Spatially explicit models of divergence and genome hitchhiking

S. M. FLAXMAN*, J. L. FEDER† & P. NOSIL*†
*Department of Ecology and Evolutionary Biology, University of Colorado, Boulder, CO, USA
†Department of Biological Sciences, University of Notre Dame, Notre Dame, IN, USA

Keywords:
barriers to gene flow;
coarse-grained;
ecological speciation;
environmental cline;
fine-grained;
gradient;
mosaic habitats.

Abstract
Strong barriers to genetic exchange can exist at divergently selected loci, whereas alleles at neutral loci flow more readily between populations, thus impeding divergence and speciation in the face of gene flow. However, ‘divergence hitchhiking’ theory posits that divergent selection can generate large regions of differentiation around selected loci. ‘Genome hitchhiking’ theory suggests that selection can also cause reductions in average genome-wide rates of gene flow, resulting in widespread genomic divergence (rather than divergence only around specific selected loci). Spatial heterogeneity is ubiquitous in nature, yet previous models of genetic barriers to gene flow have explored limited combinations of spatial and selective scenarios. Using simulations of secondary contact of populations, we explore barriers to gene flow in various selective and spatial contexts in continuous, two-dimensional, spatially explicit environments. In general, the effects of hitchhiking are strongest in environments with regular spatial patterning of starkly divergent habitat types. When divergent selection is very strong, the absence of intermediate habitat types increases the effects of hitchhiking. However, when selection is moderate or weak, regular (vs. random) spatial arrangement of habitat types becomes more important than the presence of intermediate habitats per se. We also document counterintuitive processes arising from the stochastic interplay between selection, gene flow and drift. Our results indicate that generalization of results from two-deme models requires caution and increase understanding of the genomic and geographic basis of population divergence.

Introduction
Genetic differentiation during population divergence and speciation is often heterogeneous across the genome, where divergent selection drives or maintains differences in some regions, whereas the homogenizing effects of gene flow or insufficient time for random differentiation by genetic drift preclude divergence in other regions (Via, 2001; Wu, 2001; Nosil et al., 2009; Nosil & Feder, 2012). These ideas have a long history in studies of hybrid zones and sympatric speciation (Barton, 1979, 1995, 2001; Barton & Hewitt, 1985; Via, 2001). However, it is only with recent technical and analytical advances that allow genetic divergence at many loci to be screened in most any organism that numerous studies attesting to the porous nature of the genome have emerged (e.g. for reviews, see Nielsen, 2005; Nosil et al., 2009; Strasburg et al., 2012). For example, the last decade has seen the emergence of many population genomic studies reporting ‘outlier loci’ whose genetic divergence exceeds that observed for the rest of the genome, putatively because such loci are affected (either directly or indirectly via linkage) by divergent selection (Beaumont, 2005; Foll & Gaggiotti, 2008; Gompert & Buergi, 2011).

These observations have motivated investigations of intragenomic heterogeneity (with respect to differentiation of loci) during speciation with gene flow. A recent verbal theory of ‘divergence hitchhiking’
(henceforth ‘DH’) ties the above ideas together to generate a mechanism by which speciation in the face of gene flow may be easier than previously thought (Via & West, 2008; Via, 2009, 2012). The premise is that divergent selection reduces interbreeding between populations in different habitats, for example, by causing ecologically based selection against immigrants and hybrids. This reduces interpopulation recombination, and even if recombination occurs, selection can continue to reduce the frequency of immigrant alleles by selecting against advanced-generation hybrids. This reduction in effective gene flow might allow large regions of genetic differentiation to build up in the genome around the few loci subject to strong divergent selection at the initiation of speciation (Gavrilets, 2004).

This idea rests on the assumption that divergent selection on a site will create a relatively large – with respect to recombination distance – window of reduced gene flow around it, enhancing the potential to accumulate differentiation at linked sites. For example, in host races of pea aphids and in ecotypes of whitefish, regions of differentiation away from known QTL are as large as 20 cM (Rogers & Bernatchez, 2007; Via & West, 2008; Renaut et al., 2012; Via, 2012). In many other instances, regions of divergence appear much smaller (Turner et al., 2003, 2010; Machado et al., 2007; Noor et al., 2007; Turner & Hahn, 2007; Makinen et al., 2008; Storz & Kelly, 2008; Wood et al., 2008; Baxter et al., 2010; Counterman et al., 2010; Scascatelli et al., 2010; Strasburg et al., 2012), for example sometimes spanning just a few hundred kilobases or < 1 cM (Nadeau et al., 2012).

As a nonmutually exclusive alternative to DH in a few genomic regions, speciation may be promoted by ‘multifarious’ selection acting on numerous loci distributed across the genome (which, for example, affect many different phenotypic traits: Rice & Hostert, 1993; Lawniczak et al., 2010; Michel et al., 2010). Indeed, the direct involvement of many (i.e. tens to hundreds of) loci in establishing barriers during speciation with gene flow is expected from empirical as well as theoretical considerations (Barton, 1983; Barton & Bengtsson, 1986). Reductions in average genome-wide gene flow due to such multifarious selection could facilitate further genetic differentiation, even for loci unlinked to those under selection, via a process recently termed ‘genome hitchhiking’ (Feder et al., 2012; henceforth ‘GH’). DH and GH are both concerned with effects of divergent selection. The difference is that whereas DH focuses on ‘islands’ of differentiation formed around divergently selected loci due to tight physical linkage, GH focuses on more genomically widespread consequences arising from reductions in effective migration rates. These two theories – DH and GH – are complementary; for example, fortuitous physical linkage of many loci under multifarious selection could enhance barriers to gene flow (Barton, 1983; Barton & Bengtsson, 1986).

We note that the use of the term ‘hitchhiking’ (as part of both DH and GH) in the work performed here differs from its classical usage in describing the effects of selective sweeps within populations (Maynard Smith & Haigh, 1974; Barton, 2000; Charlesworth et al., 2003). Here, we follow Barton (2000: p. 1553) in using the term to encompass ‘indirect effects of selection at one or more loci on the rest of the genome.’ In this broader sense, hitchhiking effects may arise not only from selective sweeps, but also from balanced polymorphisms, local selection, background selection or selection against hybrids in a genetic cline (Kaplan et al., 1991; Nordborg et al., 1996a,b; Charlesworth et al., 1997, 2003; Barton, 2000, 2008).

Despite decades of useful work on hitchhiking and genetic barriers, additional theory on genomic patterns of divergence is needed for at least two reasons. First, debates have arisen about the size and number of genomic ‘islands’ we expect to see during speciation with gene flow (Via & West, 2008; Feder & Nosil, 2010; Feder et al., 2012; Via, 2012). Second, much previous theory in this area has, by necessity, made limiting assumptions in order to arrive at general (analytic) expressions describing the dynamics of allele preservation/loss and evolutionary equilibria. For example, many spatial models have made one or more of the following assumptions: (i) there are only two discrete demes, (ii) there is no intrinsic spatial environmental variation in fitness, (iii) selection is weak, (iv) allele frequencies at loci under selection do not fluctuate, (v) a separation of spatial or temporal scales is possible for different biological processes, (vi) the environment, if spatially continuous, is one-dimensional, and/or (vii) populations are infinite (see Barton, 2000; Charlesworth et al., 2003 for reviews). Our simulations make none of these common assumptions.

