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Effects of metapopulation processes on measures of genetic diversity

John R. Pannell* and Brian Charlesworth

Institute of Cell, Animal and Population Biology, King's Buildings, University of Edinburgh, Edinburgh EH9 3JT, UK

Many species persist as a metapopulation under a balance between the local extinction of subpopulations or demes and their recolonization through dispersal from occupied patches. Here we review the growing body of literature dealing with the genetic consequences of such population turnover. We focus our attention principally on theoretical studies of a classical metapopulation with a 'finite-island' model of population structure, rather than on 'continent-island' models or 'source-sink' models. In particular, we concern ourselves with the subset of geographically subdivided population models in which it is assumed that all demes are liable to extinction from time to time and that all demes receive immigrants. Early studies of the genetic effects of population turnover focused on population differentiation, such as measured by F_{ST} . A key advantage of F_{ST} over absolute measures of diversity is its relative independence of the mutation process, so that different genes in the same species may be compared. Another advantage is that F_{ST} will usually equilibrate more quickly following perturbations than will absolute levels of diversity. However, because F_{ST} is a ratio of between-population differentiation to total diversity, the genetic effects of metapopulation processes may be difficult to interpret in terms of F_{ST} on its own, so that the analysis of absolute measures of diversity in addition is likely to be informative. While population turnover may either increase or decrease F_{ST} , depending on the mode of colonization, recurrent extinction and recolonization is expected always to reduce levels of both within-population and species-wide diversity (π_S and π_T , respectively). One corollary of this is that π_S cannot be used as an unbiased estimate of the scaled mutation rate, θ , as it can, with some assumptions about the migration process, in species whose demes do not fluctuate in size. The reduction of π_T in response to population turnover reflects shortened mean coalescent times, although the distribution of coalescence times under extinction-colonization equilibrium is not yet known. Finally, we review current understanding of the effect of metapopulation dynamics on the effective population size.

Keywords: coalescence; effective population size; extinction; colonization; migration; population structure

1. INTRODUCTION

The metapopulation concept was introduced into biology by ecologists wishing to take into account the fact that many species consist of an assemblage of ephemeral subpopulations or demes that persist over time in a dynamic balance between local extinction and recolonization (Levins 1968, 1969). The term was originally used specifically in the context of population turnover, i.e. a metapopulation was defined as a 'population of populations' with an age structure established by the birth of populations through colonization and their death through extinction. However, its use has broadened to cover any population system in which discrete subpopulations exchange genes with one another through dispersal. During the last decade, this broadened nomenclature has coincided with an exponential increase in the number of studies invoking the metapopulation concept in ecology,

conservation biology and population genetics (Hanski & Gilpin 1997).

There have been several recent reviews addressing both empirical and theoretical aspects of metapopulation biology (Hastings & Harrison 1994; Levin 1995; Husband & Barrett 1996; Barrett & Pannell 1999; Hanski 1998, 1999; chapters in Hanski & Gilpin 1997). Most of this work has focused on the ecological considerations of metapopulation dynamics, although McCauley (1995), Barton & Whitlock (1997) and Giles & Goudet (1997a) have reviewed various aspects of the population genetics literature. In this review, we focus on theoretical studies addressing the genetic consequences of a 'classical' metapopulation structure with recurrent local extinction of demes and their recolonization through dispersal; we thus largely restrict our attention to cases where the metapopulation concept may apply in its original, narrower, sense, as was done by Hanski (1998) in his review of the metapopulation concept in ecology.

With the increasing availability of DNA sequence data from samples of individuals within a species, there is a growing need to assess the extent to which the established theoretical background can be used to interpret observed

* Author and address for correspondence: Department of Plant Sciences, South Parks Road, Oxford OX1 3RB, UK (john.pannell@plants.ox.ac.uk).

patterns and to test hypotheses that invoke metapopulation dynamics. We thus ask to what extent available theory can allow us to infer the process of recurrent extinction and recolonization from observations of genetic variation within and between populations. Our approach differs from that adopted in the above-cited studies in that we critically assess the use of relative versus absolute measures of genetic variation to characterize population structure and the dynamics of extinction and colonization. Almost all the classic work on the genetic consequences of population structure has assumed simplified models of migration in order to estimate migration rates from ratios of within- to between-population diversity (for a recent overview, see Wilkinson-Herbots 1998), and this approach has typically been adopted in studies that incorporate extinction and colonization. A key point that we wish to make is that, despite certain advantages involving the rate at which ratios of within- to between-population diversity equilibrate over time (Crow & Aoki 1984), there is a strong case for seeking evidence concerning metapopulation dynamics from patterns of absolute levels of genetic diversity.

Several studies have considered the effects of population turnover on the effective size of a metapopulation with recurrent local extinction (Maruyama & Kimura 1980; Gilpin 1991; Lande 1992; Hedrick & Gilpin 1997; Whitlock & Barton 1997; Wang & Caballero 1999), which must be related to the total amount of diversity that can be maintained in a species at equilibrium (see §3(c)). Clearly, the capacity of a metapopulation to evolve will depend to a large extent on the amount of variation maintained in a species. In our review, we pay particular attention to the possibilities of using measures of neutral genetic diversity to detect a history of metapopulation structure and dynamics. Such evidence is needed to test hypotheses that relate to adaptive evolution in a substructured population with recurrent extinctions.

The classical model of a metapopulation involves an array of n identical demes, each of constant size N , which go extinct and are immediately recolonized at rate e per generation (e.g. Slatkin 1977; see §4). Clearly, many have concluded that this type of metapopulation is unlikely to be found very often in nature (Harrison & Taylor 1997). A more likely structure is one where the extinction rate depends on the size of individual demes. In the extreme, this might mean that some large demes never go extinct and are net exporters of migrants or colonists, while others remain at the brink of extinction and owe their existence solely to the immigration of individuals from a large source (e.g. Gaggiotti & Smouse 1996). The genetic implications of this type of structure will be very different from those of the classical metapopulation, but because the classical model has been the focus of almost all theoretical genetic studies, and has frequently been invoked in interpretations of ecology and phenotypic evolution (e.g. Slatkin & Wade 1978; Lande 1985; Gouyon & Couvet 1987; Barrett *et al.* 1989; Kalisz & McPeck 1993; Ladle *et al.* 1993; Olivieri *et al.* 1997; Pannell 1997; Ronce & Olivieri 1997; Valverde & Silvertown 1997; Pannell & Barrett 1998), it can be taken as a point of departure against which to assess alternatives.

