The University of Chicago

Evolutionary Rescue in Structured Populations.
Author(s): Hildegard Uecker, Sarah P. Otto, and Joachim Hermisson
Source: *The American Naturalist*, Vol. 183, No. 1 (January 2014), pp. E17-E35
Published by: The University of Chicago Press for The American Society of Naturalists
Stable URL: http://www.jstor.org/stable/10.1086/673914
Accessed: 18/01/2014 20:13

VOL. 183, NO. 1 THE AMERICAN NATURALIST JANUARY 2014

E-ARTICLE

Evolutionary Rescue in Structured Populations

Hildegard Uecker,[1,*] **Sarah P. Otto,**[2] **and Joachim Hermisson**[1]

1. Mathematics and Biosciences Group, Faculty of Mathematics and Max F. Perutz Laboratories, University of Vienna, A-1090 Vienna, Austria; 2. Department of Zoology and Biodiversity Research Center, University of British Columbia, 2212 Main Mall, Vancouver, British Columbia V6T1Z4, Canada

Submitted December 2, 2012; Accepted May 9, 2013; Electronically published December 3, 2013

Online enhancement: appendixes.

ABSTRACT: Environmental change, if severe, can drive a population extinct unless the population succeeds in adapting to the new conditions. How likely is a population to win the race between population decline and adaptive evolution? Assuming that environmental degradation progresses across a habitat, we analyze the impact of several ecological factors on the probability of evolutionary rescue. Specifically, we study the influence of population structure and density-dependent competition as well as the speed and severity of environmental change. We also determine the relative contribution of standing genetic variation and new mutations to evolutionary rescue. To describe population structure, we use a generalized island model, where islands are affected by environmental deterioration one after the other. Our analysis is based on the mathematical theory of time-inhomogeneous branching processes and complemented by computer simulations. We find that in the interplay of various, partially antagonistic effects, the probability of evolutionary rescue can show nontrivial and unexpected dependence on ecological characteristics. In particular, we generally observe a nonmonotonic dependence on the migration rate between islands. Counterintuitively, under some circumstances, evolutionary rescue can occur more readily in the face of harsher environmental shifts, because of the reduced competition experienced by mutant individuals. Similarly, rescue sometimes occurs more readily when the entire habitat degrades rapidly, rather than progressively over time, particularly when migration is high and competition strong.

Keywords: evolutionary rescue, rapid evolution, adaptation, population structure, density-dependent fitness.

Introduction

Environmental change can pose severe challenges to a population. A population, previously well adapted to the ecological conditions of its habitat, might become maladapted and risk extinction. Examples for such serious alterations are manifold and include global warming and its consequences, the invasion of a new species competing for the same ecological niche, or the onset of drug therapies, selecting for resistance. There are basically three ways in which a population might respond to the environmental deterioration: disperse to another still favorable habitat, adapt by phenotypic plasticity without any change in genotype, or evolve genetic adaptations. Under which conditions populations can escape extinction by rapid adaptive evolution is one of the key questions of evolutionary biology.

Empirical evidence for evolutionary rescue comes from various sources. The evolution of antibiotic or insecticide resistance in natural populations provides prominent examples with a considerable amount of data (e.g., Chevillon et al. 1999; Normark and Normark 2002; Karasov et al. 2010). A recent survey of vertebrate studies reports a number of cases of population rescue by successful adaptation (Vander Wal et al. 2013). In recent years, several lab experiments have demonstrated the ability of populations to adapt rapidly to highly stressful conditions. These studies have investigated the role of potentially important factors such as the speed of environmental deterioration, population size, genetic variation, the history of stress, modes of dispersal between subpopulations, or recombination and sexual reproduction (Bell and Gonzalez 2009, 2011; Agashe et al. 2011; Lachapelle and Bell 2012; Bell 2013; Gonzalez and Bell 2013).

On the theoretical side, research into evolutionary rescue has followed two directions: one type of study uses a quantitative genetics approach. Many loci with small effects contribute to fitness, and the additive genetic variance (often assumed to be constant) plays a key role. Usually, the focus is on a population's capacity to track an optimum that gradually changes over time (e.g., Lynch et al. 1991; Bürger and Lynch 1995; Lande and Shannon 1996) or moves in space (Pease et al. 1989; Polechová et al. 2009; Duputié et al. 2012). Adaptation after a sudden environmental change has also been analyzed in this framework (Gomulkiewicz and Holt 1995). The simulation studies by Boulding and Hay (2001) and Schiffers et al. (2013), where

---

* Corresponding author; e-mail: hildegard.uecker@univie.ac.at.

Am. Nat. 2014. Vol. 183, pp. E17–E35.
DOI: 10.1086/673914

a finite but large number of loci contribute to fitness, are similar in tracking rescue through the spread of alleles at multiple loci. The second class of theoretical studies starts from the other end of the scale: adaptation relying on a single mutation (or sometimes a series of mutations at a single locus). In this second class, all models published so far consider a panmictic population that is exposed to a sudden severe change in its environment (e.g., Gomulkiewicz and Holt 1995; Iwasa et al. 2003, 2004*a*; Bell and Collins 2008; Orr and Unckless 2008; Martin et al. 2013) or a series of catastrophes (Martin et al. 2013). As a consequence of the environmental deterioration, the population size declines. For rescue of the population, a fitter genotype—either from standing genetic variation or newly mutated—must establish before the resident population becomes extinct.

In this study, we follow the latter approach and analyze a single-locus model with two alleles, representing the wildtype and the rescue mutant. However, we include several key ecological factors that have been left aside in the previous studies, in particular population structure. We note that this latter aspect has been shown to be of importance in a recent empirical study by Bell and Gonzalez (2011). While all previous one-locus models assume a sudden change in the environment that affects the whole population at once, we consider an environmental change that proceeds gradually across the habitat. There are thus temporal refuges, where the resident population can survive for extended periods even after environmental degradation has started. Eventually, however, the whole habitat deteriorates, and the population will go extinct unless a fitter mutant establishes. This mutant might already exist in the population before the shift in the environment (evolutionary rescue from standing genetic variation) or arise afterward due to recurrent mutation (evolutionary rescue by de novo mutations). In this context, we determine how ecological factors such as density-dependent competition, migration rates, and the speed and severity of the environmental change influence the probability of evolutionary rescue.

The rate of adaptive evolution—and hence the probability of evolutionary rescue—generically depends on the genetic variation (number of mutants) in the population and on the strength of selection, which determines the establishment probability of each mutation. The habitat ecology can crucially impact both factors, either directly or via ecological interactions. Importantly, an environmental variable can affect the two quantities in various, sometimes antagonistic ways. Effects on the rate of evolutionary rescue may differ, depending on whether rescue occurs mainly from the standing genetic variation or from new mutations. The intertwined influences on genetic variation and selection can lead to surprising results. For panmictic populations, it has been pointed out that harsher environmental change can lead to higher rates of rescue if selection is density dependent, with important implications for the evolution of drug resistance (Gatenby 2009; Gatenby et al. 2009; Read et al. 2011). In this article, we examine the nontrivial patterns that can result if an additional layer of ecological complexity is added, considering gradual deterioration in a structured environment.

The structure of the article is as follows. We first introduce our model of population structure and gradual environmental degradation. We then present an overview of the phenomena observed in the full model based on simulation results. Afterward, we consider a set of simpler submodels that allow for an analytical treatment in order to crystallize the main effects and to reveal the basic principles behind them. All mathematical analyses are presented in the appendixes.

The Model

Consider a population of haploid individuals that lives in a patchy environment. We focus on one locus with two alleles: the wildtype and the rescue mutant allele. Every generation, a fraction m of the offspring enters a migrant pool, which is thereafter distributed with equal probability over all demes (the "island model"; Wright 1943). The migration probability m, along with the number of demes D, is thus a measure of the degree of fragmentation of the habitat. Initially, selection is homogeneous across space. The population is well adapted to the ecology of its habitat, such that the population size in each deme is at its carrying capacity. The mutant allele has a disadvantage relative to the resident type and is present only at low frequencies at mutation-selection-migration-drift balance. Subsequently, the environment starts to deteriorate. Environmental deterioration does not affect the whole metapopulation at once but proceeds gradually across the habitat. We assume that the change progresses at constant speed. That is, every ϑ generations another patch switches to the new environment (fig. 1), where $\vartheta = 0$ corresponds to an instantaneous degradation of the entire habitat. While the subpopulations in demes with the original environment can maintain their size at carrying capacity, the fitness of the wildtype drops below 1 in the perturbed demes, and the population size starts to decline. Whereas the wildtype cannot persist in the new environment, mutants have—at least at low population densities—a fitness greater than 1. They are, however, initially rare (or absent) in the population and therefore likely to suffer stochastic loss. At this stage, the metapopulation corresponds to a source-sink system where the unperturbed demes act as sources and the perturbed demes as sinks for wildtype individuals. Because the size of the sink grows over time and the source van-

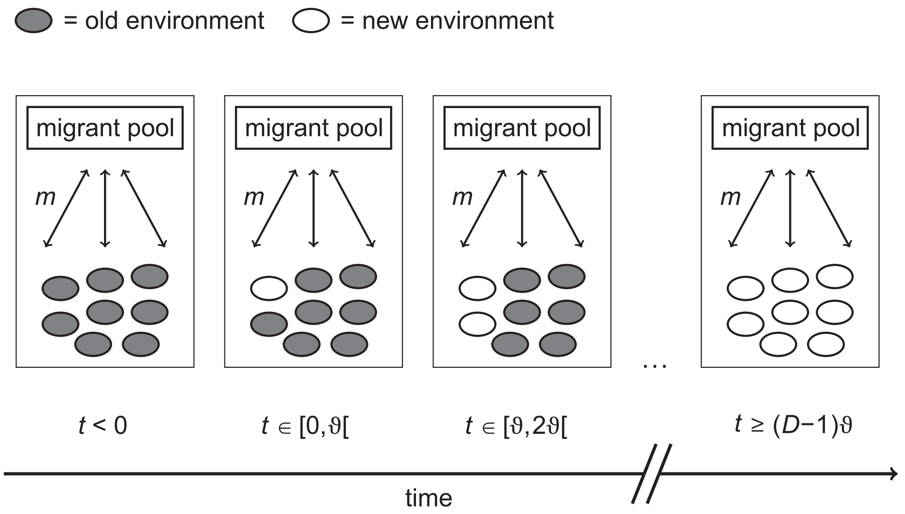

Figure 1: Sketch of the spatial and temporal habitat structure. The population lives in a patchy environment with D demes. Each generation, a fraction m of the offspring enters a migrant pool, which is then randomly distributed over the islands. Beginning at time $t = 0$, the environment changes in intervals of ϑ generations, affecting one deme at a time until all demes are affected. The environmental change is thus idealized as a discrete switch and may, for example, represent a shift in habitat type, the appearance of an invading species, or an alteration in climate.

ishes, the metapopulation will ultimately become extinct unless it is rescued by adaptive mutation.

We denote the carrying capacity for each deme as K and define $K_{\text{total}} = DK$. The numbers of wildtypes and mutants in deme i are written as $N_{\text{w}}^{(i)}$ and $N_{\text{m}}^{(i)}$, respectively. The life cycle is assumed to be as follows:

1. Reproduction and mutation. Each individual of the parent generation, irrespective of type, produces a large number X of offspring. A fraction u of the wildtype offspring mutates. Back mutation is ignored.

2. Migration. A fraction $1 - m$ of the offspring remains in its home deme, a fraction m enters the migrant pool. A fraction $1/D$ of the migrant pool settles in each deme.

3. Selection and density regulation. Each deme has a hard carrying capacity K. Under the original environmental conditions, the offspring viability is sufficiently high such that the deme is fully occupied after completion of the life cycle. Following the classical island model, we determine the genetic composition of the next generation in an unperturbed deme by binomial sampling of K individuals from the local offspring pool with frequencies weighted by fitness. The number of mutants thus follows a binomial distribution with parameter

$$p = \frac{\alpha(N_{\text{m}}^{(i)\prime} + uN_{\text{w}}^{(i)\prime})}{(1-u)N_{\text{w}}^{(i)\prime} + \alpha(N_{\text{m}}^{(i)\prime} + uN_{\text{w}}^{(i)\prime})}, \tag{1}$$

where α is the relative fitness of the mutant in the old environment and

$$N_{\text{w}}^{(i)\prime} = (1-m)N_{\text{w}}^{(i)} + \frac{m}{D}\sum_{k=1}^{D} N_{\text{w}}^{(k)},$$

$$N_{\text{m}}^{(i)\prime} = (1-m)N_{\text{m}}^{(i)} + \frac{m}{D}\sum_{k=1}^{D} N_{\text{m}}^{(k)}. \tag{2}$$

We denote by $z_0 := 1 - \alpha$ the strength of selection against mutants in unperturbed demes. Under the deteriorated conditions in the new demes, survival probabilities are lower, and at least as long as the mutant is rare, the carrying capacity will in general not be reached. Wildtype individuals are unable to replace themselves, and we set the probability of survival for each of their X offspring to $(1 - r)/X$. In contrast, mutant individuals are—at least at low densities—able to positively grow; mutant offspring survive with probability $(1 + S_i)/X$ in deme i. In the limit $X \to \infty$, the number of wildtype and mutant individuals after selection but before density regulation follows a Poisson distribution:

$$N_{w}^{(i)} \to \text{Poisson with parameter } (1-u)(1-r)N_{\text{w}}^{(i)\prime},$$

$$N_{\text{m}}^{(i)} \to \text{Poisson with parameter } (1+S_i)(N_{\text{m}}^{(i)\prime} + uN_{\text{w}}^{(i)\prime}). \tag{3}$$

If necessary, the population size is thereafter reduced to carrying capacity K. For large r, this is very rarely needed until rescue has occurred.

Note that (unless density regulation is needed) $(1 - r)$ plays the role of an absolute fitness of wildtype parents under the perturbed conditions (ignoring mutation). We

Table 1: Summary of notations

Term	Definition
D, K	No. demes and carrying capacity of a single deme, $K_{\text{total}} = KD$
$N^{(i)}_{\text{w/m}}$, $N^{(\text{old})}_{\text{w/m}}$, $N^{(\text{new})}_{\text{w/m}}$, $N^{(\text{total})}_{\text{w/m}}$	No. wildtype/mutant individuals, respectively, in deme i, the unperturbed (old) and perturbed (new) part of the habitat, and in the entire metapopulation
m	Fraction of offspring that enter the migrant pool
u	Mutation probability
ϑ	Interval between the deterioration of two demes
α, z_0	$\alpha = 1 - z_0$: relative fitness of the mutant in the old environment
$1 - r$	Absolute fitness of a wildtype parent in the new environment
$1 + S_i$	Absolute fitness of a mutant parent in deme i with the new environment (cf. eq. [4])
β	Strength of density dependence experienced by a mutant in the new environment
$1 - z$	Minimum absolute fitness of a mutant parent in the new environment (at high density) if $\beta > 0$
$1 + s$	Maximum absolute fitness of a mutant parent in the new environment (at low density) if $\beta > 0$; absolute fitness of a mutant in deme i if $\beta = 0$
s_{eff}	Effective strength of selection experienced by a mutant
$p^{(i)}_{\text{est}}$	Establishment probability of a single mutant in deme i

use r as a measure of the severity of the environmental change. Similarly, $(1 + S_i)$ is the absolute fitness of mutant parents in the perturbed deme i, where we model S_i as follows:

$$S_i = \max\left[-z, s\left(1 - \beta\frac{N_{\text{w}}^{(i)\prime} + N_{\text{m}}^{(i)\prime}}{K}\right)\right], \qquad (4)$$

with $s, z > 0$, $\beta \geq 0$. For $\beta = 0$, we have $S_i = s$, and fitness is density independent. For $\beta > 0$, growth of the mutant population is reduced in the presence of competing wildtype or mutant individuals. For $\beta > 1$, this entails an effective reduction of the mutant carrying capacity in the new environment to K/β. The parameter z sets a limit to the harmful effects of competition. Choosing $z \leq 1$ prevents absolute fitness from becoming negative. For $z = 1 - \alpha$, the absolute fitness of mutants in a fully occupied deme is the same under both environmental conditions. The effect of competition on mutants in a fully occupied deme is weaker in the new environment for $z < 1 - \alpha$ and stronger for $z > 1 - \alpha$. For simplicity, we refrain from explicitly modeling density dependence of the wildtype fitness. Note that this latter assumption is more a technicality: the relevant feature of the wildtype population size in the degraded environment is a decay that is still sufficiently fast at low densities. The rate of decay (the harshness of the environmental change) is controlled by the parameter r; the specific mode of the decay is of minor importance. Note also that under certain scenarios, mutant fitness might indeed be density dependent, while the wildtype fitness is not. For example, it is possible that mutants are able to convert a particular resource in a manner that allows them to grow in the new environment; while all individuals use up this resource, it only affects the growth rate of mutant individuals and only in the new environment.

All model parameters and further notations used throughout the article are summarized in table 1.

Simulations

Algorithm

The simulation program implements the discrete-generation life cycle, with offspring numbers in the old and the new demes determined by drawing from a binomial or a Poisson distribution, following equations (1) or (3) (plus possibly density regulation), respectively. We start the simulations with all demes fully occupied by wildtype individuals and let the population evolve for a large number of generations to generate mutation-selection-drift equilibrium before the deterioration of the habitat sets in. After all demes have deteriorated, we track the population until the wildtype has become extinct. If any mutants are present at this point, we let the simulations run until the mutant has either reached a threshold density or has become extinct. As a threshold density, we choose 90% of the total carrying capacity of the mutant if $m > 0$ and 90% of the carrying capacity of the mutant in a single deme if $m = 0$. The latter implies that the population is considered as rescued even if only a single subpopulation survives. If not stated otherwise in the figure legend, simulation points represent averages over 10^7 replicates. All computer simulations were written in the C programming language, making use of the *Gnu Scientific Library* (Galassi et al. 2009).

