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Michael Lynch; Hong-Wen Deng

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GENETIC SLIPPAGE IN RESPONSE TO SEX

MICHAEL LYNCH* AND HONG-WEN DENG

Department of Biology, University of Oregon, Eugene, Oregon 97403

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Abstract.—It is widely held that sexual reproduction enhances the potential for evolution by expanding the range of variation on which selection can act. However, when nonadditive gene action contributes to the expression of traits under selection, sexual reproduction can also result in slippage of the mean genotypic value in the direction contrary to selection. We show how the magnitude of genetic slippage depends on the extent to which segregation and recombination create maladapted genotypes. We also show how random mating can induce a change in the expressed genetic variance for a quantitative trait by eliminating Hardy-Weinberg disequilibria and reducing gametic-phase disequilibria. Depending on whether genes of like effects are in repulsion or coupling disequilibrium, this change will be positive or negative. Thus, depending on the mode of gene action and the form of the selection function, sexual reproduction can either enhance or impede the short-term response of quantitative characters to selection. Although this issue is relevant to all sexual populations, it is most easily investigated in species that infrequently engage in sex, since prolonged phases of clonal propagation can greatly exaggerate genetic disequilibria. We describe a population of the cyclical parthenogen *Daphnia pulex* in which sexual reproduction induced average changes in the means of life-history characters equivalent to approximately one-tenth of a phenotypic standard deviation. Contrary to the usual expectation, sex also caused a significant reduction in the expressed genetic variance for several traits in this population. A large fraction of the genetic variance in *Daphnia* appears to be due to dominance, and in the study population, clonal selection appears to cause a buildup of coupling disequilibrium between genes and gene combinations of like effects.

Species that reproduce both sexually and asexually provide several advantages for investigating the genetic architecture of quantitative characters. First, through clonal propagation, it is possible to estimate the total expressed genetic variance for any quantitative trait by partitioning the phenotypic variance into its within- and between-clone components. Under a suitable experimental design, the former contains all of the environmental variance for the trait, and the latter, all of the genetic variance. Second, the change in the genetic variance between a parental generation and that of its sexually produced progeny provides information on the amount of quantitative variation that was hidden (or exaggerated) in the parental generation by Hardy-Weinberg and gametic-phase disequilibria (Lynch and Gabriel 1983; Lynch 1984). Third, something close to the expressed additive genetic variance can be estimated from the covariance between parents and their sexually produced progeny. By combining these three types of analysis, insight can be gained on the extent to which genetic disequilibria and nonadditive sources of

* E-mail: mlynch@oregon.uoregon.edu.

variation (dominance and epistasis) influence patterns of quantitative-genetic variation.

During a prolonged phase of clonal propagation, directional and/or stabilizing selection can erode efficiently the expressed genetic variance of selected traits down to the level expected under selection-mutation balance in an obligate parthenogen (Lynch and Gabriel 1983). However, this need not imply that clonal populations will be depauperate with respect to genetic variation. For characters with a polygenic basis, the same phenotypic expression can be attained with a variety of underlying genotypes. For example, in the absence of epistasis, a phenotypic state of 0 can be obtained with genotypic values at two loci of +1 and -1, +2 and -2, and so on. Under stabilizing selection, such repulsion disequilibrium within and between loci can continue to accumulate in a clonal population as mutation introduces new alleles, and in the absence of segregation and recombination, it will not be revealed at the phenotypic level. However, for a polygenic character with a purely additive genetic basis, a single bout of random mating is sufficient to convert 50%–75% of the hidden genetic variance into expressed genetic variance, which is then exposed to selection in the next phase of clonal reproduction. Thus, cycles of genetic variance are expected in populations engaging in periodic sex, with the amplitude of the cycle increasing with decreasing frequency of sex (Lynch and Gabriel 1983).

Some qualitative support for this model has been reported for a cyclically parthenogenetic population of the aquatic microcrustacean *Daphnia pulex* (Lynch 1984). In that study, levels of quantitative-genetic variation for several size- and fitness-related characters were monitored over a 2-yr period. Broad-sense heritabilities were uniformly high at the beginning of the first year and declined rapidly within a few generations of clonal reproduction. Shortly thereafter, the pond dried, ensuring that all future clones would be derived from sexually produced resting eggs. When hatchlings emerged at the beginning of the next year, the heritabilities had returned to levels observed at the onset of the previous season. Tessier et al. (1992) have reported similar results from a permanent lake population of *Daphnia galeata mendotae*. They observed a complete loss of expressed genetic variance for life-history characters over a 2-mo summer period of clonal selection.

These earlier studies leave several issues unresolved. First, since resting eggs can survive for several years, it is possible that the release of genetic variance observed at recruitment is due in part to the mixing of genetically heterogeneous cohorts of hatchlings. Second, in one study (Lynch 1984), each collection of clones was assayed under the ambient pond conditions, and it is possible that the observed changes in heritabilities were due in part to environmental differences between sampling dates. Third, it is unclear whether any *Daphnia* population closely approximates the assumptions of the additive genetic model given elsewhere (Lynch and Gabriel 1983). The fact that *Daphnia* exhibit inbreeding depression (Banta 1939; Innes 1989) certainly indicates the existence of variance in nonadditive genetic factors.

The current study extends the theoretical results of earlier research (Lynch and Gabriel 1983) to include the effects of nonadditive gene action (dominance

and epistasis) on the dynamics of quantitative characters under selection. We will show that sexual reproduction can induce a change in the mean as well as in the variance of a quantitative trait in the presence of nonadditive effects. Because of the breakup of favorable gene combinations, the change in the mean will usually be in a direction opposite to that of selection, and we refer to this phenomenon as "genetic slippage." Dickerson (1955) has used this term in a broader context to describe any phenomenon, environmental or genetic, that causes the response to selection to be less than the expectation under a simple theory of additive gene action and constant environment. We also show that, by breaking up genetic factors in coupling disequilibrium, recombination can sometimes lead to a reduction in expressed genetic variance, thereby leading to cycles of variation completely out of phase with the predictions in earlier work (Lynch and Gabriel 1983). Such a pattern is contrary to the usual view that sexual reproduction expands the range of genetic variation on which selection can act. Data from a quantitative-genetic analysis of the cyclically parthenogenetic cladoceran *D. pulex* will be interpreted in light of these results.

THEORY

By favoring individuals with specific multilocus genotypes, natural selection generates disequilibria in the frequency of gene combinations within and between loci. Such disequilibria can become pronounced under prolonged phases of clonal selection since genotypes with relatively low fitness are not reconstituted by segregation and recombination. Understanding the dynamics of these disequilibria, and their statistical associations with modes of gene action, is the key to interpreting recombinationally induced changes in means and variances of quantitative characters.