Recently, Feder & Nosil (2010) used a combination of analytical and simulation approaches to expand the single-locus models of Charlesworth et al. (1997) to any number of loci under selection and to a wider range of parameter values. Their models considered two demes subject to divergent selection and exchanging migrants at a gross rate m. The main finding of Feder & Nosil (2010) was that DH around a single locus can generate large regions of neutral differentiation of up to 10 cM but only under somewhat limited conditions: strong selection, low effective population size ($N_e \leq 10^3$) and low migration rates ($m \leq 10^{-3}$). Even modest increases in $N_e$ or $m$ greatly diminished neutral differentiation around a selected gene. When multiple selected loci are considered, regions of differentiation were larger. However, with many loci under selection, effective migration rates become low enough that genome-wide divergence of neutral sites occurs via GH and isolated regions of divergence are erased. What is therefore...
required for DH to be important is that effective gene flow is significantly reduced locally in the genome without being substantially reduced globally. As an extension of this initial work, Feder et al. (2012) considered the potential for further differentiation to accumulate and reproductive isolation to increase after equilibrium was achieved via the establishment of new ecologically beneficial mutations causing habitat-associated fitness trade-offs. They found that the strongest predictor of mutation establishment was the strength of selection acting on the new mutation (relative to the migration rate), but with both DH and GH having more minor secondary effects under some conditions. Nonetheless, when a few strongly selected loci establish, GH can have important consequences for facilitating mutation establishment, whereas the effects of DH again appeared to be limited to new mutations occurring in close proximity (e.g. within 1 cM) of an already strongly selected gene.

Motivated by the fact that spatial heterogeneity is ubiquitous in nature, we here expand past work on DH and GH to a much wider range of spatial and selective scenarios using individual-based, spatially explicit models. Specifically, our simulations consider the maintenance of neutral variation in scenarios that mimic the set-up of previous models of genetic clines and introgression during secondary contact (e.g. Barton, 1983). The work thus addresses not only issues concerning genomic divergence, but also classical and ongoing debates concerning how the spatial arrangement of populations affects population differentiation (Mayr, 1963; Felsenstein, 1981; Via, 2001; Berlocher & Feder, 2002; Bolnick & Fitzpatrick, 2007; Fitzpatrick et al., 2008; Mallet et al., 2009). For example, a major consideration for the geography of speciation is whether environmental features change abruptly in space (e.g. discrete patches of different host plant species) or continuously along gradients, resulting in geographic clines (Endler, 1977).

To be sure, there are a number of previous investigations that directly compared the results from multiple different spatial scenarios (Barton, 1983, 2008; Barton & Bengtsson, 1986; Charlesworth et al., 2003). Our work extends that past work by considering a combination of realistic, biologically important features: distinct and variable individuals, drift arising naturally as a consequence of stochasticity in both migration and reproduction, selective pressures that vary in space and meiosis with stochastic recombination events. Although past models have considered some of these factors in concert, to our knowledge, no previous model of genetic barriers and secondary contact has included all of them simultaneously. Among these factors, we focus a great deal on the role of spatial environmental variation because very few previous works have included true, continuous, bounded two-dimensional environments (Charlesworth et al., 2003; Doebeli & Dieckmann, 2003; Wilkins, 2004; Barton, 2008), yet such environments typify a great deal of the terrestrial species on this planet. Considering two-dimensional space is not merely biologically relevant; conclusions derived from two-dimensional models can often differ from their one-dimensional analogues (Doebeli & Dieckmann, 2003; Wilkins, 2004; Barton, 2008).

Our results about the influences of recombination rates and the overall strength of selection on genetic barriers, DH and GH are consistent with the extensive past work cited above. However, we also found pronounced, nonintuitive effects of the other factors examined. Additionally, our results have implications for empirical studies of the gene regions involved in adaptation and speciation (Nielsen, 2005; Noor & Feder, 2006; Stinchcombe & Hoekstra, 2008). For example, our results strongly suggest that neutral ‘outlier’ loci reflect the presence of (unidentified) genes under selection that are very closely linked to the outlier (or the outliers are false positives), rather than long-distance effects of DH.

Materials and methods

Our results were generated from a stochastic, individual-based computer simulation model. The model was written in the C programming language, using the Mersenne Twister (issmt version 2.1: Saito & Matsumoto, 2006) to generate random numbers in the simulations. Source code for simulations is archived at http://sourceforge.net/projects/spatialhitchhik/files/. Spread sheets of parameter combinations used, raw data and metadata are archived on Dryad (doi:10.5061/dryad.8xc8b).

Although general, analytic results are desirable, useful analytic results are not always attainable in models with the multiple facets of biological realism we incorporated (Charlesworth et al., 1997, 2003; Doebeli & Dieckmann, 2003). For example, diffusion approximations may break down when selection is strong or when there are small, varying numbers of individuals (by chance) within a deme (Barton & Bengtsson, 1986). Indeed, due to the combination of genetic and spatial structure in our model, simplifying to the extent necessary to derive useful analytic results would result in a fundamentally different model that left out one or more of the factors we wish to consider. However, the parameter space of our model is not so large as to prevent rigorous examination of all of these factors through simulations. Additionally, by running simulations without any selection (explained below), we were able to numerically infer null statistics as points of reference for measuring the importance of DH and GH.

The model considers a population of constant size consisting of N diploid, hermaphroditic, obligately outcrossing individuals that migrate and reproduce in a continuous, spatially explicit and variable environment.
An individual in the model was defined by its genotype of \( \Lambda \) diploid loci, where \( \Lambda = 13, 14 \) or 22 for the results presented here (Table 1). Two distinct alleles segregated at each locus, represented by ‘0’ and ‘1’. Loci were arrayed along linear chromosomes, and an individual’s first locus (denoted \( L_0 \)) was always under selection. The next 11 loci, denoted \( L_1, L_2, \ldots, L_{11} \), were linked to \( L_0 \) at recombination distances \([r_1, r_2, \ldots, r_{11}] = [0.00001, 0.00002, 0.00005, 0.0001, 0.0002, 0.0005, 0.001, 0.005, 0.01, 0.05, 0.5] \). We considered an additional locus, \( L_{12} \), unlinked to any of the other loci (on a different chromosome; either allele inherited with probability 0.5). Recombination distance, \( r_p \), was defined as the probability that a crossover event would occur during a round of meiosis anywhere between locus \( L_0 \) and \( L_p \) (from 0 to \( p \) crossovers could occur). For all the results shown below, the loci \( L_1, L_2, \ldots, L_{12} \) were neutral. When selected loci in addition to \( L_0 \) were included in the simulations, they were unlinked to each other and to all other loci. In summary, our simulations considered the fates of alleles at 12 neutral loci, when \( l = 1, 2 \) or 10 additional loci were under selection.

