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A QUANTITATIVE-GENETIC MODEL FOR SELECTION ON DEVELOPMENTAL NOISE

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Abstract.—We propose a simple model for analyzing the effects of microenvironmental variation in quantitative genetics. Our model assumes that the sensitivity of the phenotype to fluctuations in microenvironment has a genetic basis and allows for genetic correlation between trait value and microenvironmental sensitivity. We analyze the effects of short-term stabilizing and directional selection on the genotypic and microenvironmental components of phenotypic variance. Our model predicts that stabilizing selection on a quantitative trait increases developmental canalization. We show that stabilizing selection can result in an increase in the heritability. Our findings may provide an explanation for the results of selection experiments in which artificial stabilizing selection did not change the heritability coefficient or increased it.

Key words.—Developmental noise, quantitative-genetic model, selection.

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The phenotype of an individual depends on both its genotype and the environment in which the individual has been developing. When discussing the sources of phenotypic variability, typically quantitative geneticists differentiate between macroenvironment and microenvironment. The former component is shared by many individuals; examples are climate conditions for natural populations, and temperature and food level for laboratory populations. But even in laboratory populations under controlled conditions individuals with similar genotypes may differ in quantitative characters in an unpredictable way. Another example of environmental effects is random difference between homological left and right parts on the same individual (fluctuating asymmetry). The reasons for such differences are small fluctuations in external or internal (for the organism) environment, or both. This source of variability is not shared by other individuals; it is unique for each individual or even for each of the two homological parts of the same individual. In these cases, one refers to the effects of the microenvironment or to developmental noise. We use both terms synonymously here.

Various characteristics of populations related to the effects of microenvironment and developmental noise have been intensively analyzed experimentally. The degree to which microenvironmental fluctuations influence the phenotype has a heritable basis (for reviews, see Palmer and Strobeck 1986; Jinks and Pooni 1988, and references herein). It is sometimes correlated with other components of phenotype (Cheverud 1988; Scheiner et al. 1991), and the reaction of a population to the microenvironmental variability can be changed by selection (Scharloo 1964, 1970; Scharloo et al. 1967, 1972; Gibson and Bradley 1974; Kaufman et al. 1977). Finally, often there is a statistically significant association between individual sensitivity to microenvironmental variability and protein heterozygosity (for reviews, see Mitton and Grant 1984; Livshits and Kobyliansky 1985; Zouros and Foltz 1987). The role of microenvironmental effects in genetics and evolution has also been discussed from a theoretical point of view in the classical literature (Schmalhausen 1949; Lerner 1954; Waddington 1957) and in recent papers (Bull 1987; Price and Schluter 1991; Møller and Pomiankowski 1993). In spite of this variety of facts and ideas, in most mathematical models of quantitative traits the influence of the microenvironment on the phenotype z has been described in a simplistic way using the model:

$$z = g + e, \tag{1}$$

where g is a contribution of the genotype and e is a random microenvironmental deviation whose distribution is assumed completely independent of the genotype. The only models we know of where the distribution of the microenvironmental deviation e depends on the genotype are those in Lewontin (1964) and Zhivotovsky and Gavrilets (1992). Lewontin (1964) presented results of a numerical investigation of a model in which the environmental variance (the variance of e in model [1]) decreases with the number of heterozygous loci. This model reflected Lerner's (1954) hypothesis of increased developmental homeostasis in multilocus heterozygotes. Zhivotovsky and Gavrilets (1992, model 4) gave the results of an analytical investigation of this model. Additionally, they (1992, model 3) presented a more general model in which the microenvironmental variance was considered as an additive trait pleiotropically controlled by the same loci that control the mean value of the trait (i.e., the value of g in model [1]). All these models postulated specific dependencies of the microenvironmental variance on the genotype.

Here, we propose a model that makes no a priori assumption about dependence of the microenvironmental variance on the genotype. Instead we begin with the standard model of an additive polygenic trait generalizing it for the case where the contributions of loci to the trait depend on the microenvironment in a linear (simplest) way. From this we derive all other properties of the system, including the specific form in which microenvironmental variance depends on the genotype. Our model for an additive trait can be considered as a modification of a model that has been used for analyzing the role of the macroenvironment in the evolution of quantitative traits under natural and artificial selection (Gavrilets 1986, 1988; Gavrilets and Scheiner 1993a,b). It is also closely related to models analyzed by de Jong (1988, 1989, 1990a,b) and Gimelfarb (1986). These and other earlier models for genotype-environment interaction have mainly focused on the effects of the environment on mean phenotypic and genotypic values. We will primarily be interested in the effects of the environment on the variances and covariances of phenotypic and genotypic values.

