J. Math. Biol. 50, 355–396 (2005)
Digital Object Identifier (DOI):
10.1007/s00285-004-0294-2

Mathematical Biology

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A multilocus analysis of intraspecific competition and stabilizing selection on a quantitative trait

Received: 29 January 2004 / Revised version: 19 August 2004 /
Published online: 20 December 2004 – © Springer-Verlag 2004

Abstract. The equilibrium structure of an additive, diallelic multilocus model of a quantitative trait under frequency- and density-dependent selection is derived. The trait is under stabilizing selection and mediates intraspecific competition as induced, for instance, by differential resource utilization. It is assumed that stabilizing selection is weak, but the strength of competition may be arbitrary relative to it. Density dependence is caused by population regulation, which may be of a very general kind. The number and effects of loci are arbitrary, and stabilizing selection is not necessarily symmetric with respect to the range of phenotypic values. All previously studied models of intraspecific competition for a continuum of resources known to the author reduce to a special case of the present model if overall selection is weak. Therefore, in this case our results are applicable as approximations to all these models. Our central result is the (nearly) complete characterization of the equilibrium and stability structure in terms of all parameters. It is derived under the sole assumption that selection is weak enough relative to recombination to ignore linkage disequilibrium. In particular, necessary and sufficient conditions on the strength of competition relative to stabilizing selection are found that ensure the maintenance of multilocus polymorphism and the occurrence of disruptive selection. In this case, explicit formulas for the number of polymorphic loci at equilibrium, the allele frequencies, the genetic variance, and the strength of disruptive selection are obtained. For two loci, the effects of linkage are investigated analytically; for several loci, they are studied numerically.

1. Introduction

Intraspecific competition is a common ecological phenomenon. It may induce (negative) frequency-dependent selection and, therefore, has been incorporated in the explanation of several important evolutionary phenomena. Most prominently, it has been invoked as an agent for maintaining high levels of genetic variation (Cockerham et al. 1972; Bulmer 1974, 1980; Slatkin and Maynard Smith 1979; Clarke 1979, 2004; Asmussen and Basnayake 1990; Gavrilets and Hastings

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Mathematics Subject Classification (2000): 92D10, 92D15, 92D40, 34C60

Key words or phrases: Density-dependent selection – frequency-dependent selection – disruptive selection – balancing selection – recombination – linkage equilibrium – genetic variation – difference equations – gradient system

1995; Bürger 2002a,b), for causing diversification within a population, e.g., sex dimorphism (Slatkin 1984; Bolnick and Doebeli 2003), and for triggering the evolution of reproductive isolation and sympatric speciation (Udovic 1980; Doebeli 1996; Dieckmann and Doebeli 1999; Matessi et al. 2001; Gavrilets 2003, 2004). In modeling such phenomena, intraspecific competition is often envisaged to occur because individuals of similar phenotype (e.g., birds with similar bill size) compete for similar resource types (e.g., seeds of similar size) from a continuously distributed, but limited, resource spectrum (for the derivation of such resource utilization models, see e.g. Roughgarden 1972; May and Oster 1976; Christiansen and Fenchel 1977; Slatkin and Maynard Smith 1979). Therefore, two conflicting selective forces act on the population: Stabilizing selection on the trait favors genotypes with intermediate phenotype because the resource distribution is assumed to be unimodal, e.g., Gaussian, whereas frequency-dependent selection favors the phenotypes that deviate most from the prevailing ones because they experience less competition. In addition, population regulation induces density-dependent selection. It is this sort of model, in which a quantitative trait is subject to a combination of frequency-independent, frequency-dependent and density-dependent selection, that will be investigated here. Other types of models of intraspecific competition involve competition for discrete, usually one or two, resources (Matessi and Gatto 1984, Wilson and Turelli 1986) or fitnesses depending on pairwise interactions (Cokerham et al. 1972; Asmussen 1983; Asmussen et al. 2004).

Quantitative characters are known to be determined by several or many gene loci (Falconer and Mackay 1996; Bürger 2000). However, in most of the ecological literature, the genetic basis of traits is either ignored or oversimplified genetic models are employed. Models of various aspects of intraspecific competition for a continuous resource are among those that have been comparatively well explored. Analytical studies have been performed on the basis of phenotypic models (Slatkin 1979), single-locus models (Bulmer 1974, 1980; May and Oster 1976; Slatkin 1979; Christiansen and Loeschcke 1980), the so-called hypergeometric model (Doebeli 1996), and of two-locus models (Loeschcke and Christiansen 1984; Bürger 2002a,b). Studies with multiple loci relied either exclusively (Clarke et al. 1988; Mani et al. 1990; Dieckmann and Doebeli 1999) or primarily (Bürger and Gimelfarb 2004) on numerical methods. In these investigations, a zoo of similar but different ecological models has been used. In many cases, the results are only qualitative in nature, e.g., conditions are given when genetic variation is maintained but not how much, or they are exemplary.

What is needed for a better understanding of the evolutionary potential of intraspecific competition is the identification of general conditions under which intraspecific competition leads to qualitative changes in the pattern of genetic variation relative to ubiquitous stabilizing selection. Because stabilizing selection can maintain only (very) low levels of genetic variation (for a review, see Bürger 2000), such qualitative changes provide one of the prerequisites for explanations of evolutionary phenomena such as intraspecific diversification or sympatric speciation in terms of disruptive selection caused by intraspecific competition. In addition, these patterns of variation have to be characterized and quantified, and the relation to the occurrence of disruptive selection must be clarified.

The main purpose of this paper is the derivation of the equilibrium structure of a general model of stabilizing selection and intraspecific competition on a polygenic trait. In our model, the number of loci and their effects are arbitrary (but they contribute additively to the trait, without dominance or epistasis), selection on the trait can be asymmetric, and population regulation is very general. All previously studied models of intraspecific competition for a continuous resource known to the author reduce to a special case of the present model if overall selection is weak. The central assumption that makes the model analytically tractable is that selection is sufficiently weak relative to recombination to neglect linkage disequilibrium. The proofs are based on recent results of Turelli and Barton (2004) on the equilibrium structure of a certain class of multilocus models of balancing selection.

Before we introduce our general model, we review the pertinent theoretical literature on this topic in order to motivate our model and to show that the previous models reduce to special cases of ours in the limit of weak selection.

Apparently, in all models of intraspecific competition mediated by a quantitative trait, the effects of competition between phenotypes g and h have been described by a function $\alpha(g, h)$ that is chosen either as

$$\alpha(g,h) = \exp\left[-\frac{(g-h)^2}{2V_\alpha}\right] \tag{1.1}$$

or as

$$\alpha(g,h) = -a(g-h)^2\,, \tag{1.2}$$

where $a = 1/(2V_\alpha)$ measures the extent of competition between individuals. As in many previous models of this type (but see Slatkin 1979; Bulmer 1980), we neglect environmental contributions to the phenotype which, in the absence of genotype-environment interaction, would only cause a slight relaxation of selection on the genotypes. Therefore, we identify phenotypic and genotypic values. Let $\pi(h)$ denote the relative frequency of individuals with phenotype h. Then the intraspecific competition function $\bar{\alpha}_\pi(g)$, which measures the strength of competition experienced by phenotype g if the population distribution is π, is given by

$$\bar{\alpha}_\pi(g) = \sum_h \alpha(g,h)\pi(h)\,, \tag{1.3}$$

and the sum has to be replaced by an integral if the distribution of types is continuous. Assuming (1.2), we obtain

$$\bar{\alpha}_\pi(g) = 1 - a[(g-\bar{g})^2 + V_\mathrm{A}]\,, \tag{1.4}$$

where $\bar{g}$ and V_A denote the mean and the variance of π, respectively. (Below, V_A will be the additive genetic variance.)

Bulmer (1974, 1980), (Bürger 2002a,b), and Bürger and Gimelfarb (2004) assumed that the fitness function is of the form

$$W_{\mathrm{B}}(g) = \left(\rho - \frac{N}{\kappa}\,\bar{\alpha}_{\pi}(g)\right) S(g)\,, \tag{1.5}$$

where ρ and κ are positive parameters, N denotes the total population size, and $S(g)$ describes (frequency-independent) stabilizing selection. (For notational simplicity, the dependence of $W_{\mathrm{B}}(g)$ on N and π is omitted.) This means that competition and stabilizing selection act independently on the trait, e.g., at different ages. This is a reasonable assumption if stabilizing selection is extrinsic for frequency dependence, for instance, caused by the requirements of a functional morphology. Bulmer (1974, 1980) assumed that $S(g)$ is Gaussian, i.e.,

$$S(g) = \exp\left[-\frac{(g-\theta)^2}{2V_{\mathrm{s}}}\right], \tag{1.6}$$

where θ is the position of the optimum and V_{s} is a measure for the strength of stabilizing selection. (Bürger 2002a,b) and Bürger and Gimelfarb (2004) chose $S(g)$ to be quadratic, i.e.,

$$S(g) = 1 - s(g-\theta)^2\,, \tag{1.7}$$

where $s = 1/(2V_{\mathrm{s}})$, because this is more amenable to mathematical analysis.

Slatkin (1979) assumed that fitness of an individual with phenotypic value g has the Lotka-Volterra functional form

$$W_{\mathrm{S}}(g) = 1 + R - \frac{RN}{k(g)}\bar{\alpha}_{\pi}(g)\,, \tag{1.8}$$

where $\bar{\alpha}_{\pi}(g)$ is given by (1.3) together with (1.1), $1+R$ is the maximum fitness in the absence of competition, and $k(g)$ represents resources that can be utilized by an individual of type g. As a model for $k(g)$, Slatkin used a function proportional to a Gaussian density, i.e., (1.6) multiplied by K, the carrying capacity. We shall denote the 'variances' of the functions k and α in his model by σ_{k}^2 and σ_{α}^2. They can be interpreted as the variance of the resource distribution and the variance of the utilization function of an individual (or the individual's niche width), respectively. Essentially the same fitness function was used by Dieckmann and Doebeli (1999). Doebeli (1996) and Bolnick and Doebeli (2003) employed a variant of Slatkin's model but used the Hassell and the Beverton-Holt equation, respectively, for population regulation (see below).

Christiansen and Loeschcke (1980) and Loeschcke and Christiansen (1984) considered a model of competition in which fitness of individuals with genotype g is given by an expression analogous to (1.8), but with $R = R(g)$ depending on g, and a constant ratio of $R(g)$ and $k(g)$, i.e., $R(g)/k(g) \equiv V$. Their fitness function can be written as

$$W_{\mathrm{CL}}(g) = 1 + V[k(g) - N\bar{\alpha}_{\pi}(g)] \tag{1.9}$$

with $\bar{\alpha}_\pi(g)$ as in (1.3). Loeschcke and Christiansen (1984) used (1.6) multiplied by K for $k(g)$ and (1.1) for $\alpha(g-h)$, whereas Christiansen and Loeschcke (1980) used the quadratic approximations (1.7) and (1.2), respectively. The functions k and α have similar ecological interpretations as in Slatkin's model. Thus, in both types of models there is an intrinsic connection between frequency dependence and stabilizing selection because the latter emerges from the assumption of a unimodal distribution of resources.

Matessi et al. (2001) used a game-theoretically motivated model to study the evolution of reproductive isolation promoted by disruptive selection. Their fitness function has the form

$$W_{\mathrm{M}}(g) = 1 + \beta_1 g^2 - (\beta_1 + \beta_2)\bar{g}g + \beta_2(\bar{g}^2 + v)\,, \tag{1.10}$$

where $\bar{g}$ and $v(\widehat{=}V_{\mathrm{A}})$ are the mean and variance of the trait. They assumed $0 < \beta_1 < \beta_2$.

In general, all these models are different. However, in the limit of weak stabilizing selection and weak competition, they can be approximated by a much simpler one. Let us introduce the quantities

$$f = a/s \;\text{ and }\; \vartheta = \rho\kappa/N - 1 \tag{1.11}$$

as a measure of the strength of competition relative to stabilizing selection and as a compound measure of the demographic effects, respectively. Then all the fitness functions introduced above share an expression equivalent to

$$W_{\mathrm{App}}(g) = \left(\rho - \frac{N}{\kappa}\right)\left[1 - s(g-\theta)^2 + s\,\frac{f}{\vartheta}\big((g-\bar{g})^2 + V_{\mathrm{A}}\big)\right] \tag{1.12}$$

as their leading-order term in s and a; i.e., if terms of order $O(s^2)$, $O(a^2)$, and $O(sa)$ are neglected, they reduce to (1.12). If f is considered as a fixed parameter, then (1.12) is obtained simply by omitting terms of order $O(s^2)$ and higher.

It is simple to show for the fitness functions used by Bulmer (1974, 1980), (Bürger 2002a,b) and Bürger and Gimelfarb (2004) that the leading-order term is given by (1.12). For Slatkin's (1979) model this assertion follows from the relations

$$\kappa = K/R\,,\quad \rho = 1 + R\,,\quad s = (2\sigma_{\mathrm{k}}^2\vartheta)^{-1}\,,\quad a = (2\sigma_\alpha^2)^{-1}\,,\quad f/\vartheta = \sigma_{\mathrm{k}}^2/\sigma_\alpha^2\,. \tag{1.13}$$

In the models of Christiansen and Loeschcke (1980) and Loeschcke and Christiansen (1984), the 'variance' of the function $\alpha(g-h)$ is denoted by $2W^2$, that of $k(g)$ by $\sigma^2 + W^2$. Then the relations

$$\begin{aligned} &\kappa = 1/V\,,\ \rho = 1 + VK\,,\ s = \frac{K}{N\vartheta}\,\frac{1}{2(\sigma^2 + W^2)}\,,\\ &a = \tfrac{1}{4}W^{-2}\,,\ f/\vartheta = \frac{N}{K}\,\frac{\sigma^2 + W^2}{2W^2} \end{aligned} \tag{1.14}$$

identify (1.12) as the leading-order term of $W_{\mathrm{CL}}(g)$ (1.9). The model of Matessi et al. (2001) is density independent (hence, $N = \kappa(\rho - 1) = K$, $\vartheta = (\rho - 1)^{-1}$, $\rho - N/\kappa = 1$) and satisfies $\theta = 0$. If we set

$$s = \tfrac{1}{2}(\beta_2 - \beta_1) \quad \text{and} \quad f/\vartheta = \frac{\beta_2 + \beta_1}{\beta_2 - \beta_1}\,, \tag{1.15}$$

then $W_{\mathrm{M}} = W_{\mathrm{App}} + s(V_{\mathrm{A}} + \bar{g}^2)$. Therefore (see (3.3) and Appendix A), in linkage equilibrium the dynamics and equilibrium structure in their model are equivalent to ours'.

Although all these models become formally equivalent in the limit of weak selection, s is density dependent in the models of Slatkin and Christiansen and Loeschcke (loc. cit).

Somewhat simplified, the main result of Slatkin's (1979) analysis is that the fitness function is disruptive and polymorphism is maintained if $\sigma_\alpha^2 < \sigma_{\mathrm{k}}^2$ (provided environmental variance is neglected). Otherwise, selection is stabilizing and no genetic variation is maintained. Bulmer's (1974, 1980) results are essentially equivalent. These genetic models are not detailed enough to obtain quantitative results, for instance to calculate the amount of genetic variation. Christiansen and Loeschcke (1980) investigated a single-locus model with four alleles at a diploid locus in a randomly mating population and showed that polymorphism is maintained whenever competition is sufficiently strong, i.e., $\sigma^2 > W^2$, which is equivalent to $\sigma_\alpha^2 < \sigma_{\mathrm{k}}^2$. However, only two alleles can be maintained at equilibrium. Loeschcke and Christiansen (1984) explored the equilibrium structure of a diallelic two-locus model, mainly under the assumption of strong competition relative to stabilizing selection and recombination. Then both loci are always polymorphic, and for certain parameter combinations stable polymorphic equilibria may coexist (see Discussion). In (Bürger 2002a,b), the equilibrium structure of a diallelic two-locus model was characterized as a function of the recombination rate and the strength of competition relative to stabilizing selection. In addition, the amount of genetic variance, the shape of the fitness function at equilibrium, and the relation between mean fitness and the location of equilibria was investigated. The (primarily) numerical study of Bürger and Gimelfarb (2004) shows that these results remain valid if up to five loci determine the trait. In particular, the role of the number of loci was examined, and it was shown that the strength of competition relative to stabilizing selection necessary to induce multilocus polymorphism is approximately independent of the number of loci and their linkage relations.

In the next section, we introduce the general model. In Section 3, the main results are presented, namely the characterization of the equilibrium and stability structure for an arbitrary number of loci under the assumptions of linkage equilibrium and a constant population size. Section 4 contains a rather complete analysis for two linked loci. In Section 5, the linkage-equilibrium (LE) approximation of Section 3 is extended to include population regulation. In addition, some results about the full model with population regulation and linkage are presented. In Section 6, numerical calculations are used to explore the range of validity of the LE approximation, as well as the similarity between the model of Bürger and Gimelfarb (2004) and that

based on (1.12). The final section is devoted to the Discussion. Proofs are relegated to the Appendix.

