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A COMPARATIVE APPROACH TO THE POPULATION-GENETICS THEORY OF SEGREGATION DISTORTION

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Abstract.—Mathematical models of four well-known naturally occurring systems of segregation distortion are compared. These include the sex-ratio chromosome of *Drosophila pseudoobscura,* the Segregation Distorter (*SD*) complex of *D. melanogaster,* the *t* locus in *Mus musculus,* and the sex-ratio system in *Aedes aegypti.* Dynamics of these models are compared with the classical one-locus multiple-allele viability system. For the *SD* complex and the sex-ratio model of *A. aegypti,* the role of recombination is reviewed. Departures from Mendelian segregation cause fascinating irregularities in the relationship between linkage and linkage disequilibrium, as well as in predictions for the evolution of recombination itself.

The discovery of segregation distortion in nature has led to the development of some fascinating mathematical theory. This theory has had two objectives. On the one hand, it is possible to design experiments that produce estimates of forces that might balance distortion, and the theory can be used to indicate whether these estimates are enough to explain the persistence of distortion and the polymorphism associated with it. On the other, one can ask questions about the evolution of segregation distortion itself, and among these, perhaps the most prominent concern the robustness of Mendelian segregation and its evolutionary stability. Reviews that address the qualitative issues posed by the existence of extreme meiotic drive are those of Zimmering et al. (1970) and Crow (1979).

Segregation distortion produces significant qualitative departures from the theoretical predictions that can be made from the mathematical theory of natural selection with Mendelian segregation. The first models to include segregation distortion treated a single gene or gene arrangement. Included among these are the studies of "sex ratio" in *Drosophila pseudoobscura,* the Segregation Distorter (*SD*) complex in *Drosophila melanogaster,* and the *t* locus in *Mus musculus.* The sex-determination system in *Aedes aegypti* has been modeled in terms of two linked genes, and the more recent treatments of *SD* have also included a second locus. These developments make it possible to compare aspects of two-locus theory with and without distortion and to consider such issues as the evolution of linkage between genes, one of which causes biased segregation. In this article, we summarize these one- and two-locus studies in a comparative manner.

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BACKGROUND

Viability Selection at One Locus with Mendelian Segregation

The following is a brief and far-from-inclusive summary of a few of the main results concerning evolution at a single autosomal locus with alleles A_i ($i = 1, 2, \ldots, k$) with the relative rates of survival of the genotypes A_iA_j given by w_{ij}. The viability matrix $\mathbf{W} = [w_{ij}]$ is nonnegative and symmetric, and it is usually assumed that all of its principal minors are nonsingular. Mating is random, and selection acts only on viability. The dynamic for the frequency x_i of allele A_i is given by

$$x_i' = x_i \sum_j w_{ij}x_j/\bar{w} = x_i w_{i\cdot}/\bar{w}, \tag{1}$$

where x_i' is the frequency of allele A_i in the next generation, the mean fitness is

$$\bar{w} = \sum_{i=1}^{k}\sum_{j=1}^{k} w_{ij}x_i x_j,$$

and the marginal average fitness of allele A_i is

$$w_{i\cdot} = \sum_{j=1}^{k} w_{ij}x_j.$$

The following are well-known facts concerning the dynamics of system (1).

1. $\bar{w}(x_1', x_2', \ldots, x_k') \geq \bar{w}(x_1, x_2, \ldots, x_k)$, with equality only at equilibria of equation (1). This is the fundamental theorem of natural selection (Fisher 1930; Kingman 1961), which in qualitative terms means that the population's average fitness increases over time. It enables us to infer global convergence of the system to one of its equilibria.
2. There are $2^k - 1$ possible equilibria of the system.
3. For generic $\mathbf{W}$ there is only one possible equilibrium $(\hat{x}_1, \hat{x}_2, \ldots, \hat{x}_k)$ with all alleles present (i.e., such that $\hat{x}_i > 0$, for $i = 1, 2, \ldots, k$).
4. This fully polymorphic equilibrium is globally stable if $\mathbf{W}$ has one positive and $k - 1$ negative eigenvalues or, equivalently, if the determinants of the principal minors of $\mathbf{W}$ alternate in sign. For example, with two alleles, the equilibrium

$$\hat{x}_1 = (w_{12} - w_{22})/(2w_{12} - w_{11} - w_{22}) \quad \text{and} \quad \hat{x}_2 = 1 - \hat{x}_1 \tag{2}$$

is globally stable if w_{12} is greater than both w_{11} and w_{22} (i.e., if there is heterozygote advantage).

