The Effective Size of a Subdivided Population

Michael C. Whitlock and N. H. Barton*

*Department of Zoology, University of British Columbia, Vancouver, BC V6T 1Z4 Canada and *Institute of Cell, Animal and Population Biology, University of Edinburgh, Edinburgh EH9 3JT, United Kingdom*

ABSTRACT

This paper derives the long-term effective size, N_e, for a general model of population subdivision, allowing for differential deme fitness, variable emigration and immigration rates, extinction, colonization, and correlations across generations in these processes. We show that various long-term measures of N_e are equivalent. The effective size of a metapopulation can be expressed in a variety of ways. At a demographic equilibrium, N_e can be derived from the demography by combining information about the ultimate contribution of each deme to the future genetic make-up of the population and Wright's F_{ST}'s. The effective size is given by $N_e = 1/(1 + \text{var}(\vartheta))\langle(1 - f_{STi})/N_i n\rangle$, where n is the number of demes, ϑ_i is the eventual contribution of individuals in deme i to the whole population (scaled such that $\Sigma_i \vartheta_i = n$), and $\langle\ \rangle$ denotes an average weighted by ϑ_i^2. This formula is applied to a catastrophic extinction model (where sites are either empty or at carrying capacity) and to a metapopulation model with explicit dynamics, where extinction is caused by demographic stochasticity and by chaos. Contrary to the expectation from the standard island model, the usual effect of population subdivision is to *decrease* the effective size relative to a panmictic population living on the same resource.

MOST species are divided into local populations, to some degree. These populations do not necessarily follow the simple assumptions of the usual models of population structure, such as the island model; instead, natural populations vary through time and space in all of the important parameters, such as population size, fitness, and emigration and immigration rates. Furthermore, demes can go extinct and recolonize. The complicated population structure that results affects many aspects of a species' evolution (BARTON and WHITLOCK 1996). In particular, the effects of subdivision on the maintenance of genetic variation are important both for understanding how natural populations evolve (WRIGHT 1931, 1939; PROVINE 1986) and for designing efficient methods of artificial selection (ROBERTSON 1961; CABALLERO et al. 1991). In this paper, we investigate the long-term effects of drift on neutral variability, as described by the effective size of species, N_e.

There are many reasons to care about the effective population size. The loss of neutral variability, while in itself somewhat interesting, is often used as a barometer for all of the genetic variation of a species, a metric often applied in conservation biology (LANDE and BARROWCLOUGH 1987). The effective population size is important in determining the rate of allelic substitutions, for neutral, deleterious and favorable mutations. While the effective size does not predict all of the behavior of the fixation of favorable alleles in subdivided popula-

tions, it does serve as a good first approximation (BARTON 1993; CABALLERO 1994). Furthermore, the effective size tells us about the limits to natural selection, as alleles whose advantage is such that $N_e s < 1$ are very likely to be lost due to drift (MARUYAMA and KIMURA 1980), and deleterious alleles are more likely to be fixed in smaller populations (KONDRASHOV 1995; LYNCH et al. 1995).

There is a large literature on the effects of subdivision on the long-term rate of drift at the metapopulation level, for both stepping-stone and island models (e.g., MARUYAMA and KIMURA 1980; NAGYLAKI 1980, 1986; EWENS 1989). However, this is restricted to either fixed deme sizes (WRIGHT 1939), random extinctions followed by immediate return to a fixed size (SLATKIN 1977; EWENS 1989, Model 1), or uncorrelated changes in population size (MARUYAMA and KIMURA 1980). EWENS (1989, Model 2) also discusses a model with an explicit population growth of one individual per generation following a founding event of one individual, but without subsequent migration.

In this paper, we present methods for calculating the effective population size with variable deme size and migration rates, local extinction, and colonization. Since there is substantial disagreement in the literature, we begin by discussing alternative definitions of "effective size". We then lay out a general framework and, by making a series of more restrictive assumptions, describe specific population structures. The effects of catastrophic local extinction are investigated explicitly in a two-state model, where patches are either extinct or occupied at a constant carrying capacity. For this model,

Corresponding author: Michael Whitlock, Department of Zoology, University of British Columbia, 6270 University Blvd., Vancouver, BC V6T 1Z4 Canada. E-mail: whitlock@zoology.ubc.ca

the effective size can be calculated for a variety of colonization patterns. We then present another model that follows explicit local population dynamics, in which extinction occurs through demographic stochasticity, possibly aided by chaotic fluctuations. For these models, the effective size can be given in terms of F_{ST} and the distribution of deme size, quantities that are in principle measurable.

DEFINING EFFECTIVE POPULATION SIZE

The "effective population size" is defined as the size of an idealized Wright-Fisher population, which would give the same value for some specified property as in the population in question (CROW and KIMURA 1970). (For simplicity, we allow selfing in this idealized population; sometimes, N_e is defined with respect to a population with no selfing. See CABALLERO 1994, p. 659). There are many effective population sizes, depending on which genetic property is considered: for example, the increase in variance in allele frequency, the balance between mutation and drift, degree of inbreeding, etc. In general, the relation between these various measures depends on the model, and so the corresponding effective sizes can differ from each other (EWENS 1979; GREGORIUS 1991; CHESSER 1993; CABALLERO 1994). In structured populations, for example, the homozygosity, the rate of change in the genetic variance, or fixation rates can change through time in different ways, even when the demographic structure is held constant; this is because the partitioning of genetic variance within and among populations can change through time (EWENS 1979, 1982; CHESSER et al. 1993). This can be understood by looking at the rate at which lines of descent coalesce into their common ancestral lineage as one looks backward in time. In a single panmictic population of N diploids, lineages coalesce with constant probability $1/2N$ per generation. In a subdivided population, in contrast, lines of descent coalesce more rapidly while they remain within the same deme, and more slowly thereafter (NEI and TAKAHATA 1993; SLATKIN 1991). Thus, the probability of fixation of favorable genes (BARTON 1993) and the rate of shifts between adaptive peaks (BARTON and ROUHANI 1991) depend on population structure differently from neutral variability. Nevertheless, the long-term effects of drift on neutral or weakly selected alleles can be summarized by a single effective size. Moreover, if the population is large enough that random drift occurs much more slowly than migration, this long term state takes a particularly simple form.

We begin by considering, in a general way, how the probability of identity by descent changes through time. We then show that, in the long term, other properties of genetic drift, which describe other kinds of effective size, are described exactly by these changes in the probability of identity by descent, so that the various mea-

sures eventually become equivalent. The probability of identity by descent is defined as the chance that two genes are descended from the same gene in some ancestral population (MALÉCOT 1948; CROW and KIMURA 1970); it is thus defined relative to this arbitrarily chosen reference population. It is important to distinguish identity by descent (which describes the structure of the genealogy and is independent of mutations that may change the allelic state of the genes) from identity in state (which describes the chance that two genes are in the same allelic state and therefore depends on the mutation process). Changes in identity by descent are due to the coalescence of lineages, and the rate of change in probability of identity by descent gives the distribution of coalescence times. Thus, once identity by descent is understood, identity in state can be derived from it by overlaying the appropriate model of mutation on the genealogy (HUDSON 1991; SLATKIN 1991). We denote identity by descent by F, and identity in state by f, throughout.

Consider now a structured population, in which genes can be in various different sites, labeled i. These "sites" might refer to demes, habitats, sexes, genetic backgrounds, or whatever; we return to their interpretation below. Let $F_{ij,t}$ be the probability that a gene chosen at random at time t from site i is identical by descent to a gene from site j in the same generation, relative to a reference population at $t = 0$. Thus, $F_{ij,0} = 0$, by definition. If the two genes come from the same site ($i = j$), in any generation, they are taken to be distinct. We suppose that identity by descent changes according to a linear recursion, of the form

$$1 - F_{ij,t+1} = \sum_{k,l} G_{ij,kl}(1 - F_{kl,t}). \qquad (1)$$

The use of such matrices was introduced by HILL (1972; see also CHARLESWORTH 1994). For this representation to give a complete recursion for the dynamics, the genes must be assigned to sites such that all the genes within each site are equivalent to each other. Here, $G_{ij,kl}$ is the chance that a gene in i is descended from a gene in k, and that a gene in j is descended from a distinct gene in l; these two probabilities may not be independent. G can be thought of as a two-dimensional matrix with all of the combinations of ij on one axis and all of the combinations of kl on the other. For the Wright-Fisher model, there is only one site; $G = (1 - 1/2N)$. In general, $G_{ij,kl}$ depends on the deme sizes and migration rates (see Equations 3 and 4 below) and may vary through time.

Under what circumstances can the complex dynamics of identity by descent, as given by Equation 1, be described by a single effective size? If the matrix G is fixed, then in the long term, lineages will coalesce at a rate given by the leading eigenvalue of G, λ_1. (We consider ways of dealing with varying G in the next section). This long term rate of coalescence (or inbreeding) defines

a natural measure of the effective size, through $\lambda_1 = (1 - 1/2N_e)$. Note that λ_1 is the leading eigenvalue of the matrix $\mathbf{G}$, which determines the increase in identity by descent. We will argue that this is necessarily equal to the leading nonunit eigenvalue of the transition matrix that gives the change in the distribution of allelic states. Therefore, the corresponding N_e is the eigenvalue effective size defined by EWENS (1979, 1982).

The probabilities of identity among the various genes will converge to $F_{ij,t} = 1 - \gamma_{ij,1}\lambda_1^t$, where $\gamma_{ij,1}$ is the leading eigenvector of $\mathbf{G}$ (see APPENDIX). Thus, the probabilities of identity depend on the locations of the genes. However, an asymptotic "effective size" can still be defined through $\Delta F_{ij} = (F_{ij,t+1} - F_{ij,t})/(1 - F_{ij,t})$, which will converge to $(1 - \lambda_1) = 1/2N_e$ for arbitrary i, j (see the APPENDIX). This is equivalent to the effective size of WRIGHT (1931), the "effective number for random extinction" introduced by HALDANE (1939), the "inbreeding effective size" used by CABALLERO (1994, p. 658), and the "asymptotic effective size" of CHESSER et al. (1993). It is also equivalent to the effective sizes derived by considering the long-term contribution of individuals to a structured population (ROBERTSON 1961; HILL 1972, 1979; CHARLESWORTH 1994; SANTIAGO and CABALLERO 1994). However, the inbreeding effective size is usually defined through the probability of identity by descent through a common ancestor in the previous generation (e.g., WRIGHT, 1939; CROW and KIMURA 1970; EWENS 1979). This can be quite different in a subdivided population and is not further considered here.

