

Simulating natural selection in landscape genetics

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Abstract

Linking landscape effects to key evolutionary processes through individual organism movement and natural selection is essential to provide a foundation for evolutionary landscape genetics. Of particular importance is determining how spatially-explicit, individual-based models differ from classic population genetics and evolutionary ecology models based on ideal panmictic populations in an allopatric setting in their predictions of population structure and frequency of fixation of adaptive alleles. We explore initial applications of a spatially-explicit, individual-based evolutionary landscape genetics program that incorporates all factors – mutation, gene flow, genetic drift and selection – that affect the frequency of an allele in a population. We incorporate natural selection by imposing differential survival rates defined by local relative fitness values on a landscape. Selection coefficients thus can vary not only for genotypes, but also in space as functions of local environmental variability. This simulator enables coupling of gene flow (governed by resistance surfaces), with natural selection (governed by selection surfaces). We validate the individual-based simulations under Wright-Fisher assumptions. We show that under isolation-by-distance processes, there are deviations in the rate of change and equilibrium values of allele frequency. The program provides a valuable tool (CDPOP v1.0; <http://cel.dbs.umt.edu/software/CDPOP/>) for the study of evolutionary landscape genetics that allows explicit evaluation of the interactions between gene flow and selection in complex landscapes.

Keywords: computer simulation, fitness surfaces, individual-based, isolation-by-distance, landscape resistance, population genetics, spatially-explicit

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Introduction

How do evolutionary processes operate on populations in non-equilibrium and spatially complex environments? Despite its importance for understanding evolutionary landscape genetics, this question has been rarely addressed (Holderegger & Wagner 2006; Balkenhol *et al.* 2009). Classical models in population genetics are founded on several critical simplifying assumptions, including discretely bounded and panmictic populations (Hartl & Clark 2007). Natural populations, in contrast, occupy spatially complex landscapes and do not meet the assumptions of the classical models. Specifically, spatial heterogeneity fundamentally alters genetic processes in ways that deviate from traditional theory (Landguth *et al.* 2010). The interaction of environmental heterogeneity with species-specific movement behaviour and life histories may cause deviations away from this classic evolutionary model. Although analytical models of dynamics are well understood for panmictic, single-locus

populations, computational models are needed for more complex situations. Analytical solutions for such complex population genetic processes are likely to be intractable; hence, simulation modelling is likely to be the most productive approach to establish mechanistic explanations and provide a foundation for spatial evolutionary genetics theory (Balkenhol *et al.* 2009; Epperson *et al.* 2010; Balkenhol & Landguth 2011).

Differential individual survival and reproduction mediated by the interaction between individual genotypes and the selective environment in which they reside is the driving force of adaptive evolution (Futuyma 2009). Examples are accumulating for rapid evolutionary change in response to strong environmental forcing, both in response to natural forces and in response to human-caused environmental changes (e.g., Hendry *et al.* 2008; Siepielski *et al.* 2009). Natural selection will operate whenever genotypes differ in fitness or the average number of offspring produced by individuals of a particular genotype is skewed. Fitness is a measure of reproductive success through variation in survival, fecundity, mating ability, and other factors that ultimately determine whether the alleles of a particular individual will be

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passed on to future generations (Hedrick 2011). It is a measure of how well individuals with a certain genetic trait (genotype) are expected to survive and reproduce. Fitness is dependent on the environment; a genotype with high fitness in one environment may have low fitness in another [see Anderson *et al.* (2011) for examples].

One of the most influential descriptions of natural selection is the fitness landscape (Wright 1932; Provine 1986; Schuller 2000; Gavrillets 2004). In this framework, survival and reproduction are driven by the interaction of genotypes in n -dimensional gene space and changes in gene frequencies of populations (i.e., movement towards peaks, ridges, or holes of an adaptive landscape). The environment in which organisms reside is spatially heterogeneous, with ecological characteristics that vary over space and time. In this context, the frequency of an allele may increase in some areas but not others as function of heterogeneous environmental conditions. Our goal is to provide a framework that can explicitly link the n -dimensional gene space with a spatially complex fitness landscape in a heterogeneous environment.

Integrating the framework of the adaptive gene landscape with spatially complex environments is the primary motivation behind this research. This integration extends landscape genetics beyond evaluations of genetic connectivity by exploring the links between gene flow and selection in complex landscapes at an individual's level. We also report initial applications of a computational program for describing and predicting evolution in complex spatial environments using individual-based, spatially-explicit simulations. We address the following research questions: (i) Can a spatially-explicit individual-based framework be used to produce theoretical changes in allele frequency from generation to generation caused by selection? and (ii) How will spatially structured populations with different dispersal strategies influence a global allele fixation or extinction?

