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GENE INTERACTION AFFECTS THE ADDITIVE GENETIC VARIANCE IN SUBDIVIDED POPULATIONS WITH MIGRATION AND EXTINCTION

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Abstract.—We investigated the effect of nonadditive genetic variance on the amount of additive genetic variance within local populations in an infinite-allele, infinite-island model with migration, extinction, and recolonization, using two-locus descent measures. For an island model with extinction, one- and two-locus descent measures are expressed in a matrix form that allows equilibrium solutions to be calculated similar to previous work on Wright's F-statistics. In a subdivided population, the additive genetic variation within a local deme depends on the dominance and epistatic genetic variation in the species. Moreover, to a good approximation, the amount of additive variance within a deme is a simple function of F_{st}, which is twice the demic fraction of genic variance. At equilibrium, it is equal to $(1 - F_{st})\ V_A$ plus $4\ F_{st}\ (1 - F_{st})\ V_{A\times A}$, where V_A and $V_{A\times A}$ are the additive and additive × additive epistatic variances at the level of the species, respectively, plus a contribution from the dominance variance and other terms including dominance. Paradoxically, with nonadditive genetic effects, drift on average increases the amount of additive genetic variance within populations, whereas migration decreases the equilibrium amount. In the presence of nonadditive genetic effects, measurements of additive genetic variance in natural populations must be taken at the proper spatial scale with respect to natural selection, or they will provide an inaccurate description of evolutionary potential both within local populations and within the species as a whole.

Key words.—Descent measures, dominance, epistasis, extinction and recolonization, genetic variance, migration, population structure, random genetic drift.

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The amount of genetic variation in a population is determined by the interaction of the fundamental processes of evolution: selection, drift, migration, and mutation. Whereas the roles of selection and mutation have been much discussed (Lande 1976; Turelli 1984; Bulmer 1989), the effects of drift and migration on quantitative trait variation are less well known, at least in the context of nonadditive genetic interactions such as dominance and epistasis. In this paper, we investigate how drift and migration affect the amount of genetic variance within populations with dominance and epistasis.

Genetic variation for phenotypic traits has traditionally been partitioned in two ways. First, within a single population, using the methods of quantitative genetics, total genetic variation can be divided into different components such as environmental, additive genetic, dominance, and epistatic genetic variance (Falconer 1981). Second, the spatial geometry of populations can lead to nonrandom mating that causes the total genetic variance to be apportioned into variance within and among populations.

It has become clear in the past few years that the geographic structuring and the quantitative genetic partitioning of variance can interact in extremely interesting ways. A fundamental relationship between additive genetic variance and population structure was demonstrated by Wright (1951) who showed that the amount of additive genetic variance within a population decreases by a factor F relative to the total outbred population. In 1952, Robertson demonstrated that with dominance the amount of additive genetic variance in an isolated line could increase with inbreeding (see also Bryant et al. 1986; Cockerham and Tachida 1988). The conditions necessary for this increase in V_A from dominance are rather restrictive, being limited to cases in which the recessive allele is rare in the ancestral outbred

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population and to overdominant alleles. Epistatic genetic variance can also lead to increases in V_A with inbreeding (Goodnight 1988; Cockerham and Tachida 1988). The genetic conditions for changes in V_A because of epistasis are less restrictive. To date, the analyses of these sorts of changes are mostly limited to population structures without migration, extinction, colonization, or other processes common to subdivided populations in nature (but see Tachida and Cockerham 1987).

In this paper, we demonstrate that a species' genetic population structure is critical in determining the amount of V_A within local populations. We show that the spatial structure can alter the ways in which genetic variation is partitioned into additive and nonadditive components and significantly change the apparent and real opportunities for evolution. In particular, we show that nonadditive genetic variance for a character or for fitness can interact with a population structure and cause a large increase in the amount of additive genetic variance within local populations.

The Model

We derive a two-locus neutral model to describe the changes in additive and nonadditive genetic variance in a subdivided population. Our basic model of population structure is Wright's island model (Wright 1951), in which the metapopulation consists of an infinite number of demes each containing N diploid breeding individuals. Migration occurs among these demes at a rate, m; migrants are not assorted by distance, but rather each population has an equal probability of receiving migrants from any other population in the species. This population structure will be further developed to account for the extinction and colonization of local populations (following Slatkin [1977], Wade and McCauley [1988], Whitlock and McCauley [1990], and Whitlock [1992b]).

Descent Measures.—Cockerham (1984), Goodnight (1987, 1988), and Tachida and Cockerham (1987) have developed the basic machinery for describing changes in genetic variance within isolated populations. We follow these authors in defining the following descent measures (see fig. 1 for a diagram of the two-locus descent measures)

F: Wright's inbreeding coefficient. F is the probability that the two alleles at the same locus in an individual are identical by descent. In this paper, we assume that individuals mate randomly within populations, and therefore F is also the probability that any two alleles from the same locus chosen at random from a population are identical by descent.