In the following section, we formulate a model of a quantitative trait, describe its static properties, and compare them with experimental data. Then we introduce selection into the model and consider the effects of natural and artificial selection on the properties of multilocus systems in the presence of developmental noise. The final section is devoted to the discussion of our approach and results. We also indicate possible generalizations of the approach.

A Model for an Additive Polygenic Trait

We begin with the standard model of an additively determined quantitative trait, which we then modify. We describe the model and our results in terms of diallelic loci for ease of presentation, but our results carry over completely to the case of more alleles per locus. Let an additive quantitative trait, z, be controlled by n diallelic loci, with alleles $\mathbf{A}_i$ and $\mathbf{a}_i$; $i = 1, \ldots, n$. We introduce the indicator variables l_i (l'_i) equal to 1 or 0 if the allele at the ith locus of the paternal (maternal) gamete is $\mathbf{A}_i$ or $\mathbf{a}_i$, respectively. Let α_i be half the difference between the contributions of the homozygous loci $\mathbf{A}_i\mathbf{A}_i$ and $\mathbf{a}_i\mathbf{a}_i$, and β_i be the contribution of the heterozygous locus $\mathbf{A}_i\mathbf{a}_i$ to the trait. We can represent the trait value as

$$z = \sum_i [\beta_i + \alpha_i(l_i + l'_i - 1)]. \tag{2a}$$

To introduce the effects of the microenvironment into the model we first define a new variable, τ, characterizing the microenvironment, and, second, assume that the locus contributions α_i and β_i are linear functions of τ.

$$\alpha_i = \zeta_i + \xi_i \tau, \tag{2b}$$

$$\beta_i = \nu_i + \mu_i \tau. \tag{2c}$$

Here ζ_i, ξ_i, ν_i, and μ_i are parameters specific for the ith locus, with ξ_i and μ_i describing the effect of alleles at locus i on sensitivity to the microenvironment. The linearity assumption is equivalent to assuming the microenvironmental effects are small. Below, we also use an alternative representation of (2):

$$z = g + \gamma\tau, \tag{3}$$

where $g = \Sigma_i[\nu_i + \zeta_i(l_i + l'_i - 1)]$ and $\gamma = \Sigma_i[\mu_i + \xi_i(l_i + l'_i - 1)]$.

We assume τ is a random variable with mean μ_τ and variance σ_τ^2. Without loss of generality we can set $\mu_\tau = 0$, possibly by redefining the scale. Model (2–3) implies that the mean value of the trait and the microenvironmental variance for the specific genotype (g, γ) are

$$E\{z \mid g, \gamma\} = g, \qquad \mathrm{var}\{z \mid g, \gamma\} = \gamma^2\sigma_\tau^2. \tag{4}$$

Thus, the value of g determines the mean value of the trait, while the value of γ is a measure of trait sensitivity to the variation in the microenvironment. This model could also be viewed as equivalent to a model of two pleiotropically determined characters: mean trait value and sensitivity to the microenvironment.

Model (2) assumes a linear dependence of the trait value on genotype and microenvironment. How good is this approximation? For a set of different genotypes, without considering that the τ value is unique for each individual, and assuming every genotype in the set experiences the same values of τ, model (2) implies regression of the trait value of each genotype on the mean value over this set of genotypes is linear, with the slope proportional to $g_{1,\iota}$. The regression on the mean model has been intensively applied for the analysis of the influence of the macroenvironment on a trait (for a review, see Jinks and Pooni 1988). Two general results from this analysis are important for us. First, linear regression is often sufficient for adequate description of data, especially if the macroenvironmental variation is small enough. A linear model would also probably be expected to be valid for a microenvironment with a smaller variability. Second, the inheritance of the mean value and the environmental sensitivity (as measured by the slope of regression) can be adequately described in terms of additive models in most cases. These results lead us to believe model (2) may be sufficient, at least in some cases. In any event, a linear model is the simplest approximation to a nonlinear one. In the final section, we describe a straightforward generalization of the model.