5. If the k-allele equilibrium $\hat{x}_1, \hat{x}_2, \ldots, \hat{x}_k$ is stable, then a new allele A_{k+1} introduced near this equilibrium increases in frequency if its marginal average fitness exceeds the population's previous average fitness, that is, if

$$w_{k+1\cdot} = \sum_{j=1}^{k} w_{j,k+1}\hat{x}_j > \hat{\bar{w}} = \sum_{i=1}^{k}\sum_{j=1}^{k} w_{ij}\hat{x}_i\hat{x}_j \tag{3}$$

(Kingman 1961). (For more details, see Karlin 1978.)

Viability Selection at Two Loci with Recombination and Normal Segregation

For the present purposes, it is enough to consider two alleles at each of the two loci A and B, with x_1, x_2, x_3, and x_4 denoting the frequencies of A_1B_1, A_1B_2, A_2B_1, and A_2B_2, respectively, and with R denoting the recombination fraction between the loci. With the chromosomes numbered in the order given, we consider a two-locus viability matrix,

$$\mathbf{W} = \begin{array}{c} \\ A_1B_1 \\ A_1B_2 \\ A_2B_1 \\ A_2B_2 \end{array} \begin{array}{c} \begin{array}{cccc} A_1B_1 & A_1B_2 & A_2B_1 & A_2B_2 \end{array} \\ \begin{pmatrix} w_{11} & w_{12} & w_{13} & w_{14} \\ & w_{22} & w_{23} & w_{24} \\ & & w_{33} & w_{34} \\ & & & w_{44} \end{pmatrix} \end{array},$$

with $w_{ij} = w_{ji}$ and the usual assumption that $w_{14} = w_{23}$, so that the two double heterozygotes are equally fit. Evolution is described by the system

$$\bar{w}x_1' = x_1w_{1\cdot} - RDw_{14}, \tag{4a}$$

$$\bar{w}x_2' = x_2w_{2\cdot} + RDw_{14}, \tag{4b}$$

$$\bar{w}x_3' = x_3w_{3\cdot} + RDw_{14}, \tag{4c}$$

$$\bar{w}x_4' = x_4w_{4\cdot} - RDw_{14}, \tag{4d}$$

where the primes signify the next generation, the mean fitness is

$$\bar{w} = \sum_{i=1}^{4}\sum_{j=1}^{4} w_{ij}x_ix_j, \tag{4e}$$

and the linkage disequilibrium is

$$D = x_1x_4 - x_2x_3. \tag{4f}$$

The following are some of the facts known about system (4). (For more details, see, e.g., Karlin 1978.)

1. It is not always true that $\bar{w}(x_1', x_2', \ldots, x_k') \geq \bar{w}(x_1, x_2, \ldots, x_k)$. This has been called the "nonexistence of adaptive topographies" (Moran 1964).

2. Seven interior equilibria have been found. It is conjectured that this is the maximum number of isolated interior equilibria in this system. Of these, at most two have been found to be simultaneously stable, and it is conjectured that no more than two fully polymorphic equilibria can be stable simultaneously (Karlin and Feldman 1970; Karlin 1975).

3. Polymorphisms and boundary equilibria can be simultaneously stable. It is conjectured that at most four boundary and two interior equilibria can be stable together (Feldman and Liberman 1979).

4. If $\hat{D} = 0$ is stable for some value R_0 of the recombination fraction, then it is stable for $R > R_0$. It is conjectured that the equilibrium value $\hat{D}$ decreases as a function of R (Karlin 1980).

5. If the stability of a boundary equilibrium depends on R, then the equilibrium

is stable for large R and unstable for smaller R, with a single value R^* dividing the two parametric ranges (see, e.g., Bodmer and Felsenstein 1967).