Methods

Simulation program

The spatial model of natural selection is built upon the existing framework of the individual-based landscape genetic program, CDPOP (Landguth & Cushman 2010). CDPOP models genetic exchange for a given resistance surface and (x, y) located individuals as functions of individual-based movement through mating and dispersal, vital dynamics and mutation. It provides a tool for simulating the emergence of spatial genetic structure in populations resulting from specified landscape resistance processes governing organism movement behaviour.

Past versions of CDPOP modelled three sources of genetic variation: gene flow, genetic drift and mutation.

These versions assumed that different genotypes have an equal probability of surviving and passing on their alleles to future generations, and thus, natural selection was not operating. This new version of CDPOP (v1.0) incorporates natural selection and enables extension of landscape genetic analyses to explicitly investigate adaptive evolution in complex landscapes. As with previous versions of CDPOP, the user specifies the genotype for each individual (i.e., number of loci and number of starting maximum alleles per locus). In CDPOP v1.0, the user also has the option of choosing a single or multiple diallelic locus selection model. For example, with 30 loci in the single-locus model, each individual has a genotype that consists of 29 neutral loci and one locus under selection. In addition, three relative fitness surfaces must be specified for the three adaptive segments of the genotype (e.g. AA, Aa and aa from the two alleles, A and a). Values for the relative fitness surfaces are spatially-explicit for each genotype and can be variable within one surface reflecting how relative fitness changes as a function of local environmental conditions. However, a user can consider classical selection models, such as overdominance, underdominance, additive, or multiplicative, by creating uniform fitness surfaces (all values in the surface for one genotype are equal) using the heterozygote effect and recessive allele effect (Gillespie 2004) and specifying the appropriate values for a given model (e.g. overdominance would include three uniform surfaces, where the relative fitness values for Aa would be greater than both the relative fitness values for AA and aa). Selection is then implemented through differential survival of offspring as a function of the relative fitness of the offspring's genotype at the location on that surface where the dispersing individual settles.

Simulation scenarios

We conducted a simple simulation modelling experiment with the following factors: number of loci (1 or 2), panmixia vs. isolation-by-distance (IBD), and IBD for two dispersal strategies (short range and long range). Six groups of simulations resulted from this combination: (i) single-locus selection with panmixia; (ii) two-locus selection with panmixia; (iii) single-locus selection governed by IBD with short-range dispersers; (iv) two-locus selection governed by IBD with short-range dispersers; (v) single-locus selection governed by IBD with long-range dispersers; and (vi) two-locus selection governed by IBD with long-range dispersers. In the single-locus selection simulations, the genotype AA was given a relative fitness value of 1.0 and the genotypes Aa and aa were given a value of 0.5. In the two-locus selection simulations, the genotype AABB was given a relative fitness value of 1.0 with the other eight possible genotypes having a value of

0.5. In the panmixia simulations, the Wright-Fisher model was assumed (i.e., random mating, sexual reproduction with both female and male with replacement, each mated pair produces one offspring, offspring randomly disperse until a constant population is reached that has an equal sex ratio, no mutation, and non-overlapping generations). We simulated IBD by specifying Euclidean distance in a resistance surface with values of 1. To address short-range species-specific movement strategies, we constrained all mate choices and dispersal distances to be $\leq 5\%$ of the maximum movement distance on the surface (6.28 km; Fig. 1). For long-range species-specific movement, we allowed all mate choices and dispersal distances to be less than or equal to the maximum movement distance on the surface (125.60 km). The probability of mate distance or dispersal distances for all IBD scenarios were chosen within the movement limit specified by an inverse-square probability function (Landguth & Cushman 2010).

In all scenarios, we used CDPOP v1.0 to simulate individual genetic exchange across 50 non-overlapping generations among 1000 randomly spatially located individuals as functions of individual-based movement, mating, dispersal, and selection. All simulated populations contained 10 diallelic loci (nine and eight neutral loci in the single locus and two-locus models, respectively), with no mutation in a two-sex, equal sex-ratio, female and male with replacement mating structure. We ran 10 Monte Carlo replicates for each simulation study.