In what follows, we refer to disequilibria involving genes within the same gamete as gametic-phase disequilibria and to disequilibria involving genes from different united gametes (whether at the same locus or different loci) as Hardy-Weinberg disequilibria. The latter are eliminated entirely by a single generation of random mating, while the reduction in gametic-phase disequilibria depends on the recombination frequency between loci. For polygenic traits, most pairs of loci will be on different chromosomes and, as a consequence, will be freely recombining, an assumption that we adhere to. We also assume that the population is large enough that random genetic drift can be ignored safely and that the entire population engages in sex simultaneously.

Our concern will be with a parental population (P) that has been under selection and with an offspring population (O) obtained by randomly mating the members of the parental population. Note that, in the case of a facultative parthenogen, the parental population may have actually been under multiple generations of clonal selection since the last bout of sexual reproduction.

Genotypic Means

For characters with a purely additive genetic basis, the mean genotypic value in a population is independent of the ways in which alleles are associated within

individuals. It depends only on allele frequencies, so sexual reproduction has no direct effect on the mean. However, with nonadditive gene action, departures from Hardy-Weinberg and/or gametic-phase equilibria can lead to a shift in the mean in response to segregation and recombination. We show below that this will occur whenever there is a tendency for parental genotypes with high (or low) genotypic values to have frequencies above their equilibrium expectations prior to sexual reproduction.

Consider, for example, a single locus for which the expected phenotypes are 0, 1, and 1 for the *aa*, *Aa*, and *AA* genotypes. Let the frequencies of both alleles be 0.5 prior to selection, so that the genotype frequencies are 0.25, 0.50, and 0.25 prior to selection and the initial mean genotypic value is 0.75. If selection then eliminates all the *aa* individuals, the remaining *Aa* and *AA* individuals will be in a 2:1 ratio, the frequency of the *a* allele will be 1/3, and the mean genotypic value will be 1. Subsequent sexual reproduction will eliminate the departure from Hardy-Weinberg expectations and, through the reconstitution of *aa* genotypes, will lead to a regression of the mean toward its value prior to selection—the new genotypic mean is 8/9. Thus, selection advanced the mean by 33%, but segregation caused it to slip back by 11%.

We will consider only the consequences of dominance and additive \times additive epistatic effects for the slippage in the mean genotypic value. We start by defining the genic effects from the standpoint of a reference population in Hardy-Weinberg and gametic-phase equilibrium. This reference population is taken to have gene frequencies equal to those in the sampled parental population, but, because the sampled population may have been under selection, the source and reference populations may have different genotype frequencies. The reference population can be viewed as the hypothetical result of mating the sampled population for many generations, in the absence of selection and random genetic drift, until all disequilibria are removed.

The mean of each type of genetic effect is defined to be equal to zero in the reference population. Letting the additive effect of allele *i* be α_i and the frequency of that allele in the sampled parental population be p_i , then $\sum_{i=1}^n p_i \alpha_i = 0$, where *n* is the number of alleles at the locus. In diploid organisms, the dominance effect δ_{ij} is defined as the deviation of the expected phenotype of the *ij*th genotype at a locus from the additive expectation ($\alpha_i + \alpha_j$). In a population in Hardy-Weinberg equilibrium, the mean dominance effect is zero, that is, $\sum_{i,j} p_i p_j \delta_{ij} = 0$. Similarly, the additive \times additive epistatic effect $(\alpha\alpha)_{ik}$ is defined to be the deviation of the expected phenotype of an individual, with an allele *i* at one locus and an allele *k* at a second locus, from the additive expectation across loci ($\alpha_i + \alpha_k$); and $\sum_i^{n_1} \sum_k^{n_2} p_i p_k (\alpha\alpha)_{ik} = 0$, where n_1 and n_2 are the numbers of alleles at the two loci.

With these definitions in hand, it is possible to describe the change in the mean genotypic value after sex in terms of genetic effects, selection intensities leading to the parental genotypic distribution, and resultant deviations from Hardy-Weinberg and gametic-phase equilibria. Dominance causes a change in the mean via Hardy-Weinberg disequilibria, while slippage of the mean due to epistasis depends on both Hardy-Weinberg and gametic-phase disequilibria. We first consider the effects of dominance.

Dominance.—Letting P_{ij} be the frequency of the ij th ordered genotype at a locus in the parental population and noting that the expected frequency of this genotype after random mating is $p_i p_j$, then $\Delta P_{ij} = P_{ij} - p_i p_j$ is the Hardy-Weinberg disequilibrium for this genotype in the parental population. Since ΔP_{ij} is the difference between genotype frequencies in parent and offspring generations and, by definition, $\sum_{i,j}^n p_i p_j \delta_{ij} = 0$, the expected slippage in the mean genotypic value due to segregation at a locus exhibiting dominance is

$$\begin{aligned} \Delta \bar{g}_D &= \bar{g}_D(O) - \bar{g}_D(P) \\ &= - \sum_{i,j}^n \Delta P_{ij} \delta_{ij} \\ &= - \sum_{i,j}^n P_{ij} \delta_{ij}, \end{aligned} \tag{1a}$$

where $\bar{g}_D(O)$ and $\bar{g}_D(P)$ are the mean dominance deviations in the offspring and parent generations.

The slippage due to dominance can also be defined in terms of the selection intensities that led to the genotype frequencies in the parental population. We define w_{ij} to be the relative fitness of the ij th genotype. For a population reproducing clonally, w_{ij} is the rate of expansion of the ij th genotype relative to the average genotype produced during the last bout of sexual reproduction. Letting p'_i be the gene frequency prior to selection, the expected frequency of the ordered ij th genotype after selection is $P_{ij} = p'_i p'_j w_{ij}$. Substituting into equation (1a),

$$\begin{aligned} \Delta \bar{g}_D &= - \sum_{i,j}^n p'_i p'_j w_{ij} \delta_{ij} \\ &= - \sum_{i,j}^n p'_i p'_j w_{ij} \delta_{ij} + \bar{\delta}' \bar{w} - \bar{\delta}' \bar{w} \\ &= - [\bar{\delta}' + \text{Cov}(w_{ij}, \delta_{ij})], \end{aligned} \tag{1b}$$

where $\bar{\delta}' = \sum_{i,j}^n p'_i p'_j \delta_{ij}$ is the mean dominance deviation prior to selection, $\bar{w} = 1$ is the mean relative fitness, and $\text{Cov}(w_{ij}, \delta_{ij})$ is the covariance of relative fitness and dominance deviation on the basis of genotype distribution in the parent population prior to selection.

