

# The Effects of Intraspecific Competition and Stabilizing Selection on a Polygenic Trait

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## ABSTRACT

The equilibrium properties of an additive multilocus model of a quantitative trait under frequency- and density-dependent selection are investigated. Two opposing evolutionary forces are assumed to act: (i) stabilizing selection on the trait, which favors genotypes with an intermediate phenotype, and (ii) intraspecific competition mediated by that trait, which favors genotypes whose effect on the trait deviates most from that of the prevailing genotypes. Accordingly, fitnesses of genotypes have a frequency-independent component describing stabilizing selection and a frequency- and density-dependent component modeling competition. We study how the equilibrium structure, in particular, number, degree of polymorphism, and genetic variance of stable equilibria, is affected by the strength of frequency dependence, and what role the number of loci, the amount of recombination, and the demographic parameters play. To this end, we employ a statistical and numerical approach, complemented by analytical results, and explore how the equilibrium properties averaged over a large number of genetic systems with a given number of loci and average amount of recombination depend on the ecological and demographic parameters. We identify two parameter regions with a transitory region in between, in which the equilibrium properties of genetic systems are distinctively different. These regions depend on the strength of frequency dependence relative to pure stabilizing selection and on the demographic parameters, but not on the number of loci or the amount of recombination. We further study the shape of the fitness function observed at equilibrium and the extent to which the dynamics in this model are adaptive, and we present examples of equilibrium distributions of genotypic values under strong frequency dependence. Consequences for the maintenance of genetic variation, the detection of disruptive selection, and models of sympatric speciation are discussed.

**M**ANY ecologically important traits are subject to frequency- and density-dependent selection. Typical situations leading to such selection include attacks of parasites, presence of predators or competitors, resource utilization, sexual dimorphism, and behavioral variability. Although it has been long known among population geneticists that frequency-dependent selection (FDS) can maintain genetic polymorphism much easier than frequency-independent selection (*e.g.*, WRIGHT 1969; COCKERHAM *et al.* 1972; MATESSI and JAYAKAR 1976; CLARKE 1979; CHRISTIANSEN and LOESCHCKE 1980; ASMUSSEN 1983; ASMUSSEN and BASNAYAKE 1990), even some pioneers in studying the evolutionary significance of frequency dependence (FD) are skeptical whether FD is responsible for a large fraction of observed polymorphisms (MAYNARD SMITH 1998). In con-

trast, CLARKE (2004) argues on the basis of an extensive review of empirical results that “The case for frequency dependence as a major factor in maintaining non-synonymous polymorphisms seems overwhelming.” However, he also stresses the importance of more empirical work needed to discriminate between FDS and other forms of balancing selection. Often, however, FDS will interact with other forms of selection, or act in addition to them, frequently on quantitative traits (*e.g.*, BULMER 1974, 1980; SLATKIN 1979; CLARKE *et al.* 1988). In such cases, an evaluation of the importance of FDS in maintaining genetic variation relative to selective pressures that are likely to be frequency independent, such as many caused by the abiotic environment or arising from the requirements of a functional morphology and developmental and physiological constraints, may be particularly difficult. One reason is that the determination of the kind and strength of selection acting on a (set of) trait(s) is everything but straightforward (*e.g.*, LANDE and ARNOLD 1983; ENDLER 1986; SCHLUTER 1988; KINGSOLVER *et al.* 2001). Second, the majority of theoretical studies of the evolutionary consequences of FDS either ignore genetics (*e.g.*, evolutionary game theory and the so-called adaptive

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dynamics approach) or are based on very simple genetic models (a single locus or a normally distributed trait with given variance). Therefore, little is known about the patterns of genetic variation maintained by FDS.

General and systematic treatments of genetic models with frequency- and density-dependent selection are available only for a single locus (NAGYLAKI 1979; ASMUSSEN 1983; ASMUSSEN and BASNAYAKE 1990). In these models, fitnesses are assigned directly to genotypes, though in a rather general way. These and other investigations clearly demonstrate that FDS may strongly influence the genetic structure of a population and has a much higher potential in maintaining genetic variation than frequency-independent selection. In addition, already for one-locus two-allele models in which genotypic fitnesses are linear functions of the genotype frequencies, complex dynamic behavior, such as chaos, may occur for relatively wide ranges of parameter values (ALTENBERG 1991; GAVRILETS and HASTINGS 1995).

We pursue a different approach by making specific assumptions on how selection acts on phenotypes. In doing so, we lose generality compared to some of the single-locus studies. However, it enables us to tackle questions such as, How strong must FD be relative to other selective forces, such as stabilizing selection, to have a noticeable impact on the genetic structure of a population? or, When is FD strong enough to be phenotypically detectable? To this end, we consider a quantitative trait that is subject to (frequency-independent) stabilizing selection and mediates frequency- and density-dependent selection through intraspecific competition; *i.e.*, individuals of similar phenotypes compete. We use a functional form for fitness of the trait introduced by BULMER (1974, 1980) that does not specify the causes of stabilizing selection, *i.e.*, whether real or induced by pleiotropic effects. Nevertheless, mathematically this model is closely related to models based on differential resource utilization and a Lotka-Volterra approach (SLATKIN 1979; CHRISTIANSEN and LOESCHCKE 1980; LOESCHCKE and CHRISTIANSEN 1984). Previous studies of this type of model assumed a single locus contributing to a normally distributed trait (BULMER 1974, 1980; SLATKIN 1979), a classical quantitative-genetics approach for a normally distributed trait (SLATKIN 1979), a single locus with multiple alleles (CHRISTIANSEN and LOESCHCKE 1980), or two recombining diallelic loci contributing additively to a quantitative trait without assumptions on its distribution (LOESCHCKE and CHRISTIANSEN 1984; BÜRGER 2002a,b). Roughly, conditions were identified under which FD is strong enough to induce disruptive selection and maintain polymorphism. In the two-locus models, the amount of genetic variation and the possible equilibrium patterns and their dependence on the parameters were derived.

Studies with simple genetics (BULMER 1974, 1980; SLATKIN 1979) have shaped our intuition of the role of intraspecific competition in maintaining genetic varia-

tion by showing that if the strength of competition relative to stabilizing selection exceeds a certain threshold, the trait is under disruptive selection; hence genetic variance should be maintained. Otherwise, the trait is under stabilizing selection, which usually depletes heritable variation (see also the DISCUSSION). However, questions concerning the extent of variation maintained by FDS or if and how conclusions depend on the underlying genetic structure can be answered only on the basis of more explicit genetic models.

We complement and extend previous studies in several directions. First, we admit multiple diallelic loci to contribute (additively) to the trait. Second, the population size is allowed to change according to its demographic dynamics. Because random genetic drift is ignored, the dynamics are still deterministic. Third, stabilizing selection that is asymmetric with respect to the existing range of phenotypic values is explored. Fourth, to cover a wide range of parameters, in particular from the high-dimensional genetic parameter space, we adopt the statistical and numerical approach of BÜRGER and GIMELFARB (1999, 2002). Thus, for a given number of loci, a range of recombination rates, and given ecological and demographic parameters, we calculate the quantities of interest by iterating a large number of genetic systems with randomly chosen locus effects and initial conditions until equilibrium is reached and then computing the appropriate averages. This numerical approach is complemented by analytical results and allows us to derive general inferences on the patterns of genetic variation resulting from the interaction of multilocus genetics with FDS. In particular, the strength of FD that leads to highly polymorphic genetic systems and to disruptive selection is determined. Also the evolution of mean fitness and of the equilibrium distribution of genotypic values under strong FD is examined.

This is not the first multilocus study exploring the amount of genetic variation maintained by FDS on a quantitative trait. CLARKE *et al.* (1988) and MANI *et al.* (1990) employed a model of selection that is similar to BULMER's (1980), but differs in the way competition and stabilizing selection are modeled. Moreover, they assume a finite population and admit several multiallelic loci with recurrent mutation. Their results are purely numerical and the main focus is on variation at the gene level. Therefore, direct comparison with the models discussed above is difficult. The purpose of our study is not to demonstrate that FDS can be important, but rather to identify conditions under which it has significant effects on the genetic structure of a population, what and how large these effects are, and how genetical and ecological parameters interact.

## THE MODEL

We consider a randomly mating diploid population with discrete generations and equivalent sexes that is

sufficiently large to ignore random genetic drift. Selection acts only through differential viabilities. Individual fitness is assumed to be determined by two components: (i) by stabilizing selection on a quantitative character and (ii) by competition among individuals. The trait is determined by  $n$  additive, diallelic loci of arbitrary effect. The model is an extension of that used in BÜRGER (2002b).

**Ecological assumptions:** The first fitness component is frequency independent and may reflect some sort of direct selection on the trait, for example, through differential supply of a resource whose utilization efficiency is phenotype dependent. However, frequency-independent stabilizing selection could as well be caused by indirect selection through pleiotropic side effects of alleles that contribute primarily to fitness-related traits (*e.g.*, ROBERTSON 1967; KEIGHTLEY and HILL 1990; BÜRGER 2000, chap. VII). We ignore environmental variation and deal directly with the fitnesses of genotypic values. In the absence of genotype-environment interaction, this is no restriction because in the present model the only effect of including environmental variance was a deflation of the selection intensity. For simplicity, we sometimes use the words genotypic value and phenotype synonymously.

Stabilizing selection is modeled by the quadratic function

$$S(g) = 1 - \frac{(g - \theta)^2}{2V_s}, \quad (1)$$

where  $V_s$  is an inverse measure for the strength of stabilizing selection and  $\theta$  is the position of the optimum. Of course,  $S(g)$  is assumed to be positive on the range of possible phenotypes, thus restricting the admissible values of  $V_s$ . We use a scale on which the range of possible phenotypes is the interval  $[0, 1]$  (see *Genetic assumptions* below). Hence, if  $\theta \geq 0.5$ , then  $V_s$  must satisfy  $V_s \geq \frac{1}{2}\theta^2$ . We exclude pure directional selection by assuming  $0 < \theta < 1$ .

The second component of fitness is FD. We assume that competition between phenotypes  $g$  and  $h$  can be described by

$$\alpha(g, h) = 1 - \frac{1}{2V_\alpha}(g - h)^2, \quad (2)$$

with the obvious constraint that the maximum difference between genotypic values must be no larger than  $\sqrt{2V_\alpha}$ . For our scaling this means  $V_\alpha \geq 0.5$ . Equation 2 implies that competition between individuals of similar phenotypes is much stronger than that between individuals of very different phenotypes, as will be the case if different phenotypes preferentially utilize different food resources. Small  $V_\alpha$  implies a strong frequency-dependent effect of competition, whereas in the limit  $V_\alpha \rightarrow \infty$ , FD vanishes. Let  $P(h)$  denote the relative frequency of individuals with phenotype  $h$ . Then the intra-

specific competition function  $\bar{\alpha}_P(g)$ , which measures the strength of competition experienced by phenotype  $g$  if the population distribution is  $P$ , is given by

$$\bar{\alpha}_P(g) = \sum_h \alpha(g, h)P(h)$$

and calculated to be

$$\bar{\alpha}_P(g) = 1 - \frac{1}{2V_\alpha}[(g - \bar{g})^2 + V_A]. \quad (3)$$

Here,  $\bar{g}$  and  $V_A$  denote the mean and (additive genetic) variance, respectively, of the distribution  $P$  of genotypic values.

Similar to BULMER's (1974, 1980) model, we assume that the absolute fitness of an individual with genotypic value (phenotype)  $g$  is given by

$$W(g) = \left( \rho - \frac{N}{\kappa} \bar{\alpha}_P(g) \right) S(g), \quad (4)$$

where  $\rho$  and  $\kappa$  are positive parameters and  $N$  denotes the total population size. For notational simplicity, the dependence of  $W(g)$  on  $N$  and  $P$  is omitted. In the context of density-dependent growth models, the parameter  $\rho$  in (4) is related to the growth rate of the population and  $\kappa$  is proportional to the carrying capacity. More precisely, in a monomorphic population in which  $g = \bar{g} = \theta$  and  $V_A = 0$ , the fitness (of the population) becomes  $\rho - N/\kappa$ ; hence the carrying capacity is

$$K = \kappa(\rho - 1). \quad (5)$$

Our model of FDS is closely related to models that are based on Lotka-Volterra equations (SLATKIN 1979; CHRISTIANSEN and LOESCHCKE 1980; LOESCHCKE and CHRISTIANSEN 1984). The relation between these models and ours is worked out in BÜRGER (2002b), where it is shown that all these ecological models lead to fitness functions that are mathematically equivalent to first order in  $1/V_s$  and  $1/V_\alpha$ . Thus, for sufficiently weak overall selection, the differences vanish. As explained in BÜRGER (2002b), the present choice of the fitness function makes the model more easily amenable to mathematical analysis and does not lead to certain special effects that a Gaussian fitness function causes under strong selection. If stabilizing selection is modeled by a Gaussian fitness function, the equilibrium structure is much more complex than with quadratic fitness. This is so in the absence of FD (NAGYLAKI 1989; WILLENSDORFER and BÜRGER 2003) as well as for very strong FD (LOESCHCKE and CHRISTIANSEN 1984). Our fitness function is also closely related to that of MATESSI *et al.* (2001); if higher-order terms are omitted, the induced dynamics and equilibrium structure become equivalent.

