Evolution of Genetic Variability and the Advantage of Sex and Recombination in Changing Environments

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ABSTRACT

The role of recombination and sexual reproduction in enhancing adaptation and population persistence in temporally varying environments is investigated on the basis of a quantitative-genetic multilocus model. Populations are finite, subject to density-dependent regulation with a finite growth rate, diploid, and either asexual or randomly mating and sexual with or without recombination. A quantitative trait is determined by a finite number of loci at which mutation generates genetic variability. The trait is under stabilizing selection with an optimum that either changes at a constant rate in one direction, exhibits periodic cycling, or fluctuates randomly. It is shown by Monte Carlo simulations that if the directional-selection component prevails, then freely recombining populations gain a substantial evolutionary advantage over nonrecombining and asexual populations that goes far beyond that recognized in previous studies. The reason is that in such populations, the genetic variance can increase substantially and thus enhance the rate of adaptation. In nonrecombining and asexual populations, no or much less increase of variance occurs. It is explored by simulation and mathematical analysis when, why, and by how much genetic variance increases in response to environmental change. In particular, it is elucidated how this change in genetic variance depends on the reproductive system, the population size, and the selective regime, and what the consequences for population persistence are.

SINCE most higher organisms reproduce sexually, it may be argued that sexual reproduction and recombination are selectively favored over asexual reproduction. This selective advantage must be large because it has to overcome the twofold cost of sex that arises from the production of "needless" males. A gene that suppresses meiosis is transmitted to its offspring with certainty instead of a probability of one half and, therefore, should spread rapidly. A number of models and theories have been proposed to explain the selective maintenance of sexual reproduction and recombination (*cf.* Williams 1975; Maynard Smith 1978; Michod and Levin 1988). This article is concerned with a class of quantitative-genetic models in which the advantage of sex is primarily due to its ability to unlink good genes from bad genotypes, which allows them to spread rapidly through the population, thereby enhancing adaptation in a changing environment.

The idea that sexual reproduction and recombination may be favored in changing environments has been revived relatively recently (Maynard Smith 1988; Crow 1992; Charlesworth 1993a,b; Kondrashov and Yampolsky 1996b; and references therein). It was noted long ago (Mather 1943) that genetic variability of a quantitative trait induces a genetic load if the trait is subject to stabilizing selection and the mean phenotype has approached the optimum. This genetic load is a consequence of the production of phenotypes that deviate from the optimum and, therefore, have lower fitness. By contrast, in a varying environment that exerts directional selection on a trait, genetic variance is essential because the response to selection will be proportional to the additive genetic variance in the population. Asexually reproducing populations, or sexually reproducing populations with suppressed recombination, are expected to have lower levels of genetic variation than corresponding sexual populations in which the trait is controlled by recombining loci, because linkage disequilibrium will hide additive genetic variance. Hence, in a stable environment asexual populations will have a lower genetic load than sexual populations, while sexuals may fare better in certain changing environments.

For various forms of environmental change, such as a directionally, periodically, or randomly changing optimum, Charlesworth (1993a,b) and Lande and Shannon (1996) investigated the conditions under which more genetic variance increases the mean fitness of a population. Basically, they showed that more genetic variance is beneficial in highly variable, but predictable, environments. Charlesworth (1993b) also investigated the conditions under which a modifier of recombination rates will spread through the population and discussed the evolutionary advantage of sex and recom-

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bination under such scenarios. These authors assumed a normal distribution of phenotypic values, that the genetic variance remains constant during evolution, and that only the mean phenotype responds to selection.

In a previous investigation of a quantitative-genetic model with a steadily moving optimum, Bürger and Lynch (1995) found that sexual populations may respond not only by shifting the mean phenotype, as predicted by classical theory, but also by an increase of additive genetic variance. The observed increase was low or negligible for very weak stabilizing selection or small effective population size, $\sim$200 or less, but reached a factor of two for population sizes of $N_e \approx 500$. This increase of variance had a positive effect on population persistence because it induced an accelerated response of the mean phenotype to the selective pressure.

More recently, Kondrashov and Yampolsky (1996a,b) performed computer simulations of a diallelic multilocus model for a quantitative trait under a balance between mutation and fluctuating or periodic stabilizing selection. They reported huge increases of genetic variability, both for amphimictic and apomictic populations, and determined conditions under which amphimixis has an evolutionary advantage over apomixis. The finding of Kondrashov and Yampolsky that genetic variance may increase by a factor of 10^3 in amphimictic populations and somewhat less in apomictic populations is in sharp contrast to the results of Bürger and Lynch (1995).

The purpose of this article is to investigate the evolutionary response of a population that has been under mutation-selection-drift balance to three kinds of environmental change: a directionally moving optimum, a periodically varying optimum, and a randomly fluctuating optimum. In particular, the evolutionary behavior of populations differing in their reproductive mode—sexual with recombination, sexual without recombination, and asexual—is studied. This is done by Monte Carlo simulations of a polygenic model in which each gene and each individual are represented and by mathematical analyses that use and extend work of Charlesworth (1993b), Lynch and Lande (1993), and Bürger and Lynch (1995, 1997). The numerical results are compared with analytical approximations.

One of the main findings is that sexual populations differ significantly from asexuals in their ability to evolve genetic variance toward higher levels, as is favorable in many changing environments. In particular, under sexual reproduction and with recombination, the genetic variance under directional selection can increase on a short time scale and confer a substantial additional evolutionary advantage to recombination, because it leads to an accelerated response of the mean phenotype and, therefore, to a substantially reduced genetic load. Asexually reproducing populations, however, show no or almost no increase of genetic variance at least for the range of genetic parameters that is supported by experimental evidence. Thus, the advantage of sexual reproduction and recombination in coping with sustained, predictable environmental change may be much larger than previously thought. It is also investigated if the advantage caused by an increase in genetic variance, as it occurs in recombining populations, can be achieved by other means such as production of more offspring or a higher population size.

Concerning the evolution of genetic variation, this study yields results that are qualitatively different from those of Kondrashov and Yampolsky (1996a). The reason for this difference is investigated and discussed. More generally, the genetic and demographic conditions are explored that lead to an increase of genetic variance in response to directional selection.

THE GENERAL MODEL

A finite population of diploid individuals that reproduces in discrete generations, either sexually with random mating and equivalent sexes or asexually, is considered. Fitness is determined by a single quantitative character under Gaussian stabilizing selection on viability, with the optimum phenotype θ_t exhibiting temporal change. The viability of an individual with phenotypic value P is assumed to be

$$W_{P,t} = \exp\left\{-\frac{(P-\theta_t)^2}{2\omega^2}\right\}, \qquad (1)$$

where ω^2 is inversely proportional to the strength of stabilizing selection and independent of the generation number t. Selection acts only through viability selection, and each individual produces B offspring. Initial populations are assumed to be in a stationary state with respect to stabilizing selection and genetic mechanisms when environmental change commences. Three kinds of environmental change are considered:

1. A phenotypic optimum that moves at a constant rate k per generation,
$$\theta_t = kt. \qquad (2)$$
2. A periodically fluctuating optimum,
$$\theta_t = A\sin(2\pi t/L), \qquad (3)$$
where A and L measure amplitude and period of the fluctuations, respectively.
3. An optimum fluctuating randomly about its expected position, according to white noise with variance V_θ and no autocorrelation.

Under each of these models, the population experiences a mixture of directional and stabilizing selection. Such models of selection were investigated previously by Maynard Smith (1988), Lynch *et al.* (1991), Charlesworth (1993a,b), Lynch and Lande (1993),

Bürger and Lynch (1995, 1997), Lande and Shannon (1996), and Kondrashov and Yampolsky (1996a,b).

The quantitative character under consideration is assumed to be determined by n mutationally equivalent loci that may be recombining or linked in the sexual case and are linked in the asexual case. 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 a genetic contribution and a normally distributed environmental effect with mean zero and variance $\sigma_E^2 = 1$. Therefore, the phenotypic mean equals the mean of the additive genetic values, $\overline{G}_t$, and the phenotypic variance is $\sigma_{P,t}^2 = \sigma_{G,t}^2 + \sigma_E^2$, where $\sigma_{G,t}^2$ designates the additive genetic variance in generation t. The parameter $V_s = \omega^2 + \sigma_E^2 = \omega^2 + 1$ is used to describe the strength of stabilizing selection on the breeding values. It may be noted that $V_s + \sigma_{G,t}^2 = \omega^2 + \sigma_{P,t}^2$.

Because this article is concerned with finite populations of effective size N_e, theoretical predictions are needed for the distribution of the mean phenotype. Let

$$s_t = \frac{\sigma_{G,t}^2}{\sigma_{G,t}^2 + V_s} \tag{4}$$

denote a measure for the strength of selection. Under the assumption of a Gaussian distribution of phenotypic values, the distribution of the mean phenotype $\overline{G}_{t+1}$ in generation $t + 1$, conditional on $\overline{G}_t$ and θ_t, is Gaussian. Its expectation is given by

$$E[\overline{G}_{t+1}|\overline{G}_t,\theta_t] = \overline{G}_t + s_t(\theta_t - \overline{G}_t) \tag{5}$$

and its variance by $\sigma_{G,t}^2/N_e$. From this, the following recursion equations for the expected mean and the expected variance of $\overline{G}$ can be derived:

$$E[\overline{G}_{t+1}] = E[\overline{G}_t] + s_t(E[\theta_t] + E[\overline{G}_t]), \tag{6a}$$

$$V[\overline{G}_{t+1}] = \frac{\sigma_{G,t}^2}{N_e} + (1 - s_t)^2 V[\overline{G}_t] \tag{6b}$$

(*cf.* Lande 1976). It follows that the mean viability of the population is

$$\overline{W}_t = \frac{\omega}{\upsilon_t} \exp[-\frac{1}{2}(\overline{G}_t - \theta_t)^2/\upsilon_t^2], \tag{7a}$$

where $\upsilon_t^2 = V_s + \sigma_{G,t}^2 + V[\overline{G}_t]$, and its (multiplicative) growth rate is

$$R_t = B\overline{W}_t \tag{7b}$$

(Latter 1970; Bürger and Lynch 1995). These formulas are very general and hold for any fitness function of the form (1) as long as phenotypic values are approximately Gaussian.