Now we consider a population of individuals assuming model (3). The mean value of the trait in the population will be $\bar{z} = \bar{g}$ while the phenotypic variance P will be

$$P = G + \mathcal{E}. \tag{5}$$

Here the genotypic variance $G \equiv var\{g\}\}$ and the microenvironmental variance $\mathcal{E}$ is

$$\mathcal{E} = (\bar{\gamma}^2 + \Gamma)\sigma_\tau^2. \tag{6}$$

where $\Gamma \equiv var\{\gamma\}$. All these values can also be expressed using model (2). Let p_i and q_i be the frequencies of alleles $\mathbf{A}_i$ and $\mathbf{a}_i$, respectively. Then $\bar{g} = \Sigma_i[\nu_i + \zeta_i(p_i - q_i)]$ and $G = \Sigma_i 2\zeta_i^2 p_i q_i + \Sigma_{i \neq j} 2\zeta_i\zeta_j \mathrm{D}_{ij}$, where D_{ij} is linkage disequilibrium between the ith and the jth loci. Mean value $\bar{\gamma}$ and variance Γ are described by the similar formulae.

The outcome of selection depends on the correlation between g and γ (see below). For model (3), the covariance C between the mean value of the trait and environmental sensitivity (as measured by γ) is

$$\begin{aligned} C &\equiv \operatorname{cov}\{g, \gamma\} \\ &= \sum_{\iota} 2\zeta_i\xi_\iota p_\iota q_i + \sum_{\iota \neq j} 2\zeta_\iota\xi_j D_{ij}. \end{aligned} \tag{7}$$

Lerner (1954) postulated that the microenvironmental variance decreases with increase in heterozygosity. This view has been a subject of controversy (see the literature cited above for references). Chakraborty (1987) analyzed the apparent association between the genotypic variance and heterozygosity. In particular, he has shown that if a trait is additive, then the genotypic variance is a decreasing function of the number of heterozygous loci. Under stabilizing selection, the mean value $\bar{\gamma}$ converges to zero (see below). If $\bar{\gamma} \approx 0$, then $\mathcal{E}$ is proportional to Γ, and the microenvironmental component of the phenotypic variance can be considered as the variance of an additive trait. Applying Chakraborty's results for this "trait," the model produces a negative association between microenvironmental variance $\mathcal{E}$ and heterozygosity, without assuming any effects of heterozygosity per se. The additivity assumption is crucial; apparent dependence of the genotypic variance of a nonadditive trait on heterozygosity can be more complex, for example, nonmonotonic (Dubrova and Gavrilets 1989). The same is true if $\bar{\gamma}$ deviates from zero. In this case, the microenvironmental variance (see eq. 6) is a sum of two variables, the first, proportional to $\bar{\gamma}^2$, increases, while the second, proportional to Γ, decreases with heterozygosity.

Dynamics of the Means and Variances under Selection.—In this section, we consider how selection on a quantitative trait influences the population structure when the trait is described by model (3). First consider stabilizing selection, which we describe by a quadratic fitness function

$$w(z) = 1 - s(z - z_0)^2, \tag{8}$$

where z_0 is the optimum phenotype, and s characterizes the strength of selection. Equation (8) implies that the optimum phenotype is the same for all microenvironments. This assumption is reasonable for describing artificial stabilizing selection experiments. Using (8), the mean fitness of the genotype (g, γ) is

$$\begin{aligned} w(g, \gamma) &= \int w(z)f(\tau)\, d\tau \\ &= 1 - s[(g - z_0)^2 + \gamma^2\sigma_\tau^2], \end{aligned} \tag{9}$$

where $f(\tau)$ is the distribution of τa,a and we again assume (without loss of generality) $E\{\tau\} = 0$. The last expression shows that quadratic stabilizing selection on the trait, z, generates separate selection components on the genotypic value, g, and on the value, γ, characterizing the sensitivity to the variation in microenvironment (cf. de Jong 1989). The resulting fitness function is equivalent to the fitness function arising when stabilizing selection acts on two pleiotropically connected traits (cf. Tachida and Cockerham 1988; Hastings and Hom 1989; Wagner 1989; Zhivotovsky and Gavrilets 1992). The optimum value for the first trait, that is, for g, is z_0, whereas for the second trait, that is, for γ, it is 0. This shows that stabilizing selection on the trait directly influences both the mean value and the sensitivity to microenvironmental variation (cf. Waddington 1957).