γ: The probability that any three gametes randomly chosen from the same population carry alleles at the same locus are identical by descent.

δ: The probability that any four gametes randomly chosen from the same population carry alleles at the same locus are identical by descent.

Δ: The one-locus descent measure that gives the probability that of two pairs of randomly chosen gametes, the two alleles of

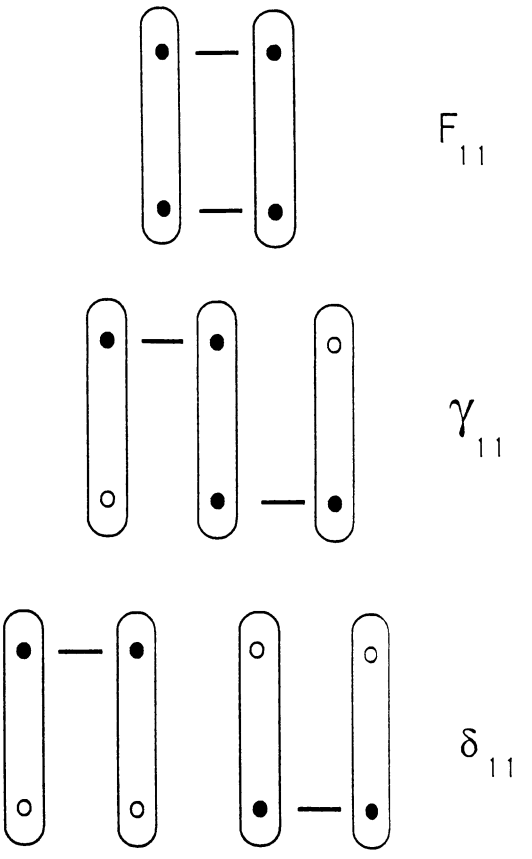

FIG. 1. The two-locus descent measures. The ellipsoids represent gametes, the small circles represent alleles at a locus, and the lines connecting alleles denote identity by descent. The three two-locus descent measures represent the probability of identity by descent for the configuration of alleles and gametes described in each cartoon.

each pair are identical by descent. The two pairs may or may not be identical with each other.

F_{11}: The descent measure for a two-locus pair analogous to F. F_{11} is the probability that two gametes chosen at random from a population carry alleles that are identical by descent for each of the two loci. This and the other measures of descent imply nothing about whether the allele at one locus is derived from the same ancestral gamete as the allele at the second locus.

γ_{11}: The probability of identity by descent for two loci when one allele is chosen from the same gamete for both loci and the other two alleles are chosen from two other gametes in the same population.

δ_{11}: The probability of identity by descent for two loci when each of the four alleles (two at each locus) are chosen from four separate gametes randomly picked from the same population.

Because of our assumption of random mating within populations, F_{11}, γ_{11}, and δ_{11} are the same whether the two gametes are chosen from the same individual or from different individuals within the same deme.

The corresponding descent measures defined by Goodnight (1987) and Tachida and Cockerham (1987) for gametes chosen from different demes (F_{B11}, γ_{B11}, δ_{B11} in Goodnight's nomenclature) are vanishingly small with the assumption of an infinite-island model, because with an infinite number of islands the probability of two individuals chosen from different demes having a common ancestor is effectively zero. This straightforward assumption greatly simplifies the cumbersome algebra of two-locus descent measures with little cost in biological generality.

Migration precedes reproduction, which occurs randomly among all individuals of the population, with selfing allowed. The two loci involved in these descent measures are allowed to recombine in all individuals at a recombination fraction, r. An infinite number of possible alleles at each locus is assumed. This two-locus model thus exactly parallels the one-locus infinite-island, infinite-allele models of population structure that have been used in the past (e.g., Maruyama 1970, Whitlock and McCauley 1990).

The transition probabilities of each descent measure can be described by a set of recurrence equations. These basic transition equations are modified from Tachida and Cockerham (1987) for the one-locus measures and from Goodnight (1987) for the two-locus measures. The one-locus equations have been modified to account for the change in the order of migration and population regulation and to include our more general model of extinction and recolonization. The two-locus measures have been modified to include migration among demes and the extinction and recolonization process. The derivation of these equations can be understood by thinking of F_{11} as a measure involving two gametes, γ_{11} as a trigametic measure, and δ_{11} as a tetragametic measure (fig. 1). For example, in the recursion for F_{11}, $1/N$ is the probability that the two gametes selected come from the same parent and $(1 - 1/N)(1 - m)^2$ is the probability that the two gametes came from two different parents in the same population. The coefficients of these two terms represent the probabilities of identity by descent for all possible recombination events weighted by the probability of recombination. γ_{11} and δ_{11} are derived similarly but are more complicated, involving three and four alleles respectively.

