MASKING OF MUTATIONS AND THE EVOLUTION OF SEX

RICHARD E. MICHEL AND TODD W. GAYLEY

Department of Ecology and Evolutionary Biology, University of Arizona, Tucson, Arizona 85721

Submitted March 19, 1990; Revised May 1, 1991; Accepted May 8, 1991

Abstract.—Outcrossing and recombination are basic aspects of sex; however, selfing maintains many of the aspects of sex, such as recombination, yet abandons outcrossing. The role of deleterious recessive alleles in the evolution of selving and outcrossing is studied by mathematical analysis of genetic models in which reproductive system is determined by a single locus. If viability is determined by heterozygote superiority at a second locus, partial outcrossing can increase when rare in a population of selvers even though inbreeding depression is less than 1/2, and mixed mating systems that are polymorphic for both outcrossing and selfing exist and are stable. In another model, the masking model, outcrossers are assumed to mask mutations by keeping them heterozygous. There are three basic parameters in this model: one measuring the difference between outcrossers and selvers in the heterozygosity of their offspring, that is, masking ability; one measuring the fitness difference between homozygous and heterozygous offspring; and a third measuring the probability that a selver is able to purge its genome of mutations. In most cases, outcrossing is stable when common so long as heterozygous offspring are more than twice as fit as mutant-homozygote offspring, mutations are nearly recessive, and the values for the masking and purging parameters are in a realistic range implied by three or more segregating mutations. The conditions for outcrossing to increase when rare are also generally favorable to outcrossing. For most combinations of parameters, a low probability of purging, along with a high mutation rate, will allow outcrossing to invade. The implication of these results for the evolution of sex is discussed.

Outcrossing brings together into the same nucleus DNA molecules from different individuals. In the vast majority of outcrossing systems, these DNA molecules break and rejoin with one another, in other words, recombine. Recombination and outcrossing are basic components of the sexual cycle and are present in a diversity of sexual systems from meiosis in eukaryotes to bacterial transformation and multiple phage infection in prokaryotes.

The DNA molecules involved in recombination may be brought together by means other than outcrossing, for example, by selfing, automixis, or endomitosis. In selfing the two DNA molecules involved in recombination come from the same individual, instead of different individuals as is the case with outcrossing. Evolution has produced a variety of reproductive systems in eukaryotes (selfing, automixis, and endomitosis) that have given up outcrossing yet maintain recombination. In contrast, there are relatively few reproductive systems, such as the diploid hybridogenetic forms of Poeciliopsis fishes (Schultz 1961, 1969; Cimino 1972), that maintain outcrossing, in the sense that two genomes from different individuals come together in the same nucleus, yet recombination does not occur. Therefore, recombination appears to be universally adaptive, or nearly so,
whereas outcrossing appears to be adaptive only in certain situations. The purpose of this article is to understand the situations that select for outcrossing.

Fisher (1941) first demonstrated the intrinsic advantage of selfing over outcrossing by considering a hypothetical plant whose ovules received pollen from itself but whose pollen was also available to other outcrossing ovules in the population. He assumed that there is no fitness difference between outcrossed and selfed offspring and that selfers and outcrossers contribute equal amounts of pollen to outcrossed ovules (this is now termed “no pollen discounting”). The intrinsic advantage of selfing over outcrossing is decreased to the extent that selfers have decreased levels of pollen output to outcrossed ovules (Nagylaki 1976; Charlesworth 1980; Uyenoyama and Waller 1991a, 1991b, 1991c), with no advantage to selfing over outcrossing in the case where the decrease in pollen output is in direct proportion to the selfing rate (complete pollen discounting). In the case of complete pollen discounting there is effectively no cost of males, because there is no pollen from selfers to compete with pollen from outcrossers. Thus, no pollen discounting contains a cost of males and represents a kind of worst case for the evolution of outcrossing. For these reasons, we focus on this case in this article.

Outcrossing may be favored over selfing if outcrossed offspring are more fit than selfed offspring. One reason that outcrossed offspring may be more fit than selfed offspring is that they are more heterozygous. This idea has had a long history in evolutionary genetics. Inbreeding depression, the lowered fitness of selfed offspring relative to that of outcrossed offspring, is commonly observed and is thought to result either from heterozygote superiority or from expression of deleterious recessive or partially recessive mutations at loci determining viability or fertility (for review see Charlesworth and Charlesworth 1987). Bernstein et al. (1981) argued that masking of deleterious alleles became an important selective factor in the maintenance of the outcrossing aspects of sex, once diplody emerged as the dominant phase in the life cycle. In haploids, outcrossing is necessary for efficient repair of damaged DNA, and so damage repair provides a selective rationale for outcrossing in haploids (Bernstein et al. 1987; Michod et al. 1990).

Using a multilocus model of mutation, Hopf et al. (1988) analyzed the effect of reproductive system on the equilibrium numbers of recessive mutations and average fitness but presented no explicit analysis of evolution of the reproductive system. They showed for multiplicative fitnesses that, at equilibrium, selfing and outcrossing populations had approximately the same average fitness, $\exp(-\mu)$, where $\mu$ is the haploid genomic mutation rate. However, the two breeding systems maintained vastly different numbers of mutations at equilibrium. Theoretical estimates for the case of recessive lethals were that selfing maintained $4\mu$ mutations per diploid genome and outcrossing maintained $2N\mu$ mutations, where $N$ is the number of functional genes per genome, which in higher organisms is probably between 40,000 and 100,000.

Bernstein et al. (1985b) argued verbally that these different numbers of mutations could create transient selection favoring outcrossing, even though all reproductive systems are equally fit at equilibrium (as far as mutational load at multipli-
cative loci is concerned). For example, in a completely selfing population, an outcrosser would mask all recessive lethals and have a fitness of 1 relative to the selfers with fitness \( \exp(-\mu) \). Likewise, in an outcrossing population, a rare selfer would most likely express one of the many hidden recessive lethals, whereas outcrossers would have a fitness of \( \exp(-\mu) \). It is difficult to evaluate this verbal argument without an explicit model taking into account, among other factors, the more effective transmission of selfing alleles.

**MODELS**

*Heterozygote Superiority or Mutation/Selection Balance*

One approach to the problem of deleterious alleles and their expression by the reproductive system is to consider two loci, one locus that affects the reproductive system and one locus that is maintained polymorphic either by recurrent mutation or by heterozygote superiority. Unfortunately, this approach does not provide much selective scope for the evolution of outcrossing, because a single fitness locus cannot generate the levels of fitness difference between selfed and outcrossed offspring expected if many loci were segregating for deleterious alleles. Nevertheless, it serves as a basic framework for a third model, the masking model, which better represents one aspect of the problem at hand, masking of mutations.

Consider a diploid, two-locus, Mendelian model with a polymorphic fitness locus and a second locus that modifies the mating system. The fitness locus, \( A/a \), is assumed to be polymorphic, either as a result of heterozygote superiority or as a result of mutation/selection balance. The second locus, \( M/m \), is the mating system locus and is assumed to modify the probability, \( \alpha \), of selfing (probability of outcrossing equal to \( 1 - \alpha \)). (We use the word outcrossing to refer to the specific case of random mating, realizing that in reality there is an outcrossing continuum between, on the one hand, close forms of inbreeding such as brother-sister mating and, on the other hand, random mating.) Let \( u, v, \) and \( w \) designate the frequencies of the three genotypes at the fitness locus, \( AA, Aa, \) and \( aa \), respectively, and let the subscripts 1, 2, and 3 denote the genotypes at the mating system locus, \( MM, Mm, \) and \( mm \), respectively. The arrays in (1) define, respectively, the probabilities of selfing, frequencies before selection, and viabilities of the different genotypes.

\[
\begin{array}{c|ccc}
& AA & Aa & aa \\
\hline
MM & \alpha_1 & \alpha_1 & \alpha_1 \\
Mm & \alpha_2 & \alpha_2 & \alpha_2 \\
mm & \alpha_3 & \alpha_3 & \alpha_3 \\
\end{array}
\]

\[
\begin{array}{c|ccc}
& AA & Aa & aa \\
\hline
MM & u_1 & v_1 & w_1 \\
Mm & u_2 & v_2, v_2 & w_2 \\
mm & u_3 & v_3 & w_3 \\
\end{array}
\]
\[
\begin{array}{c|ccc}
& AA & Aa & aa \\
\hline
MM & \sigma_{AA} & \sigma_{Aa} & \sigma_{aa} \\
Mm & \sigma_{AA} & \sigma_{Aa} & \sigma_{aa} \\
m & \sigma_{AA} & \sigma_{Aa} & \sigma_{aa} \\
\end{array}
\] (1c)

The variables \( \nu_2 \) and \( \tilde{\nu}_2 \) refer, respectively, to the frequencies of the \( AM/am \) and \( Am/aM \) double heterozygotes. The consideration of selfing prohibits the expression of the genotype frequencies in terms of the allele frequencies, so we must study the full system of genotype frequency transformation equations, constructed as follows and given in the Appendix.