2. The General Model

2.1. Assumptions on population growth and fitness

Many models of population growth in discrete time can be written in the form

$$N' = NF(N)\,, \tag{2.1}$$

where N and N' are the population sizes in consecutive generations and $F : [0, \infty) \to [0, \infty)$ is a strictly decreasing function of N (on the interval of admissible values) such that $F(N) = 1$ has a unique positive solution K, the carrying capacity. We also assume that F is twice differentiable. Throughout this paper, we are concerned only with functions F and parameter values that ensure that the ecological dynamics is simple, i.e., convergence to K occurs for all (admissible) initial conditions (see Thieme 2003, Chap. 9, for general conditions on F).

Important examples of F include the following (e.g., May and Oster 1976; Thieme 2003):

1. The so-called discrete logistic equation,

$$F(N) = \rho - N/\kappa\,, \quad 0 \le N < \rho\kappa\,. \tag{2.2}$$

The carrying capacity in this model is $K = (\rho - 1)\kappa$. Monotone convergence to K occurs for all $0 < N < \rho\kappa$ if $1 < \rho \le 2$, and oscillatory convergence (at a geometric rate) if $2 < \rho < 3$. Although the name discrete logistic equation is not really justified (there are other, sometimes more appropriate, discrete versions of the continuous logistic equation, such as the Ricker or the Beverton-Holt model; see Thieme 2003, Chap. 9), we shall use it for simplicity.

2. The Ricker difference equation (Ricker 1954),

$$F(N) = \exp[r(1 - N/K)]\,, \quad 0 \le N < \infty\,. \tag{2.3}$$

Convergence to K occurs (for all initial values $N > 0$) if and only if $r \le 2$.

3. A generalization of the models of Hassell and Maynard Smith,

$$F(N) = \frac{\lambda}{(1 + bN^{\xi})^c}\,, \quad 0 \le N < \infty\,. \tag{2.4}$$

If $\xi = 1$, this reduces to the model of Hassell (1975); if $\xi = 1$ and $c = 1$, the model of Beverton and Holt (1957) is obtained; if $c = 1$, a model suggested by Maynard Smith (1974) is obtained. The carrying capacity is $K = \left[(\lambda^{1/c} - 1)/b\right]^{1/\xi}$. For the Beverton-Holt model, it becomes $K = (\lambda - 1)/b$. We note that the Beverton-Holt model may be the most natural discretization of the continuous logistic equation because its solution is that of the continuous logistic equation evaluated at the integers (Thieme 2003, Chap. 9). All solutions with positive initial population size converge to K if and only if $\xi c \le 2$, as is trivially satisfied for the Beverton-Holt model.

We posit that the fitness of individuals with genotypic value g is

$$W(g) = F(N)[1 - s(g-\theta)^2 + s\eta(N)(g-\bar{g})^2 + s\varphi(N,\pi)]\,, \tag{2.5}$$

where

$$\eta(N) = \frac{-NF'(N)}{F(N)}\,f \tag{2.6}$$

and $\varphi(N,\pi)$ may be an arbitrary function of the population size and the distribution π of g, but is independent of g. (In the weak-selection limit analyzed in the next section, the genetic dynamics is independent of $\varphi(N,\pi)$; see below (3.4).) The quantity $\eta(N)$ can be viewed as a compound measure of the strength of frequency and density dependence relative to stabilizing selection. For the population-growth models introduced above, we obtain

$$\eta(N) = \begin{cases} f/(\rho\kappa/N - 1) & \text{if } F \text{ is given by (2.2)}\,, \\ frN/K & \text{if } F \text{ is given by (2.3)}\,, \\ f\,\dfrac{cb\xi N^{\xi}}{1+bN^{\xi}} & \text{if } F \text{ is given by (2.4)}\,. \end{cases} \tag{2.7}$$

We assume that η is strictly increasing in N, as is true in all these examples.

In accordance with (1.11) and the models discussed in the Introduction, we interpret f ($f \geq 0$) as the strength of frequency dependence relative to stabilizing selection. We will treat f as a parameter and note that, in contrast to the model of Bürger and Gimelfarb (2004), f can be arbitrarily large here.

The rationale for choosing the functional form (2.5) is that for fixed but arbitrary $f \geq 0$, $W(g)$ is the weak-selection approximation of any fitness function of the form

$$W_*(g) = F(N\bar{\alpha}_\pi(g))S(g)\,, \tag{2.8}$$

where $\bar{\alpha}_\pi(g) = 1 - sf[(g-\bar{g})^2 + V_\mathrm{A}] + O(s^2)$ and $S(g) = 1 - s(g-\theta)^2 + O(s^2)$, i.e., $W_*(g) = W(g) + O(s^2)$. In all models discussed in the Introduction, except that by Matessi et al. (2001), we have $\varphi(N,\pi) = \eta(N)V_\mathrm{A}$. In their model, $\varphi(N,\pi) = V_\mathrm{A}(1 + f/\vartheta) + \bar{g}^2$. If $F(N)$ is given by (2.2), then (2.5) reduces to (1.12). Therefore, (2.5) contains the weak-selection approximation of every model treated in the Introduction as special case.

From (2.5), the mean fitness of the population is calculated to be

$$\overline{W} = F(N)[1 - s(\Delta^2 + V_\mathrm{A}) + s\eta(N)V_\mathrm{A} + s\varphi(N,\pi)]\,, \tag{2.9}$$

where $\Delta = \bar{g} - \theta$. If we assume $\varphi(N,\pi) = \eta(N)V_\mathrm{A}$, some simple and important approximations can be derived for a population in demographic equilibrium ($\overline{W} = 1$). For example, the population size can be written as

$$\hat{N} = K + sK\left(2fV_\mathrm{A} + \frac{V_\mathrm{A} + \Delta^2}{KF'(K)}\right) + O(s^2C^2)\,. \tag{2.10}$$

where $C = \max(\Delta^2, V_A)$. For the discrete logistic and the Maynard Smith model, simple exact expressions can be obtained; see (C.1a) and (C.2). Substitution of any of these formulas into (2.6) produces approximate or explicit expressions for $\hat{\eta} = \eta(\hat{N})$; see Appendix C. Of course, V_A and Δ^2 depend on $\hat{N}$, and $\hat{N}$ may be different at different equilibria (Section 5), but the important point here is that for weak selection, sV_A and $s\Delta^2$ are small; hence $\hat{N}$ is close to K (cf. Bürger and Gimelfarb 2004, Tables 3 and 4). In general, the equilibrium values of V_A and Δ depend only weakly on the population size or, at monomorphic equilibria, are even independent of it (see Section 3).

2.2. Assumptions on genetics

Next we introduce the genetic 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 given by (2.5); thus, the trait experiences a combination of stabilizing and of frequency- and density-dependent selection. The trait is determined by n additive, diallelic loci of arbitrary effect. Dominance and epistasis are absent. We denote the alleles at locus i by A_i and a_i, their frequencies by P_i and Q_i ($P_i + Q_i = 1$), and their effects by $\frac{1}{2}\gamma_i$ and $-\frac{1}{2}\gamma_i$ ($\gamma_i > 0$). As noted by Turelli and Barton (2004), this choice is general if the difference of effects (the effect of a substitution) is γ_i because constants that determine the mean phenotype can be absorbed by θ. We assume that θ is within the range of possible genotypic values, i.e., $|\theta| \le \Gamma = \sum_{i=1}^{n} \gamma_i$. We shall call the optimum symmetric if $\theta = 0$.

The allele frequencies are sufficient to describe the multilocus dynamics only if there is linkage equilibrium. In general, we need the gamete frequencies. Gametes are designated by r, s, t, the frequency of gamete r among zygotes in consecutive generations by p_r and p_r', and the fitness of a zygote consisting of gametes s and t by W_{st} (we do not indicate the frequency and density dependence). Let $R(st \to r)$ denote the probability that a randomly chosen gamete produced by an st individual is r. The function R is determined by the pattern of recombination between loci.

2.3. The evolutionary dynamics

Since random mating is assumed and gamete frequencies are measured after reproduction and before selection, Hardy-Weinberg proportions obtain and the genetic dynamics is given by the well known system of recursion relations

$$p_r' = \overline{W}^{-1} \sum_{s,t} W_{st} p_s p_t R(st \to r) , \tag{2.11}$$

where $\overline{W} = \sum_{s,t} W_{st} p_s p_t$ is the mean fitness (e.g., Bürger 2000). We shall employ the full genetic dynamics only for numerical calculations and in the two-locus case.

The demographic dynamics follows the standard recursion relation

$$N' = N\overline{W} . \tag{2.12}$$

Thus, for a genetically monomorphic population with $g = \bar{g} = \theta$ (and $V_A = 0$), the difference equation (2.1) is obtained. The complete evolutionary dynamics is given by the coupled system (2.11) and (2.12).

In general, the complexity of this system prohibits a detailed analysis. This is why we concentrate on the case of linkage equilibrium. As will be shown below, this provides an accurate approximation unless linkage is tight.

3. Multiple Loci in Linkage Equilibrium

Previous studies of the model (1.5) with the choices (1.2), (1.7), (2.2) have shown that linkage disequilibrium becomes important only if linkage between loci is very tight (Bürger 2002b; Bürger and Gimelfarb 2004). Therefore, and to achieve analytical progress, we assume in this section that selection is sufficiently weak relative to recombination that the population is in (global) linkage equilibrium. Then its structure can be described by the allele frequencies. The functional forms of $W(g)$ and $\overline{W}$ are affected by the LE assumption only in so far as the genetic variance, V_A, has to be replaced by the linkage-equilibrium variance,

$$V_{LE} = 2\sum_i \gamma_i^2 P_i Q_i \,. \tag{3.1}$$

The population mean is not affected by this assumption and can be written as

$$\bar{g} = \sum_i \gamma_i (P_i - Q_i) \,. \tag{3.2}$$

The weak-selection limit of the full genetic dynamics (2.11), or the LE approximation, is of the much simpler form

$$\frac{d}{dt} P_i = \widetilde{W} \Delta P_i = P_i (\widetilde{W}_i - \widetilde{W}) \,, \quad i = 1, \ldots, n \,, \tag{3.3}$$

where $\widetilde{W}_i$ is the marginal fitness of allele A_i in linkage equilibrium and $\widetilde{W}$ is the mean fitness in linkage equilibrium (cf. Bürger 2000, p. 85). In particular, the dimensionality has been reduced from 2^n to n. If the population size is constant, for instance in demographic equilibrium, as we will assume for the rest of this section, then also F and η are constant, and we write

$$N \equiv \hat{N} \,, \quad F(N) \equiv \hat{F} = F(\hat{N}) \,, \quad \eta(N) \equiv \hat{\eta} = \eta(\hat{N}) \,; \tag{3.4}$$

cf. (2.10) and Appendix C. The relation between the model with constant population size and absence of linkage disequilibrium, (3.3), and the full model, in which $\hat{N}$ is not (exactly) known a priori, is investigated in Sections 5 and 6.

The allele-frequency dynamics (3.3) can be written as (Appendix A)

$$\dot{P}_i = \hat{F} s \gamma_i^2 P_i Q_i \left[(P_i - Q_i)(1 - \hat{\eta}) - 2\Delta/\gamma_i \right] \tag{3.5a}$$

$$= \hat{F} s \gamma_i^2 P_i Q_i \left[(P_i - Q_i) - 2\Delta/\gamma_i - 2\hat{\eta}(P_i - \tfrac{1}{2}) \right] . \tag{3.5b}$$

We remind the reader that $\Delta = \bar{g} - \theta$ is a function of the P_i ($i = 1, \ldots, n$). Except for a multiplicative factor, which is irrelevant for the equilibrium structure, (3.5b)

is equivalent to the system (7) in Turelli and Barton (2004), but with the simplification that their $\hat{p}_i = \frac{1}{2}$ and $v_i = \hat{\eta}$ for all i, where v_i denotes their parameter that quantifies the strength of balancing selection on locus i. Turelli and Barton (2004) derived the existence and stability conditions for monomorphic and polymorphic equilibria in their more general model. Application of their results to our model leads to some substantial simplifications and to a nearly complete characterization of the equilibrium structure of our model.

We note that the allele-frequency dynamics (3.5a), or (3.5b), is obtained not only from (2.5), but from any fitness function proportional to $\omega_0 + 2s(\theta - \hat{\eta}\bar{g})g - s(1-\hat{\eta})g^2$, where ω_0 is independent of g but may be an arbitrary function of the population distribution π (see Appendix A). As a consequence, the dynamics is independent of the term $\varphi(N, \pi)$ occuring in (2.5). Thus, effectively, frequency dependence enters the dynamics and equilibrium structure only through the mean phenotype $\bar{g}$. (In evolutionary game dynamics, such games are called population games; see Hofbauer and Sigmund 1998.) The system of equations (3.5a), or (3.5b), is also a special case of a general epistatic model introduced by Zhivotovsky and Gavrilets (1992). In their model, the expression in brackets is a linear function of the P_i.

In Appendix A it is shown that (3.5a) is a generalized gradient system (but its potential is not $\overline{W}$; see (A.7)). Therefore, all solutions converge to the set of equilibria (e.g., Bürger 2000, pp. 349-352, or Hofbauer and Sigmund 1998) and, if there is a single locally stable equilibrium, it must be globally stable.

Our main results are the following. The proofs are given in Appendix B.

Theorem 1. *Let $\hat{\eta} < 1$. Then*

(i) at most one locus can be polymorphic at a stable equilibrium;
(ii) multiple stable equilibria may coexist;
(iii) for every given set of locus effects (γ_i) such that no completely homozygous genotype matches the optimum θ, only single-locus polymorphisms can be stable if $\hat{\eta}$ is sufficiently close to 1.

Theorem 2. *Let $\hat{\eta} > 1$. Then there exists a unique (globally) asymptotically stable equilibrium. At this equilibrium, at least one locus is polymorphic.*

(i) This equilibrium is fully polymorphic if and only if

$$\gamma_i > \frac{2\,|\theta|}{2n + \hat{\eta} - 1} \quad \textit{for all } i\,. \tag{3.6}$$

The allele frequencies are

$$\hat{P}_i = \frac{1}{2} + \frac{1}{\gamma_i}\,\frac{\theta}{2n + \hat{\eta} - 1}\,. \tag{3.7}$$

(ii) A stable, fully polymorphic and symmetric equilibrium ($\hat{P}_i = \frac{1}{2}$ for all i) exists if and only if $\theta = 0$. The only stable equilibrium at which $\hat{\Delta} = 0$, i.e., $\hat{\bar{g}} = \theta$, is the fully polymorphic symmetric equilibrium.

(iii) If the unique stable equilibrium is not fully polymorphic (hence, $\theta \neq 0$), we order loci so that $\gamma_1 \leq \gamma_2 \leq \ldots \leq \gamma_n$. Then

(a) there exists a unique integer m, where $1 \leq m \leq n-1$, such that loci $1, \ldots, m$ are fixed, and loci $m+1, \ldots, n$ are polymorphic. This m is the largest integer $\leq n-1$ that satisfies

$$\gamma_m[2(n-m)+\hat{\eta}+1] + 2\sum_{i=1}^{m-1}\gamma_i < 2|\theta| \; ; \tag{3.8}$$

(b) the allele frequencies of the fixed loci are all 1 (i.e., the + allele is fixed) if $\theta > 0$, and all 0 if $\theta < 0$; the allele frequencies of the polymorphic loci are

$$\hat{P}_i = \frac{1}{2} + \frac{1}{\gamma_i}\,\frac{\theta - \delta_\theta \sum_{j=1}^{m}\gamma_j}{2(n-m)+\hat{\eta}-1}\,, \tag{3.9}$$

where $\delta_\theta = 1$ if $\theta > 0$, and $\delta_\theta = -1$ if $\theta < 0$. We have $\hat{P}_i > \frac{1}{2}$ if and only if $\theta > 0$.

These theorems demonstrate that the equilibrium structure depends crucially on whether $\hat{\eta} > 1$ or not. For the model with population regulation, this condition is deceptively simple because $\hat{\eta}$ depends on the population size, which is not (exactly) known without solving the full model. This problem is treated in Section 5. Because (2.10) informs us that in demographic equilibrium $\hat{N} = K + O(s)$, simple approximations for $\hat{\eta}$ can be derived (Appendix C). As a consequence, simple and accurate approximations for the $\hat{P}_i$ and derived quantities are obtained by approximating $\hat{\eta}$ by its leading-order term $-fKF'(K)$; see (C.4). The relative error is of order $O(s) = O(\hat{N}/K - 1)$. Numerical examples are given in Table 1.

Let us now discuss the above theorems and some of their consequences.