Fortunately, these recurrence relationships can be simply represented using a matrix formulation. Define vectors $\mathbf{F}_1 = [F, \gamma, \Delta, \delta]^T$ and $\mathbf{F}_2 = [F, F_{11}, \gamma_{11}, \delta_{11}]^T$ (where the superscript T denotes transposition). Using an additional subscript to denote the generation number, we can write

$$\mathbf{F}_{1,[t+1]} = \mathbf{A}_1\mathbf{F}_{1,[t]} + \mathbf{z}_1,$$

and

$$\mathbf{F}_{2,[t+1]} = \mathbf{A}_2\mathbf{F}_{2,[t]} + \mathbf{z}_2, \quad (1)$$

where $\boldsymbol{A}_1$ and $\boldsymbol{A}_2$ are the transitional matrices given in table 1, $\boldsymbol{z}_1$ is the vector $[1/2N, 1/4N^2, 1/4N^2, 1/8N^3]^T$, and $\boldsymbol{z}_2$ is the vector $[1/2N, 1/2N[r^2 + (1 - r)^2], 1/4N^2, 1/4N^2]$. Because the logic involved in manipulating these recurrence equations is the same for the one- and two-locus cases, we will omit the subscripts referring to the number of loci in what follows.

From equation (1), the equilibrium value for $\boldsymbol{F}$ is given by

$$\mathbf{F} = (\mathbf{I} - \mathbf{A})^{-1}\mathbf{z}, \quad (2)$$

where $\mathbf{I}$ is the four-by-four identity matrix. This solution vector is complicated when written in terms of arbitrary N, m, and r, but is easily obtained numerically by calculating $\mathbf{A}$'s and $\mathbf{z}$'s before performing the matrix operations.

Extinction and Recolonization.—It is often useful to extend the island model to account for

TABLE 1A. The one-locus transition matrix $\mathbf{A}_1$.

$(1-m)^2[(1-1/(2N)]$	0	0	0
$\frac{3(1-m)^3(2N-1)}{4N^2}$	$[(1-m)^3(1-1/N)][1-1/(2N)]$	0	0
$\frac{(1-m)^4(2N+1)(2N-1)}{4N^3}$	$\frac{2(1-m)^4(2N-2)(2N-1)}{4N^3}$	$\frac{(1-m)^4(2N-3)(2N-2)(2N-3)}{8N^3}$	0
$\frac{7(1-m)^4(1-1/(2N)}{4N^2}$	$\frac{3(1-m)^4(2N-2)(2N-1)}{4N^3}$	0	$\frac{(1-m)^4(2N-3)(2N-2)(2N-1)}{8N^3}$

TABLE 1B. The two-locus transition matrix $\mathbf{A}_2$.

$(1-m)^2[1-1/(2N)]$	0	0	0
$\frac{2r(1-r)(1-m)^2}{N}$	$\frac{[r^2+(1-r)^2]/2+(N-1)(1-r)^2(1-m)^2}{N}$	$2r(1-r)(1-1/N)(1-m)^2$	$r^2(1-1/N)(1-m)^2$
$\frac{(N-1/2)(1-m)^3}{N^2}$	$\frac{[1/4+(N-1)(1-r)/2](1-m)^3}{N^2}$	$\frac{[3(N-1)/2+(N-1)(N-2)(1-r)](1-m)^3}{N^2}$	$\frac{r[(N-1)/2+(N-1)(N-2)](1-m)^3}{N^2}$
$\frac{[1/2+5(N-1)/2+(N-1)(N-2)](1-m)^4}{N^3}$	$\frac{[1/4+(N-1)/2](1-m)^4}{N^3}$	$\frac{[3(N-1)+2(N-1)(N-2)](1-m)^4}{N^3}$	$\frac{3(N-1)/4+3(N-1)(N-2)](1-m)^4}{N^3}$ $+\frac{[(N-1)(N-2)(N-3)](1-m)^4}{N^3}$

nonequilibrium situations, such as when local populations go extinct and are colonized. Following Slatkin (1977), we define the rate of extinction per generation as e, which in a species of constant size is also the rate of colonization. Two other parameters have been shown useful for the one-locus case; k represents the number of colonists arriving in the first generation at a new population, and ϕ is the probability of common origin, that is, the probability that any two individuals came from the same source population (Whitlock and McCauley 1990). When $\phi = 1$, this corresponds to the "propagule pool" model described by Slatkin (1977), Wade (1978), and Wade and McCauley (1988), where all colonists come from the same source population. The case where $\phi = 0$ is equivalent to the "migrant pool" model of those same authors, where each colonist is chosen at random from across the entire metapopulations.

