Popul Ecol (2002) 44:51–58

SPECIAL FEATURE: ORIGINAL ARTICLE

Sergey Gavrilets · Nathan Gibson

Fixation probabilities in a spatially heterogeneous environment

Received: February 1, 2002 / Accepted: April 30, 2002

Abstract We consider a simple model of a one-locus, two-allele population inhibiting a two-patch system and experiencing spatially heterogeneous viability selection. The populaton size is finite. We use a diffusion approximation and singular perturbation techniques to find the probability of fixation of a mutant allele. We focus on situations in which each allele is advantageous in one patch and deleterious in the other patch. Our theoretical results support the previous conclusions that, under certain conditions, small populations respond faster to selection than do large populations. We emphasize that knowledge of the dependence of migration rates on population size is crucial in evaluating the effects of population size on the rate of evolution.

Key words Model · Mathematical · Selection · Evolution · Rate

Introduction

Spatial heterogeneity of both biotic and abiotic environments across a species range is ubiquitous. This heterogeneity is expected and has been repeatedly demonstrated experimentally to result in variation in selection acting on individual alleles (and traits) or their combinations (Hedrick et al. 1976; Hedrick 1986; Bell 1997; Mitton 1997; Stratton and Bennington 1998). Commonly, there are trade-offs, such that the alleles that are advantageous in one environment become deleterious in another (Futuyma and Moreno 1988; Van Tienderen 1991; Cooper and Lenski 2000). These trade-offs have very important evolutionary implications. The one that has received the most attention is an opportunity for the maintenance of genetic variation in natural populations, especially if migration is limited (Levene 1953; Dempster 1955; Felsenstein 1976; Hedrick et al. 1976; Karlin 1982; Hedrick 1986). The interaction of spatial heterogeneity in selection and restrictions on migration can also affect the rates of evolution and the likelihood of speciation.

The common textbook-type wisdom is that large populations are more responsive to selection than small populations. However, in natural populations one usually observes strong positive correlations between the population density, dispersal ability, and the species range size (Gaston 1994, 1996, 1998), which implies that the most abundant species typically face the most heterogeneous environment and have the highest dispersal ability. Ohta (1972) argued that the probability that a mutant allele is advantageous on average across a range of environmental conditions experienced by a population should decrease with population size: "... the greater the population size, the greater is the habitat diversity; the greater the diversity, the smaller is between-mutant variance of selection coefficients; the smaller the variance ..., the smaller is the probability that a new mutant will behave as if it were advantageous" (pp. 308–309). Ohta's conclusion was that the rate of advantageous gene substitutions should be higher in small populations even though the number of mutants arising in such populations is smaller than in large populations. Eldredge (1995, 2002) uses a similar reasoning to argue that abundant species will exhibit evolutionary stasis and that speciation driven by selection is expected to occur after isolation of small (peripheral) populations rather than in large widespread populations (Eldredge and Gould 1974). The question of spatial heterogeneity in selection is also relevant in the context of a recent debate on Wright's shifting balance theory and its alternatives (Gavrilets 1996; Coyne et al. 1997, 1998; Wade and Goodnight 1998). Wright's theory does appear to have serious problems (Gavrilets 1996; Coyne et al. 1997). However, the alternative advanced by Coyne et al. (1997, 1998) – simple mass selection – hinges on a questionable assumption that species experience identical selection regimes across their geographic ranges. Although some mutations are advantageous throughout the range of a

S. Gavrilets (✉)
Department of Ecology and Evolutionary Biology, University of Tennessee, Knoxville, TN 37996, USA
Tel. +1-865-974-8136; Fax +1-865-974-3067
e-mail: sergey@tiem.utk.edu

N. Gibson
Department of Mathematics, University of Tennessee, Knoxville, TN, USA

species, such mutations are expected to be rare compared with those adapting a local population to specific ecological conditions it encounters (Futuyma 1987). Spatial heterogeneity in selection also plays a prominent role in recent attempts to reconcile continuous microevolutionary change in local populations with widespread macroevolutionary stasis at the species level (Eldredge et al. submitted).

