On the Distribution of the Mean and Variance of a Quantitative Trait Under Mutation-Selection-Drift Balance

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ABSTRACT

The distributions of the mean phenotype and of the genetic variance of a polygenic trait under a balance between mutation, stabilizing selection and genetic drift are investigated. This is done by stochastic simulations in which each individual and each gene are represented. The results are compared with theoretical predictions. Some aspects of the existing theories for the evolution of quantitative traits are discussed. The maintenance of genetic variance and the average dynamics of phenotypic evolution in finite populations (with \( N_e < 1000 \)) are generally simpler than those suggested by some recent deterministic theories for infinite populations.

The importance of polygenic mutations for the maintenance of genetic variation in quantitative traits and for the response to long-term directional selection has been investigated and discussed in numerous publications (e.g., Lande 1975, 1988; Hill 1982; Turelli 1984; Lynch and Hill 1986; Keightley and Hill 1983, 1988; Slatkin 1987; Bürger et al. 1989; Houlé 1989) [cf. Bulmer (1989) and Barton and Turelli (1989) for reviews and further references]. There seems to be some consensus that mutation can contribute substantially to the maintenance of genetic variation although the extent may differ greatly between species and traits. Many other mechanisms and models have been suggested or investigated that either reduce or increase the amount of heritable variation compared to the simple mutation-selection-balance hypothesis. As a consequence of the well known disputes about this subject, fresh experimental approaches have been started (e.g., Caballero et al. 1991; Mackay et al. 1992; Santiago et al. 1992; López and López-Fanjul 1993a,b).

Many of the theoretical analyses have been devoted to deterministic models, ignoring the consequences of genetic drift in finite populations, and considerable progress in the understanding of such multilocus models has been achieved (Latter 1960; Kimura 1965; Bulmer 1972; Lande 1975; Fleming 1979; Turelli 1984; Barton 1986; Barton and Turelli 1987; Slatkin 1987; Bürger 1989; Frank and Slatkin 1990; Hastings 1990; Turelli and Barton 1990; Berger and Hofbauer 1994; to mention just a few). However, the overall conclusion that must be drawn from these investigations, and this was particularly stressed by Turelli and Barton (1990), is that the evolutionary dynamics of quantitative traits crucially depends on so many assumptions and genetic details that it is unlikely that general, simple, and reliable predictions can ever be made.

In this study, we investigate the distribution of the mean phenotype and of the genetic variance of a quantitative character under mutation-stabilizing selection balance in a finite population. We compare the simulation results with the phenotypic theory for the mean phenotype of Lande (1976) and with predictions for the distribution of the genetic variance by Lynch and Hill (1986), Barton (1989) and Bürger et al. (1989). On the basis of these and other results, we conclude that several of the complications occurring in deterministic polygenic models are simplified by genetic drift and thus are of much less importance in small or moderately large populations.

THEORY

We give a brief summary of those theoretical results on the distribution of a quantitative trait in a finite population whose validity will be investigated in the next section. We consider a randomly mating, finite population of constant effective size \( N_e \) with discrete generations. Individual fitness is determined by a single quantitative character under Gaussian stabilizing selection on viability, with the optimum phenotype at zero, i.e., the viability of an individual with phenotypic value \( z \) is assumed to be

\[
W_i = \exp\left(-\frac{z^2}{2\sigma^2}\right),
\]  

where \( \sigma^2 \) is inversely proportional to the strength of stabilizing selection.

The quantitative character under consideration is assumed to be determined by \( n \) freely recombining, equivalent loci, although in our simulations we allow for linked loci, too. The allelic effects are additive within and between loci, i.e., there is no dominance or epistasis. The phenotypic value of an individual is the sum of
the genetic contribution and a normally distributed environmental effect with mean zero and variance \( \sigma_e^2 = 1 \). Therefore, the phenotypic mean \( \bar{z} \) equals the mean of the additive genetic values, \( \bar{g} \) and the phenotypic variance is \( \sigma_e^2 = \sigma_g^2 + \sigma_e^2 \), with \( \sigma_g^2 \) denoting the (additive) genetic variance. We shall use the parameter \( V_i = \omega^2 + \sigma_e^2 = \omega^2 + 1 \) to describe the strength of stabilizing selection on the breeding values.

**Distribution of the mean phenotype:** Random sampling in a finite population induces stochasticity in the evolution of the mean phenotype and, more generally, of the whole distribution of phenotypic values. Therefore, a proper understanding of phenotypic evolution requires the knowledge of the sampling distribution of the average phenotype, of the genetic (and hence phenotypic) variance, etc. Under the empirically testable assumption of a normal distribution of phenotypic values, LANDE (1976) showed that the distribution of the average phenotype is normal under stabilizing selection as in (1). In particular, he derived the dynamics of the expected mean phenotype and of its variance. At stochastic equilibrium, the expected mean phenotype obviously coincides with the optimum phenotype zero, and LANDE’s (1976) formula (17b) yields the variance of the distribution of \( z \), i.e.,

\[
V(z) = \frac{(\sigma_g^2 + V_i)^2}{N_e(\sigma_g^2 + 2V_i)} + \frac{\sigma_e^2}{BN_e} \tag{2a}
\]

where \( \sigma_e^2 \) denotes the average genetic variance at equilibrium, and the second term in (2a) accounts for measuring the phenotype among a finite number \( BN \) of progeny before selection (\( B \) the birth rate; see below). LANDE’s theory for the distribution of the mean phenotype does not depend on specific mechanisms determining how genetic variation is maintained under stabilizing selection and random drift. It depends on the assumption that selection acts only on the phenotype, and that nothing other than selection and drift affect the mean phenotype.

**Distribution of the genetic variance:** To obtain approximations for the distribution of the genetic variance, the mechanism by which genetic variability is maintained must be specified. We assume that it is through mutation. Let \( \mu \) denote the mutation rate per haploid locus. Following CROW and KIMURA’s (1964) continuum-of-alleles model, we assume an effectively continuous distribution of possible effect for mutants with mean zero, variance \( \sigma^2 \), and no skewness. There is no restriction on the number of possible alleles per locus.

Various theories and approximations have been derived for the expected value of the additive genetic variance in a finite population under a balance between selection, mutation, and random genetic drift (see references below).