The basic life-history events in any generation are selection, mutation (in the mutation/selection balance model), recombination, and mating. Let the superscript \( \sigma \) indicate genotype frequencies after selection,

\[
\begin{align*}
\sigma_1^u &= \frac{u_1 \sigma_{AA}}{T}, & \nu_1^u &= \frac{\nu_1 \sigma_{Aa}}{T}, & w_1^u &= \frac{w_1 \sigma_{aa}}{T}, \\
\sigma_2^u &= \frac{u_2 \sigma_{AA}}{T}, & \nu_2^u &= \frac{\nu_2 \sigma_{Aa}}{T}, & \tilde{\nu}_2^u &= \frac{\tilde{\nu}_2 \sigma_{aa}}{T}, & w_2^u &= \frac{w_2 \sigma_{aa}}{T}, \\
\sigma_3^u &= \frac{u_3 \sigma_{AA}}{T}, & \nu_3^u &= \frac{\nu_3 \sigma_{Aa}}{T}, & w_3^u &= \frac{w_3 \sigma_{aa}}{T},
\end{align*}
\] (2)

with \( T \) the average fitness,

\[
T = u \sigma_{AA} + \nu \sigma_{Aa} + w \sigma_{aa},
\] (3)

and \( u, \nu, \) and \( w \) the marginal frequencies at the fitness locus

\[
\begin{align*}
u &= \nu_1 + \nu_2 + \nu_3, \\
w &= \nu_1 + w_2 + w_3.
\end{align*}
\] (4)

In the case of the mutation/selection balance model, mutation occurs from \( A \) to \( a \) at rate \( \mu \), and back mutation is ignored (see eqq. [A1]). Finally, selfing occurs for the selfing portion of the population and random union of gametes is assumed to occur for the outcrossing portion of the population (see eqq. [A2]) resulting in the complete generation-to-generation equations given in the Appendix (eqq. [A3]).

In the case of heterozygote superiority, for simplicity we consider only the symmetric case letting

\[
\sigma_{AA} = 1 - \sigma, \sigma_{Aa} = 1, \sigma_{aa} = 1 - \sigma,
\] (5)

in equations (2), which are substituted into equations (A2) and (A3). In the case of the mutation/selection balance model, equations (A2) and (A3) are used with equations (A1) considering recessive mutations only,

\[
\sigma_{AA} = 1, \sigma_{Aa} = 1, \sigma_{aa} = 1 - \sigma.
\] (6)
TABLE 1

TRANSMISSION OF PHENOTYPES IN MASKING MODEL

<table>
<thead>
<tr>
<th>Offspring</th>
<th>Selfed</th>
<th>Outcrossed</th>
<th>Selfed</th>
<th>Outcrossed</th>
<th>Selfed</th>
<th>Outcrossed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hom-wt</td>
<td>1 - µ + µ/4</td>
<td>0</td>
<td>q</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Het</td>
<td>µ/2</td>
<td>1</td>
<td>k</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Hom-mut</td>
<td>µ/4</td>
<td>0</td>
<td>1 - k - q</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

Masking Model

The masking model includes the explicit mating system locus studied above along with three fitness phenotypes that relate to the state of the genome regarding deleterious alleles: Het, Hom-wt, and Hom-mut. The three phenotypes considered represent extreme states of the genome as far as the masking hypothesis is concerned. Individuals of the Hom-wt phenotype do not contain any mutations; Het individuals contain mutations but do not effectively express them because the mutations are heterozygous; and Hom-mut individuals both contain mutations and express them because the mutations are homozygous. More specifically, it is assumed that Het individuals are heterozygous for at least one locus at which a rare recessive or partially recessive deleterious allele is segregating (the other loci are homozygous wild type); Hom-wt individuals are homozygous for wild-type alleles at all of these loci; and Hom-mut individuals are homozygous for a deleterious allele at one or more such loci. The fitnesses of these three types are assumed to be $1, 1 - h\sigma$, and $1 - \sigma$ for Hom-wt, Het, and Hom-mut, irrespective of the exact number of loci that are heterozygous and homozygous. In a real population there is a distribution of different types, each with different numbers of homozygous and heterozygous loci, and this distribution evolves as the mating system evolves. Here, we consider just three types but allow their frequencies to change as the mating system evolves.

The underlying genetical control of the three phenotypes Hom-wt, Het, and Hom-mut is not explicitly represented in the model, although assumptions are made concerning the transmission of these phenotypes that reflect genetical issues (table 1). In table 1 the phenotypes of the parents are given across the top and the phenotypes of offspring down the left side. Outcrossing parents are assumed to produce all Het offspring, regardless of the phenotype of the two parents. This is because mates mask the expression of each other’s recessive, or nearly recessive, deleterious mutations, since they likely carry mutations at different loci. This is true even for matings between Hom-mut individuals, since particular Hom-mut parents are likely to be homozygous at different loci and so still mask each other’s deleterious mutations in their offspring.

The assumption that outcrossing always produces Het offspring ignores the possibility that outcrossers can, in principle, produce offspring of any of the three types (and a whole range of types in between). As a result of recombination and
independent assortment, outcrossers can produce offspring that are either free of deleterious alleles (Hom-wt) or homozygous for them (Hom-mut). These possibilities are ignored in the masking model, since they depend on variation between the offspring of outcrossers in numbers of mutations. Variation in mutation load was hypothesized by Muller (1964) as being important in the evolution of sex and has recently been emphasized in a series of articles by Kondrashov (reviewed in Kondrashov 1988). The purpose of the masking model is not to deny that outcrossers produce offspring with different numbers of deleterious alleles but, rather, to isolate masking as a specific factor in the evolution of the outcrossing aspects of sex. Masking depends on heterozygosity within individuals and not variability between individuals. Both masking and variation in mutation load can occur together in sexual systems, but this need not be the case (see Discussion).

In any event, as a result of the assumption that the offspring of outcrossers are all Het, there are no differences between the offspring of outcrossers.

In populations with Hom-wt individuals, matings between wild-type individuals might be expected to occur, producing Hom-wt offspring. This possibility is ignored in the masking model, because a new mutation somewhere in the genome will likely convert Hom-wt individuals to Het. The primary reason mutation-free Hom-wt individuals are included in the model is to provide the possibility that selfers purge their genome of deleterious alleles.

Although the offspring of outcrossing parents are assumed to always be Het, the offspring of selfing parents are assumed to differ for the three parental types (Het, Hom-mut, or Hom-wt). Consequently, the average fitness of selfed offspring changes as the population frequencies of the parental types change. This is a basic difference that distinguishes the masking model from many inbreeding depression models that assume a constant fitness of selfed offspring (e.g., Feldman and Christiansen 1984, among many).

Consider, first, Hom-mut parents that self. Since they are homozygous for deleterious mutations at at least one locus, all their offspring must also be homozygous for these mutations. Additional mutations that may occur during the parent’s lifetime can only increase the number of homozygous mutations in their selfed offspring.

Second, consider Hom-wt parents that self. Although Hom-wt parents begin life with no mutations, they may accumulate an additional mutation with probability $\mu_D$, the genomic-wide diploid mutation rate. With probability $1 - \mu_D$, no new mutations occur and all their selfed offspring will be Hom-wt. If a new mutation occurs (again with probability $\mu_D$), their selfed offspring will be Hom-wt, Het, or Hom-mut with probabilities $1/4$, $1/2$, and $1/4$, respectively. The occurrence of multiple mutations is ignored.

Finally, consider Het parents that self. In heterozygous selfers, recombination and independent assortment cannot be ignored as they were in the case of outcrossers. As a result of recombination, Het parents may produce offspring of any of the three types. In reality, the frequencies of these types among selfed offspring of Het parents are determined by the multilocus segregation and recombination probabilities at linked and unlinked loci that are heterozygous for deleterious mutations. However, the masking model sidesteps this complex genetical issue.
by assuming constant probabilities, $q$ and $k$, that a Het parent produces by selfing Hom-wt and Het offspring, respectively, with $1 - k - q$ being the probability that a Het parent produces Hom-mut offspring by selfing. The parameter $k$ measures the masking ability of selfers relative to an assumed masking ability of 1 for outcrossers. The parameter $q$ measures the probability that all deleterious mutations are purged from the genome (by recombination and segregation), producing an offspring that is free of deleterious mutation. In a real population, $k$ and $q$ will change as the frequency of deleterious mutations evolves in response to the mating system. This level of detail is not included in the model. However, the fitness distribution of selfed offspring does change as the frequencies of the three types change.

Although the genetic control of the Het and Hom phenotypes is not explicitly represented in the model studied here, the selfing or outcrossing phenotype is assumed to be controlled by two alleles at a single Mendelian locus, as discussed above. As before, let $\alpha_1$, $\alpha_2$, and $\alpha_3$ be the selfing rates, respectively, of MM, Mm, and mm genotypes (array [1a]). These three genotypes at the mating system locus, when combined with the three fitness phenotypes, Hom-wt, Het, and Hom-mut, yield a total of nine different types in the population, with frequencies given in table 2. The frequencies after selection for the nine types are obtained in a manner similar to that given in equations (2), using the fitnesses given in table 2. The full generation recurrence equations are given in the Appendix (eqq. [A4] and [A5]).

**ANALYSIS**

**General**

For the three models of selection (heterozygote superiority, mutation/selection balance, and masking), we studied the stability of either complete outcrossing or complete selfing to invasion by alleles promoting the alternative reproductive system. In either case, the population was considered to be initially fixed for the $M$ allele. In the case of a population fixed for outcrossing, $\alpha_1 = 0$, and in a population fixed for selfing, $\alpha_1 = 1.0$ (eq. [1a]). The stability of the outcrossing equilibrium to the invasion of $m$ alleles with nonzero probabilities of selfing ($\alpha_2$, $\alpha_3 > 0$) was investigated for the three models of selection by standard linear
techniques. The stability of the selfing equilibrium to the invasion of \( m \) alleles with nonzero probabilities of outcrossing (\( \alpha_2, \alpha_3 < 1.0 \)) was investigated similarly.