The mutation effective size is defined through the probability of identity in state, f_{ij}, under the infinite alleles model with mutation rate μ. In the long term, f_{ij} approaches $\gamma_{ij,1}(1 - \lambda_1)/(1 - \lambda_1(1 - \mu)^2)$, and so varies depending on the locations of the genes (APPENDIX). If one identifies the average identity in state in the Wright-Fisher model with that calculated by taking the average of f_{ij} across all pairs of genes, this yields an effective size which in general will differ from the inbreeding effective size defined above.

Next, consider the rate of increase of variance in allele frequency, V. A simple argument shows the exact relationship with identity by descent. Suppose that each gene is labeled by $X = 1$ if it carries allele P, and 0 otherwise. The allele frequency is given by the average of the X's, and so the variance in allele frequency is the sum of covariances between all pairs of X's (including each X paired with itself). The covariance contributed by a pair of genes is $p(1 - p)$ if they are identical by descent, and zero otherwise; p is the allele frequency in the ancestral generation. Hence, the variance is equal to $p(1 - p)F_t$, where F is the average of F_{ij} across all pairs of genes. The long-term rate of increase in variance $(\Delta V = (V_{t+1} - V_t)/(p(1 - p) - V_t))$ is necessarily the same as the long-term rate of increase of identity and would define the same effective size.

Finally, consider the eigenvalue effective size. This is defined by the largest nonunit eigenvalue, λ_1^*, of the transition matrix, which gives the chance that the population will change from one configuration of allelic states to another. In a panmictic population with $2N$ genes and two alleles, there are $(2N + 1)$ states; however, in a structured population with n demes each of $2N$ biallelic genes, there are $(2N + 1)^n$ states. Denote each state by α, and let the probability distribution at time t be $\psi_{\alpha,t}$. In the long term, this approaches $\psi_{\alpha,t} = \gamma_\alpha\lambda_1^{*t} + u_0\psi_0, + u_1\psi_1$, where γ_α is the eigenvector corresponding to λ_1^*, u_0 and u_1 are the probabilities of global loss and fixation, and ψ_0, ψ_1 are the corresponding ultimate probability distributions. (We assume that the nonunit eigenvalues are distinct and that ultimately only global loss or fixation are stable). Now, the probabilities of identity by descent between pairs of genes (or indeed, any set of genes) is determined by the distribution of states, $\psi_{\alpha,t}$: By reversing the argument of the previous paragraph, we have that $F_{ij,t}$ is the covariance between allelic states, divided by $p(1 - p)$. Since the covariance is a linear function of $\psi_{\alpha,t}$, the long-term increase in inbreeding is therefore given by the leading nonunit eigenvalue of the transition matrix. The eigenvalue effective size defined by the full transition matrix is therefore equal to that defined by the much simpler matrix $G_{ij,kl}$, which only accounts for pairwise identities.

We have shown that for an arbitrarily structured population, a single effective size gives the asymptotic rate of increase in inbreeding and gene frequency variance. The mutation effective size will differ, unless there are no correlations across generations in reproductive success. However, we concentrate attention on the case in which the population consists of so many demes that drift acts slowly relative to migration. In this case, we show that the probability of identity between genes from different demes converges to a constant, independent of location. This is because lineages typically trace back through very many demes before coalescing, so that the chance of i.b.d. becomes independent of which demes are involved. Therefore, mutation effective size becomes independent of how identity in state is weighted and equivalent to the other long-term measures.

We have shown that the change in the probability of identity by descent gives enough information to define the variance, inbreeding, and eigenvalue effective population sizes. In an ideal population, the change in identity by descent in one generation is given by

$$\Delta \bar{F} = (1 - \bar{F})/2N_e. \quad (2)$$

In more complicated models, the asymptotic value of this quantity defines the effective population size.

Correlations in reproductive success across generations: The key difficulty in deriving effective population size estimates for structured populations is that variation in the qualities of a deme may persist, so that

the reproductive success of alleles is correlated across generations: alleles that happen to be found in demes that are increasing in size will increase in frequency and will tend to continue to increase. Therefore, the rate of drift will be greater in the long run than expected from simple extrapolation of single generation effects, and the long-term effective size will be smaller, in a way that depends on just how reproduction and migration are correlated across generations.

These correlations could be dealt with in two ways. First, the matrix $\mathbf{G}$ in Equation 1 may be taken as fluctuating through time. If these fluctuations are cyclic, then $\mathbf{G}$ can be replaced by its product across a complete cycle; the long-term change in identity by descent, and hence the effective size, is given by the leading eigenvalue of this matrix. If fluctuations are stochastic, it is still possible to find the long-term rate of change by taking expectations of the asymptotic rate of change of identity across the distribution of demographies (assuming that this is stationary). The next few sections of this paper will use recursions of the probability of identity to give general formulae for effective size. Calculations can be simplified by reclassifying sites so as to allow a fixed recursion from one generation to the next. For example, we will consider a model where the fate of a deme depends solely on its present size. Then, probabilities of identity also depend on the sizes of the demes involved, and so a fixed recursion is found if identities are classified according to deme size, rather than referring to particular pairs of demes. This approach could be extended to more complex structures, for example, where population dynamics vary with the amount of some limiting resource.

THE EFFECTIVE SIZE OF METAPOPULATIONS WITH VARIABLE LOCAL POPULATION SIZE AND MIGRATION RATES

We will describe a general model with few assumptions and gradually increase the number of assumptions to allow further analysis. We begin by deriving the effective population size for a general model in two ways: first, by considering the increase in the average identity as a function of all of the events that occur in a generation, and second, by considering the ultimate contribution to the gene pool of any event changing allele frequency within a deme. Finally, we consider a generalized island model, in which migration is via a single gene pool. In the following sections, we apply these results to two examples.

A general model of population structure: Consider a set of n sites: we will refer to these as demes, but the same analysis would apply to alternative genetic backgrounds. Their overall number, n, is fixed, but since we allow empty sites, this is not restrictive. Reproduction (including density-dependent growth and decline) is followed by migration. In this and all subsequent sec-

tions, reproduction within demes follows the Wright-Fisher model. Identities by descent at the beginning of the generation are denoted by F_{ij}; after reproduction, by F_{ij}^*; and after migration, by F_{ij}'. We choose to count the population immediately after migration, because in the model of explicit population dynamics it is convenient to combine the two stochastic processes of reproduction and migration. The generations are nonoverlapping, and the various events in each deme occur synchronously. With these assumptions, it is easy to write recursions for the probabilities of identity of alleles chosen at random from within any given deme or from any two demes.

The recursion for the probability of identity by descent is straightforward. Letting i, j, and k represent different demes in the metapopulation, we can define the probability of identity of an allele chosen at random from deme i and deme j as F_{ij}. The immigration rate from deme j to deme i is m_{ij}; $m_i = (1 - m_{ii}) = \Sigma_{j \neq i}\, m_{ij}$ is the total rate of immigration into i, measured at the end of the life cycle. The migration matrix $\mathbf{m}$ is defined as having elements m_{ij}.

The probability of identity by descent for alleles chosen at random from different demes is

$$F_{ij}' = \sum_{k,l} m_{ik}m_{jl}F_{kl}^* = \mathbf{m}\mathbf{F}^*\mathbf{m}^T, \qquad (3)$$

where

$$F_{ii}^* = \frac{1}{2N_i} + \left(1 - \frac{1}{2N_i}\right)F_{ii}, \qquad (4a)$$

$$F_{ij}^* = F_{ij} \quad \text{for } i \neq j. \qquad (4b)$$

Note that in these equations the immigration rate is allowed to equal 1, which is equivalent to extinction and recolonization of a deme. Each of the parameters in Equation 3 (and what is to follow) can be written with a subscript t to indicate the specific value for that parameter in the tth generation. The overall average probability of identity for alleles chosen at random from the metapopulation, $\bar{F}$, is

$$\bar{F} = \sum_i \sum_j \frac{N_i N_j F_{ij}}{n^2 \bar{N}^2}, \qquad (5)$$

where n is the number of demes in the metapopulation and $\bar{N}$ is the mean number of individuals per deme. Consider the increase in average identity. The average identity after one generation, $\bar{F}'$, is found by substituting Equation 3 into Equation 5:

$$\bar{F}' = \sum_i \sum_j \frac{N_i' N_j'}{n^2 \bar{N}^2} \sum_k \sum_l m_{ik}m_{jl}F_{kl}^*. \qquad (6)$$

The analysis is simplified by defining the number of individuals produced by deme k in the next generation, $N_k^* = \Sigma_i\, N_i' m_{ik}$. This includes the genes that remained in k, plus all those genes that emigrated successfully to

other demes. Notice that for all of the N_i^* descendants of a deme, the distribution of identity is the same. The change in $\bar{F}$ is thus

$$\Delta\bar{F} \equiv \bar{F}' - \bar{F} = \sum_i \sum_j \frac{N_i^* N_j^* F_{ij}^* - N_i N_j F_{ij}}{n^2 \bar{N}^2}$$

$$= \sum_i \frac{N_i^{*2}(1 - F_{ii})}{n^2 \bar{N}^2 (2N_i)} + \sum_i \sum_j \frac{(N_i^* N_j^* - N_i N_j) F_{ij}}{n^2 \bar{N}^2} . \quad (7)$$

The first term on the right gives the increase in identity due to drift within demes, while the second gives the increase due to the variation in reproductive success across demes. Generalizing Wright's F_{ST} coefficient, we can write the correlation of allele frequency within and among demes as $\rho_{ij} = (F_{ij} - \bar{F})/(1 - \bar{F})$ (where $\rho_{ii} = F_{ST}$ is Wright's F_{ST} for the ith deme). From the definition of $\bar{F}$, $\sum_i \sum_j \rho_{ij} = 0$. Define $w_i = N_i^*/N_i$, a measure of the relative contribution of deme i to the next generation; since we assume demographic equilibrium, $\sum_i w_i N_i = \sum_i N_i$. Then

$$\frac{\Delta\bar{F}}{1 - \bar{F}} = \sum_i \frac{N_i w_i^2 (1 - F_{ST,i})}{2n^2 \bar{N}^2} + \sum_i \sum_j \frac{w_i w_j N_i N_j \rho_{ij}}{n^2 \bar{N}^2} . \quad (8)$$

Since the definition of effective size is given by $\Delta\bar{F} = (1 - \bar{F})/2N_e$ (Equation 2), Equation 8 gives N_e, such that

$$N_e = \frac{\bar{N}n}{\displaystyle\sum_i \frac{N_i w_i^2 (1 - F_{ST,i})}{n\bar{N}} + 2 \sum_i \sum_j \frac{w_i w_j N_i N_j \rho_{ij}}{n\bar{N}}} . \quad (9)$$

Note that the derivation of this equation makes no assumptions about the nature of migration. In the short term, when the dynamic equilibrium of genetic correlations and demography has not been reached, the effective size defined by Equation 9 may vary. However, as argued above, it will eventually converge to a steady value.

