

ASSORTATIVE MATING FOR FITNESS AND THE EVOLUTION OF RECOMBINATION

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Abstract.—To understand selection on recombination, we need to consider how linkage disequilibria develop and how recombination alters these disequilibria. Any factor that affects the development of disequilibria, including nonrandom mating, can potentially change selection on recombination. Assortative mating is known to affect linkage disequilibria but its effects on the evolution of recombination have not been previously studied. Given that assortative mating for fitness can arise indirectly via a number of biologically realistic scenarios, it is plausible that weak assortative mating occurs across a diverse set of taxa. Using a modifier model, we examine how assortative mating for fitness affects the evolution of recombination under two evolutionary scenarios: selective sweeps and mutation-selection balance. We find there is no net effect of assortative mating during a selective sweep. In contrast, assortative mating could have a large effect on recombination when deleterious alleles are maintained at mutation-selection balance but only if assortative mating is sufficiently strong. Upon considering reasonable values for the number of loci affecting fitness components, the strength of selection, and the mutation rate, we conclude that the correlation in fitness between mates is unlikely to be sufficiently high for assortative mating to affect the evolution of recombination in most species.

Key words.—Assortative mating, evolution of recombination, modifier model, mutation-selection balance.

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Evolutionary biologists have struggled to understand the ubiquity of recombination (Bell 1982; Barton and Charlesworth 1998; Otto and Lenormand 2002). Although group-level advantages of recombination have been identified, a more important challenge is in understanding the conditions that favor the evolution of recombination within a population (Feldman et al. 1997). Modifier models are used to study the evolutionary pressures on a gene that alters some aspect of the genetic system such as the rate of recombination. A modifier gene that increases the rate of recombination will tend to become associated with the haplotypes that are generated by recombination. The short- and long-term success of these haplotypes determine the modifier's evolutionary fate (Lenormand and Otto 2000). If recombinant haplotypes are on average more fit than nonrecombinant haplotypes, then the modifier will experience a short-term fitness advantage. If the variance in fitness of recombinant haplotypes, is greater than nonrecombinant haplotypes, then the modifier will have a long-term fitness advantage by better responding to selection.

The distribution of haplotypes generated by recombination depends on the patterns of linkage disequilibria and how recombination modifies these disequilibria. With random mating, recombination acts to reduce the magnitude of disequilibrium. Because disequilibrium is built by selection, it is usually disadvantageous to reduce it, at least in the short term. The evolution of recombination in a large panmictic population requires that epistasis be negative, but weak (Barton 1995). Under this condition, recombination enjoys a long-term advantage that is not overwhelmed by a short-term disadvantage. However, empirical data suggest that epistatic interactions are not confined to being negative and weak (de Visser et al. 1997; Elena and Lenski 1997; Whitlock and Bourguet 2000). Moreover, variation in epistasis can cause selection against recombination even if epistasis is, on average, weakly negative (Otto and Feldman 1997).

The sensitivity to epistasis arises because epistasis is the

only force generating disequilibrium when populations are large and randomly mating, as assumed by many classic models (Feldman et al. 1980; Kondrashov 1984; Charlesworth 1990; Barton 1995). However, nonrandom mating can change the sign and magnitude of disequilibrium as well as the effect of recombination on the disequilibrium. Consequently, the conditions favoring recombination may be quite sensitive to assumptions of breeding ecology (Charlesworth et al. 1979; Lenormand and Otto 2000). For example, a recent analysis by Roze and Lenormand (2005) showed that very low rates of sporophytic selfing can greatly increase the parameter space favoring recombination.

Here we focus on assortative mating for fitness, which may be common in many species because it can arise via several different mechanisms. Assortative mating can occur through male-male competition if the best males monopolize the best females. For example, in the water strider *Gerris lateralis*, the largest and most successful males spend a disproportionate amount of time guarding the largest and most fecund females (Rowe and Arnqvist 1996). Assortative mating can also occur through female choice if the best females exhibit the strongest preference for the best males. In sticklebacks, for example, females in good condition show a stronger preference for brighter males than do females in poor condition (Bakker et al. 1999). Recent theory suggests assortative mating is expected in any species with either direct male-male competition or female choice (Fawcett and Johnstone 2003). In addition, assortative mating may exist in species that are thought to epitomize random mating. Even broadcast spawners might mate assortatively if the timing of gametic release is slightly condition dependent (e.g., individuals in worse condition shed gametes slightly later than individuals in good condition). Though assortative mating may be widespread, it is likely to be weak in many species. Here we investigate whether assortative mating alters the conditions favoring recombination and how much assortative mating is needed to do so.