Under prolonged environmental change, mean fitness may become very low. Because it is assumed that individuals can produce only a finite number, B, of offspring, a constant population size cannot necessarily be maintained. Therefore, a simple kind of density-dependent population regulation is imposed, which is described in the next section.

The simulation model and part of the theory are based on an explicit genetic model that requires specifying the mechanism by which genetic variability is maintained. It is assumed that this mechanism is mutation. Following Crow and Kimura's (1964) continuum-of-alleles model, at each locus an effectively continuous distribution of possible effects for mutants is assumed. Thus, provided an allele with effect x gives rise to a mutation, the effect of the mutant is $x + \xi$, where ξ is drawn from a distribution with mean zero, variance α^2, and no skewness (for instance, a normal distribution). The mutation rate per haploid locus is denoted by μ, the genomic mutation rate by U, and the variance introduced by mutation per generation per zygote by $V_m = U\alpha^2$.

THE SIMULATION MODEL

The analytical results in this article as well as in previous articles on related topics (Lynch *et al.* 1991; Charlesworth 1993a,b; Lynch and Lande 1993; Bürger and Lynch 1995) are based on various simplifying assumptions. This is unavoidable because of the notorious difficulties encountered in the analysis of polygenic models. Therefore, comprehensive stochastic computer simulations were performed that take into account concrete genetics and demography of populations and can be used to check the theoretical results.

The simulation model has been adapted from the one used in Bürger *et al.* (1989) and Bürger and Lynch (1995). 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. In this investigation $n = 50$ was chosen. The continuum-of-alleles model of Crow Kimura (1964) is assumed by drawing individual allelic effects from a continuous distribution, hence the number of possible segregating alleles per locus is limited only by population size. Unless otherwise stated, a Gaussian distribution of mutational effects with mean zero and variance $\alpha^2 = 0.05$ is assumed and a (diploid) genomic mutation rate of $U = 0.02$ per individual and generation. This implies that the variance introduced by mutation per generation is $V_m = 0.001$. These values have been suggested as gross averages by reviews of empirical data (*cf.* Lande 1975; Turelli 1984; Lynch and Walsh 1998). 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 $\sigma_E^2 = 1$.

The generations are discrete, and the life cycle consists of three stages: (i) random sampling without replacement of a maximum of K reproducing adults from the surviving offspring of the preceding generation; (ii) production of offspring, including mutation and, possi-

bly, segregation and recombination; and (iii) viability selection according to (1).

The maximum number K of reproducing adults may be called the carrying capacity. The $N_t(\leq K)$ adults in generation t produce BN_t offspring, an expected R_tN_t of which will survive viability selection. In this way, demographic stochasticity is induced. In a sexually reproducing population, the sex ratio is 1:1 and $N/2$ breeding pairs are formed, each producing exactly $2B$ offspring, while in the asexual case each adult produces B offspring. If the actual number of surviving offspring is $>K$, then K individuals are chosen randomly to constitute the next generation of parents. Otherwise, all surviving offspring serve as parents for the next generation. With this type of density-dependent population regulation, the number of reproducing adults remains roughly constant at K unless mean fitness decreases such that $\overline{W}_t < 1/B$. If this occurs, the population cannot replace itself. The effective population size is $N_e = 4N/V_f + 2)$, where $V_f = 2(1 - 1/B)[1 - (2B - 1)/(BN - 1)]$ is the variance in family size. For further details see Bürger *et al.* (1989) and Bürger and Lynch (1995).

For each parameter combination, a certain number of replicate runs with stochastically independent initial populations were performed. Each run was 10^5 generations unless population extinction occurred previously. Initial populations were obtained from a preceding initial phase of several thousand generations (depending on K) during which mutation-selection balance had been reached. The number of replicate runs per parameter combination was between 3 (for populations >2000 individuals and if no extinction occurred during the first 10^5 generations) and 100 (if extinction occurred in <1000 generations). Statistics were averaged over all generations of replicate runs.

MUTATION-SELECTION-DRIFT BALANCE

Understanding the evolutionary response of sexual and asexual populations in variable environments requires, as we shall see, a quantitative understanding of the stationary distribution under a balance between stabilizing selection, mutation, and random genetic drift. Models for the balance between mutation and stabilizing selection have been studied intensively. For fairly comprehensive reviews and recent results, refer to Turrelli (1988), Bulmer (1989), Bürger and Lande (1994), and Bürger (1998). In the following, I summarize the relevant results and apply them to this context.

For a single haploid locus and an infinitely large population, Kimura (1965) showed that the equilibrium density is approximately Gaussian with variance $\hat{\sigma}^2(\mathrm{G}) = \sqrt{\mu V_s \alpha^2}$, provided the variance of mutational effects, α^2, is sufficiently small. A second-order approximation for the equilibrium variance was derived by Fleming (1979) under the assumption $\alpha^2/(\mu V_s) \ll 1$ (see below). Numerical simulations (Turelli 1984; Bürger 1998) showed that his approximation is very accurate if $\alpha^2 < 9\mu V_s$. In this case, the equilibrium distribution has a low kurtosis and deviates only slightly from a Gaussian. By contrast, if $\alpha^2 > 20\mu V_s$ then Turelli's (1984) house-of-cards (HC) approximation for the equilibrium variance, $\hat{\sigma}^2(\mathrm{HC}) = 2\mu V_s$, is very accurate. In this case, the equilibrium distribution differs markedly from Gaussian. It has a high kurtosis and most variance is contributed by rare alleles of large effect.

In the present analysis, sexually reproducing diploid populations are compared with diploid asexuals. Both are assumed to have the same number of loci, n, and the same mutational parameters. The genome of an asexual diploid individual with n loci and no recombination can be identified with a single haploid locus subject to a mutation rate of $\mu_a = U = 2n\mu$. Following Turelli (1984) and assuming that the parameter V_s, which measures the strength of stabilizing selection, ranges from 2 (extremely strong selection) to 100 (very weak selection), the relation $\alpha^2 < 9\mu_a V_s$ is satisfied if $\mu_a > 0.003$. With the empirically suggested average value $\mu_a = 0.02$, Fleming's prediction will be accurate for asexuals and may be written as

$$\hat{\sigma}_a^2(F) = \sqrt{V_m V_s}\left[1 - \frac{\sqrt{V_m}}{\sqrt{V_s}}\left(\frac{\eta + 3}{16U} - \frac{19}{16}\right)\right], \qquad (8)$$

where η denotes the kurtosis of the mutation distribution ($\eta = 0$ for a normal distribution).

For sexually reproducing populations without recombination, the genetics is equivalent to that of a single diploid locus, and the equilibrium variance will be twice the haploid value but with $\mu = U/2$, *i.e.*,

$$\hat{\sigma}_0^2(F) = \sqrt{2V_m V_s}\left[1 - \frac{\sqrt{V_m}}{\sqrt{2V_s}}\left(\frac{\eta + 3}{8U} - \frac{19}{16}\right)\right]. \qquad (9)$$

This is $\sim 1.4\hat{\sigma}_a^2(F)$. Analogous arguments, but for the Gaussian prediction, may be found in Lynch *et al.* (1991) and Charlesworth (1993b).

For freely recombining populations, the HC approximation applies to single loci, unless per-locus mutation rates are extremely high or stabilizing selection is extremely weak. If the n loci determining the trait are only loosely linked, then the approximation $\hat{\sigma}^2(\mathrm{HC}) = 4n\mu V_s = 2UV_s$ for the additive genetic variance is valid (Turelli 1984; Bürger and Hofbauer 1994; Turelli and Barton 1990). It was obtained previously by Latter (1960) and Bulmer (1972) for a diallelic multilocus model.

So far, infinite population size has been assumed. For a finite population of effective size N_e, Kimura's (1965) Gaussian approximation was extended to multiple loci by Latter (1970) and Lynch and Lande (1993). Applying the arguments of Lynch and Lande to Fleming's approximations (8) and (9), the following stochastic versions are obtained. For an asexual population of effective size N_e, the expected genetic variance at mutation-selection-drift balance, $\hat{\sigma}_a^2$, is approximately

$$\hat{\sigma}_a^2 \approx \hat{\sigma}_a^2(\mathrm{SF}) = -\frac{V_s}{4N_e} + \sqrt{\left(\frac{V_s}{4N_e}\right)^2 + \hat{\sigma}_a^4(F)}. \quad (10)$$

For a nonrecombining sexually reproducing population of size N_e, the expected genetic variance $\hat{\sigma}_0^2$ is approximately

$$\hat{\sigma}_0^2 \approx \hat{\sigma}_0^2(\mathrm{SF}) = -\frac{V_s}{4N_e} + \sqrt{\left(\frac{V_s}{4N_e}\right)^2 + \hat{\sigma}_0^4(F)}. \quad (11)$$

Extensive computer simulations show that (10) and (11) provide excellent approximations to the observed average genetic variance and that the phenotypic distribution is nearly Gaussian unless $N_e < 100$ (results not shown).