The computer program Mathematica (Version 1.2 for MS-DOS and Macintosh; Wolfram 1988) was used to aid in symbolic manipulation, evaluation, and graphing of the equations and results. The Jacobian matrix of partial derivatives was calculated, simplified, and then evaluated at the various equilibria discussed below. The dominant eigenvalue of the Jacobian matrix, \( \lambda \), was then obtained for the outcrossing and selfing equilibria for the three fitness models for different parameter values. In the case of the masking model, the dominant eigenvalue, \( \lambda \), could be obtained symbolically for certain special situations. The stabilities of the various equilibria are determined by \( \lambda \). The equilibrium is unstable, meaning that the \( m \) allele specifying a different reproductive system increases, if \( \lambda > 1.0 \). Extensive global iteration of the recurrence equations (A3) or (A5) was also performed, as a test of, and complement to, the stability analyses.

**Initial Equilibria for the Three Models of Selection**

The first step is to determine the initial (\( \hat{u}_1, \hat{v}_1, \hat{w}_1 \)) equilibrium state in the pure selfing or outcrossing population. This corresponds to initial fixation of the \( M \) allele, before the introduction of variation in mode of reproduction. When these stable initial equilibria are found, they can be tested for stability to invasion of the \( m \) allele.

**Heterozygote superiority model.**—Under complete outcrossing, the equilibrium genotype frequencies at the \( A/a \) locus are given in Hardy-Weinberg proportions with the frequency of the \( A \) allele being 1/2:

\[
\hat{u}_1 = 1/4, \quad \hat{v}_1 = 1/2, \quad \hat{w}_1 = 1/4.
\]  

(7)

Under complete selfing, the equilibrium genotype frequencies at the \( A/a \) locus are

\[
\hat{u}_1 = \frac{1}{4\sigma}, \quad \hat{v}_1 = \frac{\sigma - 1/2}{\sigma}, \quad \hat{w}_1 = \frac{1}{4\sigma}
\]  

(8)

(Ziehe and Roberds 1989). For these selfing equilibria to be biologically meaningful, \( \sigma > 1/2 \); otherwise, \( \hat{v}_1 < 0 \) and selection does not maintain a polymorphism at the fitness locus. We restrict our attention to polymorphic equilibria.

**Mutation/selection balance model.**—Under complete outcrossing, the frequency of the \( a \) allele is

\[
p_a = \sqrt{\mu/\sigma},
\]  

and the equilibrium genotype frequencies at the \( A/a \) locus are given in Hardy-Weinberg proportions,

\[
\hat{u}_1 = (1 - p_a)^2, \quad \hat{v}_1 = 2p_a(1 - p_a), \quad \hat{w}_1 = p_a^2.
\]  

(9)

Under complete selfing (\( \alpha_1 = 1 \)), the equilibrium genotype frequencies at the \( A/a \) locus could not be obtained analytically without resorting to approximations. The equilibrium frequencies, \( \hat{u}_1, \hat{v}_1, \) with \( \hat{w}_1 = 1 - \hat{u}_1 - \hat{v}_1 \), are given as roots
of the following pair of equations:

\[ u_1 = \frac{(1 - \mu)(4 u_1 - 2 \mu u_1 + v_1)}{4[1 - \sigma(1 - u_1 - v_1)]} \]

and

\[ v_1 = \frac{(1 - \mu)(2 \mu u_1 + v_1)}{2[1 - \sigma(1 - u_1 - v_1)]}. \]

Equations (10) were solved numerically for roots in the interval \((0, 1)\), and the Jacobian matrix of partial derivatives was then evaluated at these equilibria to obtain the dominant eigenvalues for different values of \(\sigma, \mu, r\) (the recombination rate), \(\alpha_2\), and \(\alpha_3\) in the range \((0, 1)\).

**Masking model.**—Under complete outcrossing, the initial equilibrium frequencies are

\[ \hat{u}_1 = 0, \hat{v}_1 = 1, \hat{\omega}_1 = 0. \] (11)

Under complete selfing, the equilibrium structure of the three phenotypes is more complex. There appear to always be three equilibria, of which two at most are valid, and exactly one of which is stable. One of these equilibria (and always a valid one) is fixation of mutant homozygotes:

\[ \hat{u}_1 = 0, \hat{v}_1 = 0, \hat{\omega}_1 = 1. \] (12)

The second equilibrium has \(\hat{u}_1 = 0\) but nonzero \(\hat{v}_1\) and \(\hat{\omega}_1\), and the third equilibrium is polymorphic for all three types. There is no equilibrium for fixation of mutation-free homozygotes, \(Hom-wt\), except in the uninteresting case in which the mutation rate is zero, \(\mu_D = 0\). In the case of recessive lethal mutations with a genomic-wide diploid mutation rate of one (which is realistic for higher diploids), the initial equilibrium frequencies can be found in symbolic form (eqq. [A6] in the Appendix), by solving the following pair of equations in the range \(0 < \hat{u}_1, \hat{v}_1 < 1\),

\[ u_1 = \frac{u_1 + 4 q v_1}{4 (u_1 + v_1)} \]

and

\[ v_1 = \frac{u_1 + 2 k v_1}{2 (u_1 + v_1)}. \] (13)

If there is no probability of purging the genome of mutations, \(q = 0\), then a polymorphic equilibrium exists under complete selfing for recessive lethal mutations at

\[ \hat{u}_1 = 0, \]

\[ \hat{v}_1 = \frac{\sigma - 1 + k}{\sigma}, \] (14)
and

\[ \hat{w}_1 = \frac{1 - k}{\sigma}. \]

This equilibrium only makes biological sense if \( k + \sigma \geq 1 \), in which case it is also stable so long as \( 1/4 \leq k \).

The general conditions for the validity and stability (stability in the reduced one-locus system) of these various initial selfing equilibria are clearly complicated and are not pursued in analytic detail here. Our primary interest is in their stability to invasion by outcrossing alleles. We circumvented the need for a complete understanding of the initial equilibrium structure under selfing by numerically solving for the equilibria given specific values of \( \sigma, h \) (the dominance coefficient), \( \mu, k \), and \( q \) and then picking the stable one on the basis of numerical computation of its eigenvalues (in the one-locus system). This initial equilibrium was then used as the starting point for invasion of the outcrossing, \( m \), allele. This was done over a range of parameter values.

RESULTS

Heterozygote Superiority

There are four parameters that may vary: the selection coefficient \( \sigma \), the recombination rate \( r \), and the selfing rate in \( Mm \) and \( mm \) genotypes, \( \alpha_2 \) and \( \alpha_3 \), respectively. We consider only dominant mutations at the mating type locus by assuming \( \alpha_2 = \alpha_3 \). No effect of the recombination rate, \( r \), on the increase of the mutant, \( m \), allele was found in this case. Consequently, we focus on the effects of the selection coefficient, \( \sigma \), and the new selfing rate, \( \alpha_2 \) (= \( \alpha_3 \)).

Recall that the population is initially assumed to be fixed for the \( MM \) genotype, which is phenotypically either completely selfing (\( \alpha_1 = 1 \)) or completely outcrossing (\( \alpha_1 = 0 \)). First, consider the case of a population initially fixed for outcrossing. In this case the dominant eigenvalue of the system was studied as a function of \( \sigma \) and \( \alpha_2 \) in the range \( 0 < \sigma, \alpha_2 < 1 \). The dominant eigenvalue of the system, \( \lambda \), is always greater than 1.0 for all values of \( \sigma \) and \( \alpha_2 \) in this range. Consequently, selfing always increases in a population of outcrossers.

The situation is more interesting in the case of a population initially fixed for selfing (\( \alpha_1 = 1 \)). In figure 1a the dominant eigenvalue, \( \lambda \), is plotted as a function of the selection coefficient, \( \sigma \), assuming \( \alpha_2 = \alpha_3 = 0.9 \) and \( r = 0.5 \). Here we see that, for \( \sigma \) between 0.5 and approximately 0.62, outcrossing increases in a population of selfers. Since complete outcrossing was unstable to the evolution of selfing for this range of parameter values, a mixed breeding system might be evolutionarily stable in this range. For larger values of \( \sigma \), selfing becomes stable to the increase of outcrossing. In figure 1b inbreeding depression is plotted as a function of \( \sigma \) (see also fig. 1 in Ziehe and Roberds 1989). Inbreeding depression, \( D \), is defined as one minus the relative fitness of selfed offspring compared with that of outcrossed offspring (see eq. [15]). As shown in figure 1b, inbreeding depre-
Fig. 1.—Stability and inbreeding depression in a population fixed for selfing for heterozygote superiority model. In a, the absolute value of the dominant eigenvalue $\lambda$ is shown as a function of $\sigma$. In b, inbreeding depression is plotted as a function of $\sigma$. Parameter values: $r = 0.5$, $\alpha_2 = \alpha_3 = 0.9$. See text for more discussion.

In figure 2, the dominant eigenvalue is plotted as a function of both $\sigma$ and $\alpha_2$ ($=\alpha_3$), assuming $r = 0.5$ (although $r$ has no effect on this curve). The surface has been clipped at $\lambda = 1.0$ and only the region for which $\lambda > 1.0$ is shown. This is the region of $\alpha_2$ and $\sigma$ for which the selfing equilibrium is unstable and outcrossing increases. Only partial outcrossing ($\alpha_2$ between 1.0 and approximately 0.5) can increase for selective coefficients greater than 0.5 and less than approximately 0.66. Otherwise, complete selfing is stable.