In contrast to the abundant theoretical literature on the maintenance of genetic variation (see the references cited here), only a handful of papers studied the rates of fixation in spatially heterogeneous environments. In a pioneering paper, Pollak (1966, see also 1972) found the probability of fixation of a mutant allele under a general migration scheme using a branching process approximation. Ohta (1972) calculated the fixation probability and the rate of fixation for alleles advantageous on average, assuming implicitly that the migration rates are so high that specific spatial structure of the species is unimportant. Ohta's approach can be justified by Nagylaki's (1980) results on a high migration limit in the diffusion approximation. Pollak (1972) did not study or discuss the validity of the approach he used. His approximation was questioned by Tachida and Iizuka (1991), who wrongly believed that Pollak's method produces estimates of fixation probabilities that do not depend on migration rates. Tachida and Iizuka (1991) developed an alternative approximation for the probability of fixation that is appropriate when migration is extremely weak. They also studied several cases of migration that was not extremely weak numerically and demonstrated analytically that, if selection is very weak, then the subdivided population can be treated as panmictic with an average selection coeffcient.

Here, we study the probability of fixation of a mutant allele in a species inhabiting two discrete patches with a different selection regime. We use singular perturbation techniques (Kevorkian and Cole 1996; Grasman and van Henwaarden 1999) to solve a two-dimensional diffusion equation controlling the probability of fixation.

Model

We consider a diallelic locus with alleles **a** and **A**. The population is subdivided into two subpopulations connected by migration with rate m; that is, m is the probability of migration to a different population per generation. We assume diploid inheritance with additive fitnesses. The relative fitnesses of allele **A** are $1 + s_1$ and $1 + s_2$ in the first and second subpopulations, respectively. If the coefficient s_i is positive (negative), then the allele **A** is advantageous (deleterious) relative to the allele a in the patch i. We assume that both selection and migration are weak ($|s_1|$, $|s_2|$, $m \ll 1$).

Deterministic dynamics

Neglecting effects of random genetic drift, the deterministic dynamics of the frequencies of allele **A** in the first, p_1, and second, p_2, subpopulations are described by a system of coupled ordinary differential equations:

$$\dot{p}_1 = s_1 p_1(1 - p_1) + m(p_2 - p_1) \tag{1a}$$

$$\dot{p}_2 = s_2 p_2(1 - p_2) + m(p_1 - p_2) \tag{1b}$$

where $\dot{p}_1$ and $\dot{p}_2$ are the derivatives of p_1 and p_2 with respect to time. In these equations, the first terms specify the effects of selection for local adaptation whereas the second terms specify the homogenizing effects of migration. The dynamics of system (1) are simple. If

$$s_1 < m \quad \text{and} \quad s_2 < \frac{s_1 m}{s_1 - m} \tag{2}$$

then allele **a** is fixed for any initial conditions (that is a monomorphic equilibrium with $p_1 = 0$, $p_2 = 0$ is globally stable). If

$$s_1 > -m \quad \text{and} \quad s_2 > -\frac{s_1 m}{s_1 + m} \tag{3}$$

then allele **A** becomes fixed for any initial conditions (that is, a monomorphic equilibrium with $p_1 = 1, p_2 = 1$ is globally stable). If conditions 2 and 3 are violated simultaneously (meaning that neither monomorphic equilibrium is stable), the system evolves to a stable polymorphic equilibrium (that is, a single polymorphic equilibrium exists and is globally stable). A necessary condition for this is that selection coefficients s_1 and s_2 have opposite signs. If $s_1 > 0$, $s_2 < 0$, then the allele frequencies at the polymorphic equilibrium are given by these expressions:

$$\begin{aligned} p_1^* &= \frac{1}{2} - \frac{m}{s_1} + \sqrt{\frac{1}{4} - \frac{m^2}{s_1 s_2}}, \\ p_2^* &= \frac{1}{2} - \frac{m}{s_2} - \sqrt{\frac{1}{4} - \frac{m^2}{s_1 s_2}} \end{aligned} \tag{4}$$

If $s_1 < 0, s_2 > 0$, then the signs in front of the square roots in these expressions must be changed to the opposite. Figure 1 summarizes the conditions for existence and stability of different equilibria. This figure shows that an allele is fixed deterministically if it is advantageous in both environments or if it is advantageous in one environment and its deleterious effect in the other environment is not too strong. The population approaches a stable polymorphic state if each allele is advantageous in one environment and is deleterious in the other environment and the fitness differences are sufficiently large.