For sexually reproducing populations and free recombination, the approximate formula

$$\hat{\sigma}_{sex}^2 \approx \hat{\sigma}^2(\mathrm{SHC}) = \frac{2N_eV_m}{1 + (\alpha^2N_e/V_s)} \quad (12)$$

for the expected genetic variance was found independently and by different methods (Keightley and Hill 1988; Barton 1989; Bürger *et al.* 1989; Houle 1989). It is called the stochastic house-of-cards (SHC) approximation because, in the limit of infinite population size, it reduces to the multilocus HC approximation. In the limit of no selection, $V_s \to \infty$, (12) converges to the neutral formula $\hat{\sigma}^2(N) = 2N_eV_m$ of Lynch and Hill (1986). The validity of the SHC approximation (12) requires the same assumptions about mutation parameters as the HC approximation. Previous computer simulations have shown that (12) produces a good approximation to the average equilibrium variance for a wide range of parameters, unless loci are very tightly linked (Bürger 1989; Bürger *et al.* 1989; Bürger and Lande 1994). Moreover, although allele distributions at single loci are highly kurtotic, the phenotypic distribution is close to Gaussian (kurtosis near zero) if >10 loci determine the trait. This is a consequence of the central limit theorem.

From (7a), the expected mean fitness of a population at mutation-selection-drift balance is

$$\widehat{\overline{W}} = \omega/\upsilon, \quad (13)$$

where $\upsilon^2 = V_s(1 + 1/2N_e) + \hat{\sigma}_G^2$ and $\hat{\sigma}_G^2$ is the expected (additive) genetic variance at equilibrium. This produces a very accurate approximation to the mean fitness as calculated from computer simulations (results not shown).

Inspection of the formulas for the equilibrium genetic variance, (10), (11), and (12), shows that $\hat{\sigma}_{sex}^2 > \hat{\sigma}_0^2 > \hat{\sigma}_a^2$, provided all parameters are identical and $2UV_s > \alpha^2$. The ratio $\hat{\sigma}_{sex}^2/\hat{\sigma}_0^2$ is approximately proportional to $\sqrt{V_s}$, thus weaker stabilizing selection leads to a larger genetic variance in freely recombining populations relative to nonrecombining and asexual populations. Because of the load induced by phenotypic variance, the mean fitness of freely recombining populations is always less than that of corresponding nonrecombining populations, however, typically only by a few percent. Moreover, asexual populations approach their infinite-size expectation at population sizes of a few hundred individuals, while sexual populations of the same size have variances considerably lower than their infinite-size expectation. This effect is most pronounced with moderate or weak stabilizing selection. Therefore, for populations of effective sizes of up to several thousand individuals, the advantage of asexual *vs.* sexual reproduction in stable environments is lower than predicted from load arguments for infinitely large populations.

A DIRECTIONALLY MOVING OPTIMUM

The purpose of this section is to explore the consequences of recombination and the mode of reproduction (sexual *vs.* asexual) on mean persistence time, mean fitness, and adaptive capability of populations experiencing sustained directional environmental change. A critical role is played by the genetic variance and its evolutionary response to selection. The influence of important genetic and environmental parameters is also investigated.

Classical quantitative genetics predicts that a population experiencing directional selection responds by shifting its mean phenotype according to Equations 5 and 6. If this selection is caused by a changing optimal phenotype, then the mean phenotype lags behind the optimum. For a model in which the optimum moves at a constant rate k per generation, according to (1) and (2), a critical rate of environmental change k_c has been identified beyond which extinction is certain because the lag increases from generation to generation, thus decreasing the mean fitness of the population below $\overline{W} < 1/B$, the level at which the population starts to decline. With a smaller population size, genetic drift reduces the genetic variance, which leads to an even larger lag, to a further decrease of mean fitness, and to rapid extinction (Lynch and Lande 1993; Bürger and Lynch 1995, 1997).

If the rate of environmental change is sufficiently low, then the mean lags behind the optimum but, after several generations, evolves parallel to it, on average according to $E[\overline{G}_t] \approx kt - k/s$, where, as in (4), $s = \sigma_{move}^2/(\sigma_{move}^2 + V_s)$ and σ_{move}^2 is the asymptotic genetic variance. The variance of the mean, caused by random genetic drift, is $V[\overline{G}_t] \approx V_s/(2N_e)$ (Lynch *et al.* 1991; Lynch and Lande 1993). Hence, after a sufficiently long time, the mean phenotype lags behind the optimum by the expected amount k/s. Therefore, the expected mean fitness converges to

$$E[\overline{W}_{move}] \approx \frac{\omega}{\upsilon}\exp[-\frac{1}{2}k^2/(s^2\upsilon^2)], \quad (14)$$

where $\upsilon^2 = V_s(1 + 1/2N_e) + \sigma_{move}^2$.

The critical rate of environmental change k_c is defined as the value of k such that the population can just replace itself, *i.e.*, such that $BE[\overline{W}_{move}] = 1$. Unless population

size is very small or stabilizing selection extremely weak, k_c can be approximated by

$$k_c \approx \sigma^2_{move}\sqrt{2(\ln B)/V_s} \qquad (15)$$

(Lynch and Lande 1993; Bürger and Lynch 1995).

The formulas for the expected lag, k/s, the expected mean fitness (14), and for k_c are deceptively simple because the determinants of the genetic variance have not yet been elucidated. Actually, the genetic variance also evolves in response to environmental change and settles down to a stationary value, σ^2_{move}. This value depends on the width of the fitness function, the number of loci, the effective population size, the mutation parameters, and on the rate of environmental change k. It is higher than the equilibrium value under a resting optimum, unless population size is small (Bürger and Lynch 1995). This is not unexpected because (13) implies that a reduction in genetic variance leads to an increase of mean fitness under stabilizing selection, while (14) shows that an elevated σ^2_{move} leads to a higher mean fitness under a moving optimum, unless k is very small [$k^2 < \sigma^6_{move}/(2V_s^2)$; *cf.* Charlesworth 1993b]. For any given k, however, an extremely large increase of genetic variance may cause mean fitness to decrease, because of the stabilizing component of selection (*cf.* also Lande and Shannon 1996).

Figure 1 demonstrates the advantage that sex and recombination may confer to sexually reproducing populations in a directionally changing environment. As a function of the rate of environmental change, k, it compares the mean extinction time, the mean fitness, and the genetic variance for two sexually reproducing populations, one with and one without recombination, and for two asexual populations, which differ by the number of offspring produced. The data points are obtained from simulations, and the lines are from theory as explained below. For all data shown, the carrying capacity is $K = 2^{11} = 2048$. The number of offspring produced per adult is $B = 5$ for the two sexual and one asexual population, and $B = 50$ for the other asexual population. This value is used to show that for a large range of parameters, even a 10-fold advantage of asexual reproduction would not counterweigh the advantage of sex in this kind of changing environment.

Figure 1 (top) displays the mean time to extinction for the four types of populations. For the whole range of k values, a recombining sexual population persists indefinitely, *i.e.*, for $>10^5$ generations when simulations were stopped. Additional simulations (not displayed) show that for $k = 0.42$ this population still persists for $>10^5$ generations, while for $k = 0.48$ and $k = 0.72$, its mean extinction times are 24,000 and 17 generations, respectively. A nonrecombining segregating population can permanently withstand only a much lower rate of environmental change. It goes extinct within some 1000 generations if $k = 0.07$ and within <100 generations

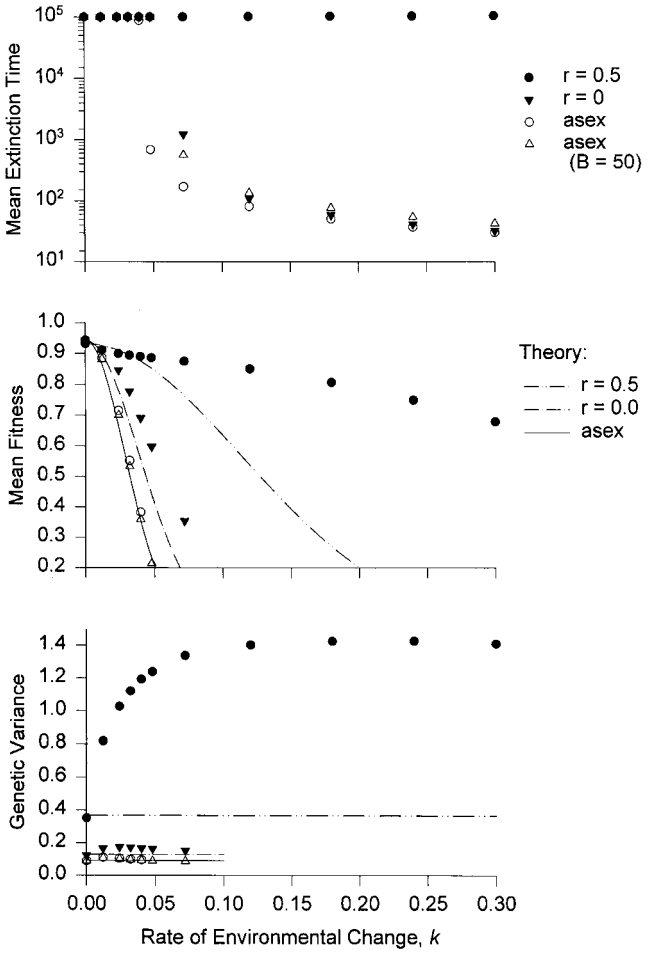

Figure 1.—Evolution and extinction of sexual and asexual populations under a directionally moving optimum. For all data shown, the genomic mutation rate is $U = 0.02$, the input of mutational variance is $V_m = 0.001$, and the mutation distribution is normal with mean zero and variance $\alpha^2 = 0.05$. The strength of stabilizing selection is $V_s = 10$, and the carrying capacity is $K = 2^{11} = 2048$. The top displays the mean time to extinction as a function of the rate of environmental change k, the middle displays the mean fitness, and the bottom the average (additive) genetic variance. Solid circles, a freely recombining sexual population ($n = 50$ loci); solid triangles, a nonrecombining sexual population; open circles, an asexual population with $B = 5$ as the two sexual populations; open triangles, an asexual population with $B = 50$. The solid lines in the middle and bottom are obtained from (14) and (10), respectively, the dash-dotted lines from (14) and (11), and the dash-double-dotted line from (14) and (12). Thus, mean fitness is calculated by assuming that the variance remains constant at its equilibrium value.

if $k \geq 0.12$. The situation is even worse for asexual populations with the same B. They go extinct within <1000 generations if $k \geq 0.05$. A 10 times larger B leads to a longer persistence time for a small range of k values, but does not help for large k. As soon as $k \geq 0.12$, which corresponds to 10% of a phenotypic standard deviation, asexual populations become extinct within <100 generations, while equivalent freely recombining populations

can easily persist through such a period of environmental change. For the recombining and nonrecombining sexual, and for the asexual populations with $B = 50$ and $B = 5$, approximate values for the critical rate of environmental change are $k_c = 0.69$, 0.085, 0.080, and 0.050, respectively. They agree reasonably well with the simulation results.