We expect assortative mating to affect the evolution of recombination because of its potential to alter linkage disequilibrium. This is most easily illustrated by considering a simple haploid two-locus, two-allele example in which all four genotypes are at the same frequency so that there is initially no linkage disequilibrium. We are interested in positive assortative mating for fitness where sexual unions between the different extreme types (*AB* and *ab*) occur less often than expected by chance under random mating and/or sexual unions between the different intermediates types (*Ab* and *aB*) occur more often than the expected. In these latter unions, *Ab* and *aB* haplotypes are converted via recombination into *AB* and *ab* haplotypes, generating positive linkage disequilibrium. The effects of assortative mating on linkage disequilibrium has been known for some time (Fisher 1918; Moran and Smith 1966; Vetta 1975), but there has been no attempt to understand how assortative mating might thereby affect the evolution of recombination.

MODEL AND RESULTS

To investigate the importance of assortative mating for fitness on the evolution of recombination, we consider a simple deterministic haploid model with two diallelic fitness loci, *A* and *B*. The model follows the general approach of other modifier models of recombination (e.g., Barton 1995; Lenormand and Otto 2000; Otto and Nuismer 2004). The fitnesses of each of the four haplotypes are given by $w_{AB} = 1$, $w_{Ab} = w_{aB} = 1 - s$, and $w_{ab} = (1 - s)^2 + \varepsilon$, where s is the selection coefficient and ε is epistasis. Alleles represented by lower-case letters are deleterious (i.e., $s > 0$). Recombination is determined by the modifier locus *M*, and the three loci are in the order *MAB*. The *M* locus affects recombination rate but not fitness (i.e., $w_{MAB} = w_{mAB} = w_{AB}$, $w_{Mab} = w_{mAb} = w_{Ab}$, etc.). With two alleles at each locus, there are eight haplotypes. The frequency of the *i*th haplotype is x_i . The frequency of the *i*th haplotype after selection is $x'_i = x_i w_i / \bar{w}$, where $\bar{w} = \sum x_i w_i$.

Mating occurs after selection. Random mating occurs with probability $1 - t$. Individuals mate assortatively (i.e., with another individual of the same fitness) with probability t . Haplotypes carrying *Ab* or *aB* are assumed to have equal fitness ($w_{Ab} = w_{aB}$), whereas haplotypes carrying *AB* or *ab* are assumed to be different from *Ab* as well as from each other. Under these assumptions, it is straightforward to calculate the frequency of different mating pairs, as illustrated here by a few examples. The frequency of matings between haplotypes *ijk* and *xyz* is given by $F_{ijk*xyz}$:

$$\begin{aligned}
 F_{MAB*MAB} &= (1 - t)x_{MAB}^2 + t\left(\frac{x_{MAB}^2}{x_{MAB} + x_{mAB}}\right), \\
 F_{MAB*mAB} &= (1 - t)(2x_{MAB}x_{mAB}) + t\left(\frac{2x_{MAB}x_{mAB}}{x_{MAB} + x_{mAB}}\right), \\
 F_{MAB*MaB} &= (1 - t)(2x_{MAB}x_{MaB}) \\
 &\quad + t\left(\frac{2x_{MAB}x_{MaB}}{x_{MAB} + x_{MaB} + x_{mAb} + x_{maB}}\right), \text{ and} \\
 F_{MAB*MaB} &= (1 - t)(2x_{MAB}x_{MaB}).
 \end{aligned}$$

As expected, the sum of all the $F_{ijk*xyz}$ is one.