Diffusion approximation

Assume that each subpopulation has a constant size N ($N \gg 1$). Let $u(x, y)$ be the probability of fixation of allele **A** given that initially $p_1 = x$, $p_2 = y$. Then, function $u(x, y)$ satisfies a partial differential equation:

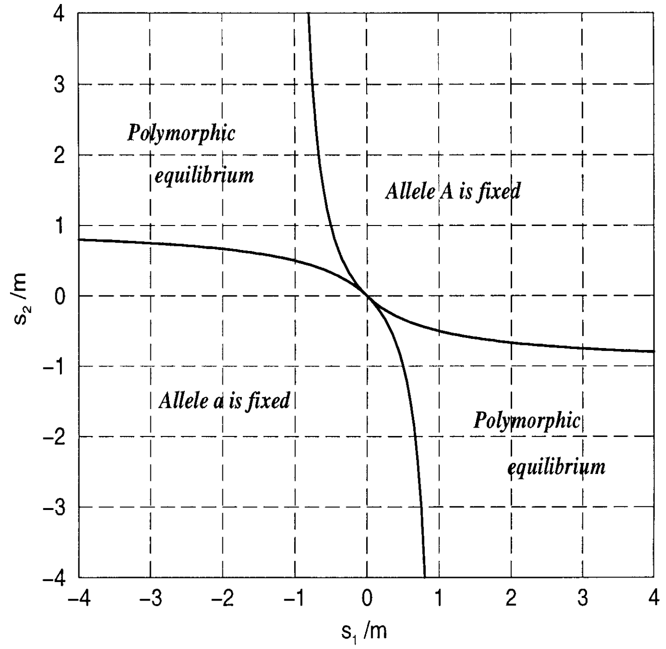


Fig. 1. Parameter space summarizing the conditions for existence and stability of different equilibria of the deterministic system (1)

$$\frac{x(1-x)}{4N}\frac{\partial^2 u}{\partial x^2}+\frac{y(1-y)}{4N}\frac{\partial^2 u}{\partial y^2}+\left[s_1x(1-x)+m(y-x)\right]\frac{\partial u}{\partial x}+\left[s_2y(1-y)+m(x-y)\right]\frac{\partial u}{\partial y}=0 \qquad (5)$$

with boundary conditions $u(0, 0) = 0$, $u(1, 1) = 1$ (Tachida and Iizuka 1991, equation 8). Here, the terms in the square brackets describe the expected changes in the frequency of allele **A** in the two subpopulations (as given by the right-hand side of Eq. 1). The terms in front of the second derivatives are equal to one-half of the expected variance of allele frequency under the Fisher–Wright binomial scheme for random genetic drift (Crow and Kimura 1970).

Results

Next, we describe some exact and approximate solutions of Eq. 5. The details of the derivations are given in the Appendix.

No heterogeneity in selection ($s_1 = s_2 = s$)

If selection coefficients are equal, then direct substitution into Eq. 5 shows that the *exact* solution is

$$u=\frac{1-\exp(-4N_T sp)}{1-\exp(-4N_T s)} \qquad (6)$$

where $N_T = 2N$ is the total size of the population and $p = (x + y)/2$ is the overall initial frequency of allele **A**. Thus, with no heterogeneity in selection, the probability of fixation is the same as in a single randomly mating population with size $2N$ (compare Eq. 6 and with a classical equation for the probability of fixation of an additive allele; e.g., Kimura 1983). Maruyama (1970) has already shown this using a different approach.