Evaluating research questions

We evaluated our first research question, 'Can a spatially-explicit individual-based framework be used to

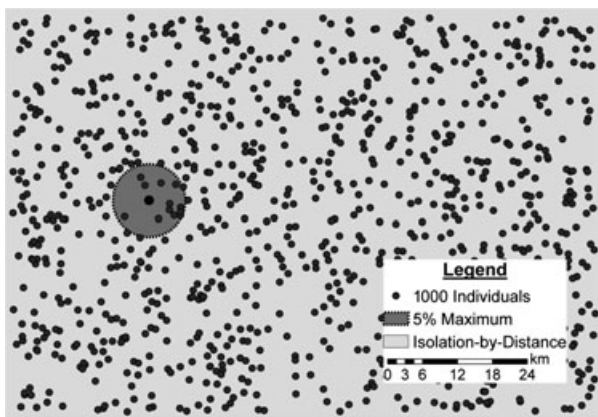


Fig. 1 An example of one simulation of 1000 randomly located individuals [dots on a resistance surface of isolation-by-distance (IBD) for a 5% maximum dispersal distance (6280 m)]. The dark circle represents the maximum dispersal and mating distance for the centre individual, i.e., the genetic neighbourhood for that individual.

produce theoretical changes in allele frequency under selection...?', by simulating selection with a global differential reproductive success under Wright-Fisher assumptions in simulations for a single and double diallelic locus. For the single diallelic locus, spatially uniform fitness surfaces were used with offspring differential reproductive success of 1.0, 0.5 and 0.5 for genotypes AA, Aa and aa, respectively. The simulated change in allele frequency was compared with the theoretical change (Δp_1) as shown by Wright (1935),

$$\Delta p_1 = \frac{p_1 q_1}{\bar{w}_1 [p_1 (w_{11} - w_{12}) + q_1 (w_{22} - w_{12})]} \quad (1)$$

where p_1 is the allele frequency for A, q_1 is the allele frequency for a, w_{11} is the relative fitness value for genotype AA, w_{12} is the relative fitness value for genotype Aa, w_{22} is the relative fitness value for genotype aa, and $\bar{w}_1 = p_1^2 w_{11} + 2p_1 q_1 w_{12} + q_1^2 w_{22}$ is the average fitness of the population. From here, a difference equation for the single-locus selection model can be derived to show the change in allele frequency for A through time,

$$p_{1,t} = \frac{p_{1,t-1} q_{1,t-1} w_{12} + p_{1,t-1}^2 w_{11}}{p_{1,t-1} w_{11} + 2p_{1,t-1} q_{1,t-1} w_{12} + q_{1,t-1}^2 w_{22}} \quad (2)$$

With the two-locus selection simulation, we compare the simulated change in allele frequency to the derived expected change in allele frequency. First, the expected frequency of the gametes after selection as

$$x'_{11} = \frac{\bar{w}_{11} (x_{11} - cD)}{\bar{w}_2}, \quad x'_{12} = \frac{\bar{w}_{12} (x_{12} + cD)}{\bar{w}_2} \quad (3a, b)$$

$$x'_{21} = \frac{\bar{w}_{21} (x_{21} + cD)}{\bar{w}_2}, \quad x'_{22} = \frac{\bar{w}_{22} (x_{22} - cD)}{\bar{w}_2} \quad (3c, d)$$

where the average relative fitness values for each gamete is $\bar{w}_{ij} = \sum_{k=1}^2 \sum_{l=1}^2 x_{kl} w_{ij,kl}$ and $\bar{w}_2 = \sum_{i=1}^2 \sum_{j=1}^2 x_{ij} \bar{w}_{ij}$ is the average relative fitness value for the population. We assumed independent assortment (i.e., free recombination, $c = 0$) and that there was no linkage disequilibrium ($D = 0$). Assuming $x_{11} = p_1 q_1$, $x_{12} = p_1 q_2$, $x_{21} = p_2 q_1$, and $x_{22} = p_2 q_2$, then the expected allele frequency after selection would be

$$p'_1 = x'_{11} + x'_{12} \quad (4)$$

Given the initial allele frequency of $p_1(0) = x_{11}(0) + x_{12}(0)$, the difference equation for the two-locus selection model becomes

$$p_{1,t} = \frac{p_{1,t-1} q_{1,t-1} \bar{w}_{11} + p_{1,t-1} q_{2,t-1} \bar{w}_{12}}{\bar{w}_2} \quad (5)$$

We evaluated our second research question: 'How will spatially structured populations influence a global allele

fixation or extinction?', by comparing results of simulations based on IBD processes across two species-specific movement strategies in both a single diallelic locus and a double diallelic locus with those under panmixia. The population genetic exchange was simulated through time and the change in allele frequency was produced to compare with the results produced from the *Selection under the Wright–Fisher model* section for both the single-locus and two-locus selection models.

