (Møller and Alatalo 1999). Males that have high mating success leave offspring that have a slight genetic propensity to high survival rates.

VARIANCE IN FITNESS AND THE OPPORTUNITY FOR SELECTION

Most of the data discussed in the preceding sections are related to the issue of whether selection on new mutations is in the same direction for males and females. In fact, selection must not only be in the same direction but must be stronger on males than females if sexual selection is to reduce mutation load relative to Haldane's calculations. A weak test of this requirement can be made by examining the variance in fitness between males and females. The variance in fitness sets an upper limit to the strength of selection because selection on a gene or trait is equal to the covariance of that gene or trait with fitness. For this reason, Crow (1958) proposed that variance in fitness standardized by the square of the mean fitness be called the opportunity for selection, $I = V(w)/\bar{w}^2$. Greater standardized variance in fitness for males than females ($I_m/I_f > 1$) implies that there is more opportunity for selection in males than females.

In many types of breeding systems there are good theoretical reasons to expect that the variance in fitness for males will be greater that of females (Wade 1979; Wade and Arnold 1980). Indeed almost all empirical studies from a diversity of taxa report $I_m/I_f > 1$: insects (Finke 1986; Nishida 1987; McVey 1988; Ferguson and Fairbairn 2001), fish (Fleming and Gross 1994), amphibians (Howard 1988; Jones et al. 2004), snakes (Madsen and Shine 1994; Prosser et al. 2002), birds (Webster et al. 2001; Whittingham and Dunn 2005; Krakauer 2008), and mammals (Clutton-Brock et al. 1988; Le Boef and Reiter 1988; Mulder 1988; Packer et al. 1988; Clutton-Brock and Pemberton 2004). However, it is important to remember that greater opportunity for selection in males does not guarantee that $s_m > s_f$. For example, even if selection against mutations is the same across the sexes, the variance in male fitness could be higher if male fitness is more sensitive to environmental noise than female fitness. Nonetheless, the relatively high variance in fitness for males is consistent with selection being stronger on males than females.

Future Directions and Missing Data

To better understand the relationship between sexual selection and mutation load, we need more empirical work, in both the laboratory and field. Ideally, we would like to obtain individual selection estimates in males and females (s_m and s_f) for a large and representative set of mutations. Such measures are the most direct assessment of the effects of sexual selection on the frequency of deleterious mutations, but there are very few data currently available on this topic, and all of which come from the same species, *D. melanogaster*. These kinds of experiments could be done in a few other outbreeding model systems in which visible mutations are available, such as *Tribolium*, *Caenorhabditis remani*, mice, *Mimulus*, etc. Future studies should not only establish whether a mutation's effect on male fitness is in the same direction as its effect on female fitness but also attempt to determine whether selective effects in males are larger than in females (i.e., is $s_m > s_f$?). At present, only a few studies even attempt to do so (Pischedda and Chippindale 2005; Sharp and Agrawal 2008). All of these studies are nonideal because they have all been done in the laboratory, under relatively artificial circumstances. To predict the true magnitude of the effects of sexual selection on mutation load, it will be necessary to measure these components in more natural settings. In particular, the laboratory measures of sexual selection do not allow much opportunity for selection on mate search intensity, and the potentially greater environmental stress in the field may generate greater variation in condition.

Although it may be difficult or impossible to measure selection on some organisms such as *D. melanogaster* in the field, it may be possible to simulate more realistic conditions in the laboratory than are typically used. For example, measures of sexual selection and behavioral analyses of experiments performed in standard fly vials compared to experiments performed in large structured flight cages may provide important insights into the relative importance of factors such as mate search intensity and courtship behavior in generating variance in mating success.

