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Increasing mutation rate of local adaptation during range expansion.

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Keywords: dispersal evolution, evolution of mutation rates, range expansion, local adaptation, spatial sorting, priority effect

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Abstract

Increasing dispersal under range expansion increases invasion speed, which implies that a species needs to adapt more rapidly to newly experienced local conditions. However, due to iterated founder effects, local genetic diversity under range expansion is low. Evolvability (mutation rate of local adaptation) has been reported to possibly be an adaptive trait itself. Thus, we expect that increased dispersal during range expansion may raise the mutation rate of local adaptation, thus increasing the survival of expanding populations. We have investigated this hypothesis with an individual-based metapopulation model. Our results show that mutation rate increases with increased dispersal rate under spatial variation experienced during range expansion, allowing a larger species range. In addition, we show that different spatial phenomena associated with range expansion, in this case spatial sorting / kin selection and priority effects, can enforce each other. These results contribute new insights into the particular genetic properties of spatial disequilibrium.

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Introduction

Many species are currently expanding their ranges, both polewards and uphill, as a response to increasing global temperatures under climate change (Parmesan and Yohe 2003; Chen et al. 2011). Range expansions are known to have profound effects on the genetic composition of populations, regarding both neutral and adaptive genetic diversity (Hewitt 1996; Thomas et al. 2001; Travis and Dytham 2002; Edmonds et al. 2004; Klopfstein et al. 2006; Phillips et al. 2006; Travis et al. 2007; Excoffier et al. 2009; Cobben et al. 2011; Cobben et al. 2012b). Traits that are to increase species' dispersal capabilities and population growth rates are selected for under range expansions due to spatial sorting (Parmesan 2006; Burton et al. 2010; Phillips et al. 2010b; Hill et al. 2011; Shine et al. 2011) and kin competition (Kubisch et al. 2013b). This may lead to the evolutionary increase of dispersal rate (Thomas et al. 2001; Travis and Dytham 2002; Kubisch et al. 2010; Henry et al. 2014), dispersal distance (Phillips et al. 2006) and effective fertility (Moreau et al. 2011) at the expanding front of the species' range. An increasing dispersal rate under range expansion will increase the invasion speed (Travis and Dytham 2002; Phillips et al. 2006) and has the implication that a species needs to be able to adapt to newly experienced local conditions more rapidly than before. In contrast, the depletion of genetic diversity at the expanding range border could limit the invasion speed if this delayed population establishment due to lack of local adaptation.

Evolvability, i.e. the set of mechanisms that facilitate evolution, can be adaptive itself under conditions that require an increased rate of adaptation, e.g. under increasing environmental stochasticity and stress (Ishii et al. 1989; Wagner and Altenberg 1996; Kirschner and Gerhart 1998; Earl and Deem 2004; Kashtan et al. 2007; Lee and Gelembiuk 2008; Brookfield 2009; Whitacre and Bender 2010). One example is the evolution of mutation rates, which can lead to increased levels of genetic diversity and thus increased evolvability (Kimura 1967; Leigh Jr 1970; Leigh Jr 1973; Ishii et al.

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1989; Sniegowski et al. 1997; Taddei et al. 1997; Metzgar and Wills 2000; Bedau and Packard 2003; Denamur and Matic 2006). In such a system a mutator gene codes for the rate of mutation at a second gene under selection. In this latter gene, the number of mutations can thus increase, generating more genetic variation for selection to act on, as such enabling adaptation to changing selection pressures (Kimura 1967; Leigh Jr 1970; Leigh Jr 1973; Taddei et al. 1997; Metzgar and Wills 2000; Sniegowski et al. 2000; Bedau and Packard 2003). During the colonization of a spatially heterogeneous environment, the mutation rate can therefore be expected to increase, by generating more genetic diversity and thereby enabling the local adaptation of recently established populations. In addition, in such a scenario of range expansion, iterated founder effects (Cobben et al. 2011) and increasing relatedness between individuals (Kubisch et al. 2013b) reduce local genetic diversity at the expansion front, while dispersal rates and invasion speed increase (Phillips et al. 2006; Phillips et al. 2010a). These combined conditions may lead to a further increased selection for high mutation rates. With the establishment of a stable range border, after range expansion, the selection pressures change and a return to lower mutation rates is expected.

