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SELECTION FOR INCREASED MUTATION RATES WITH FERTILITY DIFFERENCES BETWEEN MATINGS

K. E. HOLSINGER, M. W. FELDMAN AND L. ALTENBERG

Department of Biological Sciences, Stanford University, Stanford, California 94305-2493

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ABSTRACT

Previous studies of mutation modification have considered models in which selection is a result of viability differences that are sex symmetric. The results of a numerical study of a model in which selection is a result of fertility differences between mated pairs demonstrate that the type of selection to which a population is subject can have a significant impact on the evolution of various parameters of the genetic system. When the fertility of matings between individuals with different genotypes exceeds the fertility of at least some of the matings between individuals with the same genotype, selection may favor increased rates of mutation, in contrast to the results from all exisitng constant viability models with random mating and infinite population size. Increased mutation rates are most frequently favored when forward and back mutation occur at approximately equal rates and when the modifying locus is loosely linked to the selected locus. We present one example in which selection favors increased rates of mutation even though the selection scheme is reducible to one of differential viability between the sexes.

THE genetic system of an organism may be defined as all those features that control the expression of hereditary variability in the population, but especially its breeding system and cytogenetic characteristics. It has been recognized for many years that various features of the genetic system are themselves under hereditary control and that their characteristics may evolve in response to selection. C. D. DARLINGTON, for example, argued that selection results in genetic systems that control the variability in natural populations in a way that is beneficial to those populations. On that basis he explained much of the great variety in chromosome number and morphology as a consequence of selection for certain patterns of population variability (see especially DARLINGTON 1939, 1958). Others, including in particular KENNETH MATHER (1943, 1953), adopted and extended these ideas, concluding that the genetic system of an organism is a result of the balance between selection for immediate adaptation and long-range flexibility (see also THODAY 1953; GRANT 1958; STEBBINS 1958). In recent years the genetic system has been understood to include such properties as mutation and recombination rates, level and type of inbreeding, sex-ratio and sex determination, as well as level of gametic dispersal (*e.g.*, see MAYNARD SMITH 1978).

Much of the recent discussion of the evolution of genetic systems takes as its point of departure a model proposed by NEI (1967, 1969) for the genetic control of recombination. This model took two linked genes to be under selection while the linkage between them was controlled by a third selectively neutral locus. Some special examples of viability selection regimes in NEI's model were used by FELDMAN (1972), who phrased the evolutionary question as one of initial increase. When the modifier locus is fixed on an allele, *e.g.*, M_1, such that M_1M_1 produces a recombination fraction r_1, and the population is near an equilibrium (that depends on r_1) of the two-locus system, it has been shown that an initially rare modifying allele M_2, producing a heterozygote recombination fraction r_2, will invade the population if $r_2 < r_1$ and will be lost if $r_2 > r_1$.

Subsequently, there have been a number of studies of the evolution of neutral modifiers in terms of the initial increase of a new modifying allele that affects recombination rate (FELDMAN 1972; FELDMAN and BALKAU 1972; KARLIN and MCGREGOR 1974; TEAGUE 1976; CHARLESWORTH, CHARLESWORTH and STROBECK 1977, 1979; FELDMAN, CHRISTIANSEN and BROOKS 1980; HOLSINGER and FELDMAN 1982, 1983a), mutation rate (KARLIN and MCGREGOR 1974; GILLESPIE 1981a,b; HOLSINGER and FELDMAN 1983b; LIBERMAN and FELDMAN 1985), migration rate (BALKAU and FELDMAN 1973; KARLIN and MCGREGOR 1974; TEAGUE 1977; ASMUSSEN 1983) and level of segregation distortion (PROUT, BUNDGAARD and BRYANT 1973; HARTL 1975; THOMSON and FELDMAN 1976; LIBERMAN 1976).

A general result derived from these models is what we call the "reduction principle." This assumes that there is random mating, viability selection on the major loci that is the same in both sexes, a single modified parameter (for example recombination or mutation, but not both) and initial homozygosity at the modifier locus. Then, the principle states that a new allele at the modifier locus, introduced near an equilibrium (of the major loci) that is a function of the modified parameter, will increase when rare if it reduces the rate of the process it modifies. For mutation, a more general form of the reduction principle has recently been proved by LIBERMAN and FELDMAN (1985), who demonstrated that a new allele at a locus that controls the mutation rate at a locus undergoing viability selection will increase when rare only if it reduces the average mutation rate at that locus (see also HOLSINGER and FELDMAN 1983b). Exceptions to this general rule have been demonstrated when the modifier modifies its own transmission, as with segregation modifiers, when mating is not at random [for recombination modifiers, see CHARLESWORTH, CHARLESWORTH and STROBECK (1979) and HOLSINGER and FELDMAN (1983a); for mutation modifiers see HOLSINGER and FELDMAN (1983b)], when selection varies from generation to generation (CHARLESWORTH 1976; GILLESPIE 1981a) or when the population size is finite (GILLESPIE 1981b).