**Genetic assumptions:** The trait values  $g$  are determined additively by  $n$  diallelic loci. There is no dominance or epistasis. The contribution of one allele at each locus  $\ell$  is zero, and the contribution,  $\beta_\ell$ , of the other allele is a random number between zero and one.

It is assumed that the minimum and maximum genotypic values are always zero and one. Therefore, the actual contribution by the second allele at locus  $\ell$  is scaled to be  $\gamma_\ell = \frac{1}{2} \beta_\ell / \sum_{k=1}^n \beta_k$ . It follows that the genotypic value of the total heterozygote is always  $\frac{1}{2}$ , and the average allelic effect among the  $n$  loci controlling the trait is  $\bar{\gamma} = 1/(2n)$ . This normalization has the advantage that the strength of selection on genotypes can be compared for different numbers of contributing loci. The effect of an increasing number of loci is a finer resolution of possible phenotypes through genotypic values.

**Dynamics:** Gametes are designated by  $i$ , their frequencies among zygotes in consecutive generations by  $p_i$  and  $p'_i$ , and the fitness of a zygote consisting of gametes  $j$  and  $k$  by  $W_{jk}$  (we do not indicate the frequency and density dependence). Let  $R(jk \rightarrow i)$  denote the probability that a randomly chosen gamete produced by a  $jk$  individual is  $i$ . The function  $R$  is determined by the pattern of recombination between loci. Since random mating is assumed and gamete frequencies are measured after reproduction and before selection, Hardy-Weinberg proportions obtain and the genetic dynamics can be described in terms of gamete frequencies by the well-known system of recursion relations

$$p'_i = \bar{W}^{-1} \sum_{j,k} W_{jk} p_j p_k R(jk \rightarrow i), \quad (6)$$

where  $\bar{W} = \sum_{j,k} W_{jk} p_j p_k$  is the mean fitness (e.g., BÜRGER 2000).

The ecological dynamics follow the standard recursion

$$N' = N\bar{W}. \quad (7)$$

Thus, for a genetically monomorphic population with  $g = \bar{g} = \theta$  and  $V_A = 0$ , the classical discrete logistic equation is obtained,  $N' = N(\rho - N/\kappa)$ . As is well known, monotone convergence to the carrying capacity  $K = \kappa(\rho - 1)$  occurs if and only if  $\rho \leq 2$  and oscillatory convergence occurs if  $2 < \rho \leq 3$  (e.g., BÜRGER 2000). Throughout this study, we are concerned only with sufficiently small values  $\rho$  so that the ecological dynamics are simple; i.e., convergence to a unique equilibrium population size occurs. Also the initial  $N_0$  was chosen sufficiently small (except for exploratory reasons,  $N_0 = K$ ) so that population size always remained positive. Because this study is devoted to the equilibrium structure and the equilibrium population size is uniquely determined if  $\rho \leq 3$ , this choice of  $N_0$  is no restriction.

## THE STATISTICAL APPROACH

Usually, parameters of genetic systems controlling quantitative traits are unknown or can be inferred only indirectly. Since, in addition, the dimensionality of the parameter space and the number of gametes and genotypes increases rapidly with the number of loci, an ex-

PLICIT and analytical characterization of the equilibrium properties of multilocus models in terms of all parameters and initial conditions would be of limited value, even if it were feasible. Therefore, we use a different approach by evaluating the quantities of interest for many randomly chosen parameter sets and initial conditions and, consequently, obtaining statistical results.

We proceeded as follows. For a given set of *ecological* parameters ( $\rho, \kappa, V_\alpha, \theta, V_s$ ), a given number  $n$  of loci, and a given range of recombination rates, we constructed  $\geq 1000$  of what we call *genetic* parameter sets (allelic effects of loci and recombination rates between adjacent loci from the given range). For each genetic parameter set, allelic effects were obtained by generating values  $\beta_\ell$  ( $\ell = 1, 2, \dots, n$ ) as independent random variables, uniformly distributed between 0 and 1, and transforming them into the actual allelic effects,  $\gamma_\ell = \frac{1}{2} \beta_\ell / \sum_k \beta_k$ . The additivity assumption yields the genotypic values, and from Equations 1, 3, and 4, the genotypic fitnesses  $W_{jk}$  are calculated in each generation. Recombination rates between adjacent loci,  $r_{\ell, \ell+1}$  ( $\ell = 1, \dots, n-1$ ), were either assumed to be all  $\frac{1}{2}$  or obtained as independent random variables, uniformly distributed between 0 and 0.01. We assumed absence of interference and refer to these two scenarios as free recombination and tight linkage, respectively.

For each of such constructed genetic parameter sets, the recursion relations (6) and (7) were numerically iterated starting from 10 different randomly chosen initial gamete distributions. To make the initial distributions more evenly distributed in the gamete state space, they were chosen such that the (Euclidean) distance between any two of them was no less than a predetermined value (0.25, 0.30, and 0.35 for two, three, and four loci, respectively). An iteration was stopped after generation  $t$  when either an equilibrium was reached (in the sense that the geometric distance between gamete distributions in two consecutive generations was  $< 10^{-12}$ ), or  $t$  exceeded  $10^6$  generations (in some cases even  $10^7$ ). If equilibrium was not reached, the parameter combination was excluded from the analysis. Usually, the proportion of excluded runs was small enough not to introduce a bias. In a small region of ecological parameters (the so-called transitory region, see next section), extremely slow convergence was the rule because of very flat fitness landscapes. Since for some parameter combinations in this region only  $\sim 20\%$  of the runs converged within  $10^6$  generations, we stopped runs that had not converged only after  $10^7$  generations. At that time  $\sim 90\%$  had fulfilled our convergence criterion. If convergence within the specified maximum number of generations did not occur, it was because of extremely slow convergence of allele frequencies. Apart from a very flat fitness function, the main reason for slow convergence was the presence of alleles of extremely small effect. No instance of complicated dynamic behavior was detected.

For each parameter combination with  $n \leq 4$  loci, all statistics are based on 1000 genetic parameter sets that led to equilibration; for  $n = 5$  loci they are based on 500 such genetic parameter sets. For each parameter set we calculated the number of different equilibria, the gamete frequencies at each equilibrium, and the number of trajectories (initial distributions) converging to each equilibrium. Using this database, the equilibrium properties were analyzed. Whenever we use the term equilibrium without qualification, we mean a (locally asymptotically) stable equilibrium, unless otherwise mentioned.

Most of our numerical results are for two, three, and four loci; only a few are for five or more because some four- and most five-locus parameter combinations are extremely time consuming. With five loci, for instance, 1600 generations take  $\sim 1$  sec on an AMD Athlon processor with 1.3 GHz. Since with five loci, typical runs for weak or very strong FD equilibrate only after several hundred thousand generations (for intermediate FD more than 10 times as many), 10 initial conditions for each parameter combination are taken, and average statistics are performed over 500 genetic parameter sets, the computing time was correspondingly long. The total computer time for the project was equivalent to  $\sim 2$  CPU years, but we used several computers.

PROPERTIES OF GENETIC VARIATION AT EQUILIBRIUM

In this section, we explore how the genetic variation maintained at equilibrium is affected by the strength of FD relative to pure stabilizing selection and what role the other parameters in the model, such as number of loci, recombination rates, position of the optimum, and the demographic parameters, play. For this purpose, we study the equilibrium properties, *i.e.*, the number of stable equilibria and their degree of polymorphism, the genetic variance maintained, and the amount of linkage disequilibrium.

For each parameter combination, we recorded the equilibria to which at least 1 of the 10 trajectories converged, their number, the number of trajectories converging to a given equilibrium, the number of polymorphic loci at each equilibrium, the (additive) genetic variance,  $V_A$ , and the genic variance,  $V_{LE}$  (*i.e.*, the variance that would be observed under linkage equilibrium), at equilibrium. As a measure for global linkage disequilibrium, we use the ratio  $V_A/V_{LE}$ . To facilitate the comparison of genetic systems with different numbers of loci, we calculated the ratio  $V_r = V_A/V_{max}$  of the genetic variance and the maximum possible variance,  $V_{max}$ , in the given genetic system under the assumption of linkage equilibrium.

These values were then averaged over all 1000 genetic parameter sets, and standard deviations were calculated. This yielded our “quantities of interest” for each set of

ecological parameters, number of loci, and recombination scenario. The data presented in the figures and tables are such averages. We denote the average over  $V_r$  by  $\bar{V}_r$  and refer to it as the relative genetic variance. Its use is preferable when comparing systems with different numbers of loci, because the variance itself is strongly dependent on the average effect among loci, which decreases in proportion to  $1/(2n)$ . For a given number of loci, the relative genetic variance  $\bar{V}_r$  and the (average) genetic variance  $\bar{V}_A$  behave very similarly (results not shown). Because  $V_{max} = \frac{1}{2} \sum_i \gamma_i^2$ , the expectation (and in principle the whole distribution) of  $V_{max}$  can be calculated for each  $n$ . For  $n = 2, 3, 4$ , we have  $E[V_{max}] = \frac{1}{4}(1 - \ln 2) \approx 0.077$ ,  $\frac{1}{4}(1 + 6 \ln 2 - \frac{1}{2} \ln 3) \approx 0.054$ , and  $\frac{1}{4}(1 - 44 \ln 2 + 27 \ln 3) \approx 0.041$ , respectively. Multiplying  $\bar{V}_r$  by  $E[V_{max}]$  yields an estimate of  $\bar{V}_A$  that typically is within  $\sim 10\%$  of the “true” value (results not shown). The polymorphism displayed in the figures is the average number of polymorphic loci at a stable equilibrium, the average being taken over all 10 trajectories in all 1000 genetic parameter sets.

For later use we note that for any number of loci we have  $V_{max} \leq \frac{1}{8}$ , where the maximum is attained if the alleles at one locus have effects 0 and  $\frac{1}{2}$  and those at other loci have no effect, and  $V_A \leq \frac{1}{8}$ , where the maximum is attained if there are only the two gametes with effects 0 and  $\frac{1}{2}$  in the population, each with frequency  $\frac{1}{2}$ , because zygotes are in Hardy-Weinberg proportions.

For a given number of loci and given recombination scenario, the genetic parameter sets as well as the initial conditions are the same for all ecological parameter sets. Therefore, variation among quantities of interest comes almost exclusively from variation in the ecological parameters. Only the exclusion of slow runs leads to slight variation among the genetic parameter sets used for different ecological parameter combinations.