In figure 3, the change in gene frequency for such a partial outcrossing gene is shown for parameter values in the range of instability shown in figure 2 ($\alpha_2 = \alpha_3 = 0.9$, $\alpha_1 = 1.0$, $r = 0.5$, $\sigma = 0.60$). When rare, the gene increases to an intermediate frequency at which the population is maintained polymorphic for the two mating types ($M$ with $\alpha = 1.0$ and $m$ with $\alpha = 0.9$). Conversely, when common, such a gene decreases to the equilibrium value. Similar dynamics were observed for other parameter values in the range of instability given in figure 2. Therefore the population does not tend to either of the extreme states of complete outcrossing or complete selfing but instead maintains a mixed mating system (cf. Charlesworth and Charlesworth 1990; Uyenoyama and Waller 1991b). This is in
Fig. 2.—Increase of outcrossing in a population fixed for selfing for heterozygote superiority model. The absolute value of the dominant eigenvalue \( \lambda \) is plotted as a function of \( \sigma \) and \( \alpha_2 (= \alpha_3) \). See text for more discussion.

Fig. 3.—Evolution of modifier gene of selfing rate for heterozygote superiority model. Parameter values: \( \alpha_2 = \alpha_3 = 0.9, \alpha_1 = 1.0, r = 0.5, \sigma = 0.60 \). See text for explanation.

contrast to Lande and Schemske’s (1985) hypothesis that populations should fix on either complete outcrossing or complete selfing.

Mutation/Selection Balance

Under the two-locus mutation/selection balance model, selfing always increases when rare in a population of outcrossers and is always stable when common. For the range of parameters of biological interest, the dominant eigenvalue is always greater than one for the outcrossing equilibrium (selfing increases) and less than one for the selfing equilibrium (selfing is stable). The eigenvalue curves are not presented here because of the uniform nature of the results. There is
simply not enough fitness difference between selfed and outcrossed offspring (e.g., eq. [15]) generated in this model by the single fitness locus to make up for the intrinsic advantage of selfing, when selfers are assumed to contribute equal numbers of male gametes to the outcrossing pool as do outcrossers. In an otherwise similar model, Uyenoyama and Waller (1991a) assumed that selfers are penalized in terms of their contribution of male gametes to the outcrossing pool. In this case, mutation at a single locus can select for outcrossing.

*Masking Model*

The basic parameters in this model are \( \sigma \), the selection coefficient against mutant homozygotes (*Hom-mut*); \( h \), the dominance coefficient; \( \mu_D \), the genome-wide diploid mutation rate; and \( k \) and \( q \), the probabilities that a heterozygous selfer produces heterozygous or wild-type homozygous offspring (*Het* or *Hom-wt*), respectively (see tables 1 and 2). The final parameters are the effects of the modifier, \( m \), in heterozygous, \( \alpha_2 \), and homozygous, \( \alpha_3 \), state. We consider only dominant modifiers so that \( \alpha_2 = \alpha_3 = \alpha \).

Consider, first, the outcrossing equilibrium (\( \alpha_1 = 0 \); eq. [11]). The stability of complete outcrossing was investigated systematically for the following ranges of parameter values: \( 0 \leq q \leq 1/4 \), \( 0 \leq k \leq 1/2 \), \( 1/2 \leq \sigma \leq 1 \), \( 0 \leq \mu_D \leq 1 \), and \( 0 \leq h \leq 1 \). The mutation rate, \( \mu_D \), had little effect on the stability of the outcrossing equilibrium to modifiers of small effect (\( \alpha = 0.9 \)), whereas for modifiers of large effect (\( \alpha = 0 \)) \( \mu_D \) can have a considerable effect. This makes biological sense, because previously existing mutations masked in heterozygous state are the dominant force retarding the increase of selfing in predominantly outcrossing populations. New mutations (rate \( \mu_D \) in the model) are not as important for the evolution of selfing in predominantly outcrossing populations as they are in predominantly selfing populations (see below). New mutations only affect *Hom-wt* individuals, that is, selfers who have purged their genomes. This pool remains small if selfing modifiers have small effect.

Figure 4 shows the effects of changing \( \sigma \) and \( h \) on the stability of pure outcrossing to invasion by alleles promoting selfing. Each line in figure 4 graphs the condition \( \lambda = 1 \) for the corresponding \( \sigma \) or \( h \) value. For each line, all \( k \) and \( q \) values below and to the left have \( \lambda < 1 \), so the outcrossing equilibrium is stable against invasion. Above and to the right, \( \lambda > 1 \) and selfing invades. In figure 4a, \( h = 0 \) and \( \sigma \) varies. In figure 4b, \( \sigma = 1 \) and \( h \) varies. All curves have \( \alpha = 0.9 \) and \( m = 1 \). Figure 4a shows that selfing always increases if \( \sigma \leq 1/2 \). As the mutations become more deleterious, the range of \( k \) and \( q \) for which outcrossing is stable increases. Finally, for lethal recessives (\( \sigma = 1.0 \) line) stability is guaranteed for any \( k \) and \( q \) such that, approximately, \( k + q \leq 1/2 \). As discussed below, with more than two recessive alleles segregating, \( q \) will generally be close to zero, with \( k \) also considerably less than its one-locus maximum of 1/2. Figure 4b shows the importance of recessivity of mutations in promoting stability of outcrossing. It should be emphasized that \( h \) cannot be regarded as a per-locus dominance coefficient; because the *Het* class lumps together individuals with varying numbers of heterozygous mutations, a small per-locus dominance coefficient would correspond to a larger \( h \) value in this model. The results from figure 4 can be
Fig. 4.—Evolution of modifier gene of selfing rate for masking model at the outcrossing equilibrium. Unless otherwise marked, all lines share the following parameter values: \( \mu_D = 1, \alpha_2 = \alpha_3 = 0.1, \alpha_1 = 0, \sigma = 1.0, h = 0 \). For each line, outcrossing is stable to the invasion of selfing for \( k \) and \( q \) values below and to the left. See text for explanation.

summarized by stating that outcrossing is stable so long as there are more than two nearly recessive lethal or sublethal mutations segregating in the population.

Now consider selfing equilibria by setting \( \alpha_1 = 1 \). As noted earlier, the initial one-locus selfing equilibrium structure is complex. This complicates the analysis compared with that of the outcrossing equilibrium, where there was a single, globally stable initial equilibrium for all parameter combinations. The computer model we constructed for this analysis is therefore required to first locate each initial stable one-locus equilibrium before testing its stability to outcrossing modifiers. By knowing that we can always find the initial one-locus equilibrium, we do not need to be concerned with its form. The ranges of parameters investigated were \( 0 \leq q \leq 1/4, 0 \leq k \leq 1/2, 1/2 \leq \sigma \leq 1, 1/2 \leq \mu_D \leq 1 \), and \( 0 \leq h \leq 1 \).

Figure 5 shows the effects on the stability of pure selfing by changes in \( \sigma \) and \( h \), similarly to figure 4 for the outcrossing equilibrium. In figure 5a, for each curve, the region of \( k \) and \( q \) that is “enclosed” (to the left) is the unstable region, where outcrossing can invade. Starting from lethality (\( \sigma = 1 \)), the region of instability grows as mutations become less deleterious. For \( \sigma = 0.5 \), the whole region is unstable, but, as \( \sigma \) decreases to 0, a region of stability appears in the lower left corner and sweeps across figure 5. One reason why decreasing \( \sigma \) is favorable to outcrossing when \( \sigma \) is large derives from its effect on the initial pure selfing equilibrium: with large \( \sigma \), the initial equilibrium has few adult Hom-mut, which is the class that benefits most from making the transition to outcrossing. As \( \sigma \) decreases, this class grows, increasing the potential benefit to outcrossing modifiers. Below \( \sigma = 0.5 \), however, the fitness differences among the phenotypes become too small, and the twofold cost of males paid by outcrossing begins to dominate. Figure 5b shows that increasing dominance of mutations drastically limits the ability of outcrossing to invade. Here, the region above and to the right
Fig. 5.—Evolution of modifier gene of selfing rate for masking model at the selfing equilibrium. Unless otherwise marked, all lines share the following parameter values: $\mu_D = 1$, $\alpha_2 = \alpha_3 = 0.9$, $\alpha_1 = 1.0$, $\alpha = 0.6$, $h = 0$. a, Selfing equilibrium is unstable to invasion of outcrossing for $k$ and $q$ values to the left of each curve (within the enclosing loop). b, Selfing equilibrium is unstable above and to the right of each line, except that a small region in the upper right corner is stable for all parameters shown. See text for explanation.

of each line is unstable (except that a small but varying-sized region in the upper corner of $(q, k)$ is stable for all $h$). Unless otherwise marked, $\alpha = 0.6$ and $h = 0$. All curves have $\alpha = 0.9$ and $\mu = 1$. It is obvious from figure 5 that, for many sets of parameters, outcrossing can invade for a wide range of $k$ and $q$. In a systematic search through the range of values of $\alpha$, $h$, $\mu$, $\sigma$, $k$, and $q$, it was found that 14% of all initially stable selfing equilibria were unstable to outcrossing modifiers. One strong effect not shown in figure 5 is that of $\mu_D$. Higher $\mu_D$ enlarges the region of instability; for $\mu_D < 1/2$, outcrossing can never invade.

**Fitness of Selfed and Outcrossed Offspring**

Inbreeding depression, $D$, is defined as one minus the relative fitness of selfed and outcrossed offspring. Many workers (e.g., Lloyd 1979; Charlesworth 1980; Feldman and Christiansen 1984) have used a fixed level of inbreeding depression along with the relatedness costs of outcrossing, taken to be 1/2, as tools for understanding the evolution of selfing and outcrossing. Specifically, it is argued that, if $D > 1/2$, outcrossing should evolve; otherwise, selfing should be the favored state.