Observations

Our most significant findings from the numerical analysis are summarized in figures 2, 3, and 4. We focus on the dependence of the rescue probability on the strength of migration m, the severity of change (reflected by r), and the speed of environmental change (modeled by ϑ).

The dependence of the rescue probability on the migration rate is explored in figure 2*A* and 2*B*. In all cases, we observe a (local) maximum in the probability of evolutionary rescue for low, but nonzero levels of migration ($m_{\max} \approx s$). In some cases, rescue increases again for strong migration. This secondary increase for large m is observed if α (see fig. 2*A*) and r (see fig. 2*B*) are not too small. The chances of rescue become very high for strong migration, if r is large (cf. $r = 0.4$ in fig. 2*B*). All effects of strong migration are observed across a larger parameter range (i.e., even for smaller values of α and r), if the total number D of demes is larger. As we will see, the maximum for intermediate migration is generated by the interplay of two antagonistic effects: on the one hand, migration leads to an increased mutational input; on the other hand, by migration, mutants end up in unperturbed demes where they suffer a disadvantage (see "Evolutionary Rescue in an Island Model without Standing Genetic Variation"). The potential increase for very large m is a consequence of relaxed competition in the old environment (see "Evolutionary Rescue in a Levene Model").

Figures 2*C*, 2*D*, and 3 summarize the dependence of the rescue probability on the severity of the environmental change, $P_{\text{rescue}}(r)$. We first compare figures 2*C* and 2*D*. As expected, the rescue probability declines with r for many parameter combinations. However, we observe a counterintuitive behavior in a relevant part of the parameter space, where $P_{\text{rescue}}(r)$ exhibits a pronounced minimum. This means that a harsher environmental change (larger r) can increase the probability of survival in some cases. Figure 2*C* shows the typical behavior for weak and intermediate migration. In this case, we observe a nonmonotonic behavior for relatively high mutant fitness in the old environment and strong density dependence in the new environment (high values of both α and β). Further requirements are a sufficiently large value of s and a large, but not too large, value of z (i.e., sufficiently strong selection and density dependence in the new habitat). Figure 2*D* represents extensive migration. In this case, the parameter space yielding nonmonotonic behavior is much enlarged. We observe a nonmonotonic shape even for intermediate mutant fitness α and even in the absence of any additional density dependence in the perturbed environment ($\beta = 0$). For the parameters explored in figures 2*C* and 2*D*, standing genetic variation is required in order to observe a minimum in the rescue probability ($\alpha > 0$). However, under other parameters, $P_{\text{rescue}}(r)$ can display a nonmonotonic behavior even when $\alpha = 0$ and there is hence no standing variation, as illustrated in figure 3. This occurs if density dependence is strong (β large), selection strong relative to migration (s large, with larger values of m requiring larger values of s), and the speed of deterioration slow (ϑ large). As we will explain in the analysis section, the advantage of a faster decay (higher r) comes about because of weakened competition either on the islands with the new environment (see "Evolutionary Rescue in Panmictic Populations with $D = 1$ and Scenarios Where Habitat Structure Is Immaterial") or on the islands with the old environment (see section "Evolutionary Rescue in a Levene Model"). While a harsher change reduces the number of rescue mutations that appear by mutation, it increases the establishment probability of each single mutant due to these effects.

Figure 4 focuses on the influence of the speed of environmental change modeled by ϑ. In figure 4*A*, we see that the probability of evolutionary rescue can either increase or decrease as a function of ϑ; that is, a slowly progressing change can be better or worse for the population than an instantaneous degradation of the whole habitat. Figure 4*A* demonstrates how this depends on the strength of density dependence β. Figure 4*B* shows the probability of evolutionary rescue as a function of m for various values of ϑ. The strength of density dependence β is fixed to the value for which in figure 4*A*, a rapid change was favored over a slow one. We observe that for weak and intermediate migration, the survival probability significantly increases as ϑ gets larger (slower change), while in line with figure 4*A*, it decreases with increasing ϑ for strong migration. Overall, we find that a rapid change facilitates rescue if m, α, z, s, and r are large and β not too small. The reason for this behavior is similar to that indicated above when considering the harshness of change (faster degradation can relax competition, see section "Evolutionary Rescue in a Levene Model"), but the parameter range yielding the counterintuitive behavior is much more restricted. For strong density dependence and migration, the fitness of mutants gets strongly suppressed in the new environment due to competition with the immigrating wildtype individuals even for large r. If standing genetic variation is large and de novo mutations rare (large α, large r, small u), the probability of rescue is therefore larger for an instantaneous degradation of the entire habitat without temporal refugia.

In the following, we will explain within three analytically

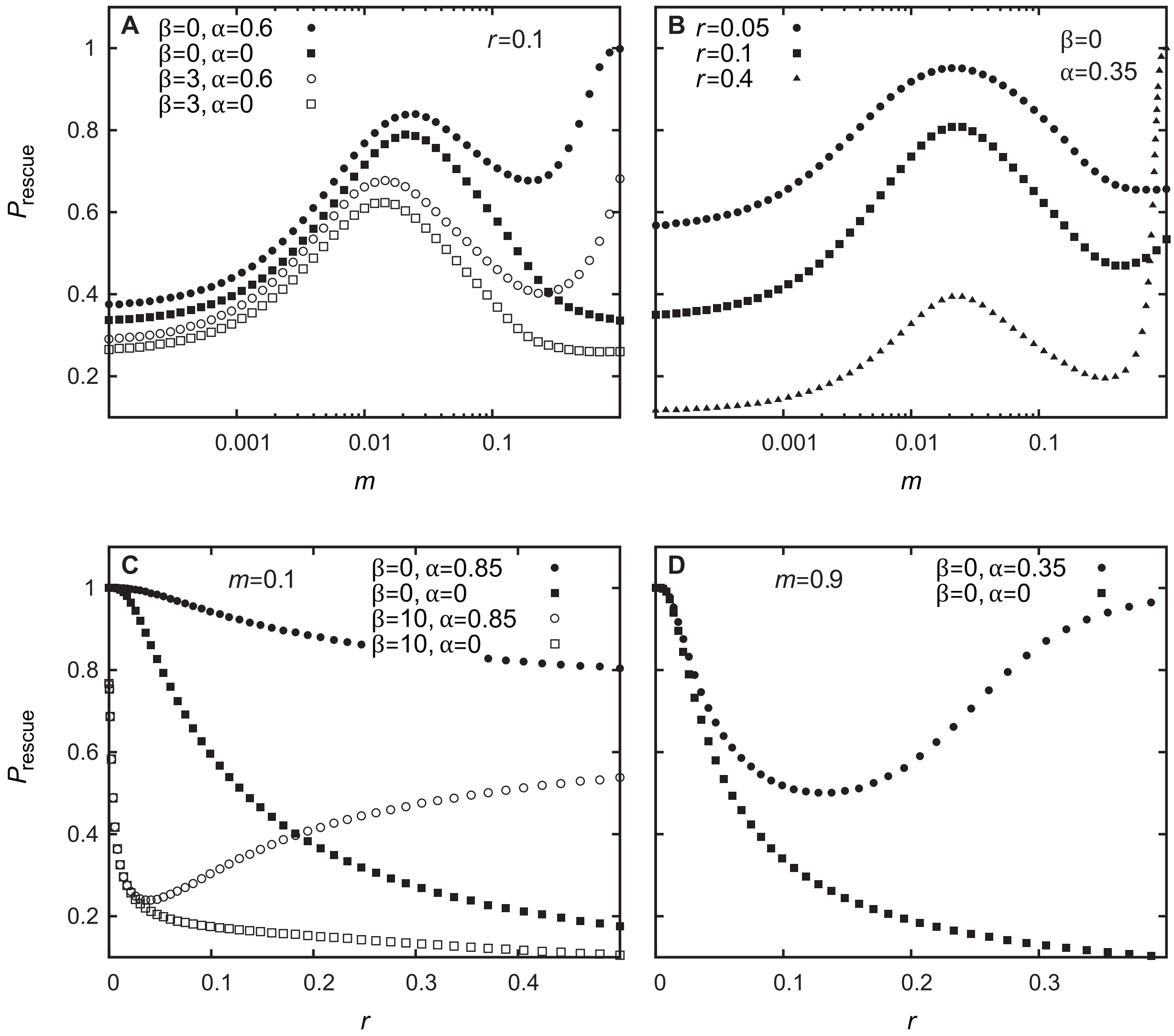

Figure 2: *A*, *B*, Probability of evolutionary rescue as a function of *m*. Filled and open symbols indicate the absence or presence of density dependence (beyond the hard carrying capacity *K*). *A*, Squares and circles distinguish scenarios with and without standing genetic variation. In all cases, we observe a local maximum for intermediate migration. In some cases, the rescue probability increases again for strong migration. *C*, *D*, Probability of evolutionary rescue as a function of *r*. Filled symbols correspond to scenarios with no explicit density dependence ($\beta = 0$), while open symbols denote strong density dependence ($\beta = 10$). Squares represent scenarios where the mutation is lethal under the original conditions ($\alpha = 0$), and circles denote scenarios with standing genetic variation ($\alpha > 0$). The plots show that a harsher change (larger *r*) is sometimes better for the survival of the population than a milder one. Each simulation point is the average over 10^6 replicates. (Parameters: $D = 8$, $z = 0.2$, $s = 0.02$, $K = 2{,}500$, $\vartheta = 250$, and $u = 0.5 \cdot 10^{-4} = 1/K_{\text{total}}$.)

tractable submodels how these patterns arise. In a first step, we will consider a class of models in which habitat structure is absent or immaterial ($D = 1$ or $m = 0$ or $\vartheta = 0$). The second submodel is a generalization of the Levene (1953) model ($m = 1$). Last, we will analyze an island model with $\alpha = \beta = 0$, that is, where the mutation is lethal in the original environment and mutant fitness in the perturbed environment is density independent.

Analysis

General Approach

The probability of evolutionary rescue is determined by the rate of successful mutants, that is, the rate of mutants that not only arise but also establish in the population. In a panmictic population, this rate is proportional to the number of wildtype individuals, which determines—to-

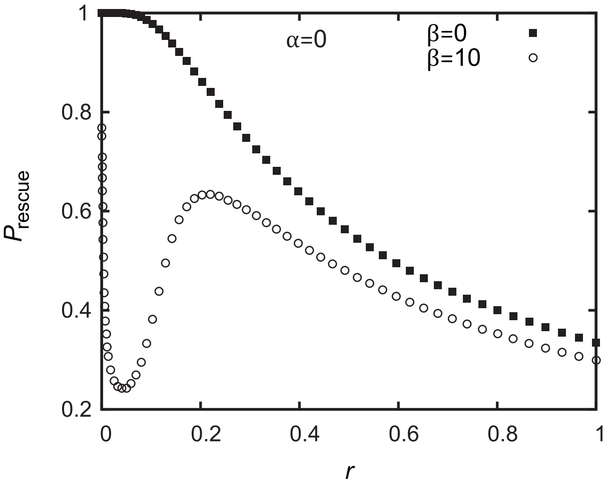

Figure 3: Probability of evolutionary rescue as a function of r. The function $P_{\text{rescue}}(r)$ can attain a minimum and a maximum for intermediate values of r. Each simulation point is the average over 10^6 replicates. (Parameters: $D = 2$, $z = 0.2$, $s = 0.02$, $m = 0.01$, $K = 10{,}000$, $\vartheta = 5{,}000$, and $u = 0.5 \cdot 10^{-4} = 1/K_{\text{total}}$.)

gether with the mutation probability u—the number of mutants that are generated each generation and the establishment probability of a new mutant. In a spatially structured population, both the mutational input and the establishment probability vary across demes. In a gradually deteriorating environment, we are inherently far from equilibrium, and both factors are time dependent.

In our model, the number of new mutations that arise in generation t and survive selection and density regulation in that generation is given by the respective terms in equations (1) and (3). As long as the rescue allele is rare, the binomial distribution in equation (1) can be approximated by a Poisson distribution with mean $u\alpha K$. Consequently, the number of successful mutants that is generated in deme i in generation t follows a Poisson distribution with mean $u\alpha K p_{\text{est}}^{(i)}(t+1)$ if the deme has not yet deteriorated and $u(1+S_i(t))N_{\text{w}}^{(i)\prime}(t)p_{\text{est}}^{(i)}(t+1)$ in the deteriorated environments, respectively. The term $p_{\text{est}}^{(i)}(t)$ is the establishment probability of a mutant in deme i in generation t at the start of the life cycle (i.e., before reproduction), and $N_{\text{w}}^{(i)\prime}(t)$ is defined as in equation (2). For a given demographic history, the probability of evolutionary rescue is hence given by

$$P_{\text{rescue}} \approx 1 - \exp\left\{-\sum_{i=1}^{D}\left[\sum_{t=-\infty}^{(i-1)\vartheta-1} u\alpha K p_{\text{est}}^{(i)}(t+1) + \sum_{t=(i-1)\vartheta}^{\infty} u(1+S_i(t))N_{\text{w}}^{(i)\prime}(t)p_{\text{est}}^{(i)}(t+1)\right]\right\}, \qquad (5)$$

where the exponential is the probability that no successful mutant is generated in any deme in any generation. The sum $\sum_{i=1}^{D}\sum_{t=-\infty}^{(i-1)\vartheta-1}$ captures the contribution of standing genetic variation (defined as mutations arising before a deme degrades), and the sum $\sum_{i=1}^{D}\sum_{t=(i-1)\vartheta}^{\infty}$ captures the contribution of de novo mutations (subsequent to environmental degradation).

Throughout the article, we model the dynamics of the wildtype population size deterministically; that is, we neglect demographic stochasticity (see Martin et al. 2013 for a study that includes demographic stochasticity). The establishment phase of new mutants, however, is characterized by strong stochasticity and thus requires a probabilistic treatment. Following a long tradition in population genetics, we calculate establishment probabilities via time-inhomogeneous branching processes (Kendall 1948; Allen 2011; Uecker and Hermisson 2011). This approach is based on the following reasoning: as long as the mutation is rare in the population, mutant offspring suffer (nearly) independent fates, and their early spread is therefore well described by a branching process. In a structured population, we must a priori distinguish several types of individuals according to deme and consequently describe the dynamics of the wildtype by a set of coupled difference equation and the spread of the mutant by a multitype branching process. In the following sections, we focus, however, on limiting cases which all allow for an effective reduction of the dimensionality of the problem. In these cases, we can model the deterministic dynamics of the wildtype by a single difference equation (see eq. [A1], available online, applicable to all three submodels) and the early phase of mutant growth by a single-type branching process with a time-dependent effective growth parameter $s_{\text{eff}}(t)$.

Details on the analysis can be found in the appendixes, available online. All numerical evaluation of integrals is done in Mathematica (Wolfram Research, Champaign, IL). Comparison to computer simulations shows that the analytical results are highly accurate.

Evolutionary Rescue in Panmictic Populations with D = 1 *and Scenarios Where Habitat Structure Is Immaterial*

We first focus on scenarios where habitat structure is either absent ($D = 1$) or proves to be immaterial, that is, does not affect the probability of evolutionary rescue. We find that habitat fragmentation is irrelevant if individuals do not migrate ($m = 0$; rescue is defined as survival of at least one subpopulation) or if the environment changes simultaneously on all islands ($\vartheta = 0$). In both cases, the probability of rescue is the same as in an unstructured population of size $K_{\text{total}} = KD$ irrespective of the number D of demes. For zero migration, this initially surprising result essentially follows because in both the unstructured

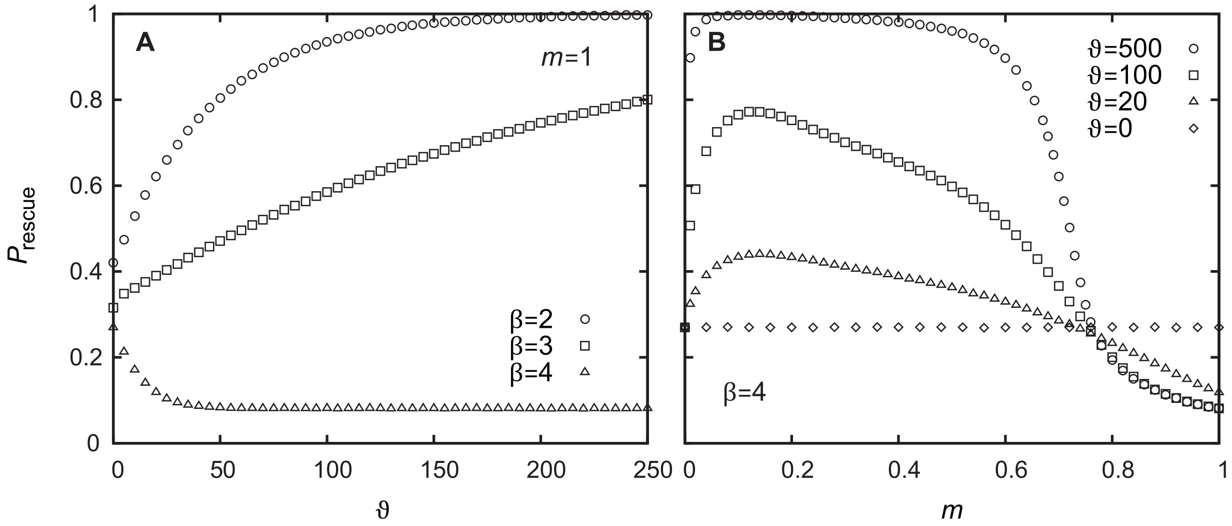

Figure 4: *A*, Probability of evolutionary rescue as a function of ϑ for three levels of density dependence. We see that for strong migration and density-dependent selection, an instantaneous deterioration of the whole habitat ($\vartheta = 0$) can be better for population survival than a slowly progressing change. *B*, Probability of evolutionary rescue as a function of *m*. For $m \gtrsim 0.8$, a fast change leads to a higher probability of evolutionary rescue than a slow change. Each simulation point is the average over 10^6 replicates. (Parameters: $D = 2$, $\alpha = 0.99$, $z = 0.685$, $s = 0.411$, $K = 10{,}000$, $r = 0.5$, and $u = 0.5 \cdot 10^{-5} = 0.1/K_{\text{total}}$.)

and the island model, the local population size declines at rate r after the local environmental shift, regardless of when this shift occurs. If the environment changes at the same time in the whole habitat ($\vartheta = 0$), the wildtype population size decays simultaneously in all demes with the same rate r as in the one-deme case, regardless of the migration rate. Hence, migration of mutants has no effect on their establishment probability, even if mutant fitness is density dependent. A formal proof of why the cases $D = 1$, $m = 0$, and $\vartheta = 0$ coincide as well as details on the analysis are given in appendix B. For simplicity, we stick to $D = 1$ in the following. In that case, we naturally deal with only one type of wildtype and one type of mutant individual.

