Polygenic local adaptation in metapopulations: a stochastic eco-evolutionary model

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Abstract

This paper analyses how allele frequencies and population sizes co-evolve in a metapopulation with infinitely many islands that are connected via migration. Each island belongs to one of several distinct ecological niches or habitats. The genetic component of fitness is influenced by an additive trait which is under habitat-specific selection. We analyse the conditions under which locally favoured alleles can be maintained in a rare habitat within the metapopulation, and clarify how demographic stochasticity, the genetic architecture of the selected trait and the relative strengths of selection, gene flow and genetic drift influence local adaptation. An important focus is to understand how the coupling between population size and multiple loci under hard selection shape eco-evolutionary outcomes. Our analysis is based on the diffusion approximation (neglecting linkage disequilibria), and yields an explicit solution for the joint distribution of allele frequencies and population size in each habitat, given the average across the whole metapopulation. We also derive simpler approximations for various limits: including when the coupling between mean fitness and population size can be neglected (the soft selection limit), when loci are close to fixation for one or other allele (the low migration limit), and when population sizes are essentially determined by the expected mean population fitness (the semi-deterministic limit). Individual-based simulations are used to test the validity of key approximations underlying the diffusion framework.

Keywords: eco-evolutionary dynamics, demographic stochasticity, polygenic selection, metapopulation, local adaptation, speciation

Introduction

Adaptation to local environmental fluctuations can be quite rapid (Thompson, 1998; Grant and Grant, 2006; Kokko and López-Sepulcre, 2007; Kinnison and Hendry, 2001), such that the time scale of evolutionary change is comparable to ecological timescales, giving rise to feedback between demography and evolution. Reciprocal interactions between population size and adaptation were described by Fisher (1930), which later led to the notion of *hard selection*, whereby high genetic load and ensuing 'selective deaths' can drive populations to extinction (Haldane, 1956). This is an extreme example of a more general feedback loop: an increase in genetic load due to deleterious variants reduces population size; smaller populations are affected more strongly by drift and gene flow, which increase the fixation of locally deleterious alleles, which further decreases size.

Eco-evolutionary feedbacks of this sort are crucial during evolutionary rescue following a sudden environmental shift (Gomulkiewicz and Holt, 1995; Gonzalez et al., 2013), and also play a key role in the survival of marginal populations (Kawecki, 2008), the colonisation of peripheral habitats (Barton and Etheridge, 2018; Sachdeva, 2019), and the emergence of sharp geographic range margins in the absence of environmental discontinuities (Polechová and Barton, 2015; Polechová, 2018).

Eco-evolutionary feedbacks are especially important in fragmented, heterogeneous habitats, where stochastic extinction and recolonisation of patches may necessitate recurrent bouts of rapid adaptation, especially if selective pressures vary. This kind of metapopulation structure may arise, for instance, if multiple hosts are available within the same region (Carroll and Boyd, 1992; Dobler and Farrell, 1999); this can favour host-specific adaptations, leading to adaptive divergence between sub-populations that specialise on different hosts. The potential for local adaptation and the stability of sub-populations then depends on the interaction between selection (which is mediated by the genetic architecture of selected traits), dispersal (which protects populations from inbreeding load and stochastic extinction, but may also introduce maladapted phenotypes, thus generating hybridisation load) and demography (which is affected by mean genetic fitness, and in turn influences the efficacy of selection).

Previous theoretical work on the persistence of subdivided populations neglects key aspects of this interplay. For instance, Blanquart et al. (2012) analyse conditions for local adaptation in a spatially heterogeneous metapopulation under *soft* selection, thus neglecting feedback between fitness and demography. Ronce and Kirkpatrick (2001) explicitly consider the coupling between fitness and population size in a metapopulation with multiple ecologically distinct habitats, but neglect all sources of stochasticity. Another modeling approach, exemplified by Hanski and Mononen (2011), assumes instant recolonisation of patches (at a fixed rate) and subsequent deterministic extinction based on population fitness. However, such approaches do not explicitly consider the coupled *stochastic* dynamics of genotype frequencies and population sizes that are likely to influence extinction thresholds in marginal habitats. Conversely, work on the effects of demographic and environmental fluctuations typically does not consider evolutionary dynamics due to genetic change (Lande, 1993).

A second challenge is to incorporate realistic assumptions about the genetic architecture of selected traits into eco-evolutionary models. At present, most metapopulation models assume one of two extreme architectures (Govaert et al., 2019; Lion, 2018), either

mutations that occur one by one (adaptive dynamics models), or a very large number of infinitesimal effect loci (quantitative genetics). Unlike adaptive dynamics, quantitative genetic models can describe response from standing genetic variation, which often underlies rapid adaptation. However, with a few exceptions (Hanski and Mononen, 2011; Rouhani and Barton, 1993; Ronce and Kirkpatrick, 2001), most such models consider migration into a *single* population (e.g., Barton and Etheridge (2018); Chevin et al. (2017); Tufto (2001)).

Here, we investigate the joint evolution of population size and allele frequencies in an idealised metapopulation, consisting of infinitely many demes that exchange genes with a common migrant pool. We assume that each island belongs to one of several habitats that are characterised by distinct selection pressures, and ask: when can demographically stable, locally adapted populations be maintained within demes despite gene flow? As we argue below, gene flow limits local adaptation not only by opposing selection at individual loci, but also via constraints arising from migration load (Lenormand, 2002). Mean fitness is reduced by at least m (the rate of migration between demes) per locally adapted locus. With hard selection, this constrains the number of locally adapted alleles that can be maintained without population collapse.

An important focus of our study is to clarify the conditions under which demes belonging to a 'rare' or marginal habitat evolve or maintain local adaptation, or instead are reduced to maladapted sink populations. Understanding evolution in marginal habitats has important implications for range limits and the long-term survival of metapopulations, and because local adaptation in marginal habitats may be the first step towards speciation.

A second focus is to understand how local adaptation is influenced by eco-evolutionary feedbacks between demography, dispersal and selection, for *polygenic* traits influenced by many (but not necessarily very many) loci. A central challenge for analysing polygenic evolution in subdivided populations is to account for statistical associations, i.e., linkage disequilibria (LD) between loci. The theoretical framework developed here neglects such associations by assuming linkage equilibrium (LE) within demes as well as within the migrant pool. This allows us to approximate the evolutionary dynamics of multi-locus genotypes solely by allele frequencies. Assuming LE does *not* imply that loci evolve independently of each other; as demonstrated below, under hard selection, evolutionary dynamics of different loci become coupled due to their aggregate effects on population size (via average fitness), which in turn influences individual loci via genetic drift.

Our analysis is based on a *diffusion approximation* for the joint stochastic evolution of allele frequencies and population size. While the diffusion approximation has been widely used in population genetics (Fisher, 1922; Kimura, 1955), it remains less prominent in ecology, and has only been used to model stochastic population dynamics, without incorporating genetics (e.g., Lande (1993); Mangel and Tier (1993)). Demographic stochasticity (i.e., stochastic fluctuations in size) has a pronounced effect when populations are small and close to the threshold of extinction. Moreover, selection is less effective in small populations, causing maladaptive alleles to fix due to genetic drift, thus further reducing fitness and size, rendering the population even more vulnerable to stochastic fluctuations. This makes it necessary to account for demographic stochasticity and genetic drift together.

Our framework incorporates both types of stochasticity, following a method presented

earlier for asymmetric continent-island migration (Banglawala, 2010). The full model requires a numerical solution, but explicit analytical predictions are possible in various biologically interesting limits. In order to assess the importance of LE and other assumptions underlying the diffusion framework, we compare our analytical predictions against individual-based simulations with a finite number of demes.

Model and Methods

Consider a metapopulation with infinitely many islands (demes) that exchange genes via a common pool. Individuals are haploid and express an additive trait that is influenced by L unlinked loci. Each locus can be in one of two alternative allelic states, denoted by $x{=}0,1$. The trait value z associated with an individual is the sum of effects of the alleles it carries: $z{=}\sum_{j=1}^{L}\gamma_j x_j$, where γ_j is the difference between effect sizes of alternative alleles at the jth locus. The additive trait is under environment-dependent directional selection: the fitness $W_i(z)$ of an individual with trait value z on island i, is $e^{\beta_i z+\theta_i}$, where β_i is the strength of selection and θ_i a constant that determines the maximum possible fitness on the ith island.

The life cycle of individuals consists of dispersal, followed by selection and mating. As our primary focus is on how gene flow influences the maintenance of polymorphisms and local adaptation, we neglect other sources of variation. However, the framework can be easily extended to incorporate mutation. In each generation, a common migrant pool is formed by drawing a fraction m from each island; migrants from this pool are then evenly redistributed across islands. The assumption of infinitely many islands is convenient, since it allows us to treat genotype frequencies in the migrant pool as deterministic (rather than following a distribution). In simulations, we model a large but finite number of islands.

We assume a model of hard selection, where population size is influenced by genetically determined mean fitness plus density-dependent regulation, which occurs locally within each island. The size n_i^* on island i, after selection and regulation, is a Poisson random variable with mean $n_i\overline{W}_i e^{r_{0,i}(1-n_i/K_i)}$. Here, $r_{0,i}$ is the baseline rate of growth, K_i the carrying capacity, n_i the population size prior to selection, and $\overline{W}_i$ the mean genetic component of fitness on island i. The n_i^* offspring are formed by randomly sampling $2n_i^*$ parents (with replacement) from the n_i individuals in proportion to individual fitness, and then creating offspring via free recombination of each pair of parental genotypes. For simplicity, $r_{0,i}$ and K_i are taken to be the same across all islands: $r_{0,i}{=}r_0$ and $K_i{=}K$. However, this can be easily generalized to island-specific growth rates and carrying capacities.

We assume that any island belongs to one of g local environments or habitats, indexed by $\alpha{=}1,2,\ldots g$, such that the environment-dependent selection strength β can take on one of g possible values. We use $\rho_1,\rho_2,\ldots\rho_g$ to denote the fraction of islands that belong to the different habitats ($\sum_i \rho_i{=}1$).

When selection is strong relative to migration and drift, and the number of loci not very large (see below), populations can adapt to their local habitat, resulting in LD between alleles favoured in a habitat. To describe such a population exactly, we would need to track the frequencies of all genotypes, which becomes cumbersome with large

numbers of loci. However, when selection per locus is weak relative to recombination, LD within a deme (generated by immigration of individuals from differently adapted habitats) is rapidly dissipated and can be neglected. Assuming LE allows us to only consider the coupled dynamics of population size and L alleles, rather than 2^L genotypes.

For weak growth, selection and migration (i.e., $r_0, \beta\gamma, m \ll 1$), we can use a continuous time approximation for allele frequency and population size dynamics. The size n_i and the allele frequency $p_{i,j}$ at the jth locus on the ith island satisfy the following *coupled* equations:

$$\frac{\partial n_i}{\partial t} = \left[r_0 (1 - \frac{n_i}{K}) + r_{g,i} \right] n_i + m(\overline{n} - n_i) + \lambda_n(t) \tag{1a}$$

$$\frac{\partial p_{i,j}}{\partial t} = p_{i,j}(1 - p_{i,j}) \frac{\partial r_{g,i}}{\partial p_{i,j}} + m \frac{\overline{n}}{n_i} [\frac{\overline{np}_j}{\overline{n}} - p_{i,j}] + \lambda_p(t) \tag{1b}$$

Here $r_{g,i} = \beta_i \langle z \rangle_i + \theta_i$ is the genetic component of the growth rate (i.e., the log fitness) averaged over all genotypes on island i; it depends on allele frequencies via the trait mean $\langle z \rangle_i = \sum_j \gamma_j p_{i,j}$ on island i. Note that the dynamics of any one deme are coupled to the dynamics of all other demes via the mean number of immigrant individuals $m\overline{n}$ and the mean number of immigrant alleles $m\overline{np_j}$ (at locus j) per unit time (where $\overline{n}$ is the population size and $\overline{np_j}$ the number of allele copies per deme, averaged across all demes in the metapopulation).

Equation (1a) describes how population size evolves over time on an island in a given habitat. The first term within the square brackets describes logistic growth, and the second the coupling between size and allele frequencies (via mean fitness): growth rates are reduced relative to the maximum r_0 due to environment-dependent selection on the additive trait. The second term describes the effects of migration, which makes a net positive contribution when the size of the focal deme is less than the average $\overline{n}$ across the metapopulation. The third term $\lambda_n(t)$ is an uncorrelated random process with $\mathbb{E}[\lambda_n] = 0$ and $\mathbb{E}[\lambda_n(t)\lambda_n(t')] = n(t)\delta(t - t')$, where $\mathbb{E}[...]$ denotes an average over independent realisations of the process. This 'noise' term describes fluctuations of population size due to the stochasticity inherent in reproduction and death. In the present model, where the number of offspring is Poisson-distributed, the variance of population sizes is $n(t)$.