This formulation of the solution has one major advantage: all of the parameters of this model are measurable in a single generation. The ρ_{ij}'s can be measured from the same genetic data as F_{ST}'s, and the reproductive success values are for a single generation's transition. Thus Equation 9 can be used to estimate N_e for a population in nature, if enough demographic data and genetic data are taken from a single generation.

Some special cases: We can now use these equations to investigate several special cases. For the standard island model with constant population size, $N_i^* = N_i = \bar{N}$ for all i, and $\rho_{ij} = -F_{ST}/(n - 1)$ for all $i \neq j$. Thus the effective size for an island model is $N_e = \bar{N}n/(1 - F_{ST})$, as has been shown previously (WRIGHT 1939). This also holds for the standard one- or two-dimensional stepping stone models, provided that deme size is constant in space and time; since $\sum_{j\neq i} \rho_{ij} = -F_{ST}$, the effective size is also $N_e = \bar{N}n/(1 - F_{ST})$.

A simple value for N_e can be derived for the case where each deme has exactly the same size, but contributes unequally to the next generation via migration. In this case all $N_i = \bar{N}$, but there is variance in the N^*'s. Let the variance among demes in allelic fitness be V. Then, for the simplified case where there is no correlation between w and F_{ST}, $\rho_{ij} = -F_{ST}/(n - 1)$, for $i \neq j$. We can then write

$$N_e = \frac{Nn}{(1 + V)(1 - F_{ST}) + 2NF_{ST}Vn/(n - 1)} , \quad (10)$$

which reduces to the island model result above. If one works in terms of the variance of allele frequency, rather than the rate of increase in identity by descent, then one can show that Equation 10 gives the variance of the change in mean allele frequency from one generation to the next, provided that the allele frequency fluctuations are uncorrelated through time, as is assumed in Equation 10.

If the level of population differentiation has reached its maximum, with $F_{ST} = 1$, then Equation 10 reduces to $N_e = (n - 1)/2V$. This is equivalent to the value of N_e for haploids with the number of demes taking the place of the number of individuals (with a variance in number of gametes produced of $2V$). This is to be expected, because a deme with complete identity is no different from a colony of haplotypes acting as a single haploid individual. If all demes contribute exactly the same number of gametes to the next generation, with no genetic variation within demes, then there is effectively no drift and the effective size is infinite.

It is also instructive to examine the case in which the variance in deme fitness is equal to the expected variance of a collection of individuals of that population size. It can be seen from Equation 10, for n large, that subdivision will decrease the effective size (relative to an undivided population) if $V > F_{ST}/(1 - F_{ST} + 2NF_{ST})$. For appreciable values of F_{ST}, this is approximately the same as that the variance among populations be greater than $1/2N$. If the distribution of reproductive success of individuals is approximately Poisson, then V will be approximately $1/2N$. If there is more variance in reproductive success than expected by this sum over individuals, however, then the effective size of the metapopulation will be reduced, sometimes drastically, as we shall see in the next section.

Using the genetic correlations among populations: In principle, Equation 9 offers the advantage that all of the parameters of this model are measurable in a single generation. The ρ_{ij}'s could be measured from the same genetic data as F_{ST}'s, and the reproductive values (w) are for a single generation's transition. For $i \neq j$, ρ_{ij} can be calculated with an analysis of covariance, extending the ANOVA approach for F_{ST}. For the value of ρ_{ij} for a given pair of populations, the analysis must be done across loci, comparing deviations of gene frequency products from the expectation. The power to

obtain reliable estimates of ρ_{ij}'s (including the F_{STi}'s) for any given pair of populations will be small, at least until genetic technology makes it possible to score very large numbers of loci and statistical methods are developed to allow for linkage among these loci.

The power to estimate ρ's increases substantially if we look at the expected genetic correlation within and among classes of populations. These classes may be defined in a variety of ways: geographically, for example, as clusters of demes; temporally, for example, age classes of demes; by size; by quality, for example, sources and sinks; or by any combination of these or other qualities. If pertinent factors can be identified, then a hierarchical ANCOVA, finding not only the F_{ST} within a class (call this F_{SC}), but also the covariance among particular classes, can be used to approximate ρ's with much more power. In the case of a geographical hierarchy, when demes are clustered and migration is more common within clusters and migration among clusters follows an island model, then approximately $\rho_{ii} = F_{ST}$, $\rho_{ij} = F_{CT}$ for demes within clusters, and

$$\rho_{ij} = -\frac{F_{ST} + (d-1)F_{SC}}{n-d}$$

for demes in different clusters, where d is the number of demes per cluster.

Weighting by ultimate contribution: In all but the simplest cases, the demographic history of a deme is correlated with its future prospects. It is therefore implausible that the genetic correlations within and between demes (ρ_{ij} in Equation 9) should be independent of reproductive output (w_i). Calculation of effective size from Equation 9 then requires knowledge of the full matrix of relative identities, essentially the same task as solving the recursions of Equations 3 and 4 directly. In this section, we show that effective size can be represented compactly in terms of a measure of the ultimate contribution of each deme to future generations. This is essentially an extension of the approach of HILL (1972) and NAGYLAKI (1980) to fluctuating deme sizes.

The change in the probability of identities occurs through the variance in reproductive success of alleles within demes and the amplification of that variation by the differential growth and migration of demes. Any change in the probability of identity within a deme changes overall allele frequencies in proportion to the ultimate reproductive success of alleles from that deme. Thus the cumulative change in identity, due to the within deme changes in one generation, is the average of the change in identity, $F_{kl}^* - F_{kl}$, weighted by the ultimate contribution of those demes to the whole population, $\vartheta_k \vartheta_i$:

$$\Delta \bar{F} = \frac{\sum_{k,l}(F_{kl}^* - F_{kl})\vartheta_k \vartheta_l}{\sum_{k,l}\vartheta_k \vartheta_l} = \frac{1}{n^2}\sum_k \vartheta_k^2 \frac{(1 - F_{kk})}{2N_k}. \quad (11)$$

This formulation requires that, regardless of the actual

sequence of migration matrices, any initial fluctuation in allele frequencies will eventually spread through the population to give the same contribution to every deme. That is, $(\mathbf{m}_{\tau-1} \cdots \mathbf{m}_\tau)\alpha_\tau$ converges to a uniform value, which we write as $(\sum_j \vartheta_{j,\tau}\alpha_{j,\tau})/n$.

The ultimate contributions can be derived easily from the migration matrix. Let $\vartheta_{j,\tau}$ be the expected contribution of a gene in deme j at time τ to the metapopulation in the distant future. For a fixed matrix, it is the left eigenvector of $\mathbf{m}$. It is defined by the recursion

$$\vartheta_{j,\tau} = \sum_{i=1}^{n} \vartheta_{i,\tau+1}m_{ij}, \quad (12)$$

where $\sum_{i=1}^{n} \vartheta_{i,\tau} = n$. Here, it is assumed that there are no subsets of demes that are completely isolated from other subsets of demes, and that at least some individuals may stay in the same deme. In other words, the matrix $\mathbf{m}$ is not reducible or periodic (see NAGYLAKI 1980). If the matrices are reducible, then the rate of loss of genetic material is ultimately zero, and the effective size is infinite.

Substituting $(1 - \bar{F})(1 - F_{STk})$ for $(1 - F_{kk})$ into Equation 11 gives the effective population size

$$\frac{1}{2N_e} = \frac{\Delta \bar{F}}{(1 - \bar{F})} = \frac{1}{n^2}\sum_k \vartheta_k^2 \frac{(1 - F_{STk})}{2N_k}. \quad (13)$$

Since the spread of identity through the population is determined by the same migration matrix as are allele frequencies, any identity $F_{ij,\tau}$ introduced at time τ will ultimately lead to a uniform increase in identity throughout the whole population of $(\sum_{ij} \vartheta_{i,\tau}\vartheta_{j,\tau}F_{ij,\tau})/n^2$. Because identity is generated in each generation by terms $(1 - F_{STk})/2N_k$ within each deme (Equation 4a), Equation 13 follows.

Equation 13 can be rewritten as

$$\frac{n}{2N_e} = (1 + \text{var }(\vartheta))\left\langle \frac{(1 - F_{ST})}{2N} \right\rangle, \quad (14)$$

where $\langle \ \rangle$ denotes an average over demes, weighted by ϑ^2. This form makes clear how effective size is decreased by variance in long-term contribution and increased by differentiation between demes, F_{ST}. Equation 14 is equivalent to Equation 10 with the same assumptions; this can be seen by remembering that $2Nm(2 - m)F_{ST} = (1 - F_{ST})(1 - m)^2$ for the island model.

The effective size of a generalized island model: To investigate the model further, we will make a set of sequentially more restrictive assumptions. We assume that the whole metapopulation is at a demographic equilibrium. The probabilities of identity by descent within and between particular demes may fluctuate as the demographic states of those demes changes, but the distribution of states and identities across the population as a whole remains constant. We further assume

that though emigration and immigration rates vary, there is no correlation between where migrants come from and go to. Emigrants, by this assumption, form a migrant pool, from which immigrants are chosen at random without replacement. This requires that $m_{ij} = m_i \varphi_j$, where φ_j is the contribution of deme j to the migrant pool, and m_i the rate of migration into deme i. Necessarily, $\Sigma_{j \neq i} \varphi_j = 1$; since the φ_j are $O(1/n)$, factors such as $(1 - \varphi_i)$ can be ignored, and so we can take $\Sigma_j \varphi_j \approx 1$.