For density-independent fitness ($\beta = 0$), we are able to derive simple analytical approximations for the rescue probability (see app. B). For s and z_0 small, we obtain

$$P_{\text{rescue}}^{\text{sgv}} \approx 1 - \exp\left[-2uK\ln\left(\frac{s + z_0}{z_0}\right)\right] = 1 - \left(\frac{s + z_0}{z_0}\right)^{-2uK}, \qquad (6)$$

$$P_{\text{rescue}}^{\text{dnm}} \approx 1 - \exp\left[-u\frac{K}{r}2s\right], \qquad (7)$$

where $P_{\text{rescue}}^{\text{sgv}}$ and $P_{\text{rescue}}^{\text{dnm}}$ denote the probability of evolutionary rescue by mutations from standing genetic variation and de novo mutations, respectively. These formulas agree with the results by Orr and Unckless (2008), who provide a detailed discussion of evolutionary rescue in unstructured populations when fitness is density independent. (Note that the absolute fitness of a mutant in the new environment is $1 + s$ in our model, while it is $1 + s_b - r$ in Orr and Unckless (2008); the parameter z_0 corresponds to s_d in Orr and Unckless 2008.) In this case, the decay rate r of the wildtype population size enters the result solely via the mutational input. As the latter is larger for smaller values of r, the probability of evolutionary rescue monotonically decreases as r increases. The probability of evolutionary rescue from standing genetic variation is unaffected by the severity of change as long as mutant fitness is density independent below the hard carrying capacity K. In contrast, if fitness is density dependent ($\beta \neq 0$), the establishment probability of mutations from both standing genetic variation and de novo mutation depends on how fast the wildtype population size decays, and more complex behavior may arise.

Figure 5 shows the probability of evolutionary rescue as a function of r for various combinations of β (affecting the strength of density dependence) and α (affecting the amount of standing genetic variation). If either α or β (or both) are small, the rescue probability decreases as a function of r (apart from barely visible nonmonotonic behavior; see app. B for details). However, when both parameters are large, we observe a pronounced minimum in the probability of evolutionary rescue. How can we understand this behavior? Both de novo mutations and mutations from standing genetic variation contribute to evolutionary rescue, and it is helpful to consider both contributions

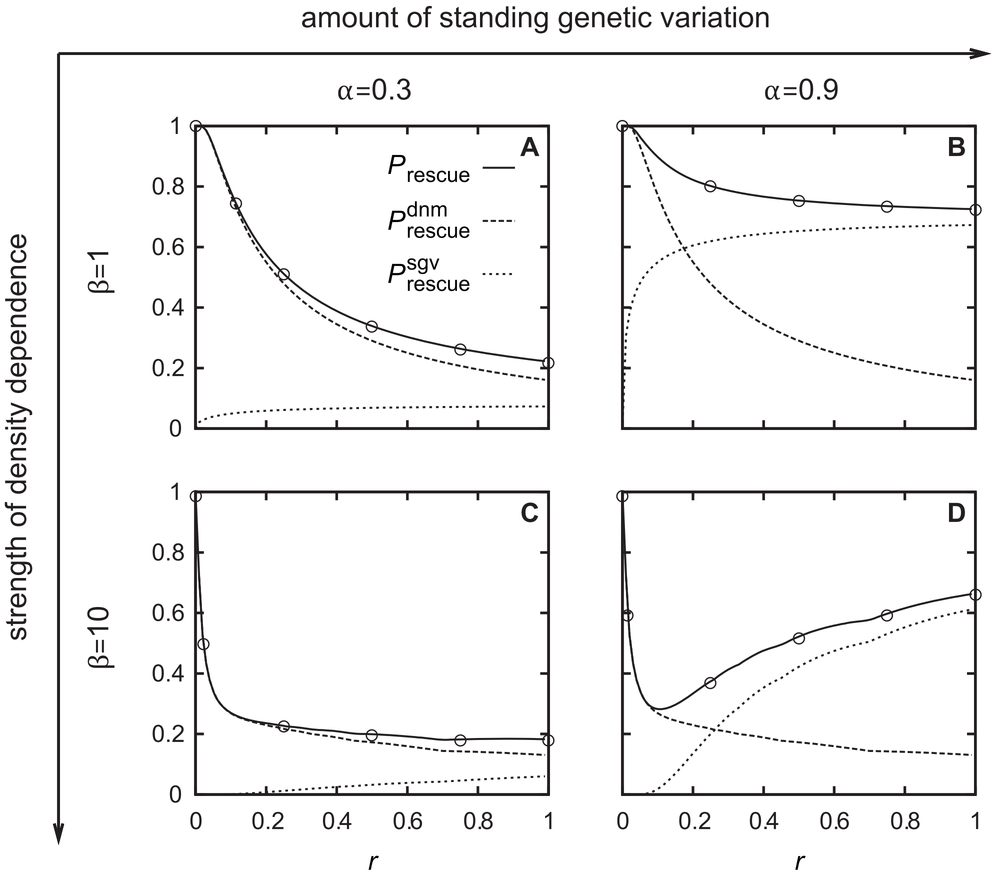

Figure 5: Evolutionary rescue in an unstructured population ($D = 1$). Dashed curves give the probability of rescue from de novo mutations (i.e., those occurring after the environmental change), while dotted curves give the probability of rescue from standing genetic variation. Depending on the amount of standing genetic variation (α) and the strength of density dependence (β), the probability of evolutionary rescue decreases with r or shows a pronounced minimum for intermediate values of r. The parameter values are $z = 0.2$, $s = 0.1$, $K = 20{,}000$, and $u = 0.5 \cdot 10^{-4} = 1/K$. The theoretical curves are based on equation (B3), available online, where the establishment probability has been calculated via equation (A7), available online. Circles denote simulation results.

separately. The mutational input ($\sim uN_{\text{w}}$) during population decline decreases as a function of r, while the establishment probability p_{est} increases because of weakened competition. The probability of evolutionary rescue by de novo mutations depends on both factors; its overall trend is governed by the declining mutational input. By contrast, the probability of evolutionary rescue from standing genetic variation increases with r because mutant fitness is density dependent. The two contributions to population survival—rescue by de novo mutations and rescue by mutations from standing genetic variation—thus exhibit opposite behavior as a function of r. When β is large, the population size has to be greatly reduced for the mutant growth parameter to become positive. In that case, the wildtype population size is already low, by the time that the establishment probability of de novo mutations becomes significant. Rescue by a de novo mutation is therefore only likely if r is very small, such that the number of mutants generated before extinction of the wildtype is nevertheless high. Consequently, $P_{\text{rescue}}^{\text{dnm}}$ decays rapidly as a function of r. At the same time, mutations from standing genetic variation can only contribute to rescue if the wildtype individuals are rapidly eliminated such that the mutants can survive up to the time when their fitness finally exceeds 1. This contribution is substantial if the amount of standing genetic variation is high (large α). This implies that if β and α are both large, the contribution from de novo mutations is high for small r and the contribution from standing genetic variation is high for large r, while for intermediate r none of the two contributions is particularly strong, leading to a minimum in the total probability of evolutionary rescue. To illustrate this point, we included the probability of evolutionary rescue from standing genetic variation and by de novo mutations individually in figure 5.

A pronounced minimum is generated if (1) density dependence is strong (sufficiently large β and z in our model) and (2) the rescue probability from standing genetic variation is high for large r. The latter condition requires large values of α and s. Furthermore, z must not be too large (in particular, $z \neq 1$), in order for mutants from the standing genetic variation to survive the first few generations after the environmental change, while the population is still large.

We point out that for extreme parameter values, a third pattern is possible: due to the antagonistic effects of r, $P_{\text{rescue}}^{\text{dnm}}$ and along with it the total probability of evolutionary rescue attains a minimum and then a maximum and decays afterward (fig. B3). For details, we refer to appendix B.

In structured populations with $m > 0$ and $\vartheta \neq 0$, additional genetic variation and targets of mutation are provided by immigration of individuals from the unperturbed to the perturbed demes. For slow change (large ϑ), the wildtype population in the perturbed demes approaches migration-selection balance. With density-dependent selection, mutants in these demes will be able to grow if and only if the density is sufficiently low, which is the case for large r. As a consequence of wildtype immigration from unperturbed to perturbed demes, the requirements on α are strongly relaxed, and we find a nonmonotonic behavior even in parameter regions with $\alpha = 0$ (cf. fig. 3).

Evolutionary Rescue in a Levene Model

As a next step, we investigate the influence of gradually changing heterogeneous selection with "good" and "bad" islands, but without population structure (i.e., $m = 1$). This leads to a variant of the Levene (1953) model with environmental deterioration. To begin with, we confine the treatment to density-independent selection ($\beta = 0$).

Since all offspring enter the migrant pool, all wildtypes are equivalent, regardless of source population, and the same holds for mutants. Thus, there is again only one kind of each allelic type, enabling analytical treatment. The crucial quantity for the understanding of the functional behavior of P_{rescue} is the effective growth parameter of a mutant (which enters the establishment probability). To derive the growth parameter, consider first a single old patch. The genetic composition of the next generation is determined by binomial sampling of K individuals, and the number of mutants follows a binomial distribution with parameter

$$\frac{\alpha N_{\text{m}}^{(\text{total})}(t)/D}{\alpha N_{\text{m}}^{(\text{total})}(t)/D + N_{\text{w}}^{(\text{total})}(t)/D} = \frac{\alpha N_{\text{m}}^{(\text{total})}(t)}{\alpha N_{\text{m}}^{(\text{total})}(t) + N_{\text{w}}^{(\text{total})}(t)}, \tag{8}$$

where $N_{\text{m}}^{(\text{total})}(t)$ and $N_{\text{w}}^{(\text{total})}(t)$ are the number of mutants and residents in the whole metapopulation. As long as mutants are rare relative to the number of wildtypes, the binomial distribution can be approximated by a Poisson distribution with parameter $\alpha(N_{\text{m}}^{(\text{total})}/N_{\text{w}}^{(\text{total})})K$. Since the offspring get distributed with equal probability over the demes, we can also (artificially) assign $N_{\text{m}}^{(\text{total})}/D$ mutant parents to each deme. For each mutant individual associated with a particular unperturbed deme, we thus obtain a Poisson distributed number of offspring with parameter

$$\alpha\frac{KD}{N_{\text{w}}^{(\text{total})}(t)}. \tag{9}$$

As $N_{\text{w}}^{(\text{total})}(t)/D$ will be smaller than K once the environmental deterioration has started, $\alpha DK/N_{\text{w}}^{(\text{total})}(t)$ will be larger than α. The reason is relaxed competition with the wildtype in this predisturbance patch: as the wildtype pop-

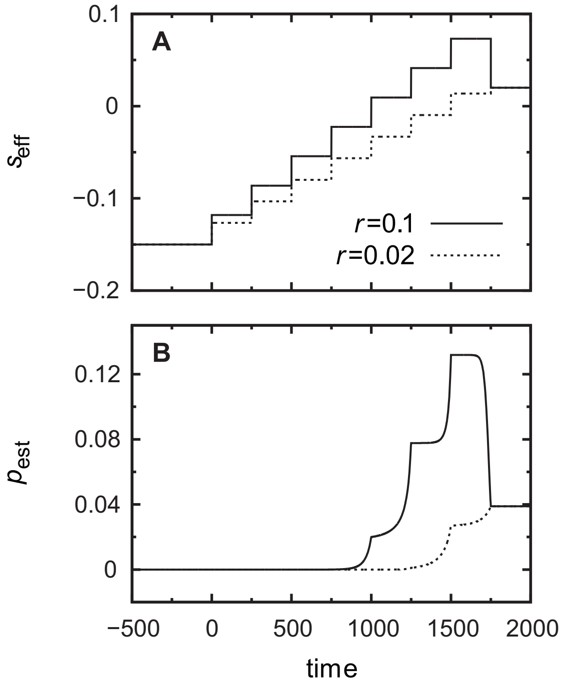

Figure 6: Effective mutant growth rate s_{eff} and establishment probability as a function of time for two values of r. Both quantities exceed their value for constant fitness s (far right) if r is large. The curves for s_{eff} and $p_{\text{est}}(t)$ follow equations (11) and (A7), available online. Parameter values: $s = 0.02$, $\beta = 0$, $\alpha = 0.85$, $D = 8$, $D\vartheta = 2{,}000$, $K_{\text{total}} = 20{,}000$, and $u = 0.5 \cdot 10^{-4} = 1/K_{\text{total}}$.

ulation size drops, fewer wildtypes contribute to the migrant pool and consequently to the local offspring pool. We now average the growth parameter of the mutant over all patches, weighting good and bad demes according to their respective numbers. For a period with d deteriorated demes, we obtain

$$s_{\mathrm{eff}}(t) = \frac{d}{D}(1+s) + \frac{D-d}{D}\alpha\frac{KD}{N_{\mathrm{w}}^{(\mathrm{total})}(t)} - 1. \tag{10}$$

In appendix C, we derive an approximation for the growth parameter of the mutant if ϑ is large enough that $N_{\mathrm{w}}^{(\mathrm{total})}(t)$ can be replaced by its stationary value, yielding

$$s_{\mathrm{eff}}(t) \approx \begin{cases} \alpha - 1 & \text{for } t < 0, \\ \alpha - 1 + \dfrac{1-\alpha+s+\alpha r}{D}d & \text{for } t \in [(d-1)\vartheta, d\vartheta[,\ d \in \{1, \dots, D-1\}, \\ s & \text{for } t \geq (D-1)\vartheta. \end{cases} \tag{11}$$

Thus, the growth parameter increases with the number of perturbed demes up to time $(D-1)\vartheta$. It might even exceed the growth parameter s in the new environment, if

$$\begin{aligned} s_{D-1} &= \alpha - 1 + \frac{1-\alpha+s+\alpha r}{D}(D-1) > s \\ \Leftrightarrow \alpha &> \frac{1+s}{1+r(D-1)}, \end{aligned} \tag{12}$$

where s_{D-1} approximates the growth parameter in the period with $D-1$ deteriorated demes, following equation (11). For "infinitely" many islands, in particular, this condition is always met except for $\alpha = 0$: the strength of effective selection goes up to $s + \alpha r$ before it drops to s after the last deme has deteriorated. The temporal development of the growth parameter for small and large r is depicted in figure 6*A*. Figure 6*B* shows the corresponding establishment probabilities. For large values of r, the effect can be quite strong. Ultimately, this is again a consequence of density-dependent fitness: density regulation in the old patches renders the absolute fitness of mutants density dependent, even if the relative fitness α is constant. When the wildtype population size decreases, competition is relaxed and the absolute fitness of mutants is increased. For the successful establishment of a mutation, absolute offspring numbers and thus the density-dependent absolute fitness matters. These considerations show that again a low fitness of the wildtype in the perturbed habitat has both a positive effect—the establishment probability increases with r, and a negative effect—the mutational input decreases. The positive effect gets stronger for larger values of α and D.

Figure 7 shows the probability of evolutionary rescue as a function of α and r, respectively. As can be seen from all three panels, P_{rescue} significantly increases with α; the increase is particularly strong for large D (fig. 7*A*) and r (fig. 7*B* and 7*C*). Note that $\alpha = 0$ implies that evolutionary rescue entirely relies on de novo mutations. We also see that due to the antagonistic effects of a fast decay of the wildtype population size, the probability of evolutionary rescue can have a pronounced minimum as a function of r (see fig. 7*B* and 7*C*). If α is small, the effect of relaxed competition is weak. In this case, the survival probability decreases as r increases because the total mutational input

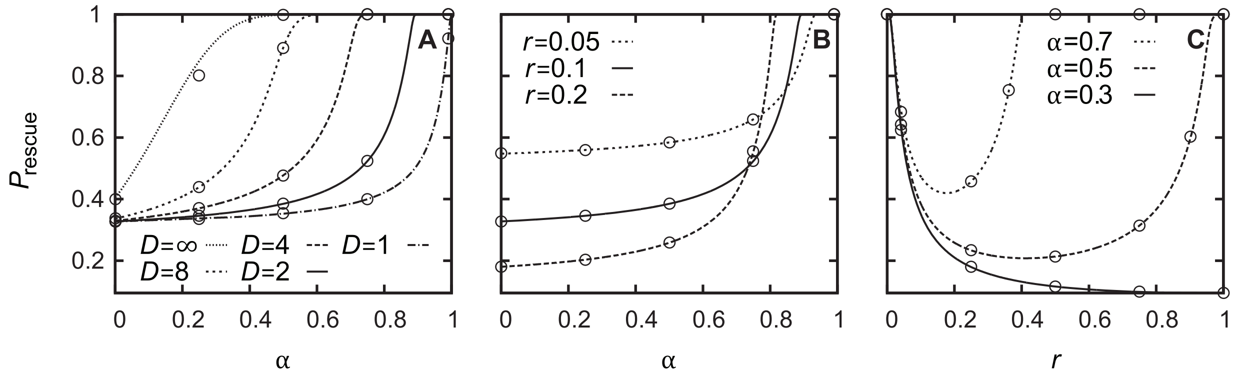

Figure 7: Evolutionary rescue in a Levene model. The probability of evolutionary rescue significantly increases with the fitness α of mutants in the unperturbed environment (*A*). For sufficiently large values of α, it has a minimum for intermediate values of r (*B*, *C*). If not specified otherwise, the parameter values are $s = 0.02$, $\beta = 0$, $D = 2$, $K_{\mathrm{total}} = 20{,}000$, $u = 0.5 \cdot 10^{-4} = 1/K_{\mathrm{total}}$, and $\vartheta = 1{,}000$; furthermore, $r = 0.1$ for *A*. The theoretical approximation for infinitely many islands is compared to simulations with $D = 100$. The theoretical curves are based on equation (C5), available online, (finite number of demes) and online equation (E12) (infinite number of demes). Circles denote simulation results.