These expressions provide two ways of visualizing the genetic slippage due to dominance. Equation (1a) shows, in purely functional terms, that the slippage is equal to the sum of the products of the genotype-specific Hardy-Weinberg deviations and their respective dominance effects. Equation (1b) shows how the Hardy-Weinberg deviations in the parental generation are related to selection. From Price's (1970, 1972) rule, the covariance term is equivalent to the selection differential on dominance deviations that led to the parental population. Thus, since $\bar{\delta}'$ is the mean dominance deviation before selection, the quantity within the brackets in equation (1b) is equivalent to the mean dominance effect after selection but before mating (relative to the equilibrium value of zero). If genotypes with positive dominance effects tend to be elevated above their Hardy-Weinberg

expectations by selection, segregation will cause a reduction in the mean genotypic value, whereas an increase is expected if there is a negative covariance between fitness and δ_{ij} . That is, restoration of Hardy-Weinberg frequencies within loci results in a change in the mean genotypic value in a direction contrary to the direction of selection in the preceding generation.

Additive \times additive epistasis.—An expression for the genetic slippage caused by additive \times additive epistatic effects can be developed in a similar manner. For each pair of loci, there are four pairwise combinations of genes within individuals—one within each of the uniting gametes and two between the uniting gametes. Thus, part of the epistatic slippage is caused by Hardy-Weinberg deviations resulting from selection on gametic combinations and part is due to gametic-phase disequilibria of genes within gametes. Let P_{ik} be the frequency of the two-locus gene combination ik (i from one locus, k from the other) within gametes that led to surviving adults, and let $P_{i\cdot k}$ be the frequency of the same combination when genes are compared across gametes. The mean additive \times additive effect in the parental population, summed over all four effects, is then

$$\bar{g}_{AA}(P) = 2 \sum_{i=1}^{n_1} \sum_{k=1}^{n_2} (P_{ik} + P_{i\cdot k})(\alpha\alpha)_{ik}. \quad (2a)$$

In the offspring generation, all gene combinations between uniting gametes will be in Hardy-Weinberg equilibrium with expected frequencies equal to $p_i p_k$. However, the gene combinations within gametes leading to the progeny are a function of the gene pairs contained within parental individuals. Under free recombination, half of the gametes produced are recombinants, and half are nonrecombinants. Thus, the frequency of gametes of the ik th type produced by the parental population is simply the mean of the gene combinations contained within the parents, $(P_{ik} + P_{i\cdot k})/2$. Summing contributions from the two within- and the two between-gamete effects, the mean additive \times additive effect in the progeny is

$$\begin{aligned} \bar{g}_{AA}(O) &= 2 \sum_{i=1}^{n_1} \sum_{k=1}^{n_2} \left(p_i p_k + \frac{P_{ik} + P_{i\cdot k}}{2} \right) (\alpha\alpha)_{ik} \\ &= \sum_{i=1}^{n_1} \sum_{k=1}^{n_2} (P_{ik} + P_{i\cdot k})(\alpha\alpha)_{ik}. \end{aligned} \quad (2b)$$

The genetic slippage due to epistasis is therefore

$$\begin{aligned} \Delta \bar{g}_{AA} &= \bar{g}_{AA}(O) - \bar{g}_{AA}(P) \\ &= - \sum_{i=1}^{n_1} \sum_{k=1}^{n_2} (P_{ik} + P_{i\cdot k})(\alpha\alpha)_{ik}. \end{aligned} \quad (3a)$$

This shows that the total advancement of the mean epistatic effect by selection is $-2\Delta \bar{g}_{AA}$ and that a generation of sexual reproduction causes the genetic mean to change in the opposite direction by half this amount.

As in the case of dominance, the epistatic slippage can also be expressed in terms of the selection intensities operating on the zygotes leading to the parental sample. Here we let w_{ik} and $w_{i \cdot k}$ be the relative fitnesses of the ik th gene combinations within and between uniting gametes that led to the parental population. In the absence of gametic-phase disequilibria involving other loci, it seems likely that $w_{i \cdot k}$ will equal w_{ik} . However, this may not be true in the presence of gametic-phase disequilibrium at multiple loci. Prior to selection, the parental population has the ik gene combination across gametes in the Hardy-Weinberg frequency $p'_i p'_k$, which is then modified by selection to $p'_i p'_k w_{i \cdot k}$. The gene frequencies after selection are $p'_i w_i$, where w_i is the marginal fitness of individuals with allele i , so the cross-gamete gene combination frequencies after sexual reproduction are $p'_i p'_k w_i w_k$. Letting the ik th gamete frequency prior to selection be P'_{ik} , then the frequency of the ik th gamete leading to surviving parents is $P'_{ik} w_{ik}$. Thus, after free recombination, the gamete frequencies, leading to the offspring generation, become $(P'_{ik} w_{ik} + p'_i p'_k w_{i \cdot k})/2$.

Letting the gametic-phase disequilibrium in the parental population prior to selection be $D'_{ik} = P'_{ik} - p'_i p'_k$ and summing the two within- and two between-gamete contributions, the slippage due to additive \times additive epistasis at a pair of loci can be expressed as

$$\Delta \bar{g}_{AA} = 2 \sum_{i,k} p'_i p'_k \left(w_i w_k - \frac{w_{ik} + w_{i \cdot k}}{2} \right) (\alpha\alpha)_{ik} - \sum_{i,k} D'_{ik} w_{ik} (\alpha\alpha)_{ik}. \quad (3b)$$

By definition from above, $\sum_{i,k} p'_i p'_k w_i w_k (\alpha\alpha)_{ik} = \sum_{i,k} p_i p_k (\alpha\alpha)_{ik} = 0$, and further through the definition of D'_{ik} , equation (3b) reduces to

$$\begin{aligned} \Delta \bar{g}_{AA} &= - \sum_{i,k} [p'_i p'_k (w_{ik} + w_{i \cdot k}) (\alpha\alpha)_{ik}] - \sum_{i,k} D'_{ik} w_{ik} (\alpha\alpha)_{ik} \\ &= - \sum_{i,k} (p'_i p'_k w_{i \cdot k} + P'_{ik} w_{ik}) (\alpha\alpha)_{ik} \\ &= - \{ \bar{\alpha}'_{i \cdot k} + \text{Cov}[w_{i \cdot k}, (\alpha\alpha)_{i \cdot k}] \} - \{ \bar{\alpha}'_{ik} + \text{Cov}[w_{ik}, (\alpha\alpha)_{ik}] \}, \end{aligned} \quad (3c)$$

where $(\bar{\alpha}')_{ik}$ and $(\bar{\alpha}')_{i \cdot k}$ are the mean additive \times additive effects for gene combinations, within and between gametes, in the parental population prior to selection. It again follows from Price's (1970, 1972) rule that the first braced term in equation (3c) is the mean between-gamete additive \times additive effect within the selected parents, whereas the second braced term is the mean within-gamete additive \times additive effect within the selected parents.