2. FACTORS AFFECTING LEVELS OF GENETIC DIVERSITY

There are many processes that can affect patterns of neutral genetic variation in a population, whether structured or not. They include mutation, local genetic drift within demes, migration between demes, local selection, hitchhiking effects, background selection, balancing selection and species bottlenecks (Wright 1932, 1940, 1951; Malécot 1951; Maynard Smith & Haigh 1974; Berry *et al.* 1991; Charlesworth *et al.* 1993, 1997; Charlesworth & Guttman 1996; Barton 1998). It is thus desirable to know how the effects of metapopulation processes will differ from those due to these other processes. Consider a set of DNA sequences that have been sampled from several individuals in each of several demes across the range of a species or metapopulation. There are at least three aspects of genetic variation that might be affected by population turnover. First, we may look for the effects of population turnover on the mean and distribution of within-deme diversity. The birth and death of demes as a result of extinction and recolonization sets up a population age structure in the metapopulation (Wade & McCauley 1988), and we should expect to find greater variation in the level of absolute within-deme diversity between demes in such a metapopulation than in a subdivided population without recurrent extinction. Second, we may look for the effects of population turnover on the total diversity maintained in the species as a whole. Here a variety of models predict that recurrent local extinction will reduce levels of species-wide diversity (Slatkin 1977; Maruyama & Kimura 1980; Lande 1992; Hedrick & Gilpin 1997; Whitlock & Barton 1997; Pannell & Charlesworth 1999). Third, we may seek a measure of the genetic differentiation among demes.

This third issue has attracted the most attention in theoretical and empirical studies of metapopulation dynamics, in accordance with the widespread use of genetic data from subdivided populations to calculate estimates of F_{ST} , the standardized genetic variance among demes (Wright 1951). Although this has not been emphasized in the metapopulation literature (but see McCauley 1995), perhaps the main advantage of using F_{ST} to indicate population structure and metapopulation processes is the rapidity at which F_{ST} equilibrates in a species (Crow & Aoki 1984; see §5). Another reason, stressed, for example, by Slatkin (1993), is that, when estimated appropriately, F_{ST} is largely independent of the mutation process, so that the same measure can be applied to several genes that differ in their mutation rates. As we shall discuss below (§6), however, this advantage may not apply to genes in different species with contrasting ecologies (Pannell & Charlesworth 1999).

The second issue above, the effect of population turnover on species-wide diversity, has attracted some theoretical work, principally in terms of calculations of the effective size of a metapopulation rather than in terms of actual estimates of diversity, although the two measures are likely to be closely related (Slatkin 1977; Maruyama & Kimura 1980; Hedrick & Gilpin 1997; Whitlock & Barton 1997). Unfortunately, the concept of the effective size of a population is broadly used in the literature to refer to several different entities, not all of which can be

used to make easily testable predictions (Ewens 1982). Finally, relatively little attention in studies of metapopulation dynamics has been focused on estimating the effects of population turnover on the distribution of neutral genetic variation within single populations. This is perhaps surprising, given that a good deal of theoretical work has involved analysing the effects of population subdivision in the absence of extinction on mean within-population diversity and coalescence times for genes sampled from single demes (Li 1976; Nagylaki 1980, 1982, 1998; Slatkin 1987; Strobeck 1987; Wilkinson-Herbots 1998).

3. MODELS WITHOUT EXTINCTION

The recognition that species are structured in space, and that this structure may have biological implications, pre-dates the ecological concept of the metapopulation of Levins (1968, 1969) and has a long history going back to Wright (1940, 1943, 1951, 1965). It was Wright's view that adaptive evolutionary change is influenced to an important extent by population subdivision, and demic structure was central to his 'shifting balance theory' (see Coyne *et al.* 1997; Wade & Goodnight 1998). Of central importance to Wright's theory is the capacity of drift in small populations to bring about genetic differentiation in the face of stabilizing selection and/or migration between demes. The degree to which demes become genetically differentiated from one another as a result of such processes was thus a focus of much of Wright's work.

Several different models of population structure were advanced and explored by Wright and have been taken up by others in his wake. These range from 'island' and 'stepping-stone' models, which assume a demic population structure, to 'continuum' models, where individuals are uniformly distributed in one- or two-dimensional space. The genetic implications of population structure with continuum properties have been discussed by Wright (1943), Malécot (1968), Felsenstein (1975), Maruyama (1977), Slatkin & Barton (1989), and Barton & Wilson (1995), and they will not concern us further; it is the classical models that assume a demic population structure that have been extended to include dynamics of extinction and colonization that are most relevant to our discussion here.

The most general of these models assumes a finite number of non-identical demes linked by gene flow through migration (e.g. Maruyama 1971, 1977; Nagylaki 1982; Wilkinson-Herbots 1998). Deme i contains N_i diploid monoecious individuals that mate at random according to the Wright–Fisher model; in populations not conforming to this idealized breeding structure, N_i is the inbreeding-effective size of deme i . (The Wright–Fisher model assumes that all individuals in a population during one generation are equally likely to be the parents of progeny in the next; this means that, in a population of constant size, each gene can expect to leave a single copy of itself in the following generation, with a variance of one; Crow & Kimura 1970.) The metapopulation is characterized by a 'backwards migration' matrix, where m_{ij} is the probability that a gene in deme i came from deme j of the previous generation. Thus m_{ii} is the proportion of resident genes in deme i , and $\sum_{j \neq i} m_{ij}$ is the proportion of

genes that are immigrants from elsewhere. Whitlock & Barton (1997) have suggested that the extinction and recolonization of deme i can be represented in the migration matrix by setting $m_{ii} = 0$ and $\sum_{j \neq i} m_{ij}$ for some deme i that is due to go extinct (i.e. all individuals in deme i are immigrants). With this formulation, the identity coefficients for extinct demes are left undefined unless immediate recolonization is assumed.

The simplest and most widely used model of geographical structure is the 'island model'. This describes an array of n demes, each containing a constant number, N , of diploid monoecious individuals. Each generation, a fraction m of the genes are replaced by immigrant genes sampled randomly from demes elsewhere in the population. The island model has formed the conceptual basis of almost all classical metapopulation models of genetic variation. Recently, Whitlock & Barton (1997) presented a more general analysis of the effects of metapopulation structure using a 'backwards migration' matrix, where m_{ij} denotes the probability that a gene in deme i came from deme j of the previous generation. Thus m_{ii} is the proportion of resident genes in deme i , and $\sum_{j \neq i} m_{ij}$ is the proportion of genes that are immigrants from elsewhere. They analysed three models: (i) a metapopulation described by a simple migration matrix; (ii) a metapopulation with stochastic catastrophic extinction and recolonization, which assumed an island model of migration; and (iii) a metapopulation model with stochastic population dynamics and migration, which could also result in the extinction and recolonization of individual demes. The second of these models is the classical metapopulation model (Slatkin 1977).

(a) *The effect of population structure on genetic differentiation*

In order to quantify the extent to which demes in a subdivided population are genetically differentiated from one another, Wright (1951) introduced the fixation index, F_{ST} , defined as the correlation between two random gametes sampled from the same population, assigning a zero correlation to two gametes sampled randomly from the population as a whole. If two alleles, A_1 and A_2 , are segregating at a single locus (or nucleotide site) at species-wide mean frequencies (\bar{p}) and $(1 - \bar{p})$, and $\text{var}(p)$ is the variance in frequency of A_1 across demes, then F_{ST} is defined by

$$F_{ST} = \frac{\text{var}(p)}{\bar{p}(1 - \bar{p})}. \quad (1)$$

If more than two alleles are found at the same locus, then F_{ST} can be generalized as Nei's (1973) G_{ST} , defined by

$$F_{ST} = G_{ST} = \frac{f_0 - \bar{f}}{1 - \bar{f}}, \quad (2)$$

where f_0 and \bar{f} are the probabilities that two genes sampled from the same deme and from the metapopulation as a whole are the same allele; with diploidy and random mating within populations, f_0 is the mean homozygosity within demes, and \bar{f} is the expected homozygosity in the metapopulation assuming no subdivision. The values of f_0 and \bar{f} will depend both on deme sizes

and migration rates as well as on the rate and mode of mutation.