(and in particular the mutational input after the last deme has deteriorated) diminishes with increasing r (solid curve in fig. 7*C*).

We now include density-dependent mutant fitness into the analysis and consider the limits $\vartheta \to 0$ and $\vartheta \to \infty$. As discussed in the previous section, the case $\vartheta = 0$ compares to a scenario with no habitat structure. If ϑ is very large, it is sufficient to focus on times after all demes but one have turned bad: two scenarios can be distinguished. In the first one, the mutant fitness in $[(D-2)\vartheta, (D-1)\vartheta[$ is larger than 1. In that case, as mutations arise recurrently, the mutant type will certainly establish during this last period. In the second one, the mutant fitness is smaller than 1. Then, mutations that were generated before time $(D-2)\vartheta$ (i.e., before the second last deme deteriorated) will not survive up to time $(D-1)\vartheta$, and we can safely ignore them. We can thus restrict our attention to a single environmental switch at time $(D-1)\vartheta$. As $m = 1$, all wildtype and all mutant individuals are equivalent with respect to selection. Therefore, the situation is once again formally equivalent to the one of an unstructured population subject to a single environmental shift (see app. C for details). For $\beta = 0$, the effective growth parameter of a mutant in the time interval $[(D-2)\vartheta, (D-1)\vartheta[$ is given by equation (11). The generalization to density-dependent mutant fitness is straightforward: we simply replace s with $S(t)$ and approximate $S(t)$ by its stationary value $\overline{S}$ (see eq. [C6], available online):

$$s_{D-1} = \alpha - 1 + \frac{1 - \alpha + \overline{S} + \alpha r}{D}(D-1). \qquad (13)$$

As discussed above, if s_{D-1} is larger than 0 and ϑ is large, the mutant type will certainly establish before the last environmental shift. If s_{D-1} is smaller than 0, a mutation-selection equilibrium will evolve. With increasing ϑ, the total probability of evolutionary rescue hence converges to a limit value. The speed of convergence is set by the time to approach equilibrium.

Figure 8 compares an instantaneous shift in all demes ($\vartheta = 0$) to a very slowly progressing change ($\vartheta = \infty$). While for the parameter values chosen for figure 8*A*, a slower change is better, we see in figure 8*B* that the rescue probability can be higher for a very fast change than for a very slow one. How can we explain this? We give an illustrative numerical example for the case of two demes: with $r = 0.5$, we find a total equilibrium wildtype population size of $4K/3$ before the last deme turns bad at time ϑ. For $\beta = 2$, we obtain $\overline{S} = -0.137$, and if we choose $\alpha = 0.99$, $s_{D-1} = 0.174 > 0$, that is, mutants have a good chance to establish. In contrast, for $\beta = 4$, we obtain $\overline{S} = -z = -0.685$ and with $\alpha = 0.99$, $s_{D-1} = -0.1$. This means that selection against the mutation is even stronger in the period $[0, \vartheta[$ than before time 0 because of the strong density dependence of growth in the new environment. Additionally, the number of wildtype individuals and thus the mutational input is lower. Consequently fewer mutants are present in the population at time ϑ than at time 0, which leads to a lower probability of evolutionary rescue for a very slowly progressing change as compared to an instantaneous degradation of the whole habitat. We note that for density-independent mutant fitness $\beta = 0$, $P_{\text{rescue}}(\vartheta = 0)$ is never larger than $P_{\text{rescue}}(\vartheta \to \infty)$; for $\alpha = \beta = 0$ and s small, $P_{\text{rescue}}(\vartheta = 0) \approx P_{\text{rescue}}(\vartheta \to \infty)$ (see app. C for a derivation).

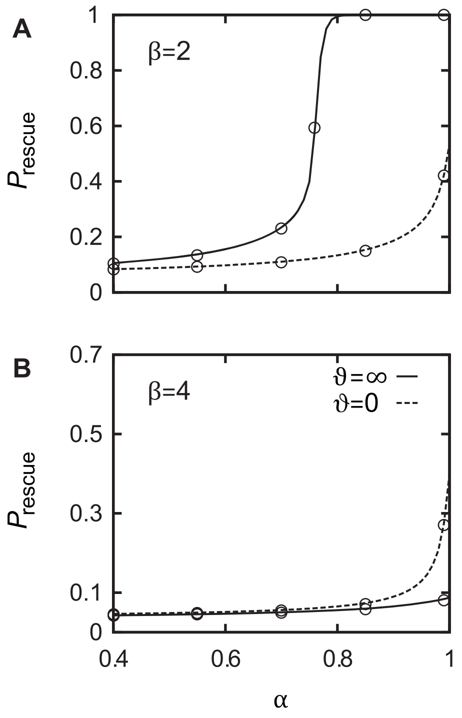

Figure 8: Evolutionary rescue in a Levene model. Comparing *A* and *B*, we see that the survival probability of the population can be higher or lower for an instantaneous degradation of the whole habitat ($\vartheta = 0$) than for a very slowly progressing change ($\vartheta = \infty$). The parameter values are $s = 0.411$, $z = 0.685$, $r = 0.5$, $D = 2$, $K_{\text{total}} = 20{,}000$, and $u = 0.5 \cdot 10^{-5} = 0.1/K_{\text{total}}$. The theoretical curves are based on equation (B3), available online (with online eq. [C8], for $\vartheta = \infty$). For the simulations, we chose $\vartheta = 5{,}000$ to represent ∞. Circles denote simulation results.

Note that the strength of s_{D-1} increases with r whenever either α or β is larger than 0. In that case, a harsher change leads to a higher establishment probability for the rescue mutant. Consequently, if $\beta > 0$, we may observe a nonmonotonic behavior of $P_{\text{rescue}}r$ even if the rescue mutation is lethal ($\alpha = 0$) under the old environmental conditions.

Evolutionary Rescue in an Island Model without Standing Genetic Variation

We now turn to an island model with arbitrary migration in order to include population structure. We assume that there is no standing genetic variation in the population for the locus in question ($\alpha = 0$); that is, the mutation is lethal in the old environment. We also restrict our investigation to density-independent selection ($\beta = 0$).

The analysis is based on the following reasoning: due to the particular migration pattern of the island model, we can merge all patches in the old environment into one habitat and all patches with the new environment into a second one. The number of wildtypes in the old part of the habitat is given by its current carrying capacity; the number of wildtypes in the new part is governed by a single difference equation (eq. [A1]). As the mutation is lethal in the old environment ($\alpha = 0$), we effectively deal with one type of mutant individuals only. As in the Levene model, it is helpful to consider the effective growth parameter of a mutant. A mutation that arises in the new environment either stays there with a probability proportional to the size of the new habitat or migrates to the old environment with a probability proportional to the size of the latter. As it cannot survive in the old habitat, its growth parameter is hence reduced by migration out of the new environment. Since the old habitat shrinks and the new habitat grows, the effective growth parameter of the mutant increases in time. This implies that again, the early spread of the mutation can be described as a time-inhomogeneous branching process with a growth parameter that gradually increases until the environmental conditions have changed on all islands. Following this reasoning, the effective growth parameter is given by

$$s_{\mathrm{eff}}(t) = \begin{cases} (1+s)\left(1 - \dfrac{D-d}{D}m\right) - 1 & \text{for } t \in [(d-1)\vartheta, d\vartheta[,\ d \in \{1, \dots, D-1\}, \\ s & \text{for } t \geq (D-1)\vartheta. \end{cases} \tag{14}$$

Migration thus reduces the effective growth parameter of mutants and along with it their establishment probability. At the same time, a large migration probability keeps the wildtype population size in the new environment high, which means that there is a large supply of new mutants that might possibly establish. Migration therefore has two antagonistic effects. As a result, the probability of evolutionary rescue has an intermediate maximum as a function of m (figs. 9*A*, 10): for small m, the positive effect of migration dominates and P_{rescue} increases with m. As m gets larger, the negative effect gets stronger and finally prevails such that the probability of evolutionary rescue decreases. For details on the analysis, we point to appendix D.

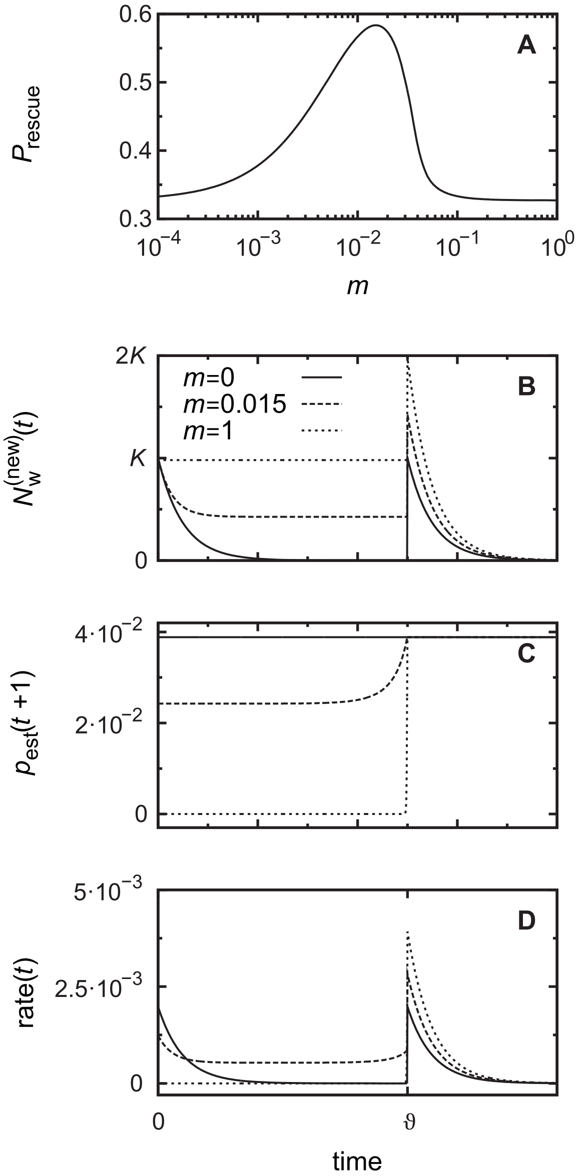

Figure 9: *A*, Probability of evolutionary rescue. The curve is based on equation (D2), available online. *B–D*, Wildtype population size in the new habitat as obtained by online equation (A1), establishment probability (calculated following online eq. [A7] with eq. [14]), and rate of successful mutations for $m = 0$, $m = 0.015$, and $m = 1$. *B–D* illustrate the existence of the maximum in *A*. The parameter values are $s = 0.02$, $\beta = 0$, $r = 0.01$, $D = 2$, $K_{\mathrm{total}} = 20{,}000$, $\vartheta = 1{,}000$, and $u = 0.5 \cdot 10^{-5} = 0.1/K_{\mathrm{total}}$.

Figure 9*B*–9*D* illustrates the dynamics for small, intermediate, and large values of m in more detail. For the sake of simplicity, we stick to a two-deme model. Figure 9*B* shows the total number of residents $N_w^{(\mathrm{new})}$ that live in the

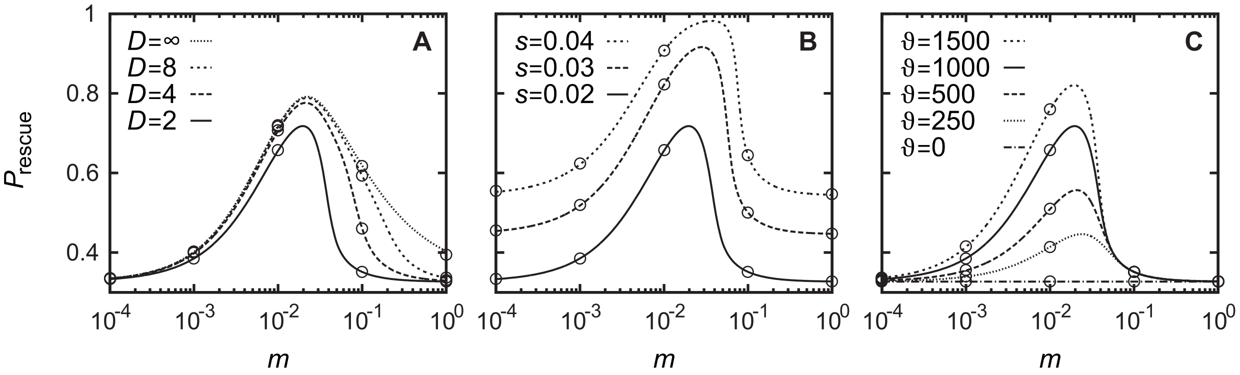

Figure 10: Probability of evolutionary rescue in an island model without standing genetic variation (mutant allele is lethal in the old environment). One observes a maximum for small values of m. If not specified otherwise in the figure legend the parameter values are $s = 0.02$, $\beta = 0$, $r = 0.1$, $D\vartheta = 2{,}000$, $K_{\text{total}} = 20{,}000$, and $u = 0.5 \cdot 10^{-4} = 1/K_{\text{total}}$. The analytical approximation for infinitely many islands is compared to simulations with $D = 40$. The theoretical curves are based on online equations (D2) (finite number of demes) and (E15) (infinitely many demes). Circles denote simulation results.

bad habitat, figure 9*C* the establishment probability of a single mutant, and figure 9*D* the rate of successful mutants. If individuals do not migrate at all, the number of wildtypes in the bad habitat exhibits two peaks: one when the first deme turns bad and the second when the second deme turns bad. The establishment probability is constant in time ($\approx 2s$). The rate of successful mutants therefore has two identical peaks; that is, a rescue mutation will most likely arise briefly after the change of the environment has occurred in one of the demes. The other extreme case is $m = 1$. In that case, $N_{\text{w}}^{(\text{new})}$ is kept relatively high. However, the establishment probability is virtually 0 up to a few generations before the second deme turns bad and then increases almost instantaneously up to $2s$. Therefore, the rate of successful mutants has only one peak (fig. 9*D*). We find that this peak comprises approximately the same area as the two peaks for $m = 0$ together, leading to approximately the same probability of evolutionary rescue. For small r and $D = 2$, as used in figure 9, this is intuitively clear: the total number of wildtype individuals stays close to K_{total} until the second deme degrades. Thus, the number of wildtypes that still exist after time ϑ (and can act as a source for rescue mutations), too, is twice as large as for $m = 0$ (see the peak in fig. 9*B*). For large r and $D > 2$, we still have $P_{\text{rescue}}(m = 0) \approx P_{\text{rescue}}(m = 1)$, although this is not obvious (see app. C for a derivation). For intermediate migration, both $N_{\text{w}}^{(\text{new})}$ and p_{est} assume nonnegligible values in the period between the deterioration of the first and the second deme, leading to a significant rate of successful mutants. Consequently, the length of this period strongly influences the survival probability of the population.

The essential elements of this discussion can also be seen in the following simple approximation, which captures the characteristic behavior of $P_{\text{rescue}}(m)$: for small s, we can approximate the establishment probability of new mutants in $[0, \vartheta[$ by

$$p_{\text{est}} \approx \max\left(2s_{\text{eff}}(t), 0\right) = \max\left[2\left(s - \frac{m}{2}\right), 0\right]. \quad (15)$$

We furthermore approximate the mutational input during this period via the equilibrium wildtype population size in the deteriorated part of the habitat (cf. eq. [D4], available online):

$$\hat{N}_{\text{w}}^{(\text{new})} = \frac{Km(1-r)}{m(1-r)+2r} \approx Km\frac{1-r}{2r}, \quad (16)$$

where the approximation is valid for $r \gg m$. This neglects the phases where the wildtype population size decays to its equilibrium or to 0, respectively, after the first and second deme deteriorates (the "peaks" in fig. 9*D*). We estimate this contribution by its value for $m = 0$ (cf. eq. [7]) and obtain for the probability of evolutionary rescuee

$$P_{\text{rescue}} \approx 1 - \exp\left\{-2u\vartheta \max\left[\left(s - \frac{m}{2}\right), 0\right] \times \frac{Km(1-r)}{2r} - \frac{2uK}{r}2s\right\}. \quad (17)$$

This simple approximation is remarkably accurate for small m and s (see fig. D1, available online). From its functional form, we see that the speed of deterioration set by ϑ has a strong effect on P_{rescue} if and only if m is in an intermediate range, such that both $\hat{N}_{\text{w}}^{(\text{new})}$ and p_{est} are nonnegligible. We also see that the maximum in $P_{\text{rescue}}(m)$ is located at $m \approx s$. These results generalize to $D > 2$ (see app. D).

We close with some observations on how various parameters shape P_{rescue}. First, we observe that the number of demes D only has a moderate influence on population survival for $D \geq 2$ (fig. 10*A*). Further, the peak for intermediate m gets broader as s increases (fig. 10*B*): the negative effect of migration sets in later for larger s. Last, as already discussed above, the value of ϑ has a strong influence on the probability of evolutionary rescue unless migration is extremely weak or quite strong (fig. 10*C*).