Equation (1b) describes allele frequency dynamics at locus j: the first term corresponds to the change due to selection on the locally favoured allele, while the second term describes the effect of migration, which tends to pull allele frequencies closer to the average amongst migrants (given by $\overline{np}_j/\overline{n}$). Note that islands with larger populations contribute more to the average allele frequency in the migrant pool. Moreover, locally favoured alleles are less prone to swamping in larger populations, since the migration term in eq. (1b) is proportional to $\overline{n}/n_i$ (a second source of coupling between allele frequency and population size). This results in a positive feedback: better adapted islands are more populous, send out more migrants and are less affected by incoming, maladapted individuals, and thus maintain local adaptation more easily (Haldane, 1956). Fluctuations about the expected allele frequency are described by $\lambda_p(t)$, which satisfies $\mathbb{E}[\lambda_p] = 0$ and $\mathbb{E}[\lambda_p(t)\lambda_p(t')] = [(p(t)q(t))/n(t)]\delta(t - t')$, as in the haploid Wright-Fisher model.

We restrict our attention to scenarios with just two alternative habitats ($g = 2$), with relative frequencies $\rho_1 = 1 - \rho$ and $\rho_2 = \rho$, where $\rho < 1/2$. Thus, ρ denotes the frequency of the rare habitat (denoted by the index 2 hereafter). We assume that directional selection

pushes traits towards the two extremes of the phenotypic range in the two habitats: thus, a genotype with all '1' alleles or all '0' alleles has maximum fitness in the first or second habitat respectively. For simplicity, the maximum possible genetic fitness is assumed to be the same in both habitats. Then the population-averaged log fitness r_g in the two habitats is $-\sum_{j=1}^{L} s_{1,j}q_{1,j}$ and $-\sum_{j=1}^{L} s_{2,j}p_{2,j}$, where p indicates the frequency of the '1' allele at any locus, and $s_{1,j}$ (or $s_{2,j}$) the strength of selection against the locally deleterious allele at locus j in habitat 1 (or 2).

These simplifying assumptions allow us to consider a reduced set of parameters (see Key Notation) and focus on key qualitative behaviours. However, equation (1) is quite general and applies to more complicated scenarios involving multiple local habitats with heterogeneous patch qualities (e.g., unequal maximum growth rates and carrying capacities).

Equations (1a) and (1b) can be re-expressed in terms of *dimensionless* parameters, constructed by rescaling population size by the carrying capacity K, and all evolutionary rates by the baseline growth rate r_0. This results in the following re-scaled parameters (denoted by uppercase letters): $T{=}r_0t$, $M{=}m/r_0$, $S{=}s/r_0$, $N{=}n/K$, and the new parameter $\zeta{=}r_0K$, which represents the number of births per unit time at carrying capacity, and hence governs the magnitude of demographic fluctuations.

Diffusion approximation for the joint distribution of allele frequencies and population size.

We can construct an equation for the time evolution of the joint probability distribution $\Psi(N, p_1, \ldots, p_L, t)$ of allele frequencies $p_1, \ldots, p_L$ and (re-scaled) population size N on any island in the metapopulation using the *diffusion approximation*. This involves approximating the evolution of the distribution by a diffusion that depends only on the mean and variance of the change in N and p per unit time. For ease of notation, the vector $(N, p_1, \ldots p_L)$ is denoted by $\mathbf{x}$. We drop the index specifying the island, since the diffusion equation has the same form on all islands; the dependence on the local habitat arises only through the population-averaged log fitness R_g, which differs between habitats. Then we have:

$$\begin{aligned}
\frac{\partial}{\partial t}\Psi(\mathbf{x},t) = & -\frac{\partial}{\partial N}\left[A_N(\mathbf{x})\Psi(\mathbf{x},t)\right] + \frac{1}{2\zeta}\frac{\partial^2}{\partial N^2}\left[B_N(\mathbf{x})\Psi(\mathbf{x},t)\right] \\
& -\sum_{j=1}^{L}\frac{\partial}{\partial p_j}\left[A_{p_j}(\mathbf{x})\Psi(\mathbf{x},t)\right] + \frac{1}{2\zeta}\sum_{j=1}^{L}\frac{\partial^2}{\partial p_j^2}\left[B_{p_j}(\mathbf{x})\Psi(\mathbf{x},t)\right] \\
& A_N(\mathbf{x}) = [1-N+R_g]N + M(\overline{N}-N) \qquad A_{p_j}(\mathbf{x}) = p_{i,j}(1-p_{i,j})\frac{\partial R_g}{\partial p_j} + M\frac{\overline{N}}{N}\left[\frac{\overline{Np_j}}{\overline{N}} - p_{i,j}\right] \\
& B_N(\mathbf{x}) = N \qquad B_{p_j}(\mathbf{x}) = \frac{p_j(1-p_j)}{N}
\end{aligned} \tag{2}$$

Here A_N and A_{p_j} specify the expected rate of change of the population size and allele frequencies (see also eq. (1)), and B_N and B_{p_j} the variance of the change per unit time

(both expressed in terms of re-scaled parameters $S, M, \ldots$). Equation (2) involves no mixed derivatives with respect to N and p_j as the covariance of fluctuations of p and N is zero (to first order in $1/N$, s, etc.). The equations also involve the average log fitness R_g given by $-\sum_{j=1}^{L} S_{1,j}q_j$ and $-\sum_{j=1}^{L} S_{2,j}p_j$ in the first and second habitats respectively.

Equation (2) describes the stochastic evolution of the joint distribution of population size and allele frequencies and in principle, can be numerically integrated to obtain the expected value, variances and co-variances of N and $\{p_j\}$ through time. However, here we focus on the equilibrium distribution, conditioned on the average number of individuals $\overline{N}$ and allele copies $\overline{Np_j}$ per deme (averaged across demes):

$$\Psi(N, \{p_j\}|\overline{N}, \{\overline{Np_j}\}) = \frac{1}{Z}\, N^{2\zeta M\overline{N}-1} \mathrm{e}^{-\zeta[(1-M)-N]^2} \prod_{j=1}^{L} \left(p_j^{2\zeta M\overline{Np}_j-1} (1-p_j)^{2\zeta M(\overline{N}-\overline{Np}_j)-1} \mathrm{e}^{-2\zeta N S_j(1-p_j)} \right) \tag{3}$$

where Z is a normalisation constant. Equation (3) specifies the stationary distribution in the first habitat; the distribution in the second (rare) habitat has the same form, except with the last term replaced by $\mathrm{e}^{-2\zeta N S_j p_j}$. Note that an explicit solution (eq. (3)) is possible only because the expected change $A_i(\mathbf{x})$ for each variable in eq. (2) can be expressed as $B_i(\mathbf{x})$ times the gradient of a (suitably-defined) potential $U(\mathbf{x})$, i.e., $A_i(\mathbf{x}) = B_i(\mathbf{x})[\partial U(\mathbf{x})/\partial x_i]$.

Numerical solution for the equilibrium. The state of each deme is determined by the average number of individuals $m\overline{N}$ and copies of each allele $m\overline{Np_j}$ (for the jth locus) that immigrate per unit time. Given these, we can find the expected numbers and allele frequencies $\{\mathbb{E}_i[N], \mathbb{E}_i[Np_j]\}$ within habitat i, by integrating over the stationary distribution (eq. (3)). Here, the expectations $\mathbb{E}[\ \ ]$ can be thought of as averages for a *given* island, obtained by either averaging over replicate metapopulations (or simulations) or by averaging over measurements at uncorrelated timepoints at equilibrium within a single simulation. The crucial point is that at equilibrium, the average across all demes in the metapopulation at any instant (denoted by $\overline{\ }$) must be equal to the weighted sum of the expected values across habitats (Rouhani and Barton, 1993; Barton and Rouhani, 1993). Thus:

$$\sum_i \rho_i \mathbb{E}_i[N] = \overline{N}, \qquad \sum_i \rho_i \mathbb{E}_i[Np_j] = \overline{Np_j} \tag{4}$$

Equilibria are located by starting at an arbitrary $\left\{\overline{N}, \overline{Np_j}\right\}$, calculating $\{\mathbb{E}_i[N], \mathbb{E}_i[Np_j]\}$ using eq. (3), then computing the new $\left\{\overline{N}, \overline{Np_j}\right\}$ using eq. (4), and iterating until a fixed point. With this procedure, either a polymorphism is found, or one or other allele is fixed. In principle, this procedure simultaneously yields the equilibrium population size and allele frequencies at all the L loci (which may have different effect sizes and hence attain different frequencies). However, iterating over an $L+1$ dimensional space is computationally intensive. We thus restrict our attention to the case where effect sizes are equal at all loci (in a given habitat), such that $S_{1,j}=S_1$ and $S_{2,j}=S_2$ for all j. Then, we need to find only the fixed point $\left\{\overline{N}, \overline{Np}\right\}$.

The procedure outlined above is exact, *given* the diffusion approximation which, however, relies on three basic assumptions. First, we assume all processes to be sufficiently

Table 1: Key Notation

g	number of distinct habitats in the metapopulation
ρ_α	fraction of islands in habitat α; we focus on two habitats (g=2), frequencies $1-\rho$ and ρ.
$r_{0,i}$	baseline growth rate on island i; $r_{0,i}=r_0$ for all i.
K_i	carrying capacity of island i; $K_i=K$ for all i.
L	number of loci influencing the trait
$s_{i,j}$	selection coefficient associated with locus j on island i
m	fraction of individuals that migrate from each island
n_i	population size on island i
$p_{i,j}$	frequency (of the '1' allele) at locus j on island i; $q_{i,j}=1-p_{i,j}$
$r_{g,i}$	genetic component of growth rate (i.e., log fitness) averaged over all genotypes on island i; $r_{g,i}$ is given by $-\sum_{j=1}^{L} s_{i,j}q_{i,j}$ and $-\sum_{j=1}^{L} s_{i,j}p_{i,j}$ for islands belonging to first and second habitats respectively
$\overline{n}$, $\overline{np_j}$	average population size per deme and average number of '1' alleles per deme at locus j, averaged across all demes contributing to the migrant pool
$\mathbb{E}_i(n)$, $\mathbb{E}_i(np_j)$	expected population size and expected number of '1' alleles at locus j for a deme in habitat i, obtained by integrating over the equilibrium joint distribution for population size and allele frequencies
Scaled parameters	
$N=n/K$	population size scaled by carrying capacity
$S=s/r_0$, $M=m/r_0$	selection coefficient, migration rate scaled by intrinsic growth rate
$\zeta=r_0K$	average number of births per unit time at carrying capacity; scales inversely with demographic fluctuations.

slow ($r_0, m, s \ll 1$) that a continuous time approximation (eq. (1)) is valid. Second, we assume infinitely many demes, such that population size and allele frequency averaged across all demes exhibit negligible fluctuations, even though within any one deme, they follow a distribution (eq. (3)). This allows us to treat the migrant pool as deterministic, and completely characterised by $\overline{N}$ and $\overline{Np_j}$. Finally, and most critically, we assume that allele frequency evolution at individual loci is unaffected by other loci (except via their joint effects on population size). More specifically, eq. (1) (which forms the basis of eqs. (2) and (3)) neglects LD within any deme as well as LD across the whole metapopulation (by neglecting LD within the migrant pool). This final assumption is justified when selection per locus is much weaker than the rate of recombination between loci. We investigate the sensitivity of our results to each of these assumptions using two types of discrete-generation individual-based simulations (SI, section C).

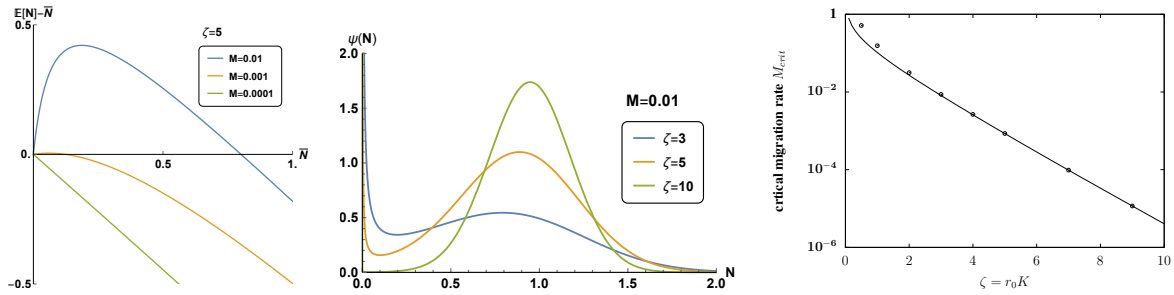
Since the full model involves several parameters, and calculating the joint distribution requires a numerical solution for $\overline{N}$ and $\overline{Np}$, it is useful to consider various limits which allow for simpler approximations. We first consider population dynamics in the absence of selection ($S_1{=}S_2{=}0$), and examine how demographic stochasticity and migration affect metapopulation survival. We then introduce selection, assuming it is weak relative to the baseline growth rate, i.e., $Ls_i \ll r_0$ or $LS_i \ll 1$ (and also neglect demographic stochasticity). In this 'soft selection' limit, population dynamics are largely unaffected by local adaptation, and populations are close to carrying capacity in both well-adapted and maladapted demes. We show when individual loci can adapt locally, despite gene flow and drift, and derive explicit expressions for the critical migration rate below which local adaptation is possible, by assuming that loci are close to fixation for one or other allele.