The Theory of Neutral Modifiers

Suppose that, in addition to the two genes under selection described above, a third locus with genotypes M_1M_1, M_1M_2, and M_2M_2 controls the rate of recombination between the A and B loci. The three genotypes produce recombination rates r_{11}, r_{12}, and r_{22}, respectively, between the A and B loci and are indistinguishable insofar as viability selection is concerned. This kind of system was introduced by Nei (1967) to describe the evolution of recombination. When M_1 is fixed, consider the equilibrium approached by the system $A_1B_1M_1$, $A_1B_2M_1$, $A_2B_1M_1$, and $A_2B_2M_1$ under the influence of selection and recombination (r_{11}). Close to this equilibrium, M_2 is introduced, and we seek conditions for the initial increase in the frequency of M_2. Provided that the four M_1 chromosomes are initially in linkage disequilibrium, M_2 increases in frequency when it is rare, provided that r_{12} is less than r_{11} (Feldman 1972; Feldman et al. 1980; Liberman and Feldman 1986). This result is independent of the recombination fraction, R, between B and M. If r_{12} is less than both r_{11} and r_{22}, then both M_1 and M_2 increase when they are rare. The frequency of M_1 in the resulting polymorphism is given by

$$\hat{P}_{M_1} = (r_{12} - r_{22})/(2r_{12} - r_{11} - r_{22}), \tag{5}$$

which is stable for R large enough and unstable for R very small (Feldman and Krakauer 1976; Liberman and Feldman 1986).

A general framework for the study of such neutral modifiers of recombination, mutation, and migration has been described (Altenberg and Feldman 1987), and the general property of such modifiers is that alleles that reduce parameters of mutation, migration, and recombination are favored. This reduction principle is likely to rely critically on properties of the mathematical rules of intergenerational transmission that are violated in the presence of modes of selection other than viability selection (Altenberg and Feldman 1987). Segregation distortion is one of these modes.

EVOLUTIONARY DYNAMICS UNDER SEGREGATION DISTORTION: ONE-LOCUS THEORY

Sex Ratio

Deterministic one-locus models for the evolution of alleles subject to segregation distortion with viability differences among genotypes reached the population-genetics literature in the early 1960s. These models were developed to describe observations from the laboratory and field concerning the Segregation Distorter complex in *Drosophila melanogaster*, the *t* locus in *Mus musculus*, and the sex-ratio chromosome in *Drosophila pseudoobscura*.

The sex-ratio chromosome, denoted X_r, causes males (whose karyotype is X_rY) to produce only daughters. Edwards (1961) developed a model to describe the

evolutionary dynamics of X_r and its normal homologue X_r and then applied his model to Wallace's (1948) experimental observations from population cages. Using viabilities estimated by Wallace, Edwards found a marked discrepancy between the dynamics predicted by his model and those Wallace observed in population cages. Edwards developed alternative estimates from Wallace's data and went on to show that the dynamics of his model, with these estimates inserted, were qualitatively compatible with those of Wallace's cages. He also used the model to develop viability estimates that would support the chromosomal frequencies in nature reported by Sturtevant and Dobzhansky (1936; Dobzhansky 1943).

A larger experimental study of sex-ratio polymorphism allowed an estimation of fertilities as well as viabilities and extended Edwards's model to include fertility differences (Curtsinger and Feldman 1980). When parameter estimates from the experiments were inserted into the model, equilibrium frequencies were obtained that agreed reasonably well with the frequencies observed in the field population from which the experimental stocks originated.

Suppose that X_r and X come to equilibrium under the forces of viability selection, fertility differences between X_rY and XY males, and segregation distortion in X_rY males whose offspring are male and female in the ratio $1 - m_1 : 1 + m_1$. It has been shown that a new sex-ratio chromosome, $X_r^{(2)}$, whose corresponding segregation bias is m_2, introduced near this equilibrium succeeds if

$$f_1(1 + m_1) < f_2(1 + m_2),$$

where $f_1 : f_2$ is the ratio of the fertilities of the X_r and $X_r^{(2)}$ males (Thomson and Feldman 1975). Clearly, in the absence of the fertility effects, increased distortion is favored.