The case $\hat{\eta} < 1$ includes pure stabilizing selection ($\hat{\eta} = 0$). Under the assumption of linkage equilibrium, Wright (1935) showed that with a symmetric optimum and quadratic stabilizing selection, at most one locus can be maintained polymorphic. Barton (1986) proved that this result remains valid for loci of equal effects and an arbitrary optimum. For two loci of arbitrary effect, an arbitrary optimum, and linkage equilibrium, Hastings and Hom (1990) characterized the equilibrium structure completely. At most two equilibria can be simultaneously stable, and a fully polymorphic equilibrium may exist but is always unstable (see also Bürger 2000, pp. 212–215). Bürger and Gimelfarb (1999) performed a numerical study of the full model with linkage, and a symmetric optimum, for up to five loci. Theorem 1 confirms and extends these results by demonstrating that for sufficiently weak frequency dependence, the equilibrium structure is very similar to that under pure stabilizing selection. Increasing strength of frequency dependence leads to a higher fraction of trajectories converging to single-locus polymorphisms, but no stable multilocus polymorphisms exist. If stabilizing selection is modeled by fitness functions other than quadratic, more complicated equilibrium structures can be obtained (Nagylaki 1989; Willensdorfer and Bürger 2003).

For the rest of this section, we assume $\hat{\eta} > 1$.

Table 1. Equilibrium structure in two six-locus systems for strong competition. The LE approximations for the allele frequencies $\hat{P}_i$ (3.9), as well as for $\hat{\Delta}$ (3.10) and $\hat{V}_{\mathrm{LE}}$ (3.11), are compared with results from numerical iteration of (2.11) and (2.12) for various recombination scenarios. The following parameters are fixed in all cases: $\rho = 2$, $\theta = 0.25$, $\Gamma = 0.5$, $s = 0.4$, $a = 0.625$ ($V_\alpha = 0.8$). Therefore, the relative fitnesses of the extreme phenotypes, $-\frac{1}{2}$ and $\frac{1}{2}$, are 0.775 and 0.975, respectively. If $N = K$ is assumed to calculate the theoretical values, we have $\hat{\eta} = f = 1.5625$, and the values in the rows 'Theory, $N = K$' are obtained. If $\hat{\eta}$ is calculated numerically from (C.3a), as described below (C.7), we obtain $\hat{\eta} = 1.633$ ($\hat{N} = 10221$) for the first set of values γ_i, and $\hat{\eta} = 1.684$ ($\hat{N} = 10375$) for the second. The exact values from numerical iteration of the full model are $\hat{\eta} = 1.634$ ($\hat{N} = 10222$) and $\hat{\eta} = 1.685$ ($\hat{N} = 10378$), respectively. For $0.005 \le r \le 0.05$, recombination rates between adjacent loci were chosen randomly from a uniform distribution and are $r = 0.0122, 0.0089, 0.0372, 0.0292, 0.0415$. In the case of two chromosomes, we have $r = 0.001, 0.001, 0.5, 0.001, 0.001$.

	$\hat{P}_1$	$\hat{P}_2$	$\hat{P}_3$	$\hat{P}_4$	$\hat{P}_5$	$\hat{P}_6$	$\hat{\Delta}$	$\hat{V}_{\mathrm{A}}$	$\hat{V}_{\mathrm{LE}}$
Effects γ_i:	0.019	0.124	0.015	0.056	0.127	0.159			
Theory, $N = K$	1.000	0.704	1.000	0.954	0.698	0.658	−0.014		0.025
Theory, (C.3a)	1.000	0.702	1.000	0.950	0.696	0.657	−0.016		0.025
$r = 0.5$	1.000	0.702	1.000	0.947	0.696	0.658	−0.016	0.025	0.025
$r = 0.1$	1.000	0.706	1.000	0.936	0.693	0.659	−0.017	0.026	0.025
$0.005 \le r \le 0.05$	1.000	0.712	1.000	0.891	0.692	0.665	−0.019	0.027	0.025
$r = 0.01$	1.000	0.731	1.000	0.764	0.679	0.675	−0.028	0.035	0.025
two chromosomes	0.956	0.848	1.000	0.645	0.643	0.643	−0.033	0.052	0.025
$r = 0.001$	0.683	0.676	0.673	0.675	0.676	0.676	−0.074	0.097	0.027
$r = 0$	0.669	0.669	0.669	0.669	0.669	0.669	−0.081	0.111	0.027
Effects γ_i:	0.004	0.015	0.148	0.062	0.266	0.006			
Theory, $N = K$	1.000	1.000	0.742	1.000	0.635	1.000	−0.020		0.041
Theory, (C.3a)	1.000	1.000	0.736	1.000	0.631	1.000	−0.024		0.041
$r = 0.5$	1.000	1.000	0.732	1.000	0.632	1.000	−0.024	0.042	0.041
$r = 0.1$	1.000	1.000	0.729	0.982	0.636	1.000	−0.026	0.042	0.041
$0.005 \le r \le 0.05$	1.000	1.000	0.731	0.862	0.653	1.000	−0.031	0.045	0.041
$r = 0.01$	1.000	1.000	0.704	0.692	0.678	1.000	−0.047	0.058	0.041
two chromosomes	1.000	0.953	0.814	0.655	0.654	0.786	−0.036	0.053	0.040
$r = 0.001$	0.855	0.683	0.673	0.673	0.673	0.729	−0.075	0.100	0.042
$r = 0$	0.669	0.669	0.669	0.669	0.669	0.669	−0.081	0.111	0.043

The existence condition (3.6) shows that increasing $\hat{\eta}$ promotes the existence of a stable, fully polymorphic equilibrium. Similarly, condition (3.8) shows that with increasing $\hat{\eta}$ the number m of fixed loci decreases. However, the conclusion that increasing n promotes existence of a fully polymorphic equilibrium cannot be drawn (see the Discussion).

An explicit expression for the deviation $\hat{\Delta}$ of the mean from the optimum is (Appendix B, proof of Theorem 2)

$$\hat{\Delta} = \frac{\delta_\theta \sum_{i=1}^{m} \gamma_i - \theta}{1 + \frac{2(n-m)}{\hat{\eta}-1}}, \tag{3.10}$$

where $\delta_\theta = 1$ if $\theta > 0$ and $\delta_\theta = -1$ if $\theta < 0$ (if $\theta = 0$, then $m = 0$ and (3.10) simplifies to (B.7)). Together with (3.8), (3.10) informs us that $\hat{\Delta} > 0$ if and only if $\theta < 0$. In particular, we have $\hat{\Delta} = 0$ if and only if $\theta = 0$, cf. (B.7). Moreover, (3.10) demonstrates that $\hat{\Delta} \to 0$ as $n \to \infty$ (or as $\hat{\eta} \to 1$ from above) as well as $\hat{\Delta} \to -\theta$ as $\hat{\eta} \to \infty$ (because then (3.6) is satisfied and $m = 0$). Hence, for sufficiently strong frequency dependence, we have $\hat{\bar{g}} \approx 0$, independently of θ.

Because for $\hat{\eta} > 1$ the locus (loci) with largest effect(s) is polymorphic, the genetic variance is usually very high even if the equilibrium is not fully polymorphic. This is supported by numerical calculations (see Figure 2a in Bürger and Gimelfarb 2004). In our model, the genetic variance at this equilibrium can be calculated explicitly by substituting (3.9) into (3.1):

$$\hat{V}_{\mathrm{LE}} = \frac{1}{2}\sum_{i\in\Omega_{\mathrm{p}}}\gamma_i^2 - 2(n-m)\frac{\left(\sum_{i\notin\Omega_{\mathrm{p}}}\gamma_i - |\theta|\right)^2}{(2(n-m)+\hat{\eta}-1)^2}\,, \tag{3.11}$$

where m is defined by (3.8) and Ω_{p} is the set of polymorphic loci (B.3); thus, $\sum_{i\notin\Omega_{\mathrm{p}}} = \sum_{i=1}^{m}$. For a fully polymorphic symmetric equilibrium, i.e., if and only if $\theta = 0$, we obtain $\hat{V}_{\mathrm{LE}} = V_{\max}$, where $V_{\max} = \frac{1}{2}\sum_{i=1}^{n}\gamma_i^2$ is the maximum variance that can be maintained by the given genetic system in linkage equilibrium. Otherwise, $\hat{V}_{\mathrm{LE}} < V_{\max}$ because $\sum_{i\notin\Omega_{\mathrm{p}}}\gamma_i = |\theta|$ is impossible. (By (3.10) this would imply $\hat{\Delta} = 0$, which can occur only at a symmetric equilibrium.) Obviously, for given allelic effects γ_i, the equilibrium variance $\hat{V}_{\mathrm{LE}}$ increases as $\hat{\eta}$ increases because, by (3.8), the latter implies that m is not increasing.

If there are alleles of equal effect, then these loci are either all fixed for the same allele or all polymorphic with identical frequencies. The reason is that the left-hand side of (3.8) is constant on sets of loci i with identical effects γ_i. If all alleles have the same effect, then the stable equilibrium is always fully polymorphic. Therefore, the assumption of equal effects is particularly favorable for competition to maintain polymorphism at many loci.

For two loci, we have a stable equilibrium with exactly one polymorphic locus if and only if

$$\gamma_1 < \frac{2\theta}{3+\hat{\eta}}\,. \tag{3.12}$$

Otherwise, both loci are polymorphic.

4. Two Linked Loci

In this section, the equilibrium structure of a two-locus version of the discrete-time model (2.11) with the fitness function (1.12) is explored, in which linkage disequilibrium is not neglected but population size is assumed constant, for instance at demographic equilibrium. We write η instead of $\hat{\eta}$. The recombination rate r is arbitrary ($0 < r \le \frac{1}{2}$).

We use the following notation. The relative frequencies of the four gametes A_1B_1, A_1B_2, A_2B_1, A_2B_2 among newly formed zygotes are p_1, p_2, p_3, p_4, respectively. The gametes are labeled $i = 1, 2, 3, 4$. Frequencies in the subsequent generation are denoted by p_i'. Let the contributions of the alleles A_1, A_2, B_1, and B_2 to the genotypic value g of the trait be $-\frac{1}{2}\gamma_1$, $\frac{1}{2}\gamma_1$, $-\frac{1}{2}\gamma_2$, and $\frac{1}{2}\gamma_2$, respectively. Because of additivity, the effects of the gametes A_1B_1, A_1B_2, A_2B_1, and A_2B_2 are $-\frac{1}{2}(\gamma_1+\gamma_2)$, $-\frac{1}{2}(\gamma_1-\gamma_2)$, $\frac{1}{2}(\gamma_1-\gamma_2)$, and $\frac{1}{2}(\gamma_1+\gamma_2)$. The resulting genotypic values are shown in Table 1 of Bürger (2002b). For definiteness, we assume $\gamma_1 \geq \gamma_2 > 0$ and refer to the A and B locus as major and minor, respectively. We denote

$$e = \frac{\gamma_1 - \gamma_2}{\gamma_1 + \gamma_2}\,, \quad t = s(\gamma_1+\gamma_2)^2\,, \tag{4.1}$$

with s as in (1.7). Then, with $\Gamma = \gamma_1 + \gamma_2$, the range of possible genotypic values is $[-\Gamma, \Gamma]$ and $\Gamma^2/4$ may be called the average (substitutional) effect of the loci on the variance of the trait. The parameter e measures the disparity of effects ($0 \leq e < 1$, and $e \geq \frac{1}{3}$ if the effects differ by a factor of two or more), and t is a scaled measure for the strength of stabilizing selection. (We have $0 \leq t \leq 1$ because $S(g)$ must be positive). A related model was investigated in Bürger (2002b), where a more detailed description including the (standard) recursion relations may be found. Here, stronger results are obtained. If s_a and c denote the parameters used in Bürger (2002b) to describe the strengths of stabilizing selection and competition, respectively, we have $t = 4s_a$ and $\eta = c/s_a$. We assume $\theta = 0$ and a constant population size, i.e., constant η. We exclude the degenerate case $\eta = 1$, in which there is a two-dimensional manifold of equilibria that, apparently, attracts all trajectories.

It is straightforward to show that if $(\hat{p}_1, \hat{p}_2, \hat{p}_3, \hat{p}_4)$ is an equilibrium, then $(\hat{p}_4, \hat{p}_3, \hat{p}_2, \hat{p}_1)$ is also an equilibrium, and both have the same stability properties. In terms of the coordinates $(x, y, z) = (p_1 + p_4, p_1 - p_4, p_2 - p_3)$, this means that the simultaneous transformation $y \to -y$ and $z \to -z$ preserves the property of being an equilibrium, as well as the stability properties of this equilibrium. Thus, all, except symmetric ($y = z = 0$), equilibria coexist in pairs. We refer to Figure 1 for a graphical representation of the equilibrium structure in two typical special cases.

4.1. Monomorphic equilibria

There always exist the four corner equilibria, at which both loci are monomorphic. Of these, the equilibria $\hat{p}_1 = 1$ and $\hat{p}_4 = 1$, i.e., fixation of one of the gametes with large genotypic effect (A_1B_1, A_2B_2), are always unstable. Analytical computation of the eigenvalues shows that the equilibria $\hat{p}_2 = 1$ (fixation of A_1B_2) and $\hat{p}_3 = 1$ (fixation of A_2B_1) are both locally asymptotically stable if and only if the following conditions are satisfied:

$$r \geq r_0 = \frac{te^2(1+\eta)}{1+te^2\eta} \tag{4.2a}$$

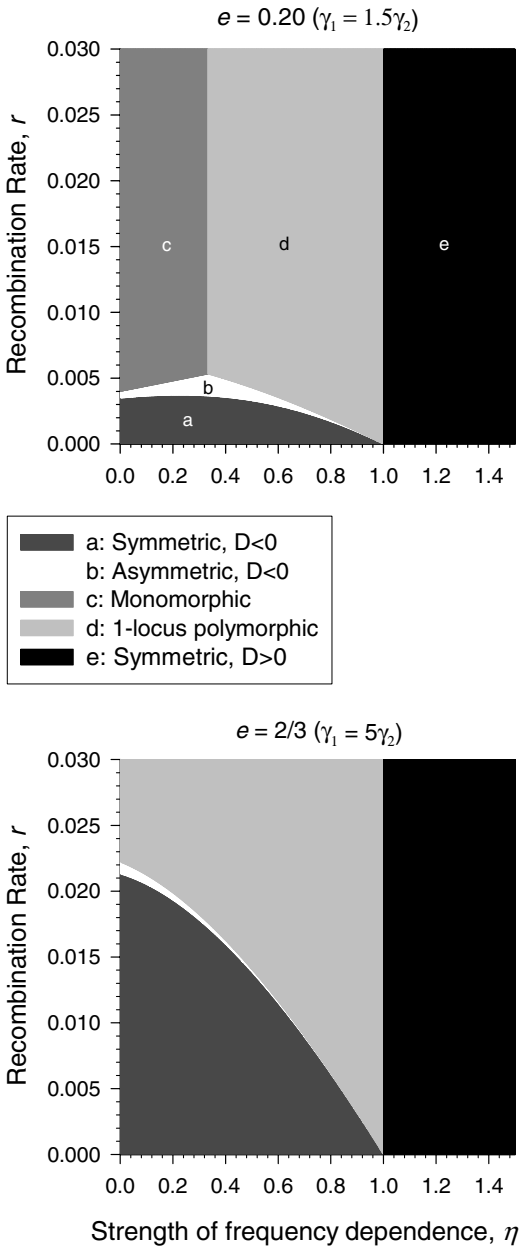

Fig. 1. Regions of stability of the five possible types of stable equilibria for the two indicated values of the disparity e of locus effects. In all cases, the strength of stabilizing selection is $t = 0.1$, so the fitness of the extreme genotypes under stabilizing selection alone is 90% of the maximum possible fitness (as in the numerical results of Section 6). The boundaries between the regions a and b, b and c, b and d, c and d, and d and e are given by r_2, r_0, r_1, η_0, and $\eta = 1$, respectively. The white region extends to $r = 0$ and $\eta = 1$ but becomes too thin to be visible. Moreover, the figures show only a restricted parameter range (small r and η) to improve the visibility of the effects of linkage. With stronger selection, the regions a and b would, of course, extend to much larger values of r; see (4.6a).

and

$$\eta \le \eta_0 = \frac{1-3e}{1+e} \,. \tag{4.2b}$$

It may be noted that $r_0 = r_0(t, \eta, e)$ is an increasing function in each of the variables t, η, and e (in η, because $te^2 \le 1$ holds by assumption). If $0 \le e \le \frac{1}{3}$, then $\eta_0 = \eta_0(t, \eta, e)$ is increasing in t and decreasing in e. Condition (4.2b) shows that the monomorphic equilibria can never be stable if $e > \frac{1}{3}$ or if $\eta > 1$. It is equivalent to $e < (1-\eta)/(3+\eta)$.