The environment was defined in terms of a two-dimensional unit square, with the \( n \) individual’s location represented by its Euclidean coordinates \((x_i, y_j)\) in the square \((\text{i.e. } x_i, y_j \in [0, 1])\), the boundaries of which were treated as fixed, impermeable barriers. The model utilizes discrete time, with each time step representing the reproductive process. Generations were nonoverlapping, and the model represented by its Euclidean coordinates \((x_i, y_j)\) was always under selection. The environment was defined in terms of a two-dimensional unit square, with the \( n \) individual’s location represented by its Euclidean coordinates \((x_i, y_j)\) in the square \((\text{i.e. } x_i, y_j \in [0, 1])\), the boundaries of which were treated as fixed, impermeable barriers. The model utilizes discrete time, with each time step representing the reproductive process. Generations were nonoverlapping, and the model represented by its Euclidean coordinates \((x_i, y_j)\) was always under selection. The environment was defined in terms of a two-dimensional unit square, with the \( n \) individual’s location represented by its Euclidean coordinates \((x_i, y_j)\) in the square \((\text{i.e. } x_i, y_j \in [0, 1])\), the boundaries of which were treated as fixed, impermeable barriers. The model utilizes discrete time, with each time step representing the reproductive process. Generations were nonoverlapping, and the model represented by its Euclidean coordinates \((x_i, y_j)\) was always under selection. The environment was defined in terms of a two-dimensional unit square, with the \( n \) individual’s location represented by its Euclidean coordinates \((x_i, y_j)\) in the square \((\text{i.e. } x_i, y_j \in [0, 1])\), the boundaries of which were treated as fixed, impermeable barriers. The model utilizes discrete time, with each time step representing the reproductive process. Generations were nonoverlapping, and the model represented by its Euclidean coordinates \((x_i, y_j)\) was always under selection.

Migration in the model was cost-free and random in direction and distance travelled (normally distributed with mean 0 and standard deviation \( \sigma \)). Movements were truncated (when necessary) to keep individuals within the borders of the unit square. With the parameters used below, the average gross migration rate (probability of patch switching per individual per generation) that emerged from the model ranged from \(~0.02\) to \(~0.15\) (see Fig. S1, Supporting Information), depending upon the granularity of the environment. In conjunction with the range of selection strengths we used (given below), we had cases in which gross migration rates were less than, equal to or greater than the strength of selection.

Recombination, selection and drift were modelled to occur during reproduction, as follows. An individual’s fitness depended upon its genotype, its location and the fitness scheme. For the purposes of representing spatial variation in the environment, the overall environment was considered to be composed of an \( n \times n \) set of square patches (demes), all of equal size (Fig. 1). We show the results below for \( n = 3 \) and 9, that is, nine and \( 81 \) patches. Hence, a scenario with nine large patches (each with area \( \approx11\% \) of the unit square) represents a ‘coarse-grained’ environment, whereas a scenario with \( 81 \) smaller patches (each with area \( \approx1.2\% \) of the unit square) represents a more ‘fine-grained’ environment.

We considered three different types of spatial variation in fitness: (i) a regular ‘gradient’ of fitness across patches (Fig. 1a,d), (ii) a ‘grey-scale mosaic’ having the same numbers and types of patches as the ‘gradient,’ but with their locations randomized (Fig. 1b,e), and (iii) an ‘extreme mosaic’ of two very different patch types (Fig. 1c,f). Comparing the results from a gradient with those from a grey-scale mosaic allowed us to determine the influence of the spatial arrangement of patches. Comparing the results from the grey-scale mosaic with the extreme mosaic gave insights into the

### Table 1
Variables and parameter values used in simulations.

<table>
<thead>
<tr>
<th>Variable/parameter</th>
<th>Meaning</th>
<th>Value(s) or range used*</th>
</tr>
</thead>
<tbody>
<tr>
<td>( N )</td>
<td>Total number of individuals in environment</td>
<td>1000, 5000, 10000</td>
</tr>
<tr>
<td>( \Lambda )</td>
<td>Total number of loci in a genome</td>
<td>13, 14, 17, 22</td>
</tr>
<tr>
<td>( l )</td>
<td>Number of loci under selection</td>
<td>1, 2, 5, 10</td>
</tr>
<tr>
<td>( L_j )</td>
<td>Locus /</td>
<td>( j = 0, 1, \ldots, \Lambda - 1 )</td>
</tr>
<tr>
<td>( r_j )</td>
<td>Probability of recombination between ( L_0 ) and ( L_j )</td>
<td>( 11 ) different values (see text)</td>
</tr>
<tr>
<td>( D )</td>
<td>Dimensionality of habitat</td>
<td>1 [unit line] or 2 [unit square]</td>
</tr>
<tr>
<td>( r_P^2 )</td>
<td>Number of patches in habitat</td>
<td>2, 3, 4, 9, 11, 25, 49, 81, 121</td>
</tr>
<tr>
<td>( S_{\text{max}} )</td>
<td>Maximum value of selection coefficient</td>
<td>0.01, 0.1, 0.5</td>
</tr>
<tr>
<td>( \sigma )</td>
<td>Standard deviation of migration movement distances (normalized to unit line)</td>
<td>0.01, 0.02, 0.05</td>
</tr>
<tr>
<td>( \delta )</td>
<td>Threshold for identifying when ( L_j (y &gt; 0) ) was decoupled from locus ( L_0 )</td>
<td>0.001, 0.1</td>
</tr>
<tr>
<td>( p )</td>
<td>Threshold for identifying when ( L_j (y &gt; 0) ), previously decoupled, had been ‘rescued’</td>
<td>( 10^{-3}, 10^{-9} )</td>
</tr>
</tbody>
</table>

*Values shown in this column are those we explored in parameter studies and sensitivity analyses. Values shown in boldface are represented in results shown here.

JOURNAL OF EVOLUTIONARY BIOLOGY © 2012 EUROPEAN SOCIETY FOR EVOLUTIONARY BIOLOGY
importance of the presence or absence of intermediate habitats.

The individuals within the boundaries of a single patch constituted the mating pool for that patch, from which gametes were drawn stochastically. The probability that an individual was selected to contribute a gamete to an offspring was proportional to the individual’s fitness relative to the fitness of all other individuals in the same patch. For scenarios with just a single locus \( L_0 \) under selection, the maximum possible contribution to fitness \((1.0 + S_{\text{max}})\) was the reverse for selected loci homozygous for the ‘0’ allele. (a–c) show ‘coarse-grained’ habitats; (d–f) depict ‘fine-grained’ variation. (a) and (d) depict gradients of fitness from the top to the bottom of the habitat; (b) and (e) depict a random mosaic with the same numbers and types of patches as the gradient; (c) and (f) depict random mosaics composed of two extreme patch types.