The Segregation Distorter Complex

The formulation here is that originally due to Hiraizumi et al. (1960). At a locus with alleles *D* and *d*, the relative viabilities of the genotypes are as follows:

genotype	*DD*	*Dd*	*dd*
viability	1	w_1	w.

(6)

The proportion of *d*-bearing gametes among all functional gametes produced by *Dd* is *k*. The relationship between the frequency of *d*-bearing gametes in consecutive generations, x and x', is

$$x' = \frac{x^2 w + 2x(1 - x)kw_1}{x^2 w + 2x(1 - x)w_1 + (1 - x)^2}. \tag{7}$$

Fixation in *D*, corresponding to $x = 0$, is unstable if

$$2kw_1 > 1; \tag{8}$$

and fixation in *d*, corresponding to $x = 1$, is unstable if

$$2(1 - k)w_1 > w. \tag{9}$$

If inequalities (8) and (9) both hold, then there is a globally stable polymorphic equilibrium with

$$\hat{x} = (2kw_1 - 1)/(2w_1 - 1 - w), \tag{10}$$

which should be compared with equilibrium (2), the result with $k = \frac{1}{2}$. We shall return to equation (10) in the context of two-locus models for the Segregation Distorter complex.

Hartl (1970*a*) extended the above model to allow for different levels of meiotic drive in the two sexes. The viability regime is as in specification (6), but now we allow parameters k and κ to be the proportions of sperm and eggs, respectively, that bear d. If x and y are the frequencies of d in sperm and eggs, respectively, evolution is described by the two-dimensional system

$$\bar{w}x' = xyw + [x(1 - y) + y(1 - x)]w_1k, \tag{11a}$$

$$\bar{w}y' = xyw + [x(1 - y) + y(1 - x)]w_1\kappa, \tag{11b}$$

where

$$\bar{w} = xyw + [x(1 - y) + y(1 - x)]w_1 + (1 - x)(1 - y). \tag{11c}$$

The fixation states (0,0) and (1,1) are both locally unstable if two conditions hold:

$$w_1(k + \kappa) > 1 \tag{12}$$

and

$$w_1(2 - k - \kappa) > w. \tag{13}$$

These reduce to inequalities (8) and (9) when $k = \kappa$. Under conditions (12) and (13), there is a "protected" polymorphism (Prout 1968). Hartl showed numerically that conditions (12) and (13) are not necessary for the existence of a stable polymorphism. In fact, the polymorphic equilibria of equations (11) are the roots of a cubic; it is possible that (0,0) and (1,1) are stable and unstable, respectively, and that two polymorphic equilibria exist, one of which is stable and the other unstable. The range of parameters required for this to occur, however, is probably too extreme to be empirically relevant. Nevertheless, it is clear that the incorporation of two meiotic-drive parameters entails a substantially increased level of complexity in the dynamics. Kimura's (1958) version of the fundamental theorem of natural selection (in continuous time) was extended by Hartl (1970*b*) in a multiple-allele framework with meiotic drive by the addition of a correction factor. To our knowledge, no equivalent representation in discrete time has been suggested (but see Ewens 1989).

The t *Locus in* Mus musculus

In his 1968 study, Lewontin incorporated both viability and male sterility into a deterministic model for the dynamics of the t allele. In terms of Hartl's parameters from the preceding section, $\kappa = 0.5$, since distortion occurs only in males. The models are not quite comparable, however, since Lewontin assumed that tt males were sterile (equivalent to $w = 0$ in males). Again writing x and y for the

frequencies of the driven t allele in sperm and ova, respectively, with $1 - x$ and $1 - y$ denoting the corresponding frequencies of the wild-type allele, the changes in these frequencies are governed by

$$x' = \frac{kw_1[x(1 - y) + y(1 - x)]}{(1 - x)(1 - y) + w_1[x(1 - y) + y(1 - x)]} \tag{14a}$$

and

$$y' = \frac{xyw + w_1[x(1 - y) + y(1 - x)]/2}{xyw + w_1[x(1 - y) + y(1 - x)] + (1 - x)(1 - y)}. \tag{14b}$$