We then consider scenarios where selection across all loci is strong enough to affect population dynamics, i.e., $LS_1, LS_2 \sim 1$ (for equal-effect loci) resulting in 'hard selection', wherein maladaptation leads to extinction. We examine the hard selection model using the numerical solution for the equilibrium distribution of $(N, p_1, \ldots p_L)$, as well as a simpler 'semi-deterministic' approximation which is valid where the population size can be treated as depending deterministically on the expected allele frequencies. In the main paper, we focus on the case where selection per favourable allele is the same in both habitats ($S_1{=}S_2{=}S$). The more general scenario with $S_1 \neq S_2$ is considered briefly in SI, section B.

Results

Effect of demographic stochasticity and migration in the absence of selection.

Consider a scenario with no selection, such that population sizes are independent of allele frequencies, and only affected by demographic fluctuations and migration. Although individual demes fluctuate, $\overline{N}$ across the entire metapopulation can be treated as deterministic. Demes are coupled through this single variable $\overline{N}$, which determines the expected number of immigrants per deme. From eq. (3), it follows that in the absence



(a) (b) (c)

Figure 1: Population size distribution, expected population size and critical migration thresholds in the absence of selection. (A) $\mathbb{E}(N)-\overline{N}$ versus $\overline{N}$ for $\zeta=r_0K=5$, where $\mathbb{E}(N)$ is the expected population size in a deme, given the average $\overline{N}$ in the metapopulation. The equilibrium solution $\mathbb{E}(N)=\overline{N}$ can be found graphically as the point at which the curve intersects the horizontal zero axis. Stable equilibria are those for which $\mathbb{E}(N)-\overline{N}$ has a negative slope at $\mathbb{E}(N)-\overline{N}=0$. The metapopulation survives ($\overline{N}>0$) only above a critical migration rate $M_c=m_c/r_0\sim0.00085$ (for $\zeta=5$). (B) Probability density $\psi[N]$ of the scaled population size $N=n/K$ for various ζ and $M=0.01$, as obtained from eq. (5). (C) The migration threshold M_c (below which the entire metapopulation goes extinct) vs. ζ. Points show exact results and the solid line depicts the large ζ approximation; M_c declines exponentially with increasing ζ.

of selection, the distribution of population size (on any island), conditioned on $\overline{N}$ is:

$$\psi[N|\overline{N}]=\frac{1}{Z_0}N^{2\zeta M\overline{N}-1}\mathrm{e}^{-\zeta[N-(1-M)]^2} \quad \text{where } Z_0=\int_0^\infty e^{-\zeta[(N-(1-M))]^2}N^{2\zeta M\overline{N}-1}\,dN \qquad (5)$$

The expected population size, $\mathbb{E}(N)$ can be obtained by integrating, and then equating $\mathbb{E}(N)=\overline{N}$ (fig. 1(a)). This yields one or more equilibria for $\overline{N}$, which can be substituted into (5) to obtain the full $\psi[N]$ (as shown in fig. 1(b)).

There is always an equilibrium at extinction ($\mathbb{E}(N)=\overline{N}=0$). Above a critical migration rate M_c, there may also be an equilibrium with $\overline{N}>0$ (fig. 1(a)). Figure 1(c) shows that as $\zeta=r_0K$ increases, the critical rate of migration required to prevent global extinction, decreases exponentially: $M_c\approx e^{-\zeta}/(2\sqrt{\pi\zeta})$. This expression for M_c follows from the fact that it is the migration rate at which the equilibrium $\overline{N}=0$ becomes unstable (SI, section A).

Above this critical migration threshold, the distribution is bimodal if the number of immigrants is small, i.e., for $2\zeta M\overline{N}=m\overline{n}<1$, which corresponds to $M\lesssim\frac{1}{2\zeta}\left(1+\frac{1}{2\zeta}\right)$ (SI, section A). In this case, some populations cluster in a Gaussian distribution around $N=1-M$ (i.e., $n=K(1-m/r_0)$), with variance $1/2\zeta=1/(2r_0K)$, whilst others are near extinction (fig. 1(b)). The parameter ζ thus governs the extent of demographic stochasticity: both the variance of the stationary distribution around carrying capacity and the risk of stochastic extinction fall with increasing ζ. In most of the paper, we will consider growth rates and carrying capacities that are sufficiently high (i.e., $\zeta=r_0K\gg1$) that well-adapted populations exhibit essentially deterministic dynamics and are not prone to stochastic extinction.

Soft selection

We now introduce selection, but assume that the evolutionary change it effects is slow compared to population growth (i.e., $\sum_j S_j \ll 1$) and that demographic stochasticity can be neglected ($\zeta = r_0 K \gg 1$). Then the model reduces to the classical infinite island model (Wright, 1932) with *fixed* size $n=K$ on each island and soft selection within demes. Unlike in the general model with hard selection, allele frequencies at different loci evolve independently under soft selection (assuming LE), since genetic drift at any locus just depends on (a fixed) population size, and not on adaptation at other loci. Thus, we need only consider the allele frequency distribution $\psi[p]$ at one locus. This distribution was first derived by Wright (1932), and also emerges from the joint distribution in eq. (3) by integrating over N (SI, section A).

The expected allele frequency $\mathbb{E}\left(p\,|\overline{p}\right)$ in a deme, given the mean $\overline{p}$ in the migrant pool, is obtained by integrating over $\psi[p]$. Allele frequencies in different demes are coupled via the mean allele frequency, $\overline{p}$, among migrants: within any deme, migration pulls the expected allele frequency towards $\overline{p}$, whereas selection drives $\mathbb{E}_1[p]$ towards 1 (or $\mathbb{E}_2[p]$ towards 0). Since all demes have equal sizes, they contribute equally to the migrant pool. Defining $\overline{p}^* = \rho\mathbb{E}_1\left(p\,|\overline{p}\,, s\right) + (1-\rho)\mathbb{E}_2\left(p\,|\overline{p}\,, -s\right)$, the difference, $\overline{p}^* - \overline{p}$ must be zero when the metapopulation is at equilibrium. The stability of equilibria can be evaluated using the derivative $\partial\overline{p}^*/\partial\overline{p}$; stable equilibria correspond to $\partial\overline{p}^*/\partial\overline{p} < 1$.

Figure 2(a) shows $\overline{p}^* - \overline{p}$ versus $\overline{p}$ for different values of $s_1 = s_2 = s$. Note that there are always equilibria corresponding to $\overline{p}=1$ or $\overline{p}=0$ (i.e., when the whole metapopulation is fixed for one or other allele). A polymorphic equilibrium (with $0<\overline{p}<1$) can be maintained when selection is sufficiently strong (fig. 2(a)), such that alleles favoured in the rare habitat can invade. As selection becomes stronger, the different habitats approach fixation for different alleles (fig. 2(b)). The critical selection strength s_c, above which a polymorphic equilibrium becomes possible, increases with migration (fig. 2(c)).

It is useful to first consider a purely deterministic analysis: this suggests that polymorphism can be maintained only above a critical selection strength $s_c = m(1-2\rho)$, where ρ denotes the frequency of the rare habitat (SI, section A). However, in general, we expect the deterministic analysis to break down close to the threshold s_c: allele frequency distributions must necessarily become bimodal as $s \to s_c$, since $Km\overline{p} \to 0$. Thus the deterministic prediction only provides a lower bound on the true s_c, as drift will further inflate the selection threshold.

In the opposite limit of low migration ($Km \to 0$), loci will be close to fixation for one or other allele. The rates of fixation towards and away from an allele with advantage s, which is at frequency $\overline{p}$ in the migrant pool, are in the ratio $\sim(\overline{p}/\overline{q})e^{2Ks}$, such that the expected frequency of the favoured allele in the deme is $\overline{p}e^{2Ks}/(\overline{p}e^{2Ks}+\overline{q})$ (SI, section A). Thus, in the symmetric case, $s_1 = s_2 = s$, the metapopulation reaches an equilibrium at:

$$\overline{p}^* = (1-\rho)\frac{\overline{p}e^{2Ks}}{\overline{p}e^{2Ks}+\overline{q}} + \rho\frac{\overline{p}}{\overline{p}+\overline{q}e^{2Ks}} \tag{6}$$

A polymorphic equilibrium at $\overline{p} = \frac{(1-\rho)e^{2Ks}-\rho}{e^{2Ks}-1}$ becomes possible if $Ks > Ks_{\mathrm{c}}$ where $Ks_{\mathrm{c}} = \frac{1}{2}\log\left(\frac{1-\rho}{\rho}\right)$ (in the $Km \to 0$ limit). We find that s_{c} increases linearly with m, and approximate this by the corresponding deterministic prediction for linear increase: $Ks_{\mathrm{c}} \approx$

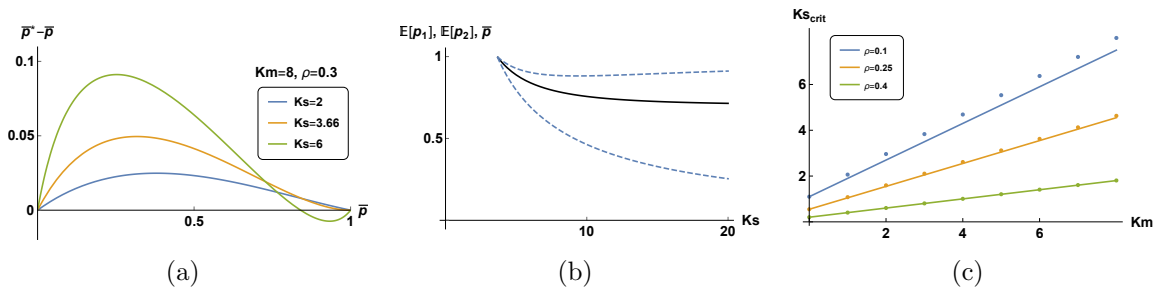


Figure 2: Local adaptation under soft selection. (A) The difference between the weighted average of the expected allele frequency across habitats and the mean in the migrant pool, $(\overline{p}^*-\overline{p})$ vs. $\overline{p}$. The equilibrium solution $\overline{p}^*-\overline{p}=0$ is where the curve intersects the horizontal axis; equilibria are stable if $\overline{p}^*-\overline{p}$ has a negative derivative at this point. A polymorphic equilibrium $0<\overline{p}<1$, exists only above a critical selection strength $Ks_c=3.66$ (orange). When selection is weaker than Ks_c, the allele favoured in the commoner habitat fixes (i.e., the stable equilibrium corresponds to $\overline{p}=1$), and local adaptation is swamped by gene flow. The frequency of the rare habitat is $\rho=0.3$, the average number of migrants per generation is $Km=8$; selection is symmetric: $s_1=s_2=s$. (B) Expected allele frequencies in the two habitats (dashed), and the overall mean across the whole metapopulation (solid), vs. Ks for $s>s_c$. (C) The critical selection strength Ks_c above which a polymorphic equilibrium with $0<\overline{p}<1$ can be maintained vs. the average number of migrants exchanged between demes Km for various fractions ρ of demes belonging to the rare habitat. Points are obtained by numerically solving for stable equilibria; lines show the approximation $Ks_c=\frac{1}{2}\log\left(\frac{1-\rho}{\rho}\right)+Km(1-2\rho)$.

$\frac{1}{2}\log\left(\frac{1-\rho}{\rho}\right)+Km(1-2\rho)$ (solid lines in fig. 2(c)). This is reasonably close to the exact results (points).

Thus, both habitats are simultaneously adapted only if $s>s_c$. For $s<s_c$, alleles that confer a selective advantage in the common habitat tend to fix across the entire metapopulation (stable equilibrium at $\overline{p}=1$ in fig. 2(a)). Interestingly, this bias towards alleles favoured in the common habitat persists even in the limit of very low migration, for which we would have expected allele frequency dynamics of different demes to decouple and be dominated by drift.

Hard selection

We now consider scenarios where mean fitness has a substantial effect on population size, such that maladapted populations go extinct with high probability. This is the case when net selection against maladapted phenotypes is comparable to the baseline growth rate, i.e., $Ls\gtrsim r_0$ or $LS\gtrsim 1$ (assuming L equal-effect loci). Note that this does not imply that selection at *individual* loci is strong. In fact, typical effect sizes may be small enough (i.e., $\zeta S=Ks\leq 1$), that drift can significantly degrade adaptation at individual loci. However, the number of loci L affecting fitness is large, so that selection, in aggregate, is strong (i.e., $L>1/S$). If local adaptation is to be possible even in large populations, then selection must be at least as strong as migration, i.e., $S>M(1-2\rho)$. Further, we focus on parameters for which stochastic extinction of well-adapted populations is extremely improbable (ζ large).

In the following, we use the joint distribution for population size and allele frequencies (eq. 3) to identify the conditions under which locally adapted, stable populations are maintained in both habitats. We first analyse one example in detail, and then explore pa-

rameter space by investigating how the critical migration (or selection) strength required for local adaptation depends on demographic stochasticity, the number of selected loci, and the frequencies of the two habitats.