Results

Selection under the Wright–Fisher model

For the single diallelic locus under panmixia, the CDPOP simulation exactly matched the expectation predicted by eqn (2). $p_{1,t}$ (labelled eqn 2) is plotted against the averaged simulated allele frequency for the 10 replicates in Fig. 2. This shows that CDPOP v1.0 implements selection under ideal Wright–Fisher conditions correctly and that outputs match theoretical expectations. For the double diallelic locus under panmixia, the CDPOP v1.0 simulation results also very closely matched the theoretical expectation of eqn (5). $p_{1,t}$ (labelled eqn 5) is plotted against the averaged simulated allele frequency for the 10 replicates in Fig. 3.

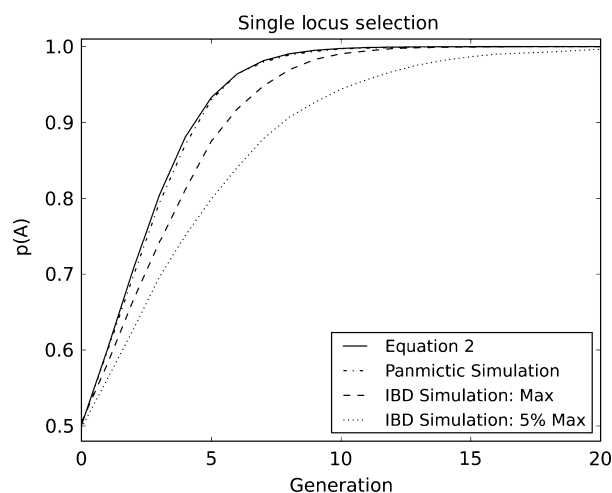


Fig. 2 The simulations for the single-locus selection model. The dashed-dotted line is the averaged simulated allele frequency from the 10 replicates for A under panmixia. The solid line is the expected allele frequency given by eqn (2). The dashed and dotted lines show the averaged simulated allele frequency from the 10 replicates for A under isolation-by-distance for the long-range and short-range dispersers, respectively. The dashed and dotted lines show the deviations away from Wright–Fisher assumptions when spatial structure is included. It should be noted that the confidence intervals generated from the 10 Monte Carlo runs are too small to be viewed at this scale.

Selection under the IBD model

For both the single-locus and two-locus model, the rate of fixation for A under IBD is slower than the expectation under ideal Wright–Fisher conditions. For example, in the single-locus simulation time to fixation increased from roughly eight generations under panmixia to 12 generations in the IBD maximum movement scenario (Fig. 2). Similarly, in the two-locus simulation, time to fixation increased from roughly 12 generations to 20 generations in the IBD maximum movement scenario (Fig. 3). This indicates that adding spatial structure to gene flow can alter the expectations for the rate at which equilibrium conditions are achieved through selection.

When comparing species-specific movement strategies (short-range vs. long-range disperses), we see that a difference occurs in the scenarios in which the movement distance is low (5%) for both the single- and two-locus results; the highly constrained mating and dispersal movements in these scenarios results in substantially slower rate of approach to fixation (equilibrium). For example, in the single-locus simulation, time to fixation increased from roughly 12 generations for the maximum movement strategy to 20 generations for the constrained 5% maximum movement strategy (Fig. 2). In the two-locus simulation, time to fixation increased from roughly 20 generations to 50 generations (Fig. 3).

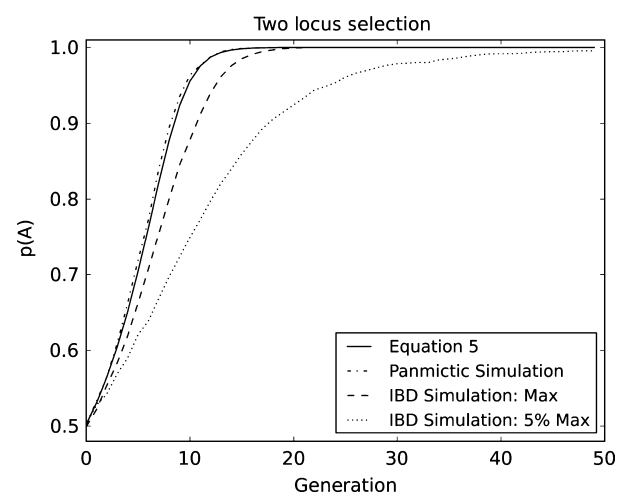


Fig. 3 The simulations for the two-locus selection model. The dashed-dotted line is the averaged simulated allele frequency from the 10 replicates for A under panmixia. The solid line is the expected allele frequency given by eqn (5). The dashed and dotted lines show the averaged simulated allele frequency from the 10 replicates for A under isolation-by-distance for the long-range and short-range dispersers, respectively. The dashed and dotted lines show the deviations away from Wright–Fisher assumptions when spatial structure is included. It should be noted that the confidence intervals generated from the 10 Monte Carlo runs are too small to be viewed at this scale.