An important role in this article is played by the quantity

$$f = \frac{V_s}{V_\alpha}, \tag{8}$$

which measures the strength of FD, *i.e.*, the strength of competition relative to stabilizing selection. If  $f = 0$ , there is no FD, whereas  $f \gg 1$  means strong FD. As we see below, the properties of our model depend on  $V_s$  and  $V_\alpha$  separately; however, to leading order in  $1/V_s$  (the strength of stabilizing selection) and  $1/V_\alpha$  (the strength of competition), they depend only on  $f$ . In addition, we introduce the compound demographic parameter

$$\mathfrak{D} = \frac{\rho K}{N} - 1. \tag{9}$$

**The symmetric case:** We begin by discussing numerical results for the symmetric case in which the optimum  $\theta$  coincides with the genotypic value of the completely heterozygote genotypes, *i.e.*,  $\theta = \frac{1}{2}$ . The demographic

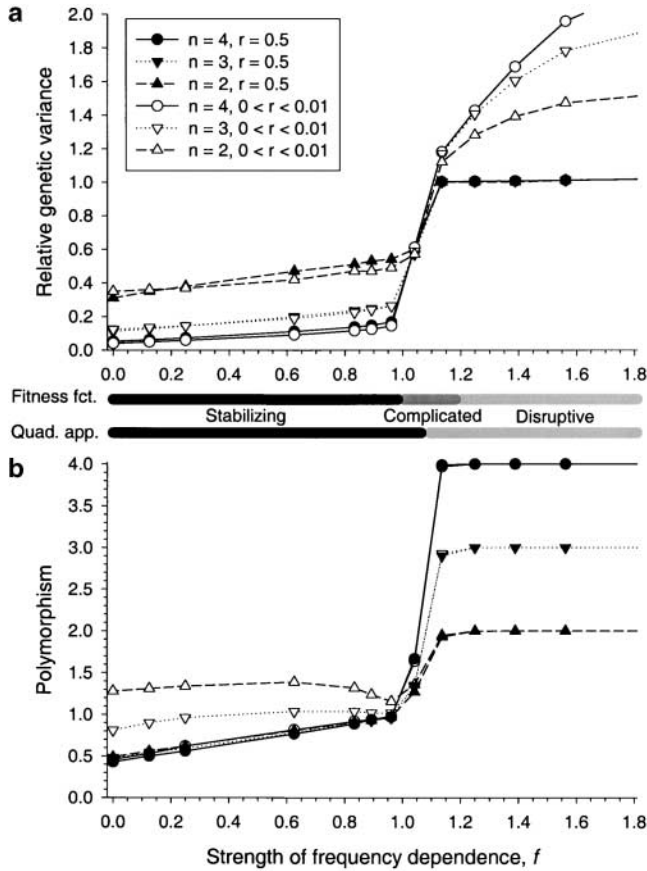


FIGURE 1.—Relative genetic variance (a) and polymorphism (b) as a function of  $f = V_s/V_\alpha$  for  $n = 2, 3,$  and  $4$  loci and free recombination (solid symbols) as well as tight linkage (open symbols). The strength of stabilizing selection is fixed ( $V_s = 1.25$ ; this reduces the fitness of the extreme genotypic values by 10%) and  $V_\alpha$  is varied [the following pairs  $(V_\alpha, f)$  correspond:  $(\infty, 0)$ ,  $(5.0, 0.25)$ ,  $(2.0, 0.63)$ ,  $(1.5, 0.83)$ ,  $(1.3, 0.96)$ ,  $(1.2, 1.04)$ ,  $(1.0, 1.25)$ ,  $(0.8, 1.56)$ , and  $(0.5, 2.5)$ ]. In addition,  $\theta = 0.5$ ,  $\rho = 2$ , and  $\kappa = 10,000$ . The bars between a and b indicate the type of fitness function observed for given  $f$ . The top bar indicates the true fitness function, the bottom bar its quadratic approximation (see DISRUPTIVE vs. STABILIZING SELECTION). Black indicates stabilizing selection ( $\cap$ -shaped); gray, a complicated fitness function (typically M-shaped); and light gray, disruptive selection ( $\cup$ -shaped).

parameters here are  $\rho = 2$  and  $\kappa = 10,000$ . This value of  $\rho$  ensures that rapid convergence of  $N$  to the carrying capacity occurs. The role of  $\rho$  and  $\kappa$  is studied further below.

Figure 1 visualizes some of the most important general findings. It shows a distinct, threshold-like dependence of the (average) relative genetic variance and the (average) amount of polymorphism on  $f$  as  $f$  increases from values  $< 1.0$  to values  $> \sim 1.2$ . This threshold is more pronounced the larger the number of loci is. The genetic variance is slowly, but steadily, increasing with  $f$  if  $f < 1$ . Then a rapid increase occurs in a narrow interval, and for free recombination the genetic variance nearly levels off as  $f$  exceeds  $\sim 1.2$ . For larger values of  $f$  and free recombination, the genetic variance

is very slightly higher than  $V_{\max}$  (actually, very slowly increasing as  $f$  increases further) and nearly independent of the number of loci. The average amount of linkage disequilibrium is very small in this case, even for large values of  $f$ ; *i.e.*, the average  $V_A/V_{LE}$  is always  $< 1.03$  (results not shown). For tight linkage, the genetic variance increases to values much higher than  $V_{\max}$  as  $f$  increases above 1.0. The increase beyond  $V_{\max}$  is almost solely due to the build-up of strong positive linkage disequilibrium; the more loci, the higher the linkage disequilibrium. If  $f \geq 1.25$ , we have  $V_{LE} = V_{\max}$  under both recombination scenarios because then a unique stable, fully polymorphic equilibrium is maintained (see Tables 1 and 2) at which all allele frequencies are  $1/2$ . Therefore, our measure  $V_A/V_{LE}$  for linkage disequilibrium equals  $V_i$  if FD is strong. For weak or moderate FD ( $f < 1$ ), linkage has only a minor, in general diminishing, effect on the genetic variance (the more loci, the weaker the effect). As under pure stabilizing selection (BÜRGER and GIMELFARB 1999), not only the (absolute) genetic variance but also the relative variance decreases with increasing number of loci if FD is weak (for some five-locus data see Table 3).

Figure 1b shows that for  $f \geq 1.25$  all equilibria are completely polymorphic, irrespective of recombination. They are also unique (Tables 1–3) and, as already noted, symmetric in the sense that all allele frequencies are  $1/2$ . They differ, of course, in their linkage disequilibria. If  $f < 1$  and recombination is free, then the average degree of polymorphism is  $< 1$  but steadily increasing and nearly independent of the number of loci. As  $f$  increases beyond 1, a marked increase of polymorphism to the maximum possible amount occurs. For tight linkage and  $f < 1$ , on average equilibria exhibit more polymorphism than for free recombination, and for a range of values  $f$  the amount of polymorphism maintained may even decrease as  $f$  increases. This latter phenomenon is more pronounced if stabilizing selection is stronger (results not shown) and was demonstrated analytically for two loci (BÜRGER 2002a,b).

The bars in different shades of gray between the top and bottom of Figure 1 indicate the shape of the fitness function at equilibrium for the corresponding value  $f$  (see DISRUPTIVE vs. STABILIZING SELECTION).

Tables 1 and 2 provide detailed insights into the effects of increasing FD on the equilibrium structure. For free recombination (Table 1), no stable equilibria with two or more polymorphic loci were found if  $f < 1$ . As Table 1 shows, the introduction of FD leads to a steady increase of single-locus polymorphisms at the expense of stable monomorphic equilibria until a complete restructuring of the equilibrium pattern occurs between  $f = 1$  and  $f = 1.25$ . If  $f > 1$ , stable monomorphic equilibria cease to exist and as soon as  $f \geq 1.25$ , there is a unique stable, fully polymorphic equilibrium. Table 2 shows that similar behavior occurs with linked loci, the difference being that with linkage and weak or moderate

**TABLE 1**  
**Equilibrium structure for  $n = 2, 3,$  and  $4$  loci and free recombination**

$f$	Two loci				Three loci					Four loci					
	No. ( $E$ )	Polymorphism			No. ( $E$ )	Polymorphism				No. ( $E$ )	Polymorphism				
		0	1	2		0	1	2	3		0	1	2	3	4
0.00	2	0.51	0.49	0	2.5 ± 1.0	0.52	0.48	0	0	3.7 ± 1.6	0.57	0.43	0	0	0
0.25	2	0.38	0.62	0	2.6 ± 1.1	0.41	0.59	0	0	3.8 ± 1.7	0.44	0.56	0	0	0
0.50	2	0.26	0.74	0	2.7 ± 1.2	0.28	0.72	0	0	4.0 ± 1.8	0.31	0.69	0	0	0
0.83	2	0.09	0.91	0	2.9 ± 1.3	0.10	0.90	0	0	4.3 ± 1.9	0.11	0.89	0	0	0
0.96	2	0.03	0.97	0	3.2 ± 1.4	0.04	0.96	0	0	4.6 ± 1.9	0.03	0.97	0	0	0
1.04	2	0	0.73	<i>0.27</i>	2.8 ± 0.9	0	0.65	<u>0.35</u>	0	3.6 ± 1.5	0	0.37	<i>0.59</i>	<i>0.04</i>	<i>0.00</i>
1.14	1.1 ± 0.3	0	0.07	<i>0.93</i>	1.1 ± 0.3	0	0.02	<u>0.07</u>	<i>0.92</i>	1.1 ± 0.5	0	0.00	<i>0.00</i>	0	<i>0.99</i>
1.25	1	0	0	<i>1</i>	1	0	0	0	<i>1</i>	1	0	0	0	0	<i>1</i>
1.56	1	0	0	<i>1</i>	1	0	0	0	<i>1</i>	1	0	0	0	0	<i>1</i>
2.50	1	0	0	<i>1</i>	1	0	0	0	<i>1</i>	1	0	0	0	0	<i>1</i>

Presented are the average number of equilibria ± the standard deviation, denoted by No. ( $E$ ), and the proportion of trajectories converging to an equilibrium with the indicated number of polymorphic loci. Italic type indicates that all equilibria of this type have nonnegative linkage disequilibrium. Underlined italic type indicates that negative and nonnegative linkage disequilibria occur. The following parameters are the same in all cases:  $\kappa = 10,000$ ,  $\rho = 2$ ,  $V_s = 1.25$ ,  $\theta = 0.5$ . Data are not shown for all values  $f$  displayed in Figure 1 but, in addition, data for the largest possible  $f$  ( $f = 2.5$ ) are included. (Integer entries such as 0, 1, or 2 mean exactly this value, *i.e.*, no variation among the 1000 genetic parameter sets was observed.)

FD, stable equilibria may exist at which two or more loci are polymorphic. But again, single-locus polymorphisms are increasing with increasing  $f$  at the expense of stable equilibria with no or more than one polymorphic locus. As in the case of free recombination, if  $f > 1$ , stable equilibria cannot be monomorphic, and if  $f \geq 1.25$ , there is a unique fully polymorphic equilibrium with all allele frequencies equaling  $\frac{1}{2}$ . We call the region in which the degree of polymorphism and genetic variance increase rapidly the transitory region.

Table 2 shows that for  $f < 1$ , multilocus polymorphisms, provided they exist, always have negative linkage disequilibrium. In the transitory region, polymorphisms with negative, zero, and positive linkage disequilibrium

may exist, whereas for large enough  $f$  all equilibria exhibit positive linkage disequilibrium. In the transitory region, the equilibrium structure may be rather complex and several stable equilibria with different degrees of polymorphism may coexist for certain parameter combinations. For instance, with four loci, free recombination,  $V_s = 1.25$ , and  $f = 1.04$  (as in Figure 1 and Table 1), an unsymmetric four-locus polymorphism coexisting with six two-locus polymorphisms was found. A detailed analytical study of the two-locus model with  $\theta = \frac{1}{2}$  was performed by BÜRGER (2002a,b). It provides a good guide for shaping the intuition on how the equilibrium structure changes under increasingly strong FD.

The occurrence of multiple stable equilibria for weak

**TABLE 2**  
**Equilibrium structure for  $n = 2, 3,$  and  $4$  loci and tight linkage ( $r$  random between 0 and 0.01)**

$f$	Two loci				Three loci					Four loci					
	No. ( $E$ )	Polymorphism			No. ( $E$ )	Polymorphism				No. ( $E$ )	Polymorphism				
		0	1	2		0	1	2	3		0	1	2	3	4
0.00	2.0 ± 0.6	0.36	0	0.64	2.0 ± 0.6	0.49	0.32	0.06	0.12	3.0 ± 1.2	0.60	0.35	0.04	0.00	0.01
0.25	2.0 ± 0.6	0.32	0.03	0.66	2.0 ± 0.6	0.37	0.41	0.11	0.11	3.2 ± 1.3	0.46	0.48	0.05	0.01	0.00
0.50	1.4 ± 0.5	0.24	0.15	0.61	2.1 ± 0.7	0.26	0.53	0.14	0.08	3.3 ± 1.4	0.33	0.62	0.05	0.01	0
0.83	2.4 ± 1.0	0.09	0.50	0.41	2.4 ± 1.0	0.10	0.78	0.10	0.02	3.7 ± 1.6	0.12	0.85	0.04	0.00	0
0.96	2.7 ± 1.2	0.04	0.77	0.20	2.7 ± 1.2	0.03	0.92	0.04	0.01	4.2 ± 1.8	0.03	0.95	0.02	0	0
1.04	2.7 ± 0.9	0	0.64	<u>0.36</u>	2.7 ± 0.9	0	0.67	<u>0.32</u>	0.00	3.5 ± 1.4	0	0.37	<u>0.59</u>	<u>0.03</u>	<u>0.00</u>
1.14	1.1 ± 0.3	0	0.06	<i>0.94</i>	1.1 ± 0.3	0	0.01	<u>0.05</u>	<i>0.94</i>	1.0 ± 0.1	0	0.00	<i>0.01</i>	<i>0.01</i>	<i>0.99</i>
1.25	1	0	0	<i>1</i>	1	0	0	0	<i>1</i>	1	0	0	0	0	<i>1</i>
1.56	1	0	0	<i>1</i>	1	0	0	0	<i>1</i>	1	0	0	0	0	<i>1</i>
2.50	1	0	0	<i>1</i>	1	0	0	0	<i>1</i>	1	0	0	0	0	<i>1</i>

See Table 1 for definition of parameters.

