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On the Evolution of Recombination in Haploids and Diploids*

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Abstract

In population genetic theory, most analytical and numerical studies of the evolution of recombination have focused on diploid genetics. In studies of the foundations and applications of genetic algorithms (GA's), however, the bit-strings are usually treated as haploid genotypes. This paper compares analytical results for the evolutionary dynamics of modifiers of recombination in haploids with results derived for diploids. The new analytical work addresses the evolution of an allele that controls the rate of recombination between two loci subject to directional selection. It is shown that the fate of a recombination modifier in both haploids and diploids is determined in a complicated way by the sign of the epistasis (interaction in fitness) between the loci, the sign of the initial linkage disequilibrium, and the amount of recombination between the modifier and the genes under selection. This theory is deterministic in that the population is regarded as infinite and no sampling occurs to produce offspring from parents.

The second part of the paper takes selection schemes that have been used recently in numerical studies of finite diploid populations and asks how recombination evolves in haploid versions of these models. Although the analysis keeps track of the recombination controlling locus rather than the time until a desired bit-string appears, our result may be of use to the practitioners of GA's. We find that as a rule high recombination evolves more easily when selection is on haploids than it does in the diploid case. This is especially true of Gaussian selection schemes with high recombination recessive to low recombination. When the fitness regime is more jagged, however, the results depend on the level of jaggedness, with high recombination favored under smoother regimes. We also find that the direction of mutation and dominance relationship among the modifying alleles affects the results. Although there remains much to be done in reconciling the two ways of approaching evolutionary properties of genetic operations, many new and interesting questions have emerged from, and will continue to be stimulated by interactions between practitioners of each approach.
Introduction

Most theoretical treatments of the evolutionary significance of recombination employ diploid genetic models. On the other hand, most investigations of either the utility or the foundations of genetic algorithms in computer science use haploid models. This paper uses models for the genetic control of recombination to compare the fate of recombination modifiers in haploid and diploid genetic systems.

Several recent studies have compared selection in haploid and diploid organisms in an effort to understand the evolution of life cycles (Kondrashov and Crow, 1991; Perrot et al, 1991; Kirkpatrick, 1994). Many of these studies have found results that are sensitive to recombination rates, which are assumed to be constant. For example, deleterious mutations are thought to be less disadvantageous in diploids, where they are masked. The advantage of masking can be eliminated, however, when genes that control the extent of the haploid and diploid phases of the life cycle are tightly linked to the genes that are subject to deleterious mutations (Bengtsson, 1992; Otto and Goldstein, 1992). Similarly, life cycle evolution has been found to depend on recombination rates in models comparing the spread of advantageous mutations in haploid and diploid organisms (Orr and Otto, 1994). These studies have generally assumed that recombination rates remain constant while life cycles evolve. Selection on recombination rates may, in turn, depend on the life cycle of an organism. Ideally, one would study the coevolution of recombination rates and life cycles. Our more limited goal is to compare the evolution of recombination rates in organisms that experience haploid selection with those that experience diploid selection. In either case, we assume that life cycles follow a regular alternation of generations.

The evolution of recombination rates can be studied by following the fate of alleles that modify linkage. This theoretical approach was introduced by Nei (1967) using a model in which two loci were under selection with the recombination between them controlled by a third locus that was selectively neutral. Studies of the evolution of recombination modifiers have assumed either that the selected loci are initially at equilibrium or that several alleles are changing in frequency within a population. In order to place our work in context, it is appropriate to review these approaches in turn.

Except in models that allow mutation or frequency-dependent selection, all studies
that investigate the evolution of recombination modifiers from equilibrium conditions have utilized diploid models. This is because simple viability selection without mutation cannot support stable polymorphic equilibria in haploid models (Feldman, 1971). When all selected loci are fixed, recombination is irrelevant and there is no induced selection on modifier alleles. Using diploid models, Feldman (1972), Feldman et al. (1980), and Feldman and Liberman (1986) developed mathematical theory showing that if the selected genes are at equilibrium with linkage disequilibrium (i.e. non-random association between the alleles at the different loci), then new alleles that reduce recombination between the selected genes would invade the population. This result, known as the "reduction principle", holds for large randomly mating populations with constant viability-level selection.

Recently, we have analysed the fate of a recombination modifier which affects recombination among an arbitrary number of loci, under weak selection (Zhivotovsky et al., 1994). Again, assuming an initial equilibrium, we showed that recombination between some pairs of loci may increase, but only if a weighted average of these pairwise recombination rates decreased. The weights were determined by the extent of epistasis between pairs of genes and their equilibrium frequencies.

The reduction principle has been shown to fail for the evolution of recombination rates under equilibrium conditions using different biological assumptions. These include models with mixed selfing and random mating (Charlesworth et al., 1979; Holsinger and Feldman, 1983), with segregation distortion (Thomson and Feldman, 1974; Feldman and Otto, 1989), with certain kinds of fluctuating selection (Charlesworth, 1976; Hamilton, 1980), and with an equilibrium between selection and mutation (Feldman et al., 1980). The final three examples can, however, be thought to involve the creation of directional selection, as meiotic drive, shifting selection, and mutation move populations away from the equilibrium attained under only constant selection. By and large, then, the reduction of recombination is favored in static populations.

Models that do not assume an initial equilibrium but instead assume that different viability alleles are co-segregating are applicable to both haploid or diploid populations. Their major drawback is, of course, that analytical results for these models are extremely scarce and restricted in scope. Most of the work on non-equilibrium situations has not
included genetic modifiers of recombination, but rather has focused on whether recombination enables a fitness optimum to be achieved more rapidly than in the absence of recombination (Fisher, 1930; Muller, 1932; Maynard Smith, 1968; Hill and Robertson, 1966; Sumida et al., 1990; Findlay and Rowe, 1990). These studies reach different conclusions about the advantage of recombination depending on assumptions about the fitness regime, the population size, and the criteria used to judge the approach to optima (Tanese, 1989; Forrest and Mitchell, 1993; Otto et al., 1994). Even when recombination is known to be advantageous, however, it is not necessarily the case that modifiers increasing the recombination rate would be favored.

Studies tracking modifiers of recombination in evolving populations have found both increases and decreases in the recombination rate. In a deterministic diploid model with directional selection acting upon two loci, high-recombination alleles were found to outcompete low-recombination alleles if selection was sufficiently strong (Maynard Smith, 1980, 1988). These results were found to depend, however, on the dominance relationships assumed and the form of selection as well as the strength of selection (Bergman and Feldman, 1990; see also Alejandre-Duran et al., 1987). In contrast, low-recombination alleles were generally favored in models with normalizing selection, at least in the absence of mutation.

Analogous results have been found in studies of finite populations. Assuming directional selection with multiplicative fitnesses acting upon several loci within haploid individuals, and assuming that new favorable alleles are introduced into the population by mutation, Felsenstein and Yokoyama (1976) showed that high-recombination alleles were generally favored. This numerical result depended on the mutation rate but was not significantly affected by the strength of selection. Using a Gaussian fitness regime, the results of Bergman and Feldman (1990) for a finite diploid population were much more ambiguous: high-recombination alleles were favored for intermediate strengths of directional selection, but low-recombination alleles were favored otherwise. With more arbitrary fitness functions, low-recombination alleles tended to be favored, especially when the fitness surface was irregular or "jagged" (Bergman and Feldman, 1992). Again, the advantage to recombination modifiers is sensitive to the properties of the fitness regime assumed, to the kind of mutation assumed, and to whether the modifier is dominant or recessive.
In summary, evolution generally favors the reduction of recombination in static populations that are at equilibrium under the action of overdominant or stabilizing selection. In changing populations, increased or decreased recombination rates can evolve, depending on the form of selection. It is not, however, known whether differences between haploid and diploid selection translate into different selective pressures upon modifiers of recombination. This question is of interest to computer scientists working with genetic algorithms as well as biologists. The former have devoted most of their attention to optimization or search using genetic operators on bit-strings, but selection is almost always assumed to act on the haploid or single bit-string. It is of interest to determine whether this choice of model has a substantial effect on the ability of GA's to achieve their goals.

In the following sections, we shall first examine some properties of a deterministic three-locus model in which two genes are under selection and the third controls the rate of recombination during the diploid phase. We will focus on a selection scheme that has the same effect on the dynamics of haploid and diploid populations. We will also briefly discuss evolution of a modifier gene with a uniquely diploid selective regime. The change at a modifier locus can be studied analytically by transforming the recursions to a coordinate system based on the gametic associations among the loci, i.e. linkage disequilibria. The initial changes in these associations can be used to make qualitative predictions about the fate of modifier alleles. Numerical iterations confirm these predictions in every case. We then proceed to analyse new results from simulations of finite populations, comparing the fate of recombination modifiers among 40 loci in haploid populations to their fate when they affect 20 loci in diploid populations. We shall see that there is no consistent difference between modifier evolution in haploid and diploid models; depending on the fitness regime chosen, increased recombination can evolve with greater, lesser, or equal ease in haploid populations.

A Deterministic Modifier Model with Selection

Some insight into the evolution of recombination modifiers can be obtained by considering their dynamics in simplified models. Here we will study a deterministic model in which selection acts at either the haploid or the diploid phase upon two loci \((A,B)\)
that recombine during a diploid phase at a rate determined by a third locus \((M)\). The alleles at the modifier locus are neutral and would not change in frequency were it not for their interactions with the major loci. Genetic associations will, however, develop between modifier alleles and alleles at the major loci, an effect that creates induced or secondary selection on the modifier (Feldman 1972; Karlin and McGregor 1974). For instance, if a modifier allele, say \(M\), were in strong linkage disequilibrium with a beneficial allele at a major locus, then the spread of this beneficial allele could carry along the modifier. We will focus on the development of disequilibria between the modifier and the major loci in order to predict the modifier’s evolution.