To incorporate extinction and recolonization into equation (2), we must first define the vector of identity coefficients for founding populations. The logic in the development of this vector is very similar to that in the development of the transition equations in stable populations. The colonist vector of identity coefficients is a function of the average vector of all existing source populations. The effect of extinction and colonization dynamics is to create variance in the age of populations. In the absence of other forms of variability in these populations, the average vector of identity coefficients is a simple function of the age of populations. With a constant probability of extinction we can write

$$\bar{\mathbf{F}} = \sum_{t=0}^{\infty} e(1 - e)^t \mathbf{F}_{[t]}, \tag{3}$$

where $\bar{\mathbf{F}}$ is the mean vector of identity coefficients, that is, $\mathbf{F}$ averaged over all population ages. With this vector, we can describe the vector of identity coefficients for colonists,

$$\mathbf{F}_{[0]} = \mathbf{P}\bar{\mathbf{F}} + \mathbf{b}, \tag{4}$$

where $\mathbf{b}_1$ is the vector $[1/2k, 1/4k^2, 1/4k^2, 1/8k^3]^T$; $\mathbf{b}_2$ is the vector $[1/2k, (r^2 + [1 - r)^2]/2k, 1/4k^2, 1/4k^2]^T$, and the matrices $\mathbf{P}_1$ and $\mathbf{P}_2$ are given in table 2. Note that $\mathbf{P}$ is a multiple of ϕ such that if $\phi = 0$, $\boldsymbol{P}$ is a zero matrix, and thus $\mathbf{F}_{[0]} = \mathbf{b}$. If $\phi > 0$, then the vector of identity coefficients for colonists depends upon the average identity in the extant source populations.

We can now obtain the vector of identity coefficients for an arbitrary age class of populations. The identity vector for generation t is

$$\mathbf{F}_{[t]} = \mathbf{A}^t\mathbf{F}_{[0]} + \sum_{x=0}^{t-1} \mathbf{A}^x\mathbf{z},$$

which becomes

$$\mathbf{F}_{[t]} = \mathbf{A}^t\mathbf{F}_{[0]} + (\mathbf{I} - \mathbf{A}^t)(\mathbf{I} - \mathbf{A})^{-1}\mathbf{z}, \tag{5}$$

such that the equilibrium value for the average vector of identity coefficients becomes, from equations (3) and (5),

$$\bar{\mathbf{F}} = (\mathbf{I} - \mathbf{A})^{-1}\mathbf{z} + e[\mathbf{I} - (1 - e)\mathbf{A}]^{-1}[\mathbf{F}_{[0]} - (\mathbf{I} - \mathbf{A})^{-1}\mathbf{z}]. \tag{6}$$

Defining $\mathbf{F}_{eq} = (\mathbf{I} - \mathbf{A})^{-1}\,\mathbf{z}$ as the equilibrium value for $\mathbf{F}$ in the absence of extinction and recolonization

$$\bar{\mathbf{F}} = \{\mathbf{I} - e[\mathbf{I} - (1 - e)\mathbf{A}]^{-1}\mathbf{P}\}^{-1} \{\mathbf{F}_{eq} + e[\mathbf{I} - (1 - e)\mathbf{A}]^{-1}(\mathbf{b} - \mathbf{F}_{eq})\} \tag{7}$$

Conversion of Variance.—From these descent measures and the partitioning of genetic variation in the outbred population, we can predict the changes in additive genetic variance in an inbred population owing to dominance and epistasis (Goodnight 1987, 1988; Cockerham 1984). We can derive an approximation for the contribution of the dominance terms to additive variance within populations. Following Cockerham (1984), we know that the amount of additive genetic variance after sampling is

$$\sigma^2_{A^*} = (1 - F)\sigma^2_A + 2(F - \gamma - 2\Delta + 2\delta)\sigma^2_D + 4(F - \gamma)d_1 + 2(\gamma - \delta)d_2 + 2(\gamma - \Delta)h, \tag{8}$$

where σ^2_A is the additive genetic variance, σ^2_D is the dominance variance, d_1 is the covariance of allelic additive and dominance effects, d_2 is the variance in homoallelic effects, and h is the "inbreeding depression." Although equation (8) seems extremely complicated, in the range of relatively small F ($F < 0.2$) that most concerns us here, γ and Δ are approximately equal to F^2, and δ is approximately F^3. Using these approximations, we find (as did Cockerham and Tachida 1988) that the additive variance becomes

$$\sigma^2_{A^*} \simeq (1 - F)\sigma^2_A + 2F(1 - F)[(1 - 2F)\sigma^2_D + 2d_1 + Fd_2]. \tag{9}$$

Equation (9) is a simpler function of only the dominance variance, the covariance between additive and dominance effects, and the variance in homoallelic effects.

TABLE 2A. The one-locus colonization matrix $\mathbf{P}_1$.

$\phi[1 - 1/(2k)]$	0	0	0
$\frac{3\phi^2(2k-1)}{4k^2}$	$\phi^2[1 - (1/k)][1 - 1/(2k)]$	0	0
$\frac{\phi^3(2k+1)(2k-1)}{4k^3}$	$\frac{2\phi^3(2k-2)(2k-1)}{4k^3}$	$\frac{\phi^3(2k-3)(2k-2)(2k-3)}{8k^3}$	0
$\frac{7\phi^3[1-1/(2k)]}{4k^2}$	$\frac{3\phi^3(2k-2)(2k-1)}{4k^3}$	0	$\frac{\phi^3(2k-3)(2k-2)(2k-1)}{8k^3}$

TABLE 2B. The two-locus colonization matrix $\mathbf{P}_2$.