**TABLE 3**  
**Summary of results for five loci**

$f$	$\bar{V}_r$	$\bar{W}/W_0$	%RF	$\hat{N}$	No. ( $E$ )	Polymorphism					
						0	1	2	3	4	5
$\theta = 0.5$											
0.00	0.024	1.013	0	9,994	$4.7 \pm 1.5$	0.62	0.38	0	0	0	0
0.96	0.086	1.001	0.00	10,010	$5.7 \pm 1.7$	0.03	0.97	0	0	0	0
1.25	1.003	1.000	0.51	10,186	1	0	0	0	0	0	1
2.50	1.026	1.000	0.47	10,551	1	0	0	0	0	0	1
$\theta = 0.75$											
0.00	0.024	1.040	0	9,994	$3.3 \pm 1.3$	0.59	0.41	0	0	0	0
0.96	0.076	1.004	0	10,008	$4.2 \pm 1.5$	0.02	0.98	0	0	0	0
1.25	0.797	0.997	1.00	10,157	1	0	0.00	0.08	0.25	0.48	0.18
2.50	0.859	0.978	0.99	10,465	1	0	0.00	0.04	0.22	0.45	0.29

The following parameters are chosen as in Figure 1 and Table 1:  $\kappa = 10,000$ ,  $\rho = 2$ ,  $V_s = 1.25$ ; recombination is free.  $\bar{V}_r$  shows the (average) relative genetic variance;  $\bar{W}/W_0$ , the average ratio of population mean fitness at equilibrium and initial mean fitness (see text for more details); %RF, the average proportion of trajectories whose mean fitness at equilibrium was reduced relative to initial mean fitness;  $\hat{N}$ , the average population size at equilibrium; and No. ( $E$ ), the average number of stable equilibria  $\pm$  standard deviation. The last six columns show the proportion of trajectories converging to an equilibrium with the indicated number of polymorphic loci.

FD is consistent with previous results of pure stabilizing selection (e.g., BARTON 1986; BÜRGER and GIMELFARB 1999). The reason is that the phenotypes of several homozygous genotypes may closely match the optimum of the stabilizing-selection fitness function and, hence, may be locally stable. Similarly, single-locus polymorphisms may be stable if both homozygous genotypes code for phenotypes close to the optimum. The equilibrium configurations for strong FD are discussed below in PHENOTYPIC DISTRIBUTIONS AT EQUILIBRIUM.

Without showing the results, we remark that the average deviation of the equilibrium mean genotypic value from the optimum is always very small. It is maximal in the absence of FD, reaching  $0.39\bar{y} = 0.09$  for two loci and  $0.24\bar{y} = 0.03$  for four loci (the maximum possible deviation is 0.5). It decreases with increasing number of loci and increasing strength of FD. If  $f > 1$ , then all deviations are  $<0.005$ ; if  $f \geq 1.25$ , they are zero because the allele frequencies are  $1/2$  at equilibrium.

Results analogous to Figure 1 and Tables 1 and 2 were obtained by fixing  $V_\alpha (= 0.5$ , the strongest possible competition in our model) and varying  $V_s$  across its full range (not shown). The main difference is that for small  $V_s$  tight linkage has a somewhat stronger effect (in the direction predicted from the above results). Results for five loci were obtained only for some parameter combinations. Therefore, they are summarized separately in Table 3.

**Analytical estimates of the transitory region:** The multilocus model is too complex to admit a complete mathematical analysis. However, the stability of the monomorphic equilibria can be determined, and this provides analytical insight into the dependence of the transitory region on the various parameters in the

model. Let  $\hat{\vartheta}$  denote the value of the compound demographic parameter  $\vartheta$  (9) at the equilibrium population size  $\hat{N}$ . In the APPENDIX, we prove that there is a critical value  $\phi_s$ , which can be written as

$$\phi_s = \hat{\vartheta} \left( 1 - \frac{\theta^2}{8V_s} \right)^{-1} = \hat{\vartheta} + \frac{\theta^2}{8V_\alpha}, \quad (10)$$

such that for  $f > \phi_s$  no stable monomorphic equilibrium can exist, whatever the allelic effects and the recombination rates are. If  $f < \phi_s$ , stable monomorphic equilibria may exist for appropriate allelic effects and recombination rates. Importantly, the critical value  $\phi_s$  is independent of the number of loci and typically only slightly larger than  $\hat{\vartheta}$ . For the parameters used in Figure 1 and Tables 1 and 2, i.e.,  $\theta = 1/2$ ,  $V_s = 1.25$ , (10) yields  $\phi_s = 1.03\hat{\vartheta}$ . Because for this range of values  $f$  (i.e.,  $f$  near one) we have  $\sim 10,000 \leq \hat{N} \leq 10,200$  (Table 4), Equation 9 gives  $1 \geq \hat{\vartheta} \geq 0.96$ , which yields a  $\phi_s$  between 1.03 and 0.99, respectively, in accordance with our numerical findings.

For two loci and a symmetric optimum, it was shown (BÜRGER 2002b) that there is a critical value  $\phi_D$ , in the present notation given by

$$\phi_D = \hat{\vartheta} \left( 1 - \frac{5}{16V_s} \right)^{-1} = \hat{\vartheta} + \frac{5}{16V_\alpha}, \quad (11)$$

such that for  $f > \phi_D$  a single, globally stable, fully polymorphic equilibrium exists at which all allele frequencies are equal to  $1/2$ . Although we cannot prove this for more than two loci, our numerical results suggest that it continues to be true. The two-locus result implies that  $f > \phi_D$  is necessary for the existence of a uniquely determined, globally stable, fully polymorphic equilib-



rium for all possible locus effects. Straightforward manipulations of the conditions  $f = \phi_s$  and  $f = \phi_D$  yield simple formulas for the corresponding critical values of  $V_\alpha$  and  $V_s$  in terms of the remaining parameters (see, e.g., the last paragraph of the APPENDIX). For the parameters used in Figure 1 and Tables 1 and 2, (11) yields  $\phi_D = 1.33\hat{\theta}$ . Because in this range of values  $f$ ,  $\hat{N}$  is between 10,200 and 10,500 (Table 4), this gives a  $\phi_D$  between 1.28 and 1.21, respectively, which again is in accordance with our numerical findings.

**The role of the demographic parameters:** Before investigating asymmetric selection, we examine how the properties of our model depend on the demographic parameters  $\rho$  and  $\kappa$  and derive an approximation for the population size expected at equilibrium. As indicated by Equations 10 and 11, a crucial role is played by the compound demographic quantity  $\hat{\vartheta}$ .

An estimate for the equilibrium population size  $\hat{N}$  can be obtained from (7) by the condition  $\bar{W} = 1$ . From (4) it is straightforward to compute an explicit expression for  $\bar{W}$  in terms of the first four moments of the phenotypic distribution at equilibrium. If the mean coincides with the optimum,  $\bar{g} = \theta$ , as is almost always satisfied to a close approximation in our numerical results (in particular, if more than two loci are involved), the following representation is obtained,

$$\bar{W} = \left(\rho - \frac{N}{\kappa}\right)\left(1 - \frac{V_A}{2V_s}\right) + \frac{N}{\kappa} \frac{V_A}{V_\alpha} - \frac{N}{\kappa} \frac{V_A^2 + M_4}{4V_\alpha V_s}, \quad (12)$$

where  $M_4$  denotes the fourth central moment. Neglecting the last term, which usually is small relative to the others because  $V_A^2 + M_4 \ll V_\alpha V_s$ , and equating the resulting expression to one, we obtain for the equilibrium population size the approximation

$$\hat{N} \approx \kappa(\rho - 1) + \kappa V_A \frac{2V_s(\rho - 1) - V_\alpha}{V_s(V_\alpha - 2V_A) + V_\alpha(V_s - V_A)}. \quad (13)$$

First, this informs us that  $\hat{N} \geq K = \kappa(\rho - 1)$  if and only if  $V_A = 0$  or

$$f \geq \frac{1}{2(\rho - 1)} \quad (14)$$

because the denominator of the last term in (13) is always positive (recall that we have  $V_A \leq \frac{1}{8}$ ,  $V_\alpha \geq \frac{1}{2}$ , and  $V_s \geq \frac{1}{8}$  if  $\theta = \frac{1}{2}$ ). Table 4 shows that (14) predicts the value  $f$  at which  $\hat{N} = K$  nearly correctly (although  $\bar{g} = \theta$  is assumed in its derivation), namely  $f = 0.5$  if  $\rho = 2$ . Second, numerical evaluation of (13) shows that it indeed provides a very accurate approximation of the numerically observed average  $\hat{N}$  (compare the last two columns in Table 4). This is also the case for all other parameter combinations of Table 4, as well as for many others (e.g., for other values of  $\rho$  and  $\kappa$ ; results not shown).

Differentiation of (13) with respect to  $V_\alpha$  shows that  $\hat{N}$  is decreasing in  $V_\alpha$  if and only if  $\rho > 2V_s/(2V_s - V_A)$ ,

TABLE 4  
Properties of equilibrium mean fitness and population size

$f$	Two loci, $r = 0.5$			Two loci, $0 < r < 0.01$			Three loci, $r = 0.5$			Three loci, $0 < r < 0.01$			Four loci, $r = 0.5$			Four loci, $0 < r < 0.01$		
	$\bar{W}/W_0$	%RF	$\hat{N}$	$\bar{W}/W_0$	%RF	$\hat{N}$	$\bar{W}/W_0$	%RF	$\hat{N}$	$\bar{W}/W_0$	%RF	$\hat{N}$	$\bar{W}/W_0$	%RF	$\hat{N}$	$\bar{W}/W_0$	%RF	$\hat{N}$
0.00	1.024	6	9,837	1.027	2	9,861	1.020	2	9,953	1.022	0	9,954	1.016	0	9,982	1.017	-	9,985
0.25	1.018	9	9,902	1.020	4	9,921	1.015	3	9,970	1.016	1	9,973	1.012	0	9,988	1.012	0	9,990
0.50	1.012	12	9,982	1.013	6	9,989	1.010	4	9,993	1.011	1	9,995	1.008	0	9,997	1.009	0	9,998
0.83	1.005	15	10,110	1.005	10	10,101	1.004	6	10,036	1.004	4	10,035	1.003	1	10,015	1.003	1	10,014
0.96	1.002	17	10,164	1.003	14	10,146	1.002	7	10,056	1.002	7	10,058	1.001	2	10,027	1.001	1	10,024
1.04	1.000	21	10,209	1.001	20	10,194	1.000	15	10,133	1.000	16	10,140	1.000	13	10,109	1.000	12	10,109
1.14	1.000	68	10,387	1.000	62	10,423	1.000	58	10,266	1.000	49	10,311	1.000	54	10,200	1.000	41	10,239
1.25	0.999	67	10,462	1.000	53	10,581	0.999	56	10,308	1.001	35	10,442	1.000	52	10,233	1.001	25	10,342
1.56	0.996	66	10,688	1.002	42	10,997	0.998	55	10,461	1.006	21	10,847	0.999	51	10,347	1.007	9	10,704
2.50	0.988	65	11,439	1.016	33	12,366	0.996	54	10,945	1.036	10	12,221	0.998	49	10,705	1.044	1	12,062

$\bar{W}/W_0$  shows the average ratio of population mean fitness at equilibrium and initial mean fitness (see text for more details); %RF, the average proportion of trajectories whose mean fitness at equilibrium was reduced relative to initial mean fitness; and  $\hat{N}$ , the average population size at equilibrium. The last column shows the population size calculated from the approximation (13) using the observed genetic variance for four tightly linked loci. The parameters  $\kappa = 10,000$ ,  $\rho = 2$ ,  $V_s = 1.25$ ,  $\theta = 0.5$  are as in Tables 1 and 2.

which is only slightly larger than one. Hence,  $\hat{N}$  increases with  $f$  unless  $\rho$  is very small. Table 4 confirms this. This is in accordance with ASMUSSEN (1983), who showed for rather general one-locus models of FDS that the population size at a stable interior equilibrium can exceed the carrying capacity if intraspecific competition between like genotypes is stronger than that between unlike genotypes. In SLATKIN's (1979) quantitative-genetic model of Lande's kind, the population size at the equilibrium with nonzero genetic variance is proportional to  $1/\sqrt{V_\alpha}$ .