Table 1 here.

We consider the usual deterministic model for the dynamics at the three loci, with two alleles at each; \(A/a, B/b, M/m\). The life cycle passes through a haploid stage, random mating of haploid genotypes, a diploid stage, and finally meiosis to form the next generation of haploids, which are censused. During meiosis, recombination occurs between the \(A\) and \(B\) loci at a rate \(r_1\) if the uniting haploids both carry the \(M\) allele, \(r_2\) if only one does, and \(r_3\) if both carry the alternate allele \(m\). Recombination can also occur between the \(M\) and \(A\) loci at a rate \(R\), which is not affected by alleles at the \(M\) locus. We assume no interference between regions in the recombination process. The dynamics are initially developed assuming selection acting on diploid genotypes as shown in Table 1a. When the diploid fitness coefficients are as shown in Table 1b, which we will call a “haplotypic” fitness scheme, the dynamics of the diploid model correspond to those of an analogous haploid model. Thus haplotypic selection will result either when it is really the haploid phase that is under selection or when selection acts independently upon the two component haplotypes of a diploid individual. With haplotypic selection acting upon diploids, epistasis can result from interactions within a chromosome but not from interactions between chromosomes (only cis effects; Nordborg et al., 1994). The exact equivalence between a haploid model and a diploid one with haplotypic fitnesses indicates that in this case selection upon recombination rates can be equivalent in haploid and diploid populations. The haplotypic model is equivalent to a purely haploid model when haploid frequencies are taken at the
appropriate census point. The numerical results summarized in Tables 3–5 are not altered by changing the point of census by reversising the order. We will focus on the evolution of recombination modifiers in the presence of directional haplotypic selection with epistasis as shown in Table 1c. We will then briefly discuss another special case of diploid selection with epistasis (Table 1d).

Let the chromosome frequencies for \{MAB, MAb, MaB, Mab, mA, Mab, mAb, mab\} be \{x_1, x_2, x_3, x_4, x_5, x_6, x_7, x_8\}. Throughout, we will use \(f_i\) to denote the frequency of any type \(i\) in the population, where \(i\) may be an allele or a haplotype. The recursions that transform the frequencies of chromosomes immediately after meiosis from one generation to the next are given by Feldman (1972). In these equations, four disequilibrium measures and three allele frequencies are sufficient to specify the dynamics of the eight chromosomes. Since we are interested in the development of disequilibria between the modifier and major loci, we can transform the equations using the following variables:

\[
\begin{align*}
    f_a &= x_3 + x_4 + x_7 + x_8, \\
    f_b &= x_2 + x_4 + x_6 + x_8, \\
    f_M &= x_1 + x_2 + x_3 + x_4, \\
    D_{Mab} &= f_{Mab} - f_M f_{ab} = x_4 - f_M (x_4 + x_8), \\
    D_{Ma} &= f_{Ma} - f_M f_a = (x_3 + x_4) - f_M f_a, \\
    D_{Mb} &= f_{Mb} - f_M f_b = (x_2 + x_4) - f_M f_b, \\
    D_{ab} &= f_{ab} - f_a f_b = (x_4 + x_8) - f_a f_b.
\end{align*}
\]

The first two terms measure the frequency of the advantageous alleles \(a\) and \(b\), the third measures the frequency of the modifier allele, \(M\). \(D_{Mab}\) measures the association between the \(M\) allele and the fittest haplotype \(ab\). \(D_{Ma}\) and \(D_{Mb}\) measure the association between the \(M\) allele and the beneficial alleles \(a\) and \(b\), respectively. \(D_{ab}\) measures the linkage disequilibrium between the \(A\) and \(B\) loci.

Let us follow changes over time in the frequency, \(f_M\), of the modifier allele, \(M\). For general fitnesses, \(\Delta f_M = f'_M - f_M\) is a complicated function of the parameters of the model. For haploid selection or haplotypic selection of the form in Table 1c, however, we
may obtain the exact recursion for the frequency of $M$,

$$\Delta f_M = \frac{D_{Mab}(s^2 + \varepsilon) + (D_{Ma} + D_{Mb})s}{\sum_{i=1}^{8} x_i w_i}. \tag{1}$$

Since the denominator is simply the average fitness of a haplotype and must be positive, the modifier will always increase in frequency through an association with the beneficial alleles considered separately ($s > 0$), but an association with the fittest chromosome ($ab$) can be beneficial or detrimental depending on the sign of $s^2 + \varepsilon$. Note that $s^2 + \varepsilon$ is equivalent to the additive epistasis between the $A$ and $B$ loci, and must be greater than $-s$ for directional selection ($w_4 > w_3$).

Predictions can be made concerning modifier evolution by examining the development of the disequilibrium measures in equation (1). If all disequilibria are initially zero, then after one generation of selection $D_{Ma}$ and $D_{Mb}$ remain zero, but the other disequilibria become:

$$D'_{ab} = \frac{\varepsilon f_a(1 - f_a)f_b(1 - f_b)(1 - \bar{r}_{AB})}{(\sum_{i=1}^{8} x_i w_i)^2},$$

$$D'_{Mab} = \frac{-\varepsilon f_a(1 - f_a)f_b(1 - f_b)f_M(1 - f_M)\Delta r}{(\sum_{i=1}^{8} x_i w_i)^2},$$

where $\bar{r}_{AB}$ represents the average recombination rate between the $A$ and $B$ loci and $\Delta r$ represents the average difference in recombination rate between carriers of the $M$ and $m$ alleles at the modifier locus:

$$\bar{r}_{AB} = f_M^2 r_1 + 2 f_M(1 - f_M)r_2 + (1 - f_M)^2 r_3,$$

$$\Delta r = f_M(r_1 - r_2) + (1 - f_M)(r_2 - r_3).$$

Once associations develop between the loci, the recursions for the disequilibria become quite complicated. If, however, we assume that the selection coefficients and, as a consequence, the disequilibria are sufficiently small, we can develop approximate recursions.
which may be used to determine how the disequilibria develop. The recursions, to linear order in \( s, \varepsilon, \) and \( D_i \) (ignoring all cross-products), are then:

\[
D'_{ab} \approx [\varepsilon f_a (1 - f_a) f_b (1 - f_b) + D_{ab}] (1 - \bar{r}_{AB}) + (D_{Ma} f_b + D_{Mb} f_a - D_{Mab}) \Delta r,
\]

\( (2) \)

\[
D'_{Mab} \approx -[\varepsilon f_a (1 - f_a) f_b (1 - f_b) + D_{ab}] f_M (1 - f_M) \Delta r + D_{Ma} f_b r_2 (1 - R) + D_{Mb} f_a r_2 R + D_{Mab} (1 - R) (1 - r_2) + K_1,
\]

\( (3) \)

where

\[
K_1 = (D_{Ma} f_b + D_{Mb} f_a - D_{Mab}) f_M (1 - f_M) (r_1 - 2 r_2 + r_3).
\]

With the approximations used above, however, \( D_{Ma} \) and \( D_{Mb} \) remain zero when they are initially set to zero. These disequilibria will grow in magnitude, but only in response to the development of \( D_{Mab} \), and only at a rate that is proportional to the cross-product of the selection coefficients and \( D_{Mab} \). Hence, to see how \( D_{Ma} \) and \( D_{Mb} \) develop, we give their recursions to linear order in the disequilibria but include all selection terms:

\[
D'_{Ma} \approx (1 - R) \left[ \frac{D_{Ma} L_1 - D_{Mab} L_2 + D_{Mab} L_3}{W^2} \right],
\]

\( (4) \)

\[
D'_{Mb} \approx \left[ \frac{(1 - R) (1 - r_2) + R r_2}{W^2} \right] \left[ - D_{Ma} L_4 + D_{Mb} L_5 + D_{Mab} L_6 \right],
\]

\( (5) \)

where \( W \) and \( L_i \) are the strictly positive functions

\[
W = 1 + s (f_a + f_b) + (s^2 + \varepsilon) f_a f_b,
\]

\[
L_1 = 1 + s (1 + f_b) + s^2 f_b + \varepsilon f_a f_b,
\]

\[
L_2 = f_a s [1 + s (1 + f_b) + s^2 f_b + \varepsilon f_b],
\]

\[
L_3 = [s (1 + s) + \varepsilon] f_b + [s (1 + s) + \varepsilon (1 - f_a)],
\]

\[
L_4 = f_b s [1 + s (1 + f_a) + s^2 f_a + \varepsilon f_a],
\]

\[
L_5 = 1 + s (1 + f_a) + s^2 f_a + \varepsilon f_a f_b,
\]

\[
L_6 = [s (1 + s) + \varepsilon] f_a + [s (1 + s) + \varepsilon (1 - f_b)].
\]

To aid in the interpretation of these equations, we will assume that \( M \) increases the recombination rate between the \( A \) and \( B \) loci and that the effects at the modifier locus
are additive. We then have that $\Delta r = +$ and $K_1 = 0$. Starting with a population in complete linkage equilibrium, we know that $D_{ab}$ develops with the sign of $\epsilon$ (Felsenstein, 1965; Eshel and Feldman, 1970) and $D_{Mab}$ develops with the sign of $-\epsilon$ after only one generation. In succeeding generations, $D_{Ma}$ and $D_{Mb}$ develop with the same sign as $D_{Mab}$, that is $-\epsilon$, but these disequilibria accumulate slowly if $R$, the recombination rate between the modifier locus and the major locus $A$, is large. While it is impossible to predict the long-term behavior of the system, the initial development of disequilibria may help predict the fate of modifiers. We will thus describe predictions formed from the above analysis and compare them to simulation results in the next section.