In this study, we investigate 1) whether there is co-evolution between dispersal rates and mutation rates during range expansion, 2) how this affects the genetic diversity across the range, and 3) the evolutionary dynamics under spatial equilibrium after range border establishment. For this, we have simulated a range establishment of a sexual, diploid species on a spatial gradient in altitude, involving both a temporal gradient requiring local adaptation, and a gradient in habitat fragmentation, i.e. dispersal mortality, to secure the establishment of a stable range border.

The Model

We are using a spatially explicit individual-based metapopulation model of a sexually reproducing species with discrete generations distributed along an elevational gradient.

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The basic model has already been successfully applied in theoretical studies, mainly focused on dispersal evolution (Travis et al. 1999; Kubisch et al. 2010; Fronhofer et al. 2011; Kubisch et al. 2013a; Kubisch et al. 2013b) and was parameterized using empirical data (Poethke et al. 1996; Amler et al. 1999). For the current study we allow the mutation rate of local adaptation to be adaptive, and investigate its interplay with the evolution of dispersal rate during and after the range establishment on an elevational gradient.

Landscape

The simulated landscape consists of 250 columns (x-dimension) of 20 patches each (y-dimension). We assume wrapped borders, building a torus. Hence, if an individual leaves the world in y-direction during dispersal, it will reenter the simulated world on the opposite side. However, if it leaves the world in the x-direction, it is lost from the simulation. While most studies investigating range expansions across an environmental gradient, for the sake of simplicity focus on a single parameter changing along space, a typical elevational gradient is known to involve both a decreasing temperature and increasing habitat fragmentation (Körner and Paulsen 2004). Thus, in our model firstly every column of patches (x-position) is characterized by its specific abiotic habitat conditions τ_x. Throughout this manuscript, τ_x will be interpreted as 'mean temperature'. This mean local temperature is used for the determination of local adaptation of individuals. To simulate a large-scale habitat gradient, x changes linearly from $\tau_{x=1} = 0$ to $\tau_{x=250} = 0$ along the x-dimension, i.e. by $\Delta_{\tau,x} = 0.04$ when moving one step in x-direction. Secondly, to account for habitat fragmentation in terms of patch isolation, each x-position is characterized by a certain degree of dispersal mortality. The probability to die upon emigration μ changes linearly from $\mu_{x=1} = 0$ to $\mu_{x=250} = 1$ along the x-dimension.

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Population dynamics and survival of offspring

Local populations are composed of individuals each of which is characterized by several traits: 1) their sex, 2) two alleles at the dispersal locus l_d coding for the individual's dispersal probability, 3) two alleles at the adaptation locus l_a coding for the individual's optimal temperature τ_{opt}, i.e. the temperature under which it survives best (see below for details), 4) another two alleles at the mutator locus l_m coding for the mutation probability of the alleles at locus l_a, so the mutation rate at the adaptation locus (see below under Genetics), and 5) a diploid neutral locus l_n, also mutating at the l_m mutation rate, for the sake of comparing with genetic diversity at the l_a locus.

Local population dynamics follow the time-discrete BevertonHolt model (Beverton and Holt 1957). Each individual female in patch x, y is therefore assigned a random male from the same habitat patch (males can potentially mate several times) and gives birth to a number of offspring drawn from a Poisson distribution with mean population growth rate λ. The offspring's sex is chosen at random. Density-dependent survival probability s_1 of offspring due to competition is calculated as:

$$s_1 = \frac{1}{1 + \frac{\lambda - 1}{K} \cdot Nx, y, t} \tag{1}$$

with K the carrying capacity and $N_{x,y,t}$ the number of individuals in patch x, y at time t. Finally, the surviving offspring experience a further density-independent mortality risk ($1s_2$) that depends on their local adaptation, so the matching of their genetically determined optimal temperature (τ_{opt}) to the temperature conditions in patch x, y (τ_x) according to the following equation:

$$s_2 = exp\left[-\frac{1}{2} \cdot \left(\frac{\tau_{opt} - \tau x}{\eta}\right)^2\right] \tag{2}$$

where describes the niche width or 'tolerance' of the species. We performed

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simulations for the species with a niche width of $\eta = 0.5$, equivalent to a decrease of survival probability of about 0.02 when dispersing one patch away from the optimal habitat. In this approach we assume that density-dependent mortality $(1 - s_1)$ acts before mortality due to maladaptation to local conditions $(1 - s_2)$. In addition, each population has an extinction probability ϵ per generation. Individual surviving offspring disperse with probability d that is determined by their dispersal locus (see below). If an individual disperses it dies with probability μ, which is calculated as the arithmetic mean of the dispersal mortality values of its natal and its target patch, respectively. This mortality accounts for various costs that may be associated with dispersal in real populations, like fertility reduction or predation risk (Bonte et al. 2012). We assume nearest-neighbor dispersal, i.e. successful dispersers settle randomly in one of the eight surrounding habitat patches.

Genetics

As mentioned above, each individual carries three unlinked, diploid loci coding for its dispersal probability, its optimum temperature (and thus its adaptation), and the mutation rate of the optimum temperature alleles, respectively, and an additional neutral locus. The phenotype of an individual is determined by calculating the arithmetic means of the two corresponding alleles, with no dominance effect involved. Hence, dispersal probability d is given by $d = \frac{l_{d,1}+l_{d,2}}{2}$ (with $l_{d,1}$ and $l_{d,2}$ giving the 2 'values' of the two dispersal alleles), optimal temperature τ_{opt} is calculated as $\tau_{opt} = \frac{l_{a,1}+l_{a,2}}{2}$ (with $l_{a,1}$ and $l_{a,2}$ giving the 'values' of the two adaptation alleles), and similarly the mutation rate of optimal temperature $m(\tau_{opt}) = 10^{-exp}$ (with $exp = \frac{l_{e,1}+l_{e,2}}{2}$, and $l_{e,1}$ and $l_{e,2}$ the 'values' of the two mutator alleles). At each of the four loci, newborn individuals inherit alleles, randomly chosen, from the corresponding loci of each of their parents. During transition from one generation to the next an allele may mutate. Alleles at the dispersal locus and the mutator locus mutate with a probability of

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$m = 10^{-4}$. Alleles at the adaptation and the neutral loci however, mutate with the probability $m(\tau_{opt})$ given by the value based on the two alleles at the mutator locus l_m as elaborated above. Mutations are simulated by adding a random number drawn from a Gaussian distribution with mean 0 and standard deviation 0.2 for the dispersal locus, standard deviation 0.5 for the adaptation and the neutral loci and standard deviation 1 for the mutator locus, to the value calculated from the mean of the inherited alleles.

Simulation Experiments

Simulations were initialized with a 'native area' (from $x = 1$ to $x = 50$) from where the species was able to colonize the world, while the rest of the world was initially kept free of individuals. Upon initialization, dispersal alleles ($l_{d,i}$) were randomly drawn from the interval $0 < l_{d,i} < 1$, and mutator alleles $l_{m,i}$ were set to 4, which set the initial mutation rate of the adaptation alleles and the neutral alleles to 10^{-4}. Populations were initialized with K locally optimally adapted individuals, i.e. adaptation alleles were initialized according to the local temperature τ_x. However, to account for some standing genetic variation we also added to every respective optimal temperature allele a Gaussian random number with mean zero and standard deviation 0.5. At the neutral locus, these individuals were initialized with random allele values with a mean of 0.5 and standard deviation 0.5. We performed 100 replicate simulations, which all covered a time span of $60,000$ generations. To establish equilibrium conditions, individuals were confined to their native area during the first $1,000$ generations. After this burn-in period, the species was allowed to pass the $x = 50$ border. Table 1 summarizes all relevant model parameters, their meanings and the standard values used for the simulations. Serving as controls, the simulations were repeated with 100 replicates for fixed values of dispersal rate, $d = 0.05$, $d = 0.1$ and $d = 0.2$, while allowing the mutator locus to evolve, and we performed final simulations with fixed values of the mutation rate of 10^{-4} and 10^{-5}, combined with evolving dispersal rate.