$\phi[1 - 1/(2k)]$	0	0	0
$\frac{2r(1-r)\phi}{k}$	$\frac{[r^2 + (1-r)^2]/2 + (k-1)(1-r)^2\phi}{k}$	$2r(1 - r)(1 - 1/k)\phi$	$r^2(1 - 1/k)\phi$
$\frac{(k-1/2)\phi^2}{k^2}$	$\frac{[1/4 + (k-1)(1-r)/2]\phi^2}{k^2}$	$\frac{[3(k-1)/2 + (k-1)(k-2)(1-r)]\phi^2}{k^2}$	$\frac{r[(k-1)/2 + (k-1)(k-2)]\phi^2}{k^2}$
$\frac{[1/2 + 5(k-1)/2 + (k-1)(k-2)]\phi^3}{k^3}$	$\frac{[1/4 + (k-1)/2]\phi^3}{k^3}$	$\frac{[3(k-1) + 2(k-1)(k-2)]\phi^3}{k^3}$	$\frac{[3(k-1)/4 + 3(k-1)(k-2)]\phi^3}{k^3} + \frac{(k-1)(k-2)(k-3)\phi^3}{k^3}$

It is also possible to obtain coefficients for additive-by-additive epistasis contribution to the within-deme additive genetic variation. (Additive-by-dominance, dominance-by-dominance, and higher order epistatic interactions require the study of six or more moments and are beyond the scope of the present paper.) Goodnight (1988) obtained the coefficient of additive-by-additive variance by an analysis of the correlation between half-sibs. If we make the useful assumption that the ancestral population is completely outbred, we can write his result for the coefficient of additive-by-additive epistatic variance as

$$4F - \frac{F_{11}(1 - 2r) - \gamma_{11}(8r^2) + \delta_{11}(3 + 10r)}{1 + 2r - 2r^2}, \tag{10}$$

or more simply, in terms of identity disequilibria,

$$4F(1 - F) - \frac{(1 - 2r)\eta_F - 8r^2\eta_\gamma + (3 + 10r)\eta_\delta}{1 + 2r - 2r^2}, \tag{11}$$

where $\eta_F = F^2 - F_{11}$, $\eta_\gamma = F^2 - \gamma_{11}$, and $\eta_\delta = F^2 - \delta_{11}$ are identity disequilibrium coefficients devised by Weir and Cockerham (1969). Unless recombination is very slow, for the cases examined previously with no migration and no extinction/recolonization, these disequilibria measures are very small. Thus, this coefficient is very close to $4F(1 - F)$.

Goodnight's (1988) formulation of the additive genetic variance is a measure taken immediately after a given degree of inbreeding occurs and therefore includes correlations among relatives caused by linkage disequilibria and differences among the three two-locus descent measures. Cockerham and Tachida (1988) have derived the contribution of epistatic variance before inbreeding to the permanent response to selection; that is, they have examined the correlations among relatives separated by sufficient time for such disequilibria to have dissolved. The contribution of epistatic variance to the additive variance involved in this permanent response was found to be $4(F - \delta_{11})$. Cockerham and Tachida observe that this quantity is approximately equivalent to $4F(1 - F)$, which is the same value we have derived here for the approximation derived from Goodnight's immediate correlation among half-sibs. The value corresponding to permanent response to selection is perhaps more pertinent for determining the possible outcomes of an evolutionary trajectory, whereas the value derived from the short-term correlation of relatives is more valuable for interpreting the results of laboratory experiments and more closely will predict what we should expect to see in natural populations. That the value for these two measures is approximately the same allows us to use the results of short-term inbreeding experiments to predict long-term changes in additive variance.

The F in these approximations corresponds exactly to the F_{ST} commonly estimated in natural populations from Wright's F-statistics, the standardized allelic variance among populations. Hence, most of the complexity in the previous models of changes in epistatic variance is unnecessary for most cases; we need consider only Wright's inbreeding coefficient to understand most of the change of epistatic variance to additive variance. As we shall see later, the identity disequilibria are very small in the case of Wright's island model as well.

Results

Although the exact model we have presented here is complex, the main implications can be illustrated graphically by example. In this section, we emphasize the accuracy of the approximations derived in the previous sections, in particular, the approximations in terms of F for the coefficients for conversion of dominance and epistatic variance in the metapopulation into additive variance within local populations. Under most circumstances, the approximations work well, for both steady-state populations and also for populations that undergo occasional local extinction and recolonization.

We will demonstrate the effects of epistasis and dominance separately for clarity. Recall that the amount of additive genetic variance in a subpopulation is composed of contributions from the additive variance, the dominance variance and covariances, and the epistatic variance in the metapopulation. In standard theory, the contribution to additive variance within a local population is $(1 - F)$ multiplied by the amount of additive variance in the metapopulation.