Figure 1 (middle) displays the observed mean fitness together with theoretical approximations obtained from (14) by substituting the following values for the genetic variance: for the two asexual populations, the stochastic Fleming approximation (10) is used for all k. This provides an accurate approximation for the observed mean fitness. For the two segregating populations and $k > 0$, no good analytical approximations for the variance σ^2_{move} are available. Substitution of the observed values of genetic variance into (14) yields precisely the observed mean fitness, thus supporting the Gaussian theory (deviations are on the order of 0.1%; results not shown). To demonstrate the extent to which the observed evolution of the genetic variance increases mean fitness, the mean fitness of equivalent sexual populations is plotted, but using the equilibrium genetic variance (dash-dotted lines). The results demonstrate that already in a slowly changing environment ($k \approx 0.05$, which corresponds to a rate of environmental change of ~5% of a phenotypic standard deviation per generation), the mean fitness of asexual populations is reduced by almost a factor of five compared with an otherwise equivalent, but recombining, population. Thus, competition between such populations will almost certainly lead to the loss of the asexual population.

Figure 1 (bottom) shows that the genetic variance increases substantially for a freely recombining population (up to approximately fourfold), while for an asexual diploid population the variance is nearly independent of k (the maximum increase being 20%), and for the segregating but nonrecombining population the maximum increase is ~40%. The variance of the asexual population with $B = 50$ is almost identical (smaller by ~3%) to that of the population with $B = 5$, because its effective size is smaller by ~10%. For $k = 0$, all observed variances are very close to their analytical approximations with relative errors <5%.

The amount by which the genetic variance increases relative to its equilibrium value depends on population size. Because of the stabilizing component of selection, the variance must remain bounded even in an infinite population. However, it is not clear how large a population has to be to approach this upper limit. For a sexual and an asexual population, Figure 2 displays the ratio of the stationary variance under a moving optimum to that under a resting optimum as a function of effective population size. The lines on the right-hand side are for $N_e = \infty$. Their values were determined by numerical iteration of the deterministic one-locus mutation-selection equation with a large number of alleles and extrapolation to 50 loci by assuming global linkage equilibrium (LE).

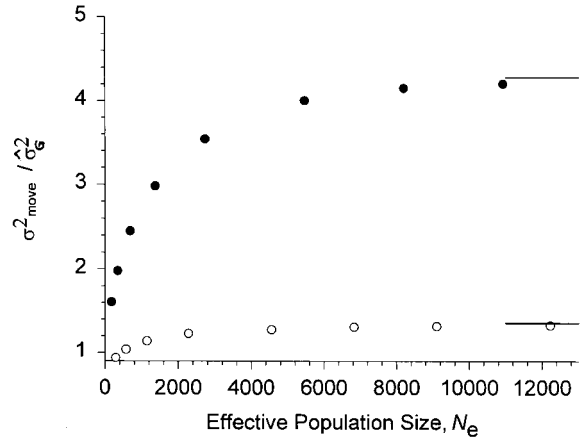

Figure 2.—Increase of genetic variance under a moving optimum as a function of population size. The mutational parameters are as in Figure 1. Solid symbols, a sexual, freely recombining population ($V_s = 10$, $k = 0.04$, and $B = 2$); open symbols, an asexual population ($V_s = 10$, $k = 0.012$, and $B = 5$). The lowest population size is $K = 2^7$ ($N_e \approx 170$). For populations $< N_e \approx 150$, rapid extinction occurs for the above values of k. The lines on the right-hand side are for $N_e = \infty$ and are calculated as described in the text.

Information about linkage disequilibrium was obtained by calculating the LE variance, *i.e.*, the variance computed from the gene frequencies by assuming Hardy-Weinberg proportions and LE [Bulmer (1980) calls this the genic variance]. In all cases, the LE variance was larger than the additive genetic variance, thus indicating repulsion linkage disequilibrium. For freely recombining populations and the data displayed in Figure 1, the average LE variance was at most 13% higher than the additive genetic variance, with a much smaller increase for a resting or very slowly moving optimum. For the nonrecombining sexual populations as well as the asexuals, the LE variance was higher by up to a factor of 17.5 (in both cases), and this occurred for a resting optimum. With a moving optimum, this factor decreased to values between 2 and 3 as k approached its maximum sustainable rate. In nonrecombining sexuals and asexuals, the amount of linkage disequilibrium increased rapidly as population size and strength of stabilizing selection increased (data not shown).

Additional simulations were performed for extremely weak ($V_s = 100$) and very strong ($V_s = 5$) stabilizing selection. Under weak selection, recombining populations responded with a much smaller increase of genetic variance ($\sigma^2_{move}/\hat{\sigma}^2_G = 1.26$ for $k = 0.04$ and $N_e = 2276$ compared with $\sigma^2_{move}/\hat{\sigma}^2_G = 3.54$ for $V_s = 10$), while under strong selection, the increase was even larger ($\sigma^2_{move}/\hat{\sigma}^2_G = 4.70$, all other parameters unchanged). By contrast, asexual populations had their variance reduced under weak stabilizing selection ($\sigma^2_{move}/\hat{\sigma}^2_G = 0.62$ for $k = 0.012$ and $N_e = 2276$), although theory predicts

that an increase would enhance mean fitness. Under very strong selection and all other parameters unchanged, the variance of asexual populations also increased ($\sigma^2_{move}/\hat{\sigma}^2_G = 1.49$). Because of their much greater genetic variance, the fitness advantage of sexual populations over asexuals even increased with weaker selection (data not shown). Given our knowledge about strength of stabilizing selection, values of V_s are more likely to be >10 instead of lower (Turelli 1984; Endler 1986).

To explore the role of the mutation rate, simulations were performed with smaller mutation rates, *i.e.*, with a genomic mutation rate of $U = 0.002$. With this mutation rate and all other parameters as in Figure 1, asexual populations responded to a moving optimum with an increase in variance of up to 80% (compared with 24% in the case $U = 0.02$), while freely recombining sexual populations experienced a maximum increase of variance by a factor of nine (compared with a factor of four if $U = 0.02$).

A PERIODICALLY CHANGING OPTIMUM

While the moving-optimum model may be applicable to sustained, long-term environmental changes, such as climatic trends, many species are subject to changes on a much shorter time scale. This is particularly true for species with short generation times. A frequently encountered scenario may be that of a periodically varying environment. We investigate population persistence, adaptive evolution, and the role of genetic variance in such an environment and compare recombining sexual populations with nonrecombining sexuals and diploid asexuals.

For the Gaussian phenotypic model, Charlesworth (1993b) and Lande and Shannon (1996) derived conditions under which an increase of genetic variance leads to an increase of mean fitness if the fitness optimum changes periodically. Charlesworth assumed discrete generations, while Lande and Shannon assumed continuous time. These conditions are more stringent than with a linearly moving optimum because, in particular with short-period fluctuations, tracking the optimum is hardly possible and a low genetic variance is favorable. As already mentioned above, there are cases where the genetic system prevents an increase of genetic variance, or even leads to a decrease, although a higher variance would increase mean fitness. Therefore, computer simulations seem to be inevitable to obtain reliable results for this complex model. In addition, we need an extension of the above-mentioned theory because, even after correcting for a misprint, Charlesworth's formula (30) for the expected log-mean fitness is accurate only for short periods L and extremely small σ^2_G/V_s. Otherwise, it underestimates the true value substantially.

The subsequent theory follows the basic approach of Charlesworth but derives an approximation that is accurate for a wide range of parameters. It assumes a Gaussian distribution of phenotypic values. The starting point is Equation 6a, which allows representation of the mean phenotype in generation t, $\bar{G}_t$, as a sum of sines, parallel to Equation 28 of Charlesworth (1993b). The resulting expression can be approximated by an integral that produces

$$\bar{G}_t = \frac{As_tL}{s_t^2L^2 + 4\pi^2}\,[2\pi e^{s_t(1-t)} - 2\pi\cos(2\pi(t-1)/L) - s_tL\sin(2\pi(t-1)/L)], \quad (16)$$

where s_t is the selection intensity (4). Defining the lag by $\Delta_t = \bar{G}_t - \theta_t$ and averaging over one period of the cycle (after a sufficiently long initial phase has elapsed), one arrives at the approximation for the expected squared lag

$$\begin{aligned} E[\Delta^2] &\approx \lim_{m\to\infty}\frac{1}{L}\int_{mL}^{mL+L}\Delta_t^2\,dt \\ &= \frac{A^2[s^2L^2(1-\cos(2\pi/L)) + 2sL\pi\sin(2\pi/L) + 2\pi^2]}{s^2L^2+4\pi^2} \\ &\approx \frac{2A^2\pi^2(1+s)^2}{s^2L^2+4\pi^2}, \end{aligned} \quad (17)$$

where s is the asymptotic value of s_t The latter approximation in (17) requires $(2\pi/L)^2 \ll 1$. Substitution of (17) into $\log \bar{W}_t$, as calculated from (7a), produces an accurate approximation for the expected log-mean fitness.