We now consider the simplest model of directional selection on a trait in which the fitness function is linear:

$$w(z) = 1 + sz, \tag{10}$$

where s characterizes the strength of selection. Obviously, the mean fitness of a genotype (g, γ) is

$$w(g, \gamma) = \int w(z) f(\tau)\, d\tau \tag{11}$$

$$= 1 + sg. \tag{12}$$

This shows that directional selection of the form (10) directly influences the mean value. If g and γ are correlated, we also expect to observe a correlated response in the sensitivity to microenvironmental variation.

We have just shown linear and quadratic selection on the trait (3) can be considered as selection on correlated traits. In the case of a single trait, the infinitesimal model (Bulmer 1980, chap. 9) seems able to describe accurately the effects of short-term selection on the dynamics of the mean and variance. This model assumes existence of a large number of unlinked loci with small effects, neglects changes in allele frequencies, and attributes the changes in the additive genetic variance to the buildup of linkage disequilibrium under selection. Bulmer (1980, eqs. 9.15 and 9.16) presented equations relating the mean and the additive genetic variance of a single quantitative trait before selection with the corresponding values in the following generation.

Below we describe a multivariate generalization of these equations. Later we will use them for analyzing the effects of linear and quadratic selection on the trait (3). We now consider m quantitative traits. Let the distribution of the genotypic values of these traits in the tth generation before selection be multivariate normal with mean vector $\bar{\mathbf{g}}$ (t) and covariance matrix $\mathbf{G}(\mathrm{t})$. A multivariate version of Bulmer's equations can be written as

$$\mathbf{g}(\mathrm{t}+1) = \mathbf{g}(\mathrm{t}) + \Delta_s\mathbf{g}(\mathrm{t}), \tag{13a}$$

$$\mathbf{G}(\mathrm{t}+1) = \mathbf{G}(\mathrm{t}) + \tfrac{1}{2}[\mathbf{G}_{\mathrm{LE}} - \mathbf{G}(\mathrm{t}) + \Delta_s\mathbf{G}(\mathrm{t})], \tag{13b}$$

where $\Delta_s\mathbf{g}(t)$ and $\Delta_s\mathbf{G}(t)$ are within-generation changes (due to selection) in the mean vector and in the covariance matrix, and $\mathbf{G}_{\mathrm{LE}}$ is the genotypic covariance matrix the current allele frequencies would produce if the population were in linkage equilibrium. There are several ways to compute the quantities $\Delta_s\mathbf{g}(t)$ and $\Delta_s\mathbf{G}(t)$. With a simple expression for the mean fitness $w(\mathbf{g})$ of genotype $\mathbf{g}$ (as we used for quadratic stabilizing and linear directional selection on the trait [3]), these quantities can be expressed in the form of covariances of $w(\mathbf{g})$ with functions of the characters,

$$\Delta_s\mathbf{g} = \mathrm{Cov}[w(\mathbf{g})/\bar{w}, \mathbf{g}], \tag{14a}$$

$$\Delta_s\mathbf{G} = \mathrm{Cov}[w(\mathbf{g})/\bar{w}, (\mathbf{g} - \bar{\mathbf{g}})(\mathbf{g} - \bar{\mathbf{g}})^{\mathrm{T}}] - (\Delta_s\mathbf{g})(\Delta_s\mathbf{g})^{\mathrm{T}} \tag{14b}$$

(Robertson 1966; Price 1970, 1972; Lande and Arnold 1983). Alternatively, if the phenotypic distribution is multivariate normal, then these quantities can be expressed in terms of changes in the phenotypic distribution. The first is described by the well-known equation $\Delta_s\mathbf{g} = \mathbf{G}^{-1}\mathbf{PS}$, where $\mathbf{S}$ is the vector of selection differentials, and $\mathbf{P}$ is the phenotypic covariance matrix (Lande 1979), while the second can be represented as

$$\Delta_s\mathbf{G} = \mathbf{GP}^{-1}(\Delta_s\mathbf{P})\mathbf{P}^{-1}\mathbf{G} \tag{15}$$