Note the difference in the denominators here compared with system (11). Lewontin showed that the fixation point (0,0) is unstable if

$$w_1(\tfrac{1}{2} + k) > 1 \tag{15}$$

(see inequality [12] with $\kappa = \frac{1}{2}$). Karlin (1972) showed that a change of variables to $u = x/(1 - x)$ and $v = y/(1 - y)$ produces a transformation that is monotonic in each of u and v and that under condition (15) there is global convergence to a unique polymorphic equilibrium, which is the root of a rather complicated cubic polynomial. Such monotonic transformations arise frequently in models of differential selection between the sexes, and their properties are useful in demonstrating convergence to equilibrium.

Because the t allele is usually found in small endogamous family units, it is likely that stochastic effects are important in the dynamics of the polymorphism. Lewontin (1968) simulated a stochastic version of the above model and found that the stochastic dynamics of the population were not sensitive to decreased survival of the tt males unless this loss was on the order of 90%.

TWO-LOCUS MODELS FOR THE MODIFICATION OF SEGREGATION DISTORTION

In the Segregation Distorter (*SD*) complex of *Drosophila melanogaster* and the sex-ratio system of *Aedes aegypti,* the extent to which segregation departs from Mendelian expectations has been shown experimentally to depend on other loci in the organism. These other genes are called modifiers of distortion. They should not be regarded as analogous to the neutral modifiers of recombination, mutation, or migration described above, because distortion modifiers affect gametic fitness and are, therefore, not neutral. It is of interest, however, to ask how two-locus distortion systems compare in their dynamics to two-locus viability systems. The two cases studied seem to exhibit some consistent differences.

The Two-Locus SD *Model*

Prout et al. (1973) proposed the following two-locus extension of the model described above (see the subsection "*The Segregation Distorter Complex*"). One locus with alleles D and d is subject to viability-level selection with the relative viabilities of DD, Dd, and dd given as 1, w_1, and w, respectively, as in specification (6). A second modifier locus with alleles M and m controls the extent of

segregation distortion in gametes produced by *Dd* individuals as follows:

modifier genotype	*MM*	*Mm*	*mm*
fraction of *d* produced	k_1	k_2	0.5

Thus, fixation of *m* entails Mendelian segregation at the *D*/*d* locus; fixation of *M* results in the dynamics described above with k_1 substituted for *k*. The recombination between the *D*/*d* and *M*/*m* loci is *r*. Let the frequencies of *DM*, *Dm*, *dM*, and *dm* be x_1, x_2, x_3, and x_4, respectively. Then, evolution at the two loci is described by the system

$$\bar{w}x_1' = x_1(x_1 + x_2) + 2x_1x_3w_1(1 - k_1) + 2w_1(1 - k_2)[rx_2x_3 + (1 - r)x_1x_4], \quad (16a)$$

$$\bar{w}x_2' = x_2(x_1 + x_2) + x_2x_4w_1 + 2w_1(1 - k_2)[rx_1x_4 + (1 - r)x_2x_3], \quad (16b)$$

$$\bar{w}x_3' = wx_3(x_3 + x_4) + 2x_1x_3w_1k_1 + 2w_1k_2[rx_1x_4 + (1 - r)x_2x_3], \quad (16c)$$

$$\bar{w}x_4' = wx_4(x_3 + x_4) + x_2x_4w_1 + 2w_1k_2[rx_2x_3 + (1 - r)x_1x_4], \quad (16d)$$

where

$$\bar{w} = (x_1 + x_2)^2 + 2(x_1 + x_2)(x_3 + x_4)w_1 + (x_3 + x_4)^2w. \quad (16e)$$

We cannot produce here a detailed description of the properties of system (16) or of the extensions discussed by Charlesworth and Hartl (1978). Instead, we list some of the interesting results and compare them with the results for viability selection at two loci, where Mendelian segregation was assumed (see above).