Discussion

Severe environmental change can drive a population extinct unless it is able to rapidly adapt to the new conditions. Environmental change is ubiquitous and greatly enhanced by human interference. A profound understanding of how such change affects biodiversity might help to develop successful conservation strategies. On the other hand, awareness of the factors that promote rapid evolution is essential whenever we seek to inhibit it, such as in treatment plans to avoid the evolution of drug resistance. In scenarios of population extinction or evolutionary rescue, evolution and ecology are necessarily intertwined. For a thorough assessment of risks and chances, it is therefore indispensable to be mindful of both evolution and ecology.

Many ecological alterations will not affect the whole habitat at once but propagate gradually across the species range. In that case, parts of the population still experience the old environment, to which it is well adapted, while others already face the new unfavorable conditions. The system corresponds to a source-sink-system with a shrinking—finally disappearing—source and a growing sink. Despite the obvious importance of population structure and gradual habitat deterioration for the probability of population survival, these aspects have not been considered in ecologically explicit models on evolutionary rescue so far. In this article, we provide a baseline model of evolutionary rescue in structured populations and investigate the implications for the probability of evolutionary rescue. In addition, we allow for density-dependent mutant fitness in the new environment. On the other hand, we restrict ourselves to the most basic genetic model of one locus with two alleles. Because of its simplicity, this basic genetic model can provide insight into the fundamental mechanisms underlying evolutionary rescue in ecologically complex scenarios. In some situations, a simple genetic basis may be appropriate. For example, mutation at a single locus can be sufficient to confer insecticide or drug resistance (Milani 1963; McKenzie et al. 1980; Daborn et al. 2002; Gerstein et al. 2012). Analysis of the model reveals several nonmonotonic relationships and unexpected patterns. In this context, three quantities—the speed of change, the severity of change, and the migration probability—are of particular interest.

The Speed of Change

How does the speed at which the deterioration proceeds across the species range influence the probability of evolutionary rescue? If $m = 0$, the survival probability of the population is independent of the speed of change, as the subpopulations in the single demes suffer independent fates. For small migration rates, the probability of evolutionary rescue is drastically increased for a slow compared to a rapid change. This is because for sufficiently weak migration, wildtype individuals are rare in the altered habitats, competition is weak, and mutations have a nonnegligible establishment probability, and the slower the change, the more mutants are generated over time. For strong migration, a more complicated picture arises: while a slower change is still often favorable, a slow deterioration of the habitat can sometimes hamper adaptation of the population if mutant fitness is strongly density dependent. We can understand this unexpected behavior as follows. For a slow change, the population encounters extended periods of environmental stasis before the last demes deteriorate. If migration is strong, the number of wildtype individuals in the perturbed demes remains relatively high during this time. As a consequence, mutant fitness, if density dependent, can be lower than it had been before the environment started deteriorating. Furthermore, the total wildtype population size and hence the number of new mutants per generation is lower than it was before time zero. The total number of mutants that are maintained in the balance of mutation, selection, and migration can therefore even be reduced relative to the number of mutants in the standing genetic variation before the environmental deterioration sets in. As a consequence, long periods of environmental stasis can lead to a reduced probability of evolutionary rescue. For density-independent mutant fitness, however, our results show that a slow change is always at least as good as a fast change (cf. app. C).

The Severity of Change

The probability of successful adaptation is usually expected to decrease with increasing maladaptation of the resident population (cf. Holt and Gomulkiewicz 2004 for an overview): the slower the decay of the wildtype population size, the more time for adaptative mutations to occur. However, it is not enough that mutations arise, they also have to survive stochastic loss and establish. Due to competition, the growth rate of new mutants will often depend negatively on the population density. In that case, a fast decay—and thus a harsh change in the environment—increases the establishment probability of mutations. As a consequence, a harsher change (larger r) is not necessarily worse for population survival than a milder one. Instead, our results show that the probability of evolutionary rescue can assume a minimum for intermediate levels of wildtype maladaptation. We find that this occurs if (1) density dependence in the new environment is strong and either the amount of standing genetic variation large or selection for the mutant strong relative to migration and the speed of change slow or if (2) migration is strong and the mutant reasonably fit in the old environment. The entire parameter space where an inverse dependence on the severity of environmental change is observed is generally larger than the parameter space where faster speed leads to higher rates of rescue. The advantage of a harsh change is that a fast decrease in the number of wildtype individuals relaxes competition, either in the new environment (scenario 1) and/or in the old environment (scenario 2). For panmictic populations without habitat structure, the first scenario has been described verbally by Read et al. (2011). In that case, rescue is likely for harsh environmental change because a fast decay of the wildtype population size enhances the establishment probability of mutations from standing genetic variation. In structured populations, not only mutants from standing genetic variation but also mutant descendants of immigrants from unperturbed to perturbed demes benefit from reduced competition in the new environment and experience a higher establishment probability for a more severe change. If standing genetic variation is low and rescue relies mainly on de novo mutations, the probability of evolutionary rescue may decrease again as r increases further because the reduced mutational input outweighs the benefits of a high establishment probability. The first scenario is also reminiscent of studies with stable source-sink dynamics, where constant mutational input from the source and low competition in the sink can lead to high rates of adaptation (Greulich et al. 2012; Hermsen et al. 2012). In the second scenario with high migration and a reasonable amount of standing variation, the positive effect of a harsh change arises for similar reasons. Fundamentally, absolute mutant fitness—and this is what decides the fate of mutations—is density dependent as a consequence of simple population regulation in the unperturbed demes. This holds true even if the relative fitness α in the old environment and the fitness $1 + S_i$ in the new environment are density independent. When the change is harsh, wildtype individuals get depleted in the perturbed part of the habitat every generation. Hence, migration between the old and the new part of the habitat is strongly unbalanced with increasing effect for stronger migration. As a consequence, competition in the old part of the habitat is relaxed and the absolute fitness of mutants accordingly enhanced. In this context, note that in our model, demes in the original environmental state get filled up to carrying capacity every generation; the genetic composition is determined by binomial sampling. This represents a certain overidealization and requires that offspring numbers are large enough. At least for not too large deme numbers D, this requirement is, however, easily fulfilled.

Awareness that intermediate environments may represent harder challenges for adaptation could be of striking importance for the design of drug treatment strategies: our results imply that a fast eradication of the pathogen might not necessarily be the best strategy to avoid drug resistance. As discussed above, in the first scenario without habitat structure, the effect is only observed if mutant fitness is strongly density dependent, which may or may not apply to a particular species. Read et al. (2011) recently discussed this idea in the context of malaria. Their arguments are based on a series of data sets showing that standing genetic variation is usually high in malaria infections and that a fast eradication of the drug sensitive pathogen allows rare resistant types to quickly amplify. This discussion of experimental evidence lends empirical support to our theory, which in turn quantifies the effect. Similarly, a recent study by Peña-Miller et al. (2013) combining deterministic mathematical models and experimental evolution in *E. coli* shows that competitive release due to a harsh treatment with a mixture of two drugs promotes the rapid emergence of drug-resistant strains.

The Migration Probability

The dependence of the rescue probability on migration is shaped by four effects: first, migration is advantageous because the old part of the habitat acts as a source for wildtype individuals that might possible mutate. Second, mutants migrate to the old habitat where they have a disadvantage with respect to the wildtype. Migration thus reduces the effective growth rate of mutants. With increasing migration, this effect outweighs the first one such that the rescue probability has a local maximum for intermediate migration. Third, when migration gets very strong, the effect of relaxed competition in the old demes sets in and the rescue probability can become again high. This latter effect only happens when the relative mutant fitness α in the old habitat, the mutant fitness $1 + S_i(t)$ in the new habitat, and the decay rate r of the wildtype population size in the new habitat are sufficiently large (the parameter range increases with increasing D). Finally, if mutant fitness in the perturbed demes is density dependent, migration leads to a reduced fitness of mutants in these demes. This counteracts the effect of relaxed competition in the old part of the habitat and can entail a very low probability of evolutionary rescue for strong migration. The interplay of all four forces can lead to a surprisingly complex dependence of the rescue probability on the migration probability (see figs. 2, 4). A maximum in the probability of successful adaptation for intermediate migration rates has been found in previous studies for partially related, partially different reasons: Gomulkiewicz et al. (1999) analyze the potential of local adaptation in a sink, which is coupled to a source. Unlike in our model, the source never degrades and the population hence never dies out. The focus of interest is niche evolution within the sink. Immigration is necessary to provide targets for mutation to act on (our first effect). The disadvantage of high immigration arises, because absolute mutant fitness in the sink is assumed to be density dependent and thus decreases for increasing immigration (our fourth effect). If immigration is too strong, absolute mutant fitness is depressed below one such that the mutation cannot spread at all. Note, however, that in our model the local maximum in the rescue probability exists even if selection is density independent in the new habitat due to migration of mutants out of the perturbed demes (our second effect). Emigration of mutants out of the sink is not taken into account in Gomulkiewicz et al. (1999). Pease et al. (1989) analyze a model of population persistence in a spatially continuous habitat. An optimum moves in space, and the population has both the possibility to adapt and to follow the optimum by migration. As space is continuous, the quantity of interest is not the migration probability (which is 1), but the mean square distance that individuals travel per generation. Similar to our model, migration is harmful in that it brings individuals to unfavorable places (cf. also Kirkpatrick and Peischl 2013). In contrast to our scenario, however, the advantage of migration arises because it is needed for the population to keep track of the moving optimum. The optimal amount of migration (in the sense of optimal mean square displacement) depends on the speed of the optimum and the additive genetic variance of the population among other factors. Likewise, an intermediate dispersal distance maximizes the probability of evolutionary rescue in a recent simulation study by Schiffers et al. (2013). The model can be seen as complementary to ours: Schiffers et al. (2013) consider a population in a deteriorating heterogeneous environment. However, the factors creating the spatial heterogeneity differ from the factors that cause the temporal degradation. In contrast to our model, the heterogeneity is thus stable in time, the gradual deterioration homogeneously affects the entire habitat. Adaptation relies on a reasonably large number of loci (15 loci per trait), making the model similar to a quantitative genetics model. Within this framework, migration has two antagonistic effects: as in our model, migration brings individuals to regions in which they are maladapted. Contrary to our model, however, this effect does not act via alleles that provide adaptation to the changing conditions—these alleles are adaptive everywhere—but on alleles that determine local adaptation to the stable heterogeneity. On the other hand, the patches are so small in Schiffers et al. (2013) that migration is necessary for the establishment of mutations that adapt the population to the globally degraded environment. This effect does not appear in our model as deme sizes are sufficiently large that the mutation can locally establish.

Limitations and Extensions of Our Model

Our analysis has several important limitations. First, our population follows the migration scheme of an island model. In particular, this implies that dispersal is global. In order to arrive at a comprehensive picture of evolutionary rescue in structured populations, local dispersal and isolation by distance should be included into the model as a next step. Experimentally, a comparison of the impact of local versus global dispersal for weak migration has been highlighted by Bell and Gonzalez (2011), showing that the rate of environmental deterioration influences how the dispersal mode affects rescue. In this context, not only a model with discrete patches, but also a model in continuous space is of interest. In experimental evolution, serial transfer of individuals with small inoculum sizes represent regular catastrophes, which would need to be included in the model for a quantitative comparison of experimental data and theory (see Martin et al. 2013). Although in some cases evolutionary rescue relies on single mutations, the simple genetic basis of adaptation is a major restriction of our study. Often, adaptation is more complex, and mutations at several loci are required to restore fitness above one. Types with only some of these mutations might potentially even perform worse (or at least not better) than the wildtype. Adaptation then includes stochastic tunneling: an inferior (or neutral) genotype is generated and has to produce a fitter mutant before it becomes extinct (Iwasa et al. 2004*b*; Weissman et al. 2009; Lynch and Abegg 2010; Martin et al. 2013). For panmictic populations, evolutionary rescue requiring stochastic tunneling has been considered by Iwasa et al. (2003) and Iwasa et al. (2004*a*) with a focus on biomedical applications (evolution of drug resistance, escape of tumor cells from chemotherapy, etc.). Last, many loci might contribute to adaptation. In that case, a quantitative genetics approach suggests itself, but also models with an explicit genetic basis of the trait would be valuable (cf. Boulding and Hay 2001 and Schiffers et al. 2013).

In conclusion, our results confirm the importance of ecological factors, specifically habitat structure and density-dependent fitness for the probability of evolutionary rescue. They provide insight into how various mechanisms intertwine to decide the race between population decline and adaptive evolution. As we have seen, this interplay of mechanisms can lead to surprising patterns in the probability of evolutionary rescue, with rapid changes in the environment (small ϑ) sometimes being easier for evolutionary rescue and sometimes harder and with rescue showing nonmonotonic relationships with both migration probability (m) and the severity of the environmental perturbation (r).

Acknowledgments

H.U. thanks the Otto lab and the Timme lab in Göttingen for helpful discussions and hospitality. We furthermore thank R. Bürger, P. Pfaffelhuber, and J. Polechová for helpful discussions and T. Day, S. Rice, and two anonymous reviewers for valuable comments on the manuscript. This work was made possible with financial support by the Vienna Science and Technology Fund (WWTF), grant MA6-01; by the Deutsche Forschungsgemeinschaft (DFG), Research Unit 1078 “Natural selection in structured populations”; by a Discovery Grant from the Natural Science and Engineering Research Council of Canada; and by travel grants from the Universities of Vienna and British Columbia.

Literature Cited

Agashe, D., J. J. Falk, and D. I. Bolnick. 2011. Effects of founding genetic variation on adaptation to a novel resource. Evolution 65: 2481–2491.

Allen, L. J. S. 2011. An introduction to stochastic processes with applications to biology. 2nd ed. Pearson Education, Upper Saddle River, NJ.

Bell, G. 2013. Evolutionary rescue of a green alga kept in the dark. Biology Letters 9:20120823.

Bell, G., and S. Collins. 2008. Adaptation, extinction and global change. Evolutionary Applications 1:3–16.

Bell, G., and A. Gonzalez. 2009. Evolutionary rescue can prevent extinction following environmental change. Ecology Letters 12: 942–948.

———. 2011. Adaptation and evolutionary rescue in metapopulations experiencing environmental deterioration. Science 332:1327-1330.

Boulding, E. G., and T. Hay. 2001. Genetic and demographic parameters determining population persistence after a discrete change in the environment. Heredity 86:313–324.

Bürger, R., and M. Lynch. 1995. Evolution and extinction in a changing environment: a quantitative genetic analysis. Evolution 49:151–163.

Chevillon, C., M. Raymond, T. Guillemaud, T. Lenormand, and N. Pasteur. 1999. Population genetics of insecticide resistance in the mosquito *Culex pipiens*. Biological Journal of the Linnean Society 68:147–157.

Daborn, P. J., J. L. Yen, M. R. Bogwitz, G. Le Goff, E. Feli, S. Jeffers, N. Tijet, et al. 2002. A single p450 allele associated with insecticide resistance in *Drosophila*. Science 297:2253–2256.

Duputié, A., F. Massol, I. Chuine, M. Kirkpatrick, and O. Ronce. 2012. How do genetic correlations affect species range shifts in a changing environment. Ecology Letters 15:251–259.

Galassi, M., J. Davies, J. Theiler, B. Gough, G. Jungman, P. Alken, M. Booth, and F. Rossi. 2009. GNU scientific library reference manual. 3rd ed. Network Theory, Bristol.

Gatenby, R. A. 2009. A change of strategy in the war on cancer. Nature 459:508–509.

Gatenby, R. A., A. S. Silva, R. J. Gillies, and B. R. Frieden. 2009. Adaptive therapy. Cancer Research 69:4894–4903.

Gerstein, A. C., D. S. Lo, and S. P. Otto. 2012. Parallel genetic changes and non-parallel gene-environment interactions underlie nystatin resistance in yeast. Genetics 192:241–252.

Gomulkiewicz, R., and R. D. Holt. 1995. When does evolution by natural selection prevent extinction? Evolution 49:201–207.

Gomulkiewicz, R., R. D. Holt, and M. Barfield. 1999. The effects of density-dependence and immigration on local adaptation and niche evolution in a black-hole sink environment. Theoretical Population Biology 55:283–296.

Gonzalez, A., and G. Bell. 2013. Evolutionary rescue and adaptation to abrupt environmental change depends upon the history of stress. Philosophical Transactions of the Royal Society B: Biological Sciences 368:20120079.

Greulich, P., B. Waclaw, and R. L. Allen. 2012. Mutational pathway determines whether drug gradients accelerate evolution of drug-resistant cells. Physical Review Letters 109:088101.

Hermisson, J., and P. S. Pennings. 2005. Soft sweeps: molecular population genetics of adaptation from standing genetic variation. Genetics 169:2335–2352.

Hermsen, R., J. B. Deris, and T. Hwa. 2012. On the rapidity of antibiotic resistance evolution facilitated by a concentration gradient. Proceedings of the National Academy of Sciences of the USA 109:10775–10780.

Holt, R. D., and R. Gomulkiewicz. 2004. Conservation implications of niche conservatism and evolution in heterogeneous environments. Pages 244–264 *in* R. Ferrière, U. Dieckmann, and D. Couvet, eds. Evolutionary conservation biology. Cambridge University Press, Cambridge.

Iwasa, Y., F. Michor, and M. A. Nowak. 2003. Evolutionary dynamics of escape from biomedical intervention. Proceedings of the Royal Society B: Biological Sciences 270:2573–2578.

———. 2004*a*. Evolutionary dynamics of invasion and escape. Journal of Theoretical Biology 226:205–214.

———. 2004*b*. Stochastic tunnels in evolutionary dynamics. Genetics 166:1571–1579.