An approximation for the average mean fitness, $\bar{W}_{per}$, can be obtained from (17) and (7a) by a straightforward Taylor approximation. Defining

$$\lambda = \frac{1}{2}E[\Delta^2]/(V_s+\sigma^2_G) \approx \frac{A^2\pi^2}{V_s(s^2L^2+4\pi^2)},$$

we get

$$\bar{W}_{per} \approx \widehat{\bar{W}}\,\exp[-\lambda + \tfrac{1}{4}\lambda^2 - \tfrac{1}{6}\lambda^3], \quad (18)$$

where $\widehat{\bar{W}}$ is the equilibrium mean fitness as given by (13). For most purposes, the term involving λ^3 can be omitted in (18). The quantity λ agrees with the load component derived by Lande and Shannon (1996) for a continuous-time model for cyclical change.

From (18), sufficient (approximate) conditions can be derived ensuring that an increase in genetic variance causes an increase in mean fitness. These are

$$A^2 > V_s \quad \text{and} \quad 0 < \frac{9\pi^2}{L^2-9\pi^2} < \frac{\sigma^2_G}{V_s} < 0.15. \quad (19)$$

Figure 3 displays the mean fitness as function of the genetic variance for five different periods, L, and (top and bottom) for two different amplitudes. It shows that for small periods L, when the optimal phenotypes

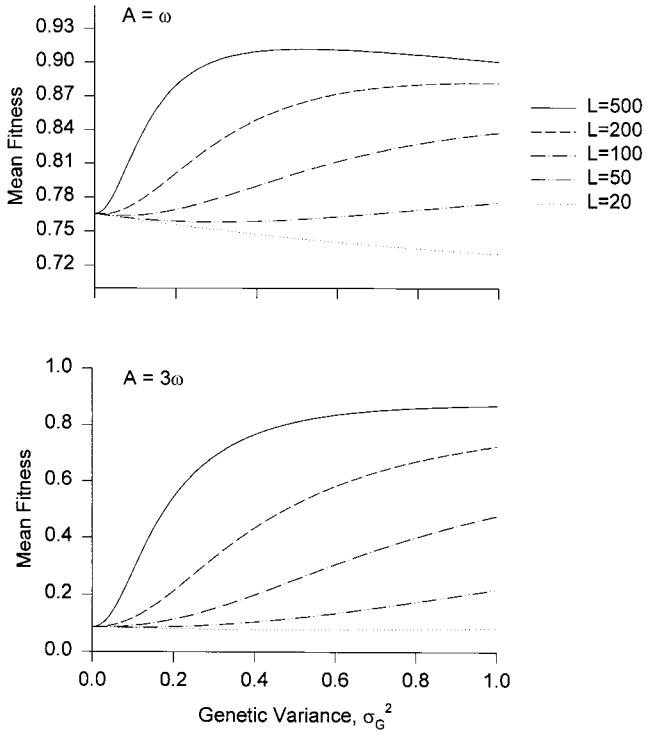

Figure 3.—Dependence of mean fitness on the genetic variance in a periodically changing environment. The population size is infinite and the strength of stabilizing selection is $V_s = 10$, *i.e.*, $\omega = 3$. The curves are calculated from (18). They are very close to exact values, as obtained from numerical integration of (7a) using (16).

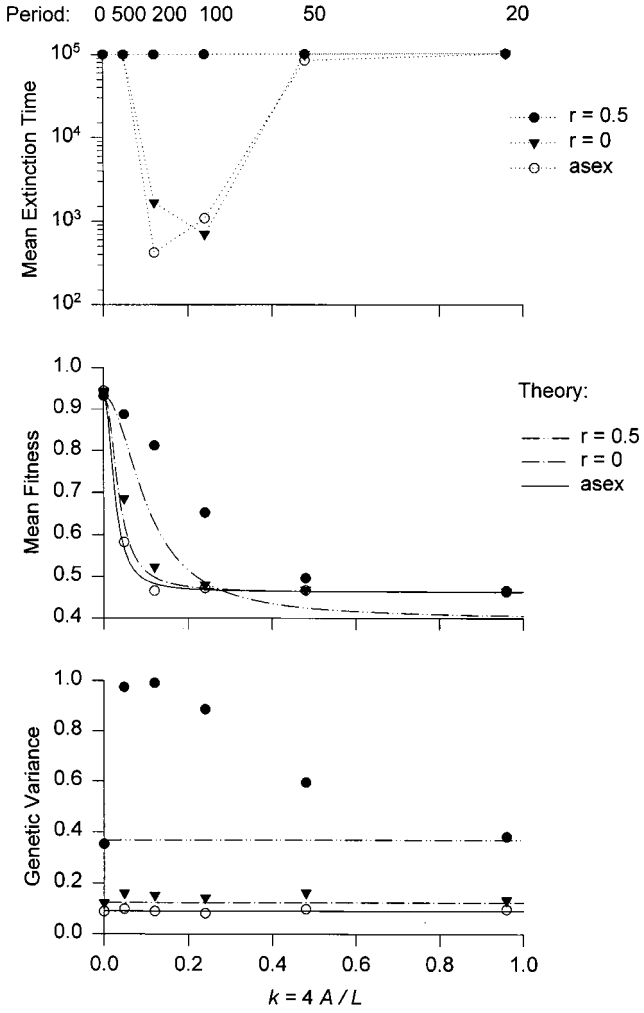

Figure 4.—Evolution and extinction of sexual and asexual populations in a periodically changing environment. The mutational parameters are as in Figure 1, the strength of stabilizing selection is $V_s = 10$ ($\omega = 3$), and the carrying capacity is $K = 2^{11} = 2048$. The amplitude (maximum displacement of the optimum) is $A = 2\omega = 6$. The top displays the mean time to extinction as function of $k = 4A/L$, which can be interpreted as the average rate of environmental change during one period of length L. The length of the period (in generations) is indicated on the top. The middle displays the mean fitness, and the bottom, the average (additive) genetic variance. Solid circles, a freely recombining sexual population ($n = 50$ loci); solid triangles, a nonrecombining sexual population; open circles, an asexual population. The solid lines in the middle and bottom are obtained from (18) and (10), respectively, the dashed lines from (18) and (11), and the dash-double-dotted line from (18) and (12). For all lines, mean fitness is calculated by assuming that the variance remains constant at its initial equilibrium value ($k = 0$).

change by major jumps, genetic variance is detrimental to mean fitness, while for medium or long periods, more genetic variance is beneficial unless the variance is extremely large. This is similar to Lande and Shannon's (1996) results but in partial contrast to Charlesworth (1993b), who underestimated the advantage of increased genetic variance. Obviously, in a periodically changing environment, an increase of genetic variance leads to an increase of mean fitness only under more restrictive conditions than in a directionally changing environment. This does not imply, however, that the genetic variance actually does increase under such conditions.

The detailed evolution of finite sexual and asexual populations in a periodically changing environment was investigated by Monte Carlo simulations as described above. No assumptions are imposed on the distribution of phenotypic (or genotypic) values. Some of the results are summarized in Figures 4 and 5. The quantities of interest are displayed as functions of $k = 4A/L$, which can be interpreted as the rate of change of the optimum averaged about one full cycle (during which the optimum moves $4A$ units, measured in multiples of σ_E^2). Dynamically, an infinite period L is equivalent to a resting optimum.

In Figure 4, the amplitude A of the periodic optimum is chosen to be 2ω, which implies that, at the most extreme position of the optimum (A units from the origin), the originally optimal phenotype (at position 0) has a fitness of 13.5%. The top shows that in this case, only the freely recombining population persists for all possible periods, while the nonrecombining sexual and the asexual die out for intermediate periods L.

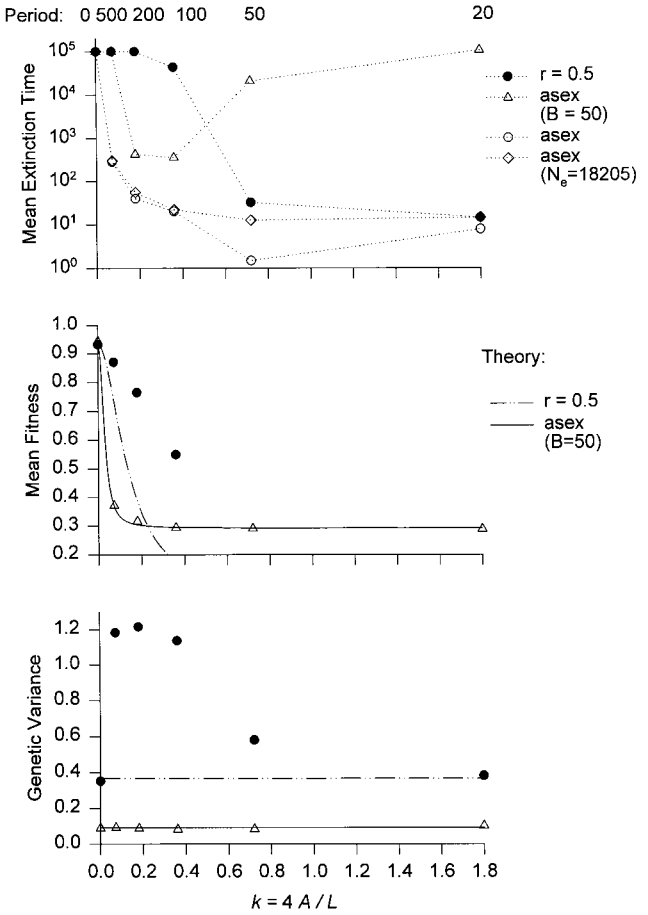

Figure 5.—Evolution and extinction of sexual and asexual populations in a periodically changing environment. This is similar to Figure 4, but with a larger amplitude of environmental fluctuations ($A = 3\omega = 9$). Solid circles, a freely recombining sexual population ($n = 50$ loci); open circles, an equivalent asexual; open triangles, an asexual with $B = 50$; open diamonds, an asexual population with $B = 5$ and $K = 2^{14}$ (effective size $N_e = 18{,}205$). The solid lines in the middle and bottom are obtained from (18) and (10), respectively, and the dash-double-dotted line from (18) and (12). For all lines, mean fitness is calculated by assuming that the variance remains constant at its initial equilibrium value ($k = 0$).