Figure 3 shows how polygenic adaptation collapses within the rare habitat as migration increases above a critical value, in a scenario with weak coupling between population size and mean fitness, i.e., $LS<1$ (figs. 3(a) and 3(b)) and in a strong coupling, i.e., $LS>1$ scenario (figs. 3(c) and 3(d)). In both cases, alternative alleles are close to fixation in the two habitats for low migration. As M increases, the frequency of the locally favoured allele (figs. 3(a) and 3(c)) and the expected population size N (figs. 3(b) and 3(d)) decline in both habitats as a result of migration load. At a critical migration rate, the rarer allele is lost, the population in the rare habitat crashes, and the overall $\overline{N}$ falls to a minimum. As M increases further, the population in the rare habitat starts increasing, signifying that the rare habitat is now a maladapted demographic sink. The emergence of source-sink dynamics at high M causes numbers in the common habitat to show a slight decline with M. This is outweighed by the faster increase in numbers in the rare habitat, resulting in a slight increase in $\overline{N}$, the average population size across the whole metapopulation, at large M. Note that there is another migration threshold below which the whole metapopulation collapses because colonisation is too rare; however, this is not visible here, since this threshold is negligibly small ($\sim e^{-\zeta}/(2\sqrt{\pi\zeta})$) for large ζ (fig. 1(c)).

Figures 3(b) and 3(d) also depict how the distribution $\psi[N]$ of the (scaled) population size in the rare habitat changes across the threshold M_c (insets). When net selection against maladapted phenotypes is weak relative to the baseline growth rate r_0, populations grow even when completely maladapted. In this weak coupling ($LS<1$) regime, population sizes are approximately normally distributed about a non-zero expected value $\mathbb{E}[N]$ irrespective of local adaptation, i.e., for both $M<M_c$ and $M>M_c$ (inset, fig. 3(b)). Further, $\mathbb{E}[N]\sim 1-LS\mathbb{E}[p]$, where $\mathbb{E}[p]$ is the expected allele frequency of the locally maladaptive allele in the habitat.

By contrast, for strong coupling (i.e., $LS>1$), the distribution of sizes is approximately normal only when the population is locally adapted, i.e., for $M<M_c$. Close to the threshold for loss of adaptation ($M\sim M_c$), the distribution $\psi[N]$ becomes bimodal, with one peak at $N\approx 1$ and the other at $N=0$, implying that a finite fraction of demes in the rare habitat is nearly extinct, while remaining demes support well-adapted populations. For $M>M_c$, the distribution is peaked at $N=0$ (i.e., most demes are extinct) and decays exponentially with N. The threshold for loss of local adaptation is sharper for larger LS— a finding that we clarify below.

Semi-deterministic approximation. The fact that population sizes are approximately normally distributed about $\mathbb{E}(N)$ for $LS\leq 1$, suggests that in this 'weak coupling' regime, a simpler approximation, in which population size is assumed to depend *deterministically* on the expected log fitness $\mathbb{E}[R_g]$, may suffice. This *semi-deterministic* approximation (details in SI, section A) assumes that fluctuations in average log fitness R_g about the expected value $\mathbb{E}[R_g]$ are negligible. Since the magnitude of fluctuations, given by $\Delta R_g \sim S[LVar(p)]^{1/2}$, must fall with number of loci L (for fixed LS), we expect the semi-deterministic approximation to become more accurate when L is large, and selective effects correspondingly small. The approximation further assumes that ζ is so large that demographic fluctuations (in well-adapted populations) are negligible, but ζS

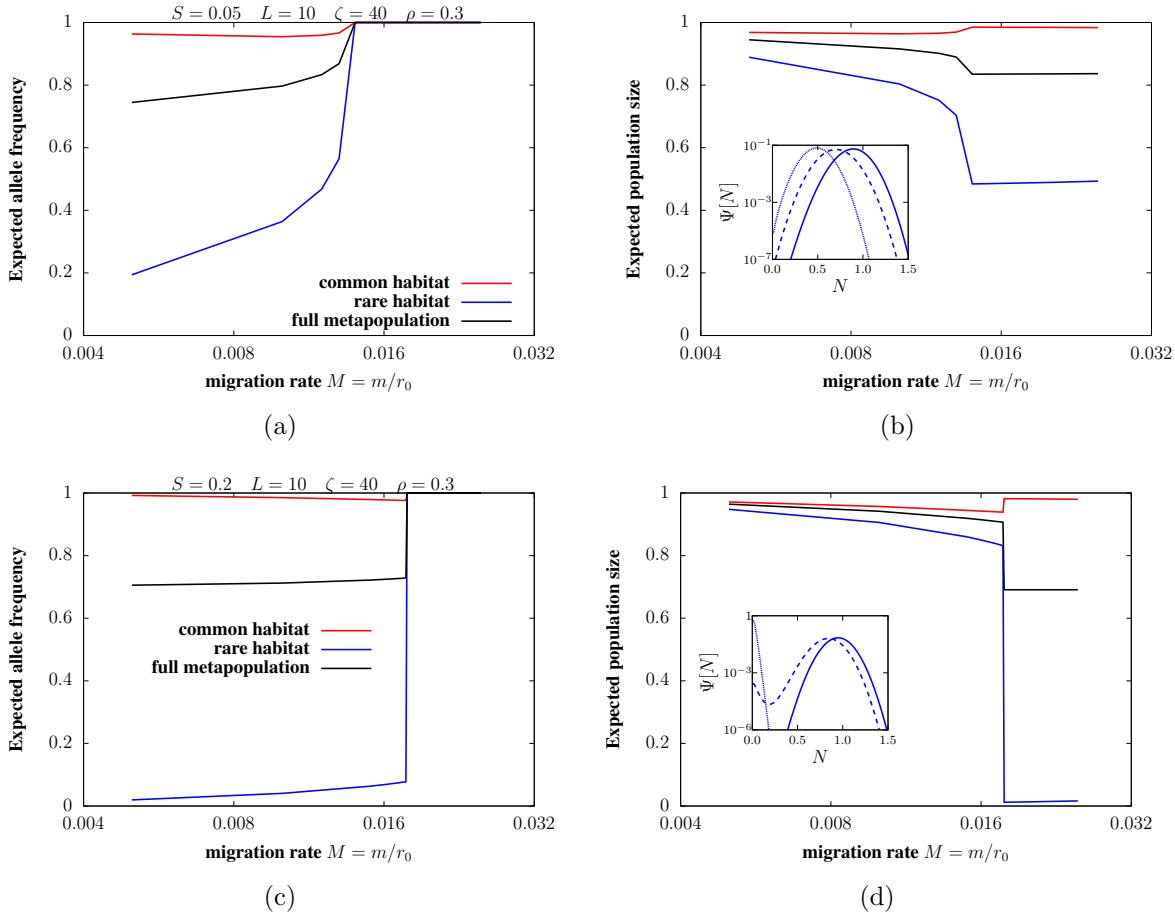


Figure 3: Loss of local adaptation at a critical migration rate under hard selection. Expected allele frequencies of the '1' allele (left panels) and expected population sizes (right panels) versus scaled migration rate $M{=}m/r_0$, for (A)-(B) weak coupling ($S{=}0.05$, $LS{=}0.5$) and (C)-(D) strong coupling ($S{=}0.2$, $LS{=}2$) between population size and mean fitness. The number of selected loci is $L{=}10$ and selection is symmetric, with $S_1{=}S_2{=}S{=}s/r_0$ at each locus; the rare habitat comprises 30% of demes ($\rho{=}0.3$) and demographic fluctuations are negligible ($\zeta{=}r_0K{=}40$). The plots show the expected allele frequencies and sizes in the rare and common habitat (blue, red) as well as the mean $\overline{p}$ and $\overline{N}$ across the whole metapopulation (black). For both weak coupling (i.e., $LS{<}1$ in A,B) and strong (i.e., $LS{>}1$ in C,D), there is a critical migration threshold M_c above which the allele favoured in the rare habitat is lost from the metapopulation. The insets in (B) and (D) depict the probability distribution $\psi[N]$ of population sizes in the rare habitat (integrated over intervals of width $\Delta N{=}0.02$) for $M{<}M_c$ (solid line), $M{\sim}M_c$ (dashed line), and $M{>}M_c$ (dotted line). For weak coupling, $\psi[N]$ peaks at some non-zero N, irrespective of M. For strong coupling, $\psi[N]$ peaks close to $N{\sim}1$ for $M{<}M_c$; becomes bimodal, i.e., has peaks at $N{=}0$ (corresponding to extinction) and $N{\sim}1$ (corresponding to a well-adapted population) at $M{\sim}M_c$; peaks at $N{=}0$ for $M{>}M_c$. All plots are obtained by numerically determining fixed points (eqs. (3) and (4)) using the joint distribution $\Psi[N, p]$.

small enough that drift has an appreciable effect at individual loci. As shown below, the semi-deterministic approximation accurately predicts the threshold for loss of local adaptation if $LS \leq 1$ (such that the distribution of N is unimodal about the expected population size), $L \gg 1$ (fluctuations in mean population fitness are negligible), and $\zeta \gg 1$ (negligible demographic fluctuations).

In these regimes (i.e., when the semi-deterministic approximation is accurate), the outcome is governed by three parameters. For a given rare habitat frequency ρ, and assuming symmetric selection $S_1 = S_2 = S$, the three parameters are: $\zeta S = Ks$, which governs the strength of drift relative to selection in a population at carrying capacity, $\zeta M = Km$, which determines the average number of migrants exchanged between demes at carrying capacity, and LS, which determines the extent to which population sizes are reduced below carrying capacity due to maladaptation. Below we clarify the roles of these parameters in the low migration limit $\zeta M \ll 1$, which is most conducive to local adaptation.

Low migration limit. When migration is rare, loci are close to fixation for one or other allele (within a deme). As with soft selection, this implies that the fixation rates of alternative alleles (at a given locus) on island i are in the ratio $\approx (\overline{Np}/\overline{N}) e^{2\zeta S_i N_i} : 1 - (\overline{Np}/\overline{N})$, where $\zeta = r_0 K$, and S_i is the (rescaled) selective advantage of the locally favoured allele at that locus on island i. Further, $\overline{Np}/\overline{N}$ is the frequency (within the migrant pool) of alleles favoured on island i. A comparison of this heuristic (for fixation rates) under hard selection with the analogous approximation under soft selection (eq. (6)) highlights two important features of allele frequency evolution under hard selection.

First, the rate of fixation and hence the frequency of the favoured allele at any locus depends on the degree of maladaptation at all other loci via the population size N_i. In particular, locally deleterious alleles at very many loci, at even modest frequencies, can have substantial effects (in aggregate) on mean fitness, thus reducing size. This further accentuates drift at individual loci, causing locally deleterious alleles to increase or even fix, further reducing population size, thus generating a positive feedback between loss of fitness and decline in numbers.

Second, any island contributes to the allele frequency $\overline{Np}/\overline{N}$ in the migrant pool in proportion to its size, which depends on the fitness of the island. Since locally adaptive alleles are at slightly lower frequency in the rare as opposed to the common habitat (even when both are locally adapted), the average population size is also somewhat lower in the rare habitat. Thus, an island belonging to the rare habitat contributes less to the allele frequency in the migrant pool than an island within the common habitat by a factor proportional to the ratio of population sizes of the two islands. This causes allele frequency in the migrant pool to shift further towards the optimal frequency in the common habitat, which increases migration load and reduces numbers in the rare habitat. This in turn reduces the contribution of the rarer habitat to the migrant pool further below ρ, generating a second positive feedback loop. Crucially, both kinds of feedback depend on the strength of coupling between population size and mean fitness, and are thus stronger for larger $LS = L(s/r_0)$. Here, we focus on how these feedback affects influence local adaptation when selection is symmetric across habitats ($S_1 = S_2 = S$) and then briefly discuss asymmetric selection in SI, section B.

First, consider how local adaptation depends on the the selective effect per locus $S = s/r_0$ or alternatively, the number of selected loci L, for a *fixed* LS under very weak