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Analysis

The individual phenotypes for the three traits were documented in time and space throughout the simulations. Genetic diversity was calculated as the variance in allelic values at the adaptation locus and the neutral locus, per x-position.

Table 1: Used parameter values.

parameter/variable	**value**	**meaning**
individual variables:		
$l_{d,1}$,$l_{d,2}$	evolving	alleles coding for the dispersal propensity
$l_{a,1}$,$l_{a,2}$	evolving	alleles coding for the optimal temperature
$l_{m,1}$,$l_{m,2}$	evolving	alleles coding for the mutation rate of the optimal temperature
$l_{n,1}$,$l_{n,2}$	evolving	neutral alleles as control
simulation parameters:		
K	100	carrying capacity
λ	2	per capita growth rate
ϵ	0.05	local extinction probability
m	10^{-4}	mutation rate for dispersal and evolvability alleles
μ_x	[0..1]	local dispersal mortality
τ_x	[0..10]	local temperature
η	0.5	niche width
x_{max}	250	extent of simulated landscape in x-direction
y_{max}		extent of simulated landscape in y-direction

Results

After the burn-in phase, the dispersal propensity d in the core area, so under low dispersal mortality, was on average approximately 0.42. Maximum population density was around 0.85 here, accompanied by a high level of local adaptation s_2 (i.e. adaptation-dependent offspring survival probability) close to one (not shown), while the mutator values $m(\tau_{opt})$ remained low, between 10^{-4} and 10^{-5} (Figure 1).

Under range expansion, the dispersal rate d increased in the populations at the expansion front, and in time decreased again as these populations got older (Figure