Allele A is advantageous on average

If allele **A** is advantageous on average (that is if $s_1 + s_2 > 0$), then the probability of fixation is approximately

$$u_+=\frac{1-\exp\left[-4N(ax+by)\right]}{1-\exp\left[-4N(a+b)\right]} \qquad (7)$$

where a and b are *positive* values satisfying a system of two nonlinear algebraic equations:

$$a^2-as_1+m(a-b)=0 \qquad (8a)$$

$$b^2-bs_2+m(b-a)=0 \qquad (8b)$$

Allele A is deleterious on average

If allele **A** is deleterious on average (that is, if $s_1 + s_2 < 0$), then the probability of fixation is approximately

$$u_-=\frac{\exp\left[4N(ax+by)\right]-1}{\exp\left[4N(a+b)\right]-1} \qquad (9)$$

where a and b are *positive* values satisfying a system of two nonlinear algebraic equations:

$$a^2+as_1+m(a-b)=0 \qquad (10a)$$

$$b^2+bs_2+m(b-a)=0 \qquad (10b)$$

Allele A is neutral on average

If allele **A** is neutral on average (that is, if $s_1 + s_2 = 0$), then the probability of fixation is approximately

$$u_0=\frac{1}{2}(u_+ + u_-) \qquad (11)$$

where u_+ and u_- are given by Eqs. 7 and 9, respectively.

Figure 5 in the Appendix shows that the approximations are rather good.

Discussion

We start discussing our results by comparing our approach with the approaches of Pollak (1966, 1972) and Tachida and Iizuka (1991). Then we consider how migration rate affects the probability of fixation, and, finally, we discuss the implications of our findings for the relative rates of evolution of small and large populations in a spatially heterogeneous environment.

Relation to previous work

Pollak (1966) found the probability of fixation using a branching process approximation. Let α_i ($= 1 + s_i$) be the relative fitness of allele **A** in the ith subpopulation ($i = 1, \ldots, n$). In Pollak's (1966) approximation, the fixation probability is

$$u = \frac{1 - \pi_1^{z_1} \ldots \pi_K^{z_K}}{1 - \pi_1^{N_1} \ldots \pi_K^{N_K}} \tag{12}$$

where z_i and N_i are the initial number of mutants and the size of the ith subpopulation, and π_i is the probability that the line descended from a single gene **A** in subpopulation i becomes extinct in the infinite population case. Probabilities π_i satisfy to a system of n nonlinear algebraic equations:

$$\pi_i = \exp\left[\alpha_i \sum_{j=1}^{n} m_{ij}\left(\pi_j - 1\right)\right] \tag{13}$$

where m_{ij} is the probability of migration from subpopulation i to subpopulation j (see Pollak 1972 for some approaches to solve these equations).

In the case of two demes ($n = 2$), Pollak's equations produce an approximation for the probability u that is identical to the one corresponding to our Eq. 7. The easiest way to see this is to switch from π_i to $\psi_i = 1 - \pi_i$ in Eq. 13, take the natural logarithm of both sides of the resulting equation, and then expand the expression in its left-hand side [that is, $\ln(1 - \psi_i)$] in a Taylor series, keeping the linear and quadratic terms. The resulting equations for ψ_1 and ψ_2 are equivalent to Eq. 8 for a and b. In a similar way, Pollak's (1966) equation 5.1 is equivalent to our approximation 9. Thus, when a mutant allele is advantageous or deleterious on average, the approximations based on branching processes and on the singular perturbation of diffusion equation give identical results. The branching processes approach, however, does not provide a satisfying way to estimate the probability of fixation when the mutant allele is neutral on average. The latter situation is expected to be common when the environment is highly heterogeneous.

Tachida and Iizuka (1991) developed an alternative Markov chain approximation for the probability of fixation that is appropriate when migration is very weak relative to selection (see Lande 1979; Slatkin 1981; Barton 1993; Gavrilets 2000 for other applications of this approximation). In a special most interesting case when the alleles are neutral on average ($s_1 = -s_2 = s > 0$), Tachida and Iizuka's approximation is

$$u = \frac{u_{adv} + u_{del}}{4}$$

where u_{adv} is the probability of fixation of an allele in an isolated population where the allele is advantageous, and u_{del} is the probability of fixation of an allele in an isolated population where it is deleterious. If selection is not too weak, then $u_{adv} \approx 2s/(1 - exp(-4Ns))$, $u_{del} \approx 0$ (Kimura 1983) resulting in

$$u \approx \frac{s/2}{1 - e^{-4Ns}} \tag{14}$$

Note that this value does not depend on the migration rate. Tachida and Iizuka demonstrated the validity of their approximation by comparing it with a numerical solution of a partial differential equation arising in the corresponding diffusion approximation. Our results support their conclusion that the Markov chain approximation is good if $m \leq 0.005$.