It is noteworthy that slippage due to epistasis can be nonzero even in the absence of selection and, because the loss of gametic-phase disequilibria is gradual, can require several generations to dissipate. In the neutral case and under random mating, $\Delta \bar{g}_{AA} = - \sum_{i,k} D'_{ik} (\alpha\alpha)_{ik}$, which shows that genetic slippage will occur as long as a correlation exists between the epistatic effects and the degree of disequilibrium for different gene combinations.

Inbreeding.—One final result that will be of use in interpreting our empirical results concerns the response of the mean phenotype to selfing the parental popu-

lation. It is well known that additive \times additive epistasis does not contribute to a change in the mean phenotype of inbred individuals (Anderson and Kempthorne 1954; Cockerham 1980; Lynch 1991), so we need only consider the effects of dominance. On selfing, parents with genotype ij produce progeny with genotypes ii , ij , and jj in a 1:2:1 ratio. The mean dominance effect in progeny obtained by selfing is therefore

$$\bar{g}_D(S) = \sum_{i,j}^n P_{ij} \left(\frac{\delta_{ij}}{2} + \frac{\delta_{ii} + \delta_{jj}}{4} \right), \tag{4}$$

where δ_{ii} is the dominance effect of the ii th homozygote.

We define the total inbreeding depression in a population (\bar{I}) to be the expected difference between the mean phenotype of totally inbred individuals and that of the parental population. Since progeny obtained by selfing are 50% inbred,

$$\begin{aligned} \bar{I} &= 2[\bar{g}_D(S) - \bar{g}_D(P)] \\ &= \sum_{i,j}^n P_{ij} \left(\frac{\delta_{ii} + \delta_{jj}}{2} - \delta_{ij} \right), \end{aligned} \tag{5a}$$

where $\bar{g}_D(P)$ is the mean dominance effect in the parents. It then follows from equation (1a) that the mean effect of homozygous genotypes is

$$\begin{aligned} \bar{H}_D &= \bar{I} - \Delta\bar{g}_D \\ &= \sum_{i,j}^n P_{ij} \left(\frac{\delta_{ii} + \delta_{jj}}{2} \right). \end{aligned} \tag{5b}$$

Note that, when the parental population is in Hardy-Weinberg equilibrium, $\Delta\bar{g}_D = -\sum_{i,j}^n P_{ij}\delta_{ij} = 0$, so $\bar{H}_D = \bar{I}$.

Assuming that most of the genetic slippage between parents and their outcrossed offspring is due to dominance, then $\Delta\bar{g}_D \cong \bar{g}(O) - \bar{g}(P)$, and \bar{H}_D can be approximated by $2\bar{g}(S) - \bar{g}(P) - \bar{g}(O)$. This allows an estimate of the mean homozygous effect to be acquired by combining the results of analyses of genetic slippage and inbreeding depression.

The preceding formulas describe changes in the mean phenotype resulting from dominance at a single locus and from additive \times additive epistasis at a pair of loci. The total expected change for a polygenic trait is defined by summing such contributions from all loci. As empirical estimators of the summed effects, we will be using

$$\bar{I} = 2[\bar{g}(S) - \bar{g}(P)], \tag{6a}$$

$$\Delta\bar{g}_D = \bar{g}(O) - \bar{g}(P), \tag{6b}$$

and

$$\bar{H}_D = 2\bar{g}(S) - \bar{g}(P) - \bar{g}(O). \quad (6c)$$

Genetic Variance

The expressed genetic variance (σ_{GE}^2) for any quantitative trait can be viewed as the sum of two components,

$$\sigma_{GE}^2 = \sigma_{GT}^2 + \Delta_{GH}, \quad (7)$$

where σ_{GT}^2 is the genetic variance that would be observed if all genes were in Hardy-Weinberg and gametic-phase equilibrium and Δ_{GH} is the deviation from this expectation due to disequilibria. When there is a negative covariance between the effects of different genes within individuals, that is, when there is repulsion disequilibrium, Δ_{GH} is negative and can be viewed as hidden genetic variance (Lynch and Gabriel 1983). However, if there is a coupling of genes with like effects, then Δ_{GH} will be positive and the expressed genetic variance will exceed the equilibrium expectation.

Only limited work has been done on the theoretical expectations for components of genetic variance for nonequilibrium systems. For outbreeding populations, this work has been confined to the situation in which there is Hardy-Weinberg equilibrium within loci, no selection, and no epistatic genetic variance (Weir et al. 1980). We develop some more general results below, although still confining attention to the case in which there are no epistatic interactions among loci.

First, we consider the expected genetic variance in the parental generation. Letting σ_A^2 and σ_D^2 be the additive and dominance components of genetic variance that would be observed in the (Hardy-Weinberg and gametic-phase) equilibrium population derived from the parental generation, then $\sigma_{GT}^2 = \sigma_A^2 + \sigma_D^2$. There are three ways in which selection leading to the sampled parents may cause the expressed genetic variance to deviate from σ_{GT}^2 :

First, for additive effects alone, the development of Hardy-Weinberg disequilibria can cause covariances between the additive effects of genes within loci, $\sigma_{A \cdot A}(w)$, as well as between genes from different loci, $\sigma_{A \cdot A}(b)$. In addition, gametic-phase disequilibria can cause covariance between the additive effects of genes acquired in the same gametes, $\sigma_{A, A}$.

Second, Hardy-Weinberg deviations within a locus x inflate the expressed dominance genetic variance in the selected parents (relative to the equilibrium expectation) by the amount $[\sum_{i,j}^n \Delta P_{ij} \delta_{ij}^2 - (\Delta \bar{g}_{Dx})^2]$, where ΔP_{ij} and δ_{ij} have been defined above, $\Delta \bar{g}_{Dx}$ is the slippage in the mean phenotype caused by dominance at the x th locus, and the summation is over all genotypes at the locus. Similarly, disequilibrium involving a pair of loci (x and y) inflates the expressed dominance genetic variance by the amount $2[\sum_{i,j,k,l} P_{ijkl} \delta_{ij} \delta_{kl} - (\Delta \bar{g}_{Dx})(\Delta \bar{g}_{Dy})]$, where P_{ijkl} is the frequency of parental genotypes with alleles i and j at locus x and alleles k and l at locus y . This quantity is simply twice the covariance of dominance effects at the two loci. Summing the one-locus and two-locus terms over all loci, the hidden genetic variance associated with dominance effects is $\Delta_D + \Delta_{D,D} -$

$(\Delta\bar{g}_D)^2$, where Δ_D is the sum of the $\sum_{i,j} \Delta P_{ij} \delta_{ij}^2$, $\Delta_{D,D}$ is the sum of the $2 \sum_{i,j,k,l} P_{ijkl} \delta_{ij} \delta_{kl}$, and $\Delta\bar{g}_D$ is the total genetic slippage in the mean phenotype due to dominance.