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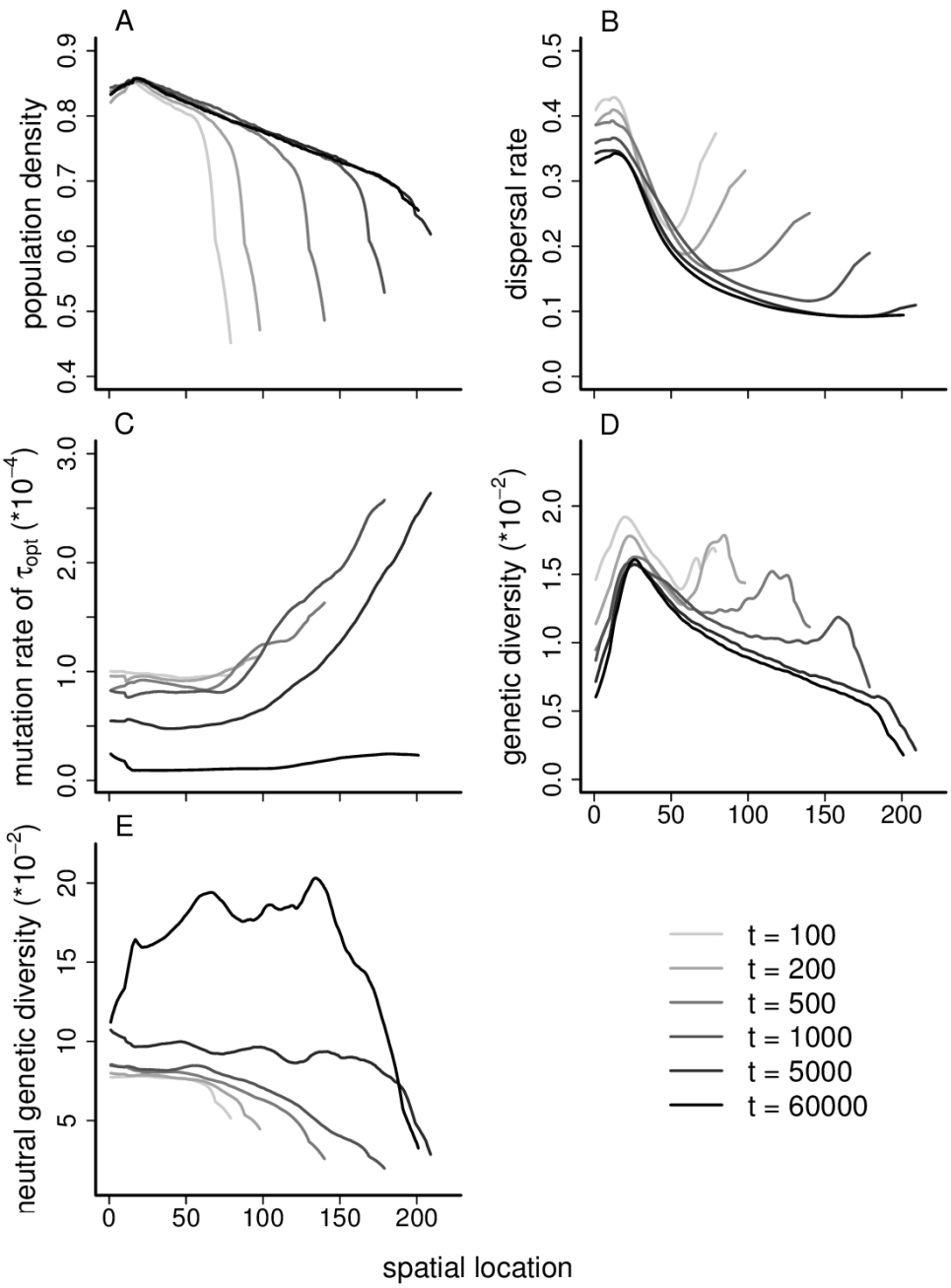

Figure 1: The average values over 100 simulations during and after range expansion across the gradient (horizontal axis) in time (gray scaling from light to dark, as time proceeds, which is given in a sequence of generations 1,000, 1,250, 1,500, 2,000, 5,000, 10,000, 60,000) of A. population density, B. dispersal rate, C. the mutation rate of the adaptation alleles, D. genetic diversity measured as the variance in adaptation alleles, and E. neutral genetic diversity, measured as the variance in alleles at the neutral locus. For reasons of clarity, a moving average with a window size of 20 has been applied (data were present in 10-generation intervals).

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1B). During range expansion the maximum established dispersal rate d was approximately 0.38 (Figure 1B). As the species expanded its range further across the gradient of increasing dispersal mortality (and increasing temperature), the maximum established dispersal rates at the range front decreased (Figure 1B). The range border established at an average dispersal mortality of 0.8, and a temperature value of 8. After reaching spatial equilibrium, the spatial distribution of dispersal rates showed a decaying exponential trend. The mutator value $m(\tau_{opt})$ showed no spatial pattern before range expansion, but rapidly increased once the species invaded the landscape. After $5,000$ generations of expansion, this mutation rate was on average five times higher at the range margin than in the core (Figure 1C). As a result of this increased mutation rate, genetic diversity at the adaptation locus was also increased at the range front, compared to regions which have been populated for a longer time (Figure 1D). At the very range margin the genetic diversity at the adaptation locus was lower, in line with the lower population densities here (Figures 1D and 1A). Diversity in the initial core area stayed at fairly high levels, due to high local dispersal rates. In contrast, the neutral genetic diversity was tenfold larger and showed a clear spatial pattern of a founder effect, with diversity decreasing with spatial location (Figure 1E).

Similar to mean dispersal propensity, mutation rates decreased again when the populations were getting older (Figure 1C). However, the time lag between the local decrease of the dispersal rate and the decrease of the mutation rate $m(\tau_{opt})$ was steadily increasing across space. At the range border it took $45,000$ generations for the mutation rate to decrease to equilibrium values after the dispersal rate had decreased. The variability in mutation rates was very high (not shown). While the maximum average mutation rate was found to be around $2.5 \cdot 10^{-4}$, the third quartile was measured at about $1.3 \cdot 10^{-3}$.