(Lande and Arnold 1983). The observed change in the phenotypic covariance matrix produced by selection within a generation $\Delta_s\mathbf{P}$ can be expressed by (14b) with substitution of z for $\mathbf{g}$, $w(z)$ for $w(\mathbf{g})$, and S for $\Delta_s\mathbf{g}$ (Lande and Arnold 1983). Equations (13–15) represent a multitrait version of Bulmer's (1980) infinitesimal model; they are valid for arbitrary fitness functions. For the specific case of a Gaussian fitness-function equation, (13b) was presented in (Turelli 1988). As was stated above, Bulmer's model assumes that the loci are unlinked. In this model, the covariance matrix $\mathbf{G}(t)$ quickly converges to an equilibrium value. Another extreme case is a model with complete linkage. In this model, the change between generations, $\mathbf{G}(t+1) - \mathbf{G}(t)$, is exactly the change within a generation, $\Delta_s\mathbf{G}(t)$, and the elements of the covariance matrix $\mathbf{G}(t)$ quickly converge to zero.

Quadratic Stabilizing Selection.—We now examine stabilizing selection (8) acting on the trait (2). Assume that the distribution $p(g, \gamma)$ of g and γ values in the population is approximately bivariate normal. For fitnesses to remain positive, we also have to assume that the parameter s is small. The equations for the changes in the means are

$$\Delta_s\bar{g} = -\frac{2s}{\bar{w}}(G\bar{g} + C\bar{\gamma}), \qquad (16a)$$

$$\Delta_s\bar{\gamma} = -\frac{2s}{\bar{w}}(C\bar{g} + \Gamma\bar{\gamma}), \qquad (16b)$$

where $\bar{w} = 1 - s(g^2 + G + \epsilon)$. For simplicity, we have assumed that $z_0 = 0$, and $\sigma_\tau^2 = 1$. In this case, equation (13a) can be written in the form $[\bar{g}(t + 1), \bar{\gamma}\ (t + 1)]^T = \mathbf{A}(\mathrm{t})[\bar{g}(\mathrm{t}); \bar{\gamma}(t)]^T$. The eigenvalues of $\mathbf{A}(t)$ are positive. Moreover, provided there is genetic variation for both g and γ, and excluding a biologically unrealistic case of perfect correlation between g and γ, these eigenvalues are less than one. This shows the mean values converge to the optimum values (zero for both g and γ). The equations for the changes in the variances G and $\mathcal{E}$ and in the covariance C are then

$$\Delta_s G = -\frac{2s}{\bar{w}}(G^2 + C^2), \qquad (17a)$$

$$\Delta_s\mathcal{E} = -\frac{2s}{\bar{w}}(\mathcal{E}^2 + C^2), \qquad (17b)$$

$$\Delta_s C = -\frac{2s}{\bar{w}}CP, \qquad (17c)$$

where for simplicity we have assumed that the mean values $\bar{g}$ and $\bar{\gamma}$ have already reached zero. The fact that both $\Delta_s G$ and $\Delta_s\mathcal{E}$ are negative, together with (13b), shows that stabilizing selection tends to reduce both components of phenotypic variance P (i.e., both G and $\mathcal{E}$) This has been demonstrated experimentally (see the references above). Our model predicts that stabilizing selection also reduces the absolute value of covariance C. The rate of change of G, $\mathcal{E}$, and C decreases with decrease in the absolute value of C. A greater component of phenotypic variance experiences a greater rate of reduction. This can result in increase in the heritability coefficient $h^2 = G/(G + \mathcal{E})$ under stabilizing selection. For example, if the population is initially at linkage equilibrium with $G = 0.25$, $\mathcal{E} = 0.75$ (and, hence, $h^2 = 0.25$), $C = 0$, and $s = 0.25$, then in the next generation $G = 0.23$, $\mathcal{E} = 0.56$, but $h^2 = 0.29 > 0.25$. Figure 1A illustrates these effects of one generation of stabilizing selection for nonzero covariance between g and γ. Absence of significant changes or even an increase in the heritability has sometimes been observed in stabilizing selection experiments (Gibson and Thoday 1963; Gibson and Bradley 1974; Kaufman et al. 1977). Classical models, which consider the microenvironmental deviation completely independent of the genotype, predict an invariable reduction in h^2.