Assuming that the $D_{Mab}$, $D_{Ma}$ and $D_{Mb}$ develop with the sign of $-\epsilon$, we may make the following predictions about the change in modifier frequency based on the terms in equation (1):

1. $\epsilon = +; (s^2 + \epsilon) = +$: The disequilibrium terms in equation (1) become negative. Since $(s^2 + \epsilon)$ and $s$ have the same sign, all these disequilibria contribute to a reduction in the frequency of $f_M$. Decreased recombination rates should be favored.

2. $\epsilon = -; (s^2 + \epsilon) = +$: The disequilibrium terms in equation (1) become positive and all add to the frequency of $f_M$. Increased recombination rates should be favored.

3. $\epsilon = +; (s^2 + \epsilon) = -$: This is an invalid case given directional selection. Nevertheless, the disequilibrium terms in equation (1) would become negative. Now $(s^2 + \epsilon)$ and $s$ have opposite signs, with a negative $D_{Ma}$ favoring the increase of recombination and negative $D_{Ma}$ and $D_{Mb}$ favoring its decrease. It is difficult to predict the outcome of these opposing influences; from the form of equations (2)-(5), however, we suspect that if $R$ plays a role in the outcome of modifier evolution, $D_{Mab}$ will command the dynamics for high $R$ (favoring increased recombination), while $D_{Ma}$ and $D_{Mb}$ would play a greater role for low $R$ (favoring reduced recombination). There may be a value of $R$, say $R_c$, below which alleles, like $M$, which increase recombination rates, will decline in frequency and above which they will increase in frequency.

4. $\epsilon = -; (s^2 + \epsilon) = -$: The disequilibrium terms in equation (1) become positive. Now again $(s^2 + \epsilon)$ and $s$ have opposite signs, with a positive $D_{Mab}$ favoring the decrease of recombination and positive $D_{Ma}$ and $D_{Mb}$ favoring its increase. From equations (2)-(5),
we again suspect that if $R$ plays a role in the outcome of modifier evolution, $D_{Ma}D_{ab}$ will command the dynamics for high $R$ (now favoring reduced recombination), while $D_{Ma}$ and $D_{Mb}$ would play a greater role for low $R$ (favoring increased recombination). If a critical value ($R_c$) exists for the recombination rate between the modifier and the major loci, increased recombination should be observed below this value and reduced recombination should be observed above this value.

In short, we expect that modifier evolution will be depend on the extent of both multiplicative epistasis ($\varepsilon$) and additive epistasis ($s^2 + \varepsilon$) in the haploid or haplotypic model considered here.

The above predictions assume that all disequilibria are initially zero. If, instead, the population is initially in linkage disequilibrium between the $A$ and $B$ loci ($D_{ab} \neq 0$; $D_{Ma} = D_{Mb} = D_{Ma} = 0$), then this disequilibrium will play a role that is analogous to that of $\varepsilon$. This happens because $D_{ab}$ enters into equations (2)-(5) only in terms of the form ($\varepsilon C + D_{ab}$), where $C$ is a positive multiplier. Therefore, starting with negative disequilibrium reduces the effective epistasis and will tend to take populations from case [1] above to case [2] and from case [3] to case [4]. Positive initial disequilibrium has the opposite tendency.

Interestingly, conditions [1]-[4] correspond exactly to mean fitness considerations only if $D_{Ma}$ and $D_{Mb}$ do not successfully oppose the effects of $D_{Ma}D_{ab}$. If one modifier allele, say $M$, is fixed ($x_5 = x_6 = x_7 = x_8 = 0$), then the mean fitness, $W$, varies with the recombination rate, $r_1$, according to $\frac{\delta W}{\delta r_1}$ which has the sign of

$$\frac{\delta D_{ab}}{\delta r_1}(s^2 + \varepsilon).$$

In turn, $\frac{\delta D_{ab}}{\delta r_1}$ has the sign of $-\varepsilon$, at least initially. Hence, we expect fitness to decrease with recombination if $\varepsilon(s^2 + \varepsilon)$ is positive and to increase if it is negative. Recombination modification complies with these mean fitness expectations in cases [1] and [2] above, but does so only in cases [3] and [4] if $D_{Ma}$ and $D_{Mb}$ are not sufficiently strong compared to $D_{Ma}D_{ab}$ to govern the evolution of the modifier. Otherwise, evolution at the modifier locus can occur in ways that reduce mean fitness.
Modifier evolution in three locus models is undoubtedly complex. Equation (1) specifies precisely how alleles that modify recombination rates would change in frequency as a function of the disequilibria that develop between the three loci with haplotypic selection. What is difficult is to determine how these disequilibria will develop, especially over many generations with moderate selection. We have given approximate arguments for how the disequilibria should develop when they all start near zero. We turn now to a numerical analysis to evaluate the sufficiency of these arguments.

**Numerical Analysis of the Three Locus Model**

Modifier evolution was numerically investigated using the full three-locus dynamics given in Feldman (1972) for the case of haplotypic selection (Table 1c). We chose four values for the selection coefficient \( \{s = 0.01, 0.1, 0.5, 5\} \), five values for the recombination rate between the \( M \) and \( A \) loci \( \{R = 0.0, 0.01, 0.1, 0.3, 0.5\} \), six sets of recombination rates between the \( A \) and \( B \) loci (Table 2), and ten values for the extent of epistasis, \( \varepsilon \). Starting with the most negative epistasis, four of these ten values represented case [4] of the last section

\[ \varepsilon = \{-s(1 + s) + 0.0001, \text{two intermediate values}, -s^2 - 0.0001\}, \]

three represented case [2]

\[ \varepsilon = \{-s^2 + 0.0001, -s^2/2, -0.0001\}, \]

and three represented case [1]

\[ \varepsilon = \{0.0001, s, 10s\}. \]

When \( s = 0.01 \), the epistasis for case [2] had to be modified slightly to become

\[ \varepsilon = \{-s^2 + 0.00001, -s^2/2, -0.00001\}. \]

Throughout, selection was strictly directional, favoring alleles \( a \) and \( b \).

**Table 2 here.**

For each combination of these parameters, a deterministic iteration was begun with the beneficial alleles, \( a \) and \( b \), each at a frequency of 0.01, the modifier allele \( M \) at a frequency
of 0.50, and no disequilibria between any of the loci. The recursions were iterated until the ab chromosome had reached a frequency of at least 0.999. Two aspects of these simulations were of particular interest: Did the disequilibria always have the expected sign? Did the modifier evolve as predicted? In the 1200 parameter sets studied, the disequilibria always developed initially according to predictions, that is, $D_{ab}$ took on the sign of $\varepsilon$ and $D_{Ma}$, $D_{Mb}$ took on the sign of $-\varepsilon$. With the exception of $D_{Mb}$, these disequilibria never changed sign during the further advance of the $ab$ chromosome. $D_{Mb}$ did later change sign in 28 of the 1200 simulations, always when $\varepsilon$ was extremely negative and when $R$ was equal to or near zero. In these cases, $D_{Ma}$ was larger in magnitude than $D_{Mb}$ and dominated the development of $D_{Mb}$ (see equation (5)). Even when the sign of $D_{Mb}$ changed from $-\varepsilon$ to $+\varepsilon$, the sum of $D_{Ma}$ and $D_{Mb}$ always had the correct sign of $-\varepsilon$. Since $D_{Mb}$ enters into equation (1) only as a part of the sum $(D_{Ma} + D_{Mb})$, the fact that it occasionally changed sign should not have had a qualitative effect on our predictions concerning modifier evolution.

The predictions concerning the fate of the modifier alleles were confirmed in every case. Specifically,

[1] $\varepsilon = +; (s^2 + \varepsilon) = +$ : Alleles that decreased the recombination rate were always favored.
[2] $\varepsilon = -; (s^2 + \varepsilon) = +$ : Alleles that increased the recombination rate were always favored.
[4] $\varepsilon = -; (s^2 + \varepsilon) = -$ : When $R$ played a role, there was a critical value ($R_c$) for the recombination rate between the modifier and the major loci below which increased recombination was favored and above which decreased recombination was favored.

Case [4] involves a conflict between the influence of $D_{Ma}$ and that of $(D_{Ma} + D_{Mb})$; the outcome of this opposition did not always depend on the value of $R$. Instead, either increased or decreased recombination rates could be favored for all values of $R$. A pattern emerged from the simulations that we interpret as shown in Figure 1: the critical value $R_c$ decreases as $(s^2 + \varepsilon) \rightarrow -s$ and increases as $s^2 + \varepsilon \rightarrow 0$. With very negative epistasis, $R_c$ may be below zero, in which case alleles that decrease recombination are favored for all $R$. In contrast, when the epistasis is just below $-s^2$, $R_c$ may be above 0.5 and increased recombination rates can be favored for all $R$. With the benefit of hindsight, this behavior is
again consistent with the form of equation (1): when $\epsilon$ is substantially less than $-s^2$, $D_{Ma}\bar{b}$ has a greater influence on the evolution of the modifier and forces down-modification of the recombination rate, but as $\epsilon \rightarrow -s^2$, the term in equation (1) involving $D_{Ma}\bar{b}$ becomes negligible and $(D_{Ma} + D_{M\bar{b}})$ dominates, leading to up-modification of recombination. Between these two extremes, the two opposing forces balance in a way that depends on the value of $R$, as predicted.