![Fig. 1 Spatial fitness schemes in the three types of environments in the model.](image)

In ‘gradient’ spatial scenarios with a single locus under selection, an individual homozygous for the ‘0’ allele at \( L_0 \) had maximum fitness \((1.0 + S_{\text{max}})\) in the upper row of patches (Fig. 1a,d). To create the ‘gradient’, moving one row ‘down’, the fitness of this \((0,0)\) homozygote is decreased by \( S_{\text{max}}/(n-1) \), such that it would have minimum fitness \((1.0)\) in the bottom row of patches of the habitat and intermediate fitness \((1.0 + 0.5S_{\text{max}})\) in the middle row of patches (Fig. 1a,d). The fitness of an individual homozygous for the ‘1’ allele at \( L_0 \) was the reverse of that just described. Finally, in the ‘gradient’ scenarios with a single locus under selection, individuals that were heterozygous at \( L_0 \) were assumed to have intermediate fitness \((1.0 + S_{\text{max}})\) in the middle row of patches, that is, in the intermediate environment where the two homozygotes had the same fitness. As we move away from that row (up or down), the fitness of a heterozygote decreases by \( S_{\text{max}}/(n-1) \), such that heterozygotes have intermediate fitness \((1.0 + 0.5S_{\text{max}})\) in the top and bottom rows (i.e. where homozygotes were most strongly favoured). We note that these assumptions created overdominance in intermediate patch types in the gradient scenarios. We ran other simulations of gradients in which heterozygote fitness was constant across all patches (as it was in the extreme mosaic scenario). The results from the latter did not change our conclusions about mosaic
vs. gradient environments (see Fig. S4, Supporting Information).

We also investigated how increasing the numbers of unlinked loci under selection influenced the potential for hitchhiking to maintain neutral variation. For multiple loci, we considered all selected loci to contribute equally to fitness, with the fitness of a genotype calculated as the product of fitness contributions across all loci under selection. We performed the calculation of this product in two different ways. (i) In our ‘root’ fitness scheme, the maximum possible fitness contribution that a selected locus could make was \( \sqrt{1.0 + S_{\text{max}}} \), where \( l \) was the number of loci under selection. Thus, in this ‘root’ fitness scheme, as \( l \) was increased, a given overall level of selection (specified by a given value of \( S_{\text{max}} \)) was constant but was spread out over increasing numbers of unlinked loci on different chromosomes across the genome. (ii) In our ‘multiplicative’ fitness scheme, the maximum possible fitness contribution from each selected locus was \( 1.0 + S_{\text{max}} \). Thus, under the multiplicative scheme, the addition of each new locus increased the total strength of selection possible by a factor of \( 1.0 + S_{\text{max}} \) (i.e., maximum potential strength of selection = \( (1.0 + S_{\text{max}})^l \)). In both the ‘root’ and ‘multiplicative’ fitness schemes, the calculation of the contribution of each locus to fitness for mosaic vs. gradient environments was accomplished as described above for the single-locus case (see also Fig. 1). We note that the multiplicative scheme with \( l = 10 \) and \( S_{\text{max}} = 0.5 \) leads to selection strengths that are unrealistically large; our purpose in presenting them is solely to demonstrate just how strong selection would have to be in order to see long-distance effects of hitchhiking on neutral loci.

The model was initialized with (1) \( N/2 = 2500 \) individuals homozygous at every locus for ‘0’ alleles, all starting at the ‘top’ of the unit square environment, and (2) \( N/2 = 2500 \) additional individuals homozygous at every locus for ‘1’ alleles, all starting at the ‘bottom’ of the environment. These initial conditions simulated an evolutionary scenario akin to that used in many previous theoretical studies: allographic populations with fixed differences at a number of loci (neutral and selected) followed by secondary contact. Thus, our model focuses on the maintenance of neutral differentiation, and future work will explore the origin of differentiation from new mutations.

Examining the efficacy of DH and GH: the loss of neutral alleles

For the 12 neutral loci \( L_1, L_2, \ldots, L_{12} \), we examined the preservation of genetic variation in the face of gene flow and recombination. Specifically, we tracked how many generations it took for either the ‘0’ or ‘1’ allele to be lost at each neutral locus, which we henceforth refer to as ‘fixation times’. This is somewhat similar to studying a coalescent process in a subdivided population with linkage, recombination, selection and drift (e.g. Kaplan et al., 1991). We recorded fixation times for 1000 independent initializations for each parameter combination and explored if and how these fixation times varied under different parameter combinations. If fixation did not occur at a locus by the end of a simulation run, then it was noted as such. Fixation times for neutral loci in the absence of any selection (\( S_{\text{max}} = 0 \)) reflect the ‘null’ expectations for the maintenance of prestanding genetic variation and differentiation following secondary contact and gene flow. These null expectations appear below as dashed horizontal lines in Figs 2–5. Increases in fixation times above these baseline values reflect the potential for hitchhiking to preserve neutral differentiation. Specifically, increases for only those neutral loci that are linked to a selected locus indicate the potential for DH to maintain prestanding neutral divergence following secondary contact. Increases in fixation times because of selection on an unlinked locus reflect the potential for GH. Because we simulated many independent replicates of the same scenario, we were also able to evaluate the extent that different loci might evolve independently by examining the correlations among loci in their fixation times.

The dynamics of divergence and loss at different loci

We also calculated \( F_{\text{ST}} \) values among patches for each locus using the standard formula \( F_{\text{ST}} = \frac{H_T - H_S}{H_T} \), where \( H_T \) was the total observed heterozygosity at a given locus at a given time step and \( H_S \) was the expected heterozygosity based upon each patch’s observed heterozygosity (Hartl & Clark, 2007). \( F_{\text{ST},L,j} \) denoted the \( F_{\text{ST}} \) value for a given locus number \( j \) at time \( t \). When an allele at neutral locus \( L_j \) was perfectly linked to an allele at the selected locus \( L_0 \), their \( F_{\text{ST}} \) values were identical (\( F_{\text{ST},L,j} = F_{\text{ST},L,j,0} \)). However, as these alleles became decoupled from one another due to gene flow and recombination, their \( F_{\text{ST}} \) values diverged. In particular, over time \( F_{\text{ST},L,j,0} \) is expected to reach a quasi-steady-state (as shown below) representing migration–selection balance. However, once decoupled from the selected locus, \( F_{\text{ST}} \) values for neutral loci should be less than those for the selected locus and eventually decay to zero as one allele goes to fixation (by chance). Hence, we recorded time series of \( F_{\text{ST}} \) values for each locus.