Third, we note that selection can cause a covariance between additive and dominance effects within individuals. Such covariance can arise within and between loci, but for our purposes this distinction is unnecessary and we denote the total covariance between additive and dominance effects in the parents by $\sigma_{A,D}$.

In summary, the expressed genetic variance in the parental population is

$$\sigma_{GE}^2(P) = \sigma_A^2 + \sigma_D^2 + [\sigma_{A \cdot A}(w) + \sigma_{A \cdot A}(b) + \sigma_{A,A} + \sigma_{A,D} + \Delta_D + \Delta_{D,D} - (\Delta\bar{g}_D)^2], \tag{8}$$

where the sum of the terms in the brackets represents the disequilibrium genetic variance, Δ_{GH} , caused by Hardy-Weinberg and gametic-phase disequilibria. With the exception of $(\Delta\bar{g}_D)^2$, all of the terms within the brackets can be either positive or negative.

Since the terms $\sigma_{A \cdot A}(w)$, $\sigma_{A \cdot A}(b)$, $\sigma_{A,D}$, Δ_D , and $\Delta\bar{g}_D$ are functions only of Hardy-Weinberg disequilibria, they become zero immediately after a generation of random mating. Thus, a description of the expressed genetic variance in the offspring generation requires only that we know how segregation and recombination modify the between-locus disequilibrium terms $\sigma_{A,A}$ and $\Delta_{D,D}$. We consider these in turn, assuming free recombination.

First, the covariance between additive effects within gametes leading to the offspring generation is simply the average of that within and between gametes that produced the surviving parents, $[\sigma_{A,A} + \sigma_{A \cdot A}(b)]/2$.

Second, the extent to which $\Delta_{D,D}$, the covariance of dominance effects, is modified by segregation and recombination depends on how the two-locus genotype frequencies P_{ijkl} change. Letting P_{ik}^* be the frequency of gametes of the ik th type produced by the parents, then the frequency of ordered $ijkl$ genotypes in the offspring generation is $P_{ik}^* P_{jl}^*$. Since the mean dominance effects in the offspring generation are scaled to equal zero, the dominance disequilibrium covariance in the offspring generation for any pair of loci can be written as $2 \sum_{i,j,k,l} P_{ik}^* P_{jl}^* \delta_{ij} \delta_{kl}$. We refer to the sum of this quantity over all pairs of loci as $\Delta_{D,D}^*$. Note that, in the absence of selection on the parent generation, $\Delta_{D,D}$ will be entirely due to gametic-phase disequilibrium and $\Delta_{D,D}^*$ will be approximately $\Delta_{D,D}/4$ since there is only a 25% probability of no recombination between the same pair of loci in two uniting gametes.

In summary, the expected expressed genetic variance among sexually produced progeny is

$$\sigma_{GE}^2(O) = \sigma_A^2 + \sigma_D^2 + \left[\frac{\sigma_{A,A} + \sigma_{A \cdot A}(b)}{2} + \Delta_{D,D}^* \right]. \tag{9}$$

Depending on the signs of the covariances between genetic effects in the parental generation, recombination can lead to either an increase or a decrease in the expressed genetic variance. In terms of components of variation, the change in

the expressed genetic variance between selected parents and their unselected progeny is

$$\begin{aligned}\Delta\sigma_{GE}^2 &= \sigma_{GE}^2(O) - \sigma_{GE}^2(P) \\ &= (\Delta\bar{g}_D)^2 - \sigma_{A \cdot A}(w) - \frac{\sigma_{A, A} + \sigma_{A \cdot A}(b)}{2} \\ &\quad - \sigma_{A, D} - \Delta_D + (\Delta_{D, D}^* - \Delta_{D, D}).\end{aligned}\tag{10}$$

The sign of $\Delta\sigma_{GE}^2$ provides an indication as to whether gene effects with the same sign were in coupling or repulsion disequilibrium in the parental population, but $\Delta\sigma_{GE}^2$ need not be strictly equivalent to Δ_{GH} . Since gametic-phase disequilibria decay asymptotically over time, not all of Δ_{GH} is eliminated in one generation, even under free recombination. However, after the first generation of random mating, in the absence of selection, all further changes in the expressed genetic variance are due to recombinationally induced changes in the covariances of additive effects within gametes and to covariances of dominance effects.

Parent-Offspring Resemblance

Finally, we consider the resemblance between parents and their sexually produced offspring. Since sexually produced progeny receive exactly one gene per locus from each parent, there is no covariance among dominance effects across generations in a random-mating population. Assuming that contributions from additive \times additive variance are of relatively minor significance, the expected covariance between parents and offspring is simply half the expressed additive genetic variance in the parental generation,

$$\sigma(P, O) = \frac{\sigma_A^2 + \Delta_{AH}}{2},\tag{11}$$

where $\Delta_{AH} = \sigma_{A \cdot A}(w) + \sigma_{A, A} + \sigma_{A \cdot A}(b)$ is the disequilibrium additive genetic variance. In the following empirical study, the narrow-sense heritability, defined to be $h_{PO}^2 = 2\sigma(P, O)/\sigma_z^2(P)$, with $\sigma_z^2(P)$ being the phenotypic variance in the parental generation, provides an estimate of the proportional contribution that expressed additive genetic variance makes to the total phenotypic variance of a trait in the parental generation. An unbiased estimate of the genetic covariance between parents and offspring is provided by the covariance between mean phenotypes of parent and offspring clones.

As noted above, estimates of the total expressed genetic variance can also be obtained with a clonally reproducing organism. We define the broad-sense heritabilities in the parental and offspring generations to be $H_P^2 = \sigma_{GE}^2(P)/\sigma_z^2(P)$ and $H_O^2 = \sigma_{GE}^2(O)/\sigma_z^2(O)$. The expressed genetic variance in each generation, $\sigma_{GE}^2(P)$ or $\sigma_{GE}^2(O)$, is estimated by the between-clone component of variance, whereas the phenotypic variance is estimated by the sum of the within- and between-clone components of variance.

METHODS

In April 1991, a population of the freshwater planktonic cladoceran *Daphnia pulex* was found to be in a phase of sexual reproduction in Amazon Pond, Eugene,

Oregon. Females that had been fertilized were identified by the presence of eggs in their ephippia, and approximately 1,000 of them were isolated into individual containers in the laboratory. Within 2 d, all females had shed their ephippia, and the latter were placed in individual vials and maintained at 4°C in the dark for several days. The vials were then placed in the light at room temperature and monitored for hatchlings for 4 d. Typically, only 10–25 resting eggs would hatch during this period, but by repeating the treatment several times, offspring from approximately 400 clones were obtained.