Dominance.—With dominance, or allelic interaction within loci, drift changes the amount of additive genetic variance within populations. Drift converts dominance variance at the level of the metapopulation into additive genetic variance within local demes. The exact amount of additive genetic variance that results from dom-

inance effects involves several parameters that are difficult if not impossible to measure. The approximation given earlier involves only the dominance variance, the term d_1, the covariance between additive and dominance effects, and d_2, the variance in homoallelic effects. Figure 2 demonstrates a simple example of the conversion of variance for a biallelic case of recessive gene action. Rare recessive alleles are believed typical of the kinds of genes contributing to inbreeding depression (Charlesworth and Charlesworth 1987), as would be expected if deleterious alleles are maintained at low frequencies by mutation-selection balance. Thus, the same alleles that contribute to inbreeding depression in fact create a circumstance for a large percent change in additive variance. This example demonstrates that the approximation from equation (9) works very well in the parameter range where F is approximately less than 0.25. Above this range, the assumptions that γ and Δ are approximately F^2 and δ is approximately F^3 are no longer valid.

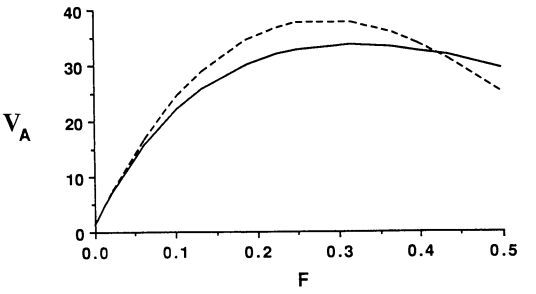

FIG. 2. The amount of additive genetic variation within local populations when variation is caused by rare recessives. The amount of V_A is standardized against $V_A = 1$ in the metapopulation, such that the vertical axis represents the ratio of V_A within populations over V_A in the species. For this example there are two alleles, one of which is at a frequency of 0.99 and is completely dominant over the other. (The variance components for this case are calculated from the Building Block model of Tachida and Cockerham 1989.) The solid line represents the exact solution, and the dashed line is the approximation given in equation (9). The amount of additive genetic variation within populations can be significantly larger than the amount in the metapopulation because of interaction of dominance and drift.

Extinction and recolonization of local populations also affects the one-locus descent measures. However, even high extinction and recolonization rates do not change the conversion of dominance effects to additive variance, for a given value of F. This constancy is much greater than the constancy with the approximations in terms of powers of F given above. Most of the effects of colonization can be predicted directly and simply by knowledge of the changes in F alone.

Epistasis.—Epistatic variance at the level of the metapopulation contributes to additive variance within populations, as well. Figure 3 plots the conversion coefficient, that is, the fraction of the epistatic variance of the metapopulation that is converted to additive variance within demes. This graph has several interesting features. First, the maximum contribution epistatic conversion coefficient occurs when F is near 1/2. The coefficient has a maximum at $F = 0.5$, because it is here that on average one out of two loci are fixed, with the other left to vary.

Second, the coefficient changes very little from $r = 0.5$ to $r = 0.1$, but there is quite a large difference between $r = 0.1$ and $r = 0$. Close linkage gives a pattern more similar to free recombination than to complete linkage. When $r = 0$, there is no meaningful sense in which the two "loci" are in fact separate or in which epistasis is measurable; here F_{11} reduces to F. As the recombination fraction gets small, alleles at the two loci experience random genetic drift less independently; that is, the drift at one locus is less likely to change the genetic context of the other locus. Thus, less epistatic variance is converted to additive variance with tight linkage, but as can be seen from equation (11), the lower limit on the conversion coefficient, even with complete linkage, is approximately $3F(1 - F)$. In natural systems, interacting genetic loci are sometimes tightly linked. Close linkage requires the exact formulae for quantitatively predicting the effects of epistasis and intense inbreeding on the immediate response to selection. Most pairs of loci are of course on average not very close; the extent to which epistatic interactions depend upon tight linkage is not known. For the values of F that are usually found in natural species ($F_{st} < 0.2$, see Hedrick and Levin 1984; McCauley and Eanes 1988), the approximations we have derived here work well even when the recombination rate between the loci is less than 0.1 (figs. 3, 4). The approximations given here work best in exactly the situations likely to be encountered in natural populations: most loci are not tightly linked and most real values of F_{st} are not very large.