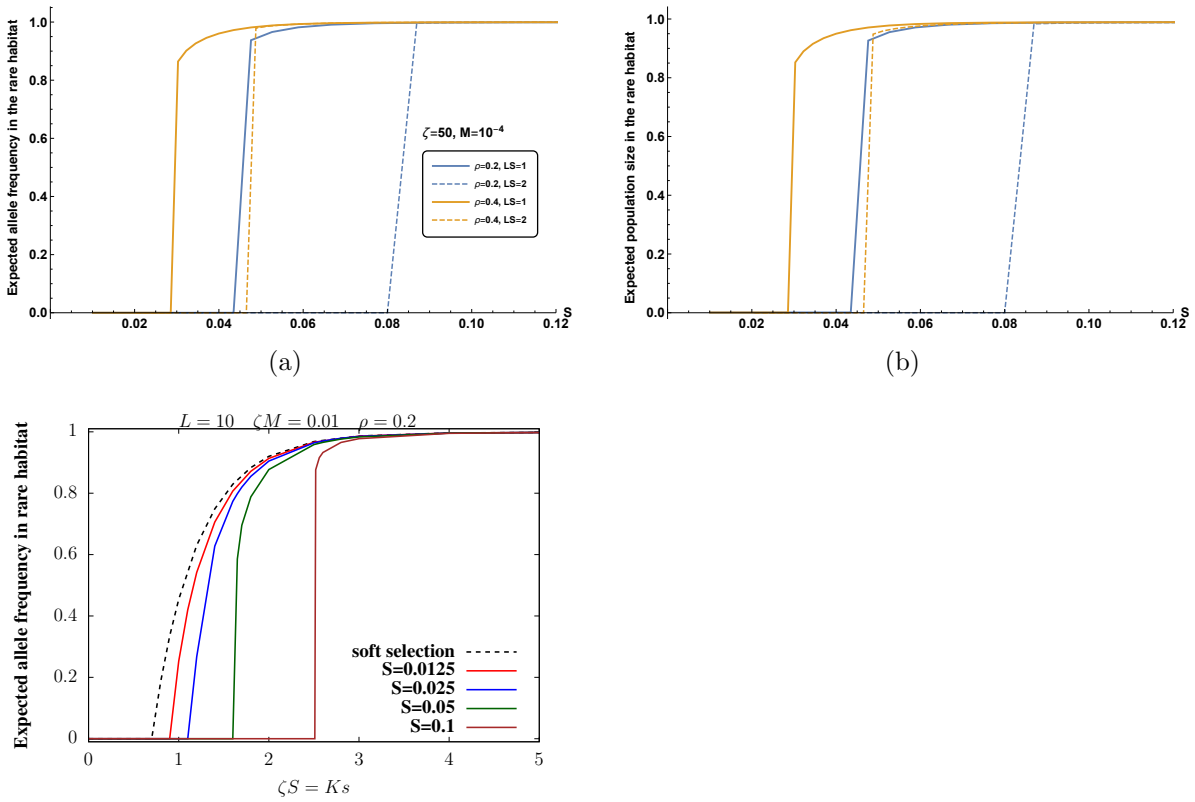


Figure 4: Local adaptation in the rare habitat, for weak migration. (A) Expected frequency of the locally favoured allele and (B) expected population size in the rare habitat vs. selective effect per locus $S{=}s/r_0$ (for symmetric selection across the two habitats $S_1{=}S_2{=}S$) for $M{=}0.0001$ and $\zeta{=}50$. In each plot, the selective effect S and the number of loci L are changed simultaneously such that maximum possible genetic load LS is constant. Different colors correspond to different frequencies ρ of the rare habitat. Solid vs dashed lines correspond to different LS. Local adaptation in the rare habitat is lost (fig A) and populations go extinct (fig B) when selective architectures are highly polygenic with weak selective effect per locus (high L, low S). (C) Expected frequency of the locally favoured allele in the rare habitat versus $\zeta S{=}Ks$ for different S, for $\zeta M{=}Km{=}0.01$. The parameter ζS is varied by varying ζ (for a given S); ζM is held constant by varying M. The dashed line shows the corresponding prediction for allele frequencies under soft selection. For a fixed ζS, populations approach the soft selection prediction as S decreases and ζ increases. All solid-line plots are obtained by determining fixed points numerically (eqs. (3) and (4)) using the joint distribution $\Psi[N, p]$; dashed line in (c) is obtained by determining exact fixed points under soft selection (SI, section A).

migration (ζM=0.005 in figs. 4(a), 4(b)). These plots thus reveal how local adaptation is influenced by the genetic architecture of (i.e., the number and selective effects of loci contributing to) genetic load, for a given (maximum possible) total load LS in the population. Figure 4(a) shows that local adaptation in the rare habitat is possible only above a critical S_c per locus. For $S<S_c$, drift overpowers selection at individual loci, causing alleles favoured in the common habitat to fix across the entire metapopulation despite very low genetic exchange, as with soft selection (fig. 2(c)). As a result, only very small maladapted populations are maintained in the rare habitat for $S<S_c$ (fig. 4(b)). Alternatively, given a certain (maximum) load LS, local adaptation is possible only if the selected trait is determined by a modest number of loci (i.e., for $L<L_c$, where $L_c=L(S/S_c)$), and fails for highly polygenic traits.

Further, local adaptation requires stronger selection per locus when the total cost of maladaptation, LS, is higher (solid vs. dashed lines in figs. 4(a) and 4(b)). In other words, the critical selection threshold S_c increases as the number of loci under divergent selection increases. In fact, for sufficiently large L, local adaptation is not possible for any S (see also fig. 5(b)). As we argue below, higher S increases the efficacy of selection at individual loci (via ζS), but also results in stronger coupling between allele frequencies and population size (via LS) which has the potential to degrade local adaptation due to the two kinds of feedback described above.

From these arguments, it follows that as one considers models of hard selection with lower and lower LS (corresponding to weaker and weaker coupling between population size and genetic fitness) while keeping ζS and ζM fixed, the behaviour of the metapopulation should converge to the predictions under soft selection with $Ks=\zeta S$ and $Km=\zeta M$. This is indeed what we see (fig. 4(c)): the frequency of the locally favoured allele increases towards the soft selection prediction on approaching lower S and consequently LS, as long as ζS is held constant (by simultaneously increasing ζ). Note however that weaker selection S by itself (for fixed ζ and L) would make local adaptation more difficult, as the increase in genetic drift (relative to selection) at low ζS damages local adaptation—an effect not compensated by the more modest increase in numbers.

Finally, note that S_c is lower for larger ρ (orange vs. blue plots in fig. 4(a)), i.e., if the rare habitat encompasses a larger fraction of demes. In this case, the rare habitat is subject to a lower migration load (since allele frequencies in the migrant pool tend to be more intermediate), resulting in a weaker reduction in population size as well as weaker swamping at individual loci.

We now ask: for a given ζM, (when) does local adaptation in the rare habitat depend only on the two composite parameters ζS (which determines the strength of drift relative to selection per locus at carrying capacity) and LS (which governs how population sizes change due to fixation of deleterious alleles)? Recall that these parameters completely determine the state of the metapopulation in the semi-deterministic ($LS\leq 1$) regime, in which sizes depend deterministically on the *expected* mean fitness. To investigate this, we determine the threshold ζ_c (such that local adaptation occurs for $\zeta>\zeta_c$), as a function of S, for various L, for fixed ζM. Here, ζM is held constant by reducing the rescaled migration rate $M=m/r_0$ as $\zeta=r_0K$ increases, such that the average number of migrants (between demes at carrying capacity) remains unchanged.

Figure 5(a) shows that the semi-deterministic prediction for $\zeta_c S$ (dashed line) is extremely accurate for $LS\lesssim 1$: in this regime, the threshold $\zeta_c S$ for local adaptation in the

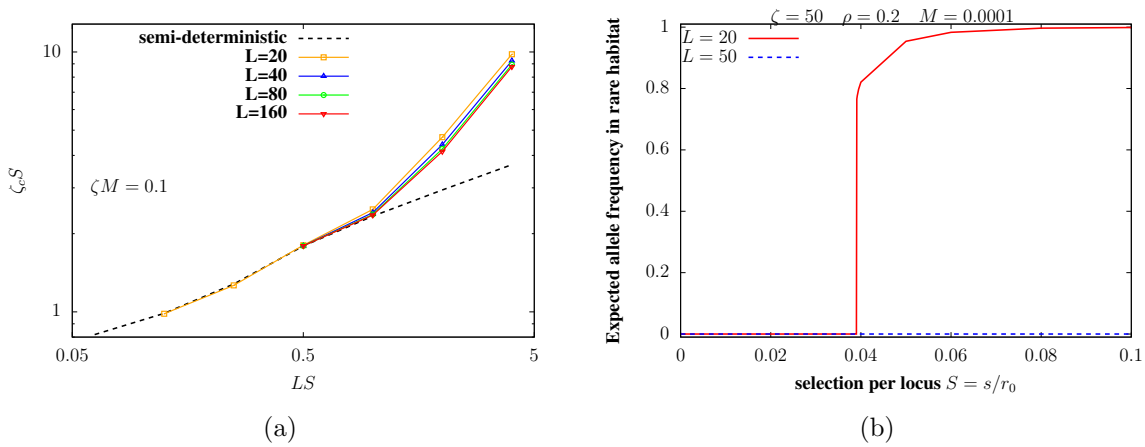


Figure 5: Exact model vs. semi-deterministic approximation in the weak migration limit. (A) The critical threshold $\zeta_c S$ for local adaptation in the rare habitat versus LS for different values of L (depicted by different symbols), for ζM=0.1 and ρ=0.2. For given L, we vary LS by changing S, and then compute the critical ζ_c for each S. The migration rate M is always varied along with ζ such that ζM is constant at 0.1. The symbols and solid lines represent predictions of the full model (obtained using eqs. (3) and (4)), while the dashed line represents predictions of the semi-deterministic approximation which treats population size as being determined by the expected allele frequencies. There is good quantitative agreement between the full model and the semi-deterministic approximation for $LS \lesssim 1$, but not for larger LS. (B) Expected frequency of the locally favoured allele in the rare habitat vs. S for L=20 (red) and L=50 (blue) for ρ=0.2, ζ=50, M=0.0001. Local adaptation in the rare habitat is not possible for any S for L=50.

rare habitat is independent of the number of selected loci, for a given LS. Moreover, this threshold only increases sub-linearly with LS for $LS \lesssim 1$. By contrast, for $LS \gtrsim 1$, the semi-deterministic approximation fails: the critical $\zeta_c S$ threshold increases much faster (nearly linearly) with LS, than predicted by the semi-deterministic approximation. However, even in this regime, the threshold for adaptation $\zeta_c S$ depends weakly on the number of loci, and is essentially governed by LS.

Increasingly stringent thresholds for local adaptation at large LS imply that when the number of loci underlying local adaptation is sufficiently high, simultaneous local adaptation across the two habitats is not possible for *any* selection strength (even for moderate ζ and very small M). For instance, with L=50 loci, local adaptation cannot be maintained in the rare habitat, even for ζS as large as 10, for ζ=50 and M=10^{-4} (blue line in fig. 5(b)). Further, for $LS \gtrsim 1$, the whole metapopulation may converge towards the alternative fixed point $\overline{p}$=1 (i.e., fix the allele favoured in the rare habitat), if the initial allele frequency is close to $\overline{p}$=1 and migration sufficiently high (results not shown).

Loss of local adaptation in the rare habitat: critical migration rates. We now consider cases where selection is strong relative to drift (so that both habitats are locally adapted under low genetic exchange), and ask: how high can migration be while still allowing local adaptation in the rare habitat and polymorphism at the level of the metapopulation? Figure 6(a) shows M_c, the critical migration rate above which polymorphism collapses, as a function of S for the case with S_1=S_2=S for two different L. The points represent results of the full model (based on the joint distribution of N and p), while dashed lines represent the predictions of the semi-deterministic approximation.

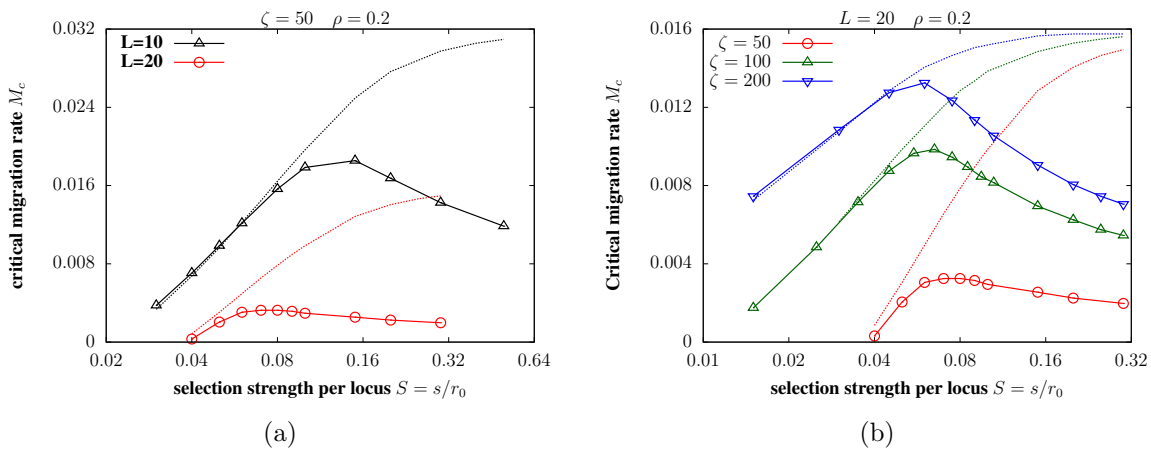


Figure 6: Critical migration rates for loss of local adaptation in the rare habitat. (A) Critical migration rate M_c=m_c/r_0 versus selection S=s/r_0 per locus for L=10 (triangles) and L=20 (circles), assuming S_1=S_2=S, ζ=50 and ρ=0.2. (B) M_c versus S for different values of ζ for L=20. Symbols depict M_c obtained via fixed point estimation from the joint distribution of population size and allele frequencies; dashed lines represent the predictions of the semi-deterministic approximation. M_c falls with S for large S, which is not captured by the semi-deterministic approximation. For any S, M_c increases with increasing ζ (in (B)), and appears to be approaching the semi-deterministic prediction.

Note that for both values of L, the critical migration rate increases with S when S is small, but then starts declining as selection increases beyond a certain threshold (which corresponds approximately to $LS{\sim}1$). Thus, the range of migration rates allowing local adaptation in the rare habitat is widest (i.e., M_c largest), for intermediate selection. As in fig. 5(a), the semi-deterministic approximation is accurate for small S, but fails to (even qualitatively) predict large S behaviour.