In this model, parameter t determines the strength of assortative mating and is equal to the correlation in fitness between mates. When $t > 0$, matings between the extreme types, *AB* and *ab*, occur less often than expected by chance, whereas matings between the intermediate types, *Ab* and *aB*, occur more often than expected by chance. Although simplistic, this model is analytically tractable and captures the critical elements of the form of assortative mating for fitness we are trying to model. (An alternative approach to modeling assortative mating is to assume that mating rates between two genotypes is related to the similarity of their fitnesses. Haploid and diploid versions of such a model are presented in the Appendix [available online only at <http://dx.doi.org/10.1554/05-502.1.s1>] and give very similar results.)

Following the standard rules of genetics, the distribution of offspring haplotypes is calculated for each mating pair. When two haploids unite to reproduce, their effective recombination rate is the average recombination induced by each parent's allele at the *M* locus. The recombination rate induced by the ancestral allele m is r_{MA} in the *M-A* interval and r_{AB} in the *A-B* interval. The alternative modifier allele *M* increases these recombination rates to $r_{MA} + \gamma_{MA}$ and $r_{AB} + \gamma_{AB}$, respectively. The distribution of haplotypes for the following generation is calculated from the weighted sum of offspring frequency distributions from all mating pairs.

To study the evolution of the modifier, we must calculate the change in the frequency of the *M* allele, Δp_M , across one complete generation. To do so, the initial haplotype frequencies are redefined in terms of allele frequencies and disequilibria. For example, $x_{MAB} = p_M p_A p_B + p_M C_{AB} + p_A C_{MB} + p_B C_{MA} + C_{MAB}$ and $x_{mAB} = (1 - p_M) p_A p_B + (1 - p_M) C_{AB} - p_A C_{MB} - p_B C_{MA} - C_{MAB}$, where C_{ij} is the two-way disequilibrium between the *i*th and *j*th loci and C_{MAB} is the three-way disequilibrium (Barton 1995). Calculating haplotype frequencies after one round of selection and reproduction, the exact change in the modifier frequency, Δp_M , is found to be:

$$\Delta p_M = \frac{(C_{MA} + C_{MB})s + (C_{MAB} - C_{MAPb} - C_{MBPa})(s^2 + \varepsilon)}{1 - (p_a + p_b)s + (C_{AB} + p_a p_b)(s^2 + \varepsilon)}. \tag{1}$$

As expected, this result shows that modifier evolves only through its associations with the selected loci because we have assumed the modifier has no direct effect on fitness (though it is easy to incorporate such an effect). To proceed, we employ the quasi-linkage equilibrium (QLE; Kimura 1965; Nagylaki 1993) to approximate the values for the associations. The QLE invokes a separation of time scales in which the disequilibria reach their steady state faster than allele frequencies change. Consequently, application of the QLE assumes that selection is weak relative to the ancestral rate of recombination, though numerical simulations indicate that the analytical approximations are surprisingly robust to this assumption. We find expressions for the evolution of the disequilibria (i.e., ΔC_{AB} , ΔC_{MA} , ΔC_{MB} , and ΔC_{MAB}), set these to zero, and solve for the steady-state values of the disequilibria. Taylor series are used to find approximate steady-state values for each disequilibrium measure. Specifically, we assume s , t , γ_{MA} , and γ_{AB} are $O(\xi)$ and ε is $O(\xi^2)$, where $\xi \ll 1$. The steady-state values are found to be:

$$\begin{aligned}
{}^{qle}C_{AB} &= V_A V_B \frac{t}{P_1} + V_A V_B \\
&\times \frac{2V_A V_B r_{AB} t^2 - P_1^2 P_2 (2 - r_{AB}) s t + P_1^3 (1 - r_{AB}) \varepsilon}{P_1^3 r_{AB}} \\
&+ o(\xi^2), \tag{2a}
\end{aligned}$$

$$\begin{aligned}
{}^{qle}C_{MA} &= \frac{\gamma_{AB} V_A V_B V_M}{r_{MA} r_{AB} r_{MAB}} \\
&\times \frac{[(p_B - p_A) r_{MA} t + (1 - r_{MA}) s](2P_2 s t - P_1 \varepsilon)}{P_1^2} \\
&+ o(\xi^4), \tag{2b}
\end{aligned}$$

$$\begin{aligned}
{}^{qle}C_{MB} &= \frac{\gamma_{AB} V_A V_B V_M}{r_{MB} r_{AB} r_{MAB}} \\
&\times \frac{[(p_A - p_B) r_{MB} t + (1 - r_{MB}) s](2P_2 s t - P_1 \varepsilon)}{P_1^2} \\
&+ o(\xi^4), \text{ and} \tag{2c}
\end{aligned}$$

$${}^{qle}C_{MAB} = \frac{\gamma_{AB} V_A V_B V_M}{r_{MA} r_{AB} r_{MAB}} \left(\frac{2P_2}{P_1} s t - \varepsilon \right) + o(\xi^3). \tag{2d}$$