It is clear that the approximation give by $4F(1 - F)$ is quite good. The maximum error possible is 33%, which occurs in the limit when the re-

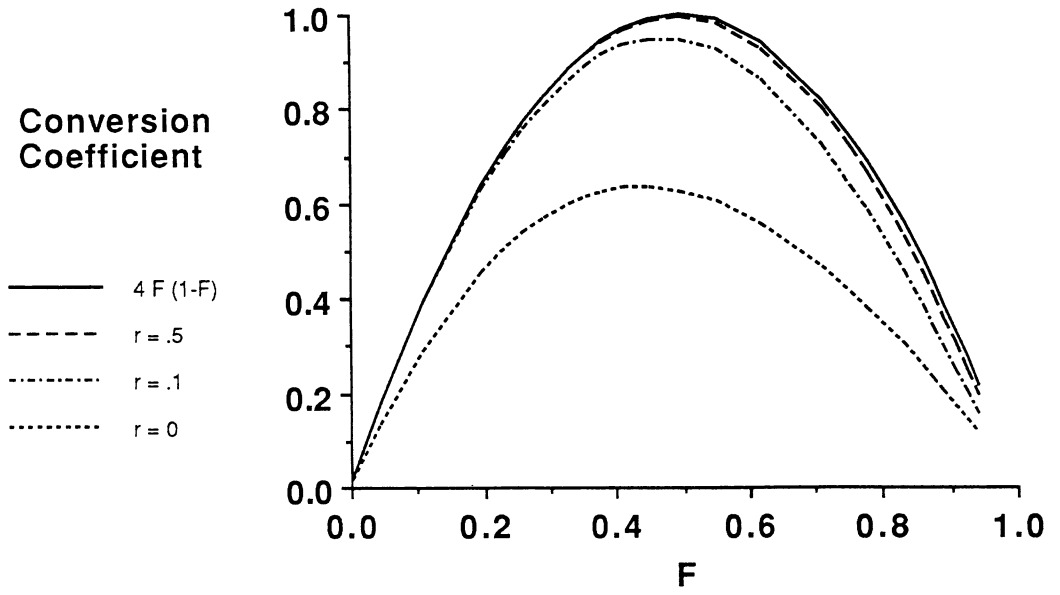

FIG. 3. The coefficient for converting epistatic genetic variance in the metapopulation to additive genetic variance within populations. The large dashed line is the approximation $4F(1 - F)$; the other lines are the exact values for differing values of the recombination rate. In this graph the migration rate is set $m = 0.005$, with N ranging from 3 to 10,000. An almost identical graph can be drawn with population size held constant and migration rate allowed to vary.

combination fraction becomes zero. When r becomes larger, the error is typically less than 2%–3%. The error increases when the migration rate is very high. The reason for this is straightforward. When the migration rate is high, many of the individuals in a population are immigrants and have no probability of identity with the resident individuals at either locus. This creates a short-term identity disequilibrium that causes slightly less of the epistatic variance to be converted to additive variance.

If local populations are subject to extinctions and subsequent recolonizations, the probabilities of identity by descent are changed, sometimes significantly. Fortunately, though, the approximation in terms of $4F(1 - F)$ is still quite accurate (fig. 4). The error of the approximation is somewhat higher in the case of extinction and recolonization than in the steady state model, but most of the variance in the change of the coefficient is caused by changes in F, not changes in the details about how the F was created.

DISCUSSION

Population structure can change many aspects of a species' evolutionary profile. In particular, variance among populations in the genotype frequencies of local populations can cause large changes in the real and apparent properties of the heritability of characters within local populations and in the partitioning of genetic variance in the species as a whole. We have shown that the changes in variance associated with population structure are such that the amount of additive genetic variance present in a local population is generally much larger if there is nonadditive genetic variance in the species than if there is not.

We have shown that the approximate conversion coefficient, $4F(1 - F)$, is accurate in reasonable cases. If the recombination rate exceeds 0.05 and migration is not extremely high, then the error of this approximation is trivial. The benefits of such approximation are obvious: population geneticists have been for years theoretically and empirically studying the effects of various population structures on F_{st}. The approximation tells us that for genes that are not tightly linked, we do not need more complicated analyses of multiple locus genotypes to understand quite well the probable amount of additive variance in a subdivided population; a simple measure of F_{st} is enough.

It is interesting to note that in the process we have described here, migration not only opposes drift at the two-locus level, but also may coun-