Because r_0 is increasing in η, and stability of $\hat{p}_2 = 1$ and $\hat{p}_3 = 1$ requires (4.2b), these monomorphic equilibria are asymptotically stable whenever (4.2b) is satisfied and

$$r \ge r_0(r, \eta_0, e) = r_{0,\max} = \frac{2te^2(1-e)}{1+e+te^2(1-3e)} \,. \tag{4.3}$$

Evaluation of r_0 at $\eta = 0$ informs us that these monomorphic equilibria are never stable if $r < te^2$.

Numerical iteration of the recursion relations suggests that each of the two monomorphic equilibria, $\hat{p}_2 = 1$ and $\hat{p}_3 = 1$, is globally attracting for half of the state space whenever it is asymptotically stable. For equal effects ($e = 0$) this follows directly from the results in Bürger (2002a) by omitting terms of order cs.

4.2. Single-locus polymorphisms

There may exist up to four equilibria with one locus polymorphic and one locus monomorphic. Only the equilibria with the major locus (the A locus) polymorphic can be asymptotically stable. They are located on the edges $p_1 + p_3 = 1$ or $p_2 + p_4 = 1$ of the simplex, and exist if and only if

$$\eta > \eta_0 = \frac{1-3e}{1+e} \,. \tag{4.4}$$

Thus, they exist only if the monomorphic equilibria are unstable. If (4.4) is fulfilled, which is always the case if $e > \frac{1}{3}$, the unique interior equilibrium on $p_1 + p_3 = 1$ is given by

$$\hat{p}_1 = \frac{\eta - 1 + e(3+\eta)}{2(1+e)(1+\eta)} \,. \tag{4.5}$$

The equilibrium coordinate $\hat{p}_1$ increases with η and satisfies $\hat{p}_1 < \frac{1}{2}$.

This equilibrium is unstable if $\eta > 1$. If $\eta_0 < \eta < 1$, then it is asymptotically stable, provided

$$r \ge r_1 = r_1(t, \eta, e) = \frac{8te(1-\eta)(1+\eta)^3}{(3+\eta)[8(1+\eta)^2 + t\eta\psi]} \tag{4.6a}$$

$$= te\,\frac{1-\eta^2}{3+\eta} + O(t^2) \,, \tag{4.6b}$$

where $\psi = \eta^2(3 - 2e + 3e^2) - 2\eta(1 - 6e + e^2) - (1 - 6e + e^2) \geq -\frac{4}{3}$ (see Appendix D). It follows that r_1 decreases (to 0) as η increases (to 1). If $\eta = \eta_0$, we have $r_1(t, \eta_0, e) = r_{0,\max}$ (4.3) if $e \leq \frac{1}{3}$, and $r_1(t, 0, e) = \frac{4}{3}et$ if $e > \frac{1}{3}$ (cf. Bürger 2000, p. 205). By symmetry, analogous results are valid for the equilibrium at the edge $p_2 + p_4 = 1$, which is obtained from (4.5) by substituting p_4 for p_1.

The single-locus polymorphic equilibria at the edges $p_1 + p_2 = 1$ and $p_3 + p_4 = 1$ exist if and only if

$$\eta > \frac{1 + 3e}{1 - e}\,.$$

These equilibria are always unstable (even within the respective single-locus system). The equilibrium value of p_1 is obtained from (4.5) by substituting $-e$ for e.

4.3. Two-locus polymorphisms

Analytically explicit determination of all interior equilibria seems to be impossible. Analytical calculations combined with numerical searches revealed that if $\eta \neq 1$, two classes of interior equilibria may exist and be stable: a symmetric equilibrium and a pair of asymmetric equilibria satisfying $D < 0$.

4.3.1. The symmetric equilibrium

There always exists one symmetric equilibrium, $\hat{p}_1 = \hat{p}_4$ and $\hat{p}_2 = \hat{p}_3$. It is the unique solution of

$$\begin{aligned} &4t(1 - e^2)(1 - \eta - 2\eta r)p_1^2 - 2[t(1 - \eta)(1 - e^2) \\ &\quad + r(4 - t\eta(1 - 3e^2))]p_1 + r(2 + t\eta e^2) = 0 \end{aligned}$$

in the interval $[0, \frac{1}{2}]$, and can be written as

$$\hat{p}_1 = \begin{cases} \dfrac{t(1 - \eta)(1 - e^2) + 4r - tr\eta(1 - 3e^2) - \sqrt{A}}{4t(1 - e^2)(1 - \eta - 2\eta r)} & \text{if } \eta \neq \dfrac{1}{1 + 2r}\,, \\ \dfrac{2 + 4r + e^2 s}{2(4 + 8r + s + e^2 s)} & \text{if } \eta = \dfrac{1}{1 + 2r}\,, \end{cases} \tag{4.7}$$

where $A = t^2(1 - e^2)^2(1 - \eta)^2 - 2t^2\eta r(1 - \eta)(1 - e^2)^2 + r^2(4 + t\eta(1 + e^2))^2$. A useful approximation is

$$\hat{p}_1 = \begin{cases} \dfrac{1}{4} - \dfrac{t(1 - e^2)(1 - \eta)}{32r} + O(t^2) & \text{if } \eta \neq \dfrac{1}{1 + 2r}\,, \\ \dfrac{1}{4} - \dfrac{t(1 - e^2)}{16(1 + 2r)} + O(t^2) & \text{if } \eta = \dfrac{1}{1 + 2r}\,. \end{cases} \tag{4.8}$$

If $\eta > 1$, then $\hat{p}_1 > \frac{1}{4}$; hence, $D > 0$, and apparently this equilibrium is globally asymptotically stable.

If $\eta < 1$, then $0 < \hat{p}_1 < \frac{1}{4}$; hence, $D < 0$. In this case, the symmetric equilibrium is asymptotically stable if and only if

$$r \leq r_2 = r_2(t, \eta, e) \,, \tag{4.9}$$

where r_2 can be computed numerically because closed, but complicated, expressions for the eigenvalues are available (provided by *Mathematica*). Iteration of the recursion relations suggests that then the symmetric equilibrium is globally stable. Because of the constraint $r > 0$, (4.9) can be satisfied only if $0 \leq \eta \leq 1$.

If $\eta = 0$, then r_2 can be determined explicitly, i.e.,

$$r_2(t, 0, e) = \tfrac{1}{6} t \left(-1 - e^2 + \sqrt{1 + 14e^2 + e^4} \right) \,,$$

and the symmetric equilibrium can be proven to be asymptotically stable (see Bürger 2000, pp. 205–207, where a different notation is used). By continuity, this extends to small (positive) values of η. Apparently, r_2 is decreasing as a function of η, whence the symmetric equilibrium with $D < 0$ can be stable only if $r \leq r_2(s, 0, e)$.

It can be shown that the position $\hat{p}_1$ of the symmetric equilibrium, and therefore the amount of linkage disequilibrium $\hat{D} = \hat{p}_1 - \frac{1}{4}$, is an increasing function of η. The absolute value of $\hat{D}$ increases with decreasing r. If $\eta > 1$, then for every $t \geq 0$ and $r > 0$, $\hat{p}_1$ approaches an upper limit $< \frac{1}{2}$ as $\eta \to \infty$.

4.3.2. Asymmetric equilibria

In the absence of competition ($\eta = 0$), asymmetric interior equilibria exist and are asymptotically stable if $e > 0$ and

$$r_2(s, 0, e) < r < \begin{cases} r_0(s, 0, e) = 4e^2 s & \text{if } e \leq \frac{1}{3} \,, \\ r_1(s, 0, e) = \frac{4}{3} e s & \text{if } e > \frac{1}{3} \,. \end{cases}$$

They can be calculated explicitly (e.g., Bürger 2000, p. 205). Because of continuity, they also exist for sufficiently small $\eta > 0$. Unfortunately, for $\eta > 0$ their explicit calculation seems to be impossible. Numerical iteration of the recursion relations and numerical solution of the equilibrium conditions suggest that they are asymptotically stable whenever they exist, which is the case if and only if

$$r_2(s, \eta, e) < r < \begin{cases} r_0(s, \eta, e) & \text{if } \eta < \eta_0 \text{ and } e \leq \frac{1}{3} \,, \\ r_1(s, \eta, e) & \text{otherwise} \,, \end{cases} \tag{4.10}$$

is satisfied. Here, r_0, r_1, and r_2 are as in (4.2a), (4.6a) and (4.9), respectively.

Apparently, none of the above-described types of equilibria can be simultaneously stable; hence there are never more than two stable equilibria.

Here is a verbal, qualitative summary of the main results of this section. If $\eta < 1$ and linkage is loose, then a pair of boundary equilibria is stable. They are monomorphic if the effects of the loci are similar (depending on η); otherwise the major locus is polymorphic. If $\eta < 1$ and linkage is sufficiently tight, then all boundary equilibria are unstable. Instead, one symmetric or a pair of asymmetric interior

equilibria is stable. These equilibria always display negative linkage disequilibrium. If $\eta > 1$, no boundary equilibrium can be stable, whatever the recombination rate. Instead, a unique interior equilibrium with all allele frequencies equal to $\frac{1}{2}$ and positive linkage disequilibrium is, apparently, globally stable. The tighter linkage, the higher is the linkage disequilibrium.

5. Analytical Results for the Full Model

The equilibrium structure in the LE approximation of Section 3 depends crucially on whether $\hat{\eta} > 1$ or not. As already noted, this condition is deceptively simple because, with population regulation, $\hat{\eta}$ is not a parameter but a function of several parameters; in particular, it depends on the population size at equilibrium. Therefore, we first consider the LE approximation and relax the assumption of a constant population size, i.e., we investigate the system (3.5a) coupled with the demographic dynamics

$$\dot{N} = N(\overline{W} - 1)\,, \tag{5.1}$$

which is the continuous-time version of (2.12). However, we assume that s is independent of N (See Introduction). At equilibrium, $\overline{W} = 1$ must be satisfied. This yields the equilibrium population size $\hat{N}$ as a function of the basic parameters and of Δ^2 and V_{LE} (see (2.10), (C.1a), (C.2) for approximate or exact expressions). It follows that $\hat{N}$ may be different at different equilibria of the same genetic system. However, this difference is order $O(s)$.

For given $\hat{N}$, the equilibria can be determined as in Section 3. The stability properties of an equilibrium of (3.5a) and (5.1) are governed by the Jacobian. Its entries in the first n rows and n columns are equal to those of the Jacobian of (3.5a) with constant population size. Assuming demographic equilibrium and using $\overline{W} = 1$ in (2.9), we obtain the entry at position $(n+1, n+1)$,

$$\frac{\partial \dot{N}}{\partial N} = F(N)^{-1}\Big[F'(N) + 2sfV_{\mathrm{LE}}(-F(N)F'(N) \\ -NF(N)F''(N) + NF'(N)^2)\Big]\,. \tag{5.2}$$

Because $F'(N) < 0$ by assumption and $V_{\mathrm{LE}} \le V_{\max}$, $\partial\dot{N}/\partial N$ is negative whenever s is small enough. The entry at position $(i, n+1)$, $1 \le i \le n$, is

$$\frac{\partial \dot{P}_i}{\partial N} = -s\gamma_i^2 F(N)\eta'(N)P_i(1-P_i)(2P_i-1)\,, \tag{5.3}$$

which is zero if locus i is fixed or if $P_i = \frac{1}{2}$. The entry at position $(n+1, i)$, $1 \le i \le n$, is

$$\frac{\partial \dot{N}}{\partial P_i} = -2s\gamma_i^2 NF(N)\left[(2P_i-1)(1-2\eta(N)) - 2\Delta/\gamma_i\right]\,. \tag{5.4}$$

By (3.5a), this simplifies to $2s\gamma_i^2 NF(N)\eta(N)(2P_i-1)$ if locus i is polymorphic at equilibrium. It follows that $\hat{N}$ is locally stable, and the eigenvalues pertaining

to the coordinates $P_1, \ldots, P_n$ differ from those of the system (3.5a) with constant population size by terms of order s^2 or smaller. Since such terms have been ignored in the derivation of the LE approximation, these differences are essentially irrelevant. It also follows that monomorphic and fully polymorphic symmetric equilibria have exactly the same eigenvalues in both kinds of models.

Because for a given genetic system, $\hat{N}$ and, hence, $\hat{\eta}$ are not uniquely determined in the model with population regulation, equilibria may stably coexist that cannot be simultaneously stable under the dynamics (3.5a) with a constant population size. As a simple example, consider two loci of equal effects ($\gamma_1 = \gamma_2$) in linkage equilibrium that evolve according to (3.5a) coupled with (5.1). For simplicity, we choose population regulation as in (2.2) with $\rho = 2$. Then, the monomorphic equilibria ($\hat{P}_1 = 1$, $\hat{P}_2 = 0$) and ($\hat{P}_1 = 0$, $\hat{P}_2 = 1$) are locally stable if and only if $f < 1$ because the equilibrium population size is $\hat{N} = K$ and $\hat{\eta} = f$. The fully polymorphic equilibrium $\hat{P}_1 = \hat{P}_2 = \frac{1}{2}$ is locally stable if and only if $f > f_c = 1/(1 + 2s\hat{V})$, where $\hat{V} = \gamma_1^2$; see (C.12). The population size at this equilibrium is $\hat{N} = K(1 - 2s\gamma_1^2)/(1 - s\gamma_1^2(1 + 2f))$, which is larger than K if $f > \frac{1}{2}$. Obviously, we have $f_c < 1$ and $\eta(\hat{N}) = 1$ if $f = f_c$. Thus, the equilibrium structure may be more complex if the demographic dynamics is taken into account.

Now we derive the equilibrium and stability structure for the LE approximation with population regulation. We use the parameter f instead of $\hat{\eta}$. We already know that the stability conditions for monomorphic and symmetric equilibria coincide with those for a constant population size, and for other equilibria, the difference is at most of order s^2.

The same argument as in Appendix E shows that no monomorphic equilibrium can be stable if $f > f_2$, where

$$f_2 = \frac{1}{-KF'(K)} \tag{5.5}$$

(note that (E.2) follows immediately from the stability conditions (B.6a) and (B.6b) of the LE approximation). Of course, monomorphic equilibria can be stable otherwise. Now suppose that there is a stable equilibrium with a single polymorphic locus and let $\frac{1}{2}f_2 < f < f_2$ (by Theorem 1, no other types of stable equilibria are possible). Then, (B.2) informs us that $\Delta \to 0$ as $\hat{\eta} \to 1$. Now (2.10) or, more generally, (2.9) imply that at such an equilibrium $\hat{N} > K$. Because η is increasing in N, we obtain $\hat{\eta} = \eta(\hat{N}) > \eta(K) = -fKF'(K)$. Since this equilibrium cannot be stable if $\hat{\eta} > 1$ (except when it is the single-locus polymorphism admitted by Theorem 2 (iii)), it looses its stability as f increases above a critical value that is $< f_2$.

The polymorphic equilibrium of Theorem 2 is locally stable if $f > f_1$, where

$$f_1 = -\frac{1}{KF'(K)} + s\hat{V}\frac{KF'(K)^2 - F'(K) - KF''(K)}{K^2F'(K)^3} + O(s^2)\,, \tag{5.6}$$

and $\hat{V}$ is given by (C.9) and satisfies $\hat{V} \le V_{\max}$ (see Appendix C). Therefore, stable coexistence of this equilibrium and monomorphic or single-locus polymorphic equilibria is possible only if

$$f_1 \le f \le f_2\,. \tag{5.7}$$

For values of f lower than f_1, Theorem 1 applies, whereas for $f > f_2$, Theorem 2 applies.

For the logistic model, (5.7) becomes (by omitting terms of order s^2 on the left-hand side)

$$\frac{1}{\rho - 1} - \frac{\rho s \hat{V}}{(\rho - 1)^2} \leq f \leq \frac{1}{\rho - 1}\,. \tag{5.8}$$

If $\rho = 2$ and $\Gamma = \frac{1}{2}$ (as used for the numerical results presented), (5.8) holds whenever $1 - \frac{1}{4}s \leq f \leq 1$ because $\hat{V} \leq V_{\max} \leq \frac{1}{2}\Gamma^2$. In particular, f_1 is always in this interval. For the Ricker and the Hassell-Maynard Smith model, inequalities corresponding to (5.8) are obtained immediately from (C.13) and (C.14), respectively.

As already pointed out at the end of Section 2.3, the full discrete-time model with linkage and density dependence, (2.11) and (2.12) with the fitness function (2.5), is too complicated to admit a detailed mathematical analysis. However, it can be proved (Appendix E) that if selection is not too strong, no monomorphic equilibrium can be stable if $f > f_2$.

A result of Nagylaki (1979, Eq. [6]) for density- and frequency-dependent selection shows that if the selection intensity s is small compared with the intrinsic growth rate of the population, then the population size converges quickly to a range of values near K, i.e., $N = K + O(s)$. This applies to our full model, because our fitness function (2.5) is of the form required in his Eq. [1a], and it is fully borne out by the numerical work below (results not shown) as well as by that of Bürger and Gimelfarb (2004). It is also in accordance with the above considerations.