The middle shows that the freely recombining population has a much higher mean fitness than the two other populations if the length of the period is between 100 and 500. The lines in the middle represent the mean fitness that would be obtained if the variance did not increase under the periodic optimum. This yields good approximations for the nonrecombining and the asexual population, but not for the recombining population, because its genetic variance increases substantially unless the period, L, is very short ($L \leq 20$). This is shown in the bottom. Thus, for this kind of environmental change, recombination improves mean fitness and increases population persistence only if the period of the cycle is long, *i.e.*, evolution is slow. This advantage of recombination is due to the fact that it enables populations to increase in genetic variance. If the optimum changes rapidly, more genetic variance is not beneficial. In this case, it makes sense for a population to stay where it is and wait until the environmental optimum returns. Clearly, this requires that the population is able to maintain a minimum viable population size during the period of low fitness.

Figure 5 is similar to Figure 4, but with a higher amplitude of environmental fluctuations ($A = 3\omega$). Then the fitness of the originally optimal phenotype is only 1.1% if the environmental optimum is at its most extreme position, A. The figure compares a freely recombining sexual population with three different diploid asexuals: one with all other parameters equal, a second that produces 10 times as many offspring ($B = 50$), and a third whose carrying capacity is 8 times higher ($K = 2^{14}$, $N_e = 18{,}205$). Again, for long periods L, *i.e.*, slow environmental change, the sexual population has the highest mean extinction time and mean fitness. For a rapidly changing optimum, however, it is the asexual population that produces $B = 50$ offspring that has the longest persistence time, although it has a much lower genetic variance than the sexual population (bottom). The lines (middle) display the mean fitness as expected with a constant genetic variance. This figure clearly demonstrates that in a rapidly changing, periodic environment, it is not the flexibility of the genome and the resulting better adaptability that improves population persistence. Instead, other strategies, such as production of more offspring, may be more successful. For a slowly changing optimum, good adaptation is the best response to environmental change.

Further simulations (results not shown) have been performed with smaller population sizes and lower amplitudes ($A = \omega$). Although for lower population sizes the increase of variance in freely recombining populations is generally much lower, they still persist longer and have a higher mean fitness than otherwise equivalent but nonrecombining sexual or asexual populations. Again, the advantage of sex and recombination is most pronounced for large amplitudes A and long periods L.

If mutational effects are drawn from a reflected gamma distribution instead of a Gaussian (*cf.* Keightley and Hill 1988; Bürger and Lande 1994), qualitatively similar results are obtained. For large recombining populations ($K = 2^{11}$, $N_e = 2276$) and medium or long periods, L, a slightly higher increase of variance occurs in comparison with otherwise equivalent populations. This yields a slightly increased mean fitness. For small recombining populations ($K = 2^8$, $N_e = 285$), such a distribution also led to a higher average genetic variance and mean fitness, but to lower mean extinction times. Actually, mean extinction times have a much higher variance in this case compared with that of a Gaussian mutation distribution, because only a few populations are picking up rare mutants with large positive effects on fitness, while others go extinct rapidly. Thus, with a highly kurtotic mutation distribution the dynamics seem to be driven to a greater extent by single, large mutational events.

Finally, it is worth mentioning that if the observed genetic variance is substituted into Equation 18, a very accurate approximation of the observed mean fitness is obtained, thus supporting the mathematical theory.

A RANDOMLY FLUCTUATING OPTIMUM

The Gaussian theory of Charlesworth (1993b) predicts that for an optimum that fluctuates randomly according to white noise with mean zero, variance V_θ, and no autocorrelation, an increase of genetic variance leads to an increase of mean fitness only if $V_\theta > 2V_s$. A similar result was obtained by Slatkin and Lande (1976), while Lande and Shannon (1996) showed that in a continuous-time model more genetic variance always increases the load.

Monte Carlo simulations with the model described above have shown that in both asexual and sexual populations the genetic variance remains virtually constant if $V_\theta \leq V_s$, in accordance with similar results of Lande (1977) and Turelli (1988). Hence, fluctuating selection with a constant average optimum and no autocorrelation is not a mechanism to increase genetic variation (Turelli 1988).

In contradistinction to theory (Slatkin and Lande 1976; Charlesworth 1993b; Lande and Shannon 1996), for fluctuations with variance $V_\theta = V_s = 10$, sexual freely recombining and asexual populations of effective size $N_e = 1140$ and with $B = 5$ went extinct after an average of ~7900 and 6600 generations, respectively (100 replicated runs). Asexual populations with twice the mutation rate and intermediate variance had a mean extinction time of 6900 generations. The mean fitnesses averaged over the persistence time, however, were ranked inversely to the genetic variances, but the differences were not significant. More genetic variance is beneficial in this case, probably because under rare large excursions of the optimum more individuals survive in populations with a broader distribution. Hence, the theory based on the assumption of a Gaussian phenotypic distribution predicts an advantage for lower genetic variability and asexual reproduction when there is none. If, however, asexuals have twice the growth rate of sexuals, then their mean persistence time is approximately tripled and, thus, higher than that of the corresponding sexual population.

For smaller V_θ, asexual populations have a slightly higher mean fitness than sexuals because of their lower genetic variance (results not shown). Indeed, monomorphic populations have the highest fitness and extinction time under such a model (*cf.* Bürger and Lynch 1995).

DISCUSSION

This investigation departs from previous work on the advantage of sex and recombination in changing environments (cited in the Introduction) primarily by using an explicit genetic multilocus model and by assuming finite population size and population regulation. Genetic variation is assumed to be maintained by mutation-selection balance. In a constant environment that exerts stabilizing selection on the trait under consideration, sexually reproducing populations have more genetic variance than mutationally and demographically equivalent asexual populations. This leads to a slightly higher equilibrium load of sexual populations. If, however, adaptation becomes necessary due to environmental change, then sexual populations can respond faster and gain a substantial selective advantage over asexuals.

In accordance with results of Charlesworth (1993a,b), this study demonstrated an advantage of recombination and sexual reproduction over asexual reproduction under sustained directional change of the environment as well as under a slowly periodically changing environment with a large amplitude. This advantage was measured both in terms of mean persistence times as well as mean fitness. However, under the present genetic model, in which mutations at each locus are drawn from a continuous distribution and the number of loci is large but finite, sufficiently large sexually reproducing populations with high levels of recombination respond to environmental change of the above-mentioned kind by a substantial increase of (additive) genetic variance, while nonrecombining sexual or asexual populations do not, or do to a much lesser extent. This flexibility of the genome confers a significant additional advantage to recombination (and sexual reproduction) that goes far beyond the evolutionary advantage recognized by Charlesworth (1993b) on the basis of the Gaussian phenotypic model that assumes that genetic variance does not change under selection.

In a constant environment, in a randomly fluctuating environment with small variance and no autocorrelation, and in a rapidly changing periodic environment with short periods, asexually reproducing populations have a higher mean fitness and a longer persistence time than freely recombining sexual populations. This is in qualitative agreement with the Gaussian theory (Slatkin and Lande 1976; Charlesworth 1993b; Lande and Shannon 1996). In such "unpredictable" environments, a higher reproductive rate is a more successful strategy for survival than elevated levels of genetic variance. In contrast to theoretical predictions, however, more genetic variation and, hence, sexual reproduction can be beneficial in a randomly fluctuating environment if the standard deviation of the fluctuations exceeds the width of the fitness function. Nonrecombining sexual populations (so that there is only segregation between chromosomes) are always in between these two extreme cases but much closer to the asexuals. It is also of interest to note that in a randomly fluctuating environment an increase of environmental variance may be beneficial (Bull 1987).

Our results demonstrate that the presently developed Gaussian phenotypic theory for the evolution of the

mean phenotype and mean fitness is accurate for directional and periodic environmental change, provided the genetic variance is known. A satisfactory theory for the genetic variance, however, exists only for a constant environment (mutation-stabilizing selection-drift balance). In this case, accurate approximations for recombining and nonrecombining sexual populations, as well as for asexuals, have been developed. Because for a range of realistic parameters, the genetic variance of nonrecombining sexual and of asexual populations remains fairly constant, their evolution can be reasonably well predicted. For recombining sexual populations this is not true. Below, we discuss why this is so.

Kondrashov and Yampolsky (1996a,b) reported an increase of genetic variance in models of periodic environmental change, but found that genetic variance increased by up to three orders of magnitude. Below, we discuss the reason for this large increase and why such a large increase seems to be unrealistic.

Evolution of genetic variance: The simulation results reported in this article lead to the following questions: Why is the increase of genetic variance in response to directional environmental change much more pronounced in sexually reproducing populations than in asexuals? Why did Kondrashov and Yampolsky (1996a) detect increases of variance that are so much higher than the present ones? More generally, we may ask what are the prerequisites on the genetic system and the mode of selection that allow evolution of the genetic variance?