Karasov, T., P. W. Messer, and D. A. Petrov. 2010. Evidence that adaptation in *Drosophila* is not limited by mutation at single sites. PLoS Genetics 6:e1000924.

Kendall, D. G. 1948. On the generalized “birth-and-death” process. Annals of Mathematical Statistics 19:1–15.

Kirkpatrick, M., and S. Peischl. 2013. Evolutionary rescue by beneficial mutations in environments that change in space and time. Philosophical Transactions of the Royal Society B: Biological Sciences 368:20120082.

Lachapelle, J., and G. Bell. 2012. Evolutionary rescue of sexual and asexual populations in a deteriorating environment. Evolution 66: 3508–3518, doi:10.1111/j.1558–5646.2012.01697.x.

Lande, R., and S. Shannon. 1996. The role of genetic variation in adaptation and population persistence in a changing environment. Evolution 50:434–437.

Levene, H. 1953. Genetic equilibrium when more than one ecological niche is available. American Naturalist 87:331–333.

Lynch, M., and A. Abegg. 2010. The rate of establishment of complex adaptations. Molecular Biology and Evolution 27:1404–1414.

Lynch, M., W. Gabriel, and A. M. Wood. 1991. Adaptive and demographic responses of plankton populations to environmental change. Limnology and Oceanography 36:1301–1312.

Martin, G., R. Aguilée, J. Ramsayer, O. Kaltz, and O. Ronce. 2013. The probability of evolutionary rescue: towards a quantitative comparison between theory and evolution experiments. Philosophical Transactions of the Royal Society B: Biological Sciences 368:20120088.

McKenzie, J. A., J. M. Dearn, and M. J. Whitten. 1980. Genetic basis of response to diazinon in Victorian populations of the Australian sheep blowfly, *Lucilia cuprina*. Australian Journal of Biological Sciences 33:85–96.

Milani, R. 1963. Genetical aspects of insecticide resistance. Bulletin of the World Health Organization 29:77–87.

Normark, B., and S. Normark. 2002. Evolution and spread of antibiotic resistance. Journal of Internal Medicine 252:91–106.

Orr, H. A., and R. L. Unckless. 2008. Population extinction and the genetics of adaptation. American Naturalist 172:160–169.

Pease, C. M., R. Lande, and J. J. Bull. 1989. A model of population growth, dispersal, and evolution in a changing environment. Ecology 70:1657–1664.

Peña-Miller, R., D. Laehnemann, G. Jansen, A. Fuentes-Hernandez, P. Rosenstiel, H. Schulenburg, and R. Beardmore. 2013. When the most potent combination of antibiotics selects for the greatest bacterial load: the smile-frown transition. PLoS Biology 11: e1001540.

Polechová, J., N. H. Barton, and G. Marion. 2009. Species' range: adaptation in space and time. American Naturalist 174:E186–E204.

Read, A. F., T. Day, and S. Huijben. 2011. The evolution of drug resistance and the curious orthodoxy of aggressive chemotherapy. Proceedings of the National Academy of Sciences of the USA 108: 10871–10877. doi:10.1073/pnas.1100299108.

Schiffers, K., E. C. Bourne, S. Lavergne, W. Thuiller, and J. M. J. Travis. 2013. Limited evolutionary rescue of locally adapted populations facing climate change. Philosophical Transactions of the Royal Society B: Biological Sciences 268:20120083.

Uecker, H., and J. Hermisson. 2011. On the fixation process of a beneficial mutation in a variable environment. Genetics 188: 915–930.

Vander Wal, E., D. Garant, M. Festa-Bianchet, and F. Pelletier. 2013. Evolutionary rescue in vertebrates: evidence, applications and uncertainty. Philosophical Transactions of the Royal Society B: Biological Sciences 368:20120090.

Weissman, D. B., M. M. Desai, D. S. Fisher, and M. W. Feldman. 2009. The rate at which asexual populations cross fitness valleys. Theoretical Population Biology 75:286–300.

Wright, S. 1943. Isolation by distance. Genetics 28:114–138.

Associate Editor: Sean H. Rice
Editor: Troy Day

Spotted owl (*Strix occidentalis*), Hereford, Arizona. Photo © 2012 Jeff Whitlock, Online Zoo, used with permission.

DOI: 10.1086/673914

Appendix A from H. Uecker et al., “Evolutionary Rescue in Structured Populations”

(Am. Nat., vol. 183, no. 1, p. E17)

General Notes on the Analysis

The Wildtype Population Size

We model the dynamics of the wildtype population size deterministically and assume that mutants are rare enough to be ignored. For the submodels considered in this article, it is not necessary to determine the number of wildtype individuals in each single deme. It is sufficient to determine the total number of wildtypes in the unperturbed (or “old”) and the total number of wildtypes in the deteriorated (or “new”) part of the habitat. Let $N_{\mathrm{w}}^{(\mathrm{new})}(t)$ be the total number of wildtype individuals that live in the new habitat at time t before migration and selection. Using equation (3) and ignoring the effects of mutation, for $t + 1 > 0$,

$$E[N_{\mathrm{w}}^{(\mathrm{new})}(t+1)|N_{\mathrm{w}}^{(\mathrm{new})}(t)] = (1-r)\left(1-m+\frac{d_t}{D}m\right)N_{w}^{(\mathrm{new})}(t) + m\frac{d_t}{D}(1-r)(D-d_t)K + K\delta((t+1)\mathrm{mod}\vartheta), \tag{A1}$$

where d_t is the number of demes in the new environmental state at time t and $\delta(0) = 1$ and $\delta(x) = 0$ otherwise. The function δ takes into account that every ϑ generations a new island turns bad, bringing with it approximately K new wildtype individuals. As demes in the old environmental state get filled up to carrying capacity every generation, the number of wildtypes in the old part of the habitat is

$$N_{\mathrm{w}}^{(\mathrm{old})}(t) = K(D-d_t).$$

Establishment Probabilities

As explained in the main text, we restrict our analytical results to scenarios where we deal with only one type of mutant individual. Across the entire life cycle (except for density regulation), each mutant produces a Poisson distributed number of offspring with mean $1 + s_{\mathrm{eff}}(t)$, where the effective growth parameter $s_{\mathrm{eff}}(t)$ depends on the specific scenario. To make use of analytical theory, we approximate the discrete-time branching process by a continuous-time branching process. As selection can be strong in scenarios of population decline and evolutionary rescue, details matter in the transition from discrete to continuous time. For the continuous-time branching process, we use the following per capita birth and death rates:

$$\lambda(t) = 0.5 + 0.5 \cdot \mathrm{sign}[\ln(1+s_{\mathrm{eff}}(t))] \cdot \min[|\ln(1+s_{\mathrm{eff}}(t))|, 1], \tag{A2a}$$

$$\mu(t) = 0.5 - 0.5 \cdot \mathrm{sign}[\ln(1+s_{\mathrm{eff}}(t))] \cdot \min[|\ln(1+s_{\mathrm{eff}}(t))|, 1], \tag{A2b}$$

and define

$$\hat{s}_{\mathrm{eff}}(t) := \mathrm{sign}[\ln(1+s_{\mathrm{eff}}(t))] \cdot \min[|\ln(1+s_{\mathrm{eff}}(t))|, 1]. \tag{A3}$$

With the logarithm, we assure that the average long-term growth $\hat{s}_{\mathrm{eff}}(t) = \lambda(t) - \mu(t)$ is the same as in the discrete-time process. The restriction to values between -1 and 1 is necessary for rates to remain nonnegative. Last, drift has to be scaled appropriately. In the continuous-time process, the sum $\lambda(t) + \mu(t)$ measures the strength of drift. In the diffusion limit, $\lambda(t) + \mu(t)$ must be 1 in order to match continuous-time and discrete-time dynamics. This leaves some freedom for the incorporation of selection (affecting the death rate or the birth rate or both). While this choice is irrelevant in the diffusion limit (and hence for weak selection), it matters if the growth parameter is large as it can be in our model. Comparison to computer simulations shows that the best agreement is obtained if we equally distribute it between the death and the birth rate, as above.

If $\exp[-\int_T^t \hat{s}_{\mathrm{eff}}(\tau)\mathrm{d}\tau] \underset{t\to\infty}{\rightarrow} 0$, the establishment probability of a mutation arising at time T is given by (Uecker and Hermisson 2011)

$$p_{\mathrm{est}}(T) = \frac{2}{1 + \int\limits_T^\infty \exp\left[-\int\limits_T^t \hat{s}_{\mathrm{eff}}(\tau)\mathrm{d}\tau\right]\mathrm{d}t}. \tag{A4}$$

In the following sections, we will encounter effective growth rates that change stepwise in time:

$$s_{\mathrm{eff}}(t) = \begin{cases} s_0 & \text{for } t < 0, \\ s_l & \text{for } t \in [(l-1)\Phi, l\Phi],\ l \in \{1, \ldots, L-1\}, \\ s_L = s & \text{for } t \geq (L-1)\Phi, \end{cases} \tag{A5}$$

where the steps occur at regular intervals Φ, depending on the model. The term $\hat{s}_{\mathrm{eff}}(t)$ is defined accordingly, with

$$\begin{aligned} &\hat{s}_i = \mathrm{sign}[\ln(1 + \mathrm{s_i})] \cdot \min[|\ln(1 + s_i)|, 1] \quad \text{for } i \in 0, \ldots, L, \\ &\hat{s} = \hat{s}_L. \end{aligned} \tag{A6}$$

Assuming that $\hat{s}_k \neq 0$ for all $k \in 0, \ldots, L$, we obtain (see below for a derivation)

$$p_{\mathrm{est}}(T) = \begin{cases} \dfrac{2}{1 + I_0(T)} & \text{for } T < 0, \\ \dfrac{2}{1 + I_l(T)} & \text{for } T \in [(l-1)\Phi, l\Phi[, \\ \dfrac{2\hat{s}_L}{1 + \hat{s}_L} & \text{for } T \geq (L-1)\Phi, \end{cases} \tag{A7}$$

with

$$I_l(T) = \frac{1}{\hat{s}_l} + \exp[\hat{s}_l \Delta T_l] \sum_{k=l}^{L-1} \frac{\hat{s}_k - \hat{s}_{k+1}}{\hat{s}_k \hat{s}_{k+1}} \exp\left[-\sum_{j=l}^{k} \hat{s}_j \Phi\right], \tag{A8}$$

where $\Delta T_l = T - (l-1)\Phi$. For $l > 0$, ΔT_l is the time that has elapsed since the lth island deteriorated. If one or more of the $\hat{s}_k$ are 0, the result is obtained by taking the limit $\hat{s}_k \to 0$.

We turn to the derivation of equation (A7) with equation (A8). We need to evaluate the integral

$$\int\limits_T^\infty \exp\left[-\int\limits_T^t \hat{s}_{\mathrm{eff}}(\tau)\mathrm{d}\tau\right]\mathrm{d}t. \tag{A9}$$

For $T \geq (L-1)\Phi$, the calculation is straightforward. So, we focus on $T < (L-1)\Phi$. We assume throughout the derivation that $\hat{s}_k \neq 0$ for all $k \in 0, \ldots, L$. For $T < l\Phi$, if $l = 0$, or $T \in [(l-1)\Phi, l\Phi[$, if $l \in \{1, \ldots, L-1\}$, we have

$$\begin{aligned} I_l(T) &= \int\limits_T^\infty \exp\left[-\int\limits_T^t \hat{s}_{\mathrm{eff}}(\tau)\mathrm{d}\tau\right]\mathrm{d}t \\ &= \int\limits_T^{l\Phi} \exp\left[-\int\limits_T^t \hat{s}_{\mathrm{eff}}(\tau)\mathrm{d}\tau\right]\mathrm{d}t + \sum_{k=l+1}^{L-1} \int\limits_{(k-1)\Phi}^{k\Phi} \exp\left[-\int\limits_T^t \hat{s}_{\mathrm{eff}}(\tau)\mathrm{d}\tau\right]\mathrm{d}t + \int\limits_{(L-1)\Phi}^{\infty} \exp\left[-\int\limits_T^t \hat{s}_{\mathrm{eff}}(\tau)\mathrm{d}\tau\right]\mathrm{d}t. \end{aligned} \tag{A10}$$

The first integral gives

$$\int\limits_T^{l\Phi} \exp\left[-\int\limits_T^t \hat{s}_{\mathrm{eff}}(\tau)\mathrm{d}\tau\right]\mathrm{d}t = \int\limits_T^{l\Phi} \exp\left[-\int\limits_T^t \hat{s}_l \mathrm{d}\tau\right]\mathrm{d}t = \int\limits_0^{l\Phi - T} \exp[-\hat{s}_l t]\mathrm{d}t = \frac{1 - \exp[-\hat{s}_l(l\Phi - T)]}{\hat{s}_l}. \tag{A11}$$

The components of the sum ($k \in \{l+1, \ldots, L-1\}$) are

$$\begin{aligned}\int_{(k-1)\Phi}^{k\Phi} \exp\left[-\int_T^t \hat{s}_{\text{eff}}(\tau)\mathrm{d}\tau\right]\mathrm{d}t &= \int_{(k-1)\Phi}^{k\Phi} \exp\left[-\int_T^{l\Phi} \hat{s}_{\text{eff}}(\tau)\mathrm{d}\tau - \sum_{j=l+1}^{k-1}\int_{(j-1)\Phi}^{j\Phi} \hat{s}_{\text{eff}}(\tau)\mathrm{d}\tau - \int_{(k-1)\Phi}^{t} \hat{s}_{\text{eff}}(\tau)\mathrm{d}\tau\right]\mathrm{d}t \\ &= \exp\left[-\hat{s}_l(l\Phi - T) - \sum_{j=l+1}^{k-1}\hat{s}_j\Phi\right]\int_0^{\Phi}\exp[-\hat{s}_k t]\mathrm{d}t \\ &= \exp\left[-\hat{s}_l(l\Phi - T) - \sum_{j=l+1}^{k-1}\hat{s}_j\Phi\right]\frac{1-\exp[-\hat{s}_k\Phi]}{\hat{s}_k}.\end{aligned} \tag{A12}$$

For the last integral, we obtain

$$\begin{aligned}\int_{(L-1)\Phi}^{\infty} \exp\left[-\int_T^t \hat{s}_{\text{eff}}(\tau)\mathrm{d}\tau\right]\mathrm{d}t &= \int_{(L-1)\Phi}^{\infty} \exp\left[-\int_T^{l\Phi} \hat{s}_l\mathrm{d}\tau - \sum_{j=l+1}^{L-1}\int_{(j-1)\Phi}^{j\Phi} \hat{s}_j\mathrm{d}\tau - \int_{(L-1)\Phi}^{t} \hat{s}_L\mathrm{d}\tau\right]\mathrm{d}t \\ &= \exp[-\hat{s}_l(l\Phi - T)]\exp\left[-\sum_{j=l+1}^{L-1}\hat{s}_j\Phi\right]\frac{1}{\hat{s}_L}.\end{aligned} \tag{A13}$$

We now use the transformation $T \rightarrow \Delta T_l = T - (l-1)\Phi$. With this, we obtain for $l \in \{0, \ldots, L-1\}$:

$$\begin{aligned}I_l(T) &= \frac{1}{\hat{s}_l} - \frac{1}{\hat{s}_l}\exp[\hat{s}_l\Delta T_l]\exp[-\hat{s}_l\Phi] + \exp[\hat{s}_l\Delta T_l]\sum_{k=l+1}^{L-1}\exp\left[-\sum_{j=l}^{k-1}\hat{s}_j\Phi\right]\frac{1-\exp[-\hat{s}_k\Phi]}{\hat{s}_k} \\ &\quad + \exp[\hat{s}_l\Delta T_l]\exp\left[-\sum_{j=l}^{L-1}\hat{s}_j\Phi\right]\frac{1}{\hat{s}_L} \\ &= \frac{1}{\hat{s}_l} - \frac{1}{\hat{s}_l}\exp[\hat{s}_l\Delta T_l]\exp[-\hat{s}_l\Phi] + \exp[\hat{s}_l\Delta T_l]\sum_{k=l}^{L-2}\exp\left(-\sum_{j=l}^{k}\hat{s}_j\Phi\right)\frac{1-\exp[-\hat{s}_{k+1}\Phi]}{\hat{s}_{k+1}} \\ &\quad + \exp[\hat{s}_l\Delta T_l]\exp\left[-\sum_{j=l}^{L-1}\hat{s}_j\Phi\right]\frac{1}{\hat{s}_L} \\ &= \frac{1}{\hat{s}_l} - \frac{1}{\hat{s}_l}\exp[\hat{s}_l\Delta T_l]\exp[-\hat{s}_l\Phi] + \exp[\hat{s}_l\Delta T_l]\sum_{k=l}^{L-2}\left[\frac{\exp[-\sum_{j=l}^{k}\hat{s}_j\Phi] - \exp[-\sum_{j=l}^{k+1}\hat{s}_j\Phi]}{\hat{s}_{k+1}}\right] \\ &\quad + \exp[\hat{s}_l\Delta T_l]\exp\left[-\sum_{j=l}^{L-1}\hat{s}_j\Phi\right]\frac{1}{\hat{s}_L} \\ &= \frac{1}{\hat{s}_l} + \exp[\hat{s}_l\Delta T_l]\sum_{k=l}^{L-1}\frac{\hat{s}_k - \hat{s}_{k+1}}{\hat{s}_k\hat{s}_{k+1}}\exp\left[-\sum_{j=l}^{k}\hat{s}_j\Phi\right],\end{aligned} \tag{A14}$$

as given by equation (A8).

DOI: 10.1086/673914

Appendix B from H. Uecker et al., "Evolutionary Rescue in Structured Populations"

(Am. Nat., vol. 183, no. 1, p. E17)

Panmictic Populations with $D = 1$ and Scenarios Where Habitat Structure Is Immaterial

We first treat the case $D = 1$ and show at the end of the section that the results coincide with the results for $D > 1$, replacing K with K_{total}, if either $m = 0$ or $\vartheta = 0$.