Under these assumptions, the ultimate contributions of each deme can be written more simply. Define Θ as the ultimate contribution to the population by the alleles in the migrant pool. This implies that

$$\Theta = \sum_i \sum_{j \neq i} \vartheta'_j m_{ji} = \sum_i \sum_{j \neq i} \vartheta'_j \varphi_i m_j. \qquad (15)$$

Since all migrants have an equal probability of success,

$$\sum_{j \neq i} \vartheta'_j m_{ji} = \varphi_i \Theta. \qquad (16)$$

We can therefore reexamine Equation 12,

$$\vartheta_i = \sum_j \vartheta'_j m_{ji} = \vartheta'_i(1 - m_i) + \sum_{j \neq i} \vartheta'_j m_{ji}$$

$$= \vartheta'_i(1 - m_i) + \varphi_i \Theta. \qquad (17)$$

This gives the following:

$$\vartheta_{i,t} = \Theta \sum_{k=0}^{\infty} \varphi_{i,t+k} \prod_{\tau=0}^{k-1} (1 - m_{i,t+\tau}). \qquad (18)$$

Substituting Equation 18 into Equation 13 gives the effective population size. The results in this paper using this derivation are exact, but an approximation to Θ can be obtained from Equation 18 and the equation $\Sigma_j \vartheta_j = n$; Θ can be roughly approximated by the harmonic mean of mn.

F_{ST} can be determined directly, either by empirical observation or by analysis of the migration matrices. If the number of demes is large, then to leading order in $1/n$:

$$F'_{STi} = (1 - m_i)^2 F^*_{STi} \quad \text{where}$$

$$F^*_{STi} = \left(\frac{1}{2N_i} + \left(1 - \frac{1}{2N_i}\right) F_{STi}\right). \qquad (19)$$

Thus, the identity within demes, relative to that between demes, is independent of changes in the population as a whole, and depends only on the sequence of immigration rates (m_i) and sizes (N_i) of the deme in question.

Under the migrant pool assumptions of this section, the same result can also be written as a function of the coalescent, by solving the recursion for F_{STk} explicitly in terms of contributions from drift in generations $\tau' < t$. Substituting this, and Equation 18 into Equation 13 gives

$$\frac{1}{2N_e} = \frac{\Theta^2}{n^2} \sum_k \sum_{\tau' < t \leq \tau} \frac{\varphi_t \varphi_\tau}{2N_{\tau'}} \left[\prod_{i=\tau'+1}^{t-1} (1 - m_i)\left(1 - \frac{1}{2N_i}\right) \right]$$
$$\times \left[\prod_{j=\tau'+1}^{\tau-1} (1 - m_j) \right] (2 - \delta_{t\tau}), \qquad (20)$$

where $\delta_{t\tau} = 1$ if $t = \tau$, and 0 otherwise. All quantities in the sum refer to deme k; the index has been suppressed for clarity. The sum is over contributions from an initial coalescence, in generation τ' (with probability $1/2N_{\tau'}$), followed by emigration events that occur subsequently, in generations t, τ (with probability φ_t, φ_τ). The factor $(2 - \delta_{t\tau})$ arises from the need to avoid counting simultaneous emigrations ($t = \tau$) twice. Tracing back from the second emigration at τ, back to the first emigration event at t, introduces the second product, since the chance that the single lineage remaining in the deme is not replaced by an immigrant as we trace back is $(1 - m_i)$ per generation. Between generations t and τ', both lineages are in the same deme without coalescing, and so the probability must be discounted by a further factor $(1 - 1/2N_j)$ in the first product. Equation 3 could be derived directly by equating the long-term rate of drift with the ultimate increase in identity due to coalescence in some particular generation, τ'. This is given by the probability of a coalescence in some deme k at time τ', multiplied by the probability that the ancestral lineages did not leave that deme, or coalesce within it, at some previous time.

As a simple check, consider the standard island model. There, $m_i = m$ for all demes, and $\varphi_i = 1/n$. From Equation 18, $\vartheta_i = 1$, and $\Theta = mn$. Substituting into Equation 13 gives $1/2N_e = (1 - F_{ST})/2nN$, as expected. Now, suppose that demes have constant demography over time, but that N, φ, and m vary between demes such that emigration and immigration balance for each deme ($\varphi_i = m_i N_i / (\Sigma_i m_i N_i)$). Then, $\vartheta_i = N_i/\bar{N}$, and the effective size is just $2n\bar{N}/(1 - F_{ST})$, where F_{ST} is the average weighted by deme size, divided by the total number in the population (MARUYAMA, 1972).

In general, deme sizes and migration rates may vary through time and may be correlated across generations. Then, Equation 13 still holds, but evaluation of the covariance between ϑ_k (which depends on the future success of genes now in deme k) and F_{STk} (which depends on their past history) is nontrivial. In the following sections, we illustrate such calculations using two explicit models.

EFFECTIVE SIZE: THE CATASTROPHIC EXTINCTION MODEL

As a special case, we wish to know the effective size of a metapopulation that is subdivided into demes that undergo extinction and recolonization. In this section we will generalize previous results to include a more general mode of colonization. Imagine (following SLATKIN 1977; WHITLOCK and McCAULEY 1990; WHITLOCK
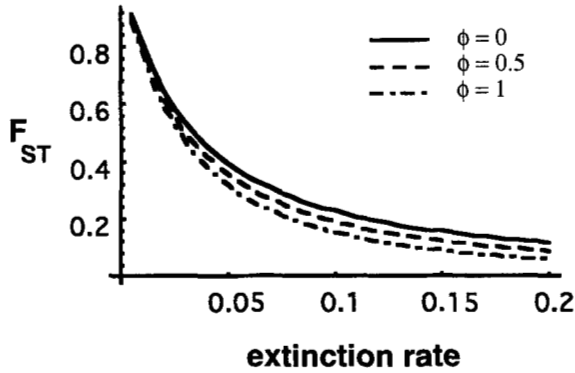
FIGURE 1.—Increasing local extinction rates decreases the effective population size of the species. $N = 50$, $k = 2$, and $m = 0.1$.
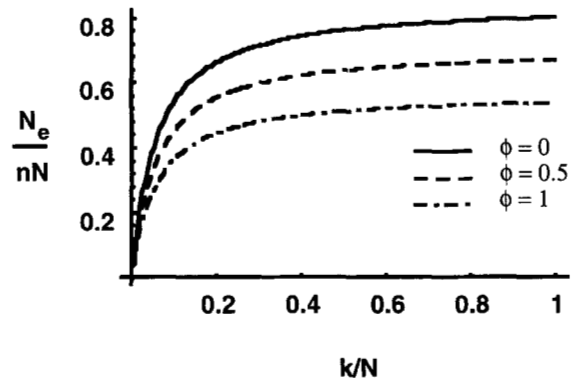

FIGURE 2.—As the number of colonists approaches the equilibrium deme size, the extinction effect on effective population size diminishes. $N = 100$, $e = m = 0.1$.

1992; see these papers for the details of the basic model) that all n demes have N diploid individuals that have a probability m of migrating to a deme chosen at random. Each of these demes go extinct with probability e per generation. Each colonized deme consists of $2k$ gametes in which each pair has a probability ϕ of having come from the same source population. For simplicity, each newly colonized deme grows to N individuals before the next generation.

For this case the value of F_{ST} has been given by WHIT-LOCK and MCCAULEY (1990):

$$F_{ST} \approx \frac{\left(1 + \frac{eN}{k}\right)}{\left(1 + 4Nm + 2Ne\left(1 - \phi\left(1 - \frac{1}{2k}\right)\right)\right)}. \quad (21)$$

With $\phi = 0$, the contribution to the next generation (N^*) is either 0 with probability e or $N/(1 - e)$ with probability $(1 - e)$. The genetic correlation among demes is on average $\rho_{ij} = -F_{ST}/(n - 1)$ for different demes.

We can write (from Equation 9),

$$N_e = \frac{Nn(1 - e)}{(1 - F_{ST}) + 2F_{ST}Ne}, \quad (22)$$

so that, with $k = n$

$$N_e \cong \frac{Nn}{4N(m + e)F_{ST}}. \quad (23)$$

It can be shown that Equation 23 is true relaxing the assumptions about ϕ and k.

The same result can be found with the method of ultimate contributions, as in Equation 13. The immediate and net contribution of genes are both zero for a deme that is about to go extinct ($\varphi_E, \vartheta_E = 0$). For the surviving demes, the net contribution depends on the number of generations that they persist before they go extinct. The net contribution of a deme which survives

x generations is $\vartheta_x = [(e + m(1 - e))/(1 - e)][(1 - e)][(1 - (1 - m)^x)/m]$. The number of demes that will last x generations without extinction is $ne(1 - e)^x$. Substituting into Equation 13, and summing over all classes of demes, gives

$$\frac{1}{2N_e} \approx F_{ST} \frac{(e + m(1 - e))}{n} (2 - e - m(1 - e))$$

$$\approx 2F_{ST} \frac{(m + e)}{n}, \quad (24)$$

which is equivalent to Equation 23 above.

Equation 23 reduces to the two approximate cases given by SLATKIN (1977) for $k = N$, at $\phi = 0$ and $\phi = 1$, and to that given by MARUYAMA and KIMURA (1980) for their model when $\phi = 1$.

If $k \ll N$ and extinction is not rare relative to migration, then the effective size can be substantially reduced (see Figures 1 and 2). For example, if $e = m = 0.10$, $N = 1000$, and $k = 1$, then the effective size is 0.0062 of what it would have been without local extinction. Local extinction can greatly reduce the effective population size.

EXPLICIT POPULATION DYNAMICS

Demographic model: As has been shown in the previous section, reducing the number of possible demographic states of demes greatly simplifies the calculation of N_e for a metapopulation. If each deme's demographic trajectory is strictly a function of its present state, and does not depend on other historical factors, then the identity measures of all demes in that state can be represented by an average, thereby simplifying the calculations. In this section, we suppose that the demographic future of a deme can be described by a single parameter, namely, deme size. The approach could be generalized to include other parameters, such as the level of some limiting resource.

In the catastrophic extinction model above (and indeed, in most models of metapopulation dynamics),

demes are taken to have constant size and to be recolonized immediately if they become extinct. The probability of extinction is imposed arbitrarily, colonization is assumed to be immediate, and numbers build up to the carrying capacity in a single generation. Here, we show how to calculate the effective size of a population with arbitrary fluctuations in deme size and illustrate the methods using a model in which extinction and recolonization are not catastrophic but are rather the consequence of the demographic stochasticity intrinsic to density-dependent population dynamics, possibly augmented by chaos in the underlying dynamics.