The semi-deterministic approximation (dashed lines) predicts that M_c should saturate to a constant, independent of S, for large S. Such saturation is also predicted by a deterministic analysis (which should be accurate as $\zeta{\to}\infty$, when drift is negligible). This is most easily demonstrated in the $\rho{\to}0$ limit, when allele frequencies in the common habitat are unaffected by immigration, such that $N_2{=}\overline{N}{=}1$ and $N_2p_2{=}\overline{Np}{=}1$. Then one can show (using eq. (1)) that the rare habitat sustains local adaptation only below a critical migration rate, $M_c{\sim}1/(4L)$ (for $L{\gg}1$ and large S). Such a selection-independent threshold M_c emerges (at large S) simply due to the constraint that under hard selection, a population is viable only while its total migration load is less than its intrinsic growth rate. Since genetic load per locus is *at least* m (and typically greater than m under hard selection), this sets a limit on the number of polymorphic loci that can be maintained without extinguishing the population.

For moderately large ζ, the actual M_c (points in fig. 6(a)) is several times less than this deterministic threshold, and *declines* with increasing S. As before, this is due to stronger coupling between population size and mean fitness (at large LS), which accentuates both drift and swamping in the rare habitat. However, even for large LS, the critical migration rate is expected to approach the deterministic prediction with increasing ζ (where higher ζ corresponds to weaker stochastic fluctuations in both population size and allele frequencies). This general expectation is supported by fig. 6(b), which shows

M_c versus S for different ζ. Note, however, that M_c converges very slowly towards the deterministic threshold with increasing ζ: for instance, in fig. 6(b), even for ζ as high as 200 (i.e., 200 births per generation in a well-adapted population), M_c is approximately half the corresponding deterministic threshold for $LS \geq 2$.

Individual-based simulations.

Our analysis is based on the diffusion framework, which involves three approximations (see also Model and Methods). First, we approximate discrete generation dynamics by the continuous time evolution of population size and allele frequencies. Second, we assume infinitely many demes such that the migrant pool is deterministic. Third, we neglect LD within any deme as well as across the whole metapopulation. The validity of each assumption is tested by comparing with individual-based simulations (SI, section C).

These comparisons reveal that the most drastic approximation is due to neglecting LD amongst migrants, which can be substantial when demes are close to fixation for alternative alleles at multiple loci. Then, immigrant genotypes entering a deme are either perfectly adapted (if they originate from the same habitat) or severely unfit (if they originate from the alternative habitat). Consequently, an immigrant allele experiences a first-generation disadvantage proportional to the aggregate effect of all alleles it is associated with; this selective disadvantage is halved in each subsequent generation (Robertson, 1961). Thus the *effective* immigration rate of an allele is lower than the raw migration rate m— an effect not captured by equation (1) or (2). As a result, the migration threshold for loss of local adaptation, as observed in simulations, is significantly higher than the M_c predicted by the diffusion approximation. This discrepancy between simulations and the diffusion approximation becomes weaker on approaching smaller growth rates r_0 and larger carrying capacities K, while holding the scaled parameters ζ, S, M constant: this corresponds to making selection weaker (relative to recombination), resulting in weaker LD.

In SI, section C, we show how the effects of LD can be partially accounted for by assuming that immigrants are drawn from two distinct pools corresponding to the two habitats (rather than a single well-mixed pool), and then considering the effective number of immigrant individuals and alleles from each pool to be weighted by their first-generation selective disadvantage in the recipient deme. However, a complete analysis along these lines (c.f. Barton and Bengtsson, 1986) is not attempted here.

Discussion

Metapopulation models have attracted much interest as idealised settings for understanding how population structure affects neutral diversity (Wright, 1932; Slatkin, 1977; Whitlock and Barton, 1997). Another line of research concerns rapid adaptation and extinction in fragmented habitats, leading to eco-evolutionary models of metapopulations (Hanski and Gilpin, 1997). Patches may have heterogeneous carrying capacities and/or different micro-environments. Metapopulation models thus also help us understand local adaptation, survival and extinction in marginal or novel habitats (i.e., "evolutionary rescue"). Yet, they have only recently been investigated in this context.

An important limitation of existing metapopulation models is that very few incorporate realistic assumptions about genetics within an eco-evolutionary framework, or explicitly consider the coupled stochastic dynamics of population size and allele frequencies. Various models do include some form of stochasticity: stochastic colonisation-extinction dynamics (Hanski and Mononen, 2011), genetic drift in structured populations (Whitlock and Barton, 1997), or demographic fluctuations in the absence of selection (Mangel and Tier, 1993; Lande et al., 2003; Black and McKane, 2012). However, none consider different sources of stochasticity together within a common framework.

Our modeling framework is based on a diffusion approximation for the joint evolution of population sizes and allele frequencies (Banglawala, 2010; Barton and Etheridge, 2018), which we extend here to a metapopulation with multiple ecological niches. It assumes a polygenic architecture for local adaptation, and accounts for both genetic drift and demographic stochasticity. It predicts the full stationary distribution of population sizes and allele frequencies in different habitats, thus yielding the conditions under which local adaptation is maintained simultaneously across habitats under divergent selection. The approximations underlying our theoretical framework (including that the migrant pool is in LE) can be formally justified as $r_0 \to 0$. Thus, they may not be accurate in typical populations, where growth rates may be high. Similarly, fluctuations in population size are assumed to be only due to demographic stochasticity, and so may be greatly underestimated. Nevertheless, our modeling approach captures key processes involved in local adaptation, and the approximations presented here apply over a broader range. We aim at understanding the fundamental processes, rather than precise prediction.

We identify two qualitatively distinct reasons why local adaptation fails within a rare habitat. First, if selection on locally favoured alleles is weak relative to drift, then alleles favoured in the common habitat tend to fix across the metapopulation, even when migration is extremely rare (fig. 4). This drift-dominated regime is also predicted under soft selection, where we obtain an explicit expression for the critical selection threshold below which polymorphism is lost: this threshold depends on the relative proportions of the two habitats, and increases as the rare habitat becomes more marginal (i.e., ρ decreases; fig. 2(c)). Interestingly, the critical selection threshold remains non-zero, implying that the bias towards alleles favoured in the common habitat persists (at low $S{=}s/r_0$), even as $M \to 0$. In practice, we expect the time scale over which swamping of the rare habitat (and loss of polymorphism) occurs to increase as $M \to 0$. Thus, under weak migration and selection, local adaptation in the rare habitat may be metastable and loss of polymorphism extremely slow: this is consistent with behaviour observed in individual-based simulations (results not shown).

Second, migration (beyond a critical rate) may swamp local adaptation even when selection per locus is strong relative to drift: this kind of migration threshold emerges quite generally even in single locus models under soft selection when loci are subject to gene flow from a differently adapted population (Haldane, 1956). In the present model (with hard selection on multiple loci), the total migration load sets a more severe constraint: it must be sufficiently low that the population can still grow. Since migration load scales with the number of loci under divergent selection, moderate maladaptation at very many loci is sufficient to cause the population to crash. Declining population size further reduces the efficacy of selection at individual loci via increased drift, but also results in stronger swamping, causing a positive feedback that extinguishes populations in the rare

habitat. This feedback sets an upper limit on the migration rate or alternatively (given M) on the number of loci that can be divergently selected across the two habitats, while still allowing local adaptation in both. In the deterministic limit (i.e., as $\zeta{=}Kr_0{\to}\ \infty$, such that both genetic drift and demographic stochasticity can be neglected), this migration threshold becomes independent of selection for large $S{=}s/r_0$, and depends solely on the number of loci and the habitat frequencies (fig. 6). However, for moderate $\zeta S{=}Ks$, the critical migration threshold decreases with increasing $S{=}s/r_0$ for $LS{\gtrsim}1$.

A key result is that hard selection renders local adaptation in the rare habitat more difficult. The extent to which selection is hard is governed by $LS{=}L(s/r_0)$. We identify two qualitatively distinct regimes demarcated by $LS{\sim}1$. For $LS{<}1$ (and $\zeta{=}Kr_0{\gg}1$), the effects of hard selection can be encapsulated by assuming that population size is reduced in proportion to the expected genetic load; the strength of drift and swamping at individual loci is then governed by this reduced size. In the $LS{<}1$ regime, an increase in selection allows populations to better withstand maladaptive gene flow and drift (fig. 4). By contrast, for $LS{>}1$, our semi-deterministic approximation that treats size as determined by expected allele frequencies fails: in this regime, the population size distribution is bimodal (fig. 3), such that there is a small probability of extinction, even when expected frequencies of locally adaptive alleles are high. This results in a somewhat paradoxical situation: the conditions for stable local adaptation become *more* restrictive as selection per locus increases in the $LS{>}1$ regime (fig. 6), because maladaptation then affects population size more strongly. Our results show that hard selection and random drift can substantially increase the damage that gene flow may cause - as, for example, when farmed fish escape into wild populations (Glover et al., 2017).

In our model, polygenic adaptation that depends on many loci, L, is difficult because both migration load and the coupling between population size and allele frequencies increases with L (for fixed S). This is because we assume an extreme form of environmental heterogeneity, in which any allele has opposite effects on fitness in the two habitats. In an alternative model with stabilizing selection (towards habitat-specific optima) on a quantitative trait, the deviation of the trait mean from the optimum and the trait variance within any deme are expected to be independent of genetic architecture in the infinitesimal $L{\to}\ \infty$ limit– provided optima lie near the centre of the phenotypic range. Then, migration load would be independent of L, and can be calculated even in the infinitesimal limit (Barton and Etheridge, 2018). This relaxes the constraint that migration load places on the number of polymorphisms that can be maintained under hard selection.

We focus here on the case where locally adapted populations are demographically stable. However, the joint distribution derived in eq. 3 can be used to explore alternative regimes. For instance, we might consider a metapopulation with many very small demes and frequent extinction (i.e., $\zeta{=}r_0K{\sim}1$). The whole metapopulation can still adapt (if migration is sufficiently high), even when selection within each deme is weaker than local drift. Indeed, Wright (1932) argued that such a 'shifting balance' allows efficient search across alternative adaptive peaks (see Rouhani and Barton, 1993; Coyne et al., 1997). However, it would not be possible for populations to adapt to local variations in environment between demes in this regime.

The framework presented here is quite general, and can be applied to metapopulations with multiple niches, or differences in patch quality. While we have focused on local adaptation, the framework can be applied to other questions in metapopulation biology.

For example, we find that in the neutral case, F_{ST} depends only on the number of incoming migrants, $\zeta M\overline{N}{=}m\overline{n}$, regardless of the size of the focal deme (Eq. 3). The model can also extend to include dominance, and so could be used to understand heterosis and inbreeding depression within a metapopulation, and their interaction with population dynamics.

Our main analysis neglects linkage disequilibrium, which arises when allele frequencies differ between habitats at multiple loci. Associations between locally adaptive alleles allow simultaneous local adaptation over a wider range of parameters than predicted by the diffusion (figs. 8(c), 8(d)), because sets of introgressing alleles from differently adapted populations are eliminated together, thus reducing the effective rate of gene flow (Barton and Bengtsson, 1986). In SI, section C, we outline a heuristic which could capture this effect. It may also be possible to estimate the extent of local adaptation, and the extent to which it reduces effective gene flow, by observing how divergence and LD vary along the genome (cf. Aeschbacher et al., 2017).

Local adaptation in a metapopulation may lead to parapatric speciation, despite gene flow: as populations diverge, selection against introgressing alleles increases, reducing effective migration, and allowing further divergence. A key issue here is whether a heterogeneous environment will lead to distinct clusters, separated by strong barriers to gene flow, which eventually become good biological species. This may depend on the distribution of available habitats. If these are broadly continuous, and select along multiple environmental dimensions, then there may be substantial local adaptation without clusters being apparent. However, with distinct environments, local adaptation may lead to strong isolation, as multiple divergent loci become coupled together (Barton and De Cara, 2009; Barton, 2010). The framework developed here may be used to investigate how the distribution of selective challenges influences whether populations evolve as generalists, adapting to a range of local environments, or split into distinct and well-isolated species.

Supplementary Information

A. Miscellaneous analytical results

Population size distribution with no selection. In the absence of selection, the joint distribution $\Psi(N, \{p_j\})$ in equation (3) can be written as the product of independent distributions for N and each of the p_j. At each locus, we simply have Wright's distribution for $\psi[p]$ (Wright, 1932) under the infinite island model. The population size distribution $\psi[N]$ is given by eq. (5). Integrating over $\psi[N]$ yields the expected population size $\mathbb{E}(N)$ in any deme, given the mean $\overline{N}$ across the metapopulation.

The equilibrium can be found by equating $\mathbb{E}(N)$ with $\overline{N}$; there is always a solution $\mathbb{E}(N){=}\overline{N}{=}0$, which corresponds to global extinction. Above a critical migration rate M_c, this solution becomes unstable, and a second solution, corresponding to a non-zero population size emerges. The threshold M_c is that migration rate for which the solution $\overline{N}{=}0$ just becomes unstable, i.e., where $\partial\mathbb{E}(N)/\partial\overline{N}|_{\overline{N}=0}{=}1$. This yields the following equation for M_c: $e^{(1-M_c)^2\zeta}\sqrt{\pi\zeta}(1{-}Erf[-(1{-}M_c)\sqrt{\zeta}])M_c{=}1$. For large ζ, the threshold M_c must be correspondingly small, such that we need only retain first order terms in M_c, and can further approximate $Erf[-(1{-}M_c)\sqrt{\zeta}]{\approx}1$. This yields $M_c{\approx}e^{-\zeta}/(2\sqrt{\pi\zeta})$ for large ζ. Only for $M{>}M_c$ is the expected population size non-zero.