Table 3 here.

Table 3 illustrates these results for $s = 0.1$ assuming that the modifier allele $M$ increases the recombination rate between the $A$ and $B$ loci with $r_1 = 0.5$, $r_2 = 0.25$, and $r_3 = 0.01$. Cases [1] and [2] may be interpreted in a straightforward manner: down-modification occurs in the former and up-modification in the latter. In these cases, the modifier undergoes a greater change in frequency when it is tightly linked ($R$ near zero) and when the epistasis is large in magnitude.

Case [4] can be interpreted in the spirit of Figure 1: $R_c$ is below zero when $\epsilon = -0.1099$, lies between $R = 0.01$ and $R = 0.10$ for $\epsilon = -0.0800$, lies between $R = 0.10$ and $R = 0.30$ for $\epsilon = -0.0400$, and finally increases beyond $R = 0.5$ for $\epsilon = -0.0101$. In this case, however, the behavior of the final modifier frequency is non-monotonic in both $R$ and $\epsilon$. These qualitative results were generally not sensitive to the dominance relations at the modifier locus; there was a slight tendency for $R_c$ to be higher when the modifier was recessive (increased recombination would then be somewhat more likely). As a final check on the generality of our results, we investigated the sensitivity of the simulations to changes in initial allele frequencies. We found no qualitative dependence on $f_a$, $f_b$, or $f_M$.

Tables 4-5 here.

In Tables 4 and 5, we investigate the potential importance of starting the population in linkage disequilibrium. As shown in Table 4, the existence of positive disequilibrium between the $A$ and $B$ loci ($D_{a\bar{b}} = 0.000098$) appears to have the effect of increasing the epistasis. For example, the simulations with $\epsilon = -0.0001$ act as if epistasis were positive and show a decrease in the high-recombination allele, $M$. In cases [1] and [2],
the initial positivity of $D_{ab}$ always leads to a reduced frequency of $M$ in comparison to the simulations begun in linkage equilibrium (Table 3). With case [4], the frequency of $M$ almost always changes in the direction of the next highest epistasis in Table 3. This may be an increase or a decrease, since the behavior is non-monotonic in $\varepsilon$. Analogous results were found with negative disequilibrium ($D_{ab} = -0.000098$), as shown in Table 5. Now, the simulations with $\varepsilon = +0.0001$ act as if epistasis were negative and show an increase in the high-recombination allele, $M$.

Analytical results describing non-equilibrium dynamical behavior are rare. We have found that disequilibria, initially absent, develop in response to epistatic selection with a sign that can be predicted based on the selective coefficients. This information can then be successfully used to predict the change in frequency of a modifier allele. In general, supermultiplicative selection ($\varepsilon > 0$) favors increased recombination rates, submultiplicative but superadditive selection ($-s^2 < \varepsilon < 0$) favors decreased recombination rates, and subadditive selection ($\varepsilon < -s^2$) favors either increased or decreased recombination rates depending on the parameters of the model. This qualitative description is summarized in Table 6. While the analysis described herein is approximate in that it extrapolates from the initial development of disequilibria, numerical iterations have confirmed the predictions in every case. Considering the complexity of three-locus models, the predictive power of our analysis suggests that it might be profitable to re-analyze such dynamical systems in terms of disequilibria, which appear to compose a more natural co-ordinate system for many problems (Uyenoyama and Bengtsson, 1989; Uyenoyama, 1991; Otto 1991).

Table 6 here.

A Diploid Model with Epistasis

The haplotypic model analyzed in the previous sections is only one of several possible special cases of the generalized diploid model with directional selection (Table 1a). In this section, we will very briefly examine the evolution of recombination modifiers under a uniquely diploid selection regime. Here selection is directional and multiplicative except that when diploid individuals carry all of the beneficial alleles, they have a fitness that
differs from \((1 + s)^4\) by \(\eta\) (Table 1d). We will call this epistatic scheme “all-or-none”. Such a viability scheme could arise either if there were an added benefit to carrying only beneficial alleles \((\eta > 0)\) or if there were a threshold in the advantage that is exceeded when four such alleles are carried \((\eta < 0)\).

Analogously to (1), we may transform the dynamical system which, in this case, becomes

\[
\Delta f_M = \frac{D_{Mab}(s^2\beta + \eta f_{ab}) + (D_{Ma} + D_{Mb})s^\beta}{\sum_i \sum_j x_i x_j w_{ij}}, \tag{6}
\]

where

\[
\beta = 1 + (f_a + f_b)s + f_{ab}s^2 \geq 1
\]

\[
f_{ab} = f_a f_b + D_{ab} \geq 0
\]

We can again follow the initial development of disequilibria. The generation after all disequilibria begin at zero, \(D_{ab}\) develops with the sign of \(\eta\), while the remaining disequilibria continue to equal zero. In the next generation, \(D_{Mab}\) develops with the sign of \(-D_{ab}\) \((-\eta)\) if, as we assume, the allele \(M\) increases the rate of recombination. In the following generations, \(D_{Ma}\) and \(D_{Mb}\) develop with the sign of \(D_{Mab} (-\eta)\), at least when selection is not extremely strong \((s \text{ less than about 10})\).

The predictions that we can make about the evolution of modifiers in this diploid model are less definitive than in the previous section. Again, if \(\eta\) is positive and selection is directional, all the disequilibria in equation (6) lead to the decrease of the allele that raises the recombination rate, \(M\). When \(\eta\) is negative but \(s^2 + \eta\) is still positive, then each disequilibrium in equation (6) leads to the increase of \(M\), thus increasing the recombination rate. Since \(\beta \geq 1\) and \(f_{ab} \leq 1\), equation (6) tells us that a necessary condition for opposition between the different disequilibria is that \(s^2 + \eta < 0\), but that this condition is no longer sufficient as it was with haplotypic selection. When \(\eta\) is sufficiently negative that \(s^2 + \eta\) becomes negative, \(s^2 \beta + \eta f_{ab}\) may still be positive and increased recombination would retain its advantage. As \(\eta\) approaches the most negative possible value consistent with directional selection, \(-s(1 + s)^3\), the term \(s^2 \beta + \eta f_{ab}\) may become negative throughout much of the
evolution of the system and $D_{Mab}$ may again oppose the effects of $D_{Ma}$ and $D_{Mb}$. As with haplotypic selection, $D_{Mab}$ is the least sensitive to the value of the recombination rate between the modifier and the major loci, $R$, so that there can be a dependence on $R$ such that $D_{Mab}$ takes on greater importance with high recombination rates (favoring decreased recombination, $r_i$, between the major loci).

Table 7 here.

Simulations were run to compare the outcome of all-or-none diploid selection to haplotypic selection. All the simulations described for haplotypic selection were repeated with an additional three values for the epistasis:

$$
\eta = \{-s(1+s)^3 + 0.0001, -s(1+s)[1+(1+s)^2]/2, -s(1+s) - 0.0001\}.
$$

These values extend the range of epistasis from its most negative possible value with haplotypic directional selection, $-s(1+s)$, to its most negative possible value with all-or-none directional selection, $-s(1+s)^3$. The results were entirely analogous to those obtained with the simpler haplotypic selective scheme. For example, the disequilibria always took the expected sign during the entire progression of $ab$ to fixation, with the exception of $D_{Mb}$ (but not $D_{Ma} + D_{Mb}$), which would occasionally change sign. Specific simulation results for the case of $s = 0.1$ and recombination set A are given in Table 7. Two quantitative differences between Table 7 and Table 3 are noteworthy: (1) the modifier tends to change less in frequency and (2) it is difficult to find sufficiently negative epistasis such that decreased recombination is favored for all $R$ (i.e. $R_c$ never decreased to below zero, see Figure 1). The first conclusion probably reflects the fact that the force behind changes in modifier frequency (epistasis) now acts in only one genotype, $aabb$. The second conclusion indicates that this diploid model favors increased recombination rates over a broader range of parameters, since $R_c$ is never low enough to favor decreased recombination rates near $R = 0$ with negative epistasis.

In summary, the haplotypic and the all-or-none selection schemes behaved similarly, with increased recombination rates favored over a slightly greater proportion of the parameter space under all-or-none selection. We see from these simple three-locus models
that during its evolution, recombination can experience the same (haplotypic fitnesses) or different (all-or-none fitnesses) selective pressures in haploid and diploid populations.

**Numerical Analyses of a Multilocus Model**

In two previous studies (Bergman and Feldman, 1990, 1992), we made numerical investigations of the dynamics of alleles at a recombination-controlling locus in diploid genetic systems. We studied both two- and multi-locus systems, although here we focus on the multilocus analyses. In our first multi-locus study (Bergman and Feldman, 1990), we considered Gaussian selection with different strengths, measured by the standard deviation, $\sigma$, and different levels of directionality as measured by the mean, $\mu$, relative to the phenotypic range. Our second study involved selection regimes of varying degrees of jaggedness as a function of the phenotype, with the degree of jaggedness controlled by a single parameter. In both studies, the population size was 100 diploid individuals, and selection occurred at twenty major diallelic loci with a twenty-first locus controlling the probability that recombination occurred among all twenty-one genes.