The fundamental model could apply to haploid or diploid populations, but for simplicity, we apply it to the haploid case. We also assume that colonization and migration are due to the same process, so that the number of colonists arriving per generation follows a Poisson distribution. As before, assume a very large number (n) of demes. These have reached a steady-state distribution of sizes, ψ_i, the mean number of genes in each deme being defined as $2\bar{N} = \Sigma_i\, i\psi_i$, where i is the number of haploid genotypes in a deme. In this section and the next, i and j are no longer just identifiers of particular populations, but mark the population size of a class of populations. (Though we use a haploid model, we define the number of genes as $2N$ for consistency with the standard formulae). As above, the population is counted immediately after migration. This simplifies the analysis, because the two stochastic processes of migration and reproduction can be combined.

The probability that a deme will go from size i to size j in one generation, as a result of reproduction followed by migration, is P_{ij}; the equilibrium distribution is determined by $\psi_j = \Sigma_i\, \psi_i P_{ij}$. The corresponding probability that a deme of size j derives from one of size i (the backwards transition matrix) is $\Gamma_{ji} = P_{ij}\psi_i/\psi_j$; $\Sigma_i\, \Gamma_{ji} = 1$. (In a diploid model, i must always be even, whereas in the haploid case, it can take any integer value). These transition matrices depend on density-dependent regulation and on migration. We assume that in each generation, a deme containing i haploid individuals produces a randomly distributed number of offspring, with expectation iw_i, where w_i decreases for large i. Throughout, we use the form $w_i = w_0\, \exp(-i/\kappa)$, where $\kappa \ln (w_0)$ corresponds to the carrying capacity of a deme. Each offspring then emigrates to some other deme with probability m. Define $\bar{M}$ as the mean number of emigrants contributed by a deme. This is also the mean number of immigrants such that $\bar{M} = m\Sigma_k\, w_k k\psi_k$. Since there are a very large number of demes, the number of immigrant genes is Poisson distributed, with expectation $\bar{M}$. The transition matrices depend on the sum of this distribution and the distribution of the number of nonmigrant offspring. The dynamics are simplest if the distribution of offspring number is Poisson. Then, the transition probability P_{ij} is a Poisson distribution over j, with expectation $\bar{M} + (1 - m)iw_i$. This can be solved to find the equilibrium distribution, ψ_i, and gives an implicit equation for $\bar{M}$, namely $\bar{M} = m\Sigma_k\, w_k k\psi_k$. [See BARTON and ROUHANI (1993) for an analogous approach to modeling gene frequencies in a metapopulation].

In a large panmictic population, the form of w_i decides whether there will be a stable equilibrium, a limit cycle, or chaos. Migration and demographic fluctuations introduce further complexities. If all offspring migrate ($m = 1$), then the distribution ψ_i is always Poisson with mean $2\bar{N}$, and the system can be described by the single variable $2\bar{N}$. If demographic fluctuations are negligible ($\kappa \gg 1$), the metapopulation reaches a stable equilibrium at $2\bar{N} = \kappa \log (w_0)$ if $1 < w_0 < e^2$, runs through limit cycles of increasing period as the growth rate increases above $w_0 = e^2 = 7.39$, and may fluctuate chaotically for $w_0 > 14.75$. When κ is small, random variation in numbers across demes increases crowding effects; averaging over the Poisson distribution shows that the system is equivalent to a panmictic population with $w_0^* = w_0\exp(-1/\kappa)$, $\kappa^* = 1/(1 - \exp(-1/\kappa))$.

If w_0^* is large enough that $\bar{N}$ shows complex dynamics with $m = 1$, then numerical iterations show that as migration decreases, $\bar{N}$ cycles through oscillations of decreasing period, and then settles to a stable value. Individual deme sizes may still fluctuate widely as a result of the underlying chaos, but change independently of each other. For example, with $w_0 = 20$, $\kappa = 3$, the population settles to a steady equilibrium with constant $\bar{N}$; a linear analysis shows this to be stable when $m < 0.26$. Higher migration rates synchronize fluctuations in different demes, so that the whole population fluctuates together. With $m = 0.5$, $\bar{N}$ alternates between 3.22 and 16.25, in a stable cycle of period 2. When $m = 1$, the population oscillates with period 8. The effect of migration on chaotic dynamics is a complicated issue (HASTINGS et al. 1993; LLOYD 1995). Here, we concentrate on cases where the overall distribution ψ_i is stable; however, local extinction may still be largely due to chaos.

Figure 3 gives examples of the equilibrium distribution, calculated numerically from the transition matrix. Each deme flips between two states: extinction or a roughly Gaussian distribution around the deterministic equilibrium. In a model where deme size varies only because of demographic fluctuations, extinction is unlikely. For example, with $w_i = w_0\, \exp(-i/\kappa)$, and $w_0 = 2$, $\kappa = 15$, the deterministic model gives a stable equilibrium at $2\bar{N} = 10.4$ (Figure 3A). Even with migration of only $m = 0.01$, only 1.65% of demes are empty, and average deme size is reduced only to $2\bar{N} = 9.38$ (Figure 3B). However, if growth rates are higher, the deterministic analog becomes chaotic, and in the stochastic model, deme size fluctuates widely. For example, with $w_0 = 20$, $\kappa = 3$, and $m = 0.2$, average deme size is $2\bar{N} = 10.0$, and 2.9% of demes are empty (Figure
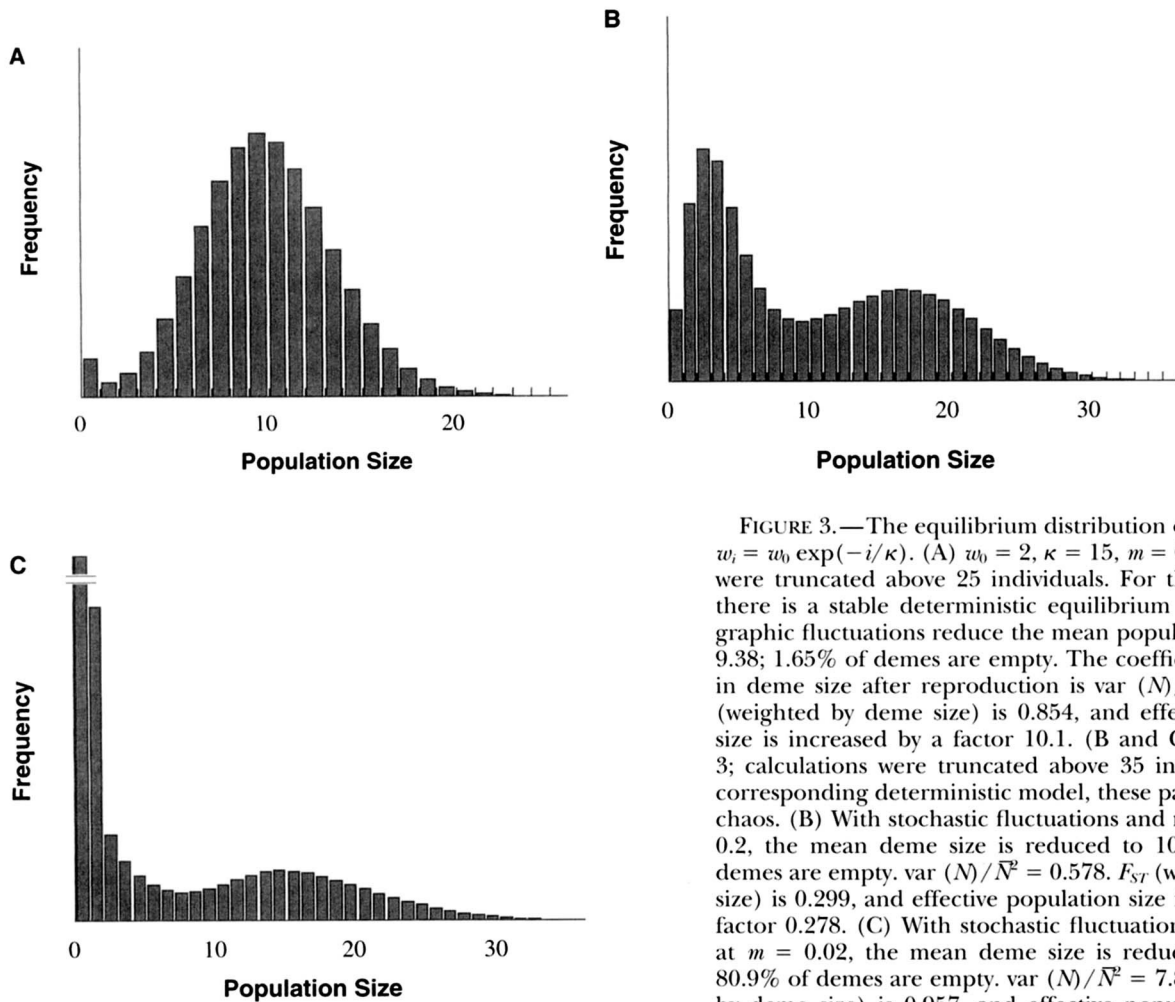
A

B

C

FIGURE 3.—The equilibrium distribution of deme sizes, for $w_i = w_0 \exp(-i/\kappa)$. (A) $w_0 = 2$, $\kappa = 15$, $m = 0.01$; calculations were truncated above 25 individuals. For these parameters, there is a stable deterministic equilibrium at 10.40. Demographic fluctuations reduce the mean population size to $\bar{N} = 9.38$; 1.65% of demes are empty. The coefficient of variation in deme size after reproduction is var $(N)/\bar{N}^2 = 0.154$. F_{ST} (weighted by deme size) is 0.854, and effective population size is increased by a factor 10.1. (B and C) $w_0 = 20$, $\kappa = 3$; calculations were truncated above 35 individuals. In the corresponding deterministic model, these parameters lead to chaos. (B) With stochastic fluctuations and migration at $m = 0.2$, the mean deme size is reduced to 10.0, and 2.9% of demes are empty. var $(N)/\bar{N}^2 = 0.578$. F_{ST} (weighted by deme size) is 0.299, and effective population size is decreased by a factor 0.278. (C) With stochastic fluctuations and migration at $m = 0.02$, the mean deme size is reduced to 1.82, and 80.9% of demes are empty. var $(N)/\bar{N}^2 = 7.81$. F_{ST} (weighted by deme size) is 0.957, and effective population size is increased by a factor 37.32.