In these equations, $V_X = p_X p_x$ is the variance at locus X , where p_X and p_x are the frequencies of alleles X and x at this locus; $P_1 = p_{Aa} + p_{aA}$ and $P_2 = p_A + p_B - 1$. The additional recombination parameters are defined as $r_{MAB} = 1 - (1 - r_{MA})(1 - r_{AB})$ and $r_{MB} = r_{MAB} - r_{MA} r_{AB}$.

These steady-state association values are then used in approximating Δp_M :

$$\begin{aligned}
\Delta p_M &\approx ({}^{qle}C_{MA} + {}^{qle}C_{MB})s + {}^{qle}C_{MAB}(s^2 + \varepsilon) + o(\xi^5) \\
&\approx \gamma_{AB} \frac{V_M V_A V_B}{r_{AB} r_{MAB}} \kappa \theta + o(\xi^5) \tag{3}
\end{aligned}$$

where $\kappa = (2P_2 s t / P_1 - \varepsilon)$ and $\theta = (s^2 + \varepsilon) + s^2(1/r_{MA} + 1/r_{MB} - 2)$. A Mathematica notebook deriving these results is available upon request.

The sign of κ indicates whether the modifier is associated with extreme or intermediate haplotypes. The modifier develops associations with particular haplotypes when the disequilibrium prior to mating deviates from ${}^{qle}C_{AB}$. It can be shown that κ reflects how selection perturbs C_{AB} away from its steady-state value. When $\kappa < 0$, selection pushes the disequilibrium above its steady state. Recombination then draws the disequilibrium back toward its steady state by generating intermediate haplotypes from the relative excess of extreme haplotypes. Consequently, a modifier that increases recombination becomes positively associated with the intermediate haplotypes it produces and negatively associated with the extreme haplotypes it destroys. Conversely, if selection pushes the disequilibrium below its steady state, as it does when $\kappa > 0$, the modifier becomes positively associated with the extreme haplotypes. Note that κ tends to be positive when beneficial alleles are common ($p_A, p_B \gg 0$) but negative when they are rare.

The factor θ describes the selective consequences for the M allele of being positively associated with the extreme haplotypes. The first and second terms of θ represent short- and

long-term effects, respectively (Barton 1995; Lenormand and Otto 2000). The long-term effect of being associated with the extreme haplotypes is positive because there is more variance in fitness associated with these haplotypes than the intermediate haplotypes. The important implication of being associated with the extreme haplotypes is that the modifier is associated with the most fit haplotype, AB , which will eventually dominate the population. The strength of the longer-term effect depends on r_{MA} and r_{MB} because these values determine how long a modifier allele remains linked to the beneficial alleles that constitute the most fit genotype. The short-term effect is positive if the average fitness of the extreme haplotypes is better than the average fitness of the intermediate haplotypes (i.e., $w_{AB} + w_{ab} > w_{Ab} + w_{aB}$), which is true when $s^2 + \varepsilon > 0$. Combining both short- and long-term effects, θ is positive provided ε is not too strongly negative.