Campbell (1986) and Holsinger (1988) argued that using constant amounts of inbreeding depression leads to incorrect predictions about mating system evolution, because inbreeding depression evolves as the mating system evolves. The need of incorporating a dynamic view of inbreeding depression has been stressed in recent work (Charlesworth and Charlesworth 1987, 1990; Charlesworth et al. 1990; Uyenoyama and Waller 1991a, 1991b, 1991c). Even if inbreeding depression is defined dynamically as a function of the genotype frequencies it may not accurately predict evolution of modifiers of the mating system (Holsinger 1988;
Uyenoyama and Waller 1991a, 1991b, 1991c; fig. 1 in this article and see below). Although Charlesworth and Charlesworth (1990) and Charlesworth et al. (1990) found counterexamples in which inbreeding depression did not predict the course of mating system evolution, they tended to view inbreeding depression as a sufficient concept for understanding their computer results.

Both the fitness distribution and the mating system distribution coevolve in the three models studied here. Consequently, the stability results reported above can be compared with fitness arguments based on the calculation of inbreeding depression at the outcrossing and selfing equilibria.

In the calculation of inbreeding depression among selfed offspring it is important to use the equilibrium genotype frequencies at the adult stage. For randomly outcrossed offspring, however, it does not matter. Either the adult genotype frequencies or the offspring genotype frequencies can be used to obtain the gene frequency that is used to calculate the Hardy-Weinberg offspring genotype frequencies. For the mutation/selection balance model, there is the additional issue of whether the selfed offspring frequencies are calculated using adult frequencies after selection or after selection and mutation. The frequencies after both selection and mutation were used below in calculating the fitness of selfed offspring for the mutation/selection balance model. For selfed and randomly outcrossed offspring, inbreeding depression can be calculated as

\[
D = 1 - \frac{\sigma_{AA} (\hat{u}_1^{aa} + 1/4 \hat{v}_1^{aa}) + 1/2 \sigma_{Aa} (\hat{v}_1^{aa} + 1/4 \hat{v}_1^{aa})}{\sigma_{AA} (\hat{u}_1 + 1/2 \hat{v}_1)^2 + 2 \sigma_{Aa} (\hat{u}_1 + 1/2 \hat{v}_1) (\hat{v}_1 + 1/2 \hat{v}_1) + \sigma_{aa} (\hat{v}_1 + 1/2 \hat{v}_1)^2}
\]  

(15)

for the heterozygote superiority model, and as

\[
D = 1 - \frac{[\hat{u}_1^q (1 - 3/4 \mu) + q \hat{v}_1^q] + (1 - h \sigma) (k \hat{v}_1^q + 1/2 \mu \hat{u}_1^q)}{+ (1 - \sigma) [\hat{v}_1^q + (1 - k - q) \hat{v}_1^q + 1/4 \mu \hat{u}_1^q]} / (1 - h \sigma)
\]  

(16)

for the masking model (since outcrossers always produce offspring with a fitness of \(1 - h \sigma\)). For the mutation/selection balance model equation (15) is used with \(m\) substituted for \(\sigma\).

For the heterozygote superiority model, equation (15) equals (using eqq. [7] and [8] in eqq. [2])

\[
D = \frac{1 - \sigma}{2 - \sigma},
\]  

(17)

for the selfing equilibrium, and

\[
D = \frac{\sigma (1 - \sigma)}{(\sigma - 2)^2},
\]  

(18)

for the outcrossing equilibrium.

For mutation/selection balance and recessive mutations (\(h = 0\); using eqq. [9] and [10] in eqq. [2] and [A1]), equation (15) equals

\[
D = -\frac{\mu - \mu^2 + \sqrt{\mu \sigma + 2 \mu^{3/2} \sqrt{\sigma - \mu \sigma}}}{2 - 2 \mu}
\]  

(19)
for the outcrossing equilibrium. The initial equilibrium at the fitness locus under complete selfing could not be obtained in explicit symbolic form for the mutation/selection balance model, so this case was studied numerically.

For the masking model at the outcrossing equilibrium, equation (16) equals (using eq. [11])

$$D = 1 - \frac{1 - \sigma + k \sigma - h k \sigma + q \sigma}{1 - h \sigma}.$$  \hspace{1cm} (20)

For the selfing equilibrium corresponding to fixation of Hom-mut (using eq. [12]),

$$D = \frac{(1 - h) \sigma}{1 - h \sigma}.$$ \hspace{1cm} (21)

For the equilibrium given by equation (14) as well as the internal selfing equilibria of the masking model, expressions for inbreeding depression are more complicated, although straightforward to obtain by substituting the corresponding equilibria into equation (16).

It can be shown using equations (18) and (19) that $D < 1/2$ is satisfied for all values of $\sigma$ for the heterozygote superiority model and all values of $\sigma$ with $\mu > \sigma$ in the mutation/homozygote balance model in outcrossing populations. Indeed, with the exception of the selfing equilibrium under heterozygote superiority, $D$ is usually less than 0.20 for these models. Nevertheless, in agreement with Holsinger (1988) and Uyenoyama and Waller (1991b), we see in figure 1 for the heterozygote superiority model that outcrossing can increase when rare in a population of selfers even though $D < 1/2$. No such counterexamples were found in the case of the mutation/selection balance model, although a systematic search was not conducted.

In the masking model, inbreeding depression is difficult to interpret in symbolic form except in limiting cases. For recessive lethal mutations at the outcrossing equilibrium (using eq. [20]), $D > 1/2$ requires

$$k + q < 1/2.$$ \hspace{1cm} (22)

This is virtually identical to the eigenvalue condition for stability of outcrossing (fig. 4a), which is for $\alpha = 0.1$ (modifier of small effect). However, for $\alpha = 1$ (modifier has large effect), the condition for stability of outcrossing is approximately

$$k + 2q < 1/2,$$

which no longer agrees with the condition based on inbreeding depression. For the selfing equilibrium corresponding to fixation of mutant homozygotes, $D > 1/2$ requires $\sigma (2 - h) > 1$, or, for recessive mutations ($h = 0$), $\sigma > 1/2$, which is consistent with the result of the stability analysis.

Recent work (Holsinger 1988; Charlesworth and Charlesworth 1990; Charlesworth et al. 1990; Uyenoyama and Waller 1991a, 1991b, 1991c) has emphasized that inbreeding depression changes as the mating system evolves, leading to associations between the genes determining the mating system and those affecting
fitness. For example, past generations of selfing may purge the line of deleterious recessives making the evolution of outcrossing less likely. Conversely, past generations of outcrossing will allow the buildup of more deleterious mutations, making the evolution of selfing more difficult.

Although the masking model, by assuming constant transmission probabilities of the Hom and Het phenotypes to offspring, cannot address these issues in a completely satisfying way, certain aspects of the model do reflect these issues. The Het frequency is less in a predominantly selfing population than in a predominantly outcrossing population. For recessive lethal mutations, we can compare inbreeding depression at the outcrossing equilibrium (eqn. [11]) with inbreeding depression at the complete selfing equilibrium given by equations (A6). In the ranges considered, $0 < q < 1/4$ and $0 < k < 1/2$, inbreeding depression is always greater at the outcrossing equilibrium than at the selfing equilibrium, reflecting the purging of deleterious alleles that occurs under selfing with probability $q$. The difference in inbreeding depression at these two equilibria derives from the fact that the fitness of selfed offspring changes as the mating system evolves in the masking model. Nevertheless, the fitness of selfed offspring is not a sufficient variable to understand the evolution of the mating system in this model.

DISCUSSION

Limitations of Models

The use of a single locus to represent fitness effects of deleterious alleles permits mathematical analysis of what, in reality, is a complicated multilocus problem. However, this same assumption is also a limitation of the models studied here. The low levels of inbreeding depression and the attendant difficulty in selecting for outcrossing in the mutation/selection and heterozygote superiority models can be traced to this single-locus assumption and the assumption of no pollen discounting (Uyenoyama and Waller 1991a, 1991b). The assumption of no pollen discounting maximizes the cost of males. The case of a single fitness locus represents a worst-case situation for the evolution of outcrossing (as does the assumption of no pollen discounting) when deleterious alleles are maintained by heterozygote superiority or mutation/selection balance. It was for this reason that the masking model was developed.

Before considering the masking model, consider the selfing equilibrium of the heterozygote superiority model (fig. 1). It is understandable why, in this two-locus system, larger selective values are unfavorable to outcrossing. This is easiest to see in the extreme case of lethal alleles, $\sigma = 1.0$. In this case, all adult genotypes must be heterozygotes and the offspring genotypes are identical whether produced by selfing or by outcrossing. Therefore, outcrossing can have no beneficial effect in terms of the fitness of its offspring when compared to selfing. Since outcrossers must still pay the costs of outcrossing, selfing is stable. Generalizing from this extreme case we can expect that, as $\sigma$ approaches 1.0, the difference between selfed and outcrossed offspring decreases and the evolution of outcrossing becomes more problematic. This is shown clearly in figure 1 as inbreeding depression decreases to zero as $\sigma$ approaches 1.0.
This effect of extreme values of \( \sigma \) is most likely an artifact of the assumption of a single fitness locus. In a multilocus setting, outcrossing mates are likely heterozygous for different lethal alleles yet the “mates” of selfers are still heterozygous for the same lethal alleles and so express them more often. This cannot be represented in the two-allele, single-locus model studied here but is assumed to be the case in the masking model.