We can also reformulate F_{ST} given by equation (2) in terms of the average times to coalescence of pairs of alleles sampled from within demes and from the population as a whole, i.e. independently of the mutation process (Slatkin 1991). Under the infinite alleles model of neutral mutations, in which each new mutation is to an allele that is not represented in the population (Kimura & Crow 1964), the probability of identity in state of two alleles, f , is approximately

$$f \approx 1 - 2u\bar{t}, \quad (3)$$

where t is the time to coalescence of the pair of alleles in question and the mutation rate per locus, u , is sufficiently small (Hudson 1990). Taking expectations over the distribution of t , and substituting into equation (2), gives

$$F_{ST} = \frac{\bar{t} - \bar{t}_0}{\bar{t}}, \quad (4)$$

where \bar{t}_0 is the average time to coalescence of two alleles sampled from the same deme and \bar{t} is the mean time to coalescence of two alleles sampled from the population as a whole (Slatkin 1991, 1993). Equations (1) and (2) are frequently used to estimate F_{ST} from allozyme or microsatellite data collected from individuals in different demes and equations (3) and (4) may be more appropriate analyses of DNA sequence data where the infinite-sites model applies (Kimura 1971). In this case we write F_{ST} in terms of average pairwise diversities per nucleotide site in samples taken from within demes, π_S , and from the total metapopulation, π_T , by overlaying the appropriate model of mutation onto the coalescence times in equation (4) (see Hudson 1990; Nagylaki 1998; Pannell & Charlesworth 1999). This gives

$$F_{ST} = \frac{\pi_T - \pi_S}{\pi_T}, \quad (5)$$

which is similar in form to Nei's G_{ST} . Various other expressions for population differentiation have also been suggested (Weir & Cockerham 1984; Lynch & Crease 1990; Hudson *et al.* 1992; Charlesworth 1998). Statistically significant departures of F_{ST} from zero signify the genetic divergence of demes through drift, or through selection when different alleles are favoured in different demes or linked to other loci that are under local selection. In a finite-island model of n demes, each with constant size N and migration rate m , the equilibrium value of F_{ST} according to equation (6) can be approximated as a function of the mean number of immigrants into each colony per generation, Nm , assuming that $m \ll 1$ (Crow & Aoki 1984). This relationship,

$$F_{ST} \approx \frac{1}{1 + 4Nm(n/(n-1))^2} \quad (6)$$

approaches Wright's classic formula for F_{ST} when n is large (Wright 1951; Crow & Aoki 1984), as does the value given by equation (5) (Charlesworth 1998):

$$F_{ST} \approx \frac{1}{1 + 4Nm}. \quad (7)$$

Wright (1951) observed that demes will become substantially differentiated from one another only if $Nm < 1$; if $Nm > 1$, different alleles are very unlikely to reach fixation in different demes, although they may still be found at different frequencies among demes. This has been the rationale for using equation (7) as an indirect means of estimating Nm , the mean number of individuals migrating into populations per generation. Although this estimate of gene flow assumes an island model with many demes and small m , it can be a useful approximation for systems with more restricted gene flow, such as two-dimensional stepping-stone models, and it has been widely used as an indirect means of estimating gene flow among subpopulations from isozyme data (Crow & Aoki 1984; Slatkin 1985; Slatkin & Barton 1989). Indeed, in studies of genetic differentiation amongst demes in subdivided populations, the calculation of F_{ST} has tended to be followed almost routinely by an estimation of Nm , tacitly assuming an island model with constant deme sizes. When these assumptions are violated, however, translating F_{ST} directly into an estimate of Nm can be misleading (Whitlock & McCauley 1999). Moreover, where sequence data are available, estimates of gene flow on the basis of F_{ST} and equations (5)–(7) alone lose valuable information, and methods that make use of the added genealogical information inherent in such data may be more efficient (Slatkin & Maddison 1990; Beerli & Felsenstein 1999).

(b) *Within-population diversity*

Under the infinite-sites model of mutation (Kimura 1971), the average within-deme nucleotide diversity, π_S , is an unbiased estimate of $\theta = 4N_Tu$ if all demes are linked by conservative migration (i.e. if migration does not change deme sizes and individuals in each deme contribute equally to the next generation; Nagylaki 1982, 1998). This result follows from the finding that, with conservative migration, the average time to coalescence of two alleles sampled from within a deme, \bar{t}_0 , is independent of further details of the migration process and is the same as that expected in a panmictic population of the same total breeding size, i.e. $\bar{t}_0 = 2N_T$ (Nagylaki 1982, 1998; Slatkin 1987; Strobeck 1987; Hey 1991; Wilkinson-Herbots 1998; reviewed in Nagylaki 2000). (Note, however, that higher moments of \bar{t}_0 are not invariant in the same way; for example, see Hudson 1990.) A generalization of this so-called geographical invariance principle to non-conservative migration has recently been derived by Nagylaki (1998). This suggests that an appropriately weighted measure of within-population nucleotide diversity might provide an approximate estimator of θ , although for it to be of practical use, information would be needed about the number of demes, deme sizes and the full matrix of migration rates between all pairs of demes. Nevertheless, the assumption of conservative migration may be reasonable in many situations, especially if the number of migrants entering each deme per generation is small, there is no substantial directionality of gene flow, and, importantly, deme sizes do not fluctuate from one generation to the next (although see Hudson 1998). This last assumption is clearly violated in a metapopulation with recurrent extinction and recolonization.

(c) *Total diversity and effective size of a metapopulation*

An important question to ask about a species is how much neutral genetic variation can be maintained under a balance between mutation and drift. This is of interest because it provides information about the role that drift has played in the past and because it informs us about the potential efficacy of selection and the possibilities for evolutionary change (Whitlock & Barton 1997). Several studies of structured populations have considered the effect of subdivision on the effective population size, which relates the effect of drift in the population of interest to that expected in an ideal population (Wright 1943). Whitlock & Barton (1997) have recently discussed the differences between various definitions of effective population sizes, which are often ignored even in discussions of the topic (e.g. Wang & Caballero 1999). They noted that the ‘variance effective size’, the ‘inbreeding effective size’, and the ‘eigenvalue effective size’ (Crow & Kimura 1970) of a subdivided population can all be summarized by a single effective size, determined by the asymptotic rate at which the probability of identity by descent increases as one follows lineages backwards in time towards their common ancestors. They found an expression for this eigenvalue (inbreeding) effective size of a metapopulation in terms of correlations of allele frequency within and among demes and the relative contribution of gametes to the next generation from different demes, and they noted that these parameters can in principle be estimated from genetic data sampled from different demes and through a knowledge of the reproductive success of each deme in the metapopulation (see also Wang 1997*a,b*; Wang & Caballero 1999).