In both of these earlier studies, the genotype at the modifier locus controlled the probability that recombination occurred, and when it occurred one, two, or three breaks had equal probabilities. We tested the effect of this assumption on the dynamics of the modifying alleles by comparing the results to simulations in which only one break was permitted; there was no qualitative and almost no quantitative change in the evolutionary outcome of the modifying alleles. Here, we shall consider only a single break when recombination occurs. We now compare the results of these earlier studies of diploids with new findings for a haploid model.

We consider forty loci in a haploid population of 200 individuals. At each locus the alleles are labelled 0 and 1 and the phenotype of an individual is constructed by summing the values at these forty loci. Selection occurs on the resulting phenotype, $\nu$, which takes on a value between zero and forty. The number 40 was chosen in the haploid case to make the range match that in our previous studies of diploids. With 40 haploid loci, the strength of selection per locus is the same in both models. The population size was chosen with the same number of adult haplotypes as in the earlier papers, so that the extent of random
genetic drift would be equivalent.

In addition to the forty loci that contribute to the phenotype, a forty-first locus controls the probability that recombination will occur, but has no effect on the phenotype. We shall use the notation CH and CL for the two alleles at the recombination-controlling locus indicating that CH produces high recombination and CL low recombination rates. The initial population is constructed by randomly choosing the alleles 0 and 1 at each of the forty major loci with equal likelihood. These loci are randomly assembled to produce the 200 forty-locus chromosomes. The initial frequency at the modifier locus depends on our choice of fitness regime: in the case of Gaussian selection we use an initial frequency of 0.5 for CH and CL, and in the jaggedness study the initial frequency of CH is 0.05. These modifier alleles are randomly assigned to the forty-locus chromosomes described above so that, on average, there is initially no linkage disequilibrium among any of the forty-one genes.

To form the next generation, two haploid parents are chosen at random to constitute a diploid phase during which recombination occurs. A recombinant offspring is chosen at random. This offspring’s phenotype is then evaluated against the fitness function and, if it survives, it is included in the pool that forms the next generation. This process is repeated until 200 offspring have survived. The process of recombination during the diploid phase has the following properties. If both chosen parents carry CH at the modifier locus, a recombination event will occur with probability $r_{11}$. That is, $r_{11}$ is the probability that a recombination event occurs at one location chosen uniformly across the forty-one loci. If one parent carries CH and the other CL, the probability of a recombination event is $r_{01}$, with $r_{00}$ the corresponding probability if both carry CL. As in our earlier studies we chose the following values: $r_{11} = 0.5$, $r_{01} = 0.5$, and $r_{00} = 0.01$ when CH is dominant and $r_{01} = 0.01$ when CH is recessive. If no recombination occurs, an offspring is a clone of a randomly chosen one of its parents. In some of our simulations, mutation is included. This occurs to both recombinant and non-recombinant offspring prior to selection. The process of random mating, recombination, mutation (if included), and selection is repeated until one of the alleles at the recombination-modifying locus has reached fixation.

In comparing the evolution of recombination in haploid and diploid systems in these
simulations, it is important to remember that the average probability of a break between two neighboring loci in the haploid case is very close to one half of that in the diploid case. In the latter case, the phenotypic range is the same as for the haploids, but there are only twenty major loci among which to select a breakpoint compared to 40 for the haploids. For this reason, we have repeated the previous diploid analyses using recombination probabilities \( r_{11}/2, r_{01}/2, \) and \( r_{00}/2, \) and refer to these results as \( D^* \) in Tables 8, 9, 10 and 11.

Gaussian Selection

The usual definition of stabilizing selection takes a particular phenotypic value, located in the central part of the phenotypic range, as having the highest fitness, with the fitness of other phenotypes decreasing monotonically with their distance from the optimum. Directional selection, on the other hand, occurs when the fitness increases monotonically towards one extreme of the phenotypic range. We examine two types of Gaussian selection regimes, one of which may be regarded as stabilizing and the other as directional. In all of our simulations, the initial mean phenotype of the population, as can be inferred from the previous section, was chosen to be at the center of the phenotypic range, i.e. 20.

In Table 8 we report the results of simulations in which the Gaussian fitness function had mean 20 and standard deviations \( \sigma = 1, 5, 10, 15, 33.33, \) in decreasing order of the strength of selection. In classical population genetic terms, this is straightforward stabilizing selection, since departures from the average phenotype result in a loss in fitness. Three kinds of mutation assumptions were tested, no mutation at all, mutation from allele 1 to allele 0 at rate 0.005 per locus, and mutation from 0 to 1 at the same mutation rate. For each parameter set, the simulation described in the previous section was repeated for one thousand randomly chosen initial populations.

Table 8 here.

The percentage of those runs that result in fixation of \( CH \) are reported in the table for both the cases when \( CH \) is dominant and when it is recessive. Since the initial frequency of \( CH \) is 0.5, if there were no effective selection on recombination, we would expect 50%
of the runs in both recessive and dominant cases to fix on CH. Departures from 50% by about 3.2% may be regarded as significant, using a two-standard-deviation rule. In Table 8 the columns headed $D^*$ refer to diploid simulations with recombination rates $r_{ij}$ taken to be half of those used in the haploid and diploid cases, headed $H$ and $D$.

From Table 8 we see that with very strong stabilizing selection ($\sigma = 1$), CL is very strongly favored in all mutation regimes. With no mutation, the advantage to CL remains as the selection weakens but becomes less pronounced. Thus, there is a general trend for CH to fix more frequently as selection weakens, although it usually does not outcompete CL. In this no mutation case, with intermediate selection strengths ($\sigma = 5, 10, 15$), there is a tendency for CH to fix more frequently when it is dominant than when it is recessive and, in most cases, CL significantly outcompetes CH in both recessive and dominant cases. With unidirectional mutation in either direction, except for the strongest and weakest selection, CH usually fixes more frequently than when mutation is absent and, in contrast to the case of no mutation, CH fixes more often when recessive than when dominant. Indeed, for intermediate selection ($\sigma = 5, 10, 15$) high-recombination significantly outperforms low-recombination for recessive modifiers. With $\sigma = 1$, there will be little asymmetry in the distribution of phenotypes after selection and mutation will be nearly irrelevant. With weaker selection and unidirectional mutation, enough asymmetry remains after mutation and selection to create a certain amount of directional selection which might allow recombination to reconstitute fitter genotypes.

Comparing the haploid and diploid columns of Table 8 with mutation, it is clear that for intermediate strengths of selection, high-recombination tends to do better with haploids than with diploids when CH is recessive. In fact in both haploid and diploid cases, with $\sigma = 5, 10, 15$, CH does significantly better when it is recessive than when dominant, to the extent that it actually significantly outcompetes CL in the former case. In all cases, CH appears never to significantly outcompete CL when the former is dominant.

An apparent anomaly is observed in Table 8 with no mutation, haploid selection, and $\sigma = 5$. Only 9.9% of the runs fixed on CH when it is recessive, a dramatically lower fraction than in the dominant case, and much lower than in the corresponding diploid selection models. This case was repeated four times with different random seeds giving
results between 9 and 11.5 percent. This case appeared so anomalous that we checked it with all integer \( \sigma \)'s between 1 and 10 observing an almost linear progression. The result is not a fluke. Comparing it with the other recessive cases for \( \sigma = 5 \), the presence of mutation (in either direction) is seen to be of even greater significance for haploids than for diploids.

Table 9 here.

Table 9 reports results for directional Gaussian selection with fitness optima at 30 and 35. The first point to observe about Table 9 is that in general \( CH \) is favored more often when selection is on haploids than when it occurs on diploids. Again, \( CH \) does better when it is recessive than when dominant. There is no doubt that in the case \( \sigma = 1 \), \( CH \) does better with directional selection than with stabilizing selection, a result which might have been predicted from our earlier two-locus work (Bergman and Feldman, 1990). As might be expected, results for the two kinds of mutation are no longer symmetric. In fact, with mutation from 1 \( \rightarrow \) 0, the advantage to high-recombination is very strong in the recessive case. As we noted in our earlier work, the advantage to \( CH \) increases as the mean of the fitness function increases (see also Maynard Smith, 1988), although we have analysed the case with mean 35 only for no mutation.

Comparing the haploid results with the two sets of diploid results, the case \( \sigma = 1 \) provides an interesting contrast between stabilizing and directional selection. In the former case, \( D^* \) results in more frequent fixation of \( CH \) than either haploid (\( H \)) or diploid (\( D \)). But in the latter, \( D^* \) is intermediate between the two. Although we have no explanation for this, it suggests that the strength of selection for or against recombination depends on the value that it takes. In most other cases where \( CH \) is significantly favored, there is not a great deal of difference between \( D \) and \( D^* \) in either Table 8 or Table 9. \( D^* \) was introduced in an attempt to make the haploid and diploid models as comparable as possible. Nevertheless, we see many cases in which the haploid results are significantly different from \( D^* \), with the general tendency to more strongly favor \( CH \) in haploids. Finally, it is worth comparing the haploid recessive result with \( \sigma = 5 \) in Tables 8 and 9. The shift of the mean to 30 has a much more pronounced effect for haploids than for diploids to the extent that
with mean 30, CH is significantly favored (fixing 64.2%). In general, the shift towards more directional Gaussian selection usually has a more dramatic effect on haploids than on diploids except in the $0 \rightarrow 1$ mutation case.