ALTENBERG (1984) suggested that the reduction principle would always hold when the genotype at the modifier locus completely determines the fidelity of transmission from parental types to offspring types at the selected loci. Consider, for example, a modifier locus that determines the mutation rate in a

randomly mating population at a locus subject to viability selection that is the same in each sex. In this case the dynamical system describing how genotype frequencies change from generation to generation can be reduced to recursions describing gamete frequency changes. The parental and offspring types are gamete types. The genotype at the modifier locus completely determines the fidelity with which gametes are transmitted from parent to offspring; one genotype may allow no mutation at the selected locus, and another may allow some fraction of the alleles at the selected locus to mutate to another allele. In this case, the genotype at the modifier locus completely determines the fidelity of transmission, and we expect selection for reduced mutation rates, as has been demonstrated (KARLIN and MCGREGOR 1974; HOLSINGER and FELDMAN 1983b; LIBERMAN and FELDMAN 1985). On the other hand, if both mutation and recombination were acting on the selected loci, a modifier that affected recombination alone would not completely control the fidelity of parent-to-offspring transmission. This is a case where reduction may be violated (FELDMAN, CHRISTIANSEN and BROOKS 1980).

When reproduction occurs entirely by self-fertilization, the dynamical system cannot be reduced to gamete frequency changes. The parental and offspring types, therefore, are genotypes, not gamete types. The genotype at the modifier locus no longer completely determines the fidelity of transmission. To see this, consider an individual that is heterozygous at the selected locus and has a modifier genotype that allows no mutation at the selected locus. Even though the gamete types will be perfectly transmitted, the genotype at the selected locus will not be. The heterozygote parent will leave both homozygous and heterozygous progeny. Thus, we expect that there can be selection for increased mutation rates under certain circumstances, as has been demonstrated (HOLSINGER and FELDMAN 1983b).

When selection occurs as a result of fertility differences between matings, the genotype at a locus controlling mutation or recombination rates does not completely control the transmission from parent to offspring. That is, we must study the dynamics in terms of genotypes, but the genotype of an offspring may be different from that of either of its parents. Thus, we might also expect departures from the reduction principle in this case. We present here the results of a numerical study of genetic modification of mutation rate when the major locus is under fertility selection. We show that, with constant fertilities and random mating, selection for increased mutation rate may occur. This includes one example that can be reduced to a viability selection scheme in which the viabilities differ between the sexes. In addition, selection for increased rates of mutation is more likely to occur if forward and back mutation rates are equal than if the mutation rate in one direction is much greater. Finally, selection for increased rates of mutation occurs more frequently when the modifying locus is only loosely linked to the locus whose mutation rate it controls than when it is tightly linked. These results differ markedly from the known theory when selection is a result of viability differences.

THE MODEL

Consider two loci with two alleles each: A/a and M/m. Selection acts through the differential fertility of mated pairs, and the fertility of the mated pair

depends only on the parental genotypes at the A locus, *i.e.*, the M locus is selectively neutral. The genotype at the M locus determines the mutation rate at the A locus. In MM genotypes the mutation rate from A to a is μ_1 and from a to A is ν_1. The corresponding rates for Mm and mm are μ_2, ν_2 and μ_3, ν_3, respectively. If all $\nu_i = 0$, the model is one of *unidirectional* mutation; if $\mu_i = \nu_i$, we call it *symmetric* mutation. Recombination occurs between the A and M loci with frequency r.

Imagine that the population is at a stable equilibrium, x^*, with A and a in a mutation-selection balance and the modifier locus fixed on one allele, *e.g.*, M. A small amount of the alternative mutation-controlling allele, m, is introduced, and we are interested in whether this new allele increases in frequency when rare. This corresponds to a local stability analysis of x^* in the full ten-dimensional genotype-frequency space. For the stability of x^* to the introduction of m, an evaluation of the largest eigenvalue of a very complicated 4×4 matrix is required. We have, therefore, chosen to study this problem numerically.