Under the assumption of a constant population size, it can be shown that for sufficiently weak selection (i.e., depending on all other parameters, which are fixed, s is chosen small enough), all trajectories of the discrete-time system (2.11) converge to an equilibrium that is a small perturbation of a locally stable equilibrium of (3.5a). The proof is outlined in Appendix F. It paralleles the proof of an important result of Nagylaki et al. (1999), and makes use of the fact that the LE approximation is a (generalized) gradient system, a so-called Svirezhev-Shahshahani gradient. In particular, if $f > f_2$, then for sufficiently small s, all trajectories of the discrete-time system converge to a small perturbation of the unique stable equilibrium given in Theorem 2. Because with population regulation, the population size converges to a range of values $N = K + O(s)$, this suggests that for sufficiently small s, also the full system, (2.11) and (2.12), has the same equilibrium and stability structure as the LE approximation with population regulation. This claim is supported by numerical iterations (results not shown).

6. Numerical Results

The accuracy of the LE approximation and its range of validity in the presence of linkage and population regulation were explored numerically by iterating the recursion relations (2.11) and (2.12) until equilibrium is reached, using a program developed by A. Gimelfarb (the one used by Bürger and Gimelfarb (2004), but with

the fitness function modified; there, a detailed description can be found). Fitness is given by (1.12), i.e., by (2.5) with logistic population regulation (2.2). In addition, we compared the equilibrium properties of this model with that used by Bürger and Gimelfarb, i.e., (1.5) with (1.2) and (1.7), henceforth called the BG-model.

The range of phenotypic values is scaled to be $[-\Gamma, \Gamma]$ with $\Gamma = \frac{1}{2}$. Table 1 displays the equilibrium structure of two typical six-locus systems with an asymmetric optimum ($\theta = 0.25$) and with allelic effects γ_i and the other parameters as given in the legend. It shows that the theoretically obtained equilibrium allele frequencies (3.9) are very accurate if loci are freely recombining ($r = 0.5$) and the leading-order approximation $f(\rho - 1)$ is substituted for $\hat{\eta}$ (which is equivalent to assuming $N = K$). Similarly, (3.10) and (3.11) provide accurate approximations for the numerically obtained $\hat{\Delta}$ and $\hat{V}_{\mathrm{LE}}$. The approximation becomes particularly accurate if $\hat{\eta}$ is calculated from (C.3a), as described in the second paragraph below (C.7). If loci are only loosely linked ($r = 0.1$ between all loci), the LE approximation remains accurate. Even for recombination rates between loci chosen randomly (uniformly) between 0.005 and 0.05, the LE approximation provides a useful guideline, although in the second example one of the loci fixed for larger r became polymorphic now (but with P close to 1). The table also shows that as linkage becomes tighter, the loci of large effects become polymorphic first. For completely linked loci, only the two extreme gametes are present at equilibrium, hence all allele frequencies become identical (and can be calculated explicitly from the corresponding single-locus model).

Analogous computations were performed for the BG-model. Instead of presenting the data, we briefly summarize the results. For free recombination, the same loci are fixed in the present and the BG-model, the allele frequencies at the polymorphic loci differ by less than five percent, and the genetic variances are nearly identical. However, in the BG-model $\left|\hat{\Delta}\right|$ is about 25% below the corresponding value in the present model. For tighter linkage, in most cases both models have the same loci fixed and allele frequencies at polymorphic loci rarely differ by more than 10%. In the BG-model, slightly tighter linkage is required to make a locus polymorphic. The differences in the genetic variances exceed 10% only in few cases. However, for complete linkage, in the BG-model $\left|\hat{\Delta}\right|$ is much smaller, about one third of the value in the present model.

As in the two-locus case (Bürger 2002b), for several tightly linked loci in a given genetic system, increasing f from zero to the critical value f_1 may induce rather complex changes in the equilibrium structure. For instance, increasing f may lead to a loss of polymorphism at equilibrium (results not shown).

We also compared the present model with the BG-model on a larger scale, by employing the statistical approach of Bürger and Gimelfarb (Table 2). For given parameters κ, ρ, s, f, and n, 1000 genetic parameter sets (locus effects γ_i, randomly chosen from a uniform distribution on [0, 1] and normalized such that $\Gamma = \sum_i \gamma_i = \frac{1}{2}$, and recombination rates, either constant or randomly chosen from an interval as indicated) were generated. For each such set, the system of recursion relations (2.11) and (2.12) was iterated from 10 randomly chosen initial conditions until equilibrium was reached, when the quantities of interest were calculated. The

Table 2. Statistical comparison of the BG-model, indicated by (1.5), and the present model, indicated by (1.12). Also the influence of recombination is presented, but only for the present model because the data from the BG-model are very similar. The data are averages over 1000 genetic parameter sets (see main text). The variances shown are (averaged) relative variances, i.e., $V_{A,R}$ is the average of V_A/V_{max}, where V_{max} is the maximum possible variance in linkage equilibrium for the given genetic system. Similarly, $V_{LE,R}$ is the average of V_{LE}/V_{max}. These relative variances are the appropriate measures if different genetic systems have to be compared (for details, see Bürger and Gimelfarb 2004). The following parameters are fixed in all cases: $\rho = 2$, $s = 0.4$, $n = 4$.

	Polymorphism							
	0	1	2	3	4	$\overline{\lvert\hat{\Delta}\rvert}$	$V_{A,R}$	$V_{LE,R}$
$\theta = 0,\ f = 0.5$								
(1.5), $r = 0.5$	0.31	0.69	0	0	0	0.019	0.097	0.097
(1.12), $r = 0.5$	0.30	0.70	0	0	0	0.019	0.098	0.098
(1.12), $0.01 \le r \le 0.5$	0.30	0.70	0	0	0	0.019	0.097	0.097
(1.12), $0 \le r \le 0.01$	0.33	0.61	0.05	0.00	0.00	0.018	0.081	0.093
$\theta = 0,\ f = 1.56$								
(1.5), $r = 0.5$	0	0	0	0	1.00	0	1.009	1.000
(1.12), $r = 0.5$	0	0	0	0	1.00	0	1.012	1.000
(1.12), $0.01 \le r \le 0.5$	0	0	0	0	1.00	0	1.032	1.000
(1.12), $0 \le r \le 0.01$	0	0	0	0	1.00	0	2.273	1.000
$\theta = 0.25,\ f = 0.5$								
(1.5), $r = 0.5$	0.32	0.68	0	0	0	0.018	0.085	0.085
(1.12), $r = 0.5$	0.32	0.68	0	0	0	0.017	0.085	0.085
(1.12), $0.01 \le r \le 0.5$	0.32	0.68	0	0	0	0.017	0.084	0.084
(1.12), $0 \le r \le 0.01$	0.36	0.60	0.04	0.00	0	0.017	0.065	0.070
$\theta = 0.25,\ f = 1.56$								
(1.5), $r = 0.5$	0	0.02	0.19	0.49	0.31	0.014	0.816	0.811
(1.12), $r = 0.5$	0	0.01	0.15	0.49	0.35	0.022	0.831	0.823
(1.12), $0.01 \le r \le 0.5$	0	0.01	0.14	0.49	0.36	0.023	0.845	0.824
(1.12), $0 \le r \le 0.01$	0	0	0.00	0.09	0.91	0.061	1.917	0.861

data in Table 2 are averages over all 1000×10 trajectories (for more details on the numerical approach, see Bürger and Gimelfarb 2004).

However, near $\hat{\eta} = 1$ these two models may behave differently. The reason is that for constant population size and with the fitness function (1.12), the equilibrium structure of a given genetic system changes suddenly as $\hat{\eta}$ increases from below one to above one, whereas in the model of (Bürger 2002a,b) and Bürger and Gimelfarb (2004) there is a small transition region with a relatively complex equilibrium structure. This is so because in models based on (1.5), the fitness function may have two maxima, i.e., be M-shaped, if $\hat{\eta}$ is close to one. With population regulation, there is a small region containing the interval from f_1 to f_2, in which the equilibrium structure of the BG-model is more complex than that of the present model.

7. Discussion

An analytical study has been performed of a simple, but general, model of a polygenic trait under balancing selection caused by the interaction of intraspecific

competition and stabilizing selection. This model can be considered as a weak-selection approximation to a number of models of intraspecific competition used in investigations of mechanisms for the maintenance of genetic variation, intraspecific diversification, and sympatric speciation (see Introduction). Our main emphasis is on elucidating the dependence of the equilibrium structure on the strength of frequency- and density-dependent selection relative to stabilizing selection. Among others, this yields exact information on the degree of polymorphism and the amount of genetic variance maintained by this form of balancing selection.

We begin by highlighting the main findings of the LE approximation which is the weak-selection approximation to all models presented in the Introduction. For constant population size, the qualitative properties of the equilibrium structure are determined by the magnitude of the compound quantity $\hat{\eta}$, defined in (2.6), which measures the strength of frequency and density dependence relative to pure stabilizing selection. The equilibrium and stability structure changes qualitatively as $\hat{\eta}$ increases from below 1 (Theorem 1) to above 1 (Theorem 2). With population regulation, these results still provide the guiding principle, although $\hat{\eta}$ is not a parameter in the proper sense because it depends on the population size at equilibrium, which is difficult to compute exactly. In particular, $\hat{\eta}$ can be different at different equilibria. However, simple approximations for $\hat{\eta}$ and the values of f that determine the stability properties of different types of equilibria are available (e.g. (5.5) – (5.8), and Appendix C).

If $f < f_1$, frequency and density dependence are relatively weak and the equilibrium structure is similar to that found in models of pure (quadratic) stabilizing selection. In particular, at most one locus can be maintained polymorphic at a stable equilibrium (Theorem 1). Hence, in general (very) little genetic variation is maintained in such a trait, the more loci are contributing to the trait, the less variance is maintained on average (cf. Bürger and Gimelfarb 1999). However, the factor by which weak frequency dependence increases the variance relative to pure stabilizing selection increases with increasing number of loci (Bürger and Gimelfarb 2004).

If $f > f_1$, the combined effects of frequency and density dependence are sufficiently strong to induce a qualitative change in the equilibrium structure. Then, a locally stable polymorphic equilibrium exists which is given by Theorem 2. If $f_1 < f < f_2$, where $f_2 - f_1 = O(s)$, this equilibrium may coexist with monomorphic or single-locus polymorphic equilibria.

If $f > f_2$ (we call this strong frequency dependence), the equilibrium given by Theorem 2 is the only locally stable equilibrium. Presumably, it is globally stable, but this was proved only under the assumption of a constant population size. Theorem 2 provides necessary and sufficient conditions on the magnitude of allelic effects for maintaining a given number of loci polymorphic. In addition to the number of loci and their effects, these conditions, (3.6) and (3.8), depend on $\hat{\eta}$ and the position θ of the optimum. If selection is completely symmetric ($\theta = 0$), this equilibrium is symmetric, i.e., all alleles have frequency $\frac{1}{2}$. This is not so if the optimum is displaced from the symmetric position $\theta = 0$. Whether such a displacement is large or not will in practice be judged in relation to the range of possible phenotypic values. In our model, this range is from $-\Gamma$ to Γ, where $\Gamma = \sum_{i=1}^{n} \gamma_i$.

If we denote the average effect of a substitution by $\bar{\gamma} = \frac{1}{n}\Gamma$, then we can rewrite condition (3.6) for a fully polymorphic equilibrium as

$$\gamma_i > \bar{\gamma}\,\frac{|\theta|\,/\,\Gamma}{1 + (\hat{\eta} - 1)/(2n)} \quad \text{for all } i\,, \tag{7.1}$$

where, according to the model assumptions, $|\theta|\,/\,\Gamma \leq 1$. This clearly shows that for $\theta \neq 0$, maintenance of a fully polymorphic stable equilibrium is greatly facilitated by loci of similar effect. For loci of equal effect, this equilibrium is always fully polymorphic. If $|\theta|\,/\,\Gamma$ is held constant, but non-zero, then increasing n makes the maintenance of a stable equilibrium with a high proportion of polymorphic loci more difficult, whereas increasing $\hat{\eta}$ facilitates it. In the limit of infinitely many loci, the loci satisfying

$$\gamma_i/\bar{\gamma} > |\theta|\,/\,\Gamma \tag{7.2}$$

are the polymorphic ones. In particular, (7.2) determines which loci are polymorphic independently of n and $\hat{\eta}$ if frequency dependence is strong.

Inequality (7.1) also yields a simple condition for the maintenance of just a single polymorphic locus under strong frequency dependence. If we set $|\theta| = \tau\Gamma = \tau n\bar{\gamma}$ $(0 \leq \tau \leq 1)$, then for $m = n - 1$, (3.8) can be rewritten as

$$\gamma_n > \tfrac{1}{2}(\hat{\eta} + 1)\gamma_{n-1} + (1 - \tau)n\bar{\gamma}\,. \tag{7.3}$$

Therefore, unless τ is close to 1, i.e., θ is near the boundary of possible genotypic values, the largest effect (γ_n) must be much larger than the second largest effect (γ_{n-1}) and, of course, much larger than the average effect $\bar{\gamma}$. As a consequence, for given Γ, even at such equilibria a large amount of genetic variance will be maintained, sometimes more than at fully polymorphic equilibria, because in the latter case all loci have fairly small effects.

This demonstrates that models based on the assumption of equal effects among loci are not representative of the general case. Under strong frequency dependence, they always have a stable fully polymorphic equilibrium, whereas for models with unequal effects this is usually not so (except in the symmetric case $\theta = 0$). If the distribution of locus effects γ_i is highly leptokurtic (as suggested by some experimental results, see Bürger (2000) for a review), so that most loci have a small effect and some a very large, the present results show that for strong frequency dependence the proportion of polymorphic loci can be much smaller than unity; yet the genetic variance will be high. For instance, if the γ_i are drawn from a gamma distribution with shape parameter 0.5 (then the kurtosis is 15), on average about 48% of the loci will satisfy $\gamma_i/\bar{\gamma} > \frac{1}{2}$; cf. (7.2). Thus, for large n only about 50% of the loci determining the trait will be polymorphic. With a shape parameter of $\frac{1}{4}$, the kurtosis is 27 and the fraction of polymorphic loci will be down to about 36% unless the number of loci is small and $\hat{\eta}$ is large. For a uniform distribution of mutational effects, as underlying the results in Table 2 and those in Bürger and Gimelfarb (2004), 75% of the loci satisfy $\gamma_i/\bar{\gamma} > \frac{1}{2}$.

The numerical results of Section 6 for the full discrete-time model with population regulation and linkage, as well as those in Bürger and Gimelfarb (2004) for

the model (1.5) with the choices (1.2) and (1.7), suggest that if $f < f_1$, Theorem 1 remains true for linked loci unless linkage is very tight. In this case, a few loci can be maintained polymorphic. For the two-locus model, this is shown analytically in Section 4 (see also Bürger 2002b). If $f > f_2$, numerical iterations of the full system show that (3.7) and (3.9) provide accurate approximations to the true equilibrium allele frequencies, and (3.11) provides a very accurate approximation to the true genetic variance. This is the case even if stabilizing selection is not very weak relative to recombination (Tables 1,2). The present numerical results as well as those of Bürger and Gimelfarb (2004) show that tight linkage always increases polymorphism and induces higher linkage disequilibrium, in particular if frequency dependence is strong. In the latter case, linkage disequilibria are positive, and highly so if linkage is tight. Then, the two extreme gametes are maintained in the population at relatively high frequency; hence, all loci are polymorphic.

The functional form (2.5) for fitness resulted from the assumption of weak selection; therefore, the results of the LE analysis in Section 3, and of its generalization in Section 5, provide approximations to all models treated in the Introduction. Most importantly, the threshold-like dependence of the equilibrium structure and of the amount of polymorphism and genetic variance is a feature of all these models. The critical values f_1 and f_2 can be calculated easily for all these models (see Introduction and Section 5). The upper value (f_2) is independent of the number and effects of loci and the linkage map; it depends on the strength of frequency-dependent competition relative to stabilizing selection and on the demographic parameters, such as the population growth rate. Therefore, the qualitative results of Bulmer (1974, 1980) and Slatkin (1979) are confirmed and extended by this study. In particular, the ecological parameters for which Dieckmann and Doebeli (1999) found sympatric speciation are contained in the parameter region $f > f_2$, which has been identified as the one leading to the maintenance of high levels of genetic variation. The genetic details matter if quantitative questions are to be answered, such as regarding the amount of variation maintained. Although we examined the accuracy of the LE approximation only for the model of Bürger and Gimelfarb (2004), there is no reason to expect that the approximation is much worse for the other models.