Discussion

CDPOP v1.0 can be used to examine processes and topics in evolutionary genetics that involve both complex genetics and spatial patterns. One such example is speciation. The genetic architecture of the reproductive barriers required for speciation is almost always complex. Early in the development of evolutionary genetics, Dobzhansky (1937) and Muller (1942) recognized that hybrid incompatibility (reproductive barriers that act after the formation of hybrid zygotes) requires gene interaction and at least two genetic changes (e.g. ancestral population consisting of AAbb must evolve to subpopulation aabb and another subpopulation to AABB). Subsequent work has characterized such Dobzhansky–Muller genetic incompatibilities (reviewed in Johnson 2010). The evolution of many reproductive barriers that act before the formation of hybrid zygotes (e.g., mating incompatibilities or incompatibilities between sperm and egg) usually require at least two genetic changes as well (Coyne & Orr 2004; Gavrilets 2004).

CDPOP v1.0 can address the question of the extent to which reproductive isolation can evolve without complete geographical separation. The evolution of reproductive barriers, either pre-mating or post-mating, with complete geographical separation is much easier than when there is gene flow (Coyne & Orr 2004). Previous theoretical models and simulations do show that such parapatric speciation can occur if selection is sufficiently strong (Gavrilets *et al.* 2000; Gavrilets 2004; Porter & Johnson 2002), but these models generally examine only pairs of populations or populations on a cline. Our framework allows for a much greater variety of spatial arrangements in an individual-based setting.

Hybrid zones are regions where hybrids of two species persist along with the parental species (Harrison & Rand 1989). Traditionally, they have been modelled in a simple clinal setting: one species is most prevalent at one end of the cline, and the other is found at the other end, and hybrids are found in between (e.g. Endler 1977; Durrett *et al.* 2000). In reality, many hybrid zones are mosaic hybrid zones, wherein the frequencies of genotypes can fluctuate substantially on a local level (Rand & Harrison 1989). The most common explanation for such mosaic hybrid zones is environmental heterogeneity on a small spatial scale (Rand & Harrison 1989; Ross & Harrison 2002). CDPOP v1.0 can be used to examine such mosaic hybrid zones, as modelling these hybrid zones requires incorporation of both genetic and spatial complexity.

CDPOP v1.0 can also incorporate sex chromosomes, which play a major role in speciation (Coyne & Orr 2004). Sex chromosomes play an important role in several of the explanations for Haldane's rule (Haldane 1922), the finding that the sex with heteromorphic sex chromosomes

being more adversely affected in hybrids from interspecific crosses (Turelli & Orr 1995; Tao & Hartl 2003; Coyne & Orr 2004). We can also allow for differences between the sexes in their dispersal patterns in studies of hybrid zones, as sexes often differ in dispersal patterns (e.g., Helbig *et al.* 2001).

Wright (1931, 1932, 1977) proposed the shifting balance theory as an explanation for both the evolution of novelty and as a means of diversification. In Wright's shifting balance, a large population is divided into many local, semi-isolated subpopulations, and these subpopulations, which experience more genetic drift, can explore more of the adaptive landscape, eventually reaching new peaks. In the shifting balance, as Wade & Goodnight (1998) put it, nature does many small experiments, and those subpopulations that successfully reached higher peaks can export their successes to the rest of the population. This process was the subject of much criticism in Wright's lifetime (see Provine 1986; for historical details), and aspects of the shifting balance process continue to be controversial (Coyne *et al.* 1997; Wade & Goodnight 1998). Part of the reason for this controversy is that only parts of the process have been modelled, not the full shifting balance. With CDPOP v1.0, we can explore the whole process of the shifting balance theory.

The ability to couple gene flow that is governed by the underlying landscape with natural selection, which is governed by spatially-explicit selection surfaces, allows for a broad range of applications in adaptive landscape genetics. For example, how does fine-scale environmental variability affect the balance of local adaptation and gene flow? What are the balances between rate of change of the environment, species-specific movement abilities, mutation rates, and selection strengths? This simulator is the basic tool needed to begin to address questions of how spatially and temporally varying environments affect the adaptation of populations to perturbations such as caused by climate change, anthropogenic changes in land use and land cover, and innate spatial and temporal dynamics of natural landscapes (see reviews Morris 2011; Neale & Kremer 2011). However, as with most modelling efforts, the goals are realism and models only get so close. Future programming work to CDPOP should involve recombination, linkage disequilibrium, multiallele and multilocus models, and different forms of selection (e.g. fecundity, gametic, sexual, frequency dependent and dynamical).

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