Iterations of the recursions described in the APPENDIX were begun with random initial frequencies, except that the modifying locus was fixed on the allele that corresponded to a mutation rate of μ_1 at the selected locus. Iterations were allowed to continue until the maximum absolute deviation between two successive sets of genotype frequencies was less than 10^{-14}. A random perturbation from this state on the order of 1% was made to simulate the introduction of a new allele at the modifying locus. Iterations were then allowed to continue for a predetermined number of generations, sufficient to determine whether or not the new allele was being eliminated. Between 5,000 and 25,000 iterations were usually required, but occasionally as many as 100,000 iterations were necessary to be certain of the fate of the new allele. Each iteration required a total of approximately 1000 floating point operations, and a single run of 5000 iterations required approximately 1¼ hr on a PDP 11/34 computer. The mutation rates were chosen to be unrealistically large so that changes in frequencies could be detected within this time. All computations were in double precision (approximately 17 decimal digits of accuracy). In view of the time involved, only a relatively small number (approximately 80) fertility matrices could be studied. Nevertheless, since we report a variety of different dynamic behaviors from this set, it seems unlikely that the qualitative conclusions of the study would be altered by consideration of a greater number.

For simplicity, only cases in which $\mu_1 > \mu_2 > \mu_3$ or $\mu_1 < \mu_2 < \mu_3$ were considered. Since we are concerned only with initial properties, when μ_1 is the initial mutation rate, μ_3 does not play a role; that is, in order to determine the direction in which selection will initially tend to move the population, consideration of the mutation rate in the rare homozygote is unnecessary.

RESULTS

In the following discussion it will be useful to consider a general fertility matrix of the sort illustrated in Table 1. If it is possible to express the $F_{ij,kl}$'s

TABLE 1

A general fertility matrix

	AA	*Aa*	*aa*
AA	$F_{11,11}$	$F_{11,12}$	$F_{11,22}$
Aa	$F_{12,11}$	$F_{12,12}$	$F_{12,22}$
aa	$F_{22,11}$	$F_{22,12}$	$F_{22,22}$

as a sum of a male virility component, m_{kl}, and a female fecundity component, f_{ij}, then the model is one of *additive* fertilities. Similarly, if the $F_{ij,kl}$'s can be expressed as the product of m_{kl}'s and f_{ij}'s, the model is one of *multiplicative* fertilities. Finally, if $F_{ij,kl} = F_{kl,ij}$ the model is said to be *sex symmetric*. BODMER (1965) and FELDMAN, CHRISTIANSEN and LIBERMAN (1983) pointed out that any fertility selection model can be changed into a dynamically equivalent model with sex symmetry by letting $F_{ij,kl} = F_{kl,ij} = (F_{ij,kl} + F_{kl,ij})/2$.

Additive fertilities: BODMER (1965) pointed out that an additive fertility model for selection at one locus with two alleles is dynamically equivalent to a model in which viability selection acts in one sex only, the other sex being selectively neutral. FELDMAN, CHRISTIANSEN and LIBERMAN (1983) extended this principle to an arbitrary number of alleles at an arbitrary number of loci. Thus, if a new allele is introduced at a mutation modifying locus with additive fertility selection, we would expect it to increase when rare only if it reduces the mutation rate at that locus. Numerical study of ten randomly chosen additive fertility matrices did not produce any counterexamples.

Multiplicative fertilities: BODMER (1965) also noted that a multiplicative fertility model for selection at one locus with two alleles is dynamically equivalent to a viability selection model in which the viabilities differ between the sexes. This principle can be extended to an arbitrary number of alleles at an arbitrary number of loci. Let the genotype of an individual be written as γ_i/γ_j, where γ_i is the haplotype received from the mother, and γ_j is the haplotype received from the father. The mating $\gamma_i/\gamma_j \times \gamma_k/\gamma_l$ has fertility $f_{ij}\, m_{kl}$, and this is the only selection in the system. Now consider a similar model in which genotype γ_i/γ_j has viability v_{ij} in females and w_{ij} in males. In the viability model, the frequency of the mating $\gamma_i/\gamma_j \times \gamma_k/\gamma_l$ is $v_{ij}g_{ij}w_{kl}g_{kl}/\bar{w}_f\,\bar{w}_m$, where g_{ij} is the frequency of genotype γ_i/γ_j in newly formed zygotes (assumed to be equal between the sexes), $\bar{w}_f = \sum_{ij} v_{ij}g_{ij}$, and $\bar{w}_m = \sum_{kl} w_{kl}g_{kl}$. Thus, the proportions among zygotes produced in this model are the same as in fertility selection model with $F_{ij,kl} = v_{ij}w_{kl}$. Therefore, by assigning the relative viabilities f_{ij} to the females of the viability selection model and m_{kl} to the males of the viability selection model, we establish the equivalence between the viability selection model with different viabilities in the two sexes and the multiplicative fertility model.