These time series revealed some surprising dynamics of allele preservation and loss. In particular, the combined forces of recombination, selection and drift interacted to produce many cases in which the neutral locus became partially decoupled from the selected locus (i.e. \( 0 < F_{\text{ST},L,j} < F_{\text{ST},L,j,0} \)), sometimes to a great extent (i.e. \( 0 < F_{\text{ST},L,j} < F_{\text{ST},L,j,0} \)). However, rather than \( F_{\text{ST},L,j} \) continuing steadily to zero from this point, the neutral locus could also become recoupled in linkage

\[ F_{\text{ST}} = \frac{H_T - H_S}{H_T} \]
disequilibrium to an allele at the selected locus, with $F_{ST,t,j}$ rising again to higher levels. At the start of a run, every ‘1’ allele at locus $L_j$ was found on a chromosome with a ‘1’ allele at $L_0$, but after sufficient rounds of recombination and reproduction, some fraction $x$ of the ‘1’ alleles at $L_j$ would be on chromosomes with a ‘0’ allele at $L_0$, generally reducing $F_{ST,t,j}$. If effective recombination rates were low enough, however, $x$ could decline from this point to zero (due to drift), resulting in a steady rise of a ‘1’ allele at $L_j$ being associated with a ‘1’ allele at $L_0$ and $F_{ST,t,j}$ rising. We refer to cases of the latter as ‘rescues’ of the alleles at the neutral locus, because the differentiation at the neutral locus that was present at the beginning of the run is restored. Like fixation time, the frequency of rescues also reflects the potential for hitchhiking to maintain population differentiation, and thus, we explored the parameters affecting rescues. The reason that ‘rescues’ reflect such potential is that they reflect effective recombination rates, in the following ways: (i) when effective recombination is close to zero, there is nothing to be rescued; (ii) when effective recombination rates are low, rescues should be possible and observed; finally, (iii) when effective recombination rates are larger than the rate of neutral allele frequency change due to drift, rescues will be rare or impossible, because recombination will break associations between alleles faster than they can be rescued.

In order to identify rescues, we needed to establish objective criteria for identifying both (i) a ‘decoupling threshold’ when a neutral locus could be classified as having become decoupled from $L_0$, and (ii) a ‘rescue threshold’ when a locus, having previously become decoupled, subsequently was rescued. In order to be conservative in the identification of rescues, we report the results for a decoupling threshold, $d$, of $F_{ST,t,0}$ $-$ $F_{ST,t,j}$ $\geq d = 0.1$, and a rescue threshold, $\rho$, of $F_{ST,t,0}$ $-$ $F_{ST,t,j}$ $\leq \rho = 10^{-9}$. To identify a rescue event, we additionally required that $F_{ST,t,0}$ $-$ $F_{ST,t,j}$ $\leq \rho$ for two consecutive generations. Rescue events could only follow a decoupling, with only one rescue event associated with each decoupling event. Likewise, only a single decoupling event was considered possible after each rescue. We document below that rescues under these criteria were relatively common, but if less conservative criteria were

![Fig. 2](image-url) Median fixation times (logarithmic scale) for 12 neutral loci when a single locus ($L_0$) is under three different levels of selection ($S_{max}$) for gradient (a, d), grey-scale mosaic (b, e) and extreme mosaic (c, f) spatial patterns of environmental variation. Recombination rates ($r_j$) of the 12 neutral loci to $L_0$ are given on the x-axis on a logarithmic scale (i.e. $-5 = \text{recombination rate of } 10^{-5}$). Results for $L_{12}$, the unlinked neutral locus on a separate chromosome, are labelled ‘unl.’ Upper panels (a–c) present results with nine patches, whereas lower panels (d–f) present results for 81 patches. The ‘null expectation’ when there is no selection on $L_0$ is denoted by the dashed line (obtained numerically by setting $S_{max} = 0$ with all other parameters the same as for the other lines in a panel). Each point is the median of results of 1000 independent simulation replicates.
used to diagnose rescues, rescues would be even more common (results not shown).

**Results**

As expected from previous theory, recombination distance ($r_j$) and the strength of selection ($S_{max}$) had strong effects on fixation times. Stronger selection (higher values of $S_{max}$) led to longer fixation times, and as recombination distance increased from very low ($r_1 = 10^{-5}$) to high levels ($r_{11} = 0.5$), the median time to fixation decreased by one to two orders of magnitude (Figs 2–4). However, in nearly all parameter combinations, this decreasing trend was almost entirely due to the fixation times of the six loci most tightly linked to the selected locus $L_0$ with $r_j \leq 0.0005$. Under most circumstances, $r_j \geq 0.001$ (~3 on the log scale) resulted in median fixation times that were not substantially longer than

Fig. 3 Median fixation times when either (a–f) two or (g–l) 10 loci are under selection and the strength of selection is given by the ‘root’ fitness calculation (see Materials and Methods). Numbers of patches, spatial scenario and fitness scheme are given above each panel. Other details are as in Fig. 2.
the null baseline expectation. This threshold was often independent of $S_{\text{max}}$, indicating that the selection/recombination ratio alone did not fully capture the effects of $S_{\text{max}}$ and $r_j$ (see also Fig. S5 in the Supporting Information).

**Spreading selection across multiple loci**

In general, a given maximum possible intensity of selection concentrated on one locus was more effective at maintaining variation at linked neutral loci than the same intensity of selection spread across multiple loci in the genome (i.e. compare Figs 2 and 3). The effect of concentrated selection was more pronounced for mosaic than for gradient scenarios (Fig. 3). Moreover, even in mosaic scenarios, the consequences of multiple selected loci were only prominent for neutral loci that were tightly linked ($r_j \leq 0.001$) to the selected locus $L_0$ (Fig. 3).

**Strength of genome-wide selection**

Increasing the total strength of selection acting genome-wide increased the fixation time for neutral

---

![Fig. 4](image-url)

*Fig. 4* Median fixation times as in Fig. 3, but with the 'multiplicative' fitness calculation (see Materials and Methods). As a result, the maximum strength of selection is greater here than in any corresponding line of Fig. 3. Other details are as in Fig. 3.
loci linked to $L_0$ (Fig. 4). In cases of the strongest genome-wide selection simulated with 10 loci having $S_{\text{max}} = 0.5$ (Fig. 4g-l), fixation times were elevated for all neutral loci in the extreme mosaic, including those unlinked to $L_0$ (although we note that the latter case involves extremely strong selection that is unlikely to be observed in natural systems). Indeed, fixation did not occur within $10^6$ generations in a majority of cases for most linked neutral loci (see points at $10^6$ for $S_{\text{max}} = 0.5$ in Fig. 4i,l). The effect of strong genome-wide selection was also more pronounced for the extreme mosaic than either of the other spatial scenarios.

**Spatial factors: coarse- vs. fine-grained environments**

In nearly all cases, the graininess of the environment had a consistent effect on median fixation time: within a given parameter set, coarse-grained environments (fewer, larger patches) had fixation times that were longer than or equal to those for fine-grained environments (a greater number of smaller-sized patches; Figs 2–4). There were a few exceptions to this pattern at the weakest level of selection (e.g. compare triangles in Fig 2c,f).

**Spatial factors: spatial arrangement of patches and the presence of intermediate patch types**

The effects of spatial arrangement and patch types depended upon both the strength of selection and the graininess of the environment. With moderate to strong selection, the grey-scale mosaic consistently produced the shortest fixation times across all scenarios. The extreme mosaic produced the longest fixation times in coarse environments with the strongest levels of selection (e.g. compare squares in Fig. 2a–c; Fig. 3a–c; Fig. 4a–c). However, when selection was weak and/or the environment was fine-grained, gradient environments produced the longest fixation times.