The parameter range that gives rise to the stable coexistence of a highly polymorphic equilibrium with monomorphisms or single-locus polymorphisms ($f_1 < f < f_2$) may be larger and lead to a richer equilibrium structure for some of the other fitness functions discussed in the Introduction. The reason is that the fitness function (2.5) changes instantaneously from concave to linear to convex as $\hat{\eta}$ increases above unity (7.4). This is not the generic case. For instance, the fitness function (1.5) is M-shaped (but very flat) in a small region near $\hat{\eta} = 1$. This leads to a transition region that is still narrow (of order s) but larger than the present one (Bürger 2002a,b; Bürger and Gimelfarb 2004). For such fitness functions, it may be necessary to replace the condition $f > f_2$ by $f > f_2 + O(s)$ in the full model.

If stabilizing selection is so strong that it cannot be approximated by a quadratic fitness function, then the LE approximation necessarily breaks down. For instance, in the absence of any frequency dependence, strong Gaussian stabilizing selection together with linkage can maintain simultaneously stable multilocus polymorphisms, even in positive linkage disequilibrium (Willensdorfer and Bürger 2003).

Such multiple stable polymorphic equilibria were also detected by Loeschcke and Christiansen (1984). However, they cannot necessarily be attributed to strong competition; rather, they seem to be generated by very strong stabilizing selection and continue to exist if competition is added.

We expect that our main results remain valid if more than two alleles can segregate because Christiansen and Loeschcke (1980) showed for a model with four possible alleles at a single locus that at equilibrium at most two alleles are maintained. This is also true for a single-locus version of our model with multiple alleles and assortative mating (K. Schneider, unpubl. manuscript).

Although not investigated here, we mention that the distribution of a trait under strong competition is nearly Gaussian if linkage is loose and there are more than about six loci (see Bürger and Gimelfarb 2004). Thus, disruptive selection does not necessarily induce departures from a normal distribution (cf. Turelli and Barton 1994). Tight linkage induces marked departures from a Gaussian, and the equilibrium distribution shows clear signs of clustering. Because of random mating, no bimodal distributions can occur in our model.

The final topic we want to discuss is the relation between the strength of competition relative to that of stabilizing selection and the occurrence of empirically detectable disruptive selection. In contrast to models based on the Lotka-Volterra approach (e.g., Roughgarden 1972; Slatkin 1979; Christiansen and Loeschcke 1980; Dieckmann and Doebeli 1999), in the present model as well as in that of Bulmer (1974, 1980), the quantitative trait may be under stabilizing selection and may mediate competition for independent reasons. It has long been known that competition must be sufficiently strong to induce disruptive selection (Bulmer 1974; Slatkin 1979). More detailed genetic models yield qualitatively similar results and show that disruptive selection occurs whenever competition is strong enough to generate multilocus polymorphism (Bürger 2002a,b; Bürger and Gimelfarb 2004). Of course, this is also true in the present model. At demographic equilibrium, (2.5) can be written as

$$W(g) = F(\hat{N})\left[1 + s(\theta^2 + \hat{\eta}\bar{g}^2 + \hat{\varphi}) + 2s(\theta - \hat{\eta}\bar{g})g - s(1-\hat{\eta})g^2\right], \qquad (7.4)$$

where $\hat{\varphi} = \varphi(\hat{N}, \hat{\pi})$. Therefore, the fitness function is convex (curved upwards) if $\hat{\eta} > 1$, linear if $\hat{\eta} = 1$, and concave if $\hat{\eta} < 1$. However, convexity does not automatically imply disruptive selection, i.e., a $\bigcup$-shaped fitness function, because, in principle, the minimum of $W(g)$ could lie outside the range of realized phenotypes. By using (3.10), it is easy to show that if $\hat{\eta} > 1$ and the population is at equilibrium, the minimum of the fitness is attained at

$$g_{\min} = \theta\,\frac{2(n-m) + \hat{\eta}(\sum_{i=1}^{m}\gamma_i/|\theta|) - 1}{2(n-m) + \hat{\eta} - 1}, \qquad (7.5)$$

which for a fully polymorphic equilibrium simplifies to

$$g_{\min} = \theta\,\frac{2n-1}{2n+\hat{\eta}-1}. \qquad (7.6)$$

Thus, the minimum satisfies $0 < |g_{\min}| < |\theta|$ and, typically, is close to θ. If θ is close to one of the extremes of the phenotypic range, it will be difficult to establish disruptive selection in experiments with statistical significance because selection may appear to be directional. It is questionable whether in such a case competitive displacement can play an important evolutionary role in triggering phenomena such as sympatric speciation because there is not only a strong directional component of selection but also the number of loci maintained polymorphic is relatively low, even if frequency dependence is strong.

Unfortunately, there is only sparse direct empirical evidence that intraspecific competition induces disruptive selection, and even that intraspecific phenotypic variation produces frequency-dependent selection (but see Bolnick 2004 and Swanson et al. 2003). Most of the empirical evidence on the role of resource competition in evolutionary diversification concerns interspecific competition (Schluter 2000). Even then, frequency-dependent selection has been established only rarely (Schluter 2003). One reason for the rarity of empirical evidence of evolutionary divergence driven by frequency-dependent selection derives from the substantial experimental difficulties in getting a handle on such systems, especially, under natural conditions. Another conceivable reason is that because stabilizing selection on quantitative traits is common (Charlesworth et al. 1979, Endler 1986; Kingsolver et al. 2001) and may act directly or indirectly (through pleiotropy) and independently of the forces causing competition, competition will often have to be rather strong to lead to detectable disruptive selection. Of course, the effects of competition must be frequency dependent; otherwise it will not induce disruptive selection. In particular, if stabilizing selection is asymmetric, the above considerations show that the frequency-dependent effects of competition must be particularly strong to induce disruptive selection, and even stronger to become empirically detectable. A high intrinsic growth rate intensifies the effects of frequency dependence, whereas a low growth rate will weaken or even nullify them. Once competition is strong enough to induce substantial multilocus polymorhism, disruptive selection should be observable (Bürger 2002b; Bürger and Gimelfarb 2004; compare also Bulmer 1980, pp. 166–168). In this connection, it is interesting that, as pointed out by Bolnick (2004), Kingsolver et al. (2001) do not distinguish between true disruptive selection and directional selection with a positive curvature. Thus, disruptive selection may be rarer than indicated by their study. There is no question that more thorough empirical studies of these issues are needed before theoreticians can be confident that the biological relevance of their models of competitive displacement mediated by a quantitative trait can be reliably assessed.

Appendix

A. Allele-frequency dynamics

A.1 First, we derive (3.5a). The main step is the calculation of the marginal fitness of allele A_i in linkage equilibrium. We designate the genotypic value of a genotype consisting of all loci except i by g^i. Let $P(g^i)$ denote its (marginal) frequency under the assumption of linkage equilibrium. By definition, the marginal fitness of

A_i in linkage equilibrium is

$$\widetilde{W}_i = \sum_{g^i} P(g^i)[W(\gamma_i + g^i)P_i + W(g^i)Q_i]\,. \tag{A.1}$$

We omit the multiplicative factor $F(N)$ and write (2.5) as

$$W(g) = \omega_0 + \omega_1 g + \omega_2 g^2\,, \tag{A.2}$$

where $\omega_0 = 1 - s\theta^2 + s\eta(N)\bar{g}^2 + s\varphi(N,\pi)$, $\omega_1 = 2s(\theta - \eta(N)\bar{g})$, $\omega_2 = -s(1 - \eta(N))$. Straightforward calculations invoking (3.2) and (3.1) show that

$$\overline{g^i} = \sum_{g^i} P(g^i)g^i = \bar{g} - \gamma_i(P_i - Q_i)\,, \tag{A.3}$$

$$\begin{aligned}\overline{g^{i\,2}} &= \sum_{g^i} P(g^i)(g^i)^2 \\ &= V_{\mathrm{LE}} + \bar{g}^2 - 2\bar{g}\gamma_i(P_i - Q_i) + \gamma_i^2(P_i^2 - 4P_iQ_i + Q_i^2)\,,\end{aligned} \tag{A.4}$$

because in linkage equilibrium, $V_{\mathrm{A}} = V_{\mathrm{LE}}$. Substituting (A.2) into (A.1), expanding and using (A.3) and (A.4), we obtain

$$\widetilde{W}_i = \omega_0 + \omega_1(\bar{g} + \gamma_i Q_i) + \omega_2(V_{\mathrm{LE}} + \bar{g}^2 + 2\bar{g}\gamma_i Q_i + \gamma_i^2 Q_i(Q_i - P_i)) \tag{A.5}$$

and, by (2.9) with V_{LE} instead of V_{A},

$$\widetilde{W}_i - \widetilde{W} = \omega_1\gamma_i Q_i + \omega_2\gamma_i Q_i(2\bar{g} + \gamma_i(Q_i - P_i))\,, \tag{A.6}$$

whence (3.5a) follows immediately. Although obvious, it is noteworthy that the dynamics in linkage equilibrium is independent of the term ω_0.

A.2 Next we show that if N, hence η, are assumed to be constant, (3.5a) is a generalized gradient system (Bürger 2000, pp. 349–352, or Hofbauer and Sigmund 1998). Let (without loss of generality) $F(N) \equiv \hat{F}$ and $\eta(N) \equiv \hat{\eta}$ and define

$$V = \hat{F}[1 - s\Delta^2 - s(1 - \hat{\eta})V_{\mathrm{LE}}]\,. \tag{A.7}$$

Replacing Q_i by $1 - P_i$, it is straightforward to check that

$$\frac{\partial V}{\partial P_i} = 2s\gamma_i^2\hat{F}[(2P_i - 1)(1 - \hat{\eta}) - 2\Delta/\gamma_i]\,;$$

hence, $\frac{dP_i}{dt} = \frac{1}{2}P_i(1 - P_i)\frac{\partial V}{\partial P_i}$. In vector notation, this reads

$$\frac{d}{dt}P = \frac{1}{2}G\nabla V\,, \tag{A.8}$$

where $\nabla V = (\partial V/\partial P_1, \ldots, \partial V/\partial P_n)^T$ is the gradient vector of first-order partial derivatives and G is a diagonal matrix with entries $P_i(1 - P_i)$ on the main diagonal.

Therefore, (A.8) is a generalized gradient system on the n-fold euclidean product of the two-dimensional simplex S^2. In particular, V is a Lyapunov function, i.e.,

$$\frac{dV}{dt} = \sum_i \frac{\partial V}{\partial P_i}\frac{dP_i}{dt} = \frac{1}{2}\sum_i P_i Q_i \left(\frac{\partial V}{\partial P_i}\right)^2 \geq 0\,.$$

For frequency-independent selection it has long been known that the LE dynamics can be written in the form (A.8) (Wright 1937; Bürger 2000, p. 84). For frequency-dependent selection the dynamics is usually not a gradient system. In the present model, the potential V differs from $\overline{W}$ (in fact, only its frequency-dependent part).

B. Proofs of Theorems 1 and 2

We begin by applying the existence and stability results of Turelli and Barton (2004) (in this appendix abbreviated TB04) to our model and formulate them in terms of our notation. It is important that their parameters v_i are all identical in our model, i.e., $v_i = \hat{\eta}$ for all i. We exclude the case $\hat{\eta} = 1$, which leads to a degenerate equilibrium structure (see (3.5a)).

From (3.5a), we see that each locus i can fall into one of three possible equilibria: $P_i = 0$, $P_i = 1$, or

$$P_i = \frac{1}{2} - \frac{1}{\gamma_i}\frac{\Delta}{\hat{\eta} - 1}\,. \tag{B.1}$$

Locus i is polymorphic if and only if

$$\hat{\eta} < 1 \text{ and } 2\,|\Delta| < \gamma_i(1 - \hat{\eta}) \tag{B.2a}$$

or

$$\hat{\eta} > 1 \text{ and } 2\,|\Delta| < \gamma_i(\hat{\eta} - 1)\,. \tag{B.2b}$$

Following TB04, for a given equilibrium we introduce the following sets of loci:

$$\Omega_0 = \{i : P_i = 0\}\,, \quad \Omega_1 = \{i : P_i = 1\}\,, \quad \Omega_\mathrm{p} = \{i : 0 < P_i < 1\}\,. \tag{B.3}$$

At such an equilibrium, we have

$$\Delta = \sum_{i\in\Omega_1}\gamma_i - \sum_{i\in\Omega_0}\gamma_i + \sum_{i\in\Omega_\mathrm{p}}\gamma_i(P_i - Q_i) - \theta\,. \tag{B.4}$$

Because $v_i \equiv \hat{\eta}$, condition (15) in TB04 (in which n denotes the number of loci in Ω_p) can never be satisfied if Ω_p contains two or more loci and $\hat{\eta} < 1$. Therefore, their condition (14) implies

if $\hat{\eta} > 1$, then all loci in Ω_p are stable; (B.5a)

if $\hat{\eta} < 1$ and Ω_p contains more than one locus, then all loci in Ω_p are unstable. (B.5b)

However, if $\hat{\eta} < 1$, then a single polymorphic locus can be stably maintained. The stability conditions for the fixed loci are (TB04, eqs. (21))

$$\gamma_i(\hat{\eta} - 1) < 2\Delta \quad \text{if } P_i = 0 \tag{B.6a}$$

and

$$\gamma_i(\hat{\eta} - 1) < -2\Delta \quad \text{if } P_i = 1\,. \tag{B.6b}$$

Hence, they are complementary to the existence conditions for polymorphic loci with $\hat{\eta} > 1$.

Proof of Theorem 1. (i) This is just the stability condition (B.5b).

(ii) This is well known for pure stabilizing selection (e.g., Barton 1986). If $0 \le \hat{\eta} < 1$ and $\theta = 0$, then for every stable equilibrium, a complimentary one is found by interchanging the frequencies of A_i and a_i at each locus. A procedure for finding alternative stable equilibria is provided by Turelli and Barton (2004).

(iii) For every monomorphic equilibrium (stable or not), the deviation from the optimum is given by $\Delta = \sum_{i\in\Omega_1}\gamma_i - \sum_{i\in\Omega_0}\gamma_i - \theta$. In the non-generic case $\Delta = 0$, the stability conditions for fixed loci, (B.6a) and (B.6b), show that such an equilibrium is stable for all $\hat{\eta} < 1$. Generically, for a given set of γ_i there is a $D_{\min} > 0$ such that $|\Delta| \ge D_{\min}$ for all monomorphic equilibria. If $\Delta \ge D_{\min}$ at such a monomorphic equilibrium, then (B.6b) cannot be satisfied if $\hat{\eta}$ increases beyond a critical value $\hat{\eta}_c < 1$, whence $\Omega_1 = \emptyset$ follows. Because θ lies in the range of possible genotypic values, i.e., $|\theta| \le \Gamma$, we get $\Delta = -\sum_{i\in\Omega_0}\gamma_i - \theta \le 0$, a contradiction. An analogous argument is valid if $\Delta \le -D_{\min}$. □

Before we prove Theorem 2, we need three auxiliary lemmas.

Lemma 1. *Let $\hat{\eta} > 1$. At every stable equilibrium, at least one of the sets Ω_0 and Ω_1 is empty.*

Proof. Suppose $i \in \Omega_0$ and $j \in \Omega_1$. Then, by (B.6a), $P_i = 0$ is stable if and only if $2\Delta > \gamma_i(\hat{\eta}-1) > 0$. Similarly, $P_j = 1$ is stable if and only if $2\Delta < \gamma_j(1-\hat{\eta}) < 0$, which yields a contradiction. □

Lemma 2. *Let $\hat{\eta} > 1$. At every stable equilibrium, Ω_p is not empty.*

Proof. By Lemma 1, at a completely monomorphic equilibrium either all loci are fixed for the plus allele or for the minus allele. Let $g_+ = \sum_{i=1}^{n}\gamma_i (= \Gamma)$ be the value of the all-plus genotype. At this equilibrium, we have $\bar{g} = g_+$. By the stability condition (B.6b), g_+ is stable if and only if $\gamma_i < 2(\theta - g_+)/(\hat{\eta} - 1)$ for all i. This, however, is impossible if $\theta \le g_+ = \Gamma$, as posited in the assumptions of the genetic model (Section 2.2). The all-minus case is analogous; thus, the lemma is proved. □

Lemma 3. *Let $\hat{\eta} > 1$. If $\theta \ge 0$ ($\theta \le 0$), then at every stable equilibrium we have $\Omega_0 = \emptyset$ ($\Omega_1 = \emptyset$).*

Proof. Let $\theta \geq 0$ and suppose $i \in \Omega_0$. Because $\hat{\eta} > 1$, stability requires $\Delta > 0$ (B.6a). Hence, (B.1) implies $P_i - Q_i < 0$ for all $i \in \Omega_p$ ($\Omega_p \neq \emptyset$ by Lemma 2). By Lemma 1, we have $\Omega_1 = \emptyset$. Therefore, $\Delta = -\sum_{i\in\Omega_0} \gamma_i + \sum_{i\in\Omega_p} \gamma_i (P_i - Q_i) - \theta < 0$, which is a contradiction.