Result 1.—Suppose that $w_1 > 1$ and $w_1 > w$ (heterozygote advantage); then, with *m* fixed, there is a one-locus two-allele stable equilibrium in the $x_2 - x_4$ boundary where *m* is fixed. Introduction of *M* near this equilibrium perturbs the segregation away from Mendelian expectations. Hartl (1975) and Liberman (1976) showed that such a distorting allele (*M*) invades the population, provided that $0 \leq r < \frac{1}{2}$ (see also Thomson and Feldman 1976). In other words, if the distortion modifier is linked to the distorted gene, then Mendelian segregation is unstable.

Result 2.—Suppose that $2w_1(1 - k_1) > w$ and $2w_1k_1 > 1$. Then, equilibrium (10) (with k_1 substituted for *k*) is stable in the $x_1 - x_3$ boundary where *M* is fixed. Near this equilibrium, *m* appears, changing the proportion of *d* gametes produced by *Dd* genotypes from k_1 to k_2 in the *Mm* heterozygotes. If the inequalities $k_2 > k_1 > \frac{1}{2}$ or $\frac{1}{2} > k_1 > k_2$ are satisfied, then *m* invades, provided that $r < (k_1 - k_2)/(1 - 2k_2)$. Otherwise, *m* invades for all recombination values. In other words, more intense distortion by *Mm*, in the same direction as that induced by *MM*, is favored if the genes are tightly linked. If *Mm* genotypes have less distortion than *MM* genotypes (e.g., if $k_1 > k_2 > \frac{1}{2}$), then *m* invades if $0 \leq r \leq \frac{1}{2}$. From results 1 and 2 we see that if invasion of a new distorting allele depends on *r*, then tighter linkage favors invasion, just as in the case of viability selection at two loci with Mendelian segregation.

Result 3.—Eshel (1985) examined the special case of $r = \frac{1}{2}$, which is excluded from result 1, and demonstrated that, if segregation at equilibrium is non-Mendelian, then invasion by any allele that reduces the average level of distortion

will occur. For $r = \frac{1}{2}$, Mendelian segregation has the property of evolutionary genetic stability (according to the definition of Eshel and Feldman 1982).

Result 4.—In an extensive analysis of the case when $k_1 = k_2 = 1$ and $w_1 = 1$, Prout et al. (1973) found a single equilibrium:

$$\begin{aligned} \hat{x}_1 &= 0\,, \\ \hat{x}_2 &= (2r - w)/(1 - w)\,, \\ \hat{x}_3 &= (1 - 2r)^2/(1 - w)\,, \\ \hat{x}_4 &= 2r(1 - 2r)/(1 - w)\,, \end{aligned} \tag{17}$$

which is locally stable if

$$\tfrac{1}{2} > r > w/2\,. \tag{18}$$

With $k_1 = k_2 \neq 1$ and $w_1 = 1$, there is a single polymorphic equilibrium whose stability depends on r according to

$$\tfrac{1}{2} > r > (2k_1 + w - 2)/2(2k_1 - 1)\,, \tag{19}$$

which reduces to inequality (18) when $k_1 = 1$. When $k_1 = k_2 \neq 1$ and $w_1 \neq 1$, the upper bound for r in the analogous condition to inequality (19) may be reduced below $\frac{1}{2}$. All these equilibria have linkage disequilibrium, but even in the simple case of equilibrium (17), the magnitude of the linkage disequilibrium is not a decreasing function of r throughout the range $\frac{1}{2} > r > w/2$. In fact, for $w/3 + \frac{1}{6} > r > w/2$, the product $\hat{x}_2\hat{x}_3$ from equilibrium (17) increases with r. It then decreases for $w/3 + \frac{1}{6} < r < \frac{1}{2}$. Thus, we have the following results (Thomson and Feldman 1976).

Result 5.—With any parameter set examined ($k_1 = k_2$ or $k_1 \neq k_2$), whenever an equilibrium with $\hat{D} \neq 0$ is stable, $|\hat{D}|$ increases as r increases, achieves a maximum, and then decreases. This is in direct contrast to the result when Mendelian segregation was assumed.

Result 6.—When $k_1 \neq k_2$, there is an equilibrium with $\hat{D} = 0$. This equilibrium is stable in an interval of recombination values strictly contained between 0 and $\frac{1}{2}$. Again, this result stands in direct contrast to the stability properties of $\hat{D} = 0$ with Mendelian segregation.