**Variance in fixation times**

Variances in median fixation time were not large for loosely linked neutral loci and were similar to the baseline null level for an unlinked neutral locus ($L_{12}$) on a separate chromosome. Moreover, variance decreased with increasing recombination distance of the neutral loci from the selected locus $L_0$ (Fig. 5).

Fig. 5 Variances in observed fixation times for cases with a single locus under selection. Sample sizes, simulation runs used, parameters and arrangement of panels are all as in Fig. 2. Note that patterns in variance qualitatively mirror the patterns in fixation times (compare lines here with corresponding panels in Fig. 2). The same was true for variances observed in cases with multiple loci under selection (results not shown). Variance estimates will be artificially low for parameter combinations and loci that had many runs reaching $10^6$ generations (e.g. panel c) before fixation occurred at a locus because the distribution of fixation times was truncated in such cases (see Materials and Methods).

JOURNAL OF EVOLUTIONARY BIOLOGY © 2012 EUROPEAN SOCIETY FOR EVOLUTIONARY BIOLOGY
Correlations among fixation times

Analysis of correlations among fixation times for neutral loci implied that, in general, there was much opportunity for even tightly linked neutral loci to evolve independently of one another. Figure 6 shows the extent to which neutral alleles at \( L_1 \) tended to share the same evolutionary trajectory as alleles at other neutral loci \( (L_2, \ldots, L_{12}) \), as demonstrated by correlations in the fixation times between pairs of loci. Correlations for other focal loci besides \( L_1 \) showed qualitatively similar patterns (results not shown). Loci that were very close together indeed often showed significant correlations among fixation times, suggesting that very tightly linked neutral loci could sometimes behave somewhat as a single ‘gene’. However, correlations were generally insignificant for any pairwise comparison of fixation times involving loci \( L_a \) through \( L_{11} \) (with \( r_{ij} \geq 0.005 \)) compared with any other locus. Thus, even for loci separated by a recombination frequency as little as 0.5 cM, evolutionary fates were usually not strongly linked.

\[ F_{ST} \text{ time series and ‘rescues’} \]

Rescue events (see Materials and Methods) were commonly observed in the simulations; an example of multiple rescues occurring within one run is shown in Fig. 7 (see Fig. S3 in the Supporting Information for additional examples). The frequency of rescues varied with the strength of selection, spatial scenario and recombination distance. In general, rescues were extremely rare or nonexistent with weak selection \((S_{\text{max}} = 0.01; \text{Fig. } 8d–f, j–l)\). This was due to a relatively high effective recombination rate in such cases and due to the fact that the selected alleles themselves could be lost by being overwhelmed by migration. In contrast, when selection was strong \((S_{\text{max}} = 0.5; \text{Fig. } 8a–c, g–i)\), even relatively large decoupling events could be rescued. The frequency of rescues was also greatly affected by recombination distance. In general, rescues were much more common for tightly than for loosely linked loci (but see Fig. 8i, discussed below). Indeed, in the majority of cases, rescues were very rare for \( r_{ij} > 0.005 \). For parameter values in which rescues were common for at least some loci (i.e. \( S_{\text{max}} = 0.5 \)), we also examined the probability of rescue following a decoupling (Fig. 9). As expected, for a given decoupling criterion, rescues were more likely for loci that were more tightly linked to the selected locus. These results were consistent with the findings for fixation time in implying that the conditions for DH to help maintain, accumulate and resurrect (rescue) neutral differentiation may be generally limited to tight linkage and strong, localized selection acting on the genome.

Discussion

Our work is distinguished from previous theory by considering the combination of (i) a wide array of spatial scenarios of intrinsic environmental variation in fitness (ii) in explicit two-dimensional, bounded space where (iii) both selection and a number of realistic sources of stochasticity determine evolutionary trajectories of (iv) various numbers of selected and neutral alleles. While including all of these features in our model made analytic treatment intractable, we were able to investigate a wide range of biologically relevant scenarios by simulation. This allowed us to expand past two-deme models (Feder & Nosil, 2010; Feder et al., 2012) of hitchhiking to a wider range of geographic scenarios.

In order to quantify the efficacy of hitchhiking, we considered a starting point that was maximally

\[ \text{Fig. 6 Correlation coefficients among fixation times between } L_1 \text{ and all other neutral loci. There are 125 correlation coefficients per box-and-whisker plot, where each correlation coefficient was calculated from approximately 200 independent simulation runs. Boxes show the median (centre line) and interquartile range (IQR; box). Whiskers span points up to 1.5 IQR beyond the IQR, and ‘+’ symbols show data points beyond the latter range.} \]

\[ \text{Fig. 7 An example of } F_{ST} \text{ time series for the selected locus (} L_0 \text{) and a neutral locus (} L_3 \text{) during one run of the model. Downward-pointing triangles indicate times when decoupling occurred; upward-pointing triangles indicate the occurrence of a ‘rescue’ event following decoupling (see Materials and Methods). In the example shown here, } L_3 \text{ is decoupled five times from } L_0 \text{, each of which is eventually followed by a rescue. However, after the 6th decoupling, fixation occurs at } L_3 \text{ (line for } L_3 \text{ goes to zero after 63 926 generations).} \]
favourable to the maintenance of neutral differentiation; namely, each neutral allele was perfectly associated with a selected allele(s), initial populations were strictly homozygous at all loci considered, and all individuals began in spatial locations that were favourable for their respective genotypes. We then measured the efficacy of hitchhiking in terms of how many generations were required for differentiation at each neutral locus to decline and be lost. This set-up specifically explored the effectiveness of forces that may promote DH and/or GH in preventing the loss of neutral divergence. Furthermore, it also enabled us to build upon the rich literature of previous theory on barriers to gene flow during secondary contact.

The roles of the strength of selection and recombination rates have been extensively explored, and our results on these factors mirror those of previous work. Briefly, strong selection and low recombination rates were required for any noticeable increase in the maintenance of neutral variation (relative to the null case of the absence of selective barriers). These results are consistent with past models demonstrating the efficacy of recombination in breaking up linkage disequilibrium (Felsenstein, 1981; Bolnick & Fitzpatrick, 2007). Quantitatively, linkage had to be extremely tight for a barrier to be effective. Our results agree with previous studies of hitchhiking in panmictic populations, which showed that hitchhiking effects are essentially absent for loci

![Fig. 8](image-url) Observed numbers of rescue events at each neutral locus as a function of model parameters. Decoupling and rescue thresholds were, respectively, \( d = 0.1 \) and \( \rho = 10^{-7} \) (see Materials and Methods), and in all panels, there were nine patches (coarse environment). (a–f): a single locus \( l_{0} \) is under selection. (g–l): 10 loci under selection with the ‘multiplicative’ fitness calculation method. Each boxplot shows the results from 1000 independent simulation runs (see Fig. 6 for explanation of box-and-whisker plots). Note that the y-axis is logarithmic.
having $r_j > 0.1 \ S_{\text{max}}$ (Maynard Smith & Haigh, 1974; see also Fig. S5). However, our results on the roles of $r_j$ and $S_{\text{max}}$ were not explained just by the $r_j/S_{\text{max}}$ ratio. We varied $S_{\text{max}}$ over 1.5 orders of magnitude, and we varied the total strength of selection over more than two orders of magnitude. Yet, in nearly all scenarios, any locus that was 0.1 cM or farther from a selected locus (i.e. $r_j \geq 10^{-3}$) showed no increase in fixation time relative to the null case. In Fig. S5, we re-plotted data from the single-locus case (Fig. 2), as a function of the $r_j/S_{\text{max}}$ ratio; the lack of overlap of lines for different $S_{\text{max}}$ values indicates that the $r_j/S_{\text{max}}$ ratio does not explain all the effects of $r_j$ and $S_{\text{max}}$.