**Interpreting \( k, q \), and \( \sigma \) in the Masking Model**

The most important parameters in the masking model are \( \sigma \), the fitness difference between heterozygotes and homozygotes, \( k \), the probability that selfers can maintain heterozygosity at all loci harboring deleterious alleles, and, \( q \), the probability that selfers can purge their genome of all deleterious alleles. The expression \( 1 - k \) can be interpreted as measuring the difference between selfers and outcrossers in masking ability, because outcrossers were assumed to maintain heterozygosity with probability 1. This might be true in an infinite population for rare deleterious alleles, but finite population size and inbreeding will reduce the masking probability for outcrossers below 1.

In the masking model, outcrossing is usually stable when common (in competition with selfing) so long as heterozygous offspring are more than twice as fit as mutant-homozygote offspring (\( \sigma > 1/2 \)), mutations are nearly recessive, outcrossers produce more than twice as many heterozygotes as do heterozygous selfers (\( k \ll 1/2 \)), and the probability that a heterozygous selfer purges its genome of mutations is low (\( q \ll 1/4 \)). These conditions should often be satisfied. For any particular locus, the frequency of heterozygotes among selfed offspring must be 1/2 by Mendel’s laws. However, the probability that a selfer produces either heterozygotes or wild-type homozygotes at all such fitness-determining loci will be less than 1/2, so long as the selfer is heterozygous at more than two such loci. For example, if an individual carried \( n \) mutations in heterozygous condition, all on separate chromosomes, the probability that a selfer produces an offspring that is heterozygous at all loci is (1/2)\(^n\). However, we also include in \textit{Het} the individuals that are heterozygous at \( n - i \) loci and homozygous wild type at \( i \) loci (0 \( \leq \) \( i \) \( < \) \( n \)). The overall probability of \textit{Het} offspring is then

\[
k = \sum_{i=0}^{n-1} \binom{n}{i} \left( \frac{1}{2} \right)^{n-i} \left( \frac{1}{4} \right)^i,
\]

which is equal to 1/2, if \( n = 1 \) or 2, and less than 1/2 if \( n > 2 \). The probability that a selfer produces an offspring that is homozygous for the wild-type allele at all loci (in other words, a \textit{Hom-wt} offspring) is \( q = (1/4)^n \). For these reasons, 1/2 and 1/4 are taken to be upper limits for \( k \) and \( q \), respectively. Most offspring, one minus the probabilities of being \textit{Het} and \textit{Hom-wt}, will be \textit{Hom-mut}, that is, homozygous for deleterious alleles for at least one of the loci. With five such loci, more than 75% of the offspring will be \textit{Hom-mut}.

For lethal recessive alleles (\( \sigma = 1.0, h = 0 \)), any \( k \) and \( q \) such that \( k + q < 1/2 \) is sufficient for outcrossing to be stable when common (see fig. 4, left). If there are more than two lethal alleles in the genome this condition will usually be satisfied. For human populations, “almost everyone carries the equivalent of
more than one lethal recessive gene in the heterozygous condition (Cavalli-Sforza and Bodmer 1971, p. 364). After their review of the data, Lande and Schemske (1985) conclude that typical individuals in large outbreeding populations are heterozygous for one or more nearly recessive lethal (or sublethal) genes. The level of lethal mutations will be much lower in predominantly selfing populations (Lande and Schemske 1985; Hopf et al. 1988), and, once selfers are able to purge the genome of mutation, outcrossers have more difficulty getting started. The conclusion of the masking model, that outcrossing is favored when common if there are more than two recessive semilethal mutations in the genome, appears to be widely met. Nevertheless, the model ignored many important genetic issues that have been addressed by recent work.

Recent Work on Inbreeding Depression and the Evolution of Outcrossing

Uyenoyama and Waller (1991a, 1991b, 1991c) have explored analytically the associations that develop between modifiers of the mating system and elements of inbreeding depression. Their work suggests that genetic associations are an important factor in the evolution of mating systems, in addition to the factors of pollen discounting and fitness of offspring. These workers argue that there is an evolutionary advantage to modifiers of mating systems that produce extremes in offspring fitness, because these extremes in fitness produce greater associations of the modifiers with high fitness genotypes. In some cases, selfing alleles produce more extreme fitness phenotypes (segregation at a single fitness locus with recurrent mutation). However, in other cases outcrossing modifiers evolve greater associations with high fitness phenotypes (two fitness loci with recurrent mutation, a single overdominant locus). Indeed, these authors find that a single overdominant locus located anywhere in the genome can dominate the evolution of the mating system, favoring outcrossing even if levels of inbreeding depression are well below 1/2.

Uyenoyama and Waller (1991a, 1991b, 1991c) and Charlesworth et al. (1990) studied the evolution of selfing and outcrossing using a model of multiple unlinked viability loci with recurrent mutation and concluded that mildly deleterious mutations are more favorable to the evolution of outcrossing than are lethal or semilethal mutations. The reason appears to be that, for lethal and semilethal mutations, selfing alleles are more able to form associations with wild-type fitness alleles. This conclusion may appear to be at odds with the masking model, which found in one case greater stability of outcrossing as the severity of the mutations increased (fig. 4a). However, in another case (fig. 5a), as the severity of the mutations decreased, the evolutionary prospects of outcrossing increased.

These effects in the masking model and the conclusions of Uyenoyama and Waller (1991a, 1991c) and Charlesworth et al. (1990) just discussed concern different matters. In analysis of the masking model, we considered only two initial states, complete outcrossing or complete selfing. Charlesworth et al. (1990) and Uyenoyama and Waller (1991a, 1991c) based their conclusion on the fact that in their models a wider range of initial outcrossing rates were stable for mildly deleterious alleles than for nearly lethal alleles, something that we have not considered.
For nearly lethal mutations, high levels of outcrossing are stable to the invasion of alleles promoting small changes in the selfing rate (Charlesworth et al. 1990, fig. 6a). However, large increases in the selfing rate are favored in predominantly outcrossing populations. In addition, these workers find that high levels of selfing are also stable for nearly lethal mutations to the invasion of outcrossing alleles. For mildly deleterious mutations, outcrossing is stable over a wider range of initial outcrossing rates. However, selfing is still stable when it dominates the population even for mildly deleterious, unlinked mutations (Charlesworth et al. 1990, fig. 6b).

The conclusions of these articles (Charlesworth et al. 1990; Uyenoyama and Waller 1991a, 1991b, 1991c) give further insights into the complexity of the problem of deleterious mutation and reproductive system. The advantage to outcrossing in masking lethal or nearly lethal mutations stems from the high probability that outcrossing mates are heterozygous at different loci. Uyenoyama and Waller (1991c) have shown that the condition for increase of modifiers of the mating system in a model of multiple unlinked viability loci undergoing mutation to lethal alleles is basically the same as it is for the case of a single viability locus. For this reason, it is not unexpected that these models are unfavorable for the evolution of outcrossing. Although they are multilocus models they give the same result (as far as the initial increase for alleles changing the mating system) as does a single-locus mutation model. With just one viability locus undergoing mutation to a lethal allele, most parents will be identical heterozygotes at the same viability locus. In this case, selfing parents and outcrossing parents have almost identical offspring distributions, because most matings will be between identical heterozygotes regardless of the mating system. The advantage of outcrossing can only be obtained when an outcrosser's mate is heterozygous at a different locus, something that cannot occur in a one-locus model. Furthermore, as discussed above in relation to figure 1, we can see in this a reason why the prospects of outcrossing are diminished as the viability effect of mutation becomes more severe.

**Masking Compared with Variance in Offspring Mutation Load**

Masking of deleterious alleles depends on heterozygosity within individuals, whereas the Fisher/Muller hypothesis for sex depends on differences between individuals in numbers of mutations. Muller (1964) first emphasized the importance of deleterious mutation in the evolution of sex. He pointed out that an asexual population incorporates a kind of ratchet mechanism by which it continually accumulates deleterious mutations. Sexual populations have the potential of avoiding this ratchet effect because offspring are produced with a variable number of mutations, some having more and some having fewer mutations than either parent. Further work has shown the ratchet effect to be most effective in small populations with mutations of small effect (Haigh 1978; Maynard Smith 1978). Kondrashov (1985, 1988) has shown that the greater variance in offspring mutation load (number of mutations) among sexuals can select for sex even in large populations. This requires that mutations interact synergistically, as proposed by Crow (1970), so that each additional mutation has a greater detrimental effect on fitness. According to the Muller/Kondrashov theory, all aspects of sex (recomb-
nation, independent assortment, and outcrossing) have a similar function in that they promote a greater between-individual variance in mutation load.

The three models studied here differ in their bearing on the Muller/Kondrashov theory and the theory that outcrossing serves to mask deleterious recessive or partially recessive alleles. The masking model was specifically developed to avoid the production of variable progeny by outcrossing and to include only the masking effects of outcrossing. The heterozygote superiority and mutation/selection balance models, although allowing outcrossers to produce progeny with variable numbers of mutations, are decidedly limited in this regard because of the assumption of a single fitness locus and should not be interpreted as a test of the Muller/Kondrashov view.

There are similarities and differences between the hypothesis that outcrossing is adaptive as a result of its effects on offspring mutation load (Muller 1964; Kondrashov 1984, 1985, 1988) and the hypothesis that outcrossing is adaptive because it masks hidden deleterious alleles (Bernstein et al. 1981). Both processes require that the parents be genetically different, that is, carry mutations at different loci. However, masking does not require between-individual variation among offspring, whereas this is the essence of the Muller/Kondrashov hypothesis. For the purpose of distinguishing between these two effects of sex, masking and variance in offspring mutation load, the masking model assumed that the offspring of outcrossers were all alike (they were all Hets).