For a neutral phenotypic character, LANCHE and HILL (1986) showed that the expected genetic variance under mutation-drift balance is

\[
\sigma_e^2(N) = V_e \frac{(2N_e - 1)^2}{2N_e} \tag{3a}
\]

where \( V_e = 2\pi \mu \sigma^2 \) is the variance introduced by mutation each generation (see also CLAYTON and ROBERTSON 1955). Their model assumes that \( 4N_e \mu < 1 \), so that it is unlikely to have more than two alleles per locus.

For stabilizing selection acting on the phenotype according to (1), the approximate formula

\[
\sigma_e^2(N) = \frac{4\pi \mu \sigma^2 N_e}{1 + (\sigma^2 N_e / V_i)} \tag{4}
\]

This is identical to the two-allele approximations of LATTER (1960) and BULMER (1972). The generality and accuracy of (5) were investigated recently by BÜRGER and HOFBAUER (1994). In the limit of weak selection, i.e., \( V_i \to \infty \), (4) reduces to TURELLI’S (1984) so-called house-of-cards (HC) approximation

\[
\sigma_e^2(N) = 4\pi \mu \sigma^2 \tag{5}
\]

The approximation (4) was derived for the continuum-of-alleles model using the HC-approximation (5) and diffusion theory (cf. BÜRGER et al. 1989), and it can be rewritten as half the harmonic mean of (3b) and (5), i.e.,

\[
\sigma_e^2(N) = \frac{\sigma_e^2(N) \sigma_e^2(HC)}{\sigma_e^2(N) + \sigma_e^2(HC)}. \tag{6}
\]

The validity of the SHC-approximation (Equation 4 or 6) requires low mutation rates per locus and a high variance \( \sigma^2 \) of the distribution of mutant effects because the HC-approximation does so and because the neutral approximation requires small \( \mu \). For high mutation rates or low \( \sigma^2 \), the Gaussian approximation of KIMURA (1965) and its multilocus extension by LANDE (1975) are more appropriate and could be inserted into (6) instead of \( \sigma_e^2(HC) \) (see also LATTER 1970; LYNCH and LANDE 1993). All the formulas in this section are based on the assumption of linkage equilibrium.

Extensive stochastic computer simulations (BÜRGER et al. 1989; BÜRGER 1989) have shown that (4) produces a surprisingly good approximation to the average
equilibrium variance for a wide range of parameters. 
Keightley and Hill (1988) obtained values of the genetic variance that are up to 30% larger than predicted by (4). The reason is that their transition matrix approach, for equal allelic effects across loci being equivalent to Bulmer's (1972) model, is based on a deterministic recursion equation with heterozygote disadvantage at each locus. This heterozygote disadvantage is a consequence of the assumption that the gene frequencies are always such that the mean phenotype is at the fitness optimum, which, however, is not satisfied in the full multilocus model. Consideration of the marginal fitness values, as appropriate under the assumption of global linkage equilibrium, shows that each locus is under directional selection and this should lead to a lower genetic variance. Barton's (1989) simulation model with two alleles per locus, is based on the correct deterministic equations for the gene frequency change in the full multilocus model and yields estimates of the genetic variance that are below those of Bulmer (1972) and Keightley and Hill (1988) but higher than (4). This is not surprising, because in Barton's simulation model alleles still occur in pairs, symmetric with respect to the optimum. The present simulations [as those in Bürger et al. (1989) and Burger (1989)] neither assume linkage equilibrium, nor equal allelic effects, nor are they based on deterministic recursion equations. It turns out that a better approximation is obtained in the case where random drift is strong compared to selection if in (6) formula (3a) is used for $\alpha^2(N)$ instead of (3b).

The distribution of the genetic variance, in particular the variance of the genetic variance, $V(\sigma^2)$, has been studied in detail only in the neutral case. Under the assumption $4N\mu < 1$, so that the likelihood of more than two segregating alleles per locus is negligible, Lynch and Hill (1986) showed that for a normal distribution of mutational effects with mean zero

$$V(\sigma^2) = \frac{\sigma^2(N)}{4N\mu + \frac{2}{3N} - \frac{1}{n}}$$  

(7a)

$$= \frac{\sigma^2(N)/\alpha^2}{1 + (\alpha^2N\mu/V)}$$  

(7b)

if $4N\mu \ll 1$ and $2\eta\mu \ll 1$.

Zeng and Cockerham (1991), using a different model of mutation with a limited range of allelic effects, obtained (7a) but with $+2/n$ instead of $-1/n$. For a neutral model without mutation, Bulmer (1980, p. 230) calculated the variance of the components of genetic variance that are due to random departures from Hardy-Weinberg equilibrium, $C_{TH}$, and linkage disequilibrium, $C_L$. Denoting the "true" variance, which would be observed in Hardy-Weinberg and linkage equilibrium for a given set of gene frequencies, by $V_T$ he showed that $\text{Var}(C_{TH}) = V_T^2/N$, and, in the absence of linkage, $\text{Var}(C_L) = 5V_T^2/3N_e$. Comparison with (7a) shows that these terms are small provided that $4\mu \ll 1$. Lynch and Hill (1986) apparently neglected variation due to Hardy-Weinberg disequilibrium and their term $2\sigma^2(N)/3N_e$, for variation due to departures from linkage equilibrium, differs from Bulmer by a factor 5/2. Avery and Hill (1977) obtained $4V_T^2/3N_e$ for that quantity. Our formula (A.27) for the variance of the genetic variance agrees, to first order, with (7b) if $4N\mu \ll 1$ and if the mutant distribution is normal.

For phenotypic characters under stabilizing selection, the variance of the genetic variance can be approximated by

$$V(\sigma^2) = \frac{\sigma^2(SH\alpha^2)}{1 + (\alpha^2N\mu/V)}$$  

(Barton 1989). In the limit of $V \to \infty$, this reduces to (7b).

Theoretical results about the distribution of the mean phenotype and the genetic variance are based on various simplifying assumptions. This is unavoidable because of the notorious difficulties encountered in the analysis of polygenic models. Therefore, we have performed comprehensive stochastic computer simulations to check these approximations.

METHODS AND RESULTS

The theoretical results about the distribution of the mean phenotype and the genetic variance are based on various simplifying assumptions. This is unavoidable because of the notorious difficulties encountered in the analysis of polygenic models. Therefore, we have performed comprehensive stochastic computer simulations to check these approximations.