Whitlock & Barton (1997) also referred to the ‘mutation effective size’ of a subdivided population. The mutation effective size is simply the size of an ideal population that will maintain the same absolute amount of neutral genetic diversity under a balance between mutation and drift as the population under consideration. In practice, this will depend on the mutational process for the genetic system in question. Under the infinite-sites model of mutation (Kimura 1971), and assuming a Wright–Fisher model of random mating, we expect a population of size N to maintain a total diversity of $\pi_T = 4Nu$ at equilibrium (Kimura 1969). Thus the mutation effective size for the infinite-sites model can be defined as $N_e = \pi_T(4u)^{-1}$, which relates directly to the mean coalescence time of two genes sampled from the metapopulation, \bar{t} , defining N_e as $\bar{t}/2$. If the mutation rate for a locus across species is constant, then their mutation effective sizes relate to one another simply as the ratio of their total diversity values. Similarly, the ratio of the mutation effective size of a population to its census size gives an indication of the effect that population structure has on the importance of drift.

The mutation and eigenvalue effective population sizes are in general not the same (Whitlock & Barton 1997), although they appear in some cases to converge for large n and sufficiently large m . Under the island model with constant deme sizes, both the mutation effective size and the eigenvalue effective size increase as a result of restricted gene flow between demes. This is due to the fact that the variance in reproductive success between individ-

uals across the whole population decreases as a result of subdivision; the output of each deme is fixed, and this reduces the effect of drift (Barton & Whitlock 1997). Whitlock & Barton (1997) noted that the expected increase in the effective size of a subdivided population under the island model when m becomes small is a consequence of the assumptions of constant deme size and that, as soon as fluctuating deme sizes are allowed, very different predictions regarding a population’s effective size are made. This difference was highlighted by McCauley (1991) in his appraisal of the likely impact of population subdivision on species of conservation importance. He suggested that a policy of artificially subdividing threatened species in an attempt to increase their effective size, in the hope of increasing the total diversity that they can maintain, may be misguided if individual populations fluctuate in size. Such fluctuations are likely to erode genetic diversity dramatically. Wang & Caballero (1999) have reviewed the theory behind this idea. Thus, if subpopulations contribute equally to the next generation, the effective population size is always increased by subdivision. However, if the variance in reproductive contribution between demes is greater than *ca.* $1/(2N-1)$, subdivision is expected to result in a decrease in the effective size (Wang & Caballero 1999).

Another definition of effective population size for a subdivided population, the ‘migration effective size’, was introduced by Nagylaki (1980). This is equal to the total number of breeding individuals in the species, N_T , multiplied by β , the inverse of the sum of the ratio of the squares of the elements of the left leading eigenvector of the migration matrix to the sizes of the corresponding demes measured relative to N_T . Under these conditions, the mean within-population diversity under the infinite-sites model, obtained by weighting the pairwise diversity for each deme by its contribution to β is equal to $4N_Tu\beta$, which generalizes the invariance principle to non-conservative migration (see above) (Nagylaki 1998). This measure is approximately equal to the total species diversity if there is ‘strong migration’, i.e. drift within populations is a weak force compared with migration, such that $1/N_i \ll m_i$, where N_i is the number of individuals in population i and m_i is the proportion of individuals in population i that are immigrants (Nagylaki 1980, 1998, 2000). The migration effective size of the metapopulation is thus in general smaller than the mutation effective size. It is also equal to N_T only if migration is conservative, as in the island model. If migration changes deme sizes, however, the migration effective population size will be reduced below the census breeding size (Nagylaki 1980, 1998). This will be the case in a metapopulation with recurrent extinctions and recolonizations (see § 4(c)).

4. MODELS WITH EXTINCTION

Metapopulation models of genetic diversity that include extinction and recolonization have almost exclusively assumed an island model of population structure (Maruyama & Kimura 1980; Wade & McCauley 1988; Whitlock & McCauley 1990; Lande 1992; Whitlock 1992*b*; Hedrick & Gilpin 1997; Ingvarsson 1997; Whitlock & Barton 1997; Pannell & Charlesworth 1999). These can all be traced back to Slatkin’s (1977) seminal paper on the

effects of population turnover on genetic diversity, in which he added the dynamics of extinction and recolonization to the basic model of a subdivided population analysed by Maruyama (1970). Previously, all formal genetic models of populations subdivided into demes had assumed constant deme sizes. However, although Slatkin (1977) provided a formal analysis of the genetic effects of population turnover, it was Wright (1940) who had first argued for the importance of recurrent local extinction in population genetics, suggesting that local extinctions and recolonizations would dramatically decrease the effective size of a population. Wright's model was motivated by a need to explain the fixation of reciprocal translocations that are strongly deleterious until they predominate in the population and that thus appear to require population sizes dramatically smaller than those actually observed. Similarly, Lande (1979, 1985) proposed a model of population turnover to explain patterns of chromosomal evolution.

Slatkin (1977) presented two metapopulation models with extinction and recolonizations: his model I assumed that migrants are drawn from a large 'continental source' in which gene frequencies are unaffected by the dynamics of the metapopulation of 'islands' (continent-island model); his model II assumed that migrants are drawn from the islands themselves, in which gene frequencies evolve in response to processes taking place in the metapopulation (finite-island model). Model II, which follows Maruyama's (1970) analysis of the same model without population turnover, is a classical metapopulation model. Its basic features are as follows.

The metapopulation consists of n identical demes, each containing N diploid monoecious individuals that reproduce according to the Wright-Fisher model. Generations are discrete. Each generation, genes mutate to new alleles at a rate u (i.e. with probability u), according to the infinite-alleles model of mutation (Kimura & Crow 1964). At the beginning of each generation, a proportion e of extant demes goes extinct; if n demes are extant, and the metapopulation is at equilibrium, ne new demes are re-established. Thus e measures the probability that a given deme is founded during the current generation. Colonization and migration may be assumed to occur concurrently after extinction.

New colonies are founded by k individuals, either originating all from a single population (the propagule-pool model; see below) or randomly sampled from the entire metapopulation (the migrant-pool model). In newly colonized demes, the size of a population increases from k to N individuals in a single generation. Migration involves the replacement of a proportion m of the individuals within each extant deme by immigrants drawn randomly from the rest of the metapopulation. Note that in the migrant-pool model, recolonization and migration are assumed to be in general quantitatively different, in that they involve the movement of different numbers of individuals into demes. In the propagule-pool model, the processes of migration and recolonization are also qualitatively different, because the source pools from which colonists and immigrants are drawn differ. Wade & McCauley (1988) have discussed the biological implications of these differences. Whitlock & McCauley (1990) generalized the colonization process of the

propagule- and migrant-pool models by introducing a parameter that accounts for the probability that two genes in the founding group of genes come from the same source population (see §4(a)).