In addition to not depending on differences among offspring in mutation load, masking is most effective without such differences. Indeed, masking is greatest without sex at all. For example, mitotic diploid reproduction can, in principle, maintain a recessive deleterious allele at each and every locus. So why is mitosis not the reproductive system of choice? Mitotically reproducing diploids cannot put their internal redundancy to good use in repair of DNA damages without recombination. But with recombination and without outcrossing, diploids pay the costs of expressing (unmasking) deleterious alleles (discussed here for selfers). It is only because of the two needs—recombinational repair of DNA damage and masking deleterious mutations—that sex, that is, outcrossing coupled with recombination, becomes the reproductive system of choice (Bernstein et al. 1985b). This view is discussed further below.

There are a variety of reproductive tactics allowed under the masking hypothesis but not under the offspring variance hypothesis. For example, a female could in principle mate with a male, keep the male genome in her somatic cells for the benefit of masking, but not pass the male genome on to her offspring. Such a female would achieve the benefits of masking but avoid the relatedness costs of outcrossing. However, it is difficult to see how such a hypothetical female could achieve the benefits of recombinational repair of DNA damages without passing on some of the male genome to its offspring. Additionally, counterselection in males may prohibit it from occurring. Nevertheless, paternal genome loss does occur in some scale insects and in pseudo-arrenotoky in the phytoseid mites (Sabelis and Nagelkerke 1988). Whether our understanding of the diversity of reproductive systems in these groups might benefit from the perspective developed in this article requires further analysis.
Outcrossing as a Process That Ensures Uncorrelated Errors, Whether in Haploids or Diploids

According to the repair hypothesis (Bernstein et al. 1984; Michod et al. 1988; Michod 1991), outcrossing originated for the function of bringing DNA template into a cell for damage repair. Implicit in this view is the assumption that outcrossing would bring in DNA that was undamaged at the sites of damage in the recipient's genome. Of course, the DNA brought in by outcrossing would likely have damages at other sites. The chances are very small that the two pieces of DNA would be damaged at exactly the same site. Thus, on a more general level, outcrossing originated for the function of bringing into a cell DNA template with uncorrelated errors, specifically, uncorrelated damages. We have seen here that outcrossing can maintain this general function of preserving uncorrelated errors in the diploid state, even when the diploid state becomes dominant, so long as we shift our attention from damages, which are nonreplicable errors, to mutations, which are replicable errors.

By their very nature, damages are nonreplicable errors, and, since damages accrue independently on homologous chromosomes even in the same cell, the two chromosomes in the diploid state are unlikely to have damages at the same sites. For this reason, outcrossing was no longer necessary for efficient damage repair, once diploidy emerged as the dominant stage in the life cycle. Once the diploid stage became the dominant stage at which selection acted in the life cycle, recessive and nearly recessive mutations accumulated, since they were masked in the diploid state. Because mutations are by their nature replicable, closed systems of reproduction, such as selfing, produce correlations in the locations of mutations in the two resulting chromosomes that end up in the diploid zygote. As shown here, their expression can lower fitness to the point that selfing becomes disadvantageous even when its twofold intrinsic advantage is taken into account.

The Evolution of Sex

Bernstein et al. (1985b) argued that the two major components of sex, recombination and outcrossing, serve different functions in diploids, although they serve a common function in haploids. According to this view, recombination originated and is maintained by the advantage of recombinational repair of DNA damages. Damages in DNA are nonreplicable but recognizable (by enzymes) errors. In contrast, mutations are replicable but nonrecognizable errors. Since damages can be recognized by enzymes, they may be repaired so long as there is a second copy of the information available. In haploid organisms, outcrossing is necessary to provide the second copy of DNA. Thus according to our view, both aspects of sex, recombination and outcrossing, originated for the function of repair of genetic damage. Experimental support for this hypothesis has been obtained in the case of natural transformation in the bacterium Bacillus subtilis (Michod et al. 1988, 1990; Wojcieszowski et al. 1989; Hoelzer and Michod 1991).

Although there is evidence that outcrossing originated in haploids for the purposes of repair, it is unlikely that it is maintained in diploid organisms for repair (Bernstein et al. 1981, 1984, 1985a, 1985b, 1985c). This is because only a second homologous chromosome is needed for recombinational repair, and, once dip-
lody emerged as the dominant stage in the life cycle, outcrossing was no longer necessary to provide this chromosome. If there were not another advantage to outcrossing, other than the need for DNA template for repair, outcrossing should have been abandoned once diploidy became the dominant stage of the life cycle in favor of closed systems of recombinational repair such as selfing or automixis. These closed systems of recombinational repair should have similar repair capacities as outcrossing (Bernstein et al. 1985b). However, they enjoy an intrinsic advantage over outcrossing if selfing individuals still contribute gametes to the outcrossing pool of pollen (Fisher 1941; Karlin and McGregor 1974; Feldman and Christiansen 1984). Bernstein et al. (1981, 1984, 1985a, 1985b, 1985c) argued that outcrossing was maintained when diploidy emerged as the dominant stage of the life cycle because of the greater masking of recessive or partially recessive deleterious mutations that occurs under outcrossing than under automixis or selfing.

The sexual cycle is a complex process involving a number of distinct components, and these components need not serve a single function. It is therefore surprising that the common assumption, at least in population genetic models, is that these different components of sex serve one basic function, the removal of linkage disequilibrium (see Felsenstein 1988 for an overview). This view is insufficient for a complete account of some of the components of sex, which are independently known to have direct effects on fitness. For example, it is well-known that recombination-deficient mutants suffer large decreases in fitness in damaging environments (for review, see Bernstein et al. 1987).

We have adopted the view that the sexual cycle is decomposable into two basic components, recombination and outcrossing, that serve different functions, at least in diploids. Recombination functions to repair DNA damages, and outcrossing functions to mask the expression of deleterious mutations that occurs with recombination in closed systems such as selfing. The present work does not address the origin and evolution of recombination, diploidy, or independent assortment. Rather, it assumes that these aspects of sex exist and addresses the question of whether they occur in the context of an "open" system like outcrossing or a "closed" system like selfing.

As mentioned above, of the two components of sex, recombination and outcrossing, recombination is more basic to life. In light of the view that recombination helps serve the basic need of DNA repair, the main unsolved problem concerning the evolution of sex is why recombination usually, but not always, occurs in an open system like outcrossing and less often in the context of closed systems such as selfing. Work on inbreeding depression and the evolution of selfing and outcrossing gains special significance when viewed in this context. The work presented and reviewed here suggests that the benefits of masking may provide enough selective force to account for the fact that recombination usually, but not always, occurs in the context of open systems like outcrossing.

ACKNOWLEDGMENTS

We thank R. B. Campbell, B. Charlesworth, D. Charlesworth, M. Feldman, K. Holsinger, S. Otto, M. Uyenoyama, and three anonymous reviewers for their
comments on previous versions of this article. We thank Uyenoyama and D. Waller for showing us their manuscripts before they were published. This work was supported by National Institutes of Health grant HD19919.

APPENDIX

RECURRENT EQUATIONS FOR HETEROZYGOTE SUPERIORITY AND MUTATION/SELECTION BALANCE MODELS

The mutation process in the mutation/selection balance model is represented as follows. Let superscript \( m \) indicate genotype frequencies after mutation and selection and \( \sigma \) the frequencies after selection (eqn. [2]):

\[
\begin{align*}
\sigma^m_i &= (1 - \mu)^2 \sigma_i^m \\
\nu_i^m &= (1 - \mu) \nu_i^m + 2 \mu (1 - \mu) u_i^m \\
w_i^m &= w_i^m + \mu^2 \sigma_i^m + \mu \nu_i^m \\
u_2^m &= (1 - \mu) \nu_2^m + (1 - \mu) \mu u_2^m \\
w_2^m &= w_2^m + \mu^2 u_2^m + \mu \nu_2^m + \mu \nu_3^m \\
u_3^m &= (1 - \mu) \nu_3^m + 2 \mu (1 - \mu) u_3^m \\
w_3^m &= w_3^m + \mu^2 u_3^m + \mu \nu_3^m
\end{align*}
\]

(A1)

The generation-to-generation recurrence equations are derived in the following way. Let \( x \)'s be the gametic frequencies in random pollen, and \( X \)'s the frequencies of all eggs of the given gametotytes that accept random pollen (the subscripts 1, 2, 3, and 4 refer, respectively, to gamete types \( AM, Am, aM \), and \( am \)). Our equations (A2) embody the assumption that selfing and outcrossing females contribute equal amounts of pollen to the pollen pool (no discounting), because the pollen frequencies do not depend on the selfing probabilities:

\[
\begin{align*}
x_1 &= u_1 + u_2 1/2 + v_1 1/2 + 1/2 (1 - r) v_2 + 1/2 r \tilde{v}_2 \\
X_1 &= (1 - \alpha_1) u_1 + (1 - \alpha_2) u_2 1/2 + (1 - \alpha_3) v_1 1/2 + 1/2 (1 - \alpha_3) (1 - \alpha_2) v_2 \\
&+ 1/2 r (1 - \alpha_3) \tilde{v}_2 \\
x_2 &= u_3 + u_2 1/2 + v_3 1/2 + \tilde{v}_2 1/2 (1 - r) 1/2 + 1/2 r v_2 \\
X_2 &= (1 - \alpha_3) u_3 + (1 - \alpha_2) u_2 1/2 + (1 - \alpha_3) v_3 1/2 + (1 - \alpha_3) \tilde{v}_2 (1 - r) 1/2 \\
&+ 1/2 r (1 - \alpha_2) v_2 \\
x_3 &= w_1 + w_2 1/2 + v_1 1/2 + (1 - r) \tilde{v}_2 1/2 + r v_2 1/2 \\
X_3 &= (1 - \alpha_3) w_1 + (1 - \alpha_2) w_2 1/2 + (1 - \alpha_3) v_1 1/2 + (1 - \alpha_2) (1 - r) \tilde{v}_2 1/2 \\
&+ (1 - \alpha_2) r v_2 1/2 \\
x_4 &= w_3 + w_2 1/2 + v_3 1/2 + r \tilde{v}_2 1/2 + (1 - r) v_2 1/2 \\
X_4 &= (1 - \alpha_3) w_3 + (1 - \alpha_2) w_2 1/2 + (1 - \alpha_3) v_3 1/2 + (1 - \alpha_2) r v_2 1/2 \\
&+ (1 - \alpha_2) (1 - r) v_2 1/2
\end{align*}
\]