The simulation model: This has been adapted from the one used in Burger et al. (1989) and Burger and Lynch (1994). It uses direct Monte-Carlo simulation, representing each individual and each gene. The genotypic value of the character is determined by $n$ additive loci with no dominance or epistasis. We chose $n = 50$ for all of our simulations. We simulate the continuum-of-alleles model of Crow and Kimura (1964) by drawing individual allelic effects from a continuous distribution, so the number of possible segregating alleles per locus is limited only by population size. The phenotypic value of an individual is obtained from the genotypic value by adding a random number drawn from a normal distribution with mean zero and variance $\sigma^2 = 1$. The generations are discrete, and the life cycle consists of three stages: (a) random sampling of breeding pairs from the surviving offspring of the preceding generation, (b) production of offspring, including mutation and recombination. (c) viability selection according to (1).

Each breeding pair produces exactly $2B$ offspring and, for all parameter values shown below, more than 90% of these survive viability selection. Random sampling of $N$ parents is performed without replacement and the sex-ratio is 1:1. Thus, the number of breeding adults is always $N$ and the mating system is dioecious and monogamous. The effective population size is $N_e = 4N/(V_1 + 2)$, where $V_1 = 2(1 - 1/B)(1 - (2B - 1)/(BN - 1))$ is the variance in family size. For further details see Burger et al. (1989) and Burger and Lynch (1994).
The distribution of the mean phenotype $\bar{z}$ and of the genetic variance $\sigma^2$ under mutation-selection-drift balance

<table>
<thead>
<tr>
<th>$N_e$</th>
<th>$V(\bar{z})$</th>
<th>$\kappa(\bar{z})$</th>
<th>$t_{\mu}(\bar{z})$</th>
<th>$\sigma^2$</th>
<th>$\kappa(\sigma^2)$</th>
<th>$V(\sigma^2)$</th>
<th>$s(\sigma^2)$</th>
<th>$\kappa(\sigma^2)$</th>
<th>$t_{\mu}(\sigma^2)$</th>
<th>$\delta$</th>
<th>$P_{\delta}$</th>
<th>$n_e$</th>
</tr>
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<tbody>
<tr>
<td>(i) $V_1 = 10$</td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>11</td>
<td>0.502</td>
<td>0.350</td>
<td>2.97</td>
<td>524</td>
<td>555</td>
<td>0.0191</td>
<td>0.0180</td>
<td>0.90</td>
<td>$10^{-3}$</td>
<td>0.93</td>
<td>$10^{-3}$</td>
<td>1.00</td>
</tr>
<tr>
<td>45</td>
<td>0.129</td>
<td>0.119</td>
<td>2.99</td>
<td>144</td>
<td>166</td>
<td>0.0694</td>
<td>0.0683</td>
<td>0.92</td>
<td>$10^{-2}$</td>
<td>0.93</td>
<td>$10^{-2}$</td>
<td>1.04</td>
</tr>
<tr>
<td>171</td>
<td>0.034</td>
<td>0.031</td>
<td>3.00</td>
<td>54</td>
<td>60</td>
<td>0.184</td>
<td>0.181</td>
<td>0.50</td>
<td>$10^{-2}$</td>
<td>0.54</td>
<td>$10^{-2}$</td>
<td>0.91</td>
</tr>
<tr>
<td>683</td>
<td>0.009</td>
<td>0.006</td>
<td>2.96</td>
<td>32</td>
<td>39</td>
<td>0.309</td>
<td>0.298</td>
<td>0.35</td>
<td>$10^{-2}$</td>
<td>0.38</td>
<td>$10^{-2}$</td>
<td>0.50</td>
</tr>
<tr>
<td>(ii) $V_2 = 100$</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>11</td>
<td>4.60</td>
<td>4.45</td>
<td>2.76</td>
<td>5025</td>
<td>4144</td>
<td>0.0199</td>
<td>0.0186</td>
<td>0.99</td>
<td>$10^{-3}$</td>
<td>0.93</td>
<td>$10^{-3}$</td>
<td>1.11</td>
</tr>
<tr>
<td>45</td>
<td>1.17</td>
<td>1.15</td>
<td>2.91</td>
<td>1215</td>
<td>1816</td>
<td>0.0823</td>
<td>0.0814</td>
<td>0.40</td>
<td>$10^{-2}$</td>
<td>0.41</td>
<td>$10^{-2}$</td>
<td>0.44</td>
</tr>
<tr>
<td>171</td>
<td>0.29</td>
<td>0.30</td>
<td>3.02</td>
<td>320</td>
<td>360</td>
<td>0.513</td>
<td>0.507</td>
<td>0.14</td>
<td>$10^{-1}$</td>
<td>0.15</td>
<td>$10^{-1}$</td>
<td>0.17</td>
</tr>
<tr>
<td>683</td>
<td>0.08</td>
<td>0.08</td>
<td>3.05</td>
<td>98</td>
<td>116</td>
<td>1.017</td>
<td>0.924</td>
<td>0.38</td>
<td>$10^{-1}$</td>
<td>0.42</td>
<td>$10^{-1}$</td>
<td>0.47</td>
</tr>
<tr>
<td>(iii) $V_3 = 1000$</td>
<td></td>
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<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>171</td>
<td>2.93</td>
<td>2.94</td>
<td>2.68</td>
<td>2967.0</td>
<td>294</td>
<td>0.337</td>
<td>0.336</td>
<td>0.17</td>
<td>$10^{-1}$</td>
<td>0.15</td>
<td>$10^{-1}$</td>
<td>0.21</td>
</tr>
<tr>
<td>Max s.e.</td>
<td>3.1%</td>
<td>2.5%</td>
<td>1.0%</td>
<td>5.0%</td>
<td>14%</td>
<td>5.7%</td>
<td>7.5%</td>
<td>0.1%</td>
<td>0.1%</td>
<td>0.2%</td>
<td>4.3%</td>
<td>5.7%</td>
</tr>
</tbody>
</table>

The symbols $V(\cdot)$, $s(\cdot)$, and $\kappa(\cdot)$ refer to the variance, the skewness, and the kurtosis, respectively. Also shown are the autocorrelation time for the mean phenotype, $t_{\mu}(\bar{z})$, the autocorrelation time of the genetic variance, $t_{\mu}(\sigma^2)$, the average kurtosis $k_e$ of genotypic values, the average number of polymorphic loci, $P_{2np}$, on a 2.5% level, and the effective number $n_e$ of segregating loci. Theoretical values are indicated by their equation number and compared to observed values from the simulation (see text). For all parameter combinations in this table, the mutational distribution is Gaussian with $\sigma^2 = 0.05$ and the mutation rate per haploid locus is $\mu = 0.0002$. This gives a genomic mutation rate of $2n\mu = 0.02$ and a mutational variance per generation of $V_{mu}/\sigma^2 = 10^{-2}$ as observed approximately in empirical studies (Lande 1975; Lynch 1988). There is free recombination between all loci. The bottom row contains the maximum standard error in percent of the mean of the data in the corresponding column.