Experimental studies of individual genes are prohibitively difficult in most organisms because it is essential to change one allele at a time. A tempting alternative that is less restrictive is to measure the effect of mutagenesis or inbreeding on mating success and other fitness components. Although such comparisons would be interesting, they will not tell us whether single mutations tend to be selected against by both natural and sexual selection. This is because traditional mutagenesis or inbreeding simultaneously affects the whole genome, and some loci may affect sexual selection alone, whereas mutations at other loci may reduce other fitness components such as viability or fecundity. It

is possible that mutagenized individuals may have both reduced mating success and reduce viability but these effects are due to separate genes (i.e., mutagenesis can generate positive linkage disequilibrium between loci affecting only sexual selection and loci that only affect other fitness components). Such a pattern does not give direct evidence for an effect of sexual selection on mutation load. However, a modification of the experimental design of Radwan (2004) offers some promise. Initially genetically homogeneous lines could be mutagenized to create a population in which all genetic variation is due to new mutations. Precautions should be taken to minimize the amount of linkage disequilibrium generated through the mutagenesis procedure (e.g., maintaining the population without any selection for some number of generations following mutagenesis to allow recombination to erode linkage disequilibrium). Mutated lines can be either exposed to sexual selection or have sexual selection experimentally removed for several generations. The resulting lines could be compared for female fitness components for individuals mated to ancestral males. If the sexually selected lines have higher female fitness, this is consistent with sexual selection acting to remove mutation load.

In some cases, experimental manipulations can be used as proxy for deleterious mutations. For example, a low-quality juvenile diet treatment can be applied as a proxy for individuals carrying deleterious alleles that reduce the ability to find and/or use resources (Bonduriansky and Rowe 2005). Individuals from high versus low diet treatments (assuming that current hunger status is controlled for) can be assessed with respect to male mating success and female fecundity. The theory predicts that mutation load is reduced when males are more affected by mutational effects than females; by analogy, we might test whether males are more affected than females by environmental challenges. More specifically, for environmental treatments that can be shown to deleteriously affect females, the experiment should investigate whether the effect on male fitness is greater than the effect on female fitness.

Obviously, extrapolating from environmental manipulations (e.g., diet treatments) to genetic effects requires a leap of faith unless a link can be properly established through independent experiments. Nonetheless, this approach vastly increases the diversity of organisms that can be used to study these issues when such extrapolations are judiciously made (e.g., Bonduriansky and Rowe 2005). To be useful, the environmental axes that are used to reduce health must be slight enough to not cause differential survival (to avoid biasing the sample of adults available to assay male mating success and female fecundity), and they must be long term in effect. For example, an acute temperature shock may either cause some weaker individuals to die or otherwise not leave long-term effects that cause differential health at the time when mating success is measured. In contrast, useful treatments may include mild exposure to long-lasting toxins (such as heavy metals) or experimental infection by sublethal parasites, in addition to the reduction in food discussed above.

For those cases in which mating success is affected by manipulation of condition, there is the opportunity to better understand the biology underlying this effect, by studying how condition affects components of male mating success such as mate search time, female encounter rates, courtship intensity, display traits, male–male fighting outcomes, etc. Many studies have shown that poor condition negatively affects secondary sexual morphological characteristics (Jennions et al. 2001; Cotton et al. 2004), but fewer have looked at the effects of condition on other components of male mating success.

Finally, it is crucial that we have better measurements of the relative mutation rates of species with high and low levels of sexual selection. These comparisons can be made on sexual versus asexual lineages, on selfing versus outcrossing species, or more directly on more monogamous versus more promiscuous species, because each of these differs in their potential for sexual selection. The best comparison may be a comparison of the rates of substitution of synonymous mutations, in order directly compare mutation rates without bias from differential probability of fixation potentially caused by other differences between species.

Discussion

The available evidence points to an important connection between sexual selection and mutation load. Various forms of evidence indicate that male mating success is condition dependent. In many cases, mutations that reduce viability and female fecundity also decrease male mating success. As a result, sexual selection probably reduces mutation load relative to the case when male mating success is not under selection.

It is less clear whether mutation load is reduced relative to the predictions of Haldane based on equal selection in both sexes. This requires that selection in males is not only in the same direction as in females but is also stronger than in females ($s_m > s_f$). This difference in selection seems likely given that the opportunity for selection is typically much larger in males than females and that many aspects of male mating success are condition dependent. Despite the intuitive appeal of this idea, there is very little direct empirical evidence and stronger support is needed.