**Jagged Fitness Landscapes**

The second class of fitness functions that we use to compare multi-locus evolution in haploids and diploids was developed by Bergman and Feldman (1992). Here we allow the degree of jaggedness of the fitness surface to be controlled by a single parameter as follows. We consider 40 haploid loci or 20 diploid loci, both with a phenotypic range, $\nu$, between zero and forty. Set $x = \nu/40$, then the fitness function is defined as

$$F(\nu) = \frac{\psi(x) - \min[\psi(x)]}{\max[\psi(x)] - \min[\psi(x)]}, \quad (7)$$

where

$$\psi(x) = \sum_{k=1}^{n} \frac{R(k) \sin \pi k x}{\sqrt{k}}, \quad (8)$$

and the $R(k), k = 1, 2, \ldots, n$ are random numbers uniformly distributed on $[0, 1]$. The "jaggedness" or, as Kaufman and Levin (1987) called it, "ruggedness" of the fitness function is controlled by varying $n$; the greater is $n$, the more jagged is $F(\cdot)$. If the combination of sine curves in (8) produces a single central maximum, the situation is described as stabilizing selection. Two extreme maxima would result in disruptive selection, while one maximum located a long way from the phenotypic mean would entail directional selection. Clearly the range of possible fitness functions described by (7) is far greater than the simple fitness landscapes generally found in textbooks on evolution. We have examined in detail $n = 2, 3, 10, 20, 40$. After $n$ is chosen, $R(k), k = 1, 2, \ldots, n$ are selected. The initial configuration of the population is chosen and the simulation proceeds until one or the other allele at the recombination controlling locus is fixed. For each set of $R(k)$ the simulation is repeated 500 times, each with a randomly chosen starting population.

For each value of $n$, 50 different sets of $\{R(k)\}$ are chosen and the results of the $50 \times 500$ runs for each $n$ constitute the data. A control experiment where the modifier locus had no effect on recombination was also carried out.
In these simulations, recombination occurred as in the previous simulations with Gaussian selection. That is, there was a neutral forty-first locus (haploids) or a twenty-first locus (diploids) that controlled the probability of a single break within the entire chromosome during meiosis. As before, this probability was 0.50 for CH/CH genotypes. In the dominant case CH/CL also produces 0.50 and in the recessive case CH/CL gives a recombination rate of 0.01; CL/CL has a probability 0.01 of a break. Following recombination but before selection one of three mutation regimes was imposed. In the first there was no mutation, in the second there was symmetric mutation (0 ↔ 1) at rate 0.005; in the third there was unidirectional mutation (0 → 1) at rate 0.005. In all cases, the initial population of chromosomes was randomly assembled from the constituent alleles; i.e. there was, on average, initial linkage equilibrium.

The initial frequency of the high recombination allele CH was 5% in the population. The simulation was pursued until either CH or CL was fixed. For each set of 500 runs with a given choice of \( R(k) \), the number which resulted in fixation of CH was tabulated and the distribution of these numbers among the 50 different sets of \( R(k) \) that were chosen for each \( n \) is recorded in Table 10 (dominant case) and Table 11 (recessive case).

Tables 10 and 11 here.

Tables 10 and 11 exhibit the patterns of observed frequencies of fixation of CH according to the jaggedness of the fitness landscape \( F \) as specified by the number of coefficients \( n \) in the dominant and recessive cases, respectively. If CH were completely neutral in its effect on the whole genotype we would expect 5%, or 25, of the 500 runs to fix on CH. The tables record the results in histogram form as a function of \( n = 2, 3, 10, 20, 40 \). The most obvious feature of the tables is that with 20 or 40 coefficients, decreased recombination rates are favored. If anything, this advantage is stronger in the dominant case (see also Bergman and Feldman, 1990, 1992).

On the other hand, there is a suggestion of some advantage to high recombination in the cases \( n = 2 \) or 3 but it is not nearly as strong an effect as the advantage of low recombination with \( n = 20 \) or 40. The role of mutation appears to be important in both recessive and dominant cases. For both, with 2 or 3 coefficients, unidirectional mutation
favors higher recombination more than in the symmetric or no mutation cases. Further, in the recessive case with large $n$, symmetric mutation gives $CL$ a greater advantage than occurs with either unidirectional or no mutation. Comparing the dominant and recessive cases, the former generally produced greater advantage to low recombination for large $n$, an effect that is more noticeable for haploids. In the cases of 2 and 3 coefficients, the haploid model of selection appears to favor high recombination (note especially the final columns of Tables 10 and 11), but this effect disappears for larger numbers of coefficients. In the dominant case (Table 10), with higher numbers of coefficients $CL$ is favored more under haploid selection than in the diploid case. This is often reversed, however, when $CH$ is recessive (Table 11).

The apparent greater success of $CH$ with 2 or 3 coefficients led us to examine the shapes of those fitness surfaces for which $CH$ was favored. The fitness mappings that favored high recombination in both haploid and diploid cases were either of the general form of directional selection or essentially U-shaped, i.e. disruptive. Fitness regimes that caused strong reduction in recombination in the haploid genetic model had the form of two peaks of similar height, each roughly Gaussian shaped, located towards the extreme phenotypes and separated by a valley where the intermediate phenotypes had the lowest fitnesses. In those cases of directional selection in which high recombination succeeded, the results were always stronger when mutation favored the opposite allele to the directional selection.

Discussion

The costs of producing both male and female individuals as well as the costs of ensuring successful mating are strikingly prohibitive for the evolution of sexual reproduction. Almost all explanations for the success of sexual systems over asexual ones revolve around a central theme: sexual reproduction allows greater mixing of a genome through both independent segregation of chromosomes and recombination within chromosomes (Kirkpatrick and Jenkins, 1989; reviews in Michod and Levin, 1988). Genetic mixis can (1) maintain and produce a wider variety of allelic combinations that might be useful in novel ecological or biological environments (Hamilton, 1980), (2) serve to collect favorable mutations from
different chromosomes onto the same chromosome (Fisher, 1930; Muller 1932; Crow and Kimura, 1965, 1969) and (3) prolong the maintenance of old allelic combinations that are lost in finite populations through deleterious mutation and drift (Muller, 1964; Kondrasov, 1988).

The issue of the evolution of recombination rates acts, in part, as a surrogate for the broader question: when is sex and genetic mixing favorable? Recombining the genome must be of sufficient advantage to offset the costs of sex or all of our theories for the success of sexual reproduction are misguided. So it must have been with some amount of consternation that modifiers that increased recombination rates were found to be selected against in almost every model that could be analytically studied (Nei, 1967, 1969; Feldman, 1972; Feldman et al., 1980; Feldman and Liberman, 1986; Altenberg and Feldman, 1987). Interestingly, the systems that could be studied analytically were ones near equilibria, where linearization techniques could be applied. At equilibrium, reproducing individuals are those that have survived selection and whose genotypes are more likely to be be favored in the next generation. In this situation, recombination will destroy the parental combinations that have survived selection and will produce new combinations that have no assurance of being favorable. In short, analytical studies were possible in the very situations in which recombination could do the most harm.

In contrast, all of the advantages described above for genetic mixis are framed against a background of change; either the environment is changing or mutations (beneficial or deleterious) are changing the genome. Indeed, analytical studies of equilibria under particular kinds of fluctuating selection (Charlesworth, 1976) or in the presence of mutation (Feldman et al., 1980) were among the first to identify cases in which increased recombination could be positively selected. Simulation studies have, appropriately, broadened our focus away from equilibria and towards dynamic populations (Felsenstein and Yokoyama, 1976; Maynard Smith, 1980, 1988; Bergman and Feldman, 1990, 1992). An advantage to modifiers that increase recombination rates is often found in these studies, especially in the presence of directional selection. The difficulty, of course, is to develop from simulations a general sense of the conditions that favor the evolution of recombination and those that oppose it.
Our goals in this paper have been two-fold. We have sought more detailed predictions concerning the fate of modifier alleles using a three-locus model with directional selection. We have also sought to compare haploid and diploid populations across a broad range of three-locus and multi-locus models in an attempt to identify the relationship between ploidy levels and the evolution of recombination rates. Systematic differences between haploids and diploids would have implications not only for the evolution of sex in organisms with different ploidy levels but also for the evolution of life cycles, which is known to depend on recombination rates (Bengtsson, 1992; Otto and Goldstein, 1992).

Predictions concerning the evolution of modifier alleles may be motivated by an examination of the role of recombination in producing favorable genotypes or by an examination of the influence of recombination on mean fitness. Eshel and Feldman (1970) studied a two-locus haploid model with haplotypic selection as described in Table 1d. Starting with a population composed of $AB$ individuals, they found that more of the beneficial double mutants, $a\delta$, would exist in a sexual population with recombination than in an asexual population without recombination if the epistasis, $\varepsilon$, were negative. The opposite result held, however, for positive epistasis. If production of the fittest genotype were to be maximized, then, we would expect increased recombination rates to evolve for negative epistasis and decreased recombination rates to evolve for positive epistasis.

Alternatively, if recombination evolved to make mean fitness as large as possible, then we have argued that increased recombination rates should evolve when $\varepsilon(s^2 + \varepsilon)$ is negative and decreased recombination rates should evolve when $\varepsilon(s^2 + \varepsilon)$ is positive. By examining the development of disequilibria and noting their influence on the frequency of a modifier allele, $M$, that increases the rate of recombination, we have developed a third set of predictions that are based on the dynamics of the system. The categories that describe how recombination rates would evolve through successive modification are shown in Table 6. Extensive simulations conform only to these latter predictions and not to those based on the production of fit genotypes or based on mean-fitness considerations. The main consequence of these results is that the evolution of modifiers of recombination should be very sensitive to the epistatic interactions assumed. Negative epistasis appears necessary but not sufficient for the evolution of increased recombination in infinite populations.
Haplotypic selection can apply to either haploids or to diploids, as long as the fitness of a diploid is based upon selection acting independently on its component chromosomes. Extending the model beyond haplotypic selection to the type of diploid selection described in Table 1d (selective interactions exist only in aabb individuals) also leads to the categorization described in Table 6. In this case, however, $R_c$ tends to be larger and has not been observed to fall below 0. Thus this mode of diploid selection tends to be more favorable to the evolution of increased recombination rates.