Slatkin (1977) framed his model in terms of probabilities of identity in state of genes sampled within demes (f_0) and between demes (f_1). In analysing his model, he distinguished between the fraction, e , of demes that were colonized in the previous generation, and the fraction, $1-e$, of demes that were extant and did not go extinct. Wade & McCauley (1988) pointed out that this effectively sets up a (geometric) distribution of colony ages, with ne colonies aged one generation, $ne(1-e)$ colonies aged two generations, $ne(1-e)^2$ colonies aged three generations, and so on. Extinction effectively increases the proportion of younger colonies in the metapopulation, and so the extent to which metapopulation processes alter the genetic properties of a species with population turnover depends entirely on the way these processes change the genetic composition of younger populations relative to those that are older. Interestingly, while this point has been used directly to seek evidence for metapopulation processes in natural populations (Couvét *et al.* 1986; Belhassen *et al.* 1989; Olivieri *et al.* 1990; Whitlock 1992a; Antobus & Lack 1994; Dybdal 1994; McCauley *et al.* 1995; Giles & Goudet 1997a,b), it has not been the explicit focus of most theoretical studies, which have effectively summed over the distribution of colony ages to derive expressions for the expectation of various parameters over the entire metapopulation (e.g. Wade & McCauley 1988; Ingvarsson 1997; Whitlock & Barton 1997), although Whitlock (1992b) presented a formula for the expected identity by descent in demes of different ages.

(a) Population differentiation

The main preoccupation of metapopulation models that include population turnover has been the question as to how these processes affect differentiation amongst demes, most commonly measured as F_{ST} . Indeed, even though Slatkin (1977) framed his results in terms of the 'effective number of alleles' for an infinite alleles model, n_e , rather than F_{ST} , he interpreted them in terms of genetic differentiation. (n_e is defined as the reciprocal of the probability of identity in state across the metapopulation, $1/\bar{f}$.) Slatkin found that extinction causes an often dramatic reduction in the effective number of alleles in a metapopulation, and he suggested that this constituted a decrease in the amount of genetic differentiation amongst demes. Wade & McCauley (1988) disagreed with this interpretation, and showed that population differentiation, as defined by F_{ST} , may increase or decrease as a result of extinction, depending on the origin and size of the propagules that found new colonies. The difference in interpretation is due to the fact that Slatkin (1977) did not pay explicit attention in his approximations to the effect that extinction has on within-population diversity. Population turnover is expected always to reduce total population diversity (π_T or n_e) and within-population diversity (π_S or $1-f_0$), but population differentiation, measured by F_{ST} , may be increased or decreased by population turnover.

Wade & McCauley (1988) and Whitlock & McCauley (1990) reframed Slatkin's (1977) model in terms of F_{ST} . Both studies assumed a metapopulation with an infinite

number of demes, and they therefore did not consider the effect of metapopulation processes on the total diversity; their approach assumed that the probability of identity in state of two individuals sampled from different demes is zero. Under this assumption, it was shown by Whitlock & McCauley (1990) that

$$F_{ST} = \frac{1 + Ne/k}{1 + 4Nm + 2Ne(1 - \phi(1 - 1/2k))}, \quad (8)$$

and that F_{ST} is increased by recurrent extinction if

$$k < \frac{2Nm}{1 - \phi} + \frac{1}{2}, \quad (9)$$

where k is the number of colonizing individuals and ϕ is the probability that any two genes in the colonizing propagule come from the same source deme (Whitlock & McCauley 1990); $\phi = 1$ and $\phi = 0$ correspond to Slatkin's propagule- and migrant-pool models, respectively. From this it can be seen that propagule-pool colonization will always cause an increase in F_{ST} relative to the case where there is no local extinction. In contrast, if colonists derive from more than a single deme, then colonization constitutes a mixing of genes, and so if k is larger than about twice the number of migrants into established demes, F_{ST} will be reduced by extinction.

The question as to whether F_{ST} will be increased or decreased by local extinction can simply be rephrased in terms of its direction of change over time after colonization. If the genetic diversity of a newly established population is initially higher than can be maintained at migration–drift equilibrium (as might occur if colonists were many and arrived from several demes and if subsequent migration was low), then local equilibration is expected to erode diversity and to cause an increase in population differentiation over time. In contrast, if colonization causes a severe local bottleneck but subsequent migration is high and from diverse sources, then equilibration towards migration–drift equilibrium should bring about an increase in diversity and a reduction in F_{ST} over time. This can be a particularly useful perspective for empirical studies in cases where the age of populations can be determined. In such situations, whether local population diversity should increase or decrease with colony age depends on the ecology of the species (Wade & McCauley 1988). In most cases, it is probably reasonable to assume that the processes of colonization and migration between extant demes are the same, i.e. that $k = Nm$. It is also likely that colonizing individuals originate most often from one or a few (nearby) demes rather than as a random sample from the metapopulation as a whole (i.e. there is a high value of ϕ , or a mode of colonization approaching the propagule-pool model). This being the case, population differentiation is expected to decrease with colony age (cf. equation (9)), and several studies have found empirical support for this by comparing F_{ST} -values between younger and older colonies (Whitlock 1992a; Antrobus & Lack 1994; McCauley *et al.* 1995; Giles & Goudet 1997a,b; but see Dybdal 1994).

Most metapopulation genetic models have assumed that the parameter values (k , N , m and e) are fixed through time. Whitlock (1992b) showed that this is an important assumption, and that when these values are

allowed to vary, estimates of F_{ST} may differ from their expected values under the assumption of fixed parameters (see also Gaggiotti & Smouse 1996; Hudson 1998). For example, fluctuations in the migration rate, m , cause an increase in the value of F_{ST} relative to its expectation in a metapopulation with the same mean m but without fluctuations. Thus fluctuations in the migration rate reduce the effective migration rate. They also tend to cause temporal fluctuations in the value of F_{ST} itself (Whitlock 1992b).

The assumption in metapopulation models that demes grow in a single generation from the number of colonists, k , to the carrying capacity of the population, N , is also unlikely to hold for most species. It is more likely that populations grow from k to N over several generations. Whitlock (1992b) and Ingvarsson (1997) have examined the effect of protracted colony growth on F_{ST} -values. If the number of immigrants into each site is the same from year to year, then the migration rate may be much higher in younger, smaller, populations, with a corresponding tendency to counteract the effects of a genetic bottleneck brought about during colonization (Whitlock 1992b; Ingvarsson 1997). Within-deme diversity will then more quickly approach a local equilibrium between the balancing forces of migration and drift.

In a classical metapopulation with island-model assumptions, no account is taken of the geographical location of demes. In reality, however, there may in fact be covariation between the age distribution of a metapopulation and the spatial location of different demes, e.g. during the range expansion of a species, where populations on the periphery of its distribution are youngest. Le Corre & Kremer (1998) have shown that, in this type of situation, the result established by Wade & McCauley (1988), that F_{ST} is increased across the metapopulation if $k < 2Nm + 1/2$ (for propagule-pool colonization), still holds. This is simply because the direction in which F_{ST} is altered by population turnover in a classical metapopulation depends only on whether newly established demes are more or less diverse than older populations, as explained above. Whether new demes replace older ones that have formerly gone extinct, as in the classical case, or whether they occur along an advancing front as the metapopulation expands its range, will not affect the direction in which F_{ST} is altered by the colonization process, as long as subsequent migration occurs according to the island model.

