



Two-locus clines on the real line with a step environment

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ABSTRACT

The shape of allele-frequency clines maintained by migration–selection balance depends not only on the properties of migration and selection, but also on the dominance relations among alleles and on linkage to other loci under selection. We investigate a two-locus model in which two diallelic, recombining loci are subject to selection caused by an abrupt environmental change. The habitat is one-dimensional and unbounded, selection at each locus is modeled by step functions such that in one region one allele at each locus is advantageous and in the other deleterious. We admit an environmentally independent, intermediate degree of dominance at both loci, including complete dominance. First, we derive an explicit expression for the single-locus cline with dominance, thus generalizing classical results by Haldane (1948). We show that the slope of the cline in the center (at the step) or, equivalently, the width of the cline, is independent of the degree of dominance. Second, under the assumption of strong recombination relative to selection and migration, the first-order approximations of the allele-frequency clines at each of the loci and of the linkage disequilibrium are derived. This may be interpreted as the quasi-linkage-equilibrium approximation of the two-locus cline. Explicit asymptotic expressions for the clines are deduced as $x \rightarrow \pm\infty$. For equivalent loci, explicit expressions for the whole clines are derived. The influence of dominance and of linkage on the slope of the cline in the center and on a global measure of steepness are investigated. This global measure reflects the influence of dominance. Finally, the accuracy of the approximations and the dependence of the shape of the two-locus cline on the full range of recombination rates is explored by numerical integration of the underlying system of partial differential equations.

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1. Introduction

A cline describes a gradual change in genotypic or phenotypic frequency as a function of spatial location. Such clines are frequently observed in natural populations and are an important and active research area in evolutionary biology and ecology (e.g., Endler, 1977; Hoffmann et al., 2002; Lohman et al., 2017). Clines typically occur in species distributed along an environmental gradient, for instance in temperature, where alternative phenotypes or genotypes are better adapted to the different extremes of the environment. Dispersal leads to mixing, reduces local adaptation, and entails a continuous, often sigmoidal, change in type frequencies across space. The study of clines can be used to obtain insight into the relative strengths of the evolutionary and ecological forces acting on this species.

Haldane (1948) devised a model in terms of a reaction–diffusion equation which approximates migration by diffusion and assumes that there is a step environment on the real line such that one allele

is advantageous if $x > 0$ and the other if $x < 0$. He derived explicit expressions for the cline, the spatially non-constant stationary solution, in terms of hyperbolic functions for the two cases of no dominance and of a completely dominant allele. The slope of the cline in the center, i.e., at the environmental step, can be expressed in terms of the selection intensity and the migration variance. He used this relation to infer the strength of selection on a population of deer mouse.

The mathematical theory of clines became a very active research area in the 1970s. Various patterns of spatial variation in fitnesses were investigated (e.g., environmental pockets, periodic changes), as were variation (e.g., barriers) or asymmetry in migration (e.g., Slatkin, 1973; Nagylaki, 1975, 1976, 1978). These works focused on the derivation of explicit results about the shape of clines. At about the same time and motivated by this work, Conley (1975), Fleming (1975), Fife and Peletier (1977), and Henry (1981) developed and employed advanced mathematical methods to investigate existence, uniqueness, and stability of clinal solutions under a variety of assumptions about fitnesses, i.e., for quite general classes of functions that describe selection caused by the environment.

Lou and Nagylaki (2002, 2004, 2006), extended much of the previous work on spatially varying selection in several directions.

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	<i>BB</i>	<i>Bb</i>	<i>bb</i>
<i>AA</i>	$\alpha(x) + \beta(x)$	$\alpha(x) + h_B\beta(x)$	$\alpha(x) - \beta(x)$
<i>Aa</i>	$h_A\alpha(x) + \beta(x)$	$h_A\alpha(x) + h_B\beta(x)$	$h_A\alpha(x) - \beta(x)$
<i>aa</i>	$-\alpha(x) + \beta(x)$	$-\alpha(x) + h_B\beta(x)$	$-\alpha(x) - \beta(x)$

(2.2)

Box 1.

In most of their analyses, migration is modeled by general elliptic operators on bounded domains in arbitrary dimensions and for wide classes of fitness functions. Such elliptic operators arise if migration is spatially inhomogeneous or anisotropic (Nagylaki, 1989). In addition, they studied the maintenance of clines at multiallelic loci, which does not only add realism but also produces new and interesting phenomena.

In the present work, we focus on the role of dominance and of linkage between loci. In particular, we investigate how the shape of a cline at one locus is affected by linkage to a second locus. We choose a step environment on the real line, such that in each of the two regions ($x > 0, x < 0$) one of the alleles at each locus is advantageous, the other deleterious. The strength of selection acting at the two loci may be different, though. The choice of a step environment on the whole real line (as opposed to a bounded interval) has the advantage that explicit results are obtained more readily.

We admit arbitrary intermediate dominance, including complete dominance, and assume that its degree is independent of the environment. The influence of dominance on the maintenance of single-locus clines has been studied before. In particular, on bounded domains the number and stability of clines depend on the degree of dominance (Henry, 1981; Lou and Nagylaki, 2002; Nagylaki and Lou, 2008; Lou et al., 2010; Nakashima et al., 2010). Explicit results about the shape of a cline seem to be rare and confined to the two cases of no dominance and complete dominance (e.g., Haldane, 1948; Nagylaki, 1975).