The shape of the distribution $\psi[N]$ is governed by the parameter $2\zeta M\overline{N}$, which is the average number of immigrants per generation per deme. For $2\zeta M\overline{N}<1$, the distribution is bimodal: a fraction of demes support large populations with $N\sim 1-M$, while the remaining fraction is close to extinction. Conversely, for $2\zeta M\overline{N}>1$, the distribution is unimodal: all demes support large populations, i.e., are close to carrying capacity.

We can obtain an explicit expression for the migration threshold M_* for which $2\zeta M_*\overline{N}(M_*)$ equals 1. Substituting the condition $2\zeta M_*\overline{N}(M_*)=1$ into the expression for $\mathbb{E}(N|\overline{N})$ and then equating with $\overline{N}$ gives us an explicit expression for $\overline{N}(M_*)$. For large ζ, this is simply $\overline{N}\approx 1-M_*$. Substituting this into $2\zeta M_*\overline{N}(M_*)=1$, yields $M_*\approx\frac{1}{2\zeta}\left(1+\frac{1}{2\zeta}\right)$. Thus, below this second threshold, i.e., for $M_c<M<M_*$, the stationary distribution of population sizes is bimodal, and there is a turnover of occupied vs. extinct demes due to frequent extinction and recolonisation events, even at equilibrium.

Allele frequency distribution and local adaptation under soft selection. In the limit $\zeta\to\infty$, $S, M\to 0$ (with $\zeta S=Ks$ and $\zeta M=Km$ held constant), we recover the soft selection model, in which each deme is at carrying capacity ($N=n/K=1$), irrespective of adaptation. Allele frequencies now evolve independently of each other (assuming LE). In a deme where the favoured allele has selective advantage s, the allele frequency distribution is:

$$\psi[p]=\frac{1}{Z_1}p^{2Km\overline{p}-1}q^{2Km\overline{q}-1}\exp(2Ksp) \quad \text{where} \quad Z_1=\Gamma\left(2Km\overline{p}\right)\Gamma\left(2Km\overline{q}\right)\ {}_1\tilde{F}_1\left(2mK\overline{p};2mK;2Ks\right)$$
$$\mathbb{E}\left(p\,|\overline{p}\,,s\right)=2mK\overline{p}\ \frac{{}_1\tilde{F}_1\left(2mK\overline{p}+1;2mK+1;2Ks\right)}{{}_1\tilde{F}_1\left(2mK\overline{p};2mK;2Ks\right)} \tag{7}$$

This distribution (Wright, 1932), can also be obtained by integrating the joint distribution in eq. (3) over N, and evaluating this integral as $\zeta\to\infty$, $S, M\to 0$ for fixed $\zeta S=Ks$ and $\zeta M=Km$. Note that the above distribution is expressed in terms of unscaled parameters s, m (since scaling by r_0 is not meaningful under soft selection). One can now calculate the equilibrium frequency by equating the average allele frequency in the migrant pool $\overline{p}$ with the expected allele frequency (average over habitats) $\overline{p}^*=\rho\mathbb{E}_1\left(p\,|\overline{p}\,,s\right)+(1-\rho)\mathbb{E}_2\left(p\,|\overline{p}\,,-s\right)$, and solving numerically for the fixed point.

However, we can obtain approximate analytical solution in various limits. First, consider the deterministic limit ($Ks\gg 1$ and $Km\gg 1$), in which allele frequencies are tightly clustered about the expected value. Then the equilibrium can be found directly from eq. (1b) by setting $\lambda_p=0$, $n_i=\overline{n}=K$ and $\overline{np}=K\overline{p}$. We can also obtain a prediction for s_c, the critical selection required for a polymorphic equilibrium in the deterministic limit, by noting that just above the threshold s_c (i.e, when a polymorphic equilibrium first appears), the difference between allele frequencies in the two habitats must be very small, and the allele frequency in the common habitat close to 1. Thus retaining only lowest order terms in $1-p_1$ and p_1-p_2 in eq. (1b) and solving for p_1, p_2 gives $s_c\approx m(1-2\rho)$. Note that this prediction just provides a lower bound on s_c, as we do not expect the deterministic analysis (which ignores variance of allele frequencies) to be accurate close to the threshold. Just above the threshold s_c, we have $\overline{q}\to 0$, such that the distribution of allele frequencies is necessarily bimodal, making it necessary to account for drift. In general, we expect drift to further degrade local adaptation in the rare habitat, thus

pushing the selection threshold s_c above the deterministic prediction.

The opposite limit is that of weak migration $Km{\to}0$, in which any locus (within a deme) are nearly fixed for one or other allele. The rates of fixation towards and away from an allele with advantage s, which is at frequency $\overline{p}$ in the migrant pool, are in the ratio $\int_0^{1/2} \psi[p]dp \Big/ \int_{1/2}^{1} \psi[p]dp$ (for a deme in the rare habitat). Since most of the weight of the distribution $\psi[p]$ is concentrated near $p{=}0$ and $p{=}1$ (for $Km{\ll}1$), we can approximate the integrand in the numerator (or in the denominator) by Taylor expanding $\psi[p]$ near $p{=}0$ (or $p{=}1$). It then follows that the rates of fixation towards and away from the favoured allele are in the ratio $\sim(\overline{p}/\overline{q})e^{2Ks}$. The expected frequency of the locally favoured allele is simply the (normalised) probability of fixation of this allele (eq. (6) in the main text).

Semi-deterministic approximation for $LS{\lesssim}1$. Under weak coupling ($LS{\lesssim}1$), population sizes are approximately normally distributed about the expected value $\mathbb{E}(N)$, irrespective of local adaptation (inset, fig. 3(a)). This allows us to approximate the stationary distribution using a simpler 'semi-deterministic' approximation: we treat population size as being determined by the expected frequencies (i.e, neglect fluctuations in N), and assume that allele frequencies are distributed according to this deterministic population size.

In practice, we replace the population-averaged log fitness r_g by its expected value $\mathbb{E}[r_g]$ in eq. (1a), neglect the stochastic term λ_n, and solve for the equilibrium size as a function of $\mathbb{E}[r_g]$. Further assuming that migration does not significantly affect population size, so that terms proportional to m in equation (1a) are also negligible, the scaled population sizes in the two habitats are $N_1^{det}{\sim}\mathrm{Max}[1{-}LS_1\mathbb{E}_1[q],0]$ and $N_2^{det}{\sim}\mathrm{Max}[1{-}LS_2\mathbb{E}_2[p],0]$: population sizes are depressed relative to carrying capacity in proportion to the genetic load. To obtain $\mathbb{E}_1[p]$ and $\mathbb{E}_2[p]$, we assume that allele frequencies are distributed as in a model with fixed and deterministic population sizes N_1^{det} and N_2^{det}. Then:

$$\mathbb{E}_i\left(p\,\middle|\,\overline{Np}\,,N_i^{det},S_i\right){=}2\zeta M\overline{Np}\;\frac{{}_1\tilde{F}_1\left(2\zeta M\overline{Np}{+}1,\;2\zeta M\overline{N}{+}1,\;2\zeta S_iN_i^{det}\right)}{{}_1\tilde{F}_1\left(2\zeta M\overline{Np},\;2\zeta M\overline{N},\;2\zeta S_iN_i^{det}\right)} \tag{8}$$
$$N_1^{det}{=}\mathrm{Max}[1{-}LS_1\mathbb{E}_1[q],0] \quad \text{and} \quad N_2^{det}{=}\mathrm{Max}[1{-}LS_2\mathbb{E}_2[p],0]$$

As before, the equilibrium $\overline{Np}$ and consequently the expected allele frequencies can be determined iteratively from: $\overline{Np}{=}(1{-}\rho)\mathbb{E}_1[p]N_1^{det}{+}\rho\mathbb{E}_2[p]N_2^{det}$.

B. Asymmetric selection across habitats

In the main text, we considered scenarios where alternative alleles are favoured in the different habitats, but selection per locally favoured allele is the same in each habitat ($S_1{=}S_2$). Here, we briefly consider the more general scenario where alternative alleles at a given locus may be selected more or less strongly in one of the two habitats ($S_1{\neq}S_2$). For simplicity, we still focus on the case where selective effects are equal across loci within a given habitat (i.e, $S_{1,j}{=}S_1$ and $S_{2,j}{=}S_2$ for all j).

Figure 7 depicts (S_1,S_2) combinations that allow simultaneous local adaptation (i.e., a polymorphic equilibrium) across the two habitats. For a given selection strength per

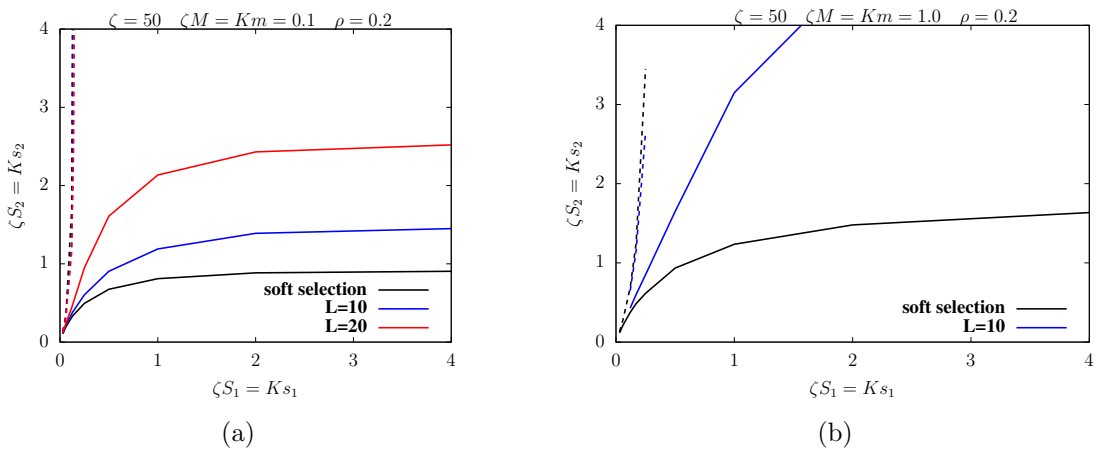


Figure 7: Local adaptation in scenarios with asymmetric selection across habitats. Critical selection thresholds $\zeta S_{2,a}$ (solid lines) and $\zeta S_{2,b}$ (dashed lines) in the rare habitat versus selection per locus, ζS_1, in the common habitat for (A) low migration (ζM=0.1) and (B) intermediate migration (ζM=1.0). Alleles favoured in the common habitat fix across the entire metapopulation for $S_2<S_{2,a}$ (below solid line); alleles favoured in the rare habitat fix across the entire metapopulation for $S_2>S_{2,b}$ (above dashed line); a polymorphic equilibrium corresponding to local adaptation across the two habitats is possible for $S_{2,a}<S_2<S_{2,b}$, i.e., for parameter combinations lying between the solid and dashed lines. The different colors correspond to different degrees of coupling between population size and mean fitness: soft selection, i.e., no coupling (black), hard selection with L=10 (blue) and L=20 (red) loci; larger L corresponds to stronger coupling (for fixed ζS_1). The region in parameter space allowing for simultaneous local adaptation shrinks with increasing L; at sufficiently high migration, there is no (S_1, S_2) combination for which polymorphism is possible with L=20 loci in (B). Selection thresholds under hard selection are obtained by determining fixed points numerically (eqs. (3) and (4)) using the joint distribution $\Psi[N, p]$; selection thresholds under soft selection are obtained via fixed point determination using the allele frequency distribution $\psi[p]$ (eq. (7)).

locus, S_1, in the common habitat, we determine two selection thresholds, $S_{2,a}$ and $S_{2,b}$, such that polymorphism is only possible for S_2 (i.e., selection strengths per locus in the rare habitat) lying between these thresholds. For $S_2<S_{2,a}$, alleles favoured in the common habitat fix, while for $S_2>S_{2,b}$, alleles favoured in the rare habitat tend to fix. Note that the threshold $S_{2,b}$ exists, i.e., strong selection in favour of alleles in the rare habitat can drive fixation of such alleles across the entire metapopulation, only if selection per locus in the common habitat is sufficiently weak.

Figure 7 shows the two selection thresholds for soft selection (black), and hard selection involving 10 (blue) or 20 (red) divergently selected loci. As before, soft selection is most conducive to simultaneous local adaptation. Under hard selection, the parameter combinations allowing for polymorphism become more restrictive with increasing L: this is consistent with the fact that larger L corresponds to stronger coupling between mean fitness and population size, which increases extinction probabilities in one or other habitat. This effect is exacerbated at higher migration rates (see fig. 7(b)): in this case, there is no (S_1, S_2) combination for which polymorphism is possible with L=20 loci (for ζ=50).

C. Individual-based simulations

The theoretical predictions detailed above are based on the diffusion framework, which involves three approximations, namely, continuous time, an infinite number of demes and linkage equilibrium (see also Model and Methods). We test the validity of each assumption by comparing analytical predictions with two types of individual-based simulations.