Equation 13 predicts that the equilibrium population size is always proportional to  $\kappa$ , and this has been verified numerically (results not shown). Another important point is (Table 4) that for a wide range of values  $f$ , the equilibrium population size deviates from  $K$  by only a few percent [cf. (13) and recall that on average  $V_A$  is very small]. Therefore, we have

$$\hat{\vartheta} = \frac{\rho\kappa}{\hat{N}} - 1 \approx \frac{1}{\rho - 1}, \quad (15)$$

which equals 1 if and only if  $\rho = 2$ . Table 4 also shows that the deviation of  $\hat{N}$  from  $K$  decreases with an increasing number of loci. This is confirmed by (13) because (unless linkage disequilibrium is extremely high) in our model the average  $V_A$  decreases with increasing number of loci since the average effect of a locus decreases in proportion to  $1/(2n)$ .

Numerical iterations for various ecological parameter sets in which  $\kappa$  has been changed by a factor of 10 show that the only statistically significant effect on the properties of the system is that the carrying capacity and, hence, the equilibrium population size are changed by the corresponding factor. Similarly, different values of  $\rho$  induce exactly the transformation indicated by (10), (11), and (13), but have no statistically significant effect on the relative genetic variance, the number of equilibria maintained, or their degree of polymorphism (results not shown). For  $\rho > 3$ , the dynamics of  $N$  become complicated and were not studied in detail. However, in the few runs performed the dynamics of gamete frequencies seemed to be nearly unaffected by the fluctuations of the population size. A similar observation was reported by CLARKE and BEAUMONT (1992).

If density dependence is ignored and the population size is assumed constant and equal to  $K$ , then up to a scale transformation of  $f$  by the factor  $(\rho - 1)\hat{\vartheta}$ , the same results as for a changing population size are obtained. For instance, for a fixed population size of 10,000, the relative genetic variance and the polymorphism at some value  $f$  are about the same as those for variable  $N$  at the value  $(\rho - 1)\hat{\vartheta}f$  (results not shown). Thus, for fixed population size, the critical values  $\phi_s$  and  $\phi_d$  are somewhat larger than those under density dependence because, by (14),  $\hat{N} > K$  if  $f > \frac{1}{2}(\rho - 1)^{-1}$ . Hence, FD must be slightly stronger to dominate pure stabilizing selection.

A potentially important conclusion resulting from Equations 10, 11, and 15 is that for small growth rates  $\rho$ , much larger  $f$ , hence stronger competition, is needed to induce a qualitative change in the equilibrium structure because  $\phi_d > \phi_s > \hat{\vartheta} \approx (\rho - 1)^{-1}$ . This is not immediately obvious for models based on the Lotka-Volterra functional form (*e.g.*, SLATKIN 1979), in which the location of this region would depend on  $\sigma_k^2/V_\alpha$ , where  $\sigma_k^2$  is the width of the available resources. However, since Equation 19 of BÜRGER (2002b) informs us that  $\sigma_k^2$  is proportional to  $V_s$  with proportionality constant  $\rho\kappa/N - 1$ , the models indeed lead to equivalent predictions.

These multilocus results confirm and generalize the conclusion of BÜRGER (2002a,b) that, compared with pure stabilizing selection, FD leads to a quantitative, but not to a qualitative change, in the equilibrium properties of genetic variation as long as  $f < \hat{\vartheta} \approx (\rho - 1)^{-1}$ . Only larger  $f$  induces a qualitative change. Notably, the critical value at which this occurs is independent of the number of loci.

**The asymmetric case:** Now we turn to the asymmetric case and explore the consequences of a shifted optimum. Even in the absence of FD, *i.e.*, for pure stabilizing selection, very little work on the asymmetric case has been done and no simple, general results are available (HASTINGS and HOM 1990; GAVRILETS and HASTINGS 1993; BÜRGER 2000, pp. 213–216). Our numerical results are based on the assumption of free recombination and that the position of the optimum is at  $\theta = 0.75$ . The main findings are summarized in Figure 2 and Tables 5 and 3, which compare the asymmetric case with the corresponding symmetric case from Figure 1 and Table 1. Figure 2 clearly demonstrates the existence of a transitory region and shows that its lower bound is nearly unaffected by the shift in the optimum, as predicted by our theoretical estimate (10) (for  $\theta = 0.75$ , we obtain  $\phi_s = 1.06\hat{\vartheta}$  instead of the previous  $1.03\hat{\vartheta}$ , and  $\hat{\vartheta}$  is nearly identical in both cases). However, although there is a distinctive increase of both the relative genetic variance and the polymorphism in a small range of values  $f$ , there is no clear upper bound of the transitory region. Instead, both quantities increase very slowly until  $f = 2.5$  is reached. For the given strength of stabilizing selection ( $V_s = 1.25$ ), this is the largest possible value in this model and attained if  $V_\alpha = 0.5$ .

For weak or moderate FD ( $f < 1$ ), the degree of polymorphism is unaffected by the change in  $\theta$  (compare Table 5 with Table 1, and see Table 3) and, except for two loci, asymmetry leads only to a slight loss of genetic variance. For five loci, the difference nearly vanishes. If FD dominates ( $f > 1.1$ ), then a shifted optimum leads to substantially reduced genetic variance and polymorphism relative to a symmetric one. Under the strongest possible FD in our model, the relative genetic variance and the average amount of polymorphism still are diminished by  $\sim 20\%$  relative to the symmetric case. Even for such strong FD, a substantial fraction of stable equilibria exists at which not all loci are

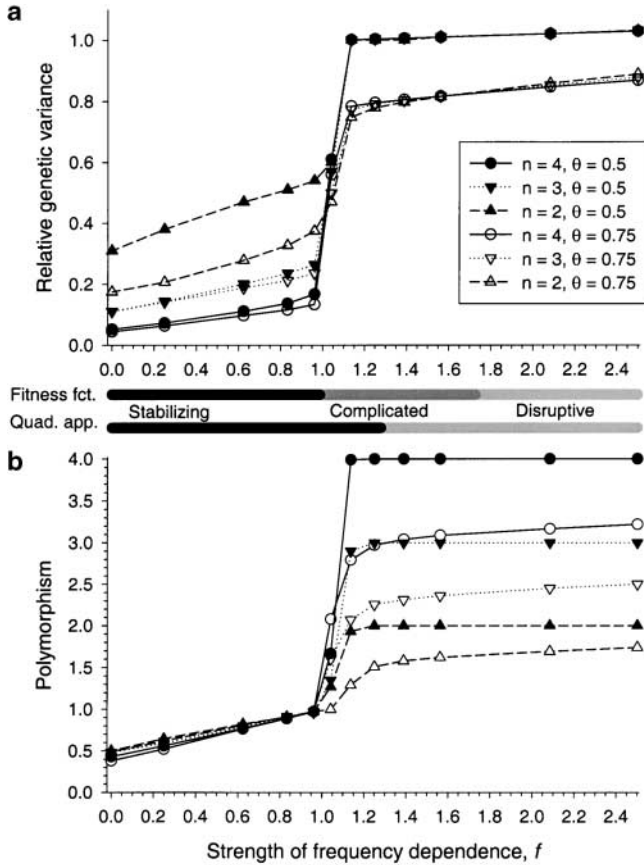


FIGURE 2.—Relative genetic variance (a) and polymorphism (b) as a function of  $f = V_s/V_\alpha$  for  $n = 2, 3, 4,$  and  $5$  loci in the case of free recombination. The symmetric case ( $\theta = 0.5$ ) is compared with the asymmetric case ( $\theta = 0.75$ ). The parameters  $V_s$ ,  $\rho$ , and  $\kappa$  are as in Figure 1 and  $V_\alpha$  is varied; hence the data for  $\theta = 0.5$  are those of Figure 1, except that data for some values  $f$  are omitted here. Instead, the range of values  $f$  is extended here up to the maximum possible  $f = 2.5$  in this model to demonstrate the effects of an asymmetric optimum more clearly. The bars between a and b indicate which type of selection was observed in the asymmetric case,  $\theta = 0.75$  (cf. Figure 1 for  $\theta = 0.5$ ).

polymorphic. Actually, the more loci there are, the lower the fraction of fully polymorphic equilibria. The relative genetic variance depends only very weakly on the number of loci. The deviation of the mean from the optimum is about as small as in the symmetric case (results not shown).

Thus, for weak or moderate FD ( $f \leq \phi_s$ ), free recombination, and three or more loci, a shift in the optimum of small or moderate size (*i.e.*,  $0.25 \leq \theta \leq 0.75$  so that  $\theta$  is closer to the middle of the phenotypic range than to its boundaries) has only a minor effect on the amount and structure of the genetic variation at equilibrium. For two loci, the effect is much larger because a shifted optimum destroys the inherent symmetries of the two-locus model that maintain much more relative genetic variance than that in models with three or more loci (see BÜRGER and GIMELFARB 1999).

For some ecological parameter combinations, results

were also obtained for an optimum at the upper boundary of phenotypic values, *i.e.*, for  $\theta = 1$ . Then the trait is under pure directional selection if FD is absent. We found that for free recombination, four loci,  $V_s = 1.25$ , and the strongest possible FD, *i.e.*,  $f = 2.5$ , the relative genetic variance is only 0.4, the average polymorphism is 2.0, and four-locus polymorphisms have a frequency of  $< 0.02$ . For weak FD ( $f = 0.83$ ), no polymorphism at all is maintained. This is consistent with the finding of LOESCHCKE and CHRISTIANSEN (1984) that for a single locus with multiple alleles, even under strong FD, no variation is maintained if the trait is under directional selection.

We also computed standard deviations of our quantities of interest. For three, four, and five loci, the standard deviation of the relative genetic variance is nearly twice the mean in the absence of FD and decreases to a value close to the mean as  $f$  increases to  $\phi_s$ . This holds for both recombination scenarios and for  $\theta = 0.5$  and  $\theta = 0.75$ . Hence, genetic variation between genetic systems varies greatly for weak to moderate FD. Under free recombination, the standard deviation decreases further in absolute terms as  $f$  increases and is always  $< 2\%$  of the mean if  $f > \phi_D$ . Hence, the genetic variance maintained under strong FD is nearly independent of the locus effects. For tight linkage, the standard deviation of the variance is between 15 and 20% of the mean if  $f > \phi_D$ ; thus in absolute terms it increases for large  $f$ .

#### DISRUPTIVE VS. STABILIZING SELECTION

Analysis of the conditions under which FDS induces disruptive selection on a trait is of importance because disruptive selection is a prerequisite for sympatric speciation if it is to be induced by competition. The fitness function in our model, (4), is a polynomial of degree 4 in  $g$ , and we classified its shape as  $\cap$ -shaped (concave with a local maximum), resulting in stabilizing selection,  $\cup$ -shaped (convex with a local minimum), resulting in disruptive selection, or else, which we call complicated selection. The fitness function was calculated at each stable equilibrium and classified according to one of the three categories. For a symmetric optimum ( $\theta = 0.5$ ), a fitness function classified as complicated is M-shaped in all cases examined; *i.e.*, there are two local optima (not at the extreme genotypic values) separated by a local minimum. The shape of the M, however, can be rather variable because the minimum can be very shallow or very deep, and the fitness of the extreme genotypic values can be very low or just slightly lower than the maximum. The M is asymmetric if  $\bar{g} \neq \theta$ . For an asymmetric optimum or at unstable equilibria in the symmetric case, other shapes may occur, such as monotone decreasing or increasing fitness, or one local maximum and one local minimum.