Effects of migration rate on fixation probability

Tachida and Iizuka (1991) argued that spatial subdivision increases the probability of fixation relative to the case of free migration between the subpopulations. Pollak's numerical results (e.g., Table 3 in Pollak 1972) lead to a similar observation. Another illustration is presented in Fig. 2, which shows fixation probabilities when $s_1 = -s_2$ for different migration rates m and population sizes N. In this figure, the lines corresponding to $m = 0.005$ would practically coincide with those based on the Tachida–Iizuka approximation. As s becomes very small, the fixation probability approaches the neutral limit $1/(4N)$. The same happens as the migration rate becomes large because in a well-mixed population the alleles become effectively neutral. Note that the increase in the probability of fixation at low migration

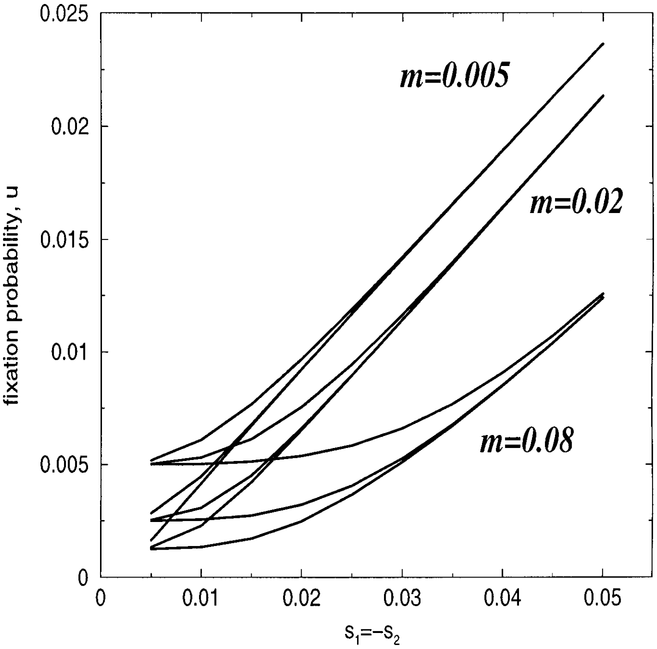


Fig. 2. Fixation probabilities when $s_1 = -s_2$ for different migration rates m and population sizes N. For each value of m there are three lines corresponding to $N = 50$, 100, and 200 (from the *top line* to the *bottom line*)

rates relative to that at high migration rates can be rather substantial, especially if the population size is large.

Relative rates of evolution of small and large populations in a spatially heterogeneous environment

Effects of population size on the rates of evolution in a heterogeneous environment were discussed by Ohta (1972) and Eldredge (1995, 2002). [Note that other previous discussions of the effects of population size on the rates of molecular evolution (Cherry 1998; Gillespie 1999, 2001) did not consider spatial factors, which do concern us here.] As illustrated in Fig. 2, the fixation probability decreases with migration rate and, unless the selection coefficient is very small, does not depend on the population size. In natural populations, population sizes are usually positively correlated with migration rates (Gaston 1994, 1996, 1998). Thus, in the case of spatially heterogeneous environment with $s_1 = -s_2$, fixation probabilities in large populations will be smaller than in small populations. By itself, this, however, does not mean that the *rates* of fixation will be smaller as well because large populations have more mutants than small populations.