The first study of a two-locus cline model is due to Slatkin (1975), who showed numerically that the linkage disequilibrium generated between the two loci tends to steepen the clines. Barton (1983, 1986, 1999) derived general results about the consequences of linkage and linkage disequilibrium among multiple loci. Although he derived them for and applied them to hybrid zones, they are also of relevance in our context.

One of the novel features of our work is that we derive an analytically explicit solution for the single-locus cline with dominance (Section 3). In particular, we show that the slope of the cline in its center or, equivalently, the width of the cline is independent of the degree of dominance. Our main achievement is the derivation of the first-order perturbation of the allele-frequency clines at each of the loci if recombination is strong relative to selection and diffusion (Section 4.1). In other words, we derive the quasi-linkage-equilibrium approximation for the two-locus cline. In Sections 4.2 and 4.5, we study two measures of steepness of clines and their dependence on dominance and linkage. We derive the asymptotic properties of the allele-frequency clines of the two-locus system in Section 4.3. For equivalent loci, we obtain an analytically explicit expression for the strong-recombination approximation of the two-locus cline (Section 4.4). In Section 5, we briefly treat the case of no recombination. Finally, we provide numerical checks of the accuracy of our approximations and illustrate the dependence of two-locus clines on the full range of recombination rates by numerical integration of the system of partial differential equations (Section 6).

2. The model

We consider a monoecious, diploid population that occupies a linear, unbounded habitat in which it is uniformly distributed and mates locally at random. Fitness of individuals depends on location and is determined by two diallelic loci, \mathcal{A} and \mathcal{B} , which recombine at rate $r \geq 0$. We model dispersal by diffusion on the real line $\mathbb{R} = (-\infty, \infty)$, and assume it is homogeneous, isotropic, and genotype-independent, with migration variance σ^2 .

The frequencies of the gametes $AB, Ab, aB,$ and ab , at position $x \in \mathbb{R}$ and time t are $p_1 = p_1(x, t), p_2 = p_2(x, t), p_3 = p_3(x, t),$ and $p_4 = p_4(x, t)$, respectively, where $p_i \geq 0$ and $\sum_{i=1}^4 p_i = 1$. Let $D = p_1p_4 - p_2p_3$ denote the usual measure of linkage disequilibrium, and let $\mathbf{p} = (p_1, p_2, p_3, p_4)^T$. If $w_{ij}(x)$ is the fitness of the diploid genotype ij ($i, j \in \{1, 2, 3, 4\}$) at location $x \in \mathbb{R}$, then $w_i = w_i(x, \mathbf{p}) = \sum_{j=1}^4 w_{ij}(x)p_j$ is the marginal fitness of gamete i , and $\bar{w} = \bar{w}(x, \mathbf{p}) = \sum_{i=1}^4 w_i p_i$ is the population mean fitness. For a glossary of symbols, see Table 1.

Throughout, we use primes, $'$, and dots, $\dot{}$, to indicate partial derivatives with respect to x and t , respectively. We assume that (i) the three evolutionary forces selection, migration, and recombination are of the same order of magnitude and sufficiently weak, (ii) migration is genotype independent and spatially uniform and symmetric, and (iii) Hardy–Weinberg proportions hold locally. Defining $\eta_1 = \eta_4 = -\eta_2 = -\eta_3 = 1$ and proceeding as in Nagylaki (1975, 1989), we derive the following diffusion approximation for the evolution of gamete frequencies:

$$\dot{p}_i = \frac{\sigma^2}{2} p_i'' + p_i(w_i - \bar{w}) - \eta_i r D, \quad i \in \{1, 2, 3, 4\}, \tag{2.1a}$$

subject to the initial conditions

$$0 \leq p_i(x, t) \leq 1, \quad \sum_{i=1}^4 p_i(x, t) = 1 \tag{2.1b}$$

for $t = 0$ and every $x \in \mathbb{R}$

(cf. Slatkin, 1975). Solutions satisfy the constraints (2.1b) for every $t \geq 0$.

Throughout, we assume absence of epistasis. Then the genotypic fitnesses can be written as given in Box 1. It is easy to show that for a continuous-time model this scaling is general because absence of epistasis is assumed (Appendix A.1). We could have introduced spatially dependent dominance coefficients, $h_A(x)$ and $h_B(x)$. However, in view of our applications, we refrained from doing so. In order to have unique single-locus clines (Fife and Peletier, 1981), we assume throughout

$$-1 \leq h_A \leq 1 \quad \text{and} \quad -1 \leq h_B \leq 1. \tag{2.3}$$

Dominance is absent at locus \mathcal{A} (\mathcal{B}) if $h_A = 0$ ($h_B = 0$).

For our purposes, it will be convenient to follow the evolution of the allele frequencies $p_A = p_1 + p_2$ and $p_B = p_1 + p_3$, and the linkage disequilibrium D . With the abbreviations

$$\vartheta_A = 1 + h_A - 2h_A p_A, \quad \vartheta_B = 1 + h_B - 2h_B p_B, \tag{2.4}$$

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