In our simulations, we chose four different population sizes, i.e., $N = 8, 52, 128, 512$ breeding adults. For all these population sizes, we chose $B = 2$. This leads to effective population sizes of $N_e = 11, 43, 171, 683$, respectively. The observed $N_e$'s in our simulations differ from these by less than 1%, for large $N$ by less than 0.1%. (The effective population size has been calculated by storing for each offspring the (indices of the) parents it came from, and then calculating the variance of family size among the offspring that survived selection.) For each parameter combination, a certain number of replicate runs with stochastically independent initial populations were performed, each run over $10^7$ generations. Initial populations were obtained from an preceding initial phase of several hundreds or thousands of generations (depending on $N$) during which mutation-selection balance had been reached. The number of replicate runs per parameter combination was 100, 40, 25, and 10 for $N = 8, 32, 128, 512$, resp. This yielded very small standard errors (see below), much smaller than in earlier simulations.

The distribution of the mean phenotype and of the genetic variance: The present simulations show, confirming a trend suggested by the simulation results in Burger et al. (1989) and Burger (1989) that the SHC-approximation (4) tends to overestimate the true equilibrium variance, in particular when genetic drift prevails. One of the reasons is that (3b) overestimates the neutral variance $\sigma^2(N)$ for small $N_e$. Also the HG-approximation overestimates the true equilibrium variance in infinite populations (cf. Burger and Hofbauer 1994). Therefore, all theoretical results below are based on choosing (6) in conjunction with (3a) as analytical approximation for the genetic variance. For the variance of the mean phenotype $V(\bar{z})$, Equation 2a in conjunction with (6) is used. Results for the distribution of the mean phenotype and the genetic variance are summarized in Tables 1 and 2. Previous simulations (Burger et al. 1989) have shown, as suggested by formulas (3) and (4), that the average genetic variance depends in a linear way on the genomic mutation rate $2n\mu$ and not on $\mu$ and $n$ separately, if the loci are unlinked and $n$ is not too small (say $n \geq 10$). Equations 2, 7, and 8 suggest that this remains true for the variance of the mean phenotype and of the genetic variance but we have not checked this by simulation.

The statistics displayed in Table 1 show that the distribution of the mean phenotype is almost perfectly Gaussian (a Gaussian distribution has a kurtosis of $\kappa = m_4/\sigma^4 = 3.0$) and Lande’s (1976) formula for the variance of the mean phenotype (Equation 2) is very accurate. Only for weak selection, $i.e.$, small $N_e/V$, is the distribution of the mean slightly platykurtic. This Gaussian theory also works well for other mutation parameters and mutant distributions, and also for linked loci (see Table 2). In contrast to our results, Barton (1989) had found that the variance of the mean phenotype is lower than predicted by (2b) which is even smaller than (2a) and yields $V(\bar{z}) = 0.0292$ for the parameters in Table 2. In his model, however, there are exactly two alleles with effects $\pm \sigma$ at each locus. This may lead to multiple stable equilibria, and the mean phenotype does not necessarily coincide with the optimum (Barton 1986). For effectively infinite populations, the multi-
HOFBAUER 1994). Then the approximation (8) for
is inserted into (8). Nevertheless, the Gaussian approxi-
variance considerably, either if the loci are very tightly
Table of the corresponding property of the HGapproximation
highly leptokurtic. This overestimate is a consequence
also BARTON 1989) and is most likely the reason for the
different results.

Concerning the average genetic variance, Table 1
confirms the finding by BÜRGER et al. (1989) that the
SHC-approximation (Equations 4 or 6) predicts the
observed genetic variance accurately, although in all cases it
gives a slight overestimate. The variance of the genetic
variance is well predicted by BARTON'S (1989) formula
(our (8)), however, it always underestimates the observed
V(σ²i) by approximately 10%. Calculating (8) on the
basis of the observed average variance σ²i* leads to a
slightly greater underestimate. For the cases where
Nₑ/Ne < 2, the approximation (7a), due to LYNCH and
Hill (1986), is included. For small Ne and very weak
selection, it is even lower than BARTON'S prediction be-
cause then (7a) is smaller than (7b) which would
respond to (8). As observed in BÜRGER (1989), the SHC-
prediction tends to overestimate the observed genetic
variance considerably, either if the loci are very tightly
linked (so that effectively there is only one locus with a
high mutation rate), or if the variance of mutational
effects becomes small, or if the mutant distribution is
highly leptokurtic. This overestimate is a consequence of
the corresponding property of the HC-approximation in
the infinite population case (see BÜRGER and HOFBRAUER 1994). Then the approximation (8) for
V(σ²i) may become rather inaccurate even if, as in
Table 2, the observed genetic variance σ²i* instead of (6)
is inserted into (8). Nevertheless, the Gaussian approxi-
mation for the distribution of the mean phenotypes re-
 mains fairly accurate, unless the genomic mutation rate
2np becomes very low, as for μ = 0.00002.

The average genetic variance is always slightly larger than
the average genetic variance but for the parameter
combinations displayed in Table 1, this difference is al-
ways less than two percent (results not displayed). This
shows that Hardy-Weinberg and linkage disequilibria
can safely be ignored unless linkage is tight (cf. LANDE

The average genetic kurtosis kₑ, i.e., the average kurtos-
is of the distribution of breeding values, is almost ex-
actly three for the two larger population sizes of Table 1,
thus suggesting a nearly Gaussian distribution of breeding
values on average. It is larger than six, which is the kurtosis of an exponential distribution reflected
about zero, only if the genomic mutation rate 2np is very
small and mutant effects very large. Leptokurtic mutant
distributions or tight linkage tend to increase the aver-
age kurtosis slightly (see Table 2). No theory seems to
be available for the distribution of the genetic kurtosis.
We have measured the variance, skewness, and kurtosis
of this distribution only for a few parameter combina-
tions. For example, for the parameter values in line 3 of
(i) of Table 1 (Ne = 171), the coefficient of variation of
the genetic kurtosis is 0.16, and the kurtosis of the kur-
tosis is 16.4, whereas for the same parameter values but
with a reflected Γ-distribution of mutational effects (line
2 of (iii) in Table 2), the coefficient of variation is 0.46,
and the kurtosis is 114.8. As a rule of thumb, the coeffi-
cient of variation and the kurtosis of the distribution of
genetic kurtosis increase rapidly as the average genetic
variance increases above three. However, as shown by
Figures 1 and 2, most of the time the genetic kurtosis is
near three, even if, as in Figure 2, its mean is higher.
This shows that the distribution of breeding values is