(A2)
The complete mixed mating genotype frequency equations are given next:

\[ u_1' = X_1 x_1 + \alpha_1 u_1 + \alpha_2 u_2 1/4 + \alpha_1 v_1 1/4 + \alpha_2 [v_2 (1 - r)^2 + \tilde{v}_2 r^2] 1/4 \]

\[ u_2' = X_1 x_2 + X_2 x_1 + \alpha_1 u_2 1/2 + \alpha_2 (v_2 + \tilde{v}_2) 2 r (1 - r) 1/4 \]

\[ u_3' = X_2 x_2 + \alpha_3 u_3 + \alpha_2 u_2 1/4 + \alpha_3 v_3 1/4 + \alpha_2 [v_2 (1 - r)^2 + \tilde{v}_2 r^2] 1/4 \]

\[ v_1' = X_1 x_3 + X_3 x_1 + \alpha_1 v_1 1/2 + \alpha_2 (v_2 + \tilde{v}_2) r (1 - r) 1/2 \]

\[ v_2' = X_1 x_4 + X_4 x_1 + \alpha_2 [v_2 (1 - r)^2 + \tilde{v}_2 r^2] 1/2 \]

\[ v_3' = X_2 x_4 + X_4 x_2 + \alpha_3 v_3 1/2 + \alpha_2 (v_2 + \tilde{v}_2) r (1 - r) 1/2 \]

\[ w_1' = X_1 x_3 + \alpha_1 w_1 + \alpha_2 w_2 1/4 + \alpha_1 v_1 1/4 + \alpha_2 [v_2 r^2 + \tilde{v}_2 (1 - r)^2] 1/4 \]

\[ w_2' = X_3 x_4 + X_4 x_3 + \alpha_1 w_2 1/2 + \alpha_1 v_2 + \tilde{v}_2 2 r (1 - r) 1/4 \]

\[ w_3' = X_4 x_4 + \alpha_3 w_3 + \alpha_2 w_2 1/4 + \alpha_3 v_3 1/4 + \alpha_2 [v_2 (1 - r)^2 + \tilde{v}_2 r^2] 1/4 \]

In equations (A2) and (A3), the superscript \( \sigma \) (eqn. [2]) or \( m \) (eqn. [A1]) notation is dropped, but it is assumed that the genotype frequencies after selection (eqn. [2] in the case of heterozygote superiority) and after selection and mutation (eqn. [A1] in the case of mutation/selection balance) are to be used in the right-hand side of equations (A2) and (A3).

Equations (A3) are similar to those studied by Karlin and McGregor (1974, eq. 9.18), except for the added complexity of selection and mutation. Fisher (1941) was the first to point out that alleles promoting selfing enjoy a considerable advantage over alleles promoting outcrossing if the selfing alleles do not affect the contribution of selfers to the pollen pool. He considered a one-locus model with additive effects at the selfing locus (the \( M/m \) locus here). His model and results were obtained from equations (A3) by setting \( \sigma_{AA} = \sigma_{aa} = 1, \mu = 0, \alpha_1 = 0, \alpha_2 = 0.5, \alpha_3 = 1.0, \) and \( v_1 = v_2 = v_3 = w_1 = w_2 = w_3 = 0. \) Likewise, equations (A3) were checked by setting \( \sigma_{AA} = \sigma_{aa} = 1 \) and \( \mu = 0 \) and by using Karlin and McGregor's (1974) parameterization of the selfing matrix,

\[
\begin{array}{ccc}
AA & Aa & aa \\
MM & \alpha_1 & \beta \\
Mm & \alpha_2 & \beta \\
mm & \alpha_3 & \beta \\
\end{array}
\]

instead of array (1a) above and comparing results of the linear stability analysis with the results reported by Karlin and McGregor (1974).

**RECURRENT EQUATIONS FOR MASKING MODEL**

Let \( x_M \) and \( x_m \) be the frequencies of \( M \) and \( m \) alleles in random pollen, and let \( X_M \) and \( X_m \) be the frequencies in eggs that accept random pollen. Again, we assume that the frequencies in pollen are not affected by the selfing phenotype (no discounting):

\[ X_M = (1 - \alpha_1) (u_1^2 + v_1^2 + w_1^2) + (1 - \alpha_2) (u_2^2 + v_2^2 + w_2^2) 1/2 \]

\[ x_M = u_1^2 + u_2^2 1/2 + v_1^2 + v_2^2 1/2 + w_1^2 + w_2^2 1/2 \]

\[ X_m = (1 - \alpha_3) (u_3^2 + v_3^2 + w_3^2) + (1 - \alpha_2) (u_2^2 + v_2^2 + w_2^2) 1/2 \]

\[ x_m = u_3^2 + u_2^2 1/2 + v_3^2 + v_2^2 1/2 + w_3^2 + w_2^2 1/2 \]

The complete generation-to-generation recurrence equations are then

\[ u_1' = q \alpha_1 v_1^2 + q \alpha_2 x_1^2 1/4 + (1 - \mu_D + \mu_D 1/4) \alpha_1 u_1^2 + (1 - \mu_D + \mu_D 1/4) \alpha_2 u_2^2 1/4 \]

\[ u_2' = q \alpha_2 v_2^2 1/2 + (1 - \mu_D + \mu_D 1/4) \alpha_2 u_2^2 1/2 \]
\[ u'_3 = q \alpha_2 v'_2 1/4 + q \alpha_3 v'_3 (1 - \mu_D + \mu_D 1/4) \alpha_2 u'_2 1/4 + (1 - \mu_D + \mu_D 1/4) \alpha_3 u'_3 \]

\[ v'_1 = \mu_D 1/2 \alpha_1 u'_1 + \mu_D 1/8 \alpha_2 u'_2 + k \alpha_1 v'_1 + k \alpha_2 v'_2 1/4 + x_M X_M \]

\[ v'_2 = \mu_D 1/4 \alpha_2 u'_2 + k \alpha_2 v'_2 1/2 + x_M X_m + x_m X_M \]

\[ v'_3 = \mu_D 1/8 \alpha_2 u'_2 + \mu_D 1/2 \alpha_3 u'_3 + k \alpha_3 v'_3 1/4 + k \alpha_3 v'_3 + X_m x_m \]

(A5)

\[ w'_1 = \mu_D 1/4 \alpha_1 u'_1 + \mu_D 1/16 \alpha_2 u'_2 + (1 - k - q) \alpha_1 v'_1 + (1 - k - q) \alpha_2 v'_2 1/4 + \alpha_1 w'_1 + \alpha_2 w'_2 1/4 \]

\[ w'_2 = \mu_D 1/8 \alpha_2 u'_2 + (1 - k - q) \alpha_2 v'_2 1/2 + \alpha_2 w'_2 1/2 \]

\[ w'_3 = \mu_D 1/16 \alpha_2 u'_2 + \mu_D 1/4 \alpha_3 u'_3 + (1 - k - q) \alpha_3 v'_3 1/4 + (1 - k - q) \alpha_3 v'_3 \]

\[ + \alpha_3 w'_3 1/4 + \alpha_3 w'_3 \].

Note that, since, by assumption, Hom phenotypes are not produced by outcrossing, the frequencies \( u'_1, u'_2, u'_3, w'_1, w'_2, \) and \( w'_3 \) do not include contributions from the frequencies in random pollen and eggs (eqq. [A4]). However, since Het phenotypes can be produced by both selfing and outcrossing, the frequencies \( v'_1, v'_2, \) and \( v'_3 \) include contributions from both the selfing and outcrossing portions of the population. These recurrence equations (A5) include the intrinsic advantage of selfing at the \( M/m \) locus studied by Fisher (1941) but involve in addition the complexities of selection among the Het and Hom phenotypes, the frequencies of which evolve as the mating system evolves.

**A SELFING EQUILIBRIUM FOR THE MASKING MODEL**

The following equilibrium frequencies apply for \( \alpha_1 = 1, \mu_D = 1, h = 0, \) and \( \sigma = 1 \):

\[ \hat{u}_1 = \frac{1 - 4 k + 12 q - 16 k q - A + 4 q A}{24 - 32 k - 32 q} \]

\[ \hat{v}_1 = \frac{1 + 6 k - 8 k^2 - 8 q + A - 2 k A}{12 - 16 k - 16 q} \]

(A6)

and

\[ \hat{w}_1 = 1 - \hat{u}_1 - \hat{v}_1, \]

in which

\[ A = (1 - 8 k + 16 k^2 + 32 q)^{1/2}. \]

**LITERATURE CITED**


*Editor: Mark D. Rauscher*