Explanations for the distinct evolutionary behavior of recombining populations can be given on two levels of sophistication: first, on an intuitive, qualitative level, and second, on a quantitative, formal one. If a new favorable mutant in a freely recombining population is not lost by random drift, it will eventually be recombined with genotypes of high fitness and can sweep rapidly through the population, thus leading to a temporary increase of genetic variation. With a constant supply of new mutations and directional selection (as caused by a gradually and predictably changing environment), this leads to an increased level of additive variation. The larger the population size, the larger the increase will be (see Figure 2). If a new favorable mutant occurs in a nonrecombining or asexual population, it will forever remain tied to its genome and all the disadvantageous mutants. This line may increase in frequency if its fitness is high enough, but the increase may be slow and weak. In particular, the line will never go to fixation unless the genomic mutation rate is extremely low.

A quantitative understanding of the evolution of genetic variance can be obtained from mutation-selection-balance theory and the equations for the rate of change of the mean and variance at a haploid locus (appendix). Let us first consider an effectively infinite population and a single haploid locus that, initially, is in mutation-stabilizing selection balance under a Gaussian fitness function. If the per-locus mutation rate is low ($20\mu V_s < \alpha^2$), then the equilibrium distribution is highly kurtotic, so that a large fraction of genetic variance is maintained by rare alleles with large effects and the equilibrium variance is closely approximated by the HC approximation. Under these conditions, the equilibrium genetic variance is much lower than the Gaussian or Fleming's (1979) approximation; *cf.* Bürger and Hofbauer (1994). It has already been shown that for various forms of directional selection such a population responds with a huge increase of variance, which is mainly caused by sweeps of rare alleles with large effects (Barton and Turelli 1987; Bürger 1993). Under the moving-optimum model, a population also responds with an increase in variance and, finally, the frequency distribution settles down to a traveling wave that lags behind the optimum by an amount $\Delta = (kV_s + \frac{1}{2}c_3)/c_2$ and has variance

$$c_2 = \sqrt{\mu V_s \alpha^2 + \Delta \cdot c_3 - \tfrac{1}{2}c_4}, \qquad (20)$$

where c_3 and c_4 are the third and fourth cumulant of the haploid allelic distribution (see appendix; for a normal distribution $c_3 = c_4 = 0$). Unless the optimum moves extremely slowly, directional selection induces a lag and a skewness such that $\Delta \cdot c_3 > \frac{1}{2}c_4$. (Iterations of the deterministic equations show that this is true if μ, V_s, and k are each varied over two orders of magnitude around the typical parameters considered in this article.) Thus, the asymptotic variance under the moving optimum is higher than the Gaussian prediction $\hat{\sigma}^2(G)$. This explains the increase of variance at a single locus with a low mutation rate. For a freely recombining population, little linkage disequilibrium builds up (as substantiated by the computer simulations) and the total genetic variance is simply the sum of the haploid single-locus variances.

These considerations not only explain the increase of variance observed for large recombining populations but also provide a rule of thumb for its magnitude. The factor by which the genetic variance increases is bounded below by $\hat{\sigma}^2(G)/\hat{\sigma}^2(HC)$, so that

$$\frac{\sigma^2_{\text{move}}}{\hat{\sigma}^2_G} \geq \frac{\alpha}{2\sqrt{\mu V_s}}, \qquad (21)$$

unless the rate of environmental change, k, is very close to zero.

In finite populations, genetic variance is eroded by random drift at a rate proportional to $1/N_e$ per generation. In particular, in small populations (N_e a few hundred or less), rare alleles of large effect occur much less frequently than in large populations and are more likely to be lost by drift. Because these are responsible for most increase of variance, this increase is smaller or absent in such populations (*cf.* Figure 2; but also Bürger 1993; Bürger and Lynch 1995). A lower bound can be obtained by dividing the stochastic version of the

Gaussian approximation through the SHC approximation, *i.e.*,

$$\frac{\sigma^2_{\text{move}}}{\hat{\sigma}^2_G} \geq \frac{\alpha}{2\sqrt{\mu V_s}} \frac{N_e + V_s/\alpha^2}{N_e + \tfrac{1}{2}\sqrt{V_s/(\mu\alpha^2)}}. \qquad (22)$$

The right-hand side approaches one as N_e becomes small. Comparison with the simulation results shows that (21) and (22) produce fairly good approximations as long as the HC approximation is much lower than the Gaussian, *i.e.*, if μV_s is sufficiently small relative to α^2.

The above approximations explain why a lower mutation rate and stronger stabilizing selection entail a higher increase of genetic variance: under such conditions the ratio of the Gaussian and the HC approximation is larger.

By contrast, if the per-locus mutation rate is high ($9\mu V_s > \alpha^2$), then in an infinite population the equilibrium distribution at a haploid locus is very close to normal and its variance is close to the Gaussian or Fleming's prediction. As discussed in the section on mutation-selection-drift balance, this situation applies to asexual and nonrecombining sexual populations. Hence, their increase of genetic variance is very small. Under weak stabilizing selection, the variance can even decrease (as mentioned above) because, then, the asymptotic distribution becomes negatively skewed and the lag very large.

The distribution of genotypic values remained close to Gaussian for all investigated cases, and this is in accordance with previous results (Bürger 1993; Turelli and Barton 1994; Bürger and Lynch 1995). More surprisingly, however, even at a haploid locus the asymptotic distribution is close to Gaussian for any choice of parameter values as long as the directional-selection component is stronger than mutation. Noticeable departures occur only if $k \ll \mu\alpha^2$ (results not shown). The reason can be seen from the cumulant equations in the appendix: without mutation, a Gaussian distribution remains Gaussian if selection occurs according to the moving optimum model and, apparently, is stable. Deviations, through increased kurtosis ($c_4 > 0$), are brought about only by mutation.

In a periodically changing environment, an increase in variance occurs that is quantitatively similar to that in a directionally changing environment, if the amplitude is large ($A > 2\omega$) and the period is long ($L \geq 100$), so that directional selection dominates (*cf.* Figures 1, 4, and 5). Otherwise, even in freely recombining populations no or very little increase occurs. This is in qualitative accordance with the Gaussian theory, which shows that under such environmental change a higher variance does not enhance mean fitness. However, usually the genetic variance does not evolve to the level at which, according to the Gaussian theory, mean fitness would be maximized. This, obviously, is a consequence of the constraints set up by the genetic system and the mode of reproduction.

Kondrashov and Yampolsky (1996a,b) investigated a quantitative trait in a periodically changing environment that is determined by equivalent diallelic loci with equal forward and back mutation rates [Barton's (1986) model]. They reported increases of variance in amphimictic populations of two and three orders of magnitude and somewhat lower increases in apomictic populations. On the basis of the above theory this can be explained by their parameter choice. Their typical parameter set consists of 36 loci with a mutation rate of 10^{-5}, yielding a gametic mutation rate of $<10^{-3}$, and very strong stabilizing selection (in our notation, $V_s/\alpha^2 \approx 1.5$). Thus, their equilibrium populations maintain almost no genetic variance under mutation-selection balance. For this parameter set, (21) predicts a >100-fold increase of genetic variance, which is in qualitative agreement with their simulation results. The problem, however, is that reviews of data suggest that gametic mutation rates are much larger (on the order of 10^{-2}) and stabilizing selection is often weaker (*cf.* Turelli 1984). The result, that in a periodically changing environment the advantage of sex and recombination is most pronounced for large amplitudes and intermediate or long periods, however, is in qualitative agreement with Kondrashov and Yampolsky (1996b).

The model employed in this article can be extended to include a modifier for the recombination rate. It would be interesting to investigate if this led to a higher selective advantage of the modifier than in Charlesworth's (1993b) investigation with a constant variance.

Other strategies for survival in a changing environment: On the basis of (15) for the maximum sustainable rate of environmental change, it can be estimated how much larger the intrinsic growth rate of a population must be to offset an increase of genetic variance. A simple calculation reveals that a rough condition is the following:

$$\frac{\ln B_2}{\ln B_1} > \left(\frac{\sigma_1^2}{\sigma_2^2}\right)^2.$$

Thus, the advantage of a doubling of the genetic variance can be achieved only by an approximate quadrupling of the *intrinsic* growth rate, ln *B*. Equivalently, a twofold cost of sex ($B_2 = 2B_1$) will be offset by an increase of variance by ~20%. It is also obvious from (14) and (15) that an increase of population size has only a negligible influence on the critical rate of change (as well as on the expected mean fitness and the expected mean extinction time), unless it leads to an increase of genetic variance. It may be of conservation biological concern that in recombining species, a noticeable increase of variance under directional selection will only occur if the effective population size is >200–300. In a periodically changing environment, a higher growth rate may substantially enhance population persistence.

Charlesworth (1993a) discussed empirical evi-

dence showing associations between artificial directional selection and correlated increase in recombination rate, which could be interpreted as possible support for models of the present kind. More recent experimental evidence (Souza *et al.* 1997) showed that in *Escherichia coli* sexual recombination yielded dramatic increases in genetic variation. This increase, however, did not lead to a higher rate of adaptation. A possible explanation for this is complex interactions between recombining genotypes and the environment, which resulted in corrupted fitness estimates. Turner and Chao (1998) found that sexual and asexual populations of the RNA virus $\phi 6$ showed a significant increase in fitness relative to the ancestor but sex did not lead to a higher rate of adaptation. Their explanation is that recombination led to biotic changes in the environment because intrahost competition caused the evolution of novel traits in the viruses.

It would be interesting to explore the ecological conditions under which closely related sexual and asexual populations live. The present theory suggests that asexuals should be found in either very stable environments or in environments that change in a rapid and unpredictable manner but such that on average the optimal phenotype remains stable.

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Note added in proof: After completing work on this project and after presenting the results at two conferences, I received the preceding article by Waxman and Peck (this volume) for review for Genetics.