After the shift in the environment, the wildtype population size decays geometrically:

$$N_{\text{w}}^{(\text{total})}(t) = \begin{cases} K & \text{for } t < 0, \\ K(1-r)^t & \text{for } t \geq 0. \end{cases} \tag{B1}$$

As we model the population size deterministically, the selection coefficient, too, becomes a deterministic function of time:

$$s_{\text{eff}}(t) = \begin{cases} \alpha - 1 = z_0 & \text{for } t < 0, \\ S(N_{\text{w}}^{(\text{total})}(t)) = S(t) & \text{for } t \geq 0. \end{cases} \tag{B2}$$

For the calculation of establishment probabilities, we approximate $s_{\text{eff}}(t)$ in continuous time as a stepped function with each step lasting one generation. We can then use equation (A7) with $\Phi = 1$ to calculate the establishment probability of a mutation, setting $s_{\text{eff}}(t) = s$ (accordingly $\hat{s}_{\text{eff}}(t) = \hat{s}$) when $K(1-r)^t < 1$. Calculations based on a continuous change in $s_{\text{eff}}(t)$ (see app. E) work well for small r but break down as r increases, since for large r the differences between discrete and continuous time dynamics become significant.

Following equation (5), the overall probability of evolutionary rescue reads:

$$P_{\text{rescue}} \approx 1 - \exp\left[-\sum_{t=-\infty}^{-1} uK\alpha p_{\text{est}}(t+1) - \sum_{t=0}^{\infty} uN_{\text{w}}^{(\text{total})}(t)(1+S(t))p_{\text{est}}(t+1)\right], \tag{B3}$$

where for numerical evaluation we again set $N_{\text{w}}^{(\text{total})}(t) = 0$ when $K(1-r)^t < 1$.

For $\beta = 0$, formula (A7) for the establishment probability reduces to

$$p_{\text{est}}(T) = \begin{cases} \dfrac{2}{1 + \exp[-\hat{z}_0 T](1/\hat{s} + 1/\hat{z}_0) - 1/\hat{z}_0} & \text{for } T < 0, \\ \dfrac{2\hat{s}}{1+\hat{s}} & \text{for } T \geq 0, \end{cases} \tag{B4}$$

with

$$\hat{z}_0 = \max[-\ln(1 - z_0), 1]. \tag{B5}$$

We can give an explicit formula for the probability of evolutionary rescue:

$$\begin{aligned} P_{\text{rescue}} &\approx 1 - \exp\left[-\sum_{t=-\infty}^{-1} uK\alpha p_{\text{est}}(t+1) - \sum_{t=0}^{\infty} uK(1-r)^t(1+s)\frac{2\hat{s}}{1+\hat{s}}\right] \\ &\approx 1 - \exp\left[-\int_{t=-\infty}^{0} uK\alpha p_{\text{est}}(t) - \sum_{t=0}^{\infty} uK(1-r)^t(1+s)\frac{2\hat{s}}{1+\hat{s}}\right] \\ &= 1 - \exp\left[-2uK\frac{\alpha}{1-\hat{z}_0}\ln\left(\frac{\hat{s}+\hat{z}_0}{(1+\hat{s})\hat{z}_0}\right) - u\frac{K}{r}(1+s)\frac{2\hat{s}}{1+\hat{s}}\right] \quad \text{for } \hat{z}_0 \neq 1. \end{aligned} \tag{B6}$$

For $\hat{z}_0 = 1$ (i.e., $\alpha \leq \exp[-1]$), we obtain

$$P_{\text{rescue}} \approx 1 - \exp\left[-2\alpha uK \frac{\hat{s}}{1+\hat{s}} - u\frac{K}{r}(1+s)\frac{2\hat{s}}{1+\hat{s}}\right]. \tag{B7}$$

Returning to equation (B6), the respective contributions of mutations from standing genetic variation and de novo mutations are given by

$$P^{\text{sgv}}_{\text{rescue}} \approx 1 - \exp\left[-2uK\frac{\alpha}{1-\hat{z}_0}\ln\left(\frac{\hat{s}+\hat{z}_0}{(1+\hat{s})\hat{z}_0}\right)\right] \approx 1 - \exp\left[-2uK\ln\left(\frac{s+z_0}{z_0}\right)\right] \tag{B8}$$

$$= 1 - \left(\frac{s+z_0}{z_0}\right)^{-2uK}, \tag{B9}$$

$$P^{\text{dnm}}_{\text{rescue}} \approx 1 - \exp\left[-u\frac{K}{r}(1+s)\frac{2\hat{s}}{1+\hat{s}}\right] \approx 1 - \exp\left[-u\frac{K}{r}2s\right], \tag{B10}$$

where the approximation is valid for small s and z_0. For small s and z_0, our results coincide with formulas (3) and (5) in Orr and Unckless (2008; note that the absolute fitness of a mutant is $1+s$ in our model, while it is $1+s_b-r$ in Orr and Unckless 2008; z_0 corresponds to s_{d} in Orr and Unckless 2008) and are similar to formula (8) for $P^{\text{sgv}}_{\text{rescue}}$ in Hermisson and Pennings (2005).

For $\beta > 0$, the formula for the probability of evolutionary rescue does not reduce to a compact expression. Evaluation of the complex formula and comparison to computer simulations shows that it yields highly accurate results. In particular, figure B1 demonstrates that the kinks in the graphs are not an artifact of our analytical approximation, but that the theory accurately reproduces the correct behavior. The existence of kinks can be understood if we consider the generation T_{c} at which for the first time $S(t) > -z$:

$$T_c = \max\left[0, \left\lfloor\frac{1}{r}\ln\left(\frac{s\beta}{s+z}\right)\right\rfloor + 1\right], \tag{B11}$$

where $\lfloor\cdot\rfloor$ denotes the floor function, which maps a real number to the largest previous integer. T_{c} takes only discrete values and therefore jumps as a function of r. As a consequence, $P_{\text{rescue}}(r)$ is not everywhere differentiable.

We pointed out in the main text that the decay of the rescue probability as a function of r is not completely monotonic in figure 5*C*. This can be seen in more detail in figure B2, which zooms in on larger r. A slight local minimum exists at $r = 0.7$. This is precisely the point where $T_c = T_c(r)$ jumps from 1 to 2 giving a little advantage to values of r larger than 0.7.

In the main text, we have discussed scenarios where the probability of evolutionary rescue either decays with r or exhibits a minimum for intermediate values of r. In addition to these patterns, a third pattern is possible: the probability of evolutionary rescue attains a minimum, then a maximum, and decays afterwards (fig. B3). This pattern can arise, because the probability that a mutation generated between time 0 and τ_0, at which $S(t)$ turns from negative to positive, rescues the population has a maximum for intermediate r: For large r, only few mutations are generated; for small r, they have a low establishment probability. If this maximum is pronounced enough, it shapes the overall curve. This is the case if β is extremely large such that the period between 0 and τ_0 is long and z small such that the establishment probability is high. The maximum gets masked if α is very large. The overall effect on the curve is generally weak, however.

It remains to prove that the results for a structured population with $m = 0$ or $\vartheta = 0$ reduce to the unstructured case with $D = 1$ (replacing K by K_{total}). To do so, we consider the general formula equation (5).

We start with $m = 0$: the dynamics in the single demes are then independent from each other. Thus, $N^{(i)\prime}_{\text{w}}(t) = N^{(1)\prime}_{\text{w}}(t -$

$(i-1)\vartheta)$ and $S_i(t) = S_1(t-(i-1)\vartheta)$. The latter implies furthermore $p_{\text{est}}^{(i)}(t) = p_{\text{est}}^{(1)}(t-(i-1)\vartheta)$. Plugging this into the formula for P_{rescue} yields

$$\begin{aligned}
P_{\text{rescue}} &\approx 1-\exp\Bigg(-\sum_{i=1}^{D}\Bigg\{\sum_{t=-\infty}^{(i-1)\vartheta-1} u\alpha K p_{\text{est}}^{(1)}[t-(i-1)\vartheta+1] \\
&\qquad + \sum_{t=(i-1)\vartheta}^{\infty} u[1+S_1(t-(i-1)\vartheta)]N_w^{(1)'}(t-(i-1)\vartheta)p_{\text{est}}^{(1)}(t-(i-1)\vartheta+1)\Bigg\}\Bigg) \\
&= 1-\exp\Bigg\{-\sum_{i=1}^{D}\Bigg[\sum_{t=-\infty}^{-1} u\alpha K p_{\text{est}}^{(1)}(t+1) + \sum_{t=0}^{\infty} u(1+S_1(t))N_{\text{w}}^{(1)'}(t)p_{\text{est}}^{(1)}(t+1)\Bigg]\Bigg\} \\
&= 1-\exp\Bigg[-\sum_{t=-\infty}^{-1} u\alpha DK p_{\text{est}}^{(1)}(t+1) + \sum_{t=0}^{\infty} u(1+S_1(t))DN_w^{(1)'}(t)p_{\text{est}}^{(1)}(t+1)\Bigg].
\end{aligned} \tag{B12}$$

For the wildtype population size, $N_{\text{w}}^{(1)'}(t) = N_{\text{w}}^{(1)}(t) = K(1-r)^t$. Using this, $S_1(t) = \max\{-z, s[1-\beta(1-r)^t]\}$. Consequently, the mutant fitness and along with it the establishment probability p_{est} of a mutation are independent of the carrying capacity. A comparison of equations (B12) and (B3) completes the proof.

We now turn to $\vartheta = 0$. In that case, the wildtype population size decays simultaneously on all demes, and we have $N_{\text{w}}^{(i)'}(t) = N_{\text{w}}^{(i)}(t) = K(1-r)^t$ and consequently $S_i(t) = \max\{-z, s[1-\beta(1-r)^t]\}$ for all $i \in \{1, \dots, D\}$. This implies in particular that the establishment probability is the same in every deme and again the same as in a population of size *KD*. We immediately obtain from equation (5)

$$P_{\text{rescue}} \approx 1-\exp\Bigg[-\sum_{t=-\infty}^{-1} u\alpha DK p_{\text{est}}^{(1)}(t+1) + \sum_{t=0}^{\infty} u(1+S_1(t))DN_{\text{w}}^{(1)'}(t)p_{\text{est}}^{(1)}(t+1)\Bigg], \tag{B13}$$

which again coincides with equation (B3).

The formulas imply that for $m = 0$ or $\vartheta = 0$, P_{rescue} depends only on the product *DK* (i.e., the carrying capacity of an equivalent unstructured population) and not on *D* and *K* separately.

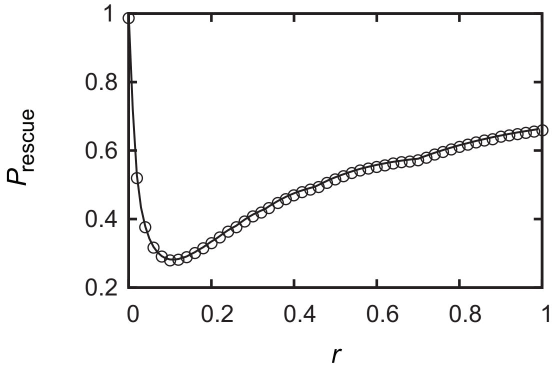

Figure B1: Probability of evolutionary rescue as a function of r with a single deme ($D = 1$). The plot shows a detailed comparison between theory and simulation results. The parameters are chosen as in figure 5*D*. The theoretical curve is based on equations (B3) and (A7). Simulation results are denoted by circles. Each simulation point is the average of 10^6 replicates.

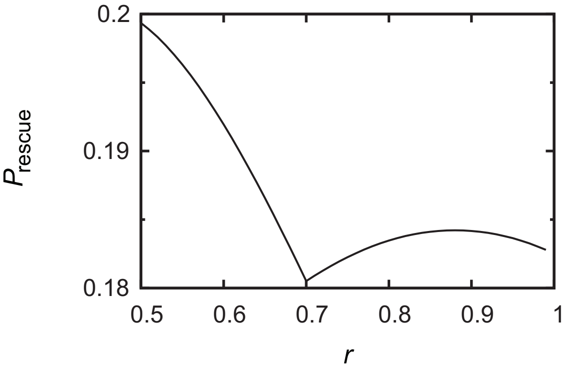

Figure B2: Probability of evolutionary rescue as a function of r with a single deme ($D = 1$). The plot expands figure 5C for large values of r, showing a minimum for $r = 0.7$. The theoretical curve is based on equations (B3) and (A7).

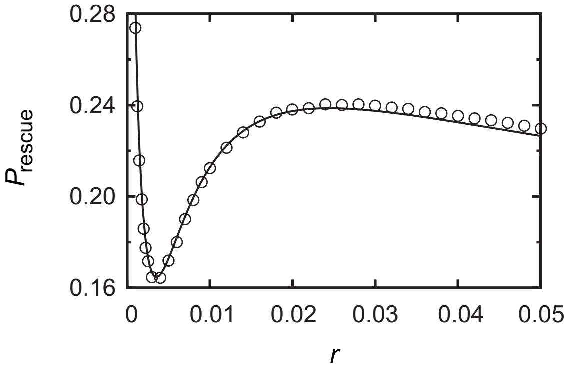

Figure B3: Probability of evolutionary rescue in an unstructured population ($D = 1$). We see that the probability of evolutionary rescue can attain a minimum, followed by a maximum. Parameter values: $\alpha = 0.9$, $z = 0.005$, $s = 0.01$, $\beta = 40$, $K = 10^6$, and $u = 1 \cdot 10^{-6} = 1/K$. The theoretical curve is based on approximation (E1). Circles denote simulation results. Each simulation point is the average of 10^6 replicates.

Appendix C from H. Uecker et al., “Evolutionary Rescue in Structured Populations”

(Am. Nat., vol. 183, no. 1, p. E17)

Levene Model

We now consider $D \geq 1$, but focus on the limiting case $m = 1$. In a first step, we furthermore restrict the analysis to $\beta = 0$. As derived in the main text equation (10), the effective growth parameter of a mutant in the metapopulation in a period with d deteriorated demes is given by

$$s_{\text{eff}}(t) = \frac{d}{D}(1+s) + \frac{D-d}{D}\alpha\frac{K}{N_{\text{w}}^{(\text{total})}(t)/D} - 1. \tag{C1}$$

The total number of wildtypes $N_w^{(\text{total})}(t) = N_w^{(\text{new})}(t) + K(D-d)$ is a function of time. However, after another deme has turned bad, it will quickly decay to its new steady state (until the next deme deteriorates). For sufficiently large values of ϑ, we can therefore approximate s_d as constant by taking the equilibrium value $\hat{N}_{\text{w},d}^{(\text{total})}$ of the total wildtype population size in the period within which d demes are perturbed. The stationary value of the total wildtype population size $\hat{N}_{\text{w},d}^{(\text{new})}$ in the bad environment is found by solving the equation

$$0 = (1-r)\frac{d}{D}[\hat{N}_{\text{w},d}^{(\text{new})} + (D-d)K] - \hat{N}_{\text{w},d}^{(\text{new})}. \tag{C2}$$

This yields

$$\hat{N}_{\text{w},d}^{(\text{new})} = \frac{(1-r)(d/D)(D-d)K}{1-(1-r)(d/D)}. \tag{C3}$$

And we obtain

$$\hat{N}_{\text{w},d}^{(\text{total})} = \hat{N}_{\text{w},d}^{(\text{new})} + K(D-d). \tag{C4}$$

Inserting equation (C4) into equation (C1) yields s_d as in equation (11). With equation (11), we can now use equation (A7) with $\Phi = \vartheta$ to determine the establishment probability of a new mutant.

The probability of evolutionary rescue in a Levene model can be approximated by (cf. eq. [5]):

$$\begin{aligned} P_{\text{rescue}} \approx 1 - \exp&\left[-u\sum_{t=-\infty}^{-1} KD\alpha p_{\text{est}}(t+1) - u\sum_{t=0}^{(D-1)\vartheta-1} N_{\text{w}}^{(\text{total})}(t)(1+s_{\text{eff}}(t))p_{\text{est}}(t+1)\right] \\ \times\ \exp&\left[-u\frac{N_{\text{w}}^{(\text{total})}((D-1)\vartheta)}{r}(1+s)\frac{2\hat{s}}{1+\hat{s}}\right], \end{aligned} \tag{C5}$$

where $N_{\text{w}}^{(\text{total})}((D-1)\vartheta)$ is the wildtype population size immediately after the last deme has deteriorated. The first sum captures the contributions of mutations that arose before time $t = 0$. The second sum takes all mutations into account that are generated as the degradation proceeds across the demes. From time $(D-1)\vartheta$ on, the population size decays geometrically, which leads to the last term in equation (C5).