Since any multiplicative fertility selection scheme can be reduced to a viability selection scheme, albeit with different viabilities in the two sexes, it might have been expected that there would always be selection for reduced rates of mutation. The fertility matrix in Table 2 illustrates a counterexample to this

TABLE 2

	AA	*Aa*	*aa*
AA	0.1138	0.1333	0.0146
Aa	0.0348	0.0408	0.0045
aa	0.2199	0.2575	0.0282

Evolutionarily stable mutation rate, μ^*			
Unidirectional mutation		Symmetric mutation	
$r = 0.0$	$r = 0.5$	$r = 0.0$	$r = 0.5$
$\mu^* < 0.001$	$\mu^* < 0.001$	$\mu^* < 0.001$ $0.3 < \mu^* < 0.5$	$0.3 < \mu^* < 0.5$

The values for μ^* are based on the fate of alleles at the modifying locus for certain initial mutation rates and are for perturbations from the polymorphic mutation-selection balance only. If only alleles that decrease the mutation rate are favored when $\mu_1 = 0.001$, then $\mu^* < 0.001$. If alleles that increase the mutation rate are favored when $\mu_1 = 0.001$, but alleles that decrease the mutation rate are favored when $\mu_1 = 0.01$, then $0.001 < \mu^* < 0.01$. A similar interpretation applies to $0.3 < \mu^* < 0.5$. $\mu^* = 0.5$ implies that alleles that alter the mutation rate when $\mu_1 = 0.5$ are eliminated. When two values for μ^* appear in the same column, the evolutionarily stable mutation rate depends on the mutation rate initially present in the population. Refer to the text for further explanation.

expectation that was found in a set of ten randomly selected multiplicative fertility matrices. There are two stable mutation-selection balance equilibria that have been found numerically for this matrix. One is a mutation-selection balance near fixation on the *AA* genotype. The other is a mutation-selection balance near a complete polymorphism. In the first case, selection always favors alleles at the modifying locus that reduce the mutation rate at the selected locus. Thus, the evolutionarily stable mutation rate, μ^*, is 0.0 when the population is near fixation on the selected locus. In the second case, selection favors alleles at the modifying locus that increase the mutation rate when $\mu_1 = 0.3$ and that decrease it if $\mu_1 = 0.5$, for $r = 0.5$ and symmetric mutation. Thus, μ^* for symmetric mutation with a modifier locus that is unlinked to the selected locus is between 0.3 and 0.5 when the population is near a complete polymorphism at the selected locus.

With $r = 0.0$ and symmetric mutation, the evolutionarily stable mutation rate depends on the mutation rate already present in the population. If $\mu_1 \leq 0.1$, for example, only alleles that decrease the mutation rate are favored by selection, and $\mu^* = 0$. If $\mu_1 = 0.3$, however, only alleles that increase the mutation rate are favored, and $0.3 < \mu^* < 0.5$.

Sex-symmetric fertilities: In the more general case when sex-symmetric fertilities are considered, selection for increased rates of mutation can also occur. When it occurs, there appears always to be a value of the mutation rate intermediate between 0 and 1 that is evolutionarily stable. The value of the evolutionarily stable mutation rate depends in a complex manner on the structure of the fertility matrix, the type of mutation and the recombination fraction between the selected locus and the modifier locus.

Out of 40 randomly chosen fertility matrices, six had an intermediate value

TABLE 3

	AA	*Aa*	*aa*
AA	0.42	0.58	0.94
Aa	0.58	0.33	0.75
aa	0.94	0.75	0.06

Evolutionarily stable mutation rate, μ^*

Unidirectional mutation		Symmetric mutation	
$r = 0.0$	$r = 0.5$	$r = 0.0$	$r = 0.5$
$\mu^* < 0.001$	$0.001 < \mu^* < 0.01$	$\mu^* = 0.5$	$\mu^* = 0.5$

See notes to Table 2.