(b) Within-deme diversity

Slatkin (1977) presented recursion equations for the probability of identity in state within (f_0) and between (f_1) demes in a finite metapopulation. However, in deriving approximations for the effective number of alleles maintained in the metapopulation at equilibrium between mutation and drift, he assumed that the number of demes, n , was large, so that

$$\bar{f} = \frac{f_0}{n} + \left(1 - \frac{1}{n}\right)f_1 \quad (10)$$

could be approximated by f_1 . Thus the effects of metapopulation dynamics on within-deme diversity were not explored. Models reframing Slatkin's (1977) analysis in

terms of F_{ST} have generally assumed a metapopulation with an infinite number of demes, such that f_1 is assumed to be zero and F_{ST} is approximated by f_0 (Wade & McCauley 1988; Whitlock & McCauley 1990; Whitlock 1992b; Ingvarsson 1997). While this equivalence is convenient (Whitlock 1992b), the assumption that $f_1 = 0$ is in general unrealistic. Moreover, it obscures the important consequences of metapopulation behaviour for within-deme diversity. As first suggested by Wright (1940), and as shown explicitly by Slatkin (1977) and others (Maruyama & Kimura 1980; Lande 1992; Whitlock & Barton 1997; Pannell & Charlesworth 1999), population turnover is expected to cause a dramatic reduction in the total diversity maintained in a metapopulation (see §4(c)). In a metapopulation that has lost almost all of its diversity, migration will clearly have little effect on within-deme diversity, just as recombination along the length of homozygous chromosomes has no genetic effect.

Recently, Pannell & Charlesworth (1999) have revisited Slatkin's recursion equations, reframing them in terms of mean nucleotide-site diversity values under the infinite-sites model rather than identities in state, to find approximations for within-deme and total metapopulation diversity. The main result concerning within-deme diversity is that it may be substantially reduced by population turnover. This reduction in mean within-deme diversity is exacerbated by the fact that the migration of individuals into recently established demes will reintroduce genetic diversity at a much slower rate than expected in the models described in (§4(a)), as migrants are drawn from demes that are likely to be genetically depauperate and similar to each other, i.e. $f_1 > 0$.

A particularly important result from metapopulation models with population turnover is the breakdown of the geographical invariance principle, which allows $\pi_S = 4Nm\theta$ to be used as an estimate of the scaled mutation rate θ (reviewed in Nagylaki 2000). Instead, a metapopulation with propagule-pool colonization, assuming a low extinction rate of the same order of magnitude as the migration rate, will have a mean within-deme diversity of

$$\pi_S \approx \frac{\theta m}{(e + m)}, \quad (11)$$

which is lower than θ ; under migrant-pool colonization, π_S will be somewhat higher (Pannell & Charlesworth 1999). If the migration rate is small and $e \gg m$, then π_S is approximated by $4ke^{-1}$, which may be difficult to distinguish from zero in natural populations.

(c) Total diversity and effective size of a metapopulation

As we have already noted, Slatkin (1977) examined the reduction of diversity in a metapopulation in terms of the effective number of alleles rather than in terms of $(1 - \bar{f})$ or π_T . Maruyama & Kimura (1980) used a similar model to derive expressions for within-deme and total metapopulation diversities, using these to find the effective size of a metapopulation with recurrent local extinction. Lande (1992) showed that, for migrant-pool colonization, the total genetic variance in a metapopulation would be substantially reduced with an extinction–recolonization

rate of about twice the migration rate. Hedrick & Gilpin (1997) used Monte Carlo simulations to calculate the effective size of a metapopulation by measuring the rate of loss of heterozygosity in a finite metapopulation from one generation to the next. A more general analysis of the eigenvalue-effective population size of a metapopulation was presented by Whitlock & Barton (1997). As predicted verbally by Wright (1940), these models all show that local extinctions cause a dramatic reduction in the effective size of a population.

The reasons for this reduction in effective size have been discussed by Whitlock & Barton (1997), Barton & Whitlock (1997) and Hedrick & Gilpin (1997). One contributing factor is simply the reduction in the census size of the metapopulation because local extinction reduces the proportion of occupied sites in any given generation. However, the most important reason is that the process of extinction–recolonization increases the variance in reproductive success among individuals across the metapopulation (reviewed in Wang & Caballero 1999). In an ideal population, population replacement from one generation to the next requires that each gene produce, on average, a single copy of itself, with a variance of one. In contrast, colonists that find themselves in a new, expanding deme in a metapopulation with recurrent extinction may produce many more copies of themselves than those in saturated demes or in demes on the verge of local extinction (which of course leave no progeny).

The reduction in effective size of a metapopulation can be seen also from the perspective of a reduction in the average time it takes for lineages to coalesce as they are traced backwards in time (Hudson 1990; Nagylaki 2000). However, expressions for the full distribution of coalescence times in a metapopulation with recurrent extinction for samples of two or more genes have not yet been published. Such an analysis, even for an island model, is likely to be complicated (e.g. Takahata 1988), but it would give us valuable information about the distribution of rare relative to more common nucleotide variants in samples of sequences that could be tested against statistics such as those of Tajima (1989), Fu & Li (1993) and Fu (1997).

Reductions in total species diversity could be due to single population bottleneck events or genetic hitchhiking events as much as to metapopulation dynamics. Reductions in diversity due to hitchhiking are likely to be found across the entire genome in self-fertilizing organisms (e.g. Nordborg *et al.* 1996; Nordborg & Donnelly 1997; Nordborg 2000; Charlesworth *et al.* 1997) and in asexuals (e.g. Berg 1995, 1996). Indeed, Barton & Whitlock (1997) have drawn an analogy between the effects of metapopulation dynamics and hitchhiking; genes that happen to be present in individuals that colonize new patches will gain an advantage through 'spatial hitchhiking' just as genes in a genetic background that is increasing in frequency as a result of selection will also be dragged to fixation. Single bottleneck events and selective sweeps affect the whole species at once, whereas spatial hitchhiking due to metapopulation dynamics affects local demes one by one (Slatkin & Wiehe 1988). These processes may all reduce the mean coalescence times and total species diversity, but the distribution of coalescence times is likely to differ between them. This possibility is foreshadowed by the

way changes in the migration rate between two demes do not alter the mean time to coalescence of pairs of genes sampled within demes but drastically alter gene-tree shape and the distribution of coalescence times (Hudson 1990; Wilkinson-Herbots 1998).

In their catastrophic-extinction model, Whitlock & Barton (1997) found that the eigenvalue effective size may be greatly reduced as a result of extinctions, and is approximated by

$$N_e \approx \frac{n}{4(m+e)F_{ST}}, \quad (12)$$

where F_{ST} is given by equation (8). This expression also appears to give the mutation effective size of the metapopulation when n is large, as long as $u \ll (nN)^{-1}$ (i.e. under the infinite-sites model (Pannell & Charlesworth 1999)). If the extinction rate is much greater than the migration rate and recolonization follows the propagule-pool model, then the mutation effective size reduces to

$$N_e \approx \frac{(1-e)n}{2e(2-e)}, \quad (13)$$

which is of the same order of magnitude as ne^{-1} and which will be much smaller than the effective size of a panmictic population of size nN if $e \ll 1/N$ (Pannell & Charlesworth 1999).