In natural populations, the shape of a fitness function is difficult to determine exactly and often approximated

TABLE 5

Equilibrium structure for  $n = 2, 3,$  and  $4$  loci, free recombination, and an asymmetric optimum ( $\theta = 0.75$ )

$f$	Two loci				Three loci					Four loci					
	No. ( $E$ )	Polymorphism			No. ( $E$ )	Polymorphism				No. ( $E$ )	Polymorphism				
		0	1	2		0	1	2	3		0	1	2	3	4
0.00	$1.5 \pm 0.5$	0.50	0.50	0	$2.4 \pm 0.8$	0.52	0.48	0	0	$2.8 \pm 1.0$	0.62	0.38	0	0	0
0.25	$1.5 \pm 0.5$	0.35	0.65	0	$2.5 \pm 0.8$	0.39	0.61	0	0	$2.9 \pm 1.1$	0.48	0.52	0	0	0
0.50	$1.5 \pm 0.5$	0.25	0.75	0	$2.6 \pm 0.9$	0.26	0.74	0	0	$3.0 \pm 1.1$	0.32	0.68	0	0	0
0.83	$1.6 \pm 0.5$	0.10	0.90	0	$2.7 \pm 0.9$	0.09	0.91	0	0	$3.3 \pm 1.2$	0.11	0.89	0	0	0
0.96	$1.7 \pm 0.5$	0.03	0.97	0	$3.0 \pm 0.9$	0.02	0.98	0	0	$3.6 \pm 1.2$	0.03	0.97	0	0	0
1.04	$1.9 \pm 0.3$	0	1	0	$2.2 \pm 0.5$	0	0.40	0.60	0	$2.7 \pm 0.7$	0	0.20	0.53	0.27	0
1.14	1	0	0.71	0.29	1	0	0.22	0.50	0.29	1	0	0.06	0.29	0.44	0.21
1.25	1	0	0.49	0.51	1	0	0.13	0.48	0.39	1	0	0.03	0.23	0.47	0.26
1.56	1	0	0.38	0.62	1	0	0.09	0.46	0.45	1	0	0.02	0.19	0.49	0.31
2.50	1	0	0.26	0.74	1	0	0.05	0.40	0.55	1	0	0.01	0.14	0.48	0.37

See Table 1 for definition of parameters.

by a quadratic polynomial through regression. Therefore, we also approximated our fitness function by a quadratic polynomial and classified it as stabilizing selection if it was concave (curved downward) and as disruptive otherwise.

In Figures 1 and 2, the horizontal bars below the top section display the dependence of the shape of the fitness function on  $f$ . Except for the region in which selection is complicated, the same type of selection occurs at all equilibria and for all genetic parameter combinations. The coincidence between the type of selection acting and the properties of genetic variation maintained at equilibrium is remarkable. The figures clearly show that complicated selection occurs in the transitory region, *i.e.*, if  $\phi_s < f < \phi_d$ . Under the assumption that the mean coincides with the optimum,  $\bar{g} = \theta$  (as is satisfied to a close approximation for the vast majority of parameter combinations if more than two loci contribute to the trait—the more loci, the better the approximation), it is straightforward to show that  $W(g)$  is  $\cap$ -shaped if and only if

$$f < \hat{\theta} + \frac{V_A}{2V_\alpha}. \tag{16}$$

Since by (10), monomorphic equilibria exist if  $f < \phi_s = \hat{\theta} + 1/(8V_\alpha)$ , (16) is satisfied for all possible genetic parameter combinations if and only if  $f < \hat{\theta}$ .

Another straightforward calculation shows that if  $\bar{g} = \theta \geq 1/2$  (as is approximately the case in our numerical results) disruptive selection occurs if and only if the derivative of  $W(g)$  at  $g = 0$  is positive. This is the case if and only if

$$f > \hat{\theta} + \frac{V_A + 2\theta^2}{2V_\alpha} = \hat{\theta} \left( 1 - \frac{V_A + 2\theta^2}{2V_s} \right)^{-1}. \tag{17}$$

If  $\theta = 1/2$  and  $V_A = 1/8$ , which is the largest possible value of  $V_A$  in Hardy-Weinberg equilibrium, the right-hand

side of (17) coincides with  $\phi_d$  (11). Therefore, disruptive selection occurs for all possible genetic systems in this model if  $f > \phi_d$ . These results suggest that in the symmetric case, disruptive selection should be almost always detectable if FD is strong enough to maintain a unique fully polymorphic equilibrium.

For the asymmetric optimum, the region with complicated selection is substantially extended and much stronger FD is needed to produce disruptive selection (Figure 2). This is also predicted by (17), which gives a critical value of  $f$  between 1.7 and 1.9 if  $V_A = 1/8$  and the numerically obtained  $\hat{N}$ 's (in this region between 10,300 and 10,800) are plugged in. In the transitory region (and only there), the fitness function is often not only complicated, but also very flat near equilibrium, thus leading to extremely slow convergence (*cf.* THE STATISTICAL APPROACH).

#### EVOLUTION OF MEAN FITNESS

For two loci and by ignoring density dependence, it was shown (BÜRGER 2002b) that under moderate or strong FD, the dynamics in this model may be highly nonadaptive; *i.e.*, mean fitness may often decrease and critical points of the fitness surface bear little relevant information about the dynamics or equilibrium properties of the model. However, even if a stable polymorphism coincides with a critical point of the fitness surface, methods relying on the invasion analysis of a rare mutant in a monomorphic population may be insufficient for deriving the correct evolutionary properties of this equilibrium (CHRISTIANSEN 1991).

For the present multilocus model we investigated such and related issues using our statistical approach. For every trajectory, we calculated the ratio  $\hat{W}/W_0$  of the mean fitness at equilibrium (which, of course, is one) and the initial mean fitness and averaged  $\hat{W}/W_0$  over all

1000 genetic parameter sets pertaining to a given ecological parameter combination. Because initial points are randomly chosen, the average ratio  $\bar{W}/W_0$  provides a measure for the net change of population mean fitness during evolution. We also calculated the percentage of trajectories, %RF, for which mean fitness at equilibrium was lower than that initially. Some of these results are summarized in Table 4.

A number of noteworthy features are observed. As  $f$  increases from zero, the average ratio  $\bar{W}/W_0$  decreases from a value  $> 1$  to 1.000 as  $f$  reaches  $\sim 1.0$  ( $\approx \phi_s$ ). In parallel, the proportion of trajectories for which fitness is reduced at equilibrium increases from nearly zero (except for two loci, when this proportion is a few percent) to 10% or more. This percentage reaches a maximum of 40% or more in the transitory region and declines as  $f$  increases beyond  $\phi_D$ . For free recombination this decline is very slow, but for tightly linked loci it is rapid; the more loci, the more rapid the decline.  $\bar{W}/W_0$  decreases slightly below one for  $f > \phi_D$  if recombination is free, but increases quite substantially if linkage is tight. Therefore, under moderate or strong FD ( $f > \phi_s$ ) the dynamics are “on average” nonadaptive if the loci are unlinked. However, if the loci are tightly linked and FD is very strong, then mean fitness decreases only with low probability and, on average, increases substantially above that of randomly chosen initial distributions. As we see by way of example in the next section, this is because with tightly linked loci, the phenotypic distribution shows signs of clustering at its extreme phenotypic values.

#### PHENOTYPIC DISTRIBUTIONS AT EQUILIBRIUM

Most ecological modeling focusing on the evolutionary consequences of FDS has relied on assumptions about the distribution of genotypic or phenotypic values. Models using the quantitative genetics approach assume that phenotypic values are normally distributed (and do not change shape), whereas models resorting to game theory or adaptive dynamics consider the fate of single mutants in otherwise monomorphic populations. Figures 3 and 4 show how distributions of genotypic values look in four- and eight-locus models if FD is strong, *i.e.*, such that a unique, fully polymorphic, stable equilibrium exists. They display seemingly fractal features; *i.e.*, typically the frequencies of neighboring genotypic values are radically different. Only a few runs with eight loci were performed with the sole purpose of demonstrating the equilibrium distribution.

Figure 3, a and b, as well as Figure 4, a and b, differ only because of different assumptions on the recombination rate; all other parameters, including the allelic effects, are the same. Comparison of these pairs of figures shows that with tight linkage a much larger fraction of genotypic values has very low frequency compared with the case of free recombination, but some genotypic values

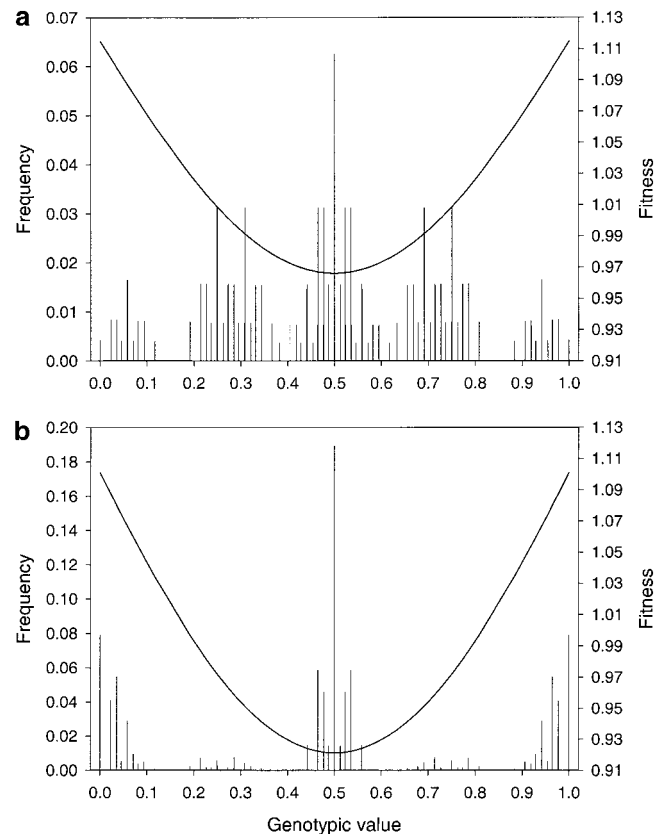


FIGURE 3.—Frequencies of genotypic values and fitness function at equilibrium for four loci. The locus effects are  $\gamma_1 = 0.036$ ,  $\gamma_2 = 0.250$ ,  $\gamma_3 = 0.191$ , and  $\gamma_4 = 0.023$ ; the ecological parameters are  $V_s = 1.25$ ,  $V_\alpha = 0.5$ ,  $\rho = 2$ , and  $\kappa = 10,000$ . Hence there is a unique, globally stable equilibrium with all allele frequencies equal to  $1/2$ . Only the linkage disequilibria depend on the genetic details. The U-shaped curve depicts the fitness function at this equilibrium. Its scale is given on the right-hand side. (a) Freely recombining loci. (b) Recombination rates between adjacent loci are randomly chosen between 0 and 0.01 and are 0.0089, 0.0037, and 0.0041 in this case. There are as many vertical bars ( $3^4 = 81$  genotypic values) in b as in a, but many are invisible because their height is so small.

have much higher frequencies. In particular, with tight linkage the extreme genotypic values occur with high frequency. Because of random mating, however, the central genotypic value is always the most frequent one.

We end with a little lesson on the central limit theorem. Despite its fractal appearance, the distribution for eight loci and free recombination in Figure 4a is nearly normal. Figure 5 displays its cumulative density function together with that of a normal distribution with the same mean and variance. Also the cumulative density functions of the other distributions displayed in Figures 3 and 4 are shown. The distribution resulting from eight tightly linked loci and those from four loci (linked or not) are markedly nonnormal. That the eight-locus distribution with free recombination is nearly normal is a consequence of the central limit theorem together with the fact that linkage equilibrium is very weak in this

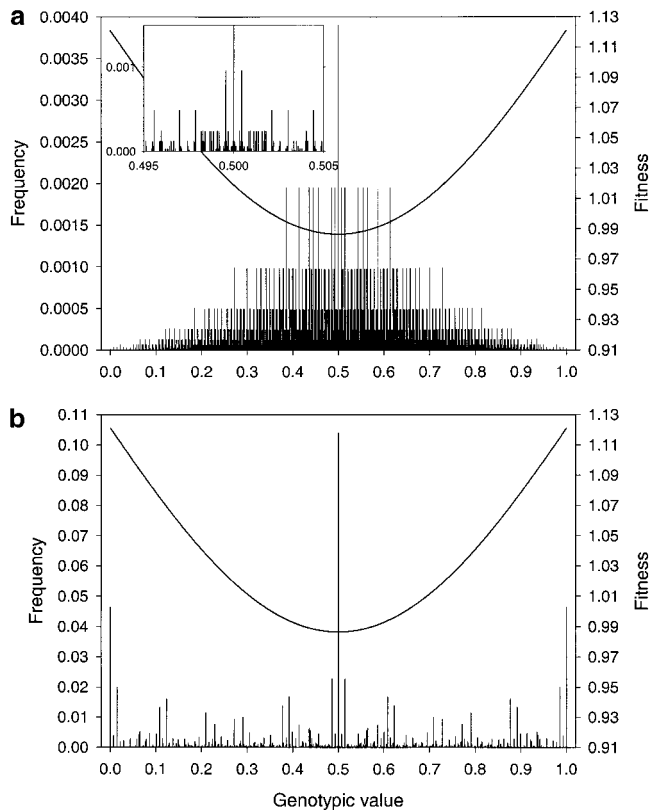


FIGURE 4.—Frequencies of genotypic values and fitness function at equilibrium for eight loci. The effects of the loci are 0.115, 0.114, 0.055, 0.007, 0.0863, 0.015, 0.044, and 0.065. There are  $3^8 = 6561$  different genotypic values, and hence as many vertical bars. The parameters  $V_s$ ,  $V_{\alpha}$ ,  $\rho$ , and  $\kappa$  are as in Figure 3. (a) Freely recombining loci. The inset is a zoomed-in version of the full figure with genotypic values restricted to the interval [0.495, 0.505] to show the seemingly fractal nature of the distribution. (b) The recombination rates between adjacent loci were randomly chosen and are 0.0016, 0.0064, 0.0006, 0.0080, 0.0073, 0.0062, and 0.0016. The locus effects and genotypic values are as in a.

case and Hardy-Weinberg proportions obtain. Because allele frequencies are  $\frac{1}{2}$ , it is closely approximated by the sum of eight independent random variables assuming the values 0,  $\gamma_i$ ,  $2\gamma_i$  with probabilities  $\frac{1}{4}$ ,  $\frac{1}{2}$ ,  $\frac{1}{4}$ , respectively. In fact, the sum of absolute differences of the frequencies of the normal and the eight-locus distribution with free recombination is  $\sim 0.01$ .