As shown in equation (3), the sign of selection on the modifier is determined by the product of κ and θ as the sign of these two terms indicate, respectively, the sign of the association between the modifier and the extreme haplotypes and whether it is selectively advantageous to be positively associated with these haplotypes. With assortative mating ($t > 0$), but not random mating, the sign of κ can change as the frequency of the alleles at the selected loci change. Thus, it is possible for the modifier to be selected in one direction when beneficial alleles are rare and in the opposite direction when beneficial alleles are common. To examine the net change in the frequency of the modifier we integrate equation (3) over the course of simultaneous selective sweeps. Following Barton (1995), we use the relationship $p_A/p_a = p_B/p_b = e^{sT}$, which reflects the logistic growth of the relative frequency of the beneficial allele. T measures time since the midpoint of the sweep ($p_A = p_B = 0.5$). The net change in the modifier is

$$\begin{aligned}
{}_{net}\Delta p_M &\approx \int_{-\infty}^{\infty} \Delta p_M dT \\
&= \gamma_{AB} \frac{V_M \theta}{r_{AB} r_{MAB}} \int_{-\infty}^{\infty} \frac{e^{sT}(e^{2sT} s t - e^{sT} \varepsilon - s t)}{(1 + e^{sT})^4} dT \\
&= -\gamma_{AB} \frac{V_M \varepsilon \theta}{6 r_{AB} r_{MAB} s}. \tag{4}
\end{aligned}$$

This value is positive when $\lambda < \varepsilon < 0$, where λ is the value of ε for which $\theta = 0$,

$$\lambda = -s^2(1/r_{MA} + 1/r_{MB} - 1).$$

The same result is obtained under random mating (Barton 1995). Thus, we find that assortative mating has no net effect on the evolution of recombination over the course of a selective sweep despite the fact that it alters the modifier's rate of evolution in each generation. As shown by equation (3), when $\lambda < \varepsilon < 0$, assortative mating will increase the modifier's rate of spread when the beneficial alleles are rare but decrease the rate when the beneficial alleles are common. These effects cancel each other out such that spread of the modifier is independent of assortative mating.

While selective sweeps happen periodically, deleterious mutations constantly occur in all genes in all populations. In

the selective sweep model, beneficial alleles move from rare to common and the effects of assortative mating cancel out in the process. In the mutation-selection balance model, beneficial alleles are always common. To incorporate deleterious mutation into the model, an additional step is added into the life cycle: selection, mating (and recombination), followed by mutation. The *A* and *B* alleles each mutate to their deleterious alternative states (*a* and *b*) at rate μ , where μ is $O(\xi^3)$. There are no backmutations at these loci or any mutations at the *M* locus. To determine the mutation-selection equilibrium with respect to the selected loci, we find expressions for Δp_A , Δp_B , and ΔC_{AB} , set these to zero and solve for p_A , p_B , and C_{AB} . Taylor series are used to find approximate equilibrium values for each.

One approach to calculating selection on the modifier at mutation-selection balance is by using the definition $\beta_M \equiv \Delta p_M / V_M$, where Δp_M , as defined in equation (3), is evaluated with the mutation-selection equilibrium values for p_A , p_B , and C_{AB} . Doing so, we find

$$\beta_M \approx \frac{\gamma_{AB}\theta\psi}{r_{AB}r_{MAB}}, \quad (5)$$

where

$$\psi = t\mu \left(1 - \frac{3\mu}{s}\right) - \frac{\varepsilon\mu^2}{s^2} + t^2\mu \left(\frac{s}{r_{AB}} + \frac{\varepsilon}{2s} - \frac{1}{2}\right), \quad (6)$$

which can be approximated more simply as $\psi \approx \mu(t - \varepsilon\mu/s^2)$ when $t \ll \varepsilon$.

This result indicates that when assortative mating is very weak, $t \ll |\varepsilon| (\mu/s^2)$, we recover Barton's (1995) condition for the evolution of recombination under random mating, that is, epistasis must be both weak and negative: $\lambda < \varepsilon < 0$. However, if assortative mating is sufficiently strong, increased recombination is favored unless epistasis is both strong and negative. That is, when $\psi > 0$, increased recombination is favored when $\varepsilon > \lambda$. In Figure 1, we show the parameter space favoring recombination.

Simulations using the exact recursions confirm the important analytical results (Fig. 1). Additional simulations confirm that the key results of this model also apply when there are more than two loci or when assortative mating is modeled as increasing the probability of matings between individuals of similar, rather than identical, fitness (i.e., $w_{Ab} = w_{aB}$ is not required). Moreover, both simulations and analytical results (see online Appendix) show that these results also apply to diploids.