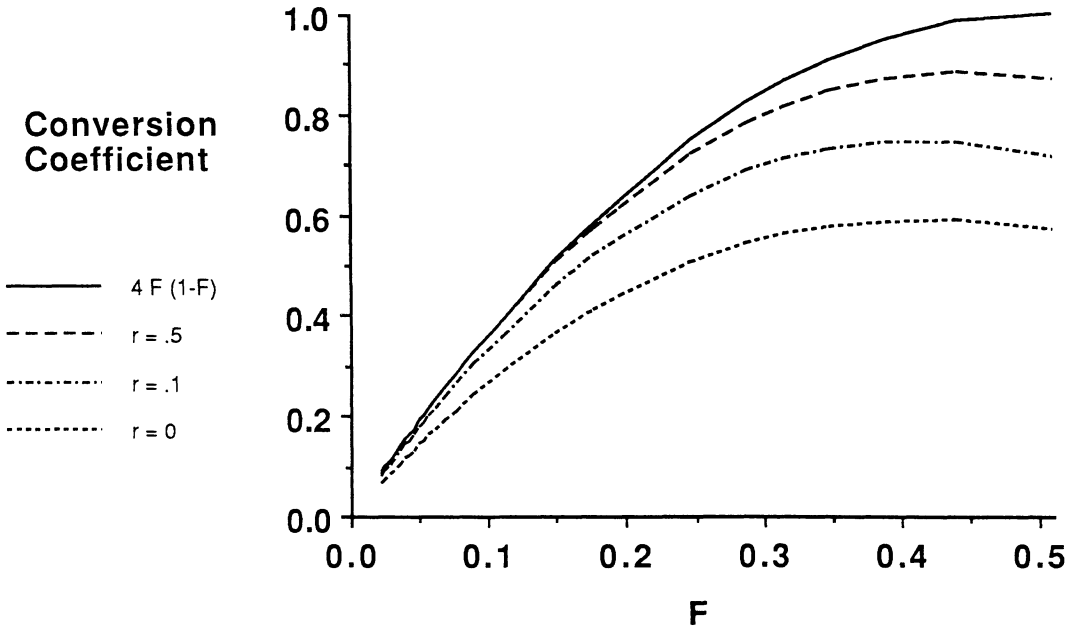

FIG. 4. The coefficient for converting epistatic genetic variance in the metapopulation to additive genetic variance within populations when local populations undergo extinction and recolonization. The large dashed line is the approximation $4F(1 - F)$; the other lines are the exact values for differing values of the recombination rate. In this graph, the migration rate is set $m = 0.05$, with N ranging from 3 to 10,000, $e = 0.05$, $\phi = 0$, and $k = 8$.

teract the increases in additive variance that migration causes at the single-locus level. As new migrants come into a local population, the allele frequencies in that population become more similar to those in the metapopulation. If in the metapopulation the frequency of an allele is such that its contribution to variance in effects is mostly nonadditive, then in the local population migration will convert additive variance into nonadditive genetic variance, even as drift drives the conversion in the opposite direction. This sort of conversion underlines the complexity illustrated by our models. In the traditional view, migration brings in new variants from other populations, and therefore increases the amount of genetic variation in a local population. However, we have shown that migration changes the genetic background for certain alleles and converts additive genetic variance back into nonadditive genetic variance. The balance between these roles for migration depends upon the relative amounts of additive and nonadditive genetic variation and, to a certain extent, upon the level of migration.

The neutral models we have given here lend some insight into the evolutionary dynamics of weakly selected gene loci. Kimura (1983, p. 146) has shown that when the product of the effective population size and the strength of stabilizing selection per locus is small, the dynamics of allele frequency change are very similar to a set of completely neutral alleles. Therefore, as long as N is small, and there is any genetic variance in the species, local populations will display additive genetic variance in spite the tendency of selection to eliminate variance. In the absence of drift, Bazykin (1973) and Phillips (1993) have shown that subdivision can permanently maintain variation if migration is weak enough relative to the strength of selection.

We have assumed a lack of mutation in these models. Lande (1992) has recently shown that the amount of additive genetic variance in a local population can be larger than that expected from the traditional Wright model even in the absence of nonadditive genetic variance if mutation is taken into account. It is unknown how mutation will affect the sort of conversion that we describe, but we can predict that the amount of additive genetic variance in subdivided populations under a mutation-selection balance would be greatly increased from the traditional expectation. This is because mutation causes increases in local

variance as described by Lande and because two-locus drift causes the nonadditive variance left by selection at the species level to be converted to local additive genetic variance, which is relatively immune to selection.

It would be useful if the descent measures developed here could be tools in the empirical study of the effects of extinction and recolonization, particularly to determine the extent to which the process of population turnover affects the genetic variance among populations (for examples, see McCauley 1989 and Whitlock 1992a). Unfortunately, the very properties of these descent measures that make them easy to approximate for a wide variety of circumstances also make them ineffective for distinguishing the effects of extinction and recolonization from the equilibrium processes of migration and drift. Figures 2 and 4 have shown that for reasonable values of F, the mode of population structure has little effect on the relationship between F and higher moments of the gene frequency distribution. Therefore, estimated values of F and the higher order descent measures probably cannot be used to distinguish equilibrium from nonequilibrium population structures.

The general pattern we have described here is that the amount of additive genetic variance within a local population can be very different from the amount in the metapopulation as a whole. In fact, the amount of additive genetic variance in the metapopulation need tell us nothing about the amount of additive variance within local populations, and vice versa. Paradoxically, for characters that have large nonadditive genetic components and not much additive genetic variance, perhaps like fitness components in many species, there can be much more additive genetic variance within a local population than in the species as as whole. The amount of additive genetic variance can actually increase as the "fixation index" increases. This seemingly counterintuitive result occurs because of the definitions of additive effects; alleles that globally have only a small additive excess because of the average genetic context in the species can have larger main effects when they are found in the context of a subpopulation where the allele frequencies of that and other loci have been allowed by small population size to drift from the global means. For this reason, we must be very careful to measure genetic parameters at precisely the right level of the genetic hierarchy. We also expect that the degree of population structure in a species may have a large role in the structure and maintenance of genetic variance.

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