From the control simulations with fixed values at the dispersal locus, it showed that the average maximum mutation rates increased with increasing (fixed) dispersal rates.

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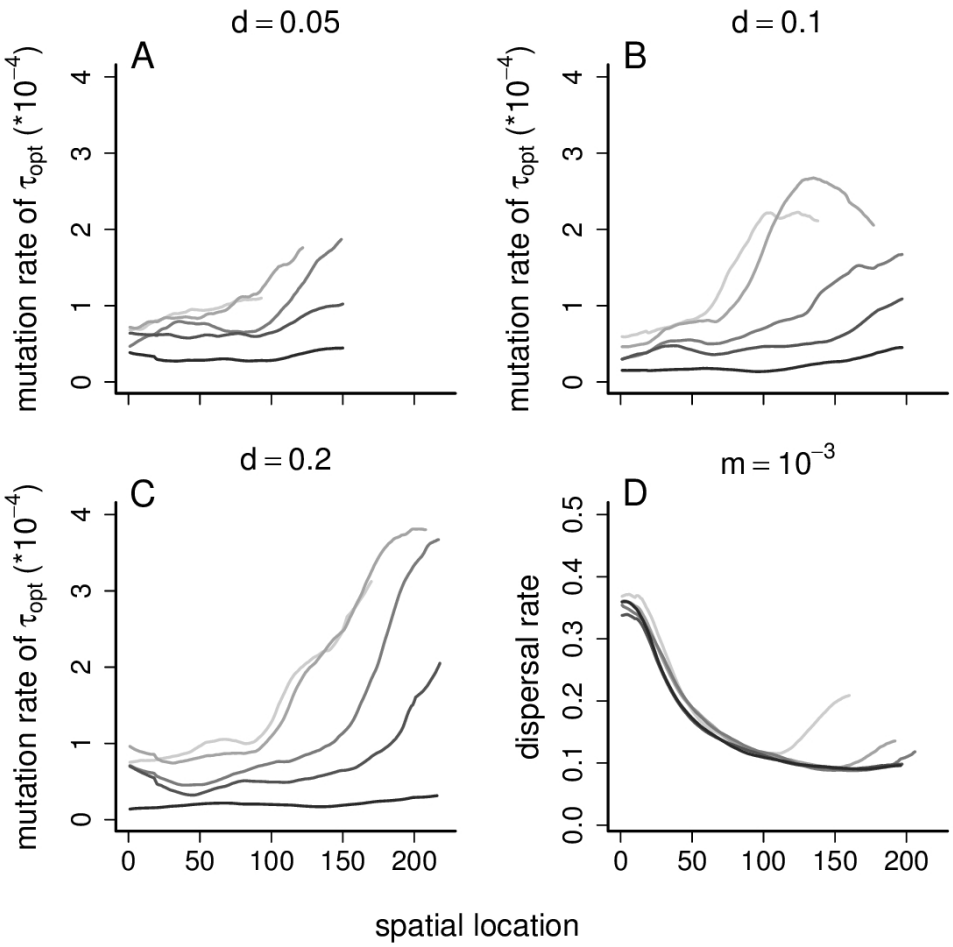

Figure 2: Results of the control simulations, with the average values of the mutation rate (A-C) during and after range expansion across the gradient (horizontal axis) in time (gray scaling from light to dark, as time proceeds, which is given in a sequence of generations $1,000$, $1,250$, $1,500$, $2,000$, $5,000$, $10,000$, $60,000$) under A. a fixed dispersal rate of 0.05, B. a fixed dispersal rate of 0.1, and C. a fixed dispersal rate of 0.2. In panel D the range border position in time (horizontal axis) is shown, averaged over 100 simulations for the original experiment with evolving mutation rate (here called 'control') and fixed mutation rates of 10^{-4} and 10^{-5}.