DISCUSSION

A gene that modifies recombination experiences indirect selection as a consequence of how recombination alters linkage disequilibrium between selected loci. If epistasis is the only force generating linkage disequilibrium, the conditions favoring recombination are quite restrictive (Feldman et al. 1980; Barton 1995). This is because recombination with random mating reduces the linkage disequilibrium toward zero, typically opposing the work of selection. However, factors other than epistasis can generate linkage disequilibrium, including drift and nonrandom mating, and so can alter the conditions favoring recombination (Lenormand and Otto

2000; Barton and Otto 2005; Martin et al. 2005; Roze and Lenormand 2005).

We have studied how a certain type of assortative mating affects the evolution of recombination. Using the simple model above and a biologically more plausible model described in the Appendix (available online), we examined models of assortative mating in which matings between different intermediate types (*Ab* and *aB*) occurred more often than expected under random mating and matings between extreme types (*AB* and *ab*) occurred less often than expected. This type of assortative mating tends to produce positive linkage disequilibrium because in matings between intermediate types recombination converts intermediate types to extreme types ($Ab \times aB \rightarrow AB, ab$). Alternative forms of assortative mating that share this characteristic would be expected to have qualitatively similar outcomes to those described here, whereas other forms of assortative mating that did not share this characteristic would likely affect the evolution of recombination differently. For example, consider a form of assortative mating that results in an excess of matings between haploid individuals with the same *AB*-genotype (e.g., $Ab \times Ab$ and $aB \times aB$ matings) but no excess of $Ab \times aB$ matings. It can be shown that this form of assortative mating does not affect linkage disequilibrium and does not affect the evolution of recombination (unpubl. results). In the discussion that follows, we refer only to the type of assortative mating we have modeled here.

Assortative mating affects linkage disequilibrium, and we have examined how it changes the conditions favoring recombination under two evolutionary scenarios: selective sweeps and mutation-selection balance. In our selective sweep model, we found that assortative mating has no net effect on the evolution of recombination over the course of the selective sweep, despite that fact that it alters the rate of change in the modifier's frequency each generation relative to the random mating expectation. This is because assortative mating has opposing effects on the modifier when beneficial alleles are common versus when they are rare.

At mutation-selection balance, beneficial alleles remain common so a net effect of assortative mating can be observed. If $t \gg |\varepsilon| (\mu/s^2)$, recombination is favored under a much greater range of epistasis values than expected under random mating. With random mating, epistasis must be both weak and negative ($\lambda < \varepsilon < 0$); with assortative mating recombination is not only favored under these conditions but also if there is no epistasis at all or if epistasis is positive, regardless of its strength (i.e., $\varepsilon > \lambda$). The striking change in the range of epistasis values favoring recombination caused by sufficiently strong assortative mating (Fig. 1) is best understood by considering what epistasis does under the different mating systems. With random mating, epistasis plays two important roles with respect to the evolution of recombination. First, the sign of epistasis determines the sign of disequilibrium between selected loci and in so doing indirectly determines whether a modifier becomes associated with the extreme (*AB* and *ab*) or intermediate (*Ab* and *aB*) haplotypes. Second, epistasis determines whether the average fitness of the extreme haplotypes is better or worse than the average fitness of the intermediate haplotypes. These dual roles of epistasis usually result in selection against the mod-