<table>
<thead>
<tr>
<th>Table 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continuation of the distribution of the mean phenotype i and of the genetic variance ( \sigma_i^2 ) under mutation-selection-drift balance</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Distribution of the mean phenotype ( \bar{z} )</th>
<th>Distribution of the genetic variance ( \sigma_i^2 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( V(\bar{z}) )</td>
<td>( \sigma_i^2 )</td>
</tr>
<tr>
<td>(2a)</td>
<td>(6)</td>
</tr>
<tr>
<td>( \delta_i^2 )</td>
<td>( \delta_i^2 )</td>
</tr>
<tr>
<td>( \kappa(\delta_i^2) )</td>
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Since, for many of the parameter combinations here, (6) does not give accurate estimates for the equilibrium genetic variance, the values of (2a), (8), and (12) are based on the observed value \( \sigma_i^2 \). In all cases, \( V_i = 10 \) and \( N_e = 171 \). NMD indicates a normal mutant distribution with variance \( \sigma_a^2 \), \( \Gamma MD \) a reflected \( \Gamma \)-distribution with variance \( \alpha^2 \), \( \Lambda MD \) a reflected \( \Lambda \)-distribution with variance \( \lambda^2 \), and \( \Lambda MD \) a reflected \( \Lambda \)-distribution with variance \( \lambda^2 \). The constants \( \lambda \) and \( \beta \) can be chosen such that this distribution has a predefined variance and kurtosis. For \( \beta = 0.5 \), the kurtosis becomes 11.7 (See KOSCHELET and HILLY 1988; BÜRGER 1993).
nearly Gaussian most of the time with occasional excursions that may be dramatic if mutational effects are large.

**Autocorrelation of the mean phenotype and the genetic variance:** The simulations show high fluctuations of the mean, variance, etc., between generations and substantial autocorrelation. This has been noticed earlier by Keightley and Hill (1983) for directional selection and by Keightley and Hill (1988) and Burger et al. (1989) for stabilizing selection. Figures 1 and 2 display the extent of this phenomenon.

In the present investigation, we have measured these autocorrelations as follows. Denote by $X(t)$ the value of a random variable (e.g., the genetic variance) in generation $t$. Then the autocorrelation function is

$$
\varphi(\tau) = \frac{\text{Cov}[X(t), X(t+\tau)]}{\sqrt{\text{Var}[X(t)]\text{Var}[X(t+\tau)]}}.
$$

In our simulations, $t$ ran from 1 to $10^5$, whereas the autocorrelation function was calculated only for $\tau$ between 1 and $5 \times 10^3$, so that the values for the $\text{Cov}[X(t), X(t+\tau)]$ are based on at least $5 \times 10^4$ data points. We found that the function $\varphi(\tau)$ declines exponentially and then fluctuates around zero for large $\tau$. Using a least squares method, an exponential function $e^{-\tau/\lambda}$ was fitted to $\varphi(\tau)$ such that $\sum_{\tau=1}^{5 \times 10^3} (\varphi(\tau) - e^{-\tau/\lambda})^2$ is minimized. The reciprocal of the unique solution $\gamma$ is called the characteristic autocorrelation time and denoted by

$$
\lambda = \frac{1}{\gamma}.
$$

Different methods, like performing the least squares approximation with weights, yielded similar results. The data (Tables 1, 2) provide quantitative estimates for the importance of the autocorrelation of the mean phenotype and the genetic variance and confirm previous qualitative observations.

An approximation for the autocorrelation function of the mean phenotype can be obtained from Lande’s (1976) analysis of genetic drift and stabilizing selection. Under weak selection ($V_s \gg 1$) and the assumption of a constant genetic variance, he identified the corresponding stochastic process as an Ornstein-Uhlenbeck diffusion process for the mean phenotype with infinitesimal mean $\mu/(V_s + \sigma_g^2)$ and variance $\sigma_g^2/N_e$. This has autocorrelation function

$$
\varphi_s(\tau) = \exp\left(-\frac{\sigma_g^2}{V_s} \tau\right)
$$

(see Cox and Miller 1965, pp. 226–228), so that the
The autocorrelation time is

$$t_m(\varepsilon) = \frac{V_1}{\sigma_\varepsilon^2}. \quad (12)$$

This result does not depend explicitly on $N_e$ and gives a rather good approximation to the observed values as long as the coefficient of variation of $\sigma_\varepsilon^2$ is small \(c.f.\) Tables 1 and 2.

We have shown for a neutral model, assuming two segregating alleles per locus, i.e., $4N_e\mu \ll 1$, and global linkage equilibrium, that the autocorrelation function for the genetic variance is given by

$$\varphi(\tau) = \left[ \left( 1 - \frac{1}{2N_e} \right) (1 - 2\mu) \right]^\tau, \quad (13)$$

so that the autocorrelation time is

$$t_m(\sigma^2_\varepsilon) \approx \frac{2N_e}{1 + 8N_e\mu} \quad (14)$$

(see APPENDIX). Bulmer (1980, p. 230) showed that random departures from Hardy-Weinberg equilibrium cause uncorrelated fluctuations of the genetic variance and, in the absence of linkage, random departures from linkage disequilibrium lead to a correlation of $1/2$ between successive values of genetic variance. The first gives an autocorrelation time of zero whereas the latter gives a value of two, which is small compared to (14) \(c.f.\) also Avery and Hill 1977). For weak selection and $4N_e\mu \ll 1$, theory and data are in reasonably good agreement \(c.f.\) Table 1.

We have also measured the autocorrelation time of the genetic kurtosis. It tends to be slightly larger than that of the genetic variance \(c.f.\) Table 1.