3C). As the migration rate decreases, $2\bar{N}$ decreases to zero at about $m = 0.015$ (Figure 4B).

Effective population size with explicit population dynamics: The N_e formulae given above must be modified, since the index i now labels the class of demes of size i, rather than one particular deme. Demes of the same size may, by chance, follow different sequences of sizes in the future, and so we must account for the variance in m_i and ϑ across demes of the same size, as well as its mean. A simplification, however, is that *for a given deme size F_{ST} and ϑ are independent*, since one depends on past events, and the other on future events. The equation for within-deme identity (Equation 19) becomes

$$F'_{STj} = \sum_i \Gamma_{ji}\{(1 - m_i)^2 + \nu_{ji}\left(F_{STi} + \frac{(1 - F_{STi})}{i} \right). \quad (25)$$

(Note that F_{ST} is not defined for demes with less than two individuals; F^*_{ST1} is the relative identity between two individuals derived from the single gene in a deme of size 1 and is necessarily 1.) The transition matrix Γ_{ij} is required to sum over all the various sizes (i) that a deme now of size j had in the previous generation. Each allele

in a deme that was of size i has probability $m_i = \bar{M}/(\bar{M} + i(1 - m)w_i)$ of being an immigrant. Note that this depends only on the number in the previous generation (i), and not on the present number (j). Necessarily, $m_0 = 1$, since a deme that has just been founded must consist solely of immigrants. The variance in immigration rate is also required and depends on both the initial and final numbers. Since the numbers of immigrants in a deme of size j is binomially distributed with probability m_i, this variance is $\nu_{ji} = m_i(1 - m_i)/j$.

Equation 13, which gives the effective population size, becomes a sum over the distribution of deme sizes, ψ_i, rather than over all demes:

$$\frac{1}{2N_e} = \frac{1}{n^2} \sum_i \psi_i(\vartheta_i^2 + V_i) \frac{(1 - F_{STi})}{2i}. \quad (26)$$

As well as the expected ultimate contribution of a deme of size i, ϑ_i, the variance in contribution, V_i, must be found. The expected immediate contribution of a deme of size i to the migrant pool is $\varphi_i = iw_i/(2n\bar{N})$; its variance is $\nu_i^* = \varphi_i/mN$. Taking the mean and variance of the recursion in Equation 18 leads to
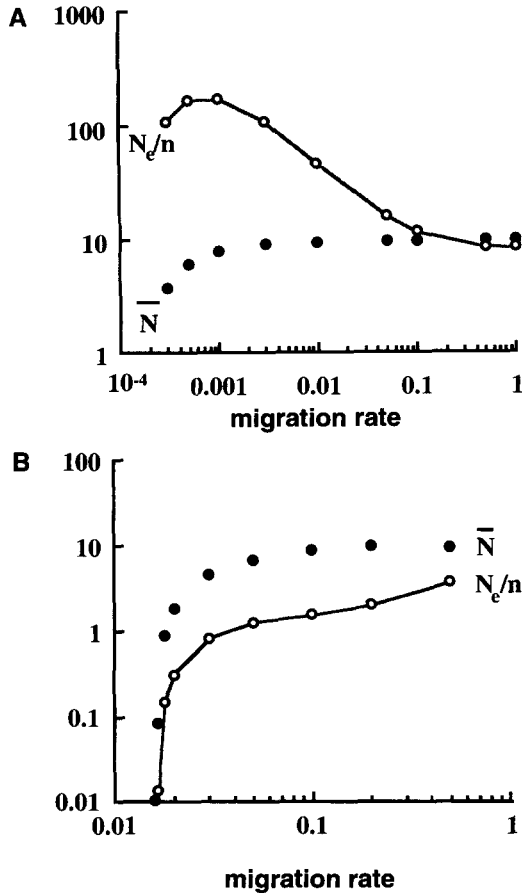
A 1000

N_e/n

$\overline{N}$

10⁻⁴ 0.001 0.01 0.1 1
migration rate

B 100

$\overline{N}$

N_e/n

0.01 0.1 1
migration rate

A 1

F_{ST}

10⁻⁴ 0.001 0.01 0.1 1
migration rate

B 1

F_{ST}

0.01 0.1 1
migration rate

FIGURE 4.—The relation between migration rate (m) and the mean deme size ($\overline{N}$; ●) and effective population size per deme (N_e/n; ○). Parameters are as in Figures 3 [(A) $w_0 = 2$, $\kappa = 15$; (B) $w_0 = 20$, $\kappa = 3$]. There is a threshold migration rate below which extinction is certain [(A) $m \approx 0.0002$, (B) $m \approx 0.016$]. The equilibrium shown in B is not stable for $m > 0.262$; in the limit $m = 1$, for example, $\overline{N}$ oscillates in a cycle of period 8. The thin lines connecting the open circles show the approximation assuming F_{ST} independent of deme size, derived from Equation 19.

$$\vartheta_i = \varphi_i + (1 - m_i) \sum_j P_{ij}\vartheta_j, \qquad (27)$$

$$V_i = \nu_i^* + (1 - m_i)^2 \left\{ \left(\sum_j P_{ij}\vartheta_j^2 \right) \right.$$

$$\left. - \left(\sum_j P_{ij}\vartheta_j \right)^2 \right\} + \left(\sum_j \nu_{ji}P_{ij}\vartheta_j^2 \right)$$

$$+ \sum_j [(1 - m_i)^2 + \nu_{ji}]P_{ij}V_j. \qquad (28)$$

The first term in Equation 28 is the variance in immediate contribution to the migrant pool. The second term is the variance in average prospects (ϑ_j) due to the change from deme size i to deme size j. The third term is due to the variance in immigration rate, ν_i.

When growth rates are low, so that the variation in deme size is due solely to demographic fluctuations, subdivision allows local extinction, and hence reduces the average deme size, $\overline{N}$ (Figure 4A). However, subdivi-
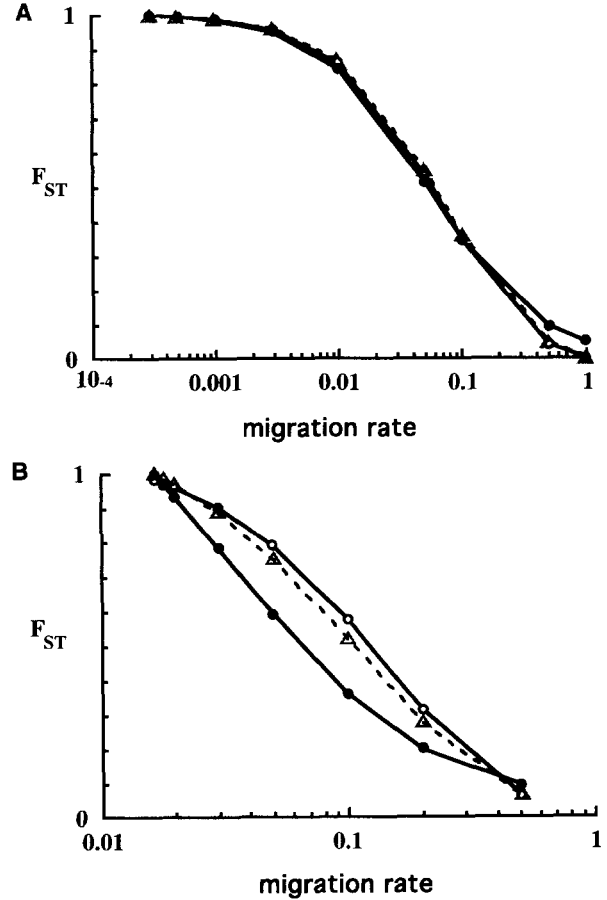
FIGURE 5.—The average F_{ST}, weighted by deme size, plotted against migration rate, m. Parameters are as above: (A) $w_0 = 2$, $\kappa = 15$; (B) $w_0 = 20$, $\kappa = 3$). The heavy line and open circles mark the exact F_{ST}; the closed circles and lighter line the island model approximation, $F_{ST} = 1/(1 + 4\overline{N}m)$, and the dotted line and triangles the approximation of Equation 29. Note that for $m > 0.262$, the solution with $\overline{N}$ constant becomes unstable.

sion also allows local differentiation (F_{ST}; Figure 5A), and overall, N_e increases substantially when $\overline{M}$ is small (Figure 4A). Note, however, that when migration approaches the critical threshold, $\overline{N}$ drops so much that the effective size also falls (left of Figure 4A). In contrast, when growth rates are high enough to give chaos in the deterministic model, deme size varies much more. The variation in success across demes caused by subdivision therefore reduces N_e even when average numbers are hardly affected (right of Figure 4B). These examples show that the combined effects of genetic differentiation (F_{st}), census numbers ($\overline{N}$) and variation in output across demes can interact in counterintuitive ways. However, note that with the parameter values that generate the low F_{ST} values most often found intraspecifically, and with demographic instability (right of Figure 4B), N_e is reduced, sometimes substantially, by subdivision.