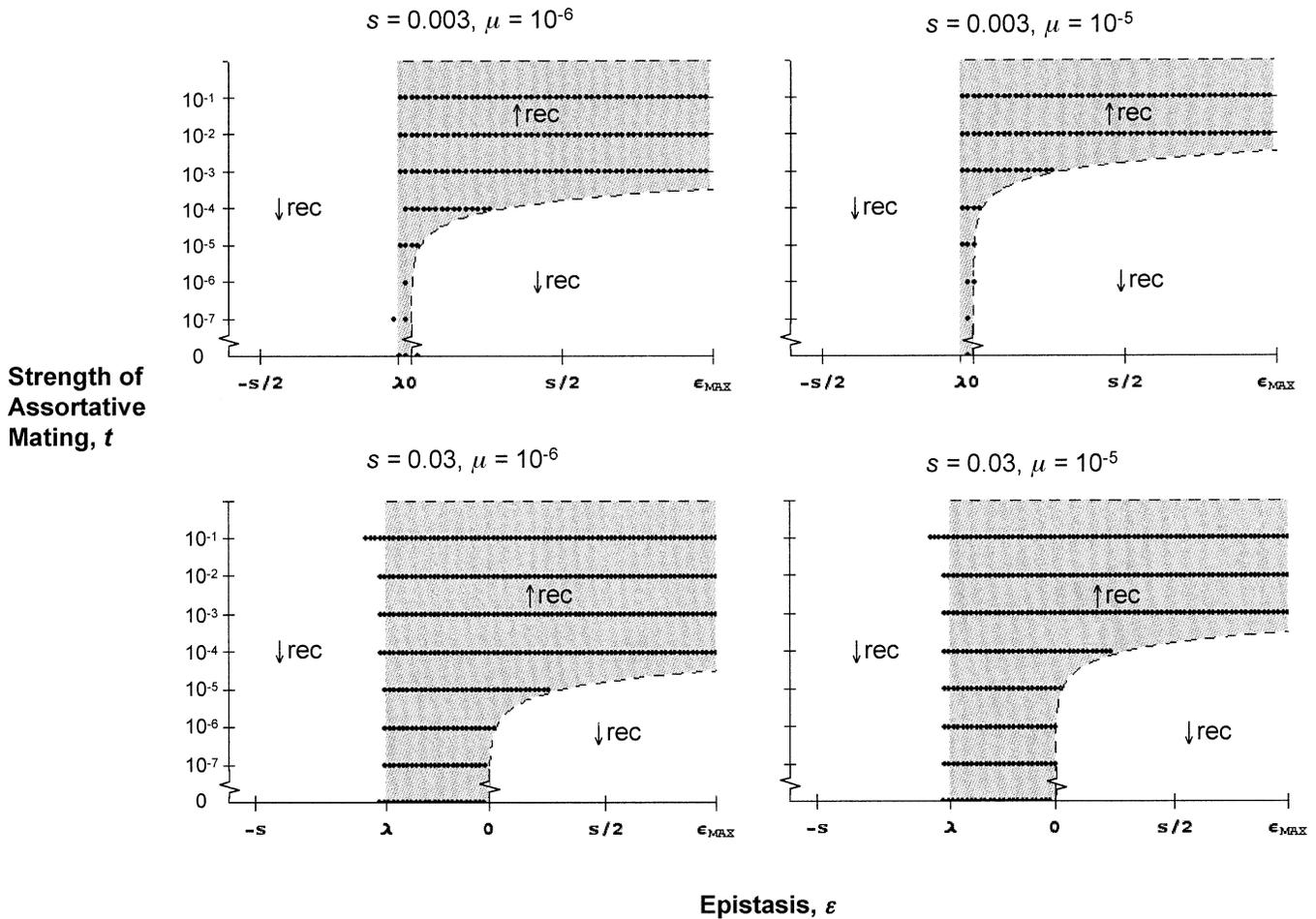


FIG. 1. Parameter space favoring recombination with assortative mating. The shaded region in each indicates the region of parameter space where increased recombination is favored as calculated using equation (6). With random mating ($t = 0$), increased recombination is favored in the range $\lambda < \epsilon < 0$. If $t \gg |\epsilon|(\mu/s^2)$, increased recombination is favored in the range, $\epsilon > \lambda$. Numerical simulations using the exact recursions were performed for $t \in \{0, 10^{-8}, 10^{-7}, 10^{-6}, 10^{-5}, 10^{-4}, 10^{-3}, 10^{-2}, 10^{-1}\}$ using 50 evenly distributed points between $\epsilon = -\epsilon_{MAX}$ and $\epsilon = \epsilon_{MAX}$. Points show the parameter values found to favor recombination in these simulations. In this model, the maximum amount of epistasis possible with a monotonic fitness function is $\epsilon_{MAX} = s(1 - s)$. Parameter values used: $r_{MA} = r_{AB} = 0.1$, $\gamma_{MA} = \gamma_{AB} = 0.01$, top row $s = 0.003$, bottom row $s = 0.03$, left column $\mu = 10^{-6}$, and right column $\mu = 10^{-5}$. Weak assortative mating can influence selection on recombination when selection is weak and mutation rates are low.