Sex-Ratio Distortion in Aedes aegypti

The genetics of sex-ratio control in mosquitoes are described by Wood and Newton (1991). Maffi and Jayakar (1981) proposed a two-locus model for the determination of sex in *Aedes aegypti*. The first gene is a sex-determination locus with alleles M and m, such that Mm individuals are males and mm individuals are females. Linked to M/m is another locus with alleles A_i, which operate to produce probabilities s_{ij} that males of genotype MA_i/mA_j transmit M; with complementary probability $1 - s_{ij}$, they transmit m. It is assumed that these segregation probabilities are symmetrical ($s_{ij} = s_{ji}$). Maffi and Jayakar studied the case of two alleles, A_1 and A_2, and the multiple-allele case was analyzed by Lessard (1987). For the present purposes, it is enough to concentrate on the two-allele

case, for which new phenomena have recently been discovered (Feldman and Otto 1989).

Suppose that x_1 and $x_2 = 1 - x_1$ are the frequencies of mA_1 and mA_2, respectively, among all gametes transmitted by females; y_1 and $y_2 = 1 - y_1$ are the frequencies of MA_1 and MA_2, respectively, among all M gametes transmitted by males; and z_1 and $z_2 = 1 - z_1$ are the frequencies of mA_1 and mA_2, respectively, among all m gametes transmitted by males. The two genes evolve according to the system

$$x_1' = (x_1 + z_1)/2, \tag{20a}$$

$$y_1' = [(1 - r)x_{1\cdot}y_1 + rx_1y_{1\cdot}]/\bar{s}, \tag{20b}$$

$$z_1' = [ry_1(1 - x_{1\cdot}) + (1 - r)x_1(1 - y_{1\cdot})]/(1 - \bar{s}), \tag{20c}$$

where

$$x_{i\cdot} = \sum_{j=1}^{2} s_{ij}x_j, \qquad y_{i\cdot} = \sum_{j=1}^{2} s_{ij}y_j, \tag{20d}$$

and

$$\bar{s} = \sum_{i=1}^{2} y_i x_{i\cdot} = \sum_{i=1}^{2} x_i y_{i\cdot} = \sum_i \sum_j s_{ij}x_i y_j \tag{20e}$$

(Lessard 1987).

Maffi and Jayakar (1981) emphasized the cases

$$s_{12} > s_{11} \text{ and } s_{22} \qquad \text{and} \qquad s_{12} < s_{11} \text{ and } s_{22} \tag{21}$$

when an equilibrium exists of the form

$$\hat{x}_1 = \hat{y}_1 = \hat{z}_1 = (s_{12} - s_{22})/(2s_{12} - s_{11} - s_{22}). \tag{22}$$

Lessard (1987) showed that, with multiple alleles, there is a corresponding isolated equilibrium with $\hat{x}_i = \hat{y}_i = \hat{z}_i$ given by the usual one-locus multi-allelic polymorphism with viability matrix $[s_{ij}]$. Equilibria of this form exhibit linkage equilibrium, since the frequencies of the A_i alleles are independent of whether they occur on MA_i or mA_i chromosomes.

Result 1.—Equilibria of the form of equilibrium (22) are stable in an interval of recombination values bounded by $r^* > 0$ and $r^{**} \leq \frac{1}{2}$. This is analogous to result 6 for the *SD* complex: in two-locus segregation-distortion models, linkage equilibrium may be stable for an interval of recombination values fully contained in the interval between 0 and $\frac{1}{2}$ (Thomson and Feldman 1976).

Result 2.—Under conditions (21) when $r < r^*$, Maffi and Jayakar (1981) found numerically that no isolated point was stable and that cycling occurred. Lessard (1987) argued that such periodic orbits are expected according to Hopf bifurcation theory.

Result 3.—When inequalities (21) do not hold, we have discovered polymorphic equilibria that have linkage disequilibrium and that may be stable for

$r \in [0, \frac{1}{2}]$ or for $r \in [0, r_0]$. In the latter case, fixation in one of the A_i becomes stable for $r \in [r_0, \frac{1}{2}]$. This new class of polymorphic equilibria may be stable for $r \in [r^{**}, \frac{1}{2}]$ (see result 2) under conditions (21) and may be stable simultaneously with fixation in one of the A alleles (Feldman and Otto 1989).