From the three-locus models, we see that the evolution of recombination can be exactly the same in haploid and diploid populations or can occur more readily in diploid populations, depending on the epistatic relationships assumed. To extend these results to more radically different models, we investigated multi-locus haploid and diploid populations. In both cases, populations were finite and the population size and number of loci were controlled to keep the extent of selection and random genetic drift per locus equivalent in haploids and diploids. We investigated two types of selective regimes: a gaussian fitness function and a more arbitrary "jagged" fitness function.

With a gaussian fitness function, the evolution of a modifier of recombination was sensitive both to the strength of selection and to whether selection was stabilizing or directional. Directional selection was generally more favorable to the evolution of increased recombination rates, although stabilizing selection in the presence of mutation also led to increased recombination rates. Interestingly, a gaussian fitness function is one characterized by negative epistasis. That is, if two points on the function are chosen as references, all intermediate points have a higher value than expected if fitnesses were multiplicative. Thus we again see that the evolution of increased recombination is possible in the presence of directional selection with negative epistasis, although in Tables 8 and 9 we also observe reduction in some cases under these conditions.

With jagged fitness landscapes, high recombination appears to have its greatest chance of success when selection is directional or extremely disruptive. These regimes appeared most often with 2 or 3 coefficients. With more jagged landscapes, i.e. $n > 10$, low recombination is strongly favored, especially when high recombination is dominant. With jagged fitnesses and 2 or 3 coefficients, the direction of selection was towards chromosomes
dominant by 0 alleles, and here 0 → 1 mutation resulted in an advantage to high recombination. This is interesting in light of our previous remarks on directional mutation with Gaussian selection. In the Gaussian case the direction of selection was towards 1 alleles and high recombination did best with 1 → 0 mutation. This suggests a possible generality that high recombination will have its best chance of success when mutation occurs away from alleles favored by directional selection. It is worth recalling in this context the analytical result of Feldman et al. (1980) that high recombination can be favored in situations of such mutation-selection conflict.

In both haploid and diploid genetic models, recessive and dominant action of CH produced an interesting difference both in the Gaussian and jagged fitness regimes. When high recombination is favored, it is favored more strongly when CH is recessive, but when low recombination is favored, its advantage is stronger when CH is dominant. This interesting finding warrants further investigation, perhaps even analytical studies with small numbers of genes.

Our numerical results on both Gaussian and jagged fitness regimes may also be of interest to scientists interested in either the foundations or applications of genetic algorithms. In GA research, as in our multilocus simulations, the population of bit-strings at any time is a very small sample of all possible bit-strings. Under assumptions on the genetic operations that affect the bit-strings, and usually with random initial conditions, the focus in GA research is to achieve the first representative of an optimal genotypic class as quickly as possible, at which time evolution is terminated. During the process, the genetic operations, i.e. mutation and recombination, are not usually subject to change. Thus, modifier genes that control the genetic operators are usually not part of the arsenal. For example, the advantage of one value of recombination over another would be evaluated only in terms of how quickly the desired bit-string is produced. Recombination is an exogenous parameter in this approach, and from a biological point of view, the model is more akin to group selection than individual selection as characterized by the modifier approach. In our finite population simulations, because we are primarily interested in the fate of alleles CH and CL, which control the rate of recombination, we terminate the process only when one of CH or CL is fixed. Combining the two approaches, allowing genetic
parameters to evolve in GA research, may improve the performance of genetic algorithms in some classes of problems. An interesting question along these lines is with unidirectional mutation, if high recombination is favored, does this automatically mean that selection is in the opposite direction to mutation?

That the shape of the selection curve plays an important role in the efficacy of GA’s as tools for optimization was recognized by Forrest and Mitchell (1993). It is interesting that the regimes in which GA’s perform badly are extremely jagged, a finding which parallels our result that high recombination does not succeed in very jagged selection regimes. In view of the tendency of recombination-increasing alleles to fix less often when selection occurs on the diploid phase than when it affects haploids, we might speculate that GA’s applied to diploid sets of bit-strings would be less efficient at optimization than when applied to haploids.

To conclude, we have found that, even with directional selection, the advantage to alleles that increase recombination rates is very sensitive to assumptions made about selective interactions. In large populations, it appears that negative epistasis is necessary for increased recombination to evolve. If directional selection is more often characterized by positive epistasis, that is if beneficial alleles tend to work together, then recombination is not favored and will not help in our search to explain the success of sexual reproduction. For large numbers of loci, there is a tendency for high recombination to be favored more in haploids than in diploids. We have examined only a limited number of classes of selection models and it may be useful to broaden the range of selection regimes to see if more definitive patterns to the fate of recombination emerge.

Acknowledgement. The authors thank Drs. Melanie Mitchell, Stephanie Forrest, John Holland, and the members of the Adaptive Computation Program at the Santa Fe Institute for many stimulating discussions.
References


Figure Legends

Fig. 1. $R_c$ is the critical value of recombination above which recombination decreases and below which it increases. $R_c$ depends on the value of $(s^2 + \varepsilon)$; it decreases as $(s^2 + \varepsilon) \rightarrow -s$ and increases as $(s^2 + \varepsilon)$ approaches zero.

Fig. 2. Epistasis in Gaussian fitness models: The vertical axis is fitness drawn on a log scale. The number of 1's on the horizontal axis is our measure of the phenotype. For any of the curves, all points on the curve between any two chosen points lie above the straight line connecting the outerpoints. This results in negative epistasis.
As \((s^2 + \epsilon)\) approaches \(-s\)

Increased recombination

\(R = 0.0\)

As \((s^2 + \epsilon)\) approaches 0

Decreased recombination

\(R = 0.5\)
### Table 1a
**Generalized Diploid Selection**

<table>
<thead>
<tr>
<th></th>
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<th>Ab</th>
<th>aB</th>
<th>ab</th>
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<td>$w_{13}$</td>
<td>$w_{14}$</td>
</tr>
<tr>
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<td>$w_{12}$</td>
<td>$w_{23}$</td>
<td>$w_{24}$</td>
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<tr>
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<td>$w_{23}$</td>
<td>$w_{34}$</td>
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<tr>
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<td>$w_{44}$</td>
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### Table 1b
**Haplotypic Selection**

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<tr>
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<td>$w_{2}w_{4}$</td>
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<td>$w_{4}^2$</td>
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</tbody>
</table>

### Table 1c
**Haplotypic Epistasis**

\[
w_1 = 1, \quad w_2 = w_3 = (1 + s), \quad w_4 = (1 + s)^2 + \epsilon; \quad s > 0
\]

### Table 1d
**All-or-none Epistasis**

\[
w_{11} = 1, \quad w_{12} = w_{13} = 1 + s, \quad w_{14} = w_{22} = w_{23} = w_{33} = (1 + s)^2, \\
w_{24} = w_{34} = (1 + s)^3, \quad w_{44} = (1 + s)^4 + \eta; \quad s > 0
\]
Table 2

<table>
<thead>
<tr>
<th>Genotype</th>
<th>$MM$</th>
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<td>Set B</td>
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<td>0.03</td>
<td>0.01</td>
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<tr>
<td>Set C</td>
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<td>0.01</td>
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<tr>
<td>Set D</td>
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<td>Set F</td>
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</table>

Effect of genotype at modifier locus on recombination rate between $A$ and $B$ loci.
### Table 3

<table>
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<th>$R = 0.01$</th>
<th>$R = 0.10$</th>
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<th>$R = 0.50$</th>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\varepsilon = -0.1099$</td>
<td>0.49992144*</td>
<td>0.47308530</td>
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<td>$\varepsilon = -0.0800$</td>
<td>0.51592720</td>
<td>0.50794302</td>
<td>0.49427731</td>
<td>0.49402509</td>
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<td>0.51526885</td>
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<tr>
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<td>0.50114412</td>
<td>0.50027430</td>
<td>0.50010633</td>
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<tr>
<td>Case [2] - Expect increase</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>$\varepsilon = -0.0099$</td>
<td>0.50498403</td>
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<tr>
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<tr>
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<td>0.50000167</td>
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<tr>
<td>Case [1] - Expect decrease</td>
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<tr>
<td>$\varepsilon = 0.0001$</td>
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<td>0.35228876</td>
<td>0.40939938</td>
</tr>
</tbody>
</table>

**Final frequency of $M$ allele after fixation of $ab$ chromosome.** Three-locus recursions (Feldman, 1972) are iterated using haplotypic selection (Table 1c). Initial frequency of the $M$ allele is 0.5; the $a$ and $b$ alleles begin at a frequency of 0.01. All loci are initially in linkage equilibrium. Example given in the table is for $s = 0.1$ and recombination set A: $r_1 = 0.5, r_2 = 0.25, r_3 = 0.01$. Only in the asterisked case (*) did the disequilibrium $D_{Mb}$ change signs from $-\varepsilon$ to $+\varepsilon$ after an initial period with the correct sign. A more detailed analysis indicates that $R_c = 0.03$ when $\varepsilon = -0.08$ and $R_c = 0.24$ when $\varepsilon = -0.04$. 
Table 4