For these examples, F_{ST} does not depend strongly on deme size, over the range of sizes commonly found
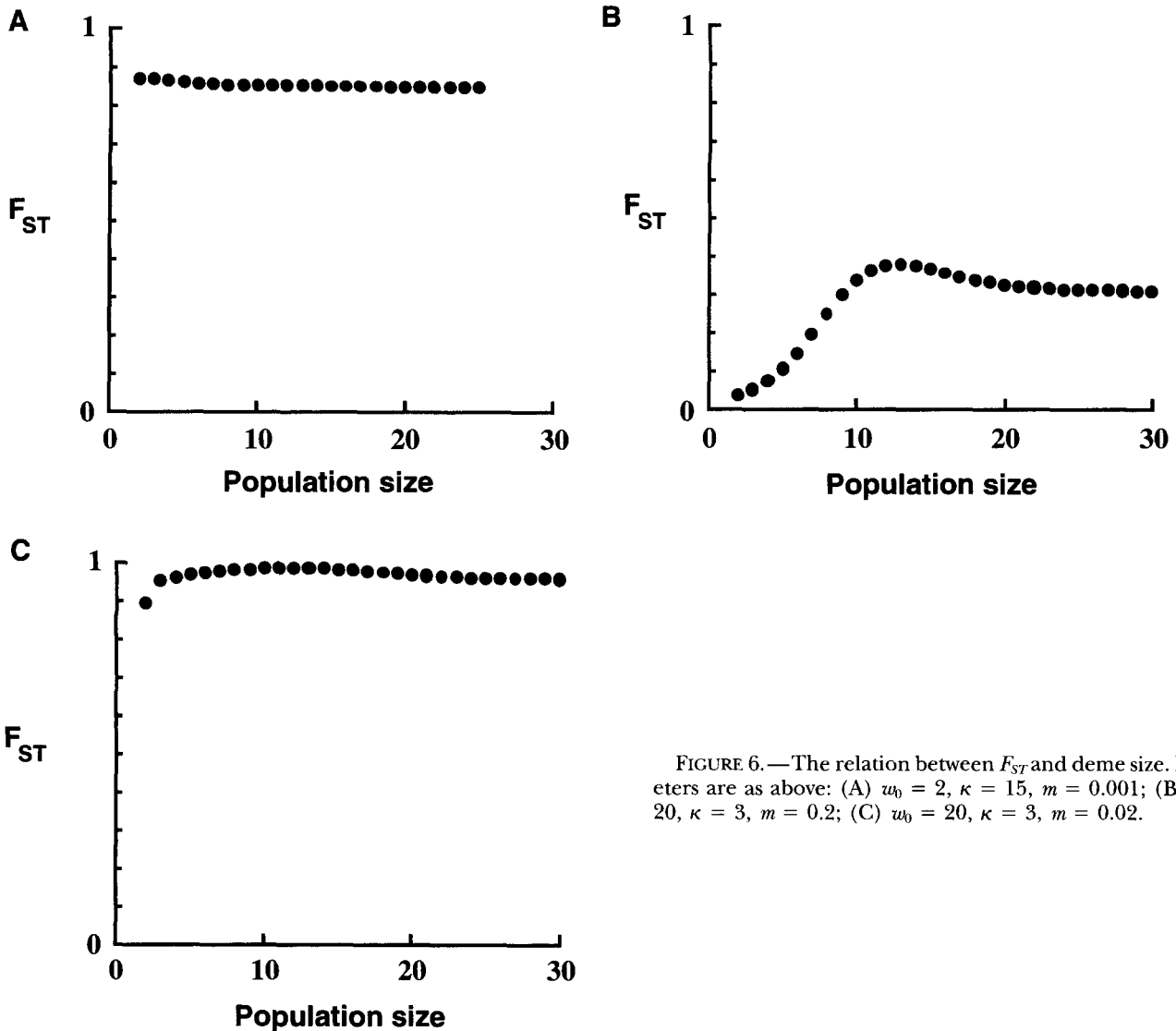
A

B

C

FIGURE 6.—The relation between F_{ST} and deme size. Parameters are as above: (A) $w_0 = 2$, $\kappa = 15$, $m = 0.001$; (B) $w_0 = 20$, $\kappa = 3$, $m = 0.2$; (C) $w_0 = 20$, $\kappa = 3$, $m = 0.02$.

in the metapopulation (Figure 6). One can obtain an accurate approximation for F_{ST} by assuming it to be independent of deme size and taking the average of Equation 25 over the equilibrium distribution, excluding deme sizes $j = 0$ and 1, for which F_{ST} is not defined:

$$F_{ST} \approx \cfrac{1}{1 + \cfrac{\sum_{i=2}^{\infty} \tilde{\psi}_i(m_i(2 - m_i) - \nu_i)}{\sum_{i=2}^{\infty} \tilde{\psi}_i((1 - m_i)^2 + \nu_i)/i}}, \qquad (29)$$

where $\tilde{\psi}_i = (\psi_i - \psi_o\Gamma_{0i} - \psi_1\Gamma_{1i})/((\psi_i - \psi_o - \psi_1)$ is the probability that a deme is of size i and will not drop to size 1 or 0 in the next generation. In the standard island model, Equation 29 clearly reduces to $1/(1 + 4Nm)$. Approximate solutions can be obtained if the mean deme size is thought of as a kind of harmonic mean deme size, weighted by $\tilde{\psi}_i$ and by the immigration rate. In the examples above, this approximation is accurate over the whole range of migration values (dotted lines in Figure 5), whereas the simple island model $1/$

$(1 + 4Nm)$ tends to underestimate F_{ST} (thin lines in Figure 5). Substituting Equation 29 into Equation 13 leads to an accurate approximation for the effective population size (thin lines in Figure 4).

DISCUSSION

We have presented general methods for finding the effective size of a population that is subdivided across many different demes, each changing in size and each contributing to a common migrant pool. We found that though the effective size can be increased by genetic differentiation across demes, it may be greatly reduced by variation in the sizes and contributions of these demes.

Finding the effective size of a spatially structured population is closely related to the analogous problem with age structure (HILL, 1972, 1979; CHARLESWORTH 1994) and with inherited variation in fitness (ROBERTSON 1961; CABALLERO 1994; SANTIAGO and CABALLERO

1994). The asymptotic rate of drift in an age-structured population can be found using a similar matrix method (HILL 1972; CHARLESWORTH 1994). However, though the long-term contribution of individuals to the population (here, ϑ_j) is the crucial quantity, the rate of drift does not simply reduce to the variance of this quantity, as for a single age-structured population (HILL 1979).

There is a close analogy with hitchhiking, where a marker allele may find itself in a variety of different genetic backgrounds. If the genetic backgrounds change in frequency, as with directional selection or a fluctuating polymorphism, then the effects of drift may be greatly amplified (MAYNARD SMITH and HAIGH 1974; HUDSON 1991). The case where families have heritable differences in fitness shares the complication that allele frequency fluctuations are correlated across generations, making the variance of changes in one generation an unsatisfactory basis for defining N_e (CABALLERO 1994). A spatially structured population is somewhat different, because once an individual moves to a new deme, it immediately acquires the fitness associated with that deme; in contrast, the correlation between descendants from a family is slowly dissipated by sexual reproduction. However, if one distinguishes genes associated with different genetic backgrounds, then recombination plays the role of migration, and the problems become similar. We speculate that the geometry imposed by recombination lies somewhere between the island model and a stepping stone-model: it transfers a gene to many genetic backgrounds (rather than to a few neighbors, as in the stepping-stone model), but nevertheless, only to a small fraction of the possible backgrounds (in contrast to the island model).

The effects of subdivision on the effective size of a species can be complex, but can be divided into several factors: the census population size, the degree of genetic differentiation, and the variance in reproductive success both between and within demes. By examining each of these effects individually, we can better understand the reasons for the changes in N_e.

Obviously, the effective size of any population relates in some way to the total number of individuals in that population, and, all else being equal, the effective size will increase in proportion to the census size. This effect, while conceptually trivial, can be a significant factor in determining the difference in effective size between a panmictic population and a subdivided population occupying the same habitat. The ecology of metapopulations is such that, for many if not most species, local extinction and demographic fluctuations in a divided population will reduce the total census size relative to an undivided population (see GILPIN and HANSKI 1989 and above). Moreover, if the number of immigrants per generation (Nm) is small enough to cause significant genetic differentiation, it is likely also to be small enough to reduce census numbers.

Most discussions of the effects of population subdivision on effective population size have focused on the effects of differentiation among demes, as measured by F_{ST} (WRIGHT 1969; GILPIN and HANSKI 1989). The genetic differentiation of populations will often increase the effective size of a metapopulation. In the extreme, with no migration among demes, any mutation that arises in a particular deme may fix in that deme, but cannot spread to other demes. Hence no allele can ever fix in the metapopulation, drift to fixation takes indefinitely long, and the effective size is infinite. This effect operates to a lesser degree when the migration rate is nonzero but limited; there is a lag between the increase of an allele frequency within a deme before that allele can change in frequency in other demes, because of the waiting time until migration of the allele. Any metapopulation with closed and stable subsets that do not exchange any migrants either directly or indirectly with other subsets will also have an infinite effective size.

Variance among demes in reproductive success decreases the effective population size, and genetic correlations among alleles within demes tend to amplify this effect substantially. The effects seen in the catastrophic extinction model demonstrate the extent to which this sort of variance can substantially decrease the effective size of a metapopulation (see Figure 1). With realistic population structures, that is, those in which the output of each deme is not rigidly determined to be exactly the same for each deme, the variance in success among demes quickly makes up for the genetic correlations within demes; little extinction or differential migration is required to reverse the direction of effect of subdivision on effective size, relative to the island model. These differences can be related to the difference between soft and hard selection: if population regulation is strictly at the level of demes, then the variance in reproductive success among demes will be small and the effective size will tend to be large. On the other hand, when individual deme size is loosely regulated, or if regulation occurs at the level of the whole metapopulation, the variance can be large among populations, and N_e small.

Local extinction and colonization have been treated directly above; in the simple catastrophic extinction model given above the effects of colonization are large. If a small number of individuals gain a large reproductive success by colonizing a new deme, this can significantly increase the variance in reproductive success in the species, decreasing its effective size. This effect is slightly enhanced if colonists tend to have a common origin (ϕ), because they are then genetically similar (see Figures 1 and 2). The variance in reproductive success is particularly increased if there are very few colonists relative to the carrying capacity ($k \ll N$). Then, extinction and colonization will greatly reduce the effective size of the species. The model given here assumes that the k colonists will grow immediately to size

N in the next generation. If demes grow more slowly and immigration continues, the variance in reproductive success due to colonization is diminished, and N_e would be closer to Nn. The effective sizes of fast-growing species with relatively low rates of dispersal are therefore expected to be the most affected by extinction and colonization processes.

Conservation biologists and resource managers are often forced to make difficult decisions about the geometry of populations and communities under their care. The amount of genetic variation maintained within species may be important for the future ability of species to adapt to new evolutionary pressures and thus affects the optimal strategy for maximizing the long-term chances of species' survival. To increase the amount of genetic variance for a given total population size, it has been suggested that the species should be subdivided into distinct subpopulations, thus allowing different alleles to be maintained in each deme. This strategy has been criticized because local extinction reduces the amount of genetic variance rather than increasing it (MCCAULEY 1991). The results in this paper suggest that the decrease in N_e with realistic population structures is a common phenomenon, and the increase in N_e with the island model is an artifact of the unnatural assumptions of that model.