Maintenance of Genetic Variability under Stabilizing Selection.—The normal approximation, which was used in the preceding section, cannot be applied for analyzing long-term stabilizing selection. For this case, a more detailed approach is needed. The fitness of a genotype (g, γ) is equivalent to the fitness function that describes stabilizing selection acting on two pleiotropically related traits (see expression [9]), allowing the use of results already known for selection on multiple traits. Here we discuss results on the maintenance of polygenic variability without mutation. Hastings and Hom (1990) have shown that if stabilizing selection is weak relative to recombination, then the number of polymorphic loci at equilibrium cannot be greater than the number of traits. In model (3), the number of traits is two; thus, no more than two loci can be maintained as polymorphic under weak selection. However, if selection is strong enough relative to the overall recombination rate or to the recombination rate within some subsets of loci, then polymorphism can be maintained in many loci (Gimelfarb 1992; Gavrilets and Hastings 1993, 1994). This conclusion applies directly to model (3).

Linear Directional Selection.—Finally, we examine directional selection (10). Again we assume the distribution $p(g, \gamma)$ of g and γ values in the population is approximately bivariate normal and the parameter, s, is small. In this case,

$$\Delta_s\bar{g} = sG/\bar{w}, \qquad (18a)$$

$$\Delta_s\bar{\gamma} = sC/\bar{w}, \qquad (18b)$$

where $\bar{w} = 1 + s\bar{g}$, and

$$\Delta_s G = -(\Delta_s\bar{g})^2 = -s^2G^2/\bar{w}^2, \qquad (19a)$$

$$\Delta_s\mathcal{E} = 2s\bar{\gamma}C/\bar{w}, \qquad (19b)$$

$$\Delta_s C = -(\Delta_s\bar{g})(\Delta_s\bar{\gamma}) = -s^2CG/\bar{w}^2. \qquad (19c)$$

Expressions (18a, 19a) describe the direct effects of selection on g, while those in (18b, 19b) describe the correlated selection on γ. The model predicts that directional selection slowly decreases the genotypic variance, G, and the absolute value of covariance C. The effects of selection on the microenvironmental variance can be more pronounced, depend on the sign of C, and vanish as C or $\bar{\gamma}$ reaches zero. Figure 1B illustrates the one-generational effects of directional selection on both components of phenotypic variance and the heritability coefficient.

DISCUSSION

Here we have proposed a new model for analyzing the effects of microenvironmental variation in quantitative genetics. This model assumes that the loci contribute additively to the trait value, and that the locus contributions are linear functions of some unobserved random microenvironmental variable. In spite of the simplicity of the model, it incorporates and is able to describe many properties of natural and experimental populations. In particular, the model assumes that microenvironmental sensitivity has a genetic basis, allows for a genetic correlation between the trait value and the microenvironmental sensitivity, and produces a negative relationship between microenvironmental variability and heterozygosity. All these properties have been repeatedly observed in experiments (see the references above), but are almost neglected in existing quantitative-genetic models. Using this model, we also analyzed the effects of short-term stabilizing and directional selection on the genotypic and the microenvironmental components of phenotypic variance and on the heritability coefficient. We have shown stabilizing selection tends to reduce both these components. This has been observed in selection experiments. A component with a larger value experiences a bigger reduction, which can result in an increase in the heritability coefficient under stabilizing selection. Our findings may provide an explanation for the results of selection experiments in which artificial stabilizing selection did not change, or even increased, the heritability coefficient (Gibson and Thoday 1963; Gibson and Bradley 1974; Kaufman et al. 1977). Standard quantitative-genetic models always imply a decrease in heritability under stabilizing selection. Our model also predicts that the reduction in the components of phenotypic variability increases with increasing covariance C between trait value and microenvironmental sensitivity, and that stabilizing selection tends to reduce this covariance. The latter prediction is also true for the directional selection which we modeled by a linear fitness function. However, the effect of directional selection on the microenvironmental variance $\mathcal{E}$ depends on the sign of C—if it is positive, we expect to observe an increase in $\mathcal{E}$.