Result 4.—Suppose that the population is fixed for A_1 ($x_2 = y_2 = z_2 = 0$) and that A_2 arises near this fixation state. Then, if $\frac{1}{2} > s_{11} > s_{12}$ or $s_{12} > s_{11} > \frac{1}{2}$, such that A_2 causes increased distortion, then A_2 increases in frequency if $r < (s_{11} - s_{12})/(1 - 2s_{12})$. Otherwise, A_2 invades for all r between 0 and $\frac{1}{2}$. If this result is compared with result 2 for the *SD* complex, substituting k_1 for s_{11} and k_2 for s_{12}, we see that the two results are equivalent (Feldman and Otto 1989).

MODIFICATION OF RECOMBINATION IN TWO-LOCUS MODELS OF SEGREGATION DISTORTION

Consider a third locus, F, with alleles f_1 and f_2, whose function is to control the extent of recombination between the major loci D/d and M/m in the *SD* complex and between M/m and A_1/A_2 in the sex-ratio model treated above. For precision, suppose that the order is *FDM* or *FMA*. The genotypes f_1f_1, f_1f_2, and f_2f_2 produce recombination rates r_{11}, r_{12}, and r_{22}, respectively, between the major loci and have no other effects on distortion or viability. Suppose further that R is the recombination fraction between F and D or between F and M and that there is no interference in the recombination process. The population is initially fixed for f_1, such that the recombination fraction between the major loci is r_{11}, and it is assumed that the population is initially at equilibrium with the major loci in linkage disequilibrium. We then ask for the conditions under which f_2 increases in frequency after its introduction near the equilibrium. Recall that in the case of Mendelian segregation, this condition was simply $r_{12} < r_{11}$ for all R, independent of the order of the three genes.

For the *SD* complex, the only case analyzed thoroughly has $k_1 = k_2 = 1$ and $w_1 = 1$, as studied by Prout et al. (1973), and the results are as follows.

Result 1.—When rare, f_2 increases in frequency, provided that

$$0 \leq R < r_{11} \quad \text{and} \quad r_{12} < r_{11} \tag{23a}$$

or that

$$R > r_{11} \quad \text{and} \quad r_{12} > r_{11} \tag{23b}$$

(Thomson and Feldman 1974). Thus, there is dependence on the linkage between F and D/d; tight linkage causes reduction of recombination between D/d and M/m, and loose linkage causes its increase.

Result 2.—A qualitatively similar result to result 1 holds for linkage modification in the model of sex-ratio distortion (Feldman and Otto 1989). For small enough R, reduced recombination between M/m and A_1/A_2 is favored, and for large enough R, increased recombination is usually favored. The cutoff points for R are not as simple as inequalities (23), and it is conjectured that more general versions of the two-locus *SD* model will also produce conditions more complicated than (23).

Result 3.—In the model of sex-ratio distortion, if r_{12} is greater than both r_{11}

and r_{22}, an equilibrium exists of the form given by equation (5), $\hat{P}_{f_1} = (r_{12} - r_{22})/(2r_{12} - r_{11} - r_{22})$, such that the frequency of f_1 is stable, for large enough R. If r_{12} is less than both r_{11} and r_{22}, this equilibrium is stable for small R, which is exactly the opposite of the condition noted with Mendelian segregation (Feldman and Otto 1989).

CONCLUSION

Most qualitative principles that can be drawn from viability selection acting alone on one or two loci are violated in the presence of gametic selection caused by meiotic drive. It is difficult to predict a priori what the nature of such violations could be. Nevertheless, the results summarized here show that there exist patterns of concordance among the various distortion models. It remains to be understood why this concordance exists and to determine whether the behavior of models with non-Mendelian segregation should be regarded as anomalous or as characteristic of more general models of natural selection than have been analyzed in detail. It might be conjectured, for example, that further development of the theory of fertility or sexual selection might reveal that the elegant behavior of classical viability models is in fact the anomaly.

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