For neutral alleles, the rate of fixation, R, is equal to the mutation rate, μ. If migration rate in the two-deme system with $s_1 = -s_2$ is large, the alleles will behave as neutral. Therefore, the rate of fixation in a heterogeneous environment in the *high population size–high migration* limit is

$$R_{high} = \mu \tag{15a}$$

In the low migration limit considered by Tachida and Iizuka (1991), the fixation rate is given by Eq. 14. With $4N\mu$ mutations per generation, this gives the *low population size–low migration* limit of the rate of fixation in a heterogeneous environment as

$$R_{low} = \mu \frac{S/2}{1 - e^{-S}} \tag{15b}$$

where $S = 4Ns$. If $S > 1.59$, then $R_{low} > R_{high}$.

Which of the two approximations (Eq. 15a, 15b) will be more general or appropriate and which populations – small or large – will evolve faster? The answers to these questions are expected to depend on how the rate of migration scales with the population size. Figure 3 describes two different hypothetical relationships between N and m. For the convex dependence A, relatively large values of N are compatible with small m. In this case, (moderately) small populations will be in the domain of approximation 15b and will have higher fixation rates than large populations, which will be in the domain of approximation 15a. In other words, for convex dependencies we expect small populations to evolve faster. For example, let $s_1 = -s_2 = 0.005$. In this case, Eq. 11 predicts that a large population with $N = 10000$ and $m = 0.1$ will fix mutations at a rate $R = 4.99\mu$. In a small population with $N = 1000$ and $m = 0.005$, the rate of fixation is $R = 6.58\mu$, which is higher than that for the large population. On the other hand, for the concave dependence B, migration rate m is large even with relatively small values of N, meaning the population is well mixed. In this case only very small populations will be in the domain of approximation (15b). However, because N is small, the fixation rates will be small as well. In other words, for concave dependencies we expect larger populations to evolve faster. For example, in a small population with $N = 1000$ and $m = 0.015$, Eq. 11 predicts that the rate of fixation is $R = 3.10\mu$, which is lower than that for the large population. These examples show that knowledge of the dependence of migration rates on population size is crucial in evaluating the effects of the population size on the rates of evolution.

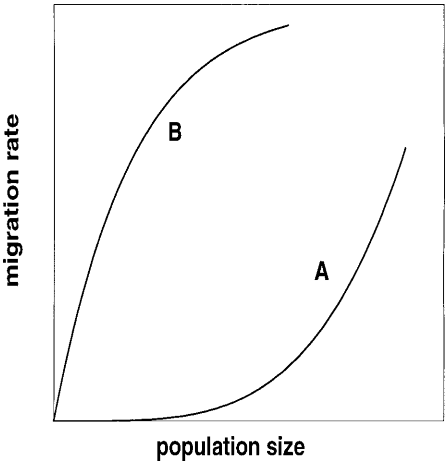


Fig. 3. Two hypothetical dependencies of the migration rate on the population size

Recently, Gillespie (2001) concluded that under certain conditions stochastic fluctuations in allele frequencies are more important in large populations than in small populations. Our results collaborate previous arguments of Ohta (1972) and Eldredge (1995, 2002) that under certain conditions selection is more important in small populations than in large populations. These examples concur with a common knowledge that certain textbook-type wisdoms occasionally require reevaluation.

Acknowledgments S. Gavrilets is grateful to T. Ohta and N. Eldredge for introducing him to the questions approached here, to E. Pollak and J. Gravner for discussions and comments, to the members of a working group organized by N. Eldredge and J.N. Thompson at the National Center for Ecological Analysis and Synthesis (NCEAS), University of California, Santa Barbara, for illuminating discussions, and to M. Kawata for inviting him to the 20th symposium of the Society of Population Ecology. We thank the reviewers for helpful comments. Supported by National Institutes of Health grant GM56693 and by National Science Foundation grant DEB-0111613.