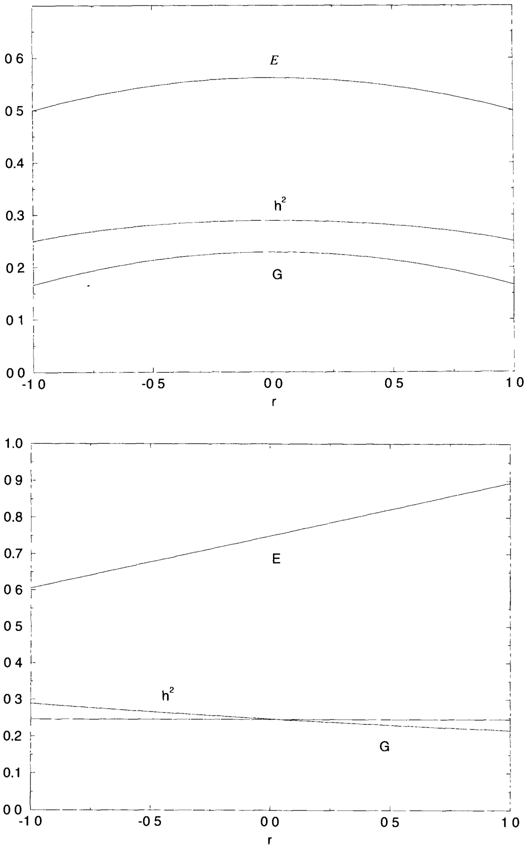

FIG. 1. Genotypic variance, G, microenvironmental variance, ϵ, and the heritability, h^2 after one generation of selection as functions of the correlation between g and fl. Before selection the population is at linkage equilibrium with $G = 0.25$, $\mathcal{E} = 0.75$, $h^2 = 0.25$. (A) stabilizing selection (8) with $s = 0.25$; (B) directional selection (10) with $s = 0.25$.

We have shown that the model considered here can produce a negative apparent association between microenvironmental variance, $\mathcal{E}$, and heterozygosity. An observed negative association between $\mathcal{E}$ and heterozygosity is a core element of Lerner's theory of genetical homeostasis. Lerner (1954) postulated that multilocus heterozygotes have lower environmental variance be-cause of better buffering against variations in the environment. In contrast, we have derived this negative association without any assumptions about the effects of heterozygosity per se. In our model, this is just an outcome of the assumptions that the parameter γ measuring the sensitivity to the microenvironmental variation is determined additively, and its mean value in the population is about zero. More complex models of genetic determination of microenvironmental sensitivity and deviation of $\bar{\gamma}$ from zero would result in other dependencies, including nonmonotonic ones. Our model's prediction that stabilizing selection on a quantitative trait reduces the sensitivity to fluctuations in the microenvironment is closely related to Waddington's (1957) ideas about developmental canalization. Waddington emphasized the role of special regulatory genes underlying this effect. Our phenomenological model does not incorporate such genes, but nevertheless is able to reproduce the effect. Our model could be modified, however, by having some genes which only affect the trait, and some which only affect the sensitivity to the microenvironment.

The basic model analyzed here was constructed, as we have described above, by taking the standard model of an additive quantitative trait (2) and assuming the locus contributions are linear functions of some unobserved variable that describes the state of the microenvironment (cf. de Jong 1988, 1989, 1990a,b). While the assumption of linearity seems justified (the fluctuations in the microenvironment are supposed to be small, and the linear approximation is expected to be valid), the assumption that a single microenvironmental variable exists may be too restrictive. The following argument shows how a more general model could be constructed. Let us consider a model that states that the character

$$z = F(\mathcal{G}, \mathcal{E}), \tag{20}$$

where $\mathcal{G}$ and $\mathcal{E}$ are vectors of variables that describe internal and external environments. The former is usually referred to in quantitative genetics as genotype, while the latter is temperature, food level, etc. Let us consider a trait value for a specific genotype in a specific fixed external macroenvironment. A natural way to model microfluctuations in the external environment is to assume that the components of ϵ are random variables distributed around some (macroenvironmental) values $\mathcal{E}_{i,macro}$. Microfluctuations in the internal environment result in the specific genotype acting as if it were a slightly different genotype. To model this, we can assume that the components of $\mathcal{G}$ are random variables distributed around "real" genotypic values $G_{i,macro}$. Assuming all these deviations are small, we can approximate F by a linear function that results in the model $z = g + e$. Here $g = F(G_{macro}, \mathcal{E}_{macro})$ and