## DISCUSSION

There is no doubt that FDS has the potential of maintaining substantial genetic variation, on the level of both quantitative traits and coding polymorphisms (see Introduction). Rather, the question is about the importance of FD in maintaining variation relative to mechanisms such as mutation-selection balance, genotype-environment interaction, spatially or temporally heterogeneous environments, or other forms of balancing selection. Focusing on quantitative traits, which are likely to be

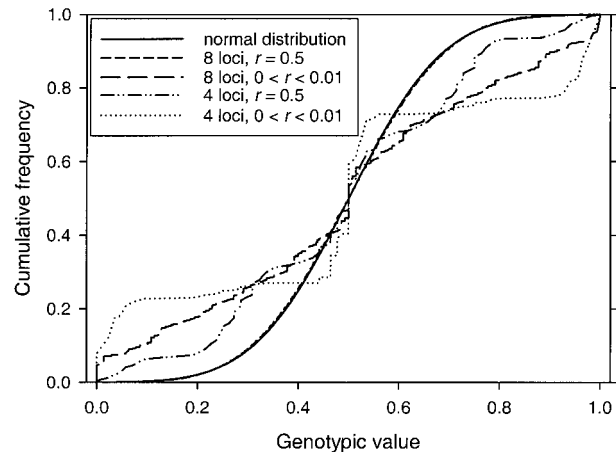


FIGURE 5.—Cumulative distribution functions of the eight-locus distribution with free recombination from Figure 4a, the corresponding normal distribution, the eight-locus distribution with tight linkage from Figure 4b, and the four-locus distributions with and without linkage from Figure 3.

not only under direct selection but also under indirect selection caused by pleiotropy (e.g., KEIGHTLEY and HILL 1990; ZHANG and HILL 2002), it seems reasonable to assume that FDS on such a trait may interact with other selective forces, for instance, directional or stabilizing selection. Among the different forms of FDS, mainly those conferring an advantage to rare genotypes (negative FD) can maintain genetic variation (e.g., ASMUSSEN and BASNAYAKE 1990; CLARKE 2002). A particularly important cause for negative FD is selection by competitors. Most of the few theoretical analyses of the evolutionary consequences of FDS on quantitative traits assume intraspecific competition mediated by a trait under stabilizing selection. These analyses are based, however, on very simple genetic models involving either a single locus or a classical quantitative genetics approach (BULMER 1974, 1980; SLATKIN 1979; CHRISTIANSEN and LOESCHCKE 1980) or on two-locus models (LOESCHCKE and CHRISTIANSEN 1984; BÜRGER 2002a,b). An exception is the numerical work of CLARKE *et al.* (1988) and MANI *et al.* (1990) for finite populations, who investigated the heterozygosity and the variance of a quantitative trait determined by up to 12 recombining loci with recurrent mutation and many possible alleles. Although their fitness is also a product of a stabilizing-selection term and a frequency-dependent term, their results are not directly comparable to ours because, among others, they model FD in a different way. The bottom line of their analysis is that FD can maintain much genetic variability.

The main purpose of this study was to investigate the extent to which conclusions from the models in which FD is induced by competition between similar phenotypes remain valid if the trait is determined by multiple additive loci and whether and how genetic details matter. We adopted the model of BULMER (1974, 1980) in which fitness has two multiplicative components, one

resulting from frequency-independent stabilizing selection, the other from competition. Formally, this is very similar to models of competition for limited resources as used by SLATKIN (1979) or CHRISTIANSEN and LOESCHCKE (1980); see BÜRGER (2002b). The most important parameter in our model is what we call the strength of FD,  $f = V_s/V_\alpha$ , (8), where  $V_s$  is the inverse measure for the strength of pure stabilizing selection and  $V_\alpha$  is that for the strength of competition. Although the properties of our model depend on  $V_s$  and  $V_\alpha$  separately, to leading order in  $1/V_s$  and  $1/V_\alpha$ , they depend on  $f$  (see Equations 10 and 11 and also Equations 14, 16, and 17).

Our most basic general finding is that for given demographic parameters ( $\rho, \kappa$ ) the properties of genetic variation maintained at stable equilibria, whether measured in terms of genetic variance of the trait or in terms of degree of polymorphism, depend (to leading order in  $1/V_s$  and  $1/V_\alpha$ ) in a nearly threshold-like way on  $f$ . We identified a critical value  $\phi_s$  (10) such that for  $f < \phi_s$ , the equilibrium structure is qualitatively similar to that under pure stabilizing selection (the genetic variance is relatively low and the vast majority of equilibria are monomorphic or maintain a single polymorphic locus). If  $f > \phi_s$ , then no stable monomorphic equilibria exist and the genetic variance and the degree of polymorphism increase rapidly. There is another critical value,  $\phi_D$  (11), which is larger than  $\phi_s$  (but usually not much), such that a globally stable, fully polymorphic equilibrium is maintained if the optimum  $\theta$  for pure stabilizing selection lies in the middle of the range of phenotypic values, *i.e.*,  $1/2$  on our scale (Figures 1 and 2, Tables 1–3). If the optimum is displaced from this symmetric position to a moderate extent, then  $\phi_D$  is larger and not all stable equilibria are fully polymorphic. However, they are unique and still maintain a rather high amount of genetic variance (Figure 2, Tables 3 and 5). The interesting and important aspect here is that the critical values  $\phi_s$  and  $\phi_D$  are independent of the number of loci and of the recombination rates in the sense that if  $f > \phi_s$ , then no genetic system can have a stable monomorphic equilibrium, and if  $f > \phi_D$ , then in every possible genetic system a unique globally stable polymorphic equilibrium exists.

These results about the threshold-like behavior are consistent with those of BULMER (1974, 1980) and SLATKIN (1979), who had much simpler genetics in their models and only a symmetric optimum. The main difference is that in their models there are only two possibilities: genetic variation is either maintained or not; its amount cannot be determined. In Bulmer’s model, a diallelic locus with an infinitesimally small contribution to the trait is maintained polymorphic if and only if

$$(\sigma_z^2 + V_s + V_\alpha)(\sigma_z^2 + V_s)^{3/2} < \rho V_s^{5/2}, \quad (18)$$

where  $\sigma_z^2$  is the phenotypic variance of the trait. Because

the left-hand side is increasing in  $\sigma_z^2$ , no polymorphism can be maintained, whatever the value of  $\sigma_z^2$ , if

$$f < (\rho - 1)^{-1}, \quad (19)$$

which is obtained by setting  $\sigma_z^2 = 0$  in (18). In view of (15), this is a close approximation to our condition  $f < \phi_s$  provided selection is weak. In the two quantitative-genetic models of Slatkin, no variation is maintained if  $\sigma_k^2 < V_\alpha$ ; otherwise, selection is disruptive and genetic variation is maintained. Because his  $\sigma_k^2 \approx V_s/\vartheta$  (BÜRGER 2002b), the condition  $\sigma_k^2 < V_\alpha$  is (approximately) equivalent to  $f < \vartheta$  and hence to (19).

In our model, the situation is more complex because genetic variation can be maintained if  $f < \phi_s$ . In the absence of linkage, however, more than one polymorphic locus never exists (Tables 1, 3, and 5). With tightly linked loci, there is a small probability of maintaining a stable multilocus polymorphism if  $f < \phi_s$  (Table 2). Figures 1 and 2 show that weak FD leads to a slow increase in genetic variation, basically by increasing the proportion of single-locus polymorphisms (Tables 1, 2, 3, and 5). Table 6 quantifies the amount by which moderate FD (*i.e.*, such that  $f$  is just below the critical value  $\phi_s$ ) increases the relative genetic variance  $\bar{V}_r$  compared to pure stabilizing selection. The message is clear: the more loci, the larger is the effect of FD. The reason is that the genetic and the relative genetic variance maintained under pure stabilizing selection decrease rapidly with increasing number of loci (see Figures 1 and 2 and BÜRGER and GIMELFARB 1999). This is the only issue for which the conclusions drawn in BÜRGER (2002b) on the basis of a two-locus model have to be revised: weak to moderate FD may maintain considerably more genetic variance than frequency-independent stabilizing selection if several loci contribute to the trait.

An important point is that the strength of FD required to induce disruptive selection and a qualitative change in the equilibrium structure depends strongly on the growth rate  $\rho$  [see (10), (11), (15), and also (19)]. Hence, for growth rates only slightly larger than one, extremely strong FD will be necessary to induce such a change (actually stronger than can be realized in our model in which competition decreases quadratically with the difference in phenotype).

We expect that qualitatively similar conclusions about the role of the demographic parameters hold for other models of population regulation. To substantiate this expectation consider the Beverton-Holt model and define the fitness function by

$$W(g) = \frac{\lambda}{1 + bN\bar{\alpha}_p} S(g), \quad (20)$$

where  $\lambda$  is the growth rate and  $(\lambda - 1)/b$  is the carrying capacity in the absence of genetic variation. In this model, the population size converges monotonically to the carrying capacity for any growth rate  $\lambda > 1$ . For a

**TABLE 6**  
**Increase of genetic variance through moderate frequency dependence**

	Two loci		Three loci		Four loci		Five loci:
	$0 < r < 0.01$	$r = 0.5$	$0 < r < 0.01$	$r = 0.5$	$0 < r < 0.01$	$r = 0.5$	$r = 0.5$
$V_s = 1.25, \theta = 0.5$	1.4	1.7	2.1	2.4	3.6	3.2	3.6
$V_s = 1.25, \theta = 0.75$	2.1	2.1	2.6	2.1	3.7	3.0	3.1

Presented is the ratio of the average relative genetic variance at the highest value  $f < \phi_s$  for which data are available and the average relative genetic variance in the absence of frequency dependence, *i.e.*,  $V_r (f = 0.96)/V_r (f = 0)$ .

monomorphic population, the solution of the discrete-time recursion is obtained directly from the continuous-time logistic equation by assuming that one generation corresponds to one time unit in continuous time. It is a simple exercise to repeat the proof in the APPENDIX for the fitness function (20) to conclude that no monomorphic equilibrium can exist if  $f > (1 + b\hat{N})/(b\hat{N})$ , as is obtained instead of  $f > \phi_s$  (10). This turns out to be also the condition ensuring that for any genetic system, the fitness function at equilibrium is U-shaped; *i.e.*, selection is disruptive, provided  $\bar{g}$  is close to  $\theta$ . The reason is that the fitness function (20) changes directly from  $\cap$ -shaped to U-shaped as  $f$  increases from small values to large values, without going through an M-shape. If also in this model, the equilibrium population size is typically close to the carrying capacity,  $(\lambda - 1)/b$ , as we assume but didn't check numerically, then we obtain  $f > \lambda/(\lambda - 1)$  as an approximate condition for FDS to dominate stabilizing selection. For model (4), the corresponding condition is  $f > 1/(\rho - 1)$ , *cf.* (19). The ratio  $\lambda/(\lambda - 1)$  converges to 1 as  $\lambda \rightarrow \infty$  and to infinity as  $\lambda \rightarrow 1$  from above. Therefore, as with discrete logistic growth, the critical value  $f$  beyond which FDS is strong enough to induce a qualitative change in the equilibrium structure increases with decreasing growth rate. Moreover, in the Beverton-Holt model, this critical value can never be  $< 1$ , which it can with discrete logistic growth if  $\rho > 2$ . (As long as  $\rho \leq 3$  convergence to the carrying capacity still occurs!) If we identify the intrinsic growth rates in both models, *i.e.*,  $\lambda = \rho$ , then  $\lambda/(\lambda - 1) > 1/(\rho - 1)$ . These considerations suggest that if population regulation is "smoother" than that in the discrete logistic model underlying our numerical results, FDS must be stronger to have similar effects.