<table>
<thead>
<tr>
<th>$R$</th>
<th>$R = 0.00$</th>
<th>$R = 0.01$</th>
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<th>$R = 0.30$</th>
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<tr>
<td>$\varepsilon = -0.1099$</td>
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</tr>
<tr>
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<td>0.51380991</td>
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<td>0.50194322</td>
<td>0.4997372</td>
<td>0.49952433</td>
</tr>
<tr>
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<td>0.50225493</td>
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<td>0.50100177</td>
<td>0.50026197</td>
<td>0.50010295</td>
</tr>
<tr>
<td>$\varepsilon = 0.0001$</td>
<td>0.50215079</td>
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<td>0.50025830</td>
<td>0.50010207</td>
</tr>
<tr>
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<td>0.50002867</td>
<td>0.50045047</td>
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<td>0.50006404</td>
</tr>
<tr>
<td>$\varepsilon = 0.0001$</td>
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<td>0.49982500</td>
<td>0.49998549</td>
<td>0.49999580</td>
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<td>0.49762281</td>
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<td>$\varepsilon = 1.0000$</td>
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<td>0.46906175</td>
<td>0.48950772</td>
<td>0.49401709</td>
</tr>
</tbody>
</table>

Final frequency of $M$ allele after fixation of $ab$ chromosome. Three-locus recursions (Feldman, 1972) are iterated using haplotypic selection (Table 1c) with initially positive disequilibrium. Initial frequency of the $M$ allele is 0.5; the $a$ and $b$ alleles begin at a frequency of 0.01. $D_{ab}$ is initially set to +0.000098; remaining disequilibria are zero. Because of this initial disequilibrium, all the disequilibrium measures develop, at first, with the wrong sign when the epistasis is negative as if the epistasis were initially positive. Example given in the table is for $s = 0.1$ and recombination set $A$: $r_1 = 0.5, r_2 = 0.25, r_3 = 0.01$. 
Table 5

<table>
<thead>
<tr>
<th>Case [4] - Expect dependence on $R_c$</th>
<th>$R = 0.00$</th>
<th>$R = 0.01$</th>
<th>$R = 0.10$</th>
<th>$R = 0.30$</th>
<th>$R = 0.50$</th>
</tr>
</thead>
<tbody>
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<td>0.49507759</td>
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<tr>
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<td>0.51255688</td>
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<td>0.49978452</td>
<td>0.49952070</td>
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<tr>
<td>$\varepsilon = -0.0101$</td>
<td>0.50795043</td>
<td>0.50600902</td>
<td>0.50128741</td>
<td>0.50028666</td>
<td>0.50010981</td>
</tr>
</tbody>
</table>

| Case [2] - Expect increase            |            |           |           |           |           |
| $\varepsilon = -0.0099$              | 0.50789618 | 0.50594343 | 0.50126940 | 0.50024920 | 0.50010901 |
| $\varepsilon = -0.0050$              | 0.50580286 | 0.50425738 | 0.50078065 | 0.50017461 | 0.50007328 |
| $\varepsilon = -0.0001$              | 0.50357234 | 0.50241380 | 0.50020295 | 0.50002181 | 0.50000754 |

| Case [1] - Expect decrease            |            |           |           |           |           |
| $\varepsilon = 0.0001$                | 0.50347769 | 0.50233521 | 0.50017753 | 0.50001467 | 0.50000425 |
| $\varepsilon = 0.1000$                | 0.42686123 | 0.43523433 | 0.47249102 | 0.46990081 | 0.49416289 |
| $\varepsilon = 1.0000$                | 0.12103831 | 0.13406083 | 0.23271017 | 0.35725042 | 0.41155108 |

**Final frequency of $M$ allele after fixation of $ab$ chromosome.** Three-locus recursions (Feldman, 1972) are iterated using haplotypic selection (Table 1c) with initially negative disequilibrium. Initial frequency of the $M$ allele is 0.5; the $a$ and $b$ alleles begin at a frequency of 0.01. $D_{ab}$ is initially set to $-0.000098$; remaining disequilibria are zero. Because of this initial disequilibrium, all the disequilibrium measures develop, at first, with the wrong sign when the epistasis is positive as if the epistasis were initially negative. Example given in the table is for $s = 0.1$ and recombination set $A$: $r_1 = 0.5, r_2 = 0.25, r_3 = 0.01$. 


Evolution of a modifier allele, $M$, that increases recombination. The existence of a critical recombination rate is inferred from the dependence of the disequilibria on $R$ (Figure 1). The exact value of $R_c$ is unknown, but it tends to be large (perhaps even greater than 1/2) when $s^2 + \epsilon$ is near zero and falls (perhaps below 0) as $s^2 + \epsilon$ becomes more negative.
### Table 7

<table>
<thead>
<tr>
<th>$\eta$</th>
<th>$R = 0.00$</th>
<th>$R = 0.01$</th>
<th>$R = 0.10$</th>
<th>$R = 0.30$</th>
<th>$R = 0.50$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case [4] - Expect dependence on $R_c$</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$-0.1330$</td>
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<td>0.49814295</td>
<td>0.4979553</td>
<td>0.49827556</td>
</tr>
<tr>
<td>$-0.1216$</td>
<td>0.50453094</td>
<td>0.50253238</td>
<td>0.49936689</td>
<td>0.49890061</td>
<td>0.49809380</td>
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<tr>
<td>$-0.1101$</td>
<td>0.50420529</td>
<td>0.50277899</td>
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<td>0.49934745</td>
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<td>0.49935355</td>
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<tr>
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<td>0.50248770</td>
<td>0.50051943</td>
<td>0.49992072</td>
<td>0.49982831</td>
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<tr>
<td>$-0.0400$</td>
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<td>0.50043039</td>
<td>0.50011565</td>
<td>0.50003177</td>
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<tr>
<td>$-0.0101$</td>
<td>0.50042252</td>
<td>0.50036725</td>
<td>0.50015045</td>
<td>0.50004949</td>
<td>0.50002339</td>
</tr>
</tbody>
</table>

| Case [2] - Expect increase |
| $-0.0099$ | 0.50041411 | 0.50036002 | 0.50014763 | 0.50004862 | 0.50002301 |
| $-0.0050$ | 0.50020955 | 0.50018285 | 0.50007651 | 0.50002597 | 0.50001269 |
| $-0.0001$ | 0.50000420 | 0.50000368 | 0.50000157 | 0.50000055 | 0.50000027 |

| Case [1] - Expect decrease |
| $0.0001$ | 0.49999580 | 0.49999362 | 0.49999343 | 0.49999445 | 0.49999972 |
| $0.1000$ | 0.49574966 | 0.49512085 | 0.49792367 | 0.49906315 | 0.49942719 |
| $1.0000$ | 0.46701768 | 0.46829844 | 0.47671081 | 0.48572423 | 0.48985956 |

**Final frequency of $M$ allele after fixation of $ab$ chromosome.** Three-locus recursions (Feldman, 1972) are iterated using all-or-none selection (Table 1d). Initial frequency of the $M$ allele is 0.5; the $a$ and $b$ alleles begin at a frequency of 0.01. All loci are initially in linkage equilibrium. Example given in the table is for $s = 0.1$ and recombination set A: $r_1 = 0.5$, $r_2 = 0.25$, $r_3 = 0.01$. Only in the case marked (*) did the disequilibrium $D_{M1}$ change signs from $-\eta$ to $+\eta$ after an initial period with the correct sign.
Table 8
Evolution of recombination in finite populations with Gaussian stabilizing selection.
Percent of runs fixed on high recombination allele CH*.

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<thead>
<tr>
<th>Mean 20</th>
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<th>Dominant</th>
<th>0.7</th>
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<th>0.1</th>
<th>1.2</th>
<th>3.4</th>
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<th>0.9</th>
<th>3.0</th>
<th>0.0</th>
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<tr>
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<td>Recessive</td>
<td>5.4</td>
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<td>4.8</td>
<td>10.9</td>
<td>4.6</td>
<td>5.2</td>
<td>11.3</td>
<td>5.9</td>
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<table>
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<tr>
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<th>( \sigma = 5 )</th>
<th>Dominant</th>
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<th>33.6</th>
<th>28.1</th>
<th>41.4</th>
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<th>32.9</th>
<th>39.1</th>
<th>42.3</th>
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<tbody>
<tr>
<td></td>
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<td>18.6</td>
<td>26.8</td>
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<td>59.4</td>
<td>68.9</td>
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<td>61.8</td>
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<table>
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*If CH were neutral, it would be expected to fix in 50% of the runs.
Table 9
Evolution of recombination in finite populations with Gaussian directional selection.
Percent of runs fixed on high recombination allele CH*.

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*If CH were neutral, it would be expected to fix in 50% of the runs.
Table 10
High recombination dominant. Distribution of fixations of the high recombination allele.

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*If \( CH \) were neutral, the expected number would be 25.
*\( Mutation \) is at 0.005 per locus per generation.
*\( Mutation \) from 0 to 1 and 1 to 0 each at 0.005 per locus per generation.
\( D^* \) is the diploid model of the first column with half of its recombination rate.
Table 11
High recombination recessive. Distribution of fixations of the high recombination allele.

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*Mutation from 0 to 1 and 1 to 0 each at 0.005 per locus per generation.
D* is the diploid model of the first column with half of its recombination rate.