$$e = \sum \gamma_{i,int}\tau_{i,int} + \sum \gamma_{j,ext}\tau_{j,ext}, \tag{21}$$

where $\tau_{i,int} = G_i - G_{i,macro}$, and $\tau_{j,ext} = \mathcal{E}_j - \mathcal{E}_{j,macro}$ account for the fluctuations in the internal and external microenvironment and can be considered random variables, while γ's are fixed coefficients (that depend on the internal and external macroenvironment). Model (3) assumes the random variable e can be approximated as $e \cong \gamma\tau$, where γ depends on the macroenvironment, and τ accounts for fluctuations in microenvironment (cf. Gimelfarb 1986). A more general model would have the form

$$z = g + \sum \gamma_i\tau_i, \tag{22}$$

where g and γ_i depend on the macroenvironment and τ_i are independent random variables that specify the microenvironmental effects. Formally, the components of γ can be interpreted as quantitative traits, which are genetically correlated, and the properties of the system under consideration can be analyzed using the existing theory of multivariate quantitative genetics (Lande 1979; Tachida and Cockerham 1988; Wagner 1989; Hastings and Hom 1989; Zhivotovsky and Gavrilets 1992). For example, quadratic stabilizing selection (8) will make the mean fitness of genotype $(g, \gamma_1, \gamma_2, \ldots)$

$$\begin{aligned} &w(g, \gamma_1, \gamma_2, \ldots) \\ &\quad = 1 - s\Big((g - z_0)^2 + \sum \gamma_i^2 var\{\tau_i\}\Big). \end{aligned}$$

This fitness function is equivalent to a fitness function acting on a set of quantitative traits. Standard approaches for analyzing models of this kind exist (Hastings and Hom 1989; Zhivotovsky and Gavrilets 1992).

Here, we have applied a framework (Gavrilets 1986, 1988; Gimelfarb 1986; de Jong 1988, 1989, 1990a,b; Gavrilets and Scheiner 1993a,b), which has been developed for analyzing the effects of macroenvironment, to the problems related to microenvironment. In principle, the existing alternative approaches could be used (see the review by Scheiner 1993). The infinite dimensional version (Gomulkiewicz and Kirkpatrick 1992) of the approach that treats quantitative traits in different (macro) environments as separate traits (Falconer 1952; Via and Lande 1985, 1987) could be used to answer questions about dynamics of the phenotypic moments under selection. However, using this approach we could not consider relationships between phenotypic characteristics and heterozygosity or demonstrate the maintenance of genetic variability without mutation. Another alternative is a model developed by Gillespie and Turelli (1989). This model, however, has some shortcomings (Gimelfarb 1990) and does not provide a simple way for predicting the effects of selection on phenotypic moments.

The approach described here can be generalized in several directions. One way is to consider the exact dynamic equations without using the assumption about bivariate normality. Dominance and epistatic effects can be included in the model. Other more complex selection regimes can also be considered, including truncation selection, which is usually used in artificial selection experiments, and Gaussian stabilizing selection. If the fitness function is Gaussian (i.e., $w(z) = Exp[-z^2/(2V_s)]$, and the τ value in model (3) has a normal distribution, then the mean fitness of genotype (g, γ) is given by

$$w(g, \gamma) \sim Exp\left\{-\frac{g^2}{2(V_s + \gamma^2\sigma_\tau^2)}\right\}.$$

Such a fitness function has been proposed for analyzing the evolution of environmental tolerance (Lynch and Gabriel 1987; Gabriel and Lynch 1992). A more detailed analysis of the relationships between the microenvironmental variance and heterozygosity can also be completed. Gavrilets and de Jong (1993 unpubl. data) have derived formulae that can be used to compute the mean fitness of the population, $\bar{w}$, conditioned on heterozygosity, H, and covariance of $\bar{w}$, and H. As soon as a genetic model of the microenvironmental sensitivity is specified, these formulae for analyzing the relation between ϵ and H can be directly applied. Another interesting application would be a generalization of the approach for the case of multiple traits and analysis of the relationships between genotypic and phenotypic covariance matrices (Cheverud 1988).

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