This further led to increased range sizes (Figures 2A-C). Mutation rates positively affected invasion speed, with decreasing (fixed) values of mutation rate causing a decreasing invasion speed (Figure 2D). The local level of adaptation s_2 was close to one in all simulations, throughout the simulation time and across the complete species range.

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Discussion

In this study we investigated whether an increase in dispersal rate under range expansion can lead to the evolution of higher mutation rate at the adaptation locus, enabling species to more rapidly adapt to local conditions with an increasing invasion speed. We found an increase of mutation rate, positively dependent on the dispersal rate. Evolved high mutation rates took an extensive period of time to return to lower mutation rates after the local dispersal rates decreased again, due to a priority effect (De Meester et al. 2002; Urban and De Meester 2009).

This modeling study shows for the first time that mutation rate can increase as a result of increased dispersal rates and spatial variation, experienced under range expansion. This high mutation rate increases genetic diversity and thus adaptive potential in newly colonized areas, causing a faster range expansion. This result is particularly interesting as selection for optimum mutation rate is associated with asexual populations (Kimura 1967; Leigh Jr 1970; Leigh Jr 1973; Sniegowski et al. 2000). Indeed, selection only operates on the adaptation locus, favoring mutations that increase local adaptation. In sexual populations, strong linkage disequilibrium is required for the (advantageous) alleles at the adaptation locus and the (high) mutation rate allele at the mutator locus to be inherited together, and as such to lead to indirect selection at the mutator locus (Sniegowski 2000). In our study, however, these two loci are genetically unlinked. Because the colonization of an empty patch requires a high genetic diversity to cope with the novel temperature (not shown), this on average occurs by individuals carrying high mutation rate alleles. A high initial population growth rate and the specific requirements for invaders in such a newly established population leads to high relatedness between individuals, where the beneficial allele at the adaptation locus and the high mutation rate allele at the mutator locus are essentially 'soft-linked' for lack of genetic diversity at the mutator locus. This also explains the high variability in mutation rates. We are not witnessing selection for

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optimum mutation rates: as long as it is accompanied by a beneficial allele at the adaptation locus, any allele at the mutator locus can establish itself.

During range expansion the dispersal rate was showing a clear signal of spatial sorting (Shine et al. 2011) and kin competition (Kubisch et al. 2013b), with good dispersers gathering at the expanding wave front (Phillips et al. 2010a). The immigration of different individuals is expected to maintain a high local level of genetic variation (Holt and Barfield 2011), from which one would expect high levels of dispersal to be accompanied by a low local mutation rate and we indeed find this pattern in the range core throughout the simulation. At the margin, however, relatedness amongst individuals increases at an advancing range front (Kubisch et al. 2013b), reducing both local genetic diversity and the diversity of immigrants. Under these conditions an increase in evolvability of local adaptation evolved, which compensated for the experienced spatial variation in local temperature. Both high rate signals of dispersal and mutation rate disappeared with time. At the range border, individuals with a high dispersal rate were locally well-adapted as a result of the high mutation rate. While a lower dispersal rate is beneficial under conditions of high dispersal mortality, slow dispersers took a long time to reach the area (genetic signature of range expansion, Phillips et al. 2010b). They were in addition hindered by the high dispersal mortality, and on top of that needed to compete with better locally adapted individuals (priority effect, De Meester et al. 2002). So we show here that different spatial phenomena associated with range expansion, in this case spatial sorting / kin competition and priority effects, can enforce each other. This has implications for field work, where the cause of an observed local high dispersal rate requires careful interpretation, as it can be the result of natural selection, spatial selection, spatial disequilibrium, or priority effects. The dispersal rate decreased first and was only after an extensive time lag of ten thousands of generations followed by a decrease in mutation rate. This again was caused by a priority effect (De Meester et al. 2002), where a high level of local adaptation prevents the establishment of individuals with a lower mutation rate. In

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addition, there is no direct selection against a high mutation rate. Selection affects the mutation rate through the mutations it has caused, and from which it has not yet been dissociated by recombination or separate inheritance (Kimura 1967; Leigh Jr 1970; Leigh Jr 1973; Sniegowski et al. 2000). So, as long as locally adapted alleles are also associated with high mutation rates, and both loci are unlinked, the low level of genetic diversity at the mutator locus together with the independent inheritance of the alleles at both loci in our study, result in a slow return to low mutation rates. In a control simulation we linked both loci, resulting in qualitatively equal spatial and temporal patterns as a consequence of recombination.