As discussed in the context of a metapopulation without extinction (§3(c)), the mutation effective size of a population translates into an estimate of the total diversity maintained in the metapopulation at equilibrium. In the limit as u approaches zero, as is true for the infinite-sites model, it can be equated to half the mean coalescence time for a pair of alleles sampled at random from the whole population, and is thus independent of the mutation rate. Expressions for the mutation-effective size of a population derived under the assumptions of the infinite-sites model can be used to make predictions regarding π_T , which can be measured by analysing DNA sequence diversity (e.g. Pannell & Charlesworth 1999). The expected reduction in diversity as a result of population dynamics will be particularly marked in species whose populations grow rapidly in size after a colonization event, as this effectively decreases the migration rate if Nm remains constant between generations (Ingvarsson 1997).

5. RATES OF EQUILIBRATION IN A METAPOPOPULATION

The models we have reviewed have generally sought expressions for population differentiation and diversity measures in a metapopulation at equilibrium, with most analyses focusing on Wright's F_{ST} . As noted earlier (§3(a)), because F_{ST} is a ratio between within-deme diversity and total diversity in the metapopulation, these latter two measures are obscured when F_{ST} alone is calculated (Charlesworth 1998). However, it is plain that both within-deme and total metapopulation diversity can be altered in important ways by recurrent local extinction, and these measures may therefore also contain signals about the role that metapopulation dynamics may have played in a species' history.

There is of course a difficulty in using equilibrium models to understand a species' past. This is simply that they can be completely uninformative about systems that have not yet reached equilibrium, or those in which major perturbations have occurred relatively recently. It is thus important to ask over how long a history we must assume relatively uniform rates of local extinction, migration and total number of demes in a species if we are to use these metapopulation models to make predictions about the amount and distribution of genetic diversity. We may gain some intuition by considering rates of equilibration for the parameters that we wish to estimate. Consider a single panmictic population. At drift-mutation equilibrium, new genetic variants will enter the population through random mutation as often as they are lost through random drift. If the diversity in the population, π_T say, is lower than that expected for its current size (for example, because the population has recently expanded from a bottleneck), then the time it takes for π_T to increase to its expected value will depend on the rate at which new mutations accumulate in the population. In such a situation, π_T will approach mutation-drift equilibrium approximately as fast as $(1-u)^{2t}$ approaches zero, where t is the time in generations. This will of course be very slow if u is small.

In the contrasting scenario, suppose that a large population that had reached mutation-drift equilibrium suffers a drastic reduction in size, so that π_T for the new, smaller, population is much higher than expected; let the reduced mutation effective population size be N'_e . In this situation, equilibration of π will occur about as rapidly as $(1-1/(2N'_e))^t$ approaches zero, i.e. over a time-scale determined by the new effective population size of the species. This, too, may be very slow if N'_e is large.

A major advantage of using F_{ST} as an index to assess the structure and metapopulation dynamics of a subdivided population is its rapid equilibration (Crow & Aoki 1984; McCauley 1995). Basically, the equilibration of F_{ST} after a perturbation involves the redistribution of the diversity already present in the population and will occur, under assumptions of the island model, approximately as fast as $[(1-1/(2N))(1-m)]^{2t}$ approaches zero. It seems most likely that, in many biologically reasonable situations, $u \ll N_e^{-1} \ll m$, so that the equilibration of F_{ST} will be much more rapid than that of either π_T or π_S . This applies equally to a metapopulation, in which recurrent extinction augments the amount of gene flow between demes; recurrent extinction causes an increase in both N_e^{-1} and in gene flow, so that time to equilibration through the loss of genetic variation by drift and through the redistribution of variation through gene flow will be reduced. Pannell & Charlesworth (1999) presented numerical calculations of equilibration times, illustrating these differences between F_{ST} , π_T and π_S . Under realistic parameter values, π_T and π_S tended to equilibrate several orders of magnitude more slowly than F_{ST} , although equilibration following decreases in the number of demes was slower for F_{ST} , illustrating the strong dependence of the F_{ST} ratio on absolute diversities. This result also highlights the fact that the rate of asymptotic convergence of F_{ST} is actually the same as that of the absolute total metapopulation and within-population diversities, i.e. as equilibrium is approached, so the rates of equilibration of

F_{ST} , π_T and π_S converge on one another. This is because the rate of convergence of all functions is controlled by the same eigenvalues. If the numerical calculations cited above were continued for long enough, the slow rate of equilibration of F_{ST} would begin to dominate (T. Nagylaki, personal communication). Nevertheless, although the asymptotic rate of approach to equilibrium will be slow, F_{ST} typically gets close to its equilibrium value relatively quickly.

6. DISCUSSION

The classic relation $F_{ST} = (1 + 4Nm)^{-1}$, derived from analysis of the island model, has provided us with an indirect means of estimating the amount of gene flow between populations in subdivided populations (Slatkin 1985; Slatkin & Barton 1989). Although natural populations are unlikely to conform to the detailed assumptions of this model, Slatkin & Barton (1989) concluded that estimates of gene flow using F_{ST} should often be accurate within a factor of two, even for population structures quite different from the island model (but see Whitlock & McCauley 1999). As these authors note, this degree of accuracy is as much as may be meaningful for situations in which we are unlikely to have detailed information on demography, population structure and especially changes in population parameters over time.

Population genetics theory has also demonstrated that, under conditions met by the island model, measures of average within-population diversity are invariant with respect to the migration rate (Slatkin 1987; Strobeck 1987; Hey 1991; reviewed in Nagylaki 2000) and that estimates of π_S can be then be used to estimate the scaled mutation rate, θ , for the species as a whole. Where assumptions of the island model are not met, e.g. when migration is not conservative or the infinite-sites model does not apply, recent analysis suggests that an appropriately weighted measure of within-population diversity may provide an approximate estimator of θ (Nagylaki 1998). The robustness of the 'invariance principle' to deviations from conservative migration is not known, but it is clear that even the simple metapopulation dynamics we have discussed here are sufficient to reduce the accuracy of estimates of θ based on within-deme diversity (Pannell & Charlesworth 1999).

In a metapopulation with population turnover, average within-deme diversity, measures of total species diversity and F_{ST} may deviate strongly from those expected in an equivalent species with a stable demography. We might thus look for evidence of these deviations in the distribution of neutral genetic diversity. This would be particularly useful for testing hypotheses of mating-system and life-history evolution that invoke selection due to metapopulation dynamics (e.g. Heuch 1978; Gouyon & Couvet 1987; Barrett *et al.* 1989; Olivieri *et al.* 1997; Pannell 1997; Ronce & Olivieri 1997; Pannell & Barrett 1998), or ecological models incorporating extinction-recolonization dynamics (see works reviewed in Hanski & Gilpin 1997; Hanski 1998, 1999). To what extent have the metapopulation models reviewed here been able to inform us about the biology of natural species?