The only pronounced cases of hitchhiking effects beyond 0.1 cM were for the most extreme strengths of genome-wide selection (Fig. 4g–i). However, the latter involve selection strengths that are unheard of in empirical studies; we present these results not because they are expected to be common, but rather to show just how strong selection would have to be in order to maintain islands of neutral differentiation that are larger than even just 0.1 cM in size. These findings reinforce the conclusions of recent work on hitchhiking that showed that the conditions for the establishment of sizeable genomic islands via DH were relatively limited (Feder & Nosil, 2010; Feder et al., 2012); here, we show that conditions for the maintenance of such islands, at least for neutral divergence, are similarly limited and are so across a range of spatial scenarios.

Although expected values of barrier strengths, coalescence times and fixation times have been examined in a number of previous studies incorporating selection and recombination, aspects of the variance in these processes have received less detailed attention (though see Petry, 1983; Hey, 1991; for examples). Here, we examined how variance in fixation times changed with values of $S_{\text{max}}$ and $r_j$. Figure 5 shows that the variance was affected by these variables in the same manner as fixation times. This suggests that neutral loci that are not tightly linked to selected loci are unlikely to exhibit high $F_{\text{ST}}$ via stochastic effects of divergence, because these stochastic effects diminished with $r_j$: variance in fixation times declined by several orders of magnitude as recombination distance was increased from $10^{0.5}$ to $10^{3}$ (Fig. 5). Based upon this, we suggest that DH is unlikely to explain empirical observations of ‘stand-alone’ neutral outliers that are only loosely linked to target loci under divergent selection. Instead, our models predict that such instances most likely reflect the operation of one or more of the following: (i) the presence of an additional, undetected selected locus that is tightly linked to the outlier, (ii) a lack of suitable marker coverage in the region of interest to detect many other neutral loci in addition to the detected outlier

Fig. 9 The proportion of decoupling events that are followed by a rescue event, shown for the subset of runs of Fig. 8 for which there were commonly rescues at one or more loci (Fig. 8a–g–i). See Fig. 6 for explanation of box-and-whisker plots.
displaying differentiation, (iii) the existence of numerous other genes under selection spread throughout the genome fostering GH, or (iv) on some occasions a false positive (i.e. the locus is not actually affected indirectly by selection).

The effects of multiple loci

Barton (1983) articulated a number of arguments for the importance of multiple loci in the maintenance of population differentiation. We considered the effects of multiple loci in two ways: the same overall strength of selection spread across increasing numbers of loci (Fig. 3), and increasing the overall strength of selection with the number of loci (Fig. 4). Whereas the effects of the latter (discussed above) were expected, the results of the former were less intuitive. For example, Barton (1983) showed that spreading the same overall strength of selection over more and more loci increased the effective strength of a barrier to gene flow; we found just the opposite. This is seen by comparing equivalent panels as the number of selected loci is increased from one (Fig. 2) to two (Fig. 3a–l) to 10 (Fig. 3g–l). The reason for the discrepancy of our predictions with previous works (Barton, 1983; Barton & Bengtsson, 1986) is due to differences in genome structure: rather than add selected loci to a map of constant size (as done in some previous works), we added selected loci that were unlinked to any of the neutral loci we were tracking. In other words, spreading the same strength of selection over more and more unlinked loci increased the effective recombination rate. This underscores the importance of understanding not just the overall strength of selection, but also where selected genes are within the genome in order to predict the strength of barriers to gene flow.

Effects of environmental granularity

The general conclusion from our analysis of spatial scenarios was that finer environmental heterogeneity generally reduces the effects of hitchhiking. Holding other parameters constant, in a majority of cases environments with fewer (larger) patches were usually as effective or more effective than environments with more (smaller) patches for retaining neutral differentiation following secondary contact and gene flow. The reason is intuitive: as the environment becomes more fine-grained, a given average migration distance becomes more likely to cause an individual to switch to a different patch of habitat.

Mosaic vs. gradient environments

For a given set of parameters, grey-scale mosaics generally showed the weakest effects of hitchhiking, and overall, neutral differentiation was maintained the longest with very strong selection in coarse-grained extreme mosaics. However, in fine-grained environments and/or with weak or moderate selection, gradients could produce longer fixation times than extreme mosaics. Although these results may appear somewhat nuanced, they are easily understood by considering two main aspects of how spatial variation impacts the maintenance of differentiation. First, the existence of regular spatial structure should facilitate the formation of clines because regular structure can decrease the migration rate between different habitat types. For example, in our gradient environments (Fig. 1a,d), movements to the left or right keep individuals in the same patch type, and changes in granularity do little to alter that. However, in either of the random mosaics (Fig. 1b,c,e,f), movement in any direction can take an individual to a new patch type, and changing patches is more likely as the environment becomes more fine-grained. Second, the absence of intermediate patch types can decrease the effective recombination rate if there is selection against heterozygotes. The grey-scale mosaic had both random structure and intermediate patch types and thus tended to produce the shortest fixation times. The gradients and extreme mosaics each had only one of these features – regular structure or the absence of intermediates, respectively – and varying granularity and $S_{\text{max}}$ allowed us to see cases where one or the other became more important. Finally, a classic two-deme model would have regular structure yet lack intermediate patch types, and thus would be predicted to be the most favourable for the maintenance of neutral variation, which is what our supplemental results showed (Fig. S2 compared to Fig. 2). The effects of hitchhiking are therefore expected to go from strongest to weakest in the following order: coarse-grained environments with strong divergent selection, regular structure and lacking intermediate patch types (Fig. S2) > coarse-grained extreme mosaics with strong divergent selection (Fig. 1c) > regular gradients (Fig. 1a,d) > fine-grained extreme mosaics (Fig. 1f) > fine-grained mosaics with intermediate patch types (Fig. 1e). The standard two-deme model of divergent ecological selection commonly used for analysing speciation with gene flow thus represents the most favourable spatial scenario for hitchhiking to contribute to population divergence.