ifier; the modifier is typically associated with the haplotypes that cause a short-term disadvantage because, with random mating, recombination acts to reduce the disequilibrium favored by epistatic selection. When there is assortative mating, epistasis loses one of its two roles—it no longer determines whether the modifier becomes associated with the extreme or intermediate haplotypes. At mutation-selection balance, assortative mating causes the modifier to become associated with the extreme haplotypes, regardless of the sign of epistasis, provided $t \gg |\epsilon|(\mu/s^2)$. This association is always advantageous to the modifier in the long term and is also beneficial in the short term provided epistasis is not too negative ($\epsilon > -s^2$). Under random mating, the modifier becomes associated with the intermediate types when epistasis is positive, an association that is disadvantageous in both the short and long term.

If t is not large relative to $|\epsilon|(\mu/s^2)$, then the conditions favoring recombination collapse back to the random mating

expectation. How large a value of t might we expect to find in natural populations? First, we must recognize that in our model we considered fitness effects of only two loci and t was the correlation between mates with respect to these two loci. Thus, t should be thought of as the correlation between mates per locus pair. In reality, assortative mating does not occur at the level of each locus pair but rather at the level of the phenotype, which is fitness or some correlate of fitness. This phenotype will be controlled by many loci at mutation-selection balance, not just two, and the correlation at the phenotypic level will be distributed among all the locus pairs affecting the phenotype. Wright (1921) found that if a polygenic trait was affected by n loci and the correlation in the trait value between mates was ρ , then the correlation between mates per locus pair would be proportional to ρ/n , provided that $\rho \ll 1$. Assuming that 10% to 100% of all loci contribute to the fitness components that form the basis for assortative mating, n should be in the range 10^3 to 10^4 . The correlation

in fitness between mates is unlikely to be more than a few percent in most species, that is, ρ is $O(10^{-2})$. Thus, we speculate that t is $O(10^{-6})$ or $O(10^{-5})$. Taking s in the range 10^{-3} to 10^{-2} , ε in the range $O(s^2)$ to $O(s)$, and μ in the range 10^{-5} to 10^{-6} , then $\varepsilon\mu/s^2$ is $O(10^{-6})$ to $O(10^{-2})$. Thus, we conclude that while assortative mating may affect the evolution of recombination in some species, it is unlikely to be of widespread importance.

In extrapolating the results of a two-locus model to the whole genome, we are ignoring higher order disequilibria (i.e., 3-, 4-, . . . , and n -way associations among selected loci) that could affect the evolution of recombination. These higher order disequilibria are typically considered to be negligible (Barton 1995), at least with random mating. To ensure that higher order associations were not having an unexpected influence when assortative mating occurs, we performed computer simulations involving 1600 loci. Results from these simulations confirm that assortative mating does not favor recombination when $t \ll |\varepsilon| (\mu/s^2)$.

Though we conclude that assortative mating is unlikely to affect recombination in most species, it is not possible to reach this conclusion by simply comparing the strength of the two factors that generate linkage disequilibrium (t and ε). Other parameters (i.e., μ , s) also affect the result in a nonintuitive fashion. If mutation rates were very low, then even small amounts of assortative mating would be sufficient to drastically change selection on recombination (Fig. 1). That is, one could say that the failure of assortative mating to affect the evolution of recombination is because mutation rates are too high rather than because the correlation in fitness between mates is too low. Such a perspective is a reminder that even minor deviations from the simplifying assumption of random mating can be important for the evolution of recombination.

While we have focused on the gene-level advantages to recombination, other authors (Davis 1995; Rice 1998; Jaffe 2000) have used computer simulations to show that assortative mating provides a group-level advantage to a sexually recombining population over an asexual population. Indeed, our analytical approximations confirm this result (not shown). However, group-level advantages of recombination do not translate into gene-level advantages. For example, recombining populations can be much fitter than nonrecombining populations at mutation-selection balance when there is strong negative epistasis (Kimura and Maruyama 1966; Kondrashov 1982), but a modifier for increased recombination would be negatively selected under these conditions (Feldman et al. 1980; Barton 1995). Nonetheless, the previously identified group-level advantage of assortative mating may have important implications for the reduction of mutation load (Rice 1998).

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