TABLE 4

	AA	*Aa*	*aa*
AA	0.83	0.27	0.66
Aa	0.27	0.10	0.72
aa	0.66	0.72	0.06

Evolutionary stable mutation rate, μ^*

Unidirectional mutation		Symmetric mutation	
$r = 0.0$	$r = 0.5$	$r = 0.0$	$r = 0.6$
$\mu^* < 0.001$	$\mu^* < 0.001$	$\mu^* < 0.001$ $0.3 < \mu^* < 0.5$	$0.3 < \mu^* < 0.5$

See notes for Table 2. The results in Table 4 are for perturbations from the polymorphic mutation-selection balance only. $\mu^* = 0$ if perturbations are made from the mutation-selection balance near fixation on *A*.

for the evolutionarily stable mutation rate. All matings between individuals of different genotypes were more fertile than were matings between individuals of the same genotype in four of these six matrices, *e.g.*, the fertility matrix in Table 3. Matings between individuals of different genotypes were more fertile than all except one of the matings between individuals of the same genotype in the remaining two matrices. In one of these (Table 4) a homozygote × homozygote mating was the most fertile of all. In this instance, again, there are two stable mutation-selection balance equilibria. For perturbations from the one near fixation on *AA*, selection always favors reduced mutation. For perturbations from the one near complete polymorphism, selection favors increased mutation when $\mu_1 < 0.5$ and decreased mutation when $\mu_1 > 0.5$, for both $r = 0.0$ and $r = 0.5$ with symmetric mutation. This suggests that the evolutionarily stable mutation rate can be different from zero only if matings between individuals of different genotypes are more fertile than at least some of the matings between individuals of the same genotype. Although this may be a necessary condition, it is clearly not sufficient.

Fifteen fertility matrices were chosen randomly, subject to the constraint

TABLE 5

	AA	*Aa*	*aa*
AA	0.3288	0.4699	0.5048
Aa	0.4699	0.4243	0.9600
aa	0.5048	0.9600	0.4233

Evolutionarily stable mutation rate, μ^*			
Unidirectional mutation		Symmetric mutation	
$r = 0.0$	$r = 0.5$	$r = 0.0$	$r = 0.5$
$\mu^* < 0.001$	$0.001 < \mu^* < 0.01$	$\mu^* < 0.001$	$\mu^* < 0.001$

See notes to Table 2.

TABLE 6

	AA	*Aa*	*aa*
AA	0.5591	0.8854	0.6437
Aa	0.8854	0.4189	0.6213
aa	0.6437	0.6213	0.3971

Evolutionarily stable mutation rate, μ^*			
Unidirectional mutation		Symmetric mutation	
$r = 0.0$	$r = 0.5$	$r = 0.0$	$r = 0.5$
$\mu^* < 0.001$	$\mu^* < 0.001$	$\mu^* < 0.001$	$\mu^* < 0.001$

See notes to Table 2.

that all matings between individuals of different genotypes be more fertile than all matings between individuals of the same genotype. An intermediate value for the evolutionarily stable mutation rate was found for only six of these 15 matrices. Thus, the evolutionarily stable mutation rate for unidirectional mutation is between 0.001 and 0.01 for the fertility matrix in Table 5 when $r = 0.5$ and is 0.0 for the fertility matrix in Table 6, regardless of the type of mutation or the recombination fraction between the modifier and the selected loci.

The fertility matrix in Table 5 also illustrates that the type of mutation can have an effect on the value of the evolutionarily stable mutation rate. Thus, when the modifying and selected loci are unlinked, the evolutionarily stable mutation rate is 0.0 for symmetric mutation and between 0.001 and 0.01 for unidirectional mutation. With the fertility matrix in Table 7, however, the evolutionarily stable mutation rate is between 0.01 and 0.02 for unidirectional mutation and is 0.5 for symmetric mutation when the modifying and selected loci are unlinked. In general, the evolutionarily stable mutation rate is higher with symmetric mutation than with unidirectional mutation. The one exception we found was with the fertility matrix in Table 5.