Holt and Barfield (2011) investigated niche evolution at species' range margins and found that local evolution was hampered when source populations of immigrating individuals were at low density, as a result of the stochastic processes in such populations (Pearson et al. 2009; Bridle et al. 2010; Turner and Wong 2010). The likelihood of observing niche evolution was further affected by the mutation rate, where dispersal limited local evolution in the sink population under a higher mutation rate, because of the increased numbers of maladapted individuals from the source (Holt and Barfield 2011). They did, however, not allow the joint evolution of mutation rate and dispersal rate, but instead used fixed rates.

Our results can be affected by the used genetic architecture, where linkage between traits (Blows and Hoffmann 2005; Hellmann and Pineda-Krch 2007), polygeny, and the magnitude of mutations can be of importance in range dynamics (Kawecki 2000; Kawecki 2008; Walsh and Blows 2009; Gomulkiewicz et al. 2010; Kimbrell 2010). For example, in a control simulation with a haploid sexual species, no patterns can be seen because all genetic diversity is lost.

In our study we have investigated the evolution of mutation rates. Dealing with novel environmental conditions or increased evolvability is however not restricted to mutation rates, but can be modeled in different ways, e.g. an increased magnitude of

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the phenotypic effect of mutations (Griswold 2006), an epigenetic effect, the evolution of modularity (Kashtan et al. 2009), degeneracy (Whitacre and Bender 2010), or the evolution of generalism or plasticity (Lee and Gelembiuk 2008; Chevin and Lande 2011). In a control simulation an increase of the niche width, i.e. increased generalism, uncoupled the link between mutation and dispersal rates, allowing for a faster expansion and a larger range. In addition, Kubisch et al. (2013a) show that when dispersal is a means of adaptation, by tracking suitable conditions during periods of change, this can prevent local adaptation altogether. Which kind of adaptation can be expected under specific ecological and environmental conditions is an interesting field of future investigation.

There is an ever-expanding pool of literature discussing the ecological and evolutionary dynamics of dispersal in the formation of species ranges (reviewed in Kubisch et al. 2014). Increased dispersal has been shown to increase invasion speeds (Thomas et al. 2001; Travis and Dytham 2002; Phillips et al. 2010a), affect the fate of neutral mutations (Travis et al. 2010), as well as the level of local adaptation (Kubisch et al. 2013a; Bourne et al. 2014), and local population dynamics (Travis et al. 2007; Burton et al. 2010), and in addition causes strong patterns of spatial disequilibrium (Ibrahim et al. 1996; Phillips et al. 2010b). This study shows that the particular genetic properties of populations under such spatial disequilibrium can have important consequences for the evolution of evolvability. While individual-based models have recently largely extended our theoretical knowledge of interactions and evolution of traits during range expansion, empirical data have been restricted to a few well-known cases (Thomas et al. 2001; Phillips et al. 2006; Moreau et al. 2011). Increasing ecological realism in our models (Cobben et al. 2011; Cobben et al. 2012a; Cobben et al. 2012b; Bocedi et al. 2014) might improve the predictability of theoretical phenomena and support field studies. These latter are, however, always constrained by the required temporal and spatial scales, which are particularly restrictive in terrestrial systems.

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Acknowledgements

We thank Troy Day and Andy Gardner for their encouragement and valuable comments, as well as two anonymous referees, who all have greatly contributed to the improvement of this manuscript. M.C. was funded by the Open Programme of the Netherlands Organisation of Scientific Research (NWO).

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