In simulations of the first kind, we simulate a single focal deme belonging to the rare habitat by drawing the number of immigrants per generation from a Poisson distribution with mean $m\overline{N}$, and assigning the '1' allele at (any) locus j in each migrant genome independently with probability $\overline{Np_j}/\overline{N}$. Here, $\overline{Np_j}$ and $\overline{N}$ are the means across the whole metapopulation, and are obtained numerically from the diffusion approximation (as described above). These simulations thus respect the infinite island assumption, since migrants are drawn from an effectively infinite pool, characterised by deterministic $\overline{N}$ and $\overline{Np}$, which are unaffected by stochastic fluctuations within the focal deme. Moreover, choosing the state of each locus in each migrant genotype independently ensures LE within the migrant pool. This set of simulations thus allows us to test the consequences of discrete time and LD *within* demes. For a given set of scaled parameters (ζ, S_1, S_2, M), we expect the results of these simulations to approach the predictions of the diffusion approximation as r_0 is reduced while holding the scaled parameters constant.

In simulations of the second kind, we simulate the full metapopulation consisting of n_D demes, of which $(1-\rho)n_D$ and ρn_D belong to the first and second habitat respectively. These simulations relax the assumption that the migrant pool is infinite and in LE. We test the importance of the infinite deme assumption by varying n_D. We also test the effects of LD within the migrant pool, by comparing simulations with the same scaled parameters but different r_0. LD in the migrant pool (which reflects LD across the whole metapopulation, when demes belonging to different local habitats are simultaneously adapted at many loci) is expected to be insignificant when $s{=}r_0S$ is weak relative to recombination. Thus, as in the first set of simulations, we expect the behaviour of individual-based simulations to converge to the diffusion approximation (which assumes LE) as r_0 is reduced (for a given combination of scaled parameters). However, the rate of convergence as $r_0{\to}0$ can be quite different for the two set of simulations, for instance, if our analytical results are more sensitive to some assumptions than to others.

Since individual-based simulations of large numbers of demes (e.g., in simulations of the second kind) with large carrying capacities ($\zeta{\gg}1$) and polygenic architectures are computationally intensive, we focus on one set of parameters and explore how the critical migration threshold for loss of local adaptation is affected by deviations from these three assumptions for this set.

Continuous time approximation. To test the validity of the continuous time approximation, we simulate a single focal deme in the rare habitat subject to immigration from a migrant pool whose state is assumed to follow the predictions of the diffusion framework (simulations of the first kind). Figure 8(a) and 8(b) show the average allele frequency (averaged across all loci) and the average population size (averaged over 100 replicates) from individual-based simulations for various r_0. The unscaled parameters s and m are decreased and the carrying capacity K increased as we reduce r_0, such that the scaled parameters $\zeta{=}r_0K$, $S{=}s/r_0$ and $M{=}m/r_0$ remain constant. Figure 8(a) and

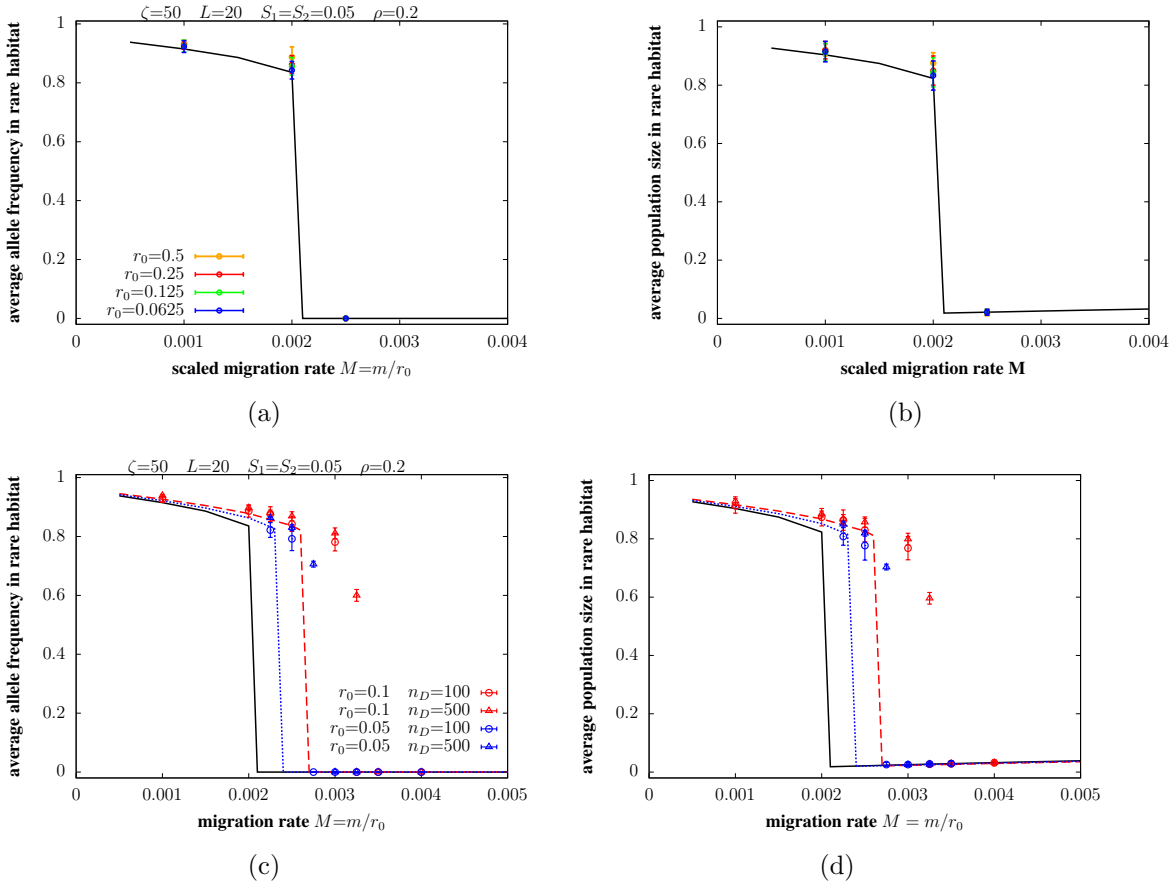


Figure 8: Comparison of individual-based simulations with predictions of the diffusion approximation (eqs. (3) and (4) in the main text). (A)-(B) Average allele frequency and population size in the rare habitat versus scaled migration rate $M{=}m/r_0$ from individual-based simulations of a focal deme which receives a Poisson-distributed number of immigrants (on average $m\overline{N}$) in each generation. Migrants are sampled from an infinite pool in LE; allele frequencies in this pool are equal to $\overline{Np}/\overline{N}$ (at each locus). The quantities $\overline{N}$ and $\overline{Np}$ are calculated using the diffusion approximation for the infinite island model (eqs. (3) and (4)). Results of individual-based simulations are shown by circles, the different colors corresponding to different values of r_0. All other unscaled parameters are varied as we vary r_0 such that the scaled parameters remain constant at $\zeta{=}50$, $S_1{=}S_2{=}0.05$. Solid line shows predictions of the diffusion approximation. (C)-(D) Average allele frequency and population size in the rare habitat versus scaled migration rate $M{=}m/r_0$ from individual-based simulations of a metapopulation with n_D demes, where circles and triangles represent results for $n_D{=}100$ and $n_D{=}500$. For each n_D and M, we simulate two sets of unscaled parameters, one with $r_0{=}0.1$ (red) and the other with $r_0{=}0.05$ (blue), both corresponding to the same scaled parameters: $\zeta{=}50$ and $S_1{=}S_2{=}0.05$. The solid black line shows predictions of the diffusion approximation (assuming LE and infinitely many islands). The dashed lines show the predictions of a more elaborate approximation that partially relaxes the LE assumption by accounting for the first generation selective disadvantage of immigrant alleles originating from different habitats due to association with other negatively selected alleles (see text). Red and blue dashed lines correspond to $r_0{=}0.1$ and $r_0{=}0.05$ respectively. The frequency of the rare habitat is $\rho{=}0.2$ and the number of selected loci is $L{=}20$ in all simulations.

8(b) show that even for $r_0 \sim 0.5$, individual-based simulations only deviate moderately from the diffusion prediction (solid line), with the agreement between the two improving for lower r_0.

The slightly higher frequencies of locally adaptive alleles in simulations (than predicted theoretically) at larger r_0 may reflect the importance of $\mathcal{O}(s^2)$ terms (which the continuous time approximation neglects) but also that the focal deme is not strictly in LE, as individuals with more recent immigrant ancestry will typically carry deleterious alleles at multiple loci (even when deleterious allele frequency is low). This kind of LD can often be adequately accounted for by assuming that immigrant alleles are introduced at an *effective* migration rate that is lower than the actual migration rate, due to their association with low-fitness genetic backgrounds (Barton and Bengtsson, 1986; Banglawala, 2010).

Finite number of demes. We also carry out individual-based simulations of metapopulations with a finite number n_D of demes (simulations of the second kind). Figures 8(c), 8(d)) show simulations with 100 versus 500 demes (circles versus triangles) of which 20% belong to the rare habitat, along with theoretical predictions for an infinite number of demes. For any given set of parameters, the average frequency of locally favourable alleles in the rare habitat (and consequently population size) is slightly higher for n_D=500, compared to n_D=100. Moreover, the migration threshold M_c itself is also somewhat higher for larger n_D. However, these effects are modest in magnitude.

Linkage equilibrium. For a given n_D, we further compare populations with different values of the baseline growth rate: r_0=0.05, K=1000 vs. r_0=0.1, K=500, (red vs. blue symbols), both of which are described by the same scaled parameters (ζ=50, S_1=s_1/r_0=s_2/r_0=S_2=0.05) and should thus exhibit the same (scaled) migration threshold M_c for loss of local adaptation (provided that the assumptions underlying the diffusion approximation are valid). However, as seen in figure 8(c), M_c differs significantly between the two set of simulations and is also much higher than the prediction of the diffusion approximation (solid black line).

As discussed above, our theoretical framework ignores LD within demes as well as LD within the migrant pool. Neglecting LD within demes (i.e., neglecting the fact that allele frequencies among residents of a deme may be different from average allele frequencies within the migrant pool at multiple loci) appears to make only a modest difference to the results (figs. 8(a) and 8(b)). However, LD within the migrant pool has a far stronger effect: neglecting such LD significantly underestimates the parameter ranges over which local adaptation can be simultaneously maintained across habitats (figs. 8(c), 8(d)).

LD within the migrant pool essentially implies that immigrant genotypes entering a particular deme may either be perfectly adapted (if they originate from other demes belonging to the same habitat) or severely unfit (if they emerge from demes belonging to the other habitat). Consequently, an immigrant allele experiences an immediate (first-generation) selective disadvantage which depends on the fitness of its genetic background in the recipient deme; this selective disadvantage is halved in each subsequent generation (Robertson, 1961). Thus, the effective migration rate of alleles differs from m and moreover, depends on both the habitat from which the allele originates and the habitat into which it migrates.

As a first approximation, we assume that immigrants entering any deme are drawn from two distinct pools (corresponding to the two habitats) with relative contributions $1-\rho$ and ρ. The 'effective' number of migrants from the ith pool to a deme within the common (or rare) habitat is assumed to be $m\overline{N_i}e^{-r_0SL[1-\overline{N_ip_i}/\overline{N_i}]}$ (or $m\overline{N_i}e^{-r_0SL[\overline{N_ip_i}/\overline{N_i}]}$) respectively. Similarly, the average number of immigrant alleles (at a given locus) from the ith pool to a deme within the common (or rare) habitat is assumed to be $m\overline{N_ip_i}e^{-r_0S(L-1)[1-\overline{N_ip_i}/\overline{N_i}]}$ and $m\overline{N_ip_i}e^{-r_0S(L-1)[\overline{N_ip_i}/\overline{N_i}]}$. Thus, in this formulation, the effective number of immigrants from each habitat is weighted by the first-generation fitness of immigrants (from that habitat) in the recipient deme. Similarly, the effective number of immigrant alleles at a particular locus is weighted by the marginal fitness of this allele, which depends on the frequencies of immigrant alleles at the other $L-1$ loci as well as their selective effects in the recipient deme. Note also that as we consider smaller and smaller unscaled parameters $r_0, s, \ldots$ (red vs blue symbols), while holding scaled parameters $\zeta, S, \ldots$ constant, the weights $e^{-r_0SL[1-\overline{N_ip_i}/\overline{N_i}]}$, $e^{-r_0SL[\overline{N_ip_i}/\overline{N_i}]}$ approach 1, so that this approximation converges to the theory in the main paper (which assumes LE).

Assuming that immigrants come from two distinct pools (corresponding to the two distinct habitats) results in a slightly more complicated theoretical approximation. Fixed points can be obtained numerically as before, but now by equating the expected values in each habitat to the corresponding average in the migrant pool derived from that habitat (i.e., by solving for $E(N_1)=\overline{N_1}$, $E(N_2)=\overline{N_2}$, $E(N_1p_1)=\overline{N_1p_1}$, $E(N_2p_2)=\overline{N_2p_2}$). The results of this approximation are depicted by dashed lines in figs. 8(c) and 8(d). Note that the critical migration rates obtained via this approximation (dashed lines) are significantly higher than those predicted by ignoring LD altogether (solid lines), but still somewhat lower than M_c found in individual-based simulations (points). A more accurate approximation can be obtained by accounting for the fact that immigrant alleles originating from differently adapted demes experience a selective disadvantage that persists over multiple generations (and not just the first generation, as assumed above). We defer details to future work.

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