At face value, our results could be interpreted as a sobering message for the potential for divergent selection to foster speciation in the face of gene flow. Scenarios with coarse spatial variation among starkly different patches (e.g. a two-deme model with extreme patch
patches had fewer individuals per deme (i.e. the continuous space analogue of a discrete two-deme model). The key consideration here, of course, is the relationship between selection, the spatial scales of environmental variation and demes, and migration distances (Slatkin, 1973; Nagylaki, 1975, 1976; Doeblei & Dieckmann, 2003; Barton, 2008). When the range of migration is greater than the spatial dimensions of habitats (patches), gene flow can be substantial and population differentiation difficult (Petry, 1983; Doeblei & Dieckmann, 2003). In contrast, for organisms with dispersal distances that are small relative to environmental granularity, migration from natal habitats, even when they abut and are interspersed with alternative environments, can be relatively rare. In these circumstances, predictions from two-deme models become more biologically realistic, with divergence more likely. Indeed, when dispersal becomes more and more limited such that organisms essentially do not leave their home environments, n-patch models become equivalent to allopatric speciation.

An interpretation of our results on environmental coarseness is that increasing subdivision of the population increased the migration rate (for constant $r$; see Fig. S1), and thus increased the effective recombination rate, thereby reducing the effects of DH and GH. This is in direct apparent contrast to previous results (Kaplan et al., 1991) predicting that population subdivision should reduce the effective recombination rate. The reason for the difference between those results and our own is that increasing subdivision in our model resulted in smaller patches (a finer spatial scale of variation). Even so, an increase in effective recombination rate was not necessarily expected, because smaller patches had fewer individuals per deme – an effect which on its own increases the efficacy of DH and GH (Feder & Nosil, 2010; Feder et al., 2012) – and also because the effects of spatial subdivision are highly dependent upon population sizes and stability (reviewed by Barton, 1998). Bierne (2010) and Kim & Maruki (2011) also found that increasing population subdivision could reduce the efficacy of hitchhiking, but for a very different reason: in those models, the environment was homogeneous, and increasing subdivision reduced the speed and scope of selective sweeps (which we did not examine).

The stochastic dynamics of selection, recombination and drift

Our conclusions above were additionally corroborated by our results on a phenomenon that has previously received very little attention: the decay and subsequent ‘rescue’ of differentiation at neutral loci (Figs 7–9, S3). In general, we observed the greatest number of rescues in the conditions that had the strongest barriers and were the most conducive to hitchhiking. Figure 8i may at first glance appear to contradict this, because it shows a greater number of rescues for loci that were farther removed or completely unlinked from the selected locus. However, within these same data, the probability of a rescue event following a decoupling was still higher for more tightly linked loci (Fig. 9f).

Future extensions

Our models considered migration to be random and independent of genotype. However, organisms are often expected to evolve and display strong behavioural habitat choice and preference (Bolnick et al., 2009; Flaxman & Lou, 2009; Flaxman et al., 2011), which can be of great importance in determining gene flow (Vuilleumier et al., 2010). In these instances, interhabitat migration can be greatly reduced, even for taxa that disperse widely, especially when they reproduce in their preferred habitats. Our results therefore underscore the significance of habitat choice for ecological speciation with gene flow (Vuilleumier et al., 2010). Future work should explore more fully whether and how the evolution of habitat choice may depend on hitchhiking with performance loci. Qualitatively, theory exists for two-allele choice models indicating that tight linkage of preference and performance loci facilitates speciation with gene flow (Johnson et al., 1996; Fry, 2003). Also, habitat-specific mating in and of itself generates a degree of disequilibrium between choice and performance genes (Nosil et al., 2006). However, we lack quantitative analyses assessing the extent to which DH and GH increase the probability that new habitat choice mutations will establish and enhance the retention and accumulation of neutral differentiation in the genome. Such work could also be extended beyond just habitat choice to ‘magic traits’ more generally; that is, traits subject to divergent selection that also generate nonrandom mating (Gavrilets, 2003, 2004; Servedio et al., 2011).

In our simulations, we considered divergent selection to act in a multiplicative manner and to generate fitness trade-offs between alternative habitats. These are assumptions about selection that may often hold in nature. However, we did not here consider the possibility of strictly additive fitness across loci, variation in the strength of selection acting on different loci or epistatic fitness interactions. Implications from previous work (Barton & Bengtsson, 1986; Feder & Nosil, 2010) suggest that epistasis may change some of the quantitative predictions from the current simulations, but not the major qualitative conclusions. For example, intuitively, we expect that epistatic interactions among loci should
reduce the effective recombination rate and thereby strengthen the potential for hitchhiking. Moreover, if a similar suite of environmental challenges is repeatedly experienced by a population through time, then it may be that co-adapted complexes of linked genes exist as standing variation, further enhancing the potential for DH. All of these aspects of selection require further theoretical inquiry to better quantify their effects, although we suspect that our qualitative conclusions are likely to hold.

More generally, several important questions remain to be resolved concerning the roles that genome structure and hitchhiking play in facilitating speciation with gene flow. Here, we concentrated on the maintenance of neutral variation as a metric for assessing the potential for DH and GH to contribute to the genetic differentiation of populations. Future work should consider the establishment of new mutations in a ‘forward approach’ in a sympatric setting to complement our current ‘backward’ approach assessing the decay of differentiation following secondary contact. This would involve extending the two-deme analysis of Feder et al. (2012) to more complex spatial scenarios. In addition, simulations of how genome-wide patterns of differentiation change during the speciation process would be highly informative. There is still much to discern about the contributions of different population genetic processes for generating observed empirical patterns of genomic differentiation.

Finally, our results provide predictions about whether DH and GH are likely to be important in a given empirical system; namely, if one can measure the strength of divergent selection acting in different habitats, our model provides a number of robust predictions about the sizes and persistence of genomic ‘islands’ of divergence that ought to be observed in the genome. As emerging technologies (e.g. high-throughput sequencing) provide ever-more extensive data sets on large numbers of individuals from natural populations, it will become increasingly feasible to empirically test (at least qualitatively) predictions from our model and others. Our model, and future extensions of it, should help to provide a theoretical basis for the empirical study of genomic divergence.

Acknowledgments

We thank R. G. Harrison and two anonymous reviewers for helpful comments on earlier versions of the model. We thank Research Computing at the University of Colorado for support and for the use of computer resources. This work utilized the Janus supercomputer, which is supported by the National Science Foundation (award number CNS-0821794) and the University of Colorado Boulder. The Janus supercomputer is a joint effort of the University of Colorado Boulder, the University of Colorado Denver and the National Center for Atmospheric Research. The work was also supported, in part, by grants from JLF from NSF and the USDA and an ERC grant to PN. The authors declare that they have no conflicts of interest.

References


Supporting information

Additional Supporting Information may be found in the online version of this article:

Figure S1 Gross migration rates in the model as a function of the number of patches.

Figure S2 Median fixation times (logarithmic scale) for 12 neutral loci when a single locus (L0) is under three different levels of selection (Smax) for a 1-dimensional environment (the unit line) with only 2 patches of habitat (a 2-deme scenario).

Figure S3 Example time series of FST values of the locus (L0) under selection and two neutral loci.

Figure S4 Fixation times when the assumption of overdominance is removed.

Figure S5 Data from Fig. 2 in the main text re-plotted so that the x-axis is the ratio rj/Smax.

Data deposited at Dryad: doi:10.5061/dryad.8sc8b

Received 5 April 2012; revised 27 August 2012; accepted 9 September 2012