The effective number of segregating factors: In the present model, the number of segregating loci is always smaller than the number of all loci potentially contributing to the trait. We calculated the effective number $n_e$ of loci according to Lande's (1981) formula

$$n_e = \pi \frac{E(\sigma^2_i)^2}{E(\sigma^2_i)}, \quad (15)$$

where $\sigma_i$ is the standard deviation of the distribution of allelic effects at one (haploid) locus, and the expectation is taken over all loci at male and female gametes. Data are displayed in Tables 1 and 2. If the number of effective loci is sufficiently high, in our simulations approximately $n_e \geq 15$, the distribution of breeding values is nearly Gaussian. In addition, we compared $n_e$ to the average polymorphism $P_{0.5%}$ on a 2.5% level. The criterion in our simulations for a locus to be polymorphic was that there were more than 5% heterozygotes at a locus which implies that the most frequent allele has a frequency of less than 97.5%.

Directional selection: It would be desirable to have a theory for the distribution of the mean phenotype and the genetic variance under directional selection. Such a theory is not currently available. Following Lynch and Lande (1993) and Bürger and Lynch (1994), we modeled directional selection by a "moving optimum," i.e.,

$$W_i = \exp \left\{ \frac{(z - k)^2}{2\omega^2} \right\}, \quad (16)$$

where $k$ is a positive constant describing the rate at which the optimum phenotype moves. For $k$ low enough \(c.f.\) a critical rate of environmental change, \(c.f.\) Lynch and Lande 1993; Bürger and Lynch 1994), populations practically persist for ever. For this kind of directional selection, the variances of the mean phenotype and of the genetic variance have a major influence on the dynamics of evolution and extinction (Bürger and Lynch 1994).

Extending these investigations, we performed several simulations for a slowly moving optimum, i.e., $k$ so small that the average mean fitness was still higher than 0.85, compared to 0.95 for pure stabilizing selection with $\omega^2 = 9$. Thus the number of breeding adults and the effective population size remained constant during the $10^6$ generations, each simulation run lasted. As shown by Lynch and Lande (1993), a steady-state distribution builds up that responds constantly to directional selection but the mean phenotype lags behind the optimum. For this "traveling wave," we found \(r.s.\) that even a very low $k$, i.e., $k \approx 4\%$ of a phenotypic standard deviation of an initial population, leads to a more than twofold increase of $\sigma^2_\varepsilon$ to a sixfold increase of $V(\sigma^2_\varepsilon)$, to a 3.5-fold increase of $V(\sigma^2_\varepsilon)$, and to a decrease of $t_m$ by a factor $1/6$, as compared to the initial equilibrium distribution (with $k = 0$). Further increasing $k$ leads to a further increase of $\sigma^2_\varepsilon$, $V(\sigma^2_\varepsilon)$, and $V(\zeta)$, and to a further decrease of $t_m$. The genetic variance $\sigma^2_\varepsilon$ however, levels off soon \(r.s.\) Bürger and Lynch 1994) and always remains below the neutral prediction (3).

DISCUSSION AND CONCLUSIONS

For many evolutionary biologists and geneticists, the only simple conclusion emerging from the last decade of theoretical investigations on the dynamics of quantitative-genetic variance and the dynamics of phenotypic evolution might be that the theories are often excessively complicated and frequently depend on a plethora of parameters that are difficult or impossible to measure. We would like to summarize below a few simple and useful results that have emerged from our simulations and other recent studies.

The majority of the theoretical studies dealt with infinite populations, i.e., they neglected random drift. It turned out that many results depend strongly on details of the assumptions. For example, under stabilizing selection the Gaussian theory of Kimura (1965) and Lande (1975), and the house-of-cards approximation of Turelli (1984) predict qualitatively different levels of genetic variation under mutation-selection balance. The
reason for the discrepancy between these approximations is that they are based on different assumptions about the mutation parameters, i.e., they are valid in different regions of the parameter space. Both approximations can be mathematically justified, and both approximations always overestimate the true equilibrium variance (Bürger and Hofbauer 1994). As is well known, Turelli (1984) and Barton and Turelli (1989) have argued that current empirical knowledge suggests parameter values in favor of the HC-approximation to be the more plausible ones.

We based many of our simulations on such parameters estimates [cf. also Lande (1975) and Lynch (1988)]. In addition, we investigated how the shape of the mutant distribution affects the equilibrium distribution of the trait because theoretical arguments (Keightley and Hill 1988) as well as recent empirical results (e.g., MacKay et al. 1992) indicate that mutant distributions may be highly leptokurtic. This means that most new mutational variance is due to few mutants with large effects whereas the majority of mutants has very little or no effect. The present simulations show, and for infinite populations this was mathematically proved by Bürger and Hofbauer (1994), that increasing the kurtosis of the mutant distribution leads to increasing deviations from the SHC-approximation (see Tables 1 and 2). Ironically, given that all other parameters are the same, Gaussian mutant distributions are more favourable to Turelli’s (1984) HC-approximation (or rare-alleles approximation) than mutant distributions dominated by rare alleles with large effects.

It is important to notice that genetic drift in finite populations reduces the discrepancy between the Gaussian and the HC-approximation, as encompassed in deterministic models. In finite populations, the genetic variance is always below that predicted by the neutral mutation-drift balance (Lynch and Hill 1986) and, in small populations, it is always very close to it. In fact, for small population size or weak selection, the SHC-prediction (6) and the stochastic version of the Gaussian approximation (cf. Latter 1970; Lynch and Lande 1993) deviate only slightly, because both are close to the neutral prediction. The present simulations confirm earlier results (Bürger et al. 1989) that the SHC-prediction is a very good approximation for a reasonably wide range of parameters. However, in most cases it is an overestimate. Our results also show that Barton’s (1989) theory for the variance of the genetic variance (8) provides good estimates as long as the SHC-approximation applies.

In deterministic multilocus models the situation is much more complicated. For example, Barton (1986) showed that many simultaneously stable equilibria, giving rise to different levels of genetic variance and to mean phenotypes deviating from the optimum, may exist. On the other hand, a deterministic multilocus model allowing for a continuum of possible alleles at each locus, yields much simpler results: the mean phenotype is always very close to the optimum (and agrees with the optimum if the mutant distributions are symmetric) and, for small mutation rates or large variance of mutational effects, the equilibrium genetic variance is closely approximated by the HC-prediction (cf. Bürger and Hofbauer 1994).