We note that Lemma 3 (or directly (B.6a), (B.6b)) implies that if $\theta = 0$ and $\hat{\eta} > 1$, a stable equilibrium is fully polymorphic. □

Proof of Theorem 2. Let $\hat{\eta} > 1$ and assume $\theta \geq 0$. Then, by Lemmas 1 and 3, for every stable equilibrium, we have $\Omega_0 = \emptyset$ and $\Omega_p \neq \emptyset$. We order the effects so that $\gamma_1 \leq \gamma_2 \leq \ldots \leq \gamma_n$. The feasibility condition (B.2b) shows that for a given equilibrium a unique m ($0 \leq m \leq n-1$) exists such that $\Omega_1 = \{1, \ldots, m\}$ and $\Omega_p = \{m+1, \ldots, n\}$. Then, invoking (B.1), we see that (B.4) becomes □

$$\Delta = \sum_{i=1}^{m} \gamma_i + \sum_{i=m+1}^{n} \gamma_i (P_i - Q_i) - \theta = \sum_{i=1}^{m} \gamma_i - 2\frac{\Delta}{\hat{\eta} - 1}(n - m) - \theta \,,$$

from which the equilibrium value of Δ is calculated to be

$$\hat{\Delta} = \frac{\sum_{i=1}^{m} \gamma_i - \theta}{1 + \frac{2(n-m)}{\hat{\eta}-1}} \,.$$

For arbitrary choice of θ, we obtain (3.10). This shows that simultaneously stable equilibria must have different values Δ and different numbers of polymorphic loci. For a fully polymorphic equilibrium ($m = 0$), (3.10) simplifies to

$$\hat{\Delta} = \frac{-\theta}{1 + 2n/(\hat{\eta} - 1)} \,. \tag{B.7}$$

(This holds for any fully polymorphic equilibrium, even if not stable, i.e., if $\hat{\eta} < 1$.) Also recall that if $\theta = 0$, then a fully polymorphic (stable) equilibrium exists.

Invoking (3.10), we see that the stability conditions (B.6a) and (B.6b) for the fixed loci can be expressed as

$$\gamma_i < 2\frac{|\theta| - \sum_{j=1}^{m} \gamma_j}{2(n - m) + \hat{\eta} - 1} \tag{B.8}$$

(it is best to consider the two cases $\theta > 0$, $\theta < 0$ separately; for $\theta = 0$, (B.6a) and (B.6b) are void). (B.8) must be satisfied by locus m, but must not be satisfied by locus $m + 1$. Simple rearrangement of (B.8) yields

$$\gamma_m [2(n - m) + \hat{\eta} + 1] + 2\sum_{i=1}^{m-1} \gamma_i < 2\,|\theta| \,. \tag{B.9}$$

It is straightforward to show that the left-hand side is non-decreasing in m. (Take the left-hand side of (B.9) for $m + 1$ and substract that for m. After rearrangement, this yields $(\gamma_{m+1} - \gamma_m)(2n - 2m + \hat{\eta} - 1) \geq 0$.) Therefore, the largest m satisfying (B.9) is uniquely determined.

Thus, we have proved that if a stable equilibrium exists, then it is uniquely determined and at least one locus is polymorphic.

Obviously, if $\hat{\eta} > 1$ and (3.6) is satisfied, then (3.7) yields a stable equilibrium that is fully polymorphic. Similarly, (3.8) and (3.9) yield a stable equilibrium with m polymorphic loci, and m is uniquely determined even if loci of equal effects occur because the left-hand side of (B.9) is constant on such sets. The allele frequencies at the fixed loci are all 1 if $\theta > 0$ and all 0 if $\theta < 0$. Since such an equilibrium satisfies the stability conditions, we have also established existence of a stable equilibrium.

To prove (i), we observe that by (B.8) this unique stable equilibrium is fully polymorphic ($m = 0$) if and only if (3.6) holds. The allele frequencies (3.7) follow immediately from (B.1) and (B.7).

To prove (ii), we first observe that the fully polymorphic equilibrium is symmetric if and only if $\theta = 0$. If $\theta = 0$, then (3.6) holds automatically and the stable equilibrium must be fully polymorphic. This proves the first assertion. If $\Delta = 0$ (and $\hat{\eta} > 1$) at a stable equilibrium, then either $\theta = 0$ (B.7), and we are finished, or $\sum_{i \notin \Omega_p} \gamma_i = |\theta|$ by (3.10). This, however, is impossible because if $\Delta = 0$, the stability conditions (B.6a), (B.6b) for fixed loci cannot be satisfied if $\hat{\eta} > 1$.

Part (iii) follows immediately from what we have proved together with (B.8), (B.9) as well as (B.1) and (3.10). We have $\hat{P}_i > \frac{1}{2}$ if and only if $\theta > 0$ because (B.8) informs us that $|\theta| > \sum_{i=1}^{m} \gamma_i$ must hold.

C. Expressions for $\hat{N}$, $\hat{\eta}$, and f_c

We assume demographic equilibrium, i.e., $\overline{W} = 1$, but initially we do not require linkage equilibrium or genetic equilibrium. For discrete logistic population growth, (2.2), and for the Maynard Smith model, (2.4) with $c = 1$, explicit expressions for $\hat{N}$ can be obtained from (2.9) by solving $\overline{W} = 1$ for N. In the first case, we get

$$\hat{N} = \kappa(\rho - 1) + \kappa s \, \frac{V_A(2f(\rho - 1) - 1) - \Delta^2}{1 - sV_A(1 + 2f) - s\Delta^2} \tag{C.1a}$$

$$= \kappa(\rho - 1) + \kappa s \left[2fV_A(\rho - 1) - V_A - \Delta^2 \right] + O(s^2 C^2)\,, \tag{C.1b}$$

where we have used (1.11) and, for (C.1b), (2.10). (C.1a) shows that $\hat{N}/\kappa$ and, hence, the resulting fitness $W(g)$ at demographic equilibrium can be expressed solely in terms of ρ, f, and the genetic parameters; κ is not needed.

For the Maynard Smith model, we obtain

$$2b\hat{N}^{\xi} = \lambda \left[1 - s(V_A + \Delta^2) + 2sf\xi V_A) \right] - 2 + \\ + \sqrt{\lambda}\sqrt{\lambda[1 - s(V_A + \Delta^2) + 2sf\xi V_A)] - 8sf\xi V_A}\,. \tag{C.2}$$

It follows that the resulting fitness $W(g)$ at demographic equilibrium can be expressed solely in terms of λ, ξ, f, and the genetic parameters; b is not needed.

If $\hat{N}$ can be calculated exactly, exact expressions for $\hat{\eta} = \eta(\hat{N})$ can be obtained. For the discrete logistic equation, we get from (2.6) and (C.1a)

$$\hat{\eta} = f\,\frac{\rho - 1 - s\rho(V_A + \Delta^2)}{1 - 2sf\rho V_A} \tag{C.3a}$$

$$= f(\rho - 1) + sf\rho\left[(2f(\rho - 1) - 1)V_A - \Delta^2\right] + O(s^2C^2)\,. \tag{C.3b}$$

In general, the following approximation for $\hat{\eta}$ is obtained from (2.10) and (2.6):

$$\hat{\eta} = \eta(\hat{N}) = -fKF'(K) + \frac{sf}{F'(K)}\left[2fV_AKF'(K) + V_A + \Delta^2\right] \times \left[KF'(K)^2 - F'(K) - KF''(K)\right] + O(s^2C^2)\,. \tag{C.4}$$

We note from the definition (2.6) of η and because $F(K) = 1$ that the leading-order term of $\hat{\eta}$ is obtained if $\hat{N} = K$. Moreover, we have $KF'(K)^2 - F'(K) - KF''(K) > 0$ if and only if $\eta'(K) > 0$. The latter, in fact even $\eta'(N) > 0$, is fulfilled in all our examples for F.

For the Ricker model, (C.4) produces

$$\hat{\eta} = fr + sf\left[(2fr - 1)V_A - \Delta^2\right] + O(s^2C^2)\,. \tag{C.5}$$

For the Hassell-Maynard Smith model, (C.4) yields

$$\hat{\eta} = fc\xi(1 - \lambda^{-1/c}) + sf\xi\lambda^{-1/c}\left[\left(2fc\xi(1 - \lambda^{-1/c}) - 1\right)V_A - \Delta^2\right] + O(s^2C^2)\,, \tag{C.6}$$

which, for the Beverton-Holt model, simplifies to

$$\hat{\eta} = f\frac{\lambda - 1}{\lambda} + s\frac{f}{\lambda}\left[\left(2f\frac{\lambda - 1}{\lambda} - 1\right)V_A - \Delta^2\right] + O(s^2C^2)\,. \tag{C.7}$$

A problem with the above relations is that the values of V_A and Δ depend on the population size $\hat{N}$, which itself is expressed in terms of V_A and Δ. Obviously, at a monomorphic equilibrium, $V_A = 0$ and explicit formulas for $\hat{N}$ and $\hat{\eta}$ are obtained if it is known which loci are fixed for the A and which for the a allele.

From now on, we assume the LE approximation of Section 3, $\hat{\eta} > 1$, and that the population is in the equilibrium given by Theorem 2. Then, the value of $\hat{\eta}$ can be calculated exactly in terms of the basic parameters. Take, for instance, (C.3a) and substitute $\hat{\Delta}$ from (3.10) and $\hat{V}_{LE}$ from (3.11) for Δ and V_A, respectively. This produces a (complicated) cubic in η that can be solved in principle to obtain $\hat{\eta}$. This method has been used to calculate numerically the values of $\hat{\eta}$ and, hence, of $\hat{N}$, $\hat{V}_{LE}$, $\hat{\Delta}$, and $\hat{P}_i$ $(i = 1, 6)$ in Table 1.

Perhaps more importantly, approximations for the critical f that yields $\hat{\eta} = 1$ can be obtained by equating $\hat{\eta}$ (2.6) to 1, developing f into a Taylor series about K, and observing (2.10). This produces

$$f = -\frac{1}{KF'(K)} + s(\hat{V}_{LE} - \hat{\Delta}^2)\frac{-F'(K) + KF'(K)^2 - KF''(K)}{K^2F'(K)^3} + O(s^2C^2)\,. \tag{C.8}$$

In the limit $\hat{\eta} \to 1$ (from above), (3.11) shows that $\hat{V}_{\mathrm{LE}}$ simplifies to

$$\hat{V} = \lim_{\hat{\eta}\to 1} \hat{V}_{\mathrm{LE}} = \tfrac{1}{2} \sum_{i\in\Omega_{\mathrm{p}}} \gamma_i^2 - \tfrac{1}{2}\Big(\sum_{i\notin\Omega_{\mathrm{p}}} \gamma_i - |\theta| \Big)^2 / (n-m)\,, \tag{C.9}$$

where m is determined by inequality (3.8) with $\hat{\eta} = 1$. Therefore, $\hat{V} \le V_{\max}$, where $V_{\max} = \frac{1}{2}\sum_{i=1}^{n} \gamma_i^2$. Moreover, (3.10) shows that $\hat{\Delta} \to 0$ as $\hat{\eta} \to 1$ from above. It follows that the critical f is given by

$$f_1 = -\frac{1}{KF'(K)} + s\hat{V}\,\frac{KF'(K)^2 - F'(K) - KF''(K)}{K^2F'(K)^3} + O(s^2V_{\max}^2)\,. \tag{C.10}$$

For the discrete logistic equation, (C.10) yields

$$f_1 = \frac{1}{\rho - 1} - \frac{\rho s\hat{V}}{(\rho-1)^2} + O(s^2V_{\max}^2)\,. \tag{C.11}$$

The exact formula

$$f_1 = \frac{1}{\rho - 1 + s\rho\hat{V}}\,, \tag{C.12}$$

is readily derived from (C.3a).

For the Ricker model, we obtain

$$f_1 = \frac{1}{r}\left(1 - \frac{s\hat{V}}{r}\right) + O(s^2V_{\max}^2)\,, \tag{C.13}$$

and for the Hassell-Maynard Smith model,

$$f_1 = \frac{\lambda^{1/c}}{c\xi(\lambda^{1/c}-1)}\left(1 - \frac{s\hat{V}}{c(\lambda^{1/c}-1)}\right) + O(s^2V_{\max}^2)\,. \tag{C.14}$$

In all cases, f_1 increases to infinity as the population growth rate decreases to unity, and $f_1 < -1/(KF'(K)) = f_2$.

D. Stability of single-locus polymorphisms in the two-locus model

If the single-locus polymorphism (4.5) exists, it is stable within its one-locus system, as is readily shown. The characteristic polynomial for the other two eigenvalues is of the form $p(x) = \frac{1}{2}p_0 + p_1x + p_2^2x^2$ (the p_2^2 is no misprint), where

$$\begin{aligned}
p_2 &= 8(1+\eta)^2 + t(1-e)^2(1-\eta)(1-3\eta-2\eta^2) + 4te(1+\eta)^2(-1+2\eta)\,,\\
p_1 &= p_2 b\,,\\
b &= -8(2-r)(1+\eta)^2 + rt\eta[(-1+\eta)(1+3\eta)(1-e)^2 + 4e(1+\eta)^2]\\
&\quad + 2t(1+e)^2(1-3\eta^2) + 4t\eta[3(1-e)^2 - 2\eta^2(1+e^2)]\,,
\end{aligned}$$

and p_0 is given below. (This and all other assertions are straightforwardly checked with *Mathematica*.) It follows immediately that $p(x)$ is convex. Simple estimates

using $0 \le t, \eta, e \le 1$ show that $p_2 \ge 3$ and $b \le -4$; hence, $p'(0) = p_1 < 0$. Therefore, $p(x)$ attains its minimum at $x_{\min} = -p_1/(2p_2^2)$, which is in (0, 1). We have

$$p(x_{\min}) = -\left[\tfrac{1}{2}ru - 4t(1-e)^2(1-\eta^2)\right]^2 - 4t^2(1-e)^2(1-\eta^2)^2\left[(1+e)^2(1+\eta)^2 - 4(1-e)^2\right],$$

where $u = 4(1+\eta)^2(2+te\eta) - t\eta(1+\eta)(1+3\eta)(1-e)^2$. Because $(1+e)^2(1+\eta)^2 - 4(1-e)^2$ increases with η and $= 0$ if $\eta = \eta_0$, we have $p(x_{\min}) < 0$ if this single-locus polymorphism exists. Therefore, there always exist two real eigenvalues, and an eigenvalue larger than 1 exists if and only if $p(1) < 0$. We have

$$p(1) = -2t(1-e)^2(\eta^2-1) \times \left\{8te(\eta-1)(1+\eta)^3 + r(3+\eta)\left[8(1+\eta)^2 + t\eta\psi\right]\right\},$$

where ψ is defined below (4.6b). Because $\psi \ge -\frac{4}{3}$, the coefficient of r is always positive. Therefore, $p(1) < 0$ whenever $\eta > 1$, and this single-locus polymorphism is unstable if $\eta > 1$.

If $\eta < 1$, then $p(1) < 0$ if and only if $r < r_1$, where r_1 is given by (4.6a), whence the equilibrium is unstable. It remains to show that the equilibrium is stable if $\eta < 1$ and $r > r_1$. From now on we assume $\eta < 1$. We already know that both eigenvalues are real. If $p(1) > 0$, they must both be less than 1 and it is sufficient to show $p(0) = \frac{1}{2}p_0 > 0$. We can write

$$p_0 = (1-2r)c_1c_2 + c_3,$$

where

$$\begin{aligned}
c_1 &= 8(1+\eta)^2 - t(1-e)^2\eta(1-\eta)(1+3\eta) + 4te\eta(1+\eta)^2 > 0,\\
c_2 &= 4(1+\eta)^2(2 - t(2-3e+2e^2) + 2t\eta(1-e+e^2))\\
&\quad + t(1-e)^2(1-\eta)(3+5\eta+4\eta^2) > 0,\\
c_3 &= 2(1+\eta)^4\left[12(2-t^2(1+e)^2) + 2(1-e) + 6e^2(1-t^2) + 3(1-e^4)\right]\\
&\quad + 8t(1+\eta)^2a_1 + (1-e^2)^2a_2 + 4ea_4 + 4t^2e^2a_6,
\end{aligned}$$

and

$$\begin{aligned}
a_1 &= (1+e)^2\eta(1+\eta)^2 + 16e\eta(1+\eta)^2 + 4(1-e)^2(1-3\eta+2\eta^2+2\eta^3) \ge 0,\\
a_2 &= 6(1+\eta)^4 - t^2(1-\eta)^2(6+9\eta-40\eta^2-43\eta^3-12\eta^4) \ge 0,\\
a_3 &= 2+9\eta-54\eta^2-2\eta^3+26\eta^4+17\eta^5+2\eta^6,\\
a_4 &= (1+\eta)^4 + t^2a_3 > 0,\\
a_5 &= 7-2\eta+86\eta^2-24\eta^3-9\eta^4+34\eta^5+20\eta^6 > 0,\\
a_6 &= a_5 + ea_3 > 0.
\end{aligned}$$

It follows that $c_3 > 0$; hence, $p_0 > 0$ whenever $t < \frac{1}{2}$ (actually, whenever $t < \sqrt{21} - 4 \approx 0.58$). Numerical results as well as analytical consideration of the case $t = 1$ suggest that this is true for all $t \le 1$.