Throughout the period of hatching, the maternal clones were kept in culture. A large fraction of the original 1,000 mothers produced progeny asexually after the release of their ephippia, so that, even though the stem mothers died eventually, their genotypes had been transmitted intact to their descendants. This provided us with the opportunity to assay the performance of maternal and progeny genotypes side by side, in the same environment. The following experiments employ 94 pairs of parents and offspring.

Two life-table experiments were performed, the first at 12°C, and the second at 20°C. In both experiments, the food consisted of a 150-mL suspension of 300,000 cells per milliliter of the green alga *Scenedesmus*. But whereas the second experiment used filtered Amazon Pond water, the pond was dry during the first experiment, and filtered Fern Ridge Reservoir water was used instead. Each experiment involved the measurement of approximately 320 individuals. The sets of parent-offspring pairs used in the two experiments were largely nonoverlapping, and both parents and offspring were replicated three times within experiments. Prior to the actual experiments, all replicate lines were raised in the experimental conditions for two generations to ensure that maternal effects did not contribute to the between-clone component of variance in the final analysis (Lynch 1985).

Individuals were examined daily for growth and reproductive characters in the second experiment, but instar durations always exceeded 2 d in the first experiment because of the cooler temperature, and it was only necessary to make measurements every other day. Measurement procedures are described elsewhere (Lynch et al. 1989). Univariate analyses were performed separately on both the parent and offspring generations in each experiment through standard one-way ANOVA. Prior to computing variance components from the observed mean squares, measurement error variance was eliminated from the within-clone component of variance as described previously (Lynch et al. 1989). Since both experiments gave comparable results after the means and variances were standardized, they are summarized in that way below.

To gain further insight into the importance of dominance, a study of inbreeding depression was also performed. Over a period of several months, resting eggs accumulated in many of the cultures of the parental clones. From a genetic standpoint, such eggs are a product of self-fertilization—their appearance requires the environmental induction of male production and subsequent fertilization of haploid eggs produced by the females of the same clone. Offspring that hatched from the resting eggs were assayed for life-history characters in an experiment also containing random parental clones. This experiment was performed in a manner identical to the second life-table experiment mentioned above.

TABLE 1

SUMMARY OF THE GENETIC PARAMETER ESTIMATES AVERAGED OVER THE TWO EXPERIMENTS

Trait	H_P^2	H_O^2	h_{PO}^2	$\Delta\sigma_{GE}^2$	$\Delta\bar{g}$
<i>B</i>	.24 (.03)	.07 (.01)	.20 (.16)	-.19 (.04)	-.09 (.03)
B_o	.44 (.09)	.30 (.04)	.30 (.24)	-.21 (.07)	-.04 (.06)
B_m	.20 (.03)	.30 (.02)	-.02 (.50)	.13 (.04)	-.11 (.10)
G_j	.38 (.09)	.18 (.14)	.28 (.12)	-.23 (.04)	.09 (.11)
G_a	.79 (.21)	.80 (.20)	-.48 (.34)	-.40 (.27)	-.07 (.02)
<i>k</i>	.38 (.02)	-.01 (.06)	.04 (.06)	-.45 (.11)	-.12 (.02)
<i>D</i>	.20 (.18)	.04 (.10)	.40 (.50)	-.13 (.23)	-.06 (.06)
<i>C</i>	.28 (.06)	.19 (.09)	.06 (.16)	-.11 (.15)	-.07 (.09)

NOTE.—Standard errors for the estimates are given in parentheses; $\Delta\sigma_{GE}^2$, the change in the between-clone variance following sex, is standardized by dividing by the mean phenotypic variance in the parent and offspring generations; $\Delta\bar{g}$, the slippage in the mean phenotype, is the offspring minus the parent mean phenotype, standardized by dividing by the mean phenotypic standard deviation in the two generations. All standard errors were obtained by Taylor expansion under the assumption that the observed mean squares were χ^2 distributed. Trait *B* denotes an instar-specific size; separate analyses were performed for each of 10 instars, and the final results were averaged. Trait B_o denotes the mean offspring size for a specific adult instar (mm); separate analyses were performed for the first four adult instars, and the final results were averaged. Traits B_m and *k* are the length (mm) and age (d) at first reproduction. Trait G_j , the juvenile growth rate, is equal to $(\ln B_t - \ln B_o)/t$, where *t* is the age at appearance of the first clutch and B_o and B_t are the lengths of the individual at times 0 and *t*. The adult growth rate is $G_a = (\ln B_{k+3} - \ln B_k)/t$, where the sizes refer to the first and third adult instars and *t* is the time between them. Trait *D* denotes the duration of a specific adult instar (d); separate analyses were performed for the first four adult instars, and the final results were averaged. Trait *C* denotes the clutch size carried in a specific adult instar; separate analyses were performed for the first five adult instars, and the final results were averaged.

RESULTS

The evidence is firm that the Amazon population is cyclically parthenogenetic, with a bout of random mating preceding the drying of the pond each year. In a routine screen of electrophoretic variation, two loci (*Pgm* and *Pgi*) were found to be polymorphic for two alleles each. Surveys involving 30–60 individuals on four dates over a 3-yr period yielded data consistent with Hardy-Weinberg expectations in all but one case. Wright's (1951) measure of local inbreeding (F_{IS}) averaged -0.12 (SE = 0.09), indicating a slight but nonsignificant excess of heterozygotes. (Throughout, numbers in parentheses refer to standard errors, and 2 SEs from zero is used as a criterion for significance.) This is consistent with expectations for an outcrossing population. Through electrophoretic markers, the method of Queller and Goodnight (1989) provided estimates of the relatedness for 34 of the pairs of parents and offspring in the life-table experiments. Such estimates have a large sampling variance when only a small number of loci are employed. The mean estimate of relatedness, 0.85 (0.65), is not significantly different from the expectation of 0.5.

The broad-sense heritability estimates indicate significant expressed genetic variance in the parent (H_P^2) and/or offspring (H_O^2) generation for all of the life-history characters analyzed, except for the duration of adult instars (table 1). On the other hand, only one of the narrow-sense heritability (h_{PO}^2) estimates is significant. Averaging over all traits, the mean broad-sense heritability in the parental

generation, 0.36 (0.07), is approximately 2.5 times greater than the mean narrow-sense heritability, 0.14 (0.06). Since the difference $H_P^2 - h_{PO}^2 \cong [\sigma_D^2 + \sigma_{A,D} + \Delta_D + \Delta_{D,D} - (\Delta\bar{g}_D)^2]/\sigma_z^2(P)$ is all due to dominance, this result suggests that approximately 22% of the phenotypic variance, and approximately two-thirds of the genetic variance, in this *Daphnia* population may be due to dominance.