Although our simulations are based on the continuum-of-alleles model, the number of actually segregating alleles per locus typically is small. Depending on the parameters, for any given point in time, a considerable fraction of loci even is monomorphic (see Tables 1 and 2 for the average polymorphism and the effective number of factors), and at the other loci two or (sometimes) more alleles segregate. This is certainly more realistic than the above deterministic models, and also more realistic than stochastic models based on di-allelic loci with symmetric effects, as in Bulmer (1972), Keightley and Hill (1988) and Barton (1989). Nevertheless, in contrast to the deterministic models, all these stochastic models, including the simulations of Houle (1989) of a model with three alleles per locus and that of Foley (1992), yield qualitatively similar results in many respects, though they differ quantitatively to a moderate extent.

The present simulations show that in finite populations the mean phenotype indeed behaves extremely simply, at least on the average. Its distribution is almost perfectly Gaussian, as predicted by Lande’s (1976) phenotypic theory, and the variance of the mean phenotype agrees closely with the phenotypic prediction \(V_r/2N_e\) (2), unless the variance of mutational effects is very large and the (genomic) mutation rate very low. This, together with the fact that the genetic variance is almost always less than or equal to the SHC-approximation, suggests that multiple stable equilibria are of little relevance in populations of small and moderate effective size.

One potentially cumbersome problem investigated and quantified by the present simulations and theory is the high autocorrelation of the genetic variance and other quantities (like mean phenotype, mean fitness, genic variance, genetic kurtosis). This was already noticed previously (Keightley and Hill 1988; Bürger et al. 1989). For a neutral model with recurrent mutation, we derived the autocorrelation function of the genetic variance (13) and found that the autocorrelation time in this case is \(2N_e/(1 + 8 N_e \mu)\). Our simulations show that for weak selection the observed autocorrelation time is somewhat below the theoretically expected value under neutrality. The autocorrelation time decreases with increasing strength of stabilizing selection and with increasing average effect of mutations because selection for or against a new mutant accelerates its fixation (Kimura and Ohta 1969). Furthermore, the autocorrelation time decreases with increasing linkage, with increasing kurtosis of the mutant distribution and with increasing mutation rate (as expected from our theory).
These high autocorrelations pose serious problems for conclusions based on measurements of genetic variance because of the long-lasting influence of random excursions of the variance.

Under directional selection according to a moving optimum (16), the autocorrelation of the genetic variance becomes much smaller. On the other hand, the variance of the mean phenotype and of the genetic variance may be an order of magnitude larger than under stabilizing selection of the same strength. Also the genetic variance increases under this form of selection and approaches a steady-state value which is higher than the SHC-prediction but lower than the neutral prediction (cf. BÜRGER and LYNCH 1994). The latter has been shown to be the asymptotic variance under both truncation selection (HILL 1982) as well as under exponential directional selection (BÜRGER 1993). In the latter case, a simple Gaussian approximation yields correct predictions for the evolution of the mean phenotype and of the genetic variance. This is not the case for a moving optimum, where the Gaussian approximation gives an approximately correct theory only for the evolution of the mean phenotype but always underestimates the lag between the optimum and the mean (cf. LYNCH and LANDE 1993; BÜRGER and LYNCH 1994). Nevertheless, in all these cases the distribution of the breeding values is approximately Gaussian unless selection becomes very strong. No satisfying theory for the distribution of the mean phenotype or the genetic variance is available for a moving optimum. Finite populations of small or moderate size (say $N_e < 500$) also behave more reasonably in response to directional selection than predicted from deterministic theory (BARTON and TURELLI 1987). Neither under exponential directional selection nor under a moving optimum is a substantial increase of genetic variance observed unless previous stabilizing selection was extremely strong (cf. BÜRGER 1993; BÜRGER and LYNCH 1994). The reason is that for such population sizes the equilibrium variance under stabilizing selection, which is approximately given by the SHC-prediction, is not much lower than the neutral prediction which appears to pose an upper limit to the genetic variance under most forms of directional selection.

To summarize, there are a number of issues that are simplified by having small population size. Among these are that (i) multiple equilibria apparently are of little relevance as suggested by the accuracy of the Gaussian theory for the mean phenotype (compare also BARTON 1989); (ii) for small populations, the stochastic analogues of the Gaussian and the house-of-cards approximation for the genetic variance do not differ very much because both are close to the neutral prediction. The stochastic house-of-cards prediction yields a good approximation; (iii) if a finite population under mutation-selection-drift balance is exposed to directional selection, a large increase of genetic variance, as predicted by the deterministic theory (BARTON and TURELLI, 1987) but usually not observed in experiments, does not occur unless the population size is very large or stabilizing selection was very strong (BÜRGER 1993; BÜRGER and LYNCH 1994; cf. also KEIGHTLEY and HILL 1989).

The general conclusion that we would like to draw from the present results and those discussed above—though with appropriate caution—is that the maintenance of genetic variance and the dynamics of phenotypic evolution appear to be simpler in finite populations of small or moderate size, compared to the corresponding dynamics in infinite populations when many details of the genetics play an important role. However, due to the stochastic nature of mutation, recombination, and selection, any single population may considerably deviate from that expected behavior of the average population.

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LITERATURE CITED


Here we derive the autocorrelation function of the genetic variance in a population of size $N_t$ under the following simple model.

(i) First, we consider a single locus with two selectively neutral alleles and equal forward and backward mutation rates $u$. If the effects of the three genotypes are 0, $a$, and $2a$, and the frequency of the alleles are $x$ and $1-x$, the genetic variance is

$$V_e(x) = 2a^2 x(1-x).$$

It is well known that there exists a stationary distribution in this model which is approximately given by

$$f(x) = \frac{\Gamma(4b)}{\Gamma(2b)} x^{2b-1}(1-x)^{2b-1},$$

where $b = 2N_t u$ (cf. Crow and Kimura 1970, Chap. 8.5).