E. Instability of monomorphic equilibria

Here, we show that in the full discrete-time model, (2.11) and (2.12), with fitness function (2.5), no monomorphic equilibrium can be locally stable if $f > f_2$ and selection is not too strong. We also assume that η is monotone increasing near K, as is the case for all examples given in Section 2. For our purpose it is sufficient to prove instability with respect to invasion of single-locus mutants. Let g denote the genotypic value of an arbitrary genotype that is homozygous in all loci. Consider a single-locus heterozygote that differs in just one locus and denote its genotypic value by $g + a$. Of course, a has to satisfy $a \neq 0$ and $-\Gamma \leq g + 2a \leq \Gamma$. From (2.9) we infer easily that at a monomorphic equilibrium, $\hat{N} = F^{-1}(1/(1 - s\Delta^2))$ because $V_A = 0$ and $\bar{g} = g$. Since F is monotone decreasing in N, this implies that at any monomorphic equilibrium, $\hat{N} \leq K$. Without loss of generality, we assume $0 \leq \theta < \Gamma$. Then the monomorphic equilibrium corresponding to g is unstable if and only if

$$W(g + a) > W(g) \tag{E.1}$$

for some (admissible) a. Because in a neighborhood of a monomorphic equilibrium, $V_A = 0$ and $\bar{g} = g$ hold to first-order approximation, a simple calculation shows that (E.1) is equivalent to

$$\eta(\hat{N}) > 1 + \frac{2\Delta}{a} . \tag{E.2}$$

Thus, all monomorphic states are unstable if for every possible g an admissible a exists such that (E.2) is fulfilled.

If $g = \theta$, then $\hat{N} = K$ and (E.2) simplifies to $\eta(K) > 1$, which is equivalent to $f > f_2$. Therefore, $f > f_2$ is necessary.

Now suppose $g > \theta$, i.e., $\Delta > 0$. Then (E.2) will be satisfied if $f > f_2$ holds and

$$\eta(\hat{N}) > \eta(K) + 2\Delta/a . \tag{E.3}$$

We show that $a < 0$ exists such that this is satisfied. Indeed, for $a < 0$ and because $K < \hat{N}$ implies $\eta(K) < \eta(\hat{N})$, (E.3) is equivalent to

$$-a < \frac{2\Delta}{\eta(K) - \eta(\hat{N})} . \tag{E.4}$$

Developing $\eta(\hat{N})$ into a Taylor series about K and dropping terms of order s^2 and smaller, we see that (E.4) becomes

$$-a < \frac{2KF'(K)^2}{s\eta'(K)\Delta} . \tag{E.5}$$

Hence, for sufficiently small s, an admissible a can be found in every genetic system. An analogous argument is valid if $g < \theta$. Therefore, $f > f_2$ is also sufficient.

If, for instance, population growth is logistic, i.e., F is given by (2.2), then (E.4) becomes

$$-a < \frac{2(\rho - 1)}{s\rho\Delta} \,. \tag{E.6}$$

A simple calculation shows that an admissible a can be found whenever $s\Gamma^2 \leq \frac{4}{3}(\rho - 1)/\rho$. Unless ρ is close to one, this is a weak restriction because $s\Gamma^2 \leq 1$ must hold anyway.

F. Convergence to QLE

In this appendix, we make heavy use of the notation, arguments and results in Nagylaki et al. (1999). We abbreviate this article by NHB. We assume that all two-locus recombination rates are positive. We consider all parameters as fixed and assume that the strength of selection, s, is sufficiently small (where 'small' may depend on the other parameters). In the absence of selection ($s = 0$) the dynamics (2.11) with constant population size $N = \hat{N}$ simplifies to

$$p_k' = p_k - D_k \,, \tag{F.1}$$

where p_k denotes the frequency of gamete k ($k = 1, \ldots, 2^n$) and D_k is a measure of linkage disequilibrium in gamete k as defined in Eq. (1.5) of NHB. Let us write $\mathbf{p}$ for the vector of dimension 2^n consisting of the p_k (in arbitrary but fixed order). For the system (F.1), the linkage-equilibrium manifold $\Lambda_0 = \{\mathbf{p} : \mathbf{D} = \mathbf{0}\}$ (cf. Eq. (3.2) in NHB) is invariant and globally attracting at a uniform geometric rate (NHB, p. 114).

For sufficiently weak selection, the theory of normally hyperbolic manifolds (see Fenichel 1971; or Hirsch et al. 1977) implies the existence of a smooth invariant manifold Λ_s close to Λ_0, which is globally attracting at a geometric rate for the system (2.11). The recursion relations for the gene frequencies on the invariant manifold Λ_s can be written as (Nagylaki 1993, Eq. 56)

$$P_i' = P_i + sP_iu_i(\mathbf{P})/\bar{w}(\mathbf{P}) + O(s^2) \,, \tag{F.2}$$

where $\bar{w}(\mathbf{P}) = \overline{W}$ evaluated on Λ_s and

$$u_i(\mathbf{P}) = F(\hat{N})\gamma_i^2 Q_i \left[(P_i - Q_i)(1 - \hat{\eta}) - 2\Delta/\gamma_i\right] . \tag{F.3}$$

Note that sP_iu_i is the right-hand side of (3.5a). Equation (F.2) corresponds to Eq. (3.10) or, equivalently, to Eq. (3.5) of NHB. Because selection is frequency independent in NHB (otherwise, their main results are not valid), it is important to note that Eq. (56) in Nagylaki (1993) was derived for frequency-dependent selection; thus, it has the generality needed to yield (F.2) as a special case.

By rescaling time and letting $s \to 0$ as in NHB, we see that the difference equation (F.2) approaches the differential equation (3.5a). Their fixed points coincide. As shown in Appendix A.2, (3.5a) is a (generalized) gradient system; hence, all eigenvalues of the Jacobian are real. Therefore, all equilibria of (3.5a) are hyperbolic if none of the eigenvalues is zero. This is equivalent to the hypothesis that (F.2) has

no fixed points with an eigenvalue 1. This clearly is a generic assumption because it is violated only if the solution of $(P_i - Q_i)(1 - \hat{\eta}) - 2\Delta/\gamma_i = 0$ (F.3) happens to coincide with $P_i = 0$ or $P_i = 1$.

Now the same proof as that of Theorem 3.1 of NHB shows that all trajectories of the discrete-time system (2.11) converge to a fixed point. This fixed point is a perturbation of a fixed point of the linkage equilibrium approximation (3.5a).

Acknowledgements. The computer program, on which all numerical results are based, was provided by Sasha Gimelfarb, who died on May 11, 2004. I am deeply grateful to him for the many years of friendship and collaboration. Many thanks to Dan Bolnick for sharing an unpublished manuscript and providing numerous useful comments on an earlier version of this manuscript. Also the comments by Thomas Nagylaki and an anonymous reviewer are appreciated. This work was supported by grant P16474-N04 of the Austrian Science Foundation (FWF). Part of this work was done during the Program on Mathematical Population Genetics and Statistical Physics sponsored by the Erwin Schrödinger International Institute of Mathematical Physics (ESI).

References

Asmussen, M.A.: Density-dependent selection incorporating intraspecific competition. II. A diploid model. Genetics **103**, 335–350 (1983)

Asmussen, M.A., Basnayake, E.: Frequency-dependent selection: The high potential for permanent genetic variation in the diallelic, pairwise interaction model. Genetics **125**, 215–230 (1990)

Asmussen, M.A., Cartwright, R.A., Spencer, H.G.: Frequency-dependent selection with dominance: A window onto the behavior of mean fitness. Genetics **167**, 499–512 (2004)

Barton, N.H.: The maintenance of polygenic variation through a balance between mutation and stabilizing selection. Genet. Res. **47**, 209–216 (1986)

Beverton, R.J.H., Holt, S.J.: On the dynamics of exploitedfsfs fish populations. Fishery Investigations Series 2, Vol. **19**, HMSO 1957

Bolnick, D.I.: Can intraspecific competition drive disruptive selection? An experimental test in natural populations of sticklebacks. Evolution **58**, 608–613 (2004)

Bolnick, D.I., Doebeli, M.: Sexual dimorphism and adaptive speciation: two sides of the same ecological coin. Evolution **57**, 2433–2449 (2003)

Bulmer, M.G.: Density-dependent selection and character displacement. American Naturalist **108**, 45–58 (1974)

Bulmer, M.G.: The Mathematical Theory of Quantitative Genetics. Oxford, UK: Clarendon Press, 1980

Bürger, R.: The Mathematical Theory of Selection, Recombination, and Mutation. Chichester: Wiley, 2000

Bürger, R.: Additive genetic variation under intraspecific competition and stabilizing selection: A two-locus study. Theor. Popul. Biol. **61**, 197–213 (2002a)

Bürger, R.: On a genetic model of intraspecific competition and stabilizing selection. Am. Natur. 160, 661–682 (2002b)

Bürger, R., Gimelfarb, A.: Genetic variation maintained in multilocus models of additive quantitative traits under stabilizing selection. Genetics **152**, 807–820 (1999)

Bürger, R., Gimelfarb, A.: The effects of intraspecific competition and stabilizing selection on a polygenic trait. Genetics **167**, 1425–1443 (2004)

Charlesworth, B., Lande, R., Slatkin, M.: A neo-Darwinian commentary on macroevolution. Evolution **36**, 474–498 (1982)

Christiansen, F.B., Fenchel, T.M.: Theories of Populations in Biological Communities. Berlin Heidelberg New York: Springer Verlag, 1977

Christiansen, F.B., Loeschcke, V.: Evolution and intraspecific exploitative competition. II. One-locus theory for small additive gene effects. Theor. Popul. Biol. **18**, 297–313 (1980)
Clarke, B.C.: The evolution of genetic diversity. Proc. R. Soc. London, B **205**, 453–474 (1979)
Clarke, B.C.: Non-synonymous polymorphisms and frequency-dependent selection. In: Singh, R., and M. Uyenoyama (eds) Evolution of Population Biology: Beyond the Modern Synthesis. Cambridge: University Press, 2004, pp. 156–177
Clarke, B.C., Shelton, P.R., Mani, G.S.: Frequency-dependent selection, metrical characters and molecular evolution. Phil. Trans. R. Soc. Lond, B **319**, 631–640 (1988)
Cockerham, C.C., Burrows, P.M., Young, S.S., Prout, T.: Frequency-dependent selection in randomly mating populations. American Naturalist **106**, 493–515 (1972)
Dieckmann, U., Doebeli, M.: On the origin of species by sympatric speciation. Nature **400**, 354–357 (1999)
Doebeli, M.: A quantitative genetic competition model for sympatric speciation. J. Evol. Biol. **9**, 893–909 (1996)
Endler, J.A.: Natural Selection in the Wild. Princeton University Press, 1986
Fenichel, N.: Persistence and smoothness of invariant manifolds for flows. Ind. Univ. Math. J. **21**, 193–226 (1971)
Falconer, D.S., Mackay, T.F.C.: Introduction to Quantitative Genetics, 4th edn. Harlow, Essex, UK: Addison Wesley Longman, 1996
Gavrilets, S.: Models of speciation: what have we learned in 40 years? Evolution **57**, 2197–2215 (2003)
Gavrilets, S.: Fitness Landscapes and the Origin of Species. Princeton: Univ. Press, 2004
Gavrilets, S., Hastings, A.: Intermittency and transient chaos from simple frequency-dependent selection. Proc. R. Soc. London, B **261**, 233–238 (1995)
Hassell, M.P.: Density-dependence in single-species populations. J. Animal Ecol. **44**, 283–296 (1975)
Hastings, A., Hom, C.L.: Multiple equilibria and maintenance of additive genetic variance in a model of pleiotropy. Evolution **44**, 1153–1163 (1990)
Hirsch, M.W., Pugh, C., Shub, M.: Invariant Manifolds. Lect. Notes Math. 583. Berlin heidelberg New York: Springer, 1977
Hofbauer, J., Sigmund, K.: *Evolutionary Games and Population Dynamics.* Cambridge: University Press, 1998
Kingsolver, J.G., Hoekstra, H.E., Hoekstra, J.M., Berrigan, D., Vignieri, S.N., Hill, C.E., Hoang, A., Gibert, P., Beerli, P.: The strength of phenotypic selection in natural populations. American Naturalist **157**, 245–261 (2001)
Loeschcke, V., Christiansen, F.B.: Evolution and intraspecific exploitative competition. II. A two-locus model for additive gene effects. Theor. Popul. Biol. **26**, 228–264 (1984)
Mani, G.S., Clarke, B.C., Shelton, P.R.: A model of quantitative traits under frequency-dependent balancing selection. Proc. R. Soc. Lond. B **240**, 15–28 (1990)
Matessi, C., Gatto, M.: Does K-selection imply prudent predation? Theor. Population Biol. **25**, 347–363 (1984)
Matessi, C., Jayakar, S.D.: Models of density-frequency dependent selection for the exploitation of resources I. Intraspecific competition. In: Karlin S. and E. Nevo (eds.) Population Genetics and Ecology. pp. 707–720, New York: Academic Press, 1976
Matessi, C., Gimelfarb, A., Gavrilets, S.: Long-term buildup of reproductive isolation promoted by disruptive selection: How far does it go? Selection **2**, 41–64 (2001)
May, R.M., Oster, G.F.: Bifurcations and dynamic complexity in simple ecological models. Am. Natur. **110**, 573–599 (1976)
Maynard Smith, J.: Models in Ecology. Cambridge: Univ. Press, 1974
Nagylaki, T.: Dynamics of density- and frequency-dependent selection. Proc. Natl. Acad. Sci. USA **76**, 438-441 (1979)
Nagylaki, T.: The maintenance of genetic variability in two-locus models of stabilizing selection. Genetics **122**, 235–248 (1989)

Nagylaki, T.: The evolution of multilocus systems under weak selection. Genetics **134**, 627–647 (1993)
Nagylaki, T., Hofbauer, J., Brunovský, P.: Convergence of multilocus systems under weak epistasis or weak selection. J. Math. Biol. **38**, 103–133 (1999)
Ricker, W.E.: Stock and recruitment. J. Fisheries. Res. Board Can. **11**, 559–623 (1954)
Roughgarden, J.: Evolution of niche width. Am. Natur. **106**, 683–718 (1972)
Schluter, D.: The Ecology of Adaptive Radiation. Oxford: Univ. Press, 2000
Schluter, D.: Frequency dependent natural selection during character displacement in sticklebacks. Evolution **57**, 1142–1150 (2003)
Slatkin, M.: Frequency- and density-dependent selection on a quantitative character. Genetics **93**, 755–771 (1979)
Slatkin, M.: Ecological causes of sexual dimorphism. Evolution **38**, 662-630 (1984)
Slatkin, M., Smith J.M.: Models of coevolution. Quarterly Rev. Biol. **54**, 233–263 (1979)
Swanson, B.O., Gibb, A.C., Marks, J.C., Hendrickson, D.A.: Trophic polymorphism and behavioral differences decrease intraspecific competition in a cichlid, *Herichthys Minckleyi*. Ecology **84**, 1441–1446 (2003)
Thieme, H.: Mathematics in Population Biology. Princeton: Univ. Press, 2003
Turelli, M., Barton, N.H.: Genetic and statistical analyses of strong selection on polygenic traits: What, me normal? Genetics **138**, 913–941 (1994)
Turelli, M., Barton, N.H.: Polygenic variation maintained by balancing selection: Pleiotropy, sex-dependent allelic effects and G×E interactions. Genetics **166**, 1053–1079 (2004)
Udovic, D.: Frequency-dependent selection, disruptive selection, and the evolution of reproductive isolation. Am. Natur. **116**, 621–641 (1980)
Willensdorfer, M., Bürger, R.: The two-locus model of Gaussian stabilizing selection. Theor. Popul. Biol. **64**, 101–117 (2003)
Wilson, D.S., Turelli, M.: Stable underdominance and the evolutionary invasion of empty niches. American Naturalist **127**, 835–850 (1989)
Wright, S.: Evolution in populations in approximate equilibrium. J. Genetics **30**, 257–266 (1935)
Wright, S.: The distribution of gene frequencies in populations. Proc. Natl. Acad. Sci. USA **23**, 307–320 (1937)
Zhivotovsky, L.A., Gavrilets, S.: Quantitative variability and multilocus polymorphism under epistatic selection. Theor. Pop. Biol. **42**, 254–283 (1992)