From a conservation standpoint, the maintenance of genetic variance should play a secondary role to other concerns. Homozygosity can be increased substantially by local extinction or by the isolation of demes (see WHITLOCK and MCCAULEY 1990). With low migration rates and deme sizes, this homozygosity can cause significant inbreeding depression and diminish a population's chances of survival (FRANKHAM 1995). From a genetic point of view, subdivision of a species, especially if there is a risk of local extinction, is not a good management strategy. Some ecological factors, such as the risk of epidemics or local disaster, can cause the risk of species extinction to be significantly reduced by population subdivision. Other ecological factors, such as low recruitment to new demes, can significantly increase the probability of metapopulation extinction for subdivided populations (see HANSKI 1989 for review). These ecological factors are undoubtedly often more important than genetic considerations and should be given full consideration in management strategy (LANDE 1988).

Most species are divided into demes with more or less limited migration between them. The effective size of such species can be strongly affected by this subdivision, particularly when there is variance in the reproductive success of the demes. Much more empirical work is needed to know the extent of the various parameters shown to be important here; particularly we know very little about the actual variance in reproductive success across demes or the correlations across generations of this success. Drift at the metapopulation level may

prove crucial to understanding the distribution of alleles within species or, perhaps, for the better design of conservation strategies.

LITERATURE CITED

BARTON, N. H., 1993   The probability of fixation of a favoured allele in a subdivided population. Genet. Res. **62:** 149–158.

BARTON, N. H., and S. ROUHANI, 1991   The probability of fixation of a new karyotype in a continuous population. Evolution **45:** 499–517.

BARTON, N. H., and S. ROUHANI, 1993   Adaptation and the 'shifting balance'. Genet. Res. **61:** 57–74.

BARTON, N. H., and M. C. WHITLOCK, 1996   The evolution of metapopulations, pp. 183–210 in *Metapopulation Dynamics: Ecology, Genetics, and Evolution,* edited by I. HANSKI and M. GILPIN. Academic Press, New York.

CABALLERO, A., 1994   Developments in the prediction of effective population size. Heredity **73:** 657–679.

CABALLERO, A., P. D. KEIGHTLEY and W. G. HILL, 1991   Strategies for increasing fixation probabilities of recessive mutations. Genet. Res. **58:** 129–138.

CHARLESWORTH, B., 1994   The effect of background selection against deleterious mutations on weakly selected, linked variants. Genet. Res. Camb. **63:** 213–228.

CHESSER, R. K., O. E. RHODES, D. W. SUGG and A. SCHNABEL, 1993   Effective sizes for subdivided populations. Genetics **135:** 1221–1232.

CROW, J. F., and M. KIMURA, 1970   *An Introduction to Population Genetics Theory.* Harper and Row, New York.

EWENS, W. J., 1979   *Mathematical Population Genetics.* Springer-Verlag, Berlin.

EWENS, W. J., 1982   On the concept of the effective population size. Theor. Pop. Biol. **21:** 373–378.

EWENS, W. J., 1989   The effective population size in the presence of catastrophes, pp. 9–25 in *Mathematical Evolutionary Theory,* edited by M. FELDMAN. Princeton University Press, Princeton, NJ.

FRANKHAM, R., 1995   Inbreeding and extinction; a threshold effect. Conserv. Biol. **9:** 792–799.

GILPIN, M., and I. HANSKI (Editors), 1989   *Metapopulation Dynamics: Empirical and Theoretical Investigations.* Academic Press, London.

GREGORIUS, H. R., 1991   On the concept of effective number. Theor. Pop. Biol. **40:** 269–283.

HALDANE, J. B. S., 1939   The equilibrium between mutation and random extinction. Ann. Eugen. **9:** 400–405.

HANSKI, I., 1989   Metapopulation dynamics: does it help to have more of the same? Trends Ecol. Evol. **4:** 113–114.

HASTINGS, A., C. L. HOM, C. S. ELLNER, P. TURCHIN and H. C. J. GODFRAY, 1993   Chaos in ecology: is mother nature a strange attractor? Annu. Rev. Ecol. Syst. **24:** 1–33.

HILL, W. G., 1972   Effective size of populations with overlapping generations. Theor. Popul. Biol. **3:** 278–289.

HILL, W. G., 1979   A note on effective population size with overlapping generations. Genetics **92:** 317–322.

HUDSON, R., 1991   Gene genealogies and the coalescent process. Oxf. Surv. Evol. Biol. **7:** 1–44.

KONDRASHOV, A. S., 1995   Contamination of the genome by very slightly deleterious mutations: why have we not died 100 times over? J. Theor. Biol. **175:** 583–594.

LANDE, R., 1988   Genetics and demography in biological conservation. Science **241:** 1455–1460.

LANDE, R., and G. F. BARROWCLOUGH, 1987   Effective population size, genetic variation, and their use in population management,

pp. 87–123 in *Viable Populations for Conservation*, edited by M. E. SOULÉ. Cambridge University Press, Cambridge.

LLOYD, A. L., 1995 The coupled logistic map: a simple model for the effects of spatial heterogeneity on population dynamics. J. Theor. Biol. **173**: 217–230.

LYNCH, M., J. CONERY, and R. BURGER, 1995 Mutation accumulation and the extinction of small populations. Am. Nat. **146**: 489–518.

MALÉCOT, G., 1948 *Les Mathématiques de l'Hérédité*. Masson et Cie, Paris.

MARUYAMA, T., 1972 Rate of decrease of genetic variability in a two-dimensional continuous population of finite size. Genetics **70**: 639–651.

MARUYAMA, T., and M. KIMURA, 1980 Genetic variability and effective population size when local extinction and recolonization of subpopulations are frequent. Proc. Natl. Acad. Sci. USA **77**: 6710–6714.

MAYNARD SMITH, J., and J. HAIGH, 1974 The hitch-hiking effect of a favourable gene. Genet. Res. **23**: 23–35.

McCAULEY, D. E., 1991 Genetic consequences of local-population extinction and recolonization. Trends Ecol. Evol. **6**: 5–8.

NAGYLAKI, T., 1980 The strong-migration limit in geographically structured populations. J. Math. Biol. **9**: 101–114.

NEI, M., and N. TAKAHATA, 1993 Effective population size, genetic diversity and coalescence time in subdivided populations. J. Mol. Evol. **37**: 240–244.

PROVINE, W., 1986 *SEWALL WRIGHT and Evolutionary Biology*. University of Chicago Press, Chicago.

ROBERTSON, A., 1961 Inbreeding in artificial selection programmes. Genet. Res. **2**: 189–194.

SANTIAGO, E., and A. CABALLERO, 1995 Effective size of populations under selection. Genetics **139**: 1013–1030.

SLATKIN, M., 1977 Gene flow and genetic drift in a species subject to frequent local extinctions. Theor. Popul. Biol. **12**: 253–262.

SLATKIN, M., 1991 Inbreeding coefficients and coalescence times. Genet. Res. **58**: 167–175.

WHITLOCK, M. C., 1992 Temporal fluctuations in demographic parameters and the genetic variance among populations. Evolution **46**: 608–615.

WHITLOCK, M. C., and D. E. McCAULEY, 1990 Some population genetic consequences of colony formation and extinction: genetic correlations within founding groups. Evolution **44**: 1717–1724.

WRIGHT, S., 1931 Evolution in Mendelian populations. Genetics **16**: 97–159.

WRIGHT, S., 1939 *Statistical genetics in relation to evolution*. Actualites scientifiques et industrielles 802. Exposes de biometrie et de la statistique biologique XIII. Hermann et Cie. Paris.

WRIGHT, S., 1969 *Evolution and the Genetics of Populations II. The Theory of Gene Frequencies*. University of Chicago Press, Chicago.

APPENDIX

Relation between mutation effective size and inbreeding effective size: Let the eigenvalues of the matrix $G_{ij,kl}$ be λ_α, the largest being λ_1. Define ξ_{ij} as $1 - F_{ij}$. We can then write the transition for ξ as $\xi^t = G^t\xi_0$

$= AD^tA^{-1}\xi_0$, where **A** has columns of the eigenvectors, γ_α and **D** is the diagonal matrix of the corresponding eigenvalues. If we scale the eigenvectors γ_α such that A^{-1} has an eigenvalue of 1 with an associated eigenvector of $(1, 1, 1, 1\cdots)$, then $A^{-1}\xi_o = \xi_o$. Since initially all $F_{ij} = 0$, $\xi_0 = (1, 1, 1, 1\cdots)$, and therefore $\xi^t = AD^t\xi_0$.

The solution for F_{ij} at time t can therefore be written as a sum of eigenvectors:

$$F_{ij} = 1 - \sum_\alpha \gamma_{ij,\alpha}\lambda_\alpha^t. \qquad (A1)$$

Asymptotically, the identities converge to $F_{ij,t} \approx 1 - \gamma_{ij,1}\lambda_1^t$. Thus the rate of change of the probability of identity is governed by the same eigenvalue for all demes.

Now, consider the equilibrium identity in state, f_{ij}. This is given by the sum over the probability that lineages coalesce at time $t(F_{ij,t} - F_{ij,t-1})$, multiplied by the probability that no mutations occurred over the $2t$ generations that separate them, $(1 - \mu)^{2t}$. Substituting from Equation A1,

$$f_{ij} = \sum_{t=1}^\infty (1 - \mu)^{2t}(F_{ij,t} - F_{ij,t-1})$$

$$= (1 - \mu)^2 \sum_\alpha \gamma_{ij,\alpha} \frac{(1 - \lambda_\alpha)}{(1 - \lambda_\alpha(1 - \mu)^2)}. \qquad (A2)$$

The identity in state depends on location in a complicated way. For very small mutation rates ($N_e\mu \ll 1$, where $2N_e \equiv 1/(1 - \lambda_1)$), it is dominated by the term associated with the leading eigenvalue; however, this is not the case for $N_e\mu \approx 1$. The average identity in state takes a simple form only if the average is weighted according to the leading eigenvector:

$$\bar{f} \equiv \frac{\Sigma_{i,j} \gamma_{ij,1}f_{ij}}{\Sigma_{i,j} \gamma_{ij,1}} = (1 - \mu)^2 \frac{(1 - \lambda_1)}{(1 - \lambda_1(1 - \mu)^2)}. \qquad (A3)$$

Equating this with the identity in state under the Wright-Fisher model, $f = (1 - \mu)^2(2N - 1)/(2N - (2N - 1)(1 - \mu)^2)$, shows that with this particular definition of average identity, the mutation effective size is equal to the inbreeding effective size. This is true for arbitrary times and arbitrary mutation rates.