The only direct evidence that $s_m > s_f$ comes from a handful of genes in *D. melanogaster*. For example, taking the estimates from Sharp and Agrawal (2008) of the selection coefficients against deleterious mutations, we can calculate that the average ratio of s_f/s is approximately 0.8. (We have excluded one locus [*U*] that demonstrates sexual conflict, because we want to focus on deleterious alleles.) With this s_f/s ratio and assuming a deleterious mutation rate of one per genome per generation, mean fitness

with respect to mutation load is expected to be approximately 22% higher with sexual selection than without. For species with higher deleterious mutation rates, this effect is greater; with lower mutation rates the effect of sexual selection on load is reduced.

However, sexual selection allows for other sources of reduction in mean fitness. Because of conflict in the optimal strategies of males and females, the presence of sexual selection can lead to greatly reduced fitness, either indirectly by causing individuals of each sex to deviate from their optima because of genetic correlations of expression between the sexes or directly by the negative effects of (usually) males on females (and the costs of the females' evolved responses to these effects). When this "conflict load" is accounted for, sexual selection may have a less beneficial, or even deleterious, effect on the mean fitness of a species. Moreover, mutation rates may increase with some kinds of sexual selection in males, because the increased need for sperm production causes an increase in the number of cell divisions per generation.

On the other hand, changes in mutation load may offset the expected reduction in fitness expected by sexual conflict. Supporting this view, reductions in the mean fitness of populations experiencing sexual selection have been observed in relatively short-term studies conducted in constant environments (e.g., Holland and Rice 1999). However, it is interesting to note that in every study done in changing environments, sexual selection either improves (Fricke and Arnqvist 2007) or has no measurable effect (Holland 2002; Rundle et al. 2006) on the mean fitness of the population. Sexual conflict may reduce the fitness of populations, but the available evidence suggests that the other effects of sexual selection, including more effective selection on adaptive and deleterious alleles throughout the genome, are sufficient to counterbalance the effects of conflict. The evidence about the cumulative effects of sexual selection on mean fitness is still scant, but seems to point toward a very weak effect. However, the available evidence is all based on relatively short-term experiments, and as we have discussed above, short-term experiments may not adequately predict, either quantitatively or qualitatively, the long-term effects of sexual selection.

Sexual selection may affect the evolution of sex, but it is unlikely to be the main factor promoting sexuality. On the one hand, sexual reproduction allows for conflict between sexes and reduced fitness of sexual populations relative to asexual ones. On the other hand, it has been suggested that sexual reproduction can reduce mutation load sufficiently to counterbalance the twofold cost of sex. Using the ratio of $s_f/s = 0.8$ calculated above from the Sharp and Agrawal data, the genomic deleterious mutation rate would have to be about 3.5 for mutation load alone to make up for the twofold cost of sex. Not only does this calculation not account for the deleterious effects of sexual conflict, but also 3.5 is higher than most estimates for even long-lived organisms. Moreover, this calculation is based on the assumption that mutation rates are not affected by sexual selection. Stronger selection in males than in females resulting from sexual selection helps to reduce load but perhaps not enough to offset the elevated input of mutations that enter a sexual population through male germ-lines. Taken together, it is very unlikely that sexual selection offsets the twofold cost of sex.

In thinking about the relationship between sexual selection and genetic load, it becomes clear that there is a great deal of potential for sexual selection to affect the fate of many (or most) loci throughout the genome. This requires us to look more broadly to the cause of differential mating success, beyond the classic study of embellished secondary sexual characteristics such stag antlers and peacock tails. In the traditional sexual selection literature, the importance of "good genes" relies on the maintenance of enough genetic variance for fitness (as expressed through the correlation with a display trait) that mate choice can contribute sufficient indirect genetic effects to the offspring of choosy females. In order for sexual selection to have an effect on mutation load, however, the conditions are much less stringent: the effect is relative to the amount of genetic variance for fitness that exists, and there need not be an intermediate morphological trait or even female choice. Differential activity or mating intensity among males, differences in male intrasexual interactions, and all female choice (even when not correlated with particular display traits) are all potentially effective in generating the selection necessary to reduce load. However, we currently have extremely little information about the magnitude or importance of such selection, and we propose that studies that examine sexual selection more broadly would be extremely valuable.

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