The overlap concerns only the section a directionally moving optimum in this article. The models considered are closely related in spirit and come up with qualitatively similar though quantitatively different conclusions. They differ in several details, such as choice of discrete- *vs.* continuous-time modeling, finite *vs.* infinite population size, different sorts of population regulation, assumptions about linkage equilibrium, and their choice of the magnitudes of several parameters. Finally, they differ with respect to analytical methods and with respect to the level of providing explanations for the observed results.

LITERATURE CITED

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

Barton, N. H., 1989 Divergence of a polygenic system subject to stabilizing selection, mutation and drift. Genet. Res. **54:** 59–77.

Barton, N. H., and M. Turelli, 1987 Adaptive landscapes, genetic distance and the evolution of quantitative characters. Genet. Res. **49:** 157–173.

Bull, J. J., 1987 Evolution of phenotypic variance. Evolution **41:** 303–315.

Bulmer, M. G., 1972 The genetic variability of polygenic characters under optimising selection, mutation and drift. Genet. Res. **19:** 17–25.

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

Bulmer, M. G., 1989 Maintenance of genetic variability by mutation-selection balance: a child's guide through the jungle. Genome **31:** 761–767.

Bürger, R., 1989 Linkage and the maintenance of heritable variation by mutation-selection balance. Genetics **121:** 175–184.

Bürger, R., 1991 Moments, cumulants, and polygenic dynamics. J. Math. Biol. **30:** 199–213.

Bürger, R., 1993 Predictions for the dynamics of a polygenic character under directional selection. J. Theor. Biol. **162:** 487–513.

Bürger, R., 1998 Mathematical properties of mutation-selection models. Genetica **102/103:** 279–298.

Bürger, R., and J. Hofbauer, 1994 Mutation load and mutation-selection-balance in quantitative genetic traits. J. Math. Biol. **32:** 193–218.

Bürger, R., and R. Lande, 1994 On the distribution of the mean and variance of a quantitative trait under mutation-selection-drift balance. Genetics **138:** 901–912.

Bürger, R., and M. Lynch, 1995 Evolution and extinction in a changing environment: a quantitative-genetic analysis. Evolution **49:** 151–163.

Bürger, R., and M. Lynch, 1997 Adaptation and extinction in changing environments. pp. 209–239 in *Environmental Stress, Adaptation and Evolution*, edited by R. Bijlsma and V. Loeschcke. Birkhäuser, Basel.

Bürger, R., G. P. Wagner and F. Stettinger, 1989 How much heritable variation can be maintained in finite populations by mutation-selection balance? Evolution **43:** 1748–1766.

Charlesworth, B., 1993a The evolution of sex and recombination in a varying environment. J. Hered. **84:** 345–350.

Charlesworth, B., 1993b Directional selection and the evolution of sex and recombination. Genet. Res. **61:** 205–224.

Crow, J. F., 1992 An advantage of sexual reproduction in a rapidly changing environment. J. Hered. **83:** 169–173.

Crow, J. F., and M. Kimura, 1964 The theory of genetic loads, pp. 495–505 in *Proceedings of the XI International Congress of Genetics*, edited by S. J. Geerts. Pergamon, Oxford.

Endler, J. A., 1986 *Natural Selection in the Wild*. University Press, Princeton, NJ.

Fleming, W. H., 1979 Equilibrium distributions of continuous polygenic traits. SIAM J. Appl. Math. **36:** 148–168.

Houle, D., 1989 The maintenance of polygenic variation in finite populations. Evolution **43:** 1767–1780.

Keightley, P. D., and W. G. Hill, 1988 Quantitative genetic variation maintained by mutation-stabilizing selection balance in finite populations. Genet. Res. **52:** 33–43.

Kimura, M., 1965 A stochastic model concerning the maintenance of genetic variability in quantitative characters. Proc. Natl. Acad. Sci. USA **54:** 731–736.

Kondrashov, A. S., and L. Yu. Yampolsky, 1996a High genetic variability under the balance between symmetric mutation and fluctuating stabilizing selection. Genet. Res. **68:** 157–164.

Kondrashov, A. S., and L. Yu. Yampolsky, 1996b Evolution of amphimixis and recombination under fluctuating selection in one and many traits. Genet. Res. **68:** 165–173.

Lande, R., 1975 The maintenance of genetic variation by mutation in a polygenic character with linked loci. Genet. Res. **26:** 221–235.

Lande, R., 1976 Natural selection and random genetic drift in phenotypic evolution. Evolution **30:** 314–334.

Lande, R., 1977 The influence of the mating system on the maintenance of genetic variability in polygenic character. Genetics **86:** 485–498.

Lande, R., and S. Shannon, 1996 The role of genetic variation in adaptation and population persistence in a changing environment. Evolution **50:** 434–437.

Latter, B. D. H., 1960 Natural selection for an intermediate optimum. Aust. J. Biol. Sci. **13:** 30–35.

Latter, B. D. H., 1970 Selection in finite populations with multiple alleles. II. Centripetal selection, mutation, and isoallelic variation. Genetics **66:** 165–186.

Lynch, M., and W. G. Hill, 1986 Phenotypic evolution by neutral mutation. Evolution **40:** 915–935.

Lynch, M., and R. Lande, 1993 Evolution and extinction in response to environmental change, pp. 234–250 in *Biotic Interactions and Global Change*, edited by P. M. Kareiva, J. G. Kingsolver and R. B. Huey. Sinauer, Sunderland, MA.

Lynch, M., and J. B. Walsh, 1998 *Genetics and Analysis of Quantitative Traits*. Sinauer, Sunderland, MA.

Lynch, M., W. Gabriel and A. M. Wood, 1991 Adaptive and demographic responses of plankton populations to environmental change. Limnol. Oceanogr. **36:** 1301–1312.

Mather, K., 1943 Polygenic inheritance and natural selection. Biol. Rev. **18:** 32–64.
Maynard Smith, J., 1978 *The Evolution of Sex*. Cambridge University Press, Cambridge, United Kingdom.
Maynard Smith, J., 1988 Selection for recombination in a polygenic model—the mechanism. Genet. Res. **51:** 59–63.
Michod, M., and B. R. Levin 1988. *The Evolution of Sex*. Sinauer, Sunderland, MA.
Slatkin, M., and R. Lande, 1976 Niche width in a fluctuating environment-density independent model. Am. Nat. **110:** 31–55.
Souza, V., P. E. Turner and R. E. Lenski, 1997 Long-term experimental evolution in *Escherichia coli*. V. Effects of recombination with immigrant genotypes on the rate of bacterial evolution. J. Evol. Biol. **10:** 743–769.
Turelli, M., 1984 Heritable genetic variation via mutation-selection balance: Lerch's zeta meets the abdominal bristle. Theor. Popul. Biol. **25:** 138–193.
Turelli, M., 1988 Population genetic models for polygenic variation and evolution, pp. 601–618 in *Proceedings of the Second International Conference on Quantitative Genetics*, edited by B. S. Weir, E. J. Eisen, M. M. Goodman and G. Namkoong. Sinauer, Sunderland, MA.
Turelli, M., and N. H. Barton, 1990 Dynamics of polygenic characters under selection. Theor. Popul. Biol. **38:** 1–57.
Turelli, M., and N. H. Barton, 1994 Genetic and statistical analyses of strong selection on polygenic traits: what, me normal? Genetics **138:** 913–941.
Turner, P. E., and L. Chao, 1998 Sex and the evolution of intrahost competition in RNA virus ϕ6. Genetics **150:** 523–532.
Williams, G. C., 1975 *Sex and Evolution*. University Press, Princeton, NJ.

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APPENDIX

In Bürger (1991), equations were derived for the change of cumulants of the frequency distribution at a haploid locus under mutation and selection. Cumulants are related to moments but have properties that make them a useful tool in quantitative genetics (Bürger 1993; Turelli and Barton 1994). The first cumulant, denoted by c_1, is equal to the mean; the second, c_2, is the variance; the third, c_3, is the third central moment; and the fourth, c_4, is equal to the fourth central moment minus three times the squared variance. For a normal distribution all cumulants of order three and higher vanish. Assume that selection is sufficiently weak, so that the fitness function acting on genotypic values [which has the same form as (1) but with $V_s = \omega^2 + 1$ instead of ω^2] can be approximated by the quadratic function $m(G) = -(G - \theta_t)^2/(2V_s)$, where $\theta_t = kt$. If n equivalent diploid loci contribute to the trait value, G, and are in linkage equilibrium, then each haploid locus experiences the same fitness function but with $\theta_t = k_1 t = kt/(2n)$. The average lag at a single haploid locus is $\Delta(t) = kt/(2n) - c_1(t)$. Applying the cumulant equations in Bürger (1991) to this case, one obtains for the between-generation change of the lag and the cumulants of order two and three

$$\Delta' - \Delta \approx k_1 - \frac{1}{V_s}\Delta \cdot c_2 + \frac{1}{2V_s}c_3$$

$$c'_2 - c_2 \approx \frac{1}{V_s}\Delta \cdot c_3 - \frac{1}{2V_s}(c_4 + 2c_2^2) + \mu\alpha^2$$

$$c'_3 - c_3 \approx \frac{1}{V_s}\Delta \cdot c_4 - \frac{1}{2V_s}(c_5 + 6c_2c_3),$$

where α^2 is the variance of the mutation distribution. Formulas for higher-order cumulants can be given explicitly, but will not be used. The above recursion relations are exact in the limit of weak selection.

It follows that a traveling-wave solution exists ($\Delta' = \Delta$, $c'_i = c_i$), which lags behind the optimum by the amount

$$(k_1V_s + \frac{1}{2}c_3)/c_2$$

and has the stationary variance

$$c_2 = \sqrt{\mu V_s\alpha^2 + \Delta \cdot c_3 - \tfrac{1}{2}c_4}.$$

Note that if this distribution is normal (or very close to normal), then the lag is k_1V_s/c_2, in agreement with the expression k/s found in a directionally moving optimum.