Recently, Giles & Goudet (1997a) have reviewed the few empirical studies aimed at testing these models

(Whitlock 1992a; Antrobus & Lack 1994; Dybdal 1994; McCauley *et al.* 1995; Giles & Goudet 1997b; see also Ingvarsson *et al.* 1997; Ingvarsson 1998). All but one of these case studies confirmed the prediction of equation (9) that F_{ST} is increased as a result of population turnover if colonization occurs through a similar process to migration (i.e. $k \approx Nm$), and particularly if colonization follows a propagule-pool model more closely than a migrant-pool model. In these studies, F_{ST} calculated among younger populations was found to be higher than that calculated among older populations. This agreement between field data and theory is encouraging, especially given the simplicity of the underlying models. However, in these models, measures of neutral diversity are sensitive to the value of several different parameters, such as the population size, N , the number of demes, n , the number of immigrants into extant sites per generation, Nm , the number of individuals that make up founding propagules, k , the source of those propagules, ϕ ($\phi = 1$ for propagule-pool colonization, $\phi = 0$ for migrant-pool colonization), the extinction rate, e , and the mutation rate, u . Variation in any one of these parameters leads to changes in predictions of F_{ST} and within- and among-deme diversity, although F_{ST} is independent of u for small Nnu , as discussed in § 5 (Whitlock & Barton 1997; see also Pannell & Charlesworth 1999).

Thus, in contrast to species with constant local population sizes and a population structure adequately approximated by an island model, estimates of F_{ST} for species that are influenced by population turnover will be informative about patterns of gene flow only where we have estimates of other parameters in the model, too. Whitlock (1992a) was able to estimate all the parameters of his model using both genetic analysis as well as demographic census and mark-recapture data from the mycophagous beetle *Bolitotherus cornutus*, and he found good correspondence with the quantitative predictions. Similarly, Ingvarsson *et al.* (1997) estimated e , m , N , k and ϕ for a metapopulation of the mycophagous beetle *Phalacrus substriatus* and found good agreement between the theoretical prediction of F_{ST} based on these estimates, and F_{ST} calculated using genetic data. In particular, he found that colonists had a high probability of common origin (high ϕ) and a high degree of relatedness.

In a study of a metapopulation of the plant *Silene dioica* growing on islands of different ages in an archipelago, Giles & Goudet (1997b) inferred the mode of colonization and the nature of subsequent immigration into extant demes by comparing correlations of genetic and geographical distances between groups of populations of different ages. They found evidence for isolation by distance in a positive correlation between geographical and genetic distance and suggested that the lack of any trace of distance-dependent migration in the youngest populations might be due to migrant-pool colonization. However, in a subsequent study, Giles *et al.* (1998) concluded that patches of plants growing on islands were the result of propagule-pool colonization, whereas gene flow between islands followed a migrant-pool model. An interesting aspect of these studies on *S. dioica* was the finding that old populations, which are on the verge of extinction as a result of successional processes and which no longer recruit juveniles or immigrants, were more

differentiated from one another than the larger populations of intermediate age (Giles & Goudet 1997*b*). As the authors point out, this result is not predicted by the standard metapopulation models, which assume a continual influx of immigrants into populations of all ages and an increase in size before catastrophic extinction occurs (Giles & Goudet 1997*a,b*).

A further study that set out to compare genetic differentiation between newly founded and older demes was performed on tide-pool populations of copepods in a littoral zone by Dybdal (1994). As in the other studies, it was predicted that the process of colony founding would give rise to greater differentiation amongst demes. However, the opposite result was obtained; older populations, which occurred higher in the littoral zone, were more differentiated than the younger populations, which were more frequently disturbed by tidal movement. This result was taken to indicate departures from the simple structure assumed in the classical metapopulation models that we have been discussing here. It appears that the older copepod populations were less closely connected to each other and to the rest of the metapopulation, i.e. that migration between them was negligible (Dybdal 1994).

These empirical studies have sought to describe more closely the dynamics of species that were already known to have a metapopulation structure. In an important sense, they have resulted as much in support for the hypothesis of a metapopulation structure in the species under investigation (e.g. Whitlock 1992*a*; Ingvarsson *et al.* 1997) as in drawing attention to aspects of the models that do not adequately describe the species history (e.g. Dybdal 1994; Giles & Goudet 1997*a,b*). Recently, it was suggested that patterns of diversity in inbreeding populations of the plant *Leavenworthia* might be due to a history of population turnover (Liu *et al.* 1998). However, comparison of predictions of metapopulation models with the genetic data showed that a history of recurrent extinctions and recolonizations was an unlikely explanation for the observations; metapopulation processes should lead to a reduction in both within-population and species-wide diversity (Pannell & Charlesworth 1999), whereas genetic diversity between inbreeding populations of *Leavenworthia* was high despite an almost total absence of diversity within populations (Liu *et al.* 1998). Thus in this case, too, the simple metapopulation models we have been discussing were useful in allowing a rejection of a simple model of population structure and dynamics.

Given the expectation of the small effective population size of a metapopulation (Harrison & Hastings 1996; Whitlock & Barton 1997; Wang & Caballero 1999), it is noteworthy that in those empirical studies to have found evidence for a history of metapopulation dynamics, sufficient genetic variation could still be found for estimates of F_{ST} to be made. This suggests either that the total breeding number of the species, nN , is, or has recently been, very large indeed (i.e. that the number of demes is particularly high), or that the erosion of neutral diversity within the metapopulation is being counteracted by continued gene flow from a larger source outside the metapopulation under examination. This second alternative seems to be quite likely, and would describe the expansion of a species range as new demes are established along a moving front (Nichols & Hewitt 1994; Ibrahim

et al. 1996; Le Corre & Kremer 1998; and see below), for example, as a species colonizes new habitat after an ice age, or in the example described above where *S. dioica* has been able to expand its range by colonizing new islands rising out of the sea. Le Corre & Kremer (1998) showed that, for stepping-stone colonization, within-population heterozygosity will be much reduced at the colonization front relative to heterozygosity in the migrant source. In a model examining the effects of migration from a source population to a sink, Gaggiotti & Smouse (1996) similarly showed that genetic variation can be maintained in a small sink population only through the continued influx of genes from a large source. Moreover, they emphasized the importance of stochasticity in the migration process, noting that it is as much the stochastic nature of migration as the mean migration rate that will determine how much variation can be maintained in sink populations (see also Whitlock 1992*b*).

Unfortunately, despite the usefulness of the metapopulation concept in understanding the genetic implications of population turnover, we are still far from being able to apply theoretical models to genetic data in order to estimate important demographic parameters such as rates of extinction. This contrasts with the possibility of using F_{ST} -values to estimate levels of gene flow among demographically stable populations (Slatkin 1985; Slatkin & Barton 1989). Gaggiotti & Smouse (1996, p. 944) concluded the discussion of their source–sink analysis by noting that ‘it does not seem possible to infer anything of interest about the applicable model, based on estimates of genetic parameters [that are] sensitive to the details of the model and to time in nonequilibrium populations’. Nevertheless, with the increasing availability of nucleotide sequence data sampled from within and among populations of individual species, it may yet be possible to detect signatures of metapopulation dynamics in much the same way that signatures of departures from neutrality have been sought (e.g. Tajima 1989; Fu & Li 1993; Fu 1997). If so, then a coalescence analysis of the effects of metapopulation dynamics on the shapes of gene trees may prove fruitful (e.g. Austerlitz *et al.* 1997; Takahata *et al.* 1997; Wakeley 1999).

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