The fertility matrix in Table 7 also illustrates how the evolutionarily stable

TABLE 7

	AA	*Aa*	*aa*
AA	0.03	0.93	0.48
Aa	0.93	0.04	0.74
aa	0.48	0.74	0.31

Evolutionarily stable mutation rate, μ^*

Unidirectional mutation		Symmetric mutation	
$r = 0.0$	$r = 0.5$	$r = 0.0$	$r = 0.5$
$\mu^* < 0.001$	$0.01 < \mu^* < 0.02$	$\mu^* < 0.001$ $0.3 < \mu^* < 0.5$	$0.3 < \mu^* < 0.5$

See notes to Table 2.

mutation rate depends on the recombination fraction. With complete linkage, the evolutionarily stable mutation rate is 0.0 for both unidirectional and symmetric mutation. (With symmetric mutation and $r = 0.0$, $\mu^* = 0.0$ only if the mutation rate originally present in the population is not too great.) With free recombination, the evolutionarily stable mutation rate is between 0.01 and 0.02 for unidirectional mutation and is 0.5 for symmetric mutation. In all cases examined, the evolutionarily stable mutation rate increases, or at least does not decline, as the linkage between the modifying and selected loci is weakened.

DISCUSSION

Several examples now exist to illustrate that the mating system of an organism can have a dramatic impact on the fate of alleles at a neutral locus that controls mutation or recombination rates at other loci subject to viability selection. Thus, with random mating, only alleles at a modifier locus that reduce the recombination rate between two loci subject to viability selection are favored by selection (FELDMAN 1972; FELDMAN, CHRISTIANSEN and BROOKS 1980). Similarly, only alleles that reduce the mutation rate at a viability selected locus are favored with random mating (KARLIN and MCGREGOR 1974; HOLSINGER and FELDMAN 1983b; LIBERMAN and FELDMAN 1985). However, both of these results can be reversed for certain viability regimes when the population reproduces by a mixture of self-fertilization and random mating (CHARLESWORTH, CHARLESWORTH and STROBECK 1979; HOLSINGER and FELDMAN 1983a,b).

We have demonstrated here that the type of selection to which a population is subject can also have an important impact on the evolution of mutation rates and, we conjecture, on the evolution of other parameters of the the genetic system as well. Specifically, when selection is a result of fertility differences or viability differences that are not sex symmetric, the evolutionarily stable mutation rate need not be zero as it is in all constant viability, infinite population size models with random mating that have been studied to date (KARLIN and MCGREGOR 1974; HOLSINGER and FELDMAN 1983b; ALTENBERG 1984; LIB-

ERMAN and FELDMAN 1985). If the fertility of matings between individuals with different genotypes is greater than that of some of the matings between individuals with the same genotype, the evolutionarily stable mutation rate may be at some value intermediate between 0 and 1.

Although the dynamics of mutation modification are quite complex, certain general patterns have emerged. The evolutionarily stable mutation rate will apparently be different from zero only if all matings between individuals with different genotypes are more fertile than at least some of the matings between individuals with the same genotype. This is analogous to the result for complete self-fertilization with viability selection (HOLSINGER and FELDMAN 1983b). In that case the evolutionary stable mutation rate was positive for some patterns of overdominance. In these situations, mutation increases the frequency of the most viable genotype. Mutation in the model considered here increases (or at least does not decrease) the diversity of genotypes produced from any mating. When matings between different genotypes are more fertile than matings between the same genotypes, individuals with a high mutation rate will tend to have offspring that are more fecund than those of individuals with lower mutation rates. This condition, however, is only necessary, not sufficient. Furthermore, the evolutionarily stable mutation rate is more likely to be different from zero if the linkage between the modifying locus and the selected locus is loose rather than tight and if the mutation is symmetric rather than unidirectional. We did illustrate one example in which the evolutionarily stable mutation rate was higher for unidirectional mutation than for symmetric mutation.

The type of mutation-selection balance at the selected locus may also determine the evolutionarily stable mutation rate. If the mutation-selected balance is near a fixation state at the selected locus, the evolutionarily stable mutation rate is zero. If the mutation-selection balance is near a polymorphic state, the evolutionarily stable mutation rate may be different from zero.

When selection is a result of viability differences between genotypes, the mean fitness is a decreasing function of the mutation rate (KARLIN and MCGREGOR 1974; HOLSINGER and FELDMAN 1983b), so that selection for decreased mutation rate corresponds to increasing the mean fitness, regardless of linkage. The analogous principle does not hold when selection is a result of fertility differences between matings, at least for tight linkage. For the fertility matrix in Table 2 with symmetric mutation and $\mu_1 = 0.5$, the mean fertility is 0.0875. With $\mu_1 = 0.02$, the mean fertility is 0.0858, yet only alleles that decrease the mutation rate are favored when $r = 0$. This may not be too surprising when we realize that the mean fertility does not necessarily increase from generation to generation in fertility selection models (POLLAK 1978).