Contrary to expectations, sexual reproduction did not lead to a release of genetic variance in this study. The average broad-sense heritability for the offspring generation, 0.23 (0.09), is about two-thirds of that seen in the parental generation, 0.36 (0.07). Seven of the eight estimates of $\Delta\sigma_{GE}^2$ (scaled relative to the phenotypic variance in table 1) are negative (significantly so in four cases). The one exception was size at first reproductive investment, B_m , which exhibited significantly positive $\Delta\sigma_{GE}^2$, consistent with a release of hidden genetic variance.

The mean phenotypes for three of the eight characters changed significantly after sex (table 1). We estimated the total genetic slippage $\Delta\bar{g}$ by the difference between offspring and parent means. In units of phenotypic SDs, the average absolute change in mean phenotypes is 0.08 (0.01). In other words, the mean phenotype of an average trait changed by about 0.1 phenotypic SDs following sex. The general trend was for individuals to become smaller and reproduce earlier.

Note that in all cases the square of the standardized slippage, $(\Delta\bar{g})^2/\sigma_z^2$, given in the last column of table 1, is less than 0.02. Recalling equation (10), this implies that slippage contributes little to the observed changes in the genetic variance. Thus, the differences between H_P^2 and h_{PO}^2 , noted above, must be due almost entirely to one or more terms in $(\sigma_D^2 + \sigma_{A,D} + \Delta_D + \Delta_{D,D})$.

Self-fertilization resulted in substantial inbreeding depression. Mean egg viability declined from 81% (14%) to 43% (7%), while the probability of survival to the fifth instar (the approximate age at maturity) declined from 67% (7%) to 38% (7%). In absolute value, changes of other life-history characters range from 0.4 to 1.2 in units of parental phenotypic SDs (left column of table 2). Body size, growth rate, and clutch sizes declined, while the age at first reproduction increased. The expected average effect of complete homozygosity, \bar{H}_D , ranges from a change of approximately 1 to 3 phenotypic SDs (table 2). With the phenotypic data on the right of the table, complete inbreeding is expected to reduce offspring length by about 0.03 mm, size at maturity by about 0.08 mm, and the size of the second clutch by about 11 eggs, and to increase the age at first reproduction by about 6.6 d. These estimates of the consequences of inbreeding are almost certainly downwardly biased since considerable mortality of inbred clones occurred prior to analysis.

DISCUSSION

It is well known that the mean *phenotypic value* of the offspring of a selected population will regress toward the mean of the parental generation prior to selection unless the heritability of a trait is equal to one (Falconer 1981). This occurs even in the absence of nonadditive gene action because the phenotypes of selected parents are a function of genetic and environmental factors and the envi-

TABLE 2
MAGNITUDE OF INBREEDING DEPRESSION RESULTING FROM SELFING

Trait	$\bar{g}(S) - \bar{g}(P)$	\bar{H}_D	Mean (SD)
<i>B</i>	-1.24 (.19)	-2.39 (.38)	. . .
<i>B_o</i>	-.44 (.61)	-.84 (1.22)	.555 (.032)*
<i>B_m</i>	-.43 (.21)	-.75 (.43)	1.328 (.104)
<i>G_j</i>	-.82 (.30)	-1.73 (.61)	.117 (.028)
<i>k</i>	1.24 (.15)	2.60 (.30)	12.28 (2.54)
<i>D</i>	.58 (.37)	1.22 (.74)	3.55 (.48)†
<i>C</i>	-1.02 (.13)	-1.97 (.28)	13.1 (5.7)‡

NOTE.—Standard errors are given in parentheses; $\bar{g}(S)$ and $\bar{g}(P)$ are the mean phenotypes of progeny obtained by selfing and of their parents. The estimated mean effect of total homozygosity, \bar{H}_D , is measured as $2\bar{g}(S) - \bar{g}(P) - \bar{g}(O)$. Both $\bar{g}(S) - \bar{g}(P)$ and \bar{H}_D are given in units of phenotypic standard deviations in the parental generation. The characters on the left are described in table 1. For reference, the means and phenotypic standard deviations for several characters are given on the right as averages for the parental generations assayed in the two main experiments; these values are given only to provide an indication of the absolute magnitude of change that would be expected in completely homozygous individuals.

* Value is *B_o*, mean offspring size for the second adult instar (mm).

† Value is *D₁*, duration of the first adult instar (d).

‡ Value is *C₂*, size of the second clutch.

ronmental effects usually are not transmitted across generations. However, the focus of this article is not the shift of mean *environmental effects* across generations but the change in the mean *genotypic value*.

With a clonally reproducing organism, it is possible to maintain the parental genotype intact and to assay it subsequently in the same environment as its sexually produced progeny. Under such a design, the distribution of environmental effects on parents and offspring should be identical, and any significant changes in mean phenotypes across generations should be due to shifts in the average genotypic values in response to segregation and recombination. As noted above, such changes can only occur if three conditions are met: nonadditive interactions must exist between genetic effects within and/or between loci, the relevant genes must be in Hardy-Weinberg and/or gametic-phase disequilibrium prior to sexual reproduction, and there must be a correlation between the effects of genetic factors and their degree of disequilibrium. The second two conditions are also required for sexual reproduction to induce a shift in the expressed genetic variance for a quantitative trait. Our observation of significant changes in phenotypic means and expressed genetic variance after sexual reproduction indicates that all three conditions were fulfilled in our study population of *Daphnia*.

A substantial fraction of the total phenotypic variance in the study population had a genetic basis. However, for most of the characters, even though there was significant genetic variance among clones, there was very little phenotypic resemblance between parents and their sexually produced progeny. This should not have occurred if the mode of gene action was entirely additive, since in this

case broad-sense and narrow-sense heritabilities should be equal. Although we did not formally consider the importance of epistatic genetic variance in our development of the theory, it is known that one-half of the expressed additive \times additive genetic variance contributes to narrow-sense heritability, as estimated by parent-offspring regression (Falconer 1981). Thus, the nearly complete absence of significant parent-offspring resemblance also suggests that the amount of expressed additive \times additive genetic variance may be relatively small in this population. We conclude that most of the expressed genetic variance must be due to dominance.

The data from the selfing experiment provide independent evidence on this matter. Inbreeding depression for a trait requires dominance genetic variance, so the results of our inbreeding experiments clearly indicate that $\sigma_D^2 \neq 0$ in the Amazon population. Banta (1939) also found evidence for substantial inbreeding depression in clones of *Daphnia laevis*—hatchability of resting eggs, fertility, and growth rate of the surviving hatchlings all declined by about 50% after selfing. Similar results were obtained by Innes (1989) with *Daphnia obtusa*. Quantitatively, these earlier studies are in striking agreement with those reported above—we observed declines of 47% in egg viability, 43% in survival rate to maturity, 20% in juvenile growth rate, and 44% in clutch size.