This stationary distribution allows for a relatively simple calculation of the terms needed for the autocorrelation function $\phi(t)$ in (9). Let the random variable $X(t)$ in (9) be given by $X(t) = V_e(x_t)$. Then, due to stationarity, the following hold:

$$E[V_e(x_t)] = 2a^2 \int_0^1 x(1-x)f(x) \, dx,$$

$$E[V_e(x_t)^2] = 4a^4 \int_0^1 x^2(1-x)^2f(x) \, dx,$$

$$E\left[\frac{V_e(x_t)}{V_e(x_{t+\tau})}\right] = 4a^4 \int_0^1 x(1-x)E[x_{t+\tau}(1-x_{t+\tau})] \, dx,$$

where $E[x_t] = \lim_{T \to \infty} (1/T) \int_0^T x(\delta t) \, dt$ (cf. Gardiner 1983, Sect. 3). The integrals in (A.3) and (A.4) are easily evaluated and one obtains

$$E[V_e(x_t)] = 2a^2 \frac{b}{1+4b},$$

$$\text{Var}[V_e(x_t)] = 2a^4 \frac{b}{(1+4b)^2(3+4b)}.$$
$x_{i+1} = x_i + \delta x_i$ and denote the expectation of a random change of $\delta x_i$ by $E_{\delta}$. Then a straightforward calculation shows that

$$E_{\delta}[\delta x_i] = u(1 - 2x_i)$$

(A8)

and

$$E_{\delta}[(\delta x_i)^2] = a_0 + a_1 x_i - a_2 x_i^2$$

(A9)

where

$$a_0 = \frac{u}{2N_e} + u^2 \left(1 - \frac{1}{2N_e}\right),$$

(A10)

$$a_1 = \frac{1}{2N_e} - (1 - 4u) - 4u^2 \left(1 - \frac{1}{2N_e}\right),$$

(A11)

Then, proceeding as in Crow and Kimura (1970, Chap. 7.4), we obtain the following recursions

$$\mu_1(t + 1) = u + (1 - 2u)\mu_1(t),$$

(A12)

$$\mu_2(t + 1) = a_0 + a_2 \mu_1(t) + C\mu_2(t),$$

(A13)

where

$$a_2 = \frac{1}{2N_e} + 2u \left(1 - \frac{1}{N_e}\right) - 4u^2 \left(1 - \frac{1}{2N_e}\right),$$

(A14)

$$C = \left(1 - \frac{1}{2N_e}\right)(1 - 2u)^2.$$  

(A15)

The solutions of the difference equations (A.12) and (A.13) are

$$\mu_1(t) = \frac{1}{2} + (\mu_1(0) - \frac{1}{2})(1 - 2u)^t,$$

(A16)

$$\mu_2(t) = \left(a_0 + \frac{a_2}{2}\right) \frac{C - 1}{C - 1} + \left(\mu_1(0) - \frac{a_2}{2}\right)(1 - 2u) \frac{C - (1 - 2u)}{C - (1 - 2u)} + \mu_2(0)C,$$

(A17)

respectively. With $\mu_1(0) = x$ and $\mu_2(0) = x^2$, this gives

$$\mu_1(t) - x = A_t + xB_t - x^2C,$$

(A18)

where

$$A_t = \frac{1}{4} \left(1 + \frac{1}{2N_e(C - 1)}\right)(1 - C)$$

(A19)

$$+ \frac{a_0}{2} (C - (1 - 2u)^t),$$

$$B_t = C - a_2 (C - (1 - 2u)^t),$$

(A20)

$$x_t = 2u + 4u^2(2N_e - 1)$$

$$1 + 2u(2N_e - 1)$$

(A21)

and C is as in (A.15).

Now we can evaluate (A.5) because

$$E(x_{i+1}(1 - x_{i+1})| x_i = x)$$

$$= \mu_1(\tau) - \mu_2(\tau) = A_t + xB_t - x^2C.$$  

(A22)

Integration of (A.5) using (A.22), and subsequent insertion of the resulting expression together with (A.6) and (A.7) into (9), yields the autocorrelation function of the genetic variance,

$$\varphi(\tau) = -2b(3 + 4b)$$

$$+ (1 + 4b)(3 + 4b)(2A_t + B_t)$$

(A23)

$$- 2(1 + b)(1 + 4b)C.$$

From (A.19) and (A.20) we have

$$2A_t + B_t = \frac{1}{2} + \frac{1}{4N_e(C - 1)}$$

$$+ C \left(\frac{1}{2} - \frac{1}{4N_e(C - 1)}\right)$$

and this is exact. However, formula (A.2) for the stationary distribution $f$ is only approximate because it is based on the diffusion approximation which assumes that $b = 2N_eu$ is of order one. Therefore, we have to use the approximation

$$2N_e(C - 1) = -(1 + 4b) + 4u(1 + b) - 4u^2$$

$$\approx -(1 + 4b),$$

(A24)

to obtain

$$\varphi(\tau) = C$$

with $C$ as in (A.15). This gives an autocorrelation time for the genetic variance of

$$t_w(V_e) = -\left[\ln \left(1 - \frac{1}{2N_e}\right) + 2\ln(1 - 2u)\right]^{-1}$$

(A25)

$$\approx \frac{2N_e}{1 + 8N_eu}.$$

The autocorrelation function of the mean genotype at a single diallelic locus is easily calculated to be

$$1 - 2u)^t, giving an autocorrelation time of approximately $1/(2u)$.

(ii) More generally, we assume $n$ loci in linkage equilibrium and assume that the mutational effects $a$ are distributed with mean zero, variance $\sigma^2$, and kurtosis $\kappa$, so that $E_a(a^4) = \kappa a^4$, where $E_a$ denotes the expectation with respect to the distribution of mutational effects $a$. For a normal distribution of mutational effects one has $\kappa = 3$. Assuming that $4N_eu \ll 1$, so that only two alleles are likely to be segregating at any one time, one obtains the expected value and the variance of the genetic variance
\( \sigma^2_i = \sum_{i=1}^n v_i^0 \) from (A.6) and (A.7), by taking expectations over mutational effects and summing over all loci \( i \):

\[
\sigma^2_i = E[\sigma^2_i] = 2na^2 \frac{b}{1 + 4b},
\]

(A26)

\[
\text{Var}[\sigma^2_i] = 2n\kappa a^4 \frac{b}{(1 + 4b)^2(3 + b)}.
\]

(A27)

Similarly, \( \text{Cov}[\sigma^2(t), \sigma^2(t + \tau)] = 2n\kappa \text{Cov}[V_j(t), V_j(t + \tau)] \), so that the autocorrelation function and the autocorrelation time are given by (A.24) and (A.25), respectively.

For \( n \) diallelic loci in the absence of selection, the variance of the mean phenotype is calculated to be

\[
\text{Var}[\bar{z}] = \frac{na^2}{1 + 8N_e u}.
\]

(A28)

This may be compared with Equation 2 from the phenotypic theory. The autocorrelation function of the mean phenotype in the \( n \)-locus case is, as with one locus, \( (1 - 2u)^t \). This leads to an autocorrelation time of

\[
t_{ac}(\bar{z}) = \frac{1}{2u}
\]

(A29)

which is again qualitatively different from (12).