A number of interesting robustness properties deserve to be highlighted. Under weak to moderate FD ( $f < \phi_s$ ), the relative genetic variance maintained is nearly independent of the amount of recombination. If there are more than two loci and the displacement of the optimum is not extreme ( $0.25 \leq \theta \leq 0.75$ ), then the variance is nearly independent of the optimum's position  $\theta$ . Further, if  $f < \phi_s$  then the average amount of polymorphism is nearly independent of the number of loci, the strength of selection (*i.e.*, only  $f$  matters, not the size of  $V_s$  and  $V_\alpha$ ), and the position of the optimum

unless the displacement is extreme. For four loci, both recombination scenarios yield nearly the same degree of polymorphism unless stabilizing selection is very strong. Preliminary results indicate that this is also true for five loci (and probably more). For strong FD ( $f > \phi_D$ ) and free recombination the relative genetic variance is independent of the number of loci and the strength of selection. This is valid for a symmetric and a nonsymmetric optimum. The average polymorphism under strong FD is independent of the amount of recombination if  $\theta$  is symmetric; otherwise very tight linkage promotes stability of a fully polymorphic equilibrium. In contrast to the polymorphism, the variance is much more sensitive to the level of recombination because for strong FD and tight linkage, large positive linkage disequilibria that inflate the variance substantially are generated.

Summarizing, under weak to moderate FD an asymmetric optimum has little effect on the amount of genetic variation maintained, whether measured in terms of variance of the trait or in terms of polymorphism, provided more than two loci contribute to the trait and the displacement is not so large that directional selection dominates. The reason is that with several loci any position of the optimum can be closely matched by a homozygous genotype and variation is maintained in at most one locus. For strong FD and an asymmetric optimum, less variance and less polymorphism than with a symmetric one are maintained. The obvious reason is that pure stabilizing selection on phenotypes that are at the far side of the optimum becomes too strong relative to FD to maintain them in the population, at least at appreciable frequency. If the position of the optimum lies at the boundary or outside of the range of phenotypic values, so that in the absence of FD the trait is under directional selection, then even strong FD maintains not much genetic variation. For two loci, this was shown by LOESCHKE and CHRISTIANSEN (1984), and we confirmed it for four loci (results not shown).

We expect that qualitatively similar results hold if more than two alleles can segregate at a locus. It is known, however, that under constant selection a large number of alleles can be maintained at a single locus (*e.g.*, SPENCER and MARKS 1992) and that under frequency-dependent selection, the dynamics with multiple alleles can be different from those with just two



alleles (*e.g.*, SEGER 1986). In contrast, CHRISTIANSEN and LOESCHKE (1980) showed for a model with four possible alleles at a single locus, which otherwise is closely related to ours (see Introduction and BÜRGER 2002b), at equilibrium only two alleles can segregate. This is also true for a single-locus version of our model with multiple alleles (K. SCHNEIDER, personal communication).

Our study, as well as others mentioned, clearly supports the conclusion of ASMUSSEN (1983) that FDS may have a strong influence on the equilibrium structure. In particular, depending on its strength, FD can maintain almost any amount of genetic variance and polymorphism. Therefore, it may be very difficult to discriminate FD from other factors maintaining genetic variation by studying the amount and pattern of variation. An exception may be strong FD acting on linked loci because then high positive linkage disequilibria are generated according to our model.

A possibility to detect FDS on a quantitative trait is by looking for disruptive selection. Our results for a symmetric optimum show that the fitness function is U-shaped at equilibrium, hence detectable by quadratic approximation whenever FD is strong enough to maintain a fully polymorphic equilibrium ( $f > \phi_D$ ). For moderate FD, as in the transitory region, disruptive selection may be difficult or impossible to detect because then the fitness function is very flat and may be complicated. If the optimum is shifted away from the middle of the phenotypic range, stronger FD is needed to induce disruptive selection [see (17) and compare the middle parts of Figures 1 and 2], and even very strong FD is not sufficient for the existence of a fully polymorphic equilibrium.

Figures 3 and 4 show that at equilibrium there may be substantial fitness differences (the maximum reduction in fitness relative to the best genotype is between 10 and 15%). This is more than in the absence of FD, where for  $V_s = 1.25$  (as in these figures) the maximum possible reduction is exactly 10%. At equilibrium, however, such genotypes are never present if selection is frequency independent because they are wiped out by selection. Therefore, we conclude that disruptive selection should be detectable empirically if it is strong enough to induce an equilibrium structure that is qualitatively different from that expected under frequency-independent stabilizing selection. Hence, if FD is as important as sometimes asserted in the ecological literature, then strong disruptive selection should be common.

Detection of disruptive selection, however, does not automatically imply that FDS is acting on that trait. An example may be provided by the African finch *Pyrenestes* for which disruptive selection on bill characters has been well documented (SMITH 1990, 1993). There are two morphs that differ substantially in lower mandible width and are randomly breeding with respect to this and related traits. Disruptive selection is most likely

related to seed quality, because large morphs feed more efficiently on a hard-seeded species of sedge and small morphs on a soft-seeded species. It is not obvious that this case of disruptive selection can be explained in terms of a model like the present one, because there is no continuous resource spectrum, but there are simply two very different types of seed available. Hence, there is no competition between similar phenotypes that would induce frequency-dependent fitnesses. Therefore, and because the environment in which these finches live appears to be rather constant over many years, it seems likely that a model with a fixed, frequency-independent bimodal fitness function is appropriate for describing selection. However, as pointed out by a reviewer, it could be envisaged that the degree of preference for one or the other resource is a quantitative trait of the type studied here.

The question of how frequent disruptive selection is remains unresolved and deserves further investigation. In contrast to previous studies (ENDLER 1986), KINGSOLVER *et al.* (2001) found that disruptive selection is not necessarily rarer than stabilizing selection. Both kinds, however, are usually not very strong.

As already noted, a quantitative assessment of the importance of FDS relative to other mechanisms seems to be difficult because little is known about how frequent and how strong FD is and because FD can induce almost any amount of genetic variation. A few comparisons, however, might be possible. In BÜRGER and GIMELFARB (2002), we investigated the influence of fluctuating environments on the genetic variation maintained in quantitative traits by methods very similar to those used here. There we found that with a cycling optimum (with or without additional stochastic fluctuations), the relative genetic variance of a trait determined by four diallelic loci, each subject to recurrent mutation of rates  $5 \times 10^{-5}$  to  $5 \times 10^{-6}$ , may be increased by a factor of at most 4 to 5 relative to pure stabilizing selection if the period of the optimum is sufficiently long ( $\sim 20$  generations or longer). With six loci, this increase was nearly twice as high. Table 6 shows that weak FD does not increase genetic variance that much, but still significantly. Whereas a fluctuating environment leads to a large increase of genetic variance only under certain conditions, FDS always increases the genetic variance, even to a very high level if FD is sufficiently strong.

Models of FDS of the kind used here are popular among ecologists and have been used, for instance, to explore character displacement (SLATKIN 1980) or, more recently, sympatric speciation (DIECKMANN and DOEBELI 1999). To obtain conditions under which such models may lead to sympatric speciation, it would be necessary to examine how much assortative mating is needed to get a bimodal distribution of the trait and how the necessary degree of assortment depends on the ecological, demographic, and genetic parameters of the model. Very little work in this direction has been performed yet, exceptions being UDOVIC (1980), MATESSI *et al.* (2001),

and GAVRILETS (2003). As a subsequent step, the conditions for the evolution of modifiers for assortment could be studied, thus providing theoretical insight into the conditions required for FDS to trigger sympatric speciation. The present analysis suggests that strong FD ( $f > \phi_D$ ) is likely to be necessary (hence, small growth rates  $\rho$  will be disadvantageous), selection should be rather symmetric, and tight linkage may be very favorable. No prediction about the role of the number of loci contributing to the trait seems to be possible.

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APPENDIX: INSTABILITY OF MONOMORPHIC EQUILIBRIA

Here we show that  $f > \phi_s$  (10) implies instability of all monomorphic equilibria in any genetic system satisfying our model. In general, the stability of a monomorphic equilibrium may depend on the recombination rates, and it does so in the present model (see BÜRGER 2002b for the two-locus case). However, for our purpose it is sufficient to investigate instability with respect to invasion of single-locus mutants. Therefore, let an arbitrary genotype that is homozygous in all loci have genotypic value  $g$ . Consider a single-locus heterozygote that differs at just one locus and denote its genotypic value by  $g + a$  ( $a \neq 0$ ). Recall that we assume that genotypic values are restricted to the interval  $[0, 1]$ . Without loss of generality, we assume  $\frac{1}{2} \leq \theta < 1$ . Then the haploid genotype corresponding to  $g$  gives rise to an unstable equilibrium if

$$W(g + a) > W(g). \tag{A1}$$

Because at this monomorphic equilibrium (and to a first-order approximation also in its neighborhood)  $V_\lambda = 0$  and  $\bar{g} = g$ , a simple calculation shows that (A1) is equivalent to

$$f > \hat{\vartheta} \frac{1 + 2(g - \theta)/a}{1 - (a + g - \theta)^2/(2V_s)}, \tag{A2}$$

where  $\hat{\vartheta} = (\rho - 1)^{-1}$  because  $\hat{N} = K$ . Thus, all monomorphic states are unstable if for every possible  $g$  an admissible  $a$  exists (*i.e.*,  $a \neq 0$ ,  $0 \leq g + 2a \leq 1$ ) such that (A2) is fulfilled.

If  $g = \theta$ , then (A2) simplifies to

$$f > \hat{\vartheta} \left(1 - \frac{a^2}{2V_s}\right)^{-1}. \tag{A3}$$

The right-hand side is increasing in  $a^2$  and attains its maximum if  $a = \frac{1}{2}\theta$  (because  $g + 2a \in [0, 1]$ ). We prove that

$$f > \phi_s = \hat{\vartheta} \left(1 - \frac{\theta^2}{8V_s}\right)^{-1} \tag{A4}$$

implies that for every  $g \in [0, 1]$  an admissible  $a$  exists such that (A2) holds.

Let  $g$  be given and consider first the case  $x = g - \theta > 0$ . Then a heterozygous effect  $a$  is admissible if and only if  $-\frac{1}{2}(\theta + x) \leq a \leq \frac{1}{2}(1 - \theta - x)$ . Let us define

$$\psi(a, x) = \frac{1 + 2x/a}{1 - s(a + x)^2}, \tag{A5}$$

where  $s = (2V_s)^{-1}$ , and observe that the right-hand side of (A2) is  $\hat{\vartheta}\psi(a, g - \theta)$ . A simple calculation shows that  $\psi(a, x)$  is decreasing in  $x$  if  $x \geq 0$  and  $-\frac{1}{2}(\theta + x) < a < 0$ . Therefore, for any such  $a$  and  $x$ , we have

$$\psi(a, x) \leq \psi(a, 0) \leq \psi\left(-\frac{1}{2}\theta, 0\right) = \phi_s/\hat{\vartheta}, \tag{A6}$$

and hence any allele with negative effect can invade the monomorphic equilibrium corresponding to  $g$  provided (A4) holds. An analogous argument shows that for  $x = g - \theta < 0$  and  $0 < a < \frac{1}{2}(1 - \theta - x)$ ,  $\psi(a, x)$  is increasing in  $x$ ; hence any allele with admissible  $a > 0$  can invade if  $f > \hat{\vartheta}(1 - (1 - \theta)^2/(8V_s))^{-1}$ , which is weaker than (A4) because  $\theta \geq \frac{1}{2}$  is assumed.

Finally, very simple rearrangements show that the equations  $f = \hat{\vartheta}(1 - \theta^2/(8V_s))^{-1}$ ,  $V_s = \hat{\vartheta}V_\alpha + \frac{1}{8}\theta^2$ , and  $f = \hat{\vartheta} + \theta^2/(8V_\alpha)$  are equivalent. Therefore,  $\phi_s$  can be expressed in both ways given in (10). The same applies to Equation 11.