Although the idea that sex accelerates the rate of evolution seems to be generally valid for characters with an additive genetic basis (Lynch and Gabriel 1983; Charlesworth 1993), our results suggest two reasons this conclusion might not always apply to quantitative characters with a strong nonadditive genetic component. First, although all components of expressed genetic variation (additive and nonadditive) contribute to the response to selection during clonal propagation, only the additive component of variance contributes to the long-term response to selection after sexual reproduction (Falconer 1981). Second, as emphasized by Shields (1982), when natural selection induces disequilibria between genes with nonadditive effects, the breakup of favorable gene combinations by segregation and recombination leads to slippage of the mean genotypic value in a direction opposite that of previous selection. Such slippage does not occur in obligately clonal populations.

A critical question is whether the price of segregational and recombinational breakdown that sexual populations pay each generation can ever offset the evolutionary advantage of higher levels of genetic variance that might be maintained by the same phenomena. But that is not the only issue. Contrary to the usual view, our theoretical and empirical results show that sexual reproduction need not always enhance the level of expressed genetic variance. Sexual reproduction can lead to a reduction in the amount of expressed genetic variance when genes with like effects tend to be associated in the same parental individuals, that is, when there is coupling disequilibrium rather than the repulsion disequilibrium predicted under stabilizing selection. Although disruptive selection of most types will cause coupling disequilibrium, a U-shaped fitness function is not a necessary condition for it. Shnol and Kondrashov (1993) have shown that selection can inflate the expressed genetic variance of a normally distributed trait if the second derivative of the logarithm of relative fitness with respect to phenotype is positive.

That is, if the average relationship of $\ln w(z)$ and z (where z denotes the phenotypic value) is concave upward, directional selection can lead to an inflation of the genetic variance relative to its equilibrium expectation.

The ecological factors that might have led to coupling disequilibria in our study population are unknown. However, some hint of the form of selection that might have been operating is provided by the direction of slippage in the mean phenotype. As noted above, sexual reproduction is expected to induce a shift in the mean phenotype in a direction opposite the force of previous selection. A major selection pressure on the Amazon *Daphnia* is probably the invertebrate predator *Chaoborus*, which attains moderately high densities in the pond. In laboratory selection experiments, Spitze (1991) found that *Chaoborus* predation leads to the evolution of larger size at maturity in *Daphnia pulex*. Our observation that sex led to a decrease in adult body size is consistent with expectations if selection were favoring larger size. Spitze also showed that *Chaoborus* predation favored earlier reproduction in the prey. However, in our study, sex caused a reduction in the age at maturity, contrary to the expectation if selection were favoring earlier reproduction.

Recently, Ebert et al. (1993) performed an experiment with *Daphnia magna* using a design very similar to that described above. The population had been reproducing clonally for about 2 mo prior to its sexual phase. Data from 23 pairs of parents and offspring were sufficient to demonstrate a substantially lower narrow-sense than broad-sense heritability for many life-history traits. For some of the traits, nearly all of the genetic variance appeared to be nonadditive, consistent with our observations. Contrary to the Amazon population and to an earlier study (Lynch 1984), no obvious changes in the broad-sense heritabilities arose between parent and offspring generations, but with only 23 parent-offspring pairs, the statistical power of this study was relatively low.

Our study does not provide a direct partitioning of the contributions of Hardy-Weinberg and gametic-phase disequilibria to the observed changes in means and variances. However, since our isozyme surveys gave results that were concordant with Hardy-Weinberg expectations, it seems likely that gametic-phase disequilibria play the major, if not the entire, role. This is not completely unexpected, since Hardy-Weinberg deviations are transient in a randomly mating population, while gametic-phase disequilibria can build up over multiple generations.

Genetic slippage in the mean and variance of quantitative traits is not unique to cyclical parthenogens. It is a potential property of any sexual species with nonadditive gene action. However, although it almost certainly occurs, slippage in the mean genotypic value is difficult to detect in purely sexual species for two reasons. First, when selection operates on multilocus genotypes for only a single generation prior to sexual reproduction, departures from the equilibrium genotype frequencies are expected to be relatively small since segregation eliminates all departures from Hardy-Weinberg expectations and recombination eliminates a fraction of the gametic-phase disequilibria each generation. This is different from the situation in clonal populations, in which genotypic lineages remain intact for extended periods of selection, causing the effects of selection to be magnified

greatly. Second, an unambiguous detection of genetic slippage requires that the phenotypes of parents and offspring be measured in the same environment. This is often not possible for species that reproduce solely by sexual reproduction.

For purely practical reasons, much of the theory of quantitative genetics has been developed under the assumption that gametic-phase disequilibria are of negligible significance in natural populations (for contrasting views, see Mather 1942, 1943; Thompson 1976). There is actually very little empirical information on the issue. Although numerous studies of electrophoretic variation have concluded that gametic-phase disequilibria are usually very weak in randomly mating populations (Barker 1979), most of these studies have low statistical power, and more recent analyses suggest the opposite (Zapata and Alvarez 1992, 1993). Moreover, weak disequilibria for single pairs of marker loci do not rule out the possibility that cumulative gametic-phase disequilibria involving *multiple quantitative-trait loci* are common in nature, and at least one line of indirect evidence suggests they may be. Experiments comparing the properties of recombinant and nonrecombinant chromosomes extracted from populations of several species of *Drosophila* have shown that the recombinant chromosomes are almost always associated with reduced fitness (Spassky et al. 1958; Dobzhansky et al. 1959; Spiess 1959; Krimbas 1961; Spiess and Allen 1961; Allen 1966; Kosuda and Moriwaki 1971; Charlesworth and Charlesworth 1975). It is difficult to reconcile these observations without invoking coupling disequilibria of genes with favorable epistatic effects on fitness.

For sexual species in which individuals can be propagated vegetatively and/or seeds preserved, there is a fairly straightforward way in which the contribution of gametic-phase disequilibria to the variance of quantitative characters might be evaluated, and it is somewhat surprising that this has not yet been done. Monitoring a population in a controlled environment, under relaxed selection, for several generations of random mating is all that is necessary. If gametic-phase disequilibria are of significance, then the phenotypic variance is expected to change progressively in response to random mating, although at a diminishing rate with increasing numbers of generations. If the disequilibria involve nonadditive effects, a shift in the mean phenotype should be observed as well. In principle, maternal environmental effects can contribute to such changes, but these can be factored out by the use of parallel control lines maintained by vegetative propagation. Experiments of this sort could provide useful insight into the genetic architecture underlying quantitative traits in natural populations, without requiring the detailed pedigree analyses that are normally necessary in studies concerned with variance-component estimation.

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