We now allow for density-dependent mutant fitness ($\beta \geq 0$). We assume that the periods of environmental stasis are very long. As discussed in the main text, it is in that case sufficient to consider the two phases where either one or no deme is unperturbed. We can approximate $S(t)$ during the phase where all but one deme have deteriorated by its steady state value:

$$\bar{S} = \max\left[-z, s\left(1-\beta\frac{\hat{N}_{\text{w},D-1}^{(\text{total})}/D}{K}\right)\right] \tag{C6}$$

with

$$\hat{N}_{\text{w},D-1}^{(\text{total})} = \frac{KD}{(D-1)r+1}. \tag{C7}$$

Analogously to equation (11), we then obtain equation (13) for the effective growth parameter during that period. In the main text, we pointed out that the situation corresponds to an unstructured population with a single environmental change. We can thus use equation (B3) with the following substitutions to calculate the probability of evolutionary rescue:

$$\begin{aligned} &K \text{ is substituted by } \hat{N}^{(\text{total})}_{\text{w},D-1}, \\ &\alpha \text{ is substituted by } 1+s_{D-1}, \\ &\beta \text{ is substituted by } \frac{\beta\hat{N}^{(\text{total})}_{\text{w},D-1}}{DK}. \end{aligned} \tag{C8}$$

We close the section with a comparison of $P_{\text{rescue}}(\vartheta \to 0)$ and $P_{\text{rescue}}(\vartheta \to \infty)$ if $\beta = 0$. In order to do so, we approximate the amount of genetic variation which is present at the time when the last deme deteriorates by its expected value. We only consider the case $s_{D-1} < 0$. For $\vartheta = 0$ and $\vartheta \to \infty$, we obtain

$$\text{E}[\text{sgv}_0] = uDK\frac{\alpha}{1-\alpha} \text{ and } E[\text{sgv}_\infty] = u\hat{N}^{(\text{total})}_{\text{w},D-1}\frac{1+s_{D-1}}{-s_{D-1}}, \tag{C9}$$

respectively. Analogously, we introduce

$$\text{E}[\text{dnm}_0] = \frac{uKD(1+s)}{r} \text{ and } \text{E}[\text{dnm}_\infty] = \frac{u\hat{N}^{(\text{total})}_{w,D-1}(1+s)}{r} \tag{C10}$$

for the expected number of de novo mutations that are generated after deterioration of the last deme in both scenarios. With this notation,

$$P_{\text{rescue}}(\vartheta = 0) \approx 1 - \exp\left[-(E[\text{sgv}_0] + E[\text{dnm}_0])\frac{2\hat{s}}{1+\hat{s}}\right], \tag{C11a}$$

$$P_{\text{rescue}}(\vartheta \to \infty) \approx 1 - \exp\left[-(E[\text{sgv}_\infty] + E[\text{dnm}_\infty])\frac{2\hat{s}}{1+\hat{s}}\right]. \tag{C11b}$$

We now compare the exponents:

$$\begin{aligned} \frac{\text{E}[\text{sgv}_\infty] + \text{E}[\text{dnm}_\infty]}{\text{E}[\text{sgv}_0] + \text{E}[\text{dnm}_0]} &= \frac{\hat{N}^{(\text{total})}_{\text{w},D-1}}{DK} \cdot \frac{(1+s_{D-1})/(-s_{D-1}) + 1/r}{[\alpha/(1-\alpha)] + 1/r} \\ &= \frac{\hat{N}^{(\text{total})}_{\text{w},D-1}}{DK} \cdot \frac{1-\alpha}{-s_{D-1}} \cdot \frac{r - s_{D-1}(1-r)}{1-\alpha+\alpha r} \begin{pmatrix} \text{Note: This expression gets minimal when} - s_{D-1} \text{ gets maximal.} \\ -s_{D-1} \text{ as a function of } s \text{ gets maximal for } s \to 0. \end{pmatrix} \\ &= \frac{1}{1+r(D-1)} \cdot \frac{1}{1+(D-1)r - [(s+r)/(1-\alpha)](D-1)} \cdot \frac{[r+s+(1-\alpha)(1-r)][1+(D-1)r] - sD}{1-\alpha+\alpha r} \\ &= \frac{1}{1+(D-1)r - [(s+r)/(1-\alpha)](D-1)} \cdot \frac{1-\alpha+\alpha r + s - sD/[1+r(D-1)]}{1-\alpha+\alpha r} \overset{s\to 0}{\geq} \frac{1}{1-[\alpha/(1-\alpha)](D-1)r} \geq 1. \end{aligned} \tag{C12}$$

This means that for $\beta = 0$, $P_{\text{rescue}}(\vartheta \to \infty) \geq P_{\text{rescue}}(\vartheta = 0)$. For $\alpha = 0$, we obtain equality. The approximation thus suggests that for arbitrary values of r, the probability of evolutionary rescue is approximately the same for a very fast and a very slowly progressing change if $\alpha = 0$ and s small, which is confirmed by computer simulations (not shown). This implies in particular, that for $\alpha = 0$, s small, and ϑ large, $P_{\text{rescue}}(m = 0) \approx P_{\text{rescue}}(m = 1)$, as can be seen in figure 10*A*.

Appendix D from H. Uecker et al., “Evolutionary Rescue in Structured Populations”

(Am. Nat., vol. 183, no. 1, p. E17)

Island Model without Standing Genetic Variation

We here restrict ourselves to $\alpha = 0$ (i.e., mutants are lethal in the old environment) and $\beta = 0$ (no additional density dependence beyond the hard carrying capacity). In the main text equation (14), we derived the following effective growth parameter of a mutant:

$$s_{\mathrm{eff}}(t) = \begin{cases} (1+s)(1-m) + (1+s)m\dfrac{d}{D} - 1 & \text{for } t \in [(d-1)\vartheta, d\vartheta[,\ d \in \{1, \dots, D-1\}, \\ s & \text{for } t \geq (D-1)\vartheta. \end{cases} \tag{D1}$$

Using this, we can calculate the establishment probability with equation (A7), setting again $\Phi = \vartheta$. For the total rescue probability, we obtain (cf. eq. [5]):

$$\begin{aligned} P_{\mathrm{rescue}} \approx 1 - \exp&\left[-u \sum_{t=0}^{(D-1)\vartheta-1} (1+s)\left(1 - m + \frac{d_t}{D}m\right) N_{\mathrm{w}}^{(\mathrm{new})}(t) p_{\mathrm{est}}(t+1)\right] \\ \times \exp&\left[-u \sum_{t=0}^{(D-1)\vartheta-1} (1+s)mK(D-d_t)\frac{d_t}{D} p_{\mathrm{est}}(t+1)\right] \times \exp\left[-u(1+s)\frac{N_{\mathrm{w}}^{(\mathrm{total})}((D-1)\vartheta)}{r}\frac{2\hat{s}}{1+\hat{s}}\right], \end{aligned} \tag{D2}$$

where $N_{\mathrm{w}}^{(\mathrm{total})}((D-1)\vartheta)$ is the wildtype population size immediately after the last deme has deteriorated. The first term takes mutants into account that originate in the new part of the habitat. The second term considers mutant offspring of individuals from old demes that migrate to the new part where they can survive. The last term is the same as in the Levene model. As $\alpha = 0$, there are no mutants in the population before time $t = 0$.

In the main text, we gave an approximation for the probability of evolutionary rescue for $D = 2$ (see eq. [17]), which generalizes to more than two islands in a straightforward way. The stationary value $\hat{N}_{w,d}^{(\mathrm{new})}$ of wildtype individuals in the perturbed part of the habitat in a period with d deteriorated demes is obtained as the solution of

$$0 = (1-r)\left(1 - \frac{D-d}{D}m\right)\hat{N}_{w,d}^{(\mathrm{new})} + m\frac{d}{D}(1-r)(D-d)K - \hat{N}_{w,d}^{(\mathrm{new})}. \tag{D3}$$

This yields

$$\hat{N}_{\mathrm{w},d}^{(\mathrm{new})} = \frac{d(D-d)Km(1-r)}{(D-d)m(1-r) + Dr}, \tag{D4}$$

and with

$$2s_{\mathrm{eff}}(t) \approx 2\left(s - m + m\frac{d_t}{D}\right), \tag{D5}$$

we obtain

$$P_{\mathrm{rescue}} \approx 1 - \exp\left\{-u\vartheta \sum_{d=1}^{D-1} 2\max\left[\left(s - m + m\frac{d}{D}\right), 0\right] \frac{d(D-d)Km(1-r)}{(D-d)m(1-r) + Dr} - u\frac{DK}{r}2s\right\}. \tag{D6}$$

Figure D1 shows a comparison between the exact formula (D2) and the approximation. The approximation captures the behavior for small m very well. In particular, it reproduces the maximum in the probability of evolutionary rescue. As m increases, the approximation becomes worse.

If the number of demes D is large and $r \gg m$, we can approximate equation (D6) with

$$\begin{aligned} P_{\text{rescue}} &\approx 1 - \exp\left\{-u\vartheta \int_0^D 2\max\left[\left(s - m + m\frac{d}{D}\right), 0\right]\frac{d(D-d)Km(1-r)}{Dr}\,\mathrm{d}d - u\frac{DK}{r}2s\right\}, \\ &= 1 - \exp\left\{-u\vartheta\frac{1}{3}D^2Km\frac{1-r}{r}\max\left[\left(s - \frac{1}{2}m\right), 0\right] - u\frac{DK}{r}2s\right\}. \end{aligned} \tag{D7}$$

From equations (17) and (D7), we find that the maximum is at $m \approx s$.

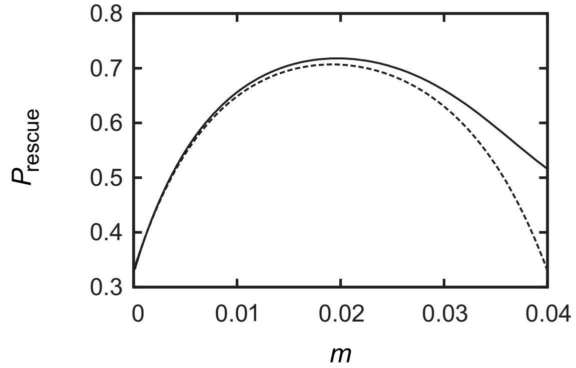

Figure D1: Evolutionary rescue in a two-island model. The plot compares the exact result (D2) (solid line) with approximation (17) (dashed line). The parameter values are the same as in figure 10.

© 2013 by The University of Chicago. All rights reserved. DOI: 10.1086/673914

Appendix E from H. Uecker et al., “Evolutionary Rescue in Structured Populations”

(Am. Nat., vol. 183, no. 1, p. E17)

Further Approximations

Unstructured Population, Small *r* and *s*

The calculation of P_{rescue} based on equations (B3) and (A7) gets computationally expensive for small r. An approximation for small r can be obtained when we assume that the selection $s_{\text{eff}}(t)$ changes continuously in time and additionally replace sums by integrals in equation (B3). We furthermore approximate $\ln(1+s[1-\beta N_{\text{w}}(t)/K]) \approx s(1-\beta N_{\text{w}}(t)/K)$ and $-\ln(1-r) \approx r$. For $\hat{z} \neq 0$, the establishment probability of a mutation then is

$$p_{\text{est}}(T) = \begin{cases} \dfrac{2}{1+\left[-(1/\hat{z}_0)+\exp(-\hat{z}_0T)\left((1/\hat{z}_0)-(1/\hat{z})+(1/\hat{z})\exp(\hat{z}T_c)+\exp(\hat{z}T_c)\int_0^\infty \exp\{-st+(s\beta/r)\exp(rT_c)[1-\exp(rt)]\}\mathrm{d}t\right)\right]}, & T \leq 0, \\ \dfrac{2}{1+\left[-(1/\hat{z})+\exp[-\hat{z}(T-T_c)]\left((1/\hat{z})+\int_0^\infty \exp\{-st-(s\beta/r)\exp(rT_c)[1-\exp(rt)]\}\mathrm{d}t\right)\right]}, & 0 \leq T < T_c, \\ \dfrac{2}{1+\int_0^\infty \exp\{-st-(s\beta/r)\exp(rT)[1-\exp(rt)]\}\mathrm{d}t}, & T \geq T_c, \end{cases} \tag{E1}$$

with

$$\hat{z}_0 = \max[-\ln(\alpha), 1], \tag{E2}$$

$$\hat{z} = \max[-\ln(1-z), 1]. \tag{E3}$$

To obtain the result for $\hat{z} = 0$, use $\lim_{\hat{z}\to 0}[\exp(\hat{z}T)-1]/\hat{z} = T$.

Infinitely Many Islands

We here give an approximation for the probability of evolutionary rescue, when the number D of demes is large. We take the limits $D \to \infty$, $\vartheta \to 0$, $K \to 0$ with $D\vartheta = \Theta$, and $DK = K_{\text{total}}$ considered constant. We treat time as continuous and use the correspondence $d/D \triangleq t/\Theta$.

We obtain the following differential equation for the number of wildtype individuals in the new part of the habitat (cf. the difference equation [A1]):

$$\dot{N}_{\text{w}}^{(\text{new})}(t) = -rN_{\text{w}}^{(\text{new})} + (1-r)m\left(\frac{t}{\Theta}-1\right)N_{\text{w}}^{(\text{new})} + m\frac{t}{\Theta}(1-r)\left(1-\frac{t}{\Theta}\right)K_{\text{total}} + \frac{K_{\text{total}}}{\Theta}. \tag{E4}$$

We now turn to the establishment probability of a new mutant. Both in the Levene and in the island model, s_d takes the form $s_d = \sigma_0 + \sigma_1 d/D$, $d \in \{1, \dots, D-1\}$. We can approximate this as $s_{\text{eff}}(t) = \sigma_0 + \tilde{\sigma}_1 t$ with $\tilde{\sigma}_1 = \sigma_1/\Theta$ for $0 \leq t < \Theta$. We state the establishment probability for

$$\hat{s}_{\text{eff}}(t) = \begin{cases} \hat{s}_0 & \text{for } t < T_c^{(1)}, \\ \ln(1+\tilde{\sigma}_0+\tilde{\sigma}_1 t) & \text{for } T_c^{(1)} \leq t < T_c^{(2)}, \\ 1 & \text{for } T_c^{(2)} \leq t < \Theta, \\ \hat{s} & \text{for } t \geq \Theta, \end{cases} \tag{E5}$$

with

$$T_c^{(1)} = \min\left\{0, \frac{1}{\tilde{\sigma}_1}[\exp(-1)-1-\tilde{\sigma}_0]\right\},$$

$$T_c^{(2)} = \min\left\{\Theta, \frac{1}{\tilde{\sigma}_1}[\exp(1)-1-\tilde{\sigma}_0]\right\}. \tag{E6}$$

We obtain

$$p_{\mathrm{est}}(T) = \begin{cases} \dfrac{2}{1+\tilde{I}_0(T)} & \text{for } T < T_c^{(1)}, \\[2ex] \dfrac{2}{1+\tilde{I}_1(T)} & \text{for } T_c^{(1)} \le T < T_c^{(2)}, \\[2ex] \dfrac{2}{1+\tilde{I}_2(T)} & \text{for } T_c^{(2)} \le T < \Theta, \\[2ex] \dfrac{2\hat{s}}{1+\hat{s}} & \text{for } T \ge \Theta, \end{cases} \tag{E7}$$

with

$$\begin{aligned} \tilde{I}_0(T) &= \frac{1}{\hat{s}_0} + \exp\left[\hat{s}_0(T - T_c)\right]\left[-\frac{1}{\hat{s}_0} + \exp\left(f(T_c^{(1)})\right)\int_{T_c^{(1)}}^{T_c^{(2)}} \exp\left(f(t)\right)\mathrm{d}t \right. \\ &\quad \left. + \frac{1}{\hat{s}}\exp\left(-f(T_c^{(2)}) + f(T_c^{(1)}) - \Theta + T_c^{(2)}\right)\right], \\ \tilde{I}_1(T) &= \exp\left(f(T)\right)\int_{T}^{T_c^{(2)}} \exp\left(f(t)\right)\mathrm{d}t \\ &\quad + \exp\left(-f(T_c^{(2)}) + f(T)\right)\left[1 - \exp\left(\Theta - T_c^{(2)}\right)\right] + \exp\left(-f(T_c^{(2)}) + f(T) - \Theta + T_c^{(2)}\right)\frac{1}{\hat{s}}, \\ \tilde{I}_2(T) &= \left(\frac{1}{\hat{s}} - 1\right)\exp\left[-(\Theta - T)\right] + 1, \end{aligned} \tag{E8}$$

and

$$f(t) = -t + \frac{(1+\tilde{\sigma}_0+\tilde{\sigma}_1 t)\ln(1+\tilde{\sigma}_0+\tilde{\sigma}_1 t)}{\tilde{\sigma}_1}. \tag{E9}$$

In the Levene model, we find

$$\sigma_0 = \alpha - 1, \tag{E10}$$

$$\tilde{\sigma}_1 = (1 - \alpha + s + \alpha r)\frac{1}{\Theta}. \tag{E11}$$

Analogously to equation (C5), we obtain

$$\begin{aligned} P_{\mathrm{rescue}} \approx 1 - \exp&\left\{-u\int_{-\infty}^{0} \alpha K_{\mathrm{total}}\, p_{\mathrm{est}}(t+1)\mathrm{d}t - u\int_{0}^{\Theta}(1 + s_{\mathrm{eff}}(t))\left[N_{\mathrm{w}}^{(\mathrm{new})} + K_{\mathrm{total}}\left(1 - \frac{t}{\Theta}\right)\right]p_{\mathrm{est}}(t+1)\mathrm{d}t\right\} \\ &\times \exp\left[-u\frac{N_{\mathrm{w}}^{(\mathrm{new})}(\Theta)}{r}(1+s)\frac{2\hat{s}}{1+\hat{s}}\right]. \end{aligned} \tag{E12}$$

Finally, in the island model with $\alpha = \beta = 0$, we have

$$\sigma_0 = (1+s)(1-m) - 1, \tag{E13}$$

$$\tilde{\sigma}_1 = (1+s)m\frac{1}{\Theta}. \tag{E14}$$

The total probability of evolutionary rescue becomes

$$
\begin{aligned}
P_{\mathrm{rescue}} \approx 1 - \exp\left\{-u\int_0^{\Theta}(1+s)\left[N_w^{(\mathrm{new})}(t)\left(1-m+m\frac{t}{\Theta}\right)+m\left(1-\frac{t}{\Theta}K_{\mathrm{total}}\frac{t}{\Theta}\right)\right]p_{\mathrm{est}}(t+1)\mathrm{d}t\right\} \\
\times\ \exp\left[-u\frac{N_{\mathrm{w}}^{\mathrm{new}}(\Theta)}{r}(1+s)\frac{2\hat{s}}{1+\hat{s}}\right].
\end{aligned}
\tag{E15}
$$