Clearly, these results suggest that evolutionists should interpret carefully the results of population genetic models with purely sex-symmetric viability selection, bearing in mind that the predictions could be reversed if a different sort of selection scheme were modeled. It was already known that the dynamics and equilibrium structure of fertility models could be quite different from those of viability selection models (HADELER and LIBERMAN 1975; FELDMAN, CHRISTIANSEN and LIBERMAN 1983). We have now demonstrated that fertility

selection and sex-asymmetric viability selection can cause at least some of the parameters of the genetic system to evolve in a direction opposite to that predicted from consideration of sex-symmetric viability selection alone. It is natural to speculate that modifiers of linkage between major genes under fertility selection (FELDMAN and LIBERMAN 1985) may also evolve to increase recombination.

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APPENDIX: DESCRIPTION OF THE RECURSIONS USED IN THE NUMERICAL STUDY

To write explicit recursions for how the genotype frequencies in one generation depend on those in the preceding generation would require calculation of the frequency of 100 different possible matings and an analysis of the frequency of each of the ten genotypes produced by each mating. We used the following indirect method for determining how genotype frequencies in one generation depend on those in the preceding generation:

1. Calculate (for given r, μ_i, and ν_i) the segregation table according to the formulas in Table 8. Let $R_{ij,k}$ be the fraction of gametes of type k produced by genotype γ_i/γ_j. Consider the mating between a female of genotype γ_i/γ_j and a male of genotype γ_k/γ_l. A fraction $2R_{ij,m}R_{kl,n}$ of the progeny will be of genotype γ_m/γ_n for $m \neq n$, and a fraction $R_{ij,m}R_{kl,n}$ of the progeny will be of genotype γ_m/γ_n for $m = n$. This mating takes place with frequency $x_{ij}x_{kl}$,

TABLE 8

The segregation table used in constructing the recursions

Genotype	Gametes			
	AM	*aM*	*Am*	*an*
Am/*AM*	$1 - \mu_1$	μ_1	0	0
aM/*AM*	$\frac{1 - \mu_1 + \nu_1}{2}$	$\frac{1 + \mu_1 - \nu_1}{2}$	0	0
Am/*AM*	$\frac{1 - \mu_2}{2}$	$\frac{\mu_2}{2}$	$\frac{1 - \mu_2}{2}$	$\frac{\mu_2}{2}$
am/*AM*	$\frac{(1 - \mu_2)(1 - r) + \nu_2 r}{2}$	$\frac{\mu_2 (1 - r) + (1 - \nu_2) r}{2}$	$\frac{(1 - \mu_2) r + \nu_2 (1 - r)}{2}$	$\frac{\mu_2 r + (1 - \nu_2)(1 - r)}{2}$
aM/*aM*	ν_1	$1 - \nu_1$	0	0
Am/*aM*	$\frac{(1 - \mu_2) r + \nu_2 (1 - r)}{2}$	$\frac{\mu_2 r + (1 - \nu_2)(1 - r)}{2}$	$\frac{(1 - \mu_2)(1 - r) + \nu_2 r}{2}$	$\frac{\mu_2 (1 - r) + (1 - \nu_2) r}{2}$
am/*aM*	$\frac{\nu_2}{2}$	$\frac{1 - \nu_2}{2}$	$\frac{\nu_2}{2}$	$\frac{1 - \nu_2}{2}$
Am/*Am*	0	0	$1 - \mu_3$	μ_3
am/*Am*	0	0	$\frac{1 - \mu_3 + \nu_3}{2}$	$\frac{1 - \mu_3 - \nu_3}{2}$
am/*an*	0	0	ν_3	$1 - \nu_3$

where x_{ij} is the frequency of the genotype γ_i/γ_j (assumed equal between the sexes), and its fertility is $F_{ij,kl}$.

2. For each possible mating calculate the fraction of progeny that are of each genotype and accumulate these genotypic proportions across the possible matings, assigning to each mating a weight corresponding to the frequency with which it occurs multiplied by its fertility.

3. Normalize the new genotypic frequencies.