Appendix

To find approximate solutions of Eq. 5, we used singular perturbations techniques (Kevorkian and Cole 1996; Grasman and van Henwaarden 1999). This equation can be rewritten as

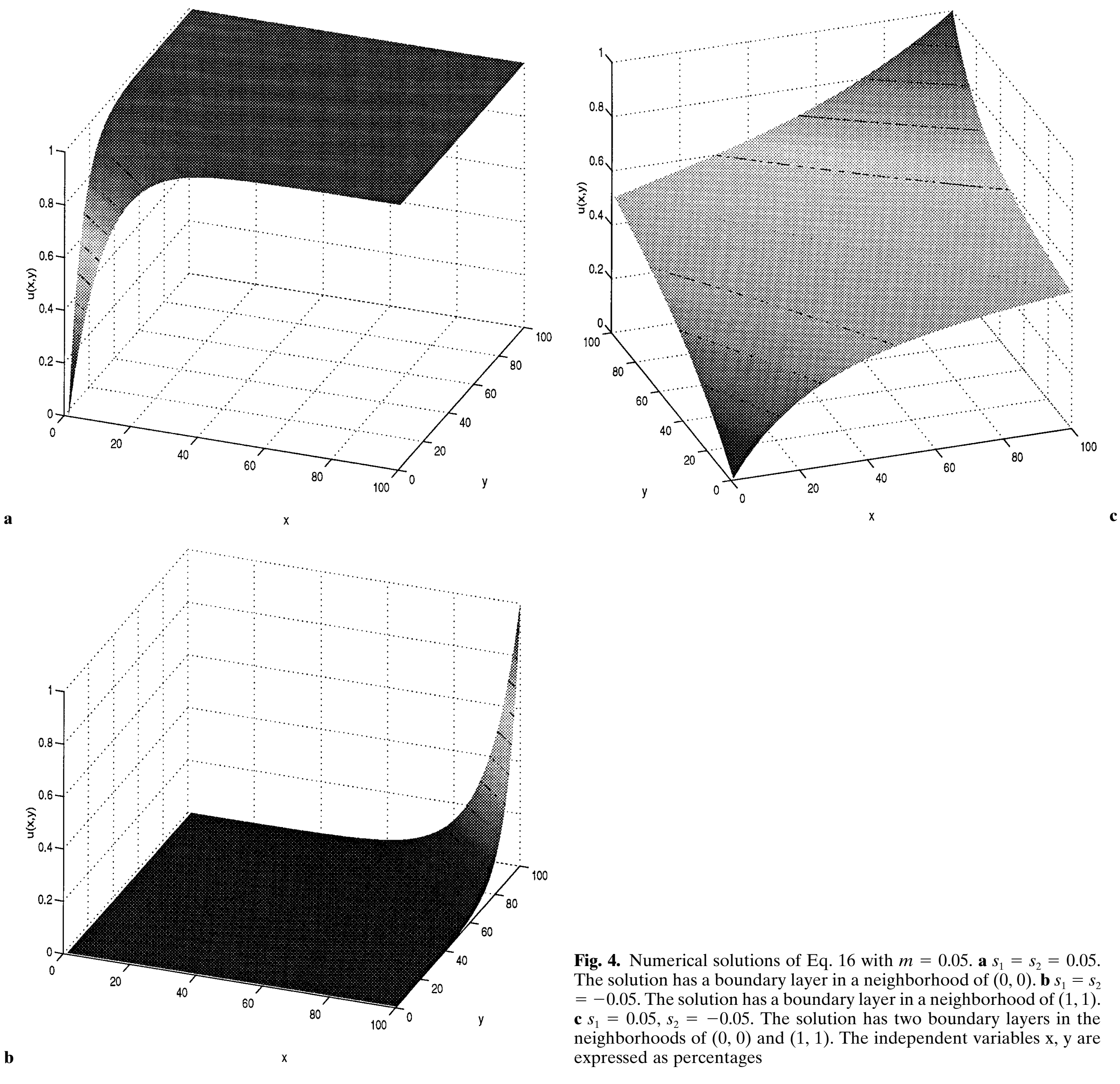


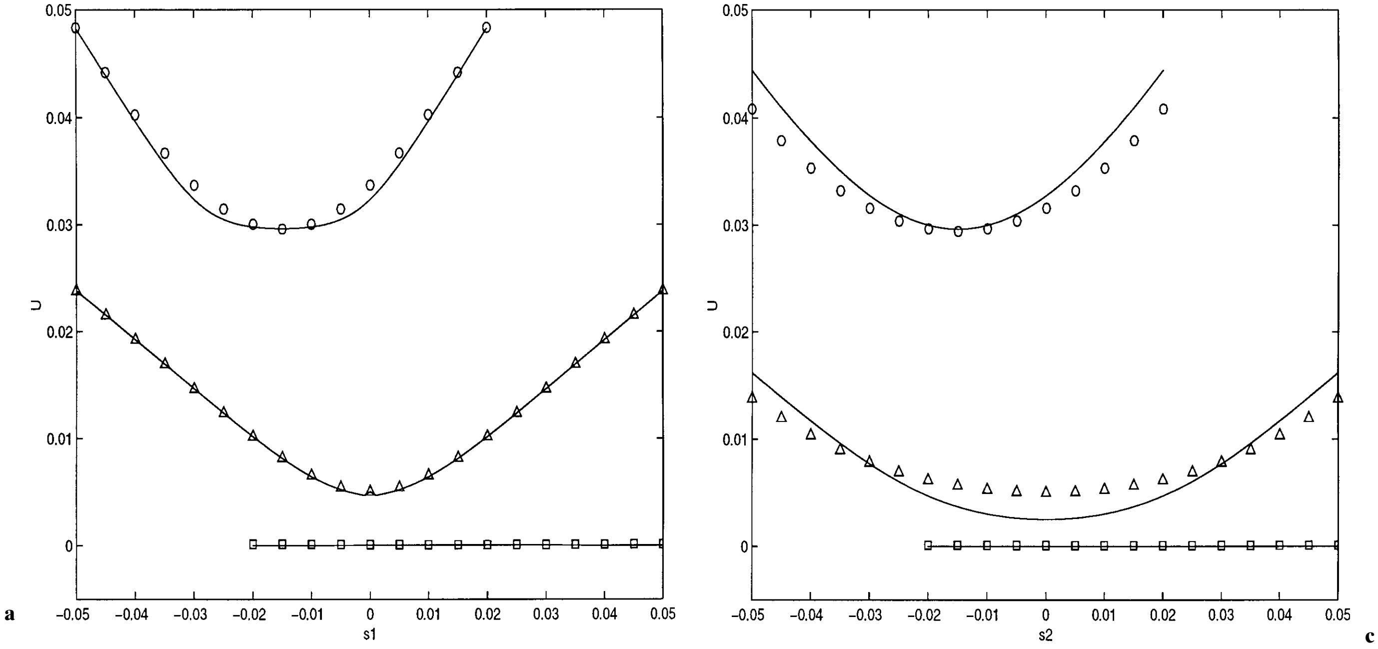
Fig. 4. Numerical solutions of Eq. 16 with $m = 0.05$. **a** $s_1 = s_2 = 0.05$. The solution has a boundary layer in a neighborhood of (0, 0). **b** $s_1 = s_2 = -0.05$. The solution has a boundary layer in a neighborhood of (1, 1). **c** $s_1 = 0.05$, $s_2 = -0.05$. The solution has two boundary layers in the neighborhoods of (0, 0) and (1, 1). The independent variables x, y are expressed as percentages

$$\varepsilon^2 x(1-x)\frac{\partial^2 u}{\partial x^2} + \varepsilon^2 y(1-y)\frac{\partial^2 u}{\partial y^2} + \left[s_1 x(1-x) + m(y-x)\right]\frac{\partial u}{\partial x} + \left[s_2 y(1-y) + m(x-y)\right]\frac{\partial u}{\partial y} = 0 \tag{16}$$

where $\varepsilon^2 = 1/(4N)$.

Deterministic equilibrium (1, 1) is stable. Assume that the values of the parameters guarantee the stability of equilibrium (1, 1) in the deterministic case. If $\varepsilon^2 \ll 1$, we expect that $u \approx 1$ for x and y away from the point (0, 0) and that the solution u has a boundary layer in a neighborhood of this point (see Fig. 4a). We introduce new variables ξ and η such that $x = \varepsilon^\alpha \xi$, $y = \varepsilon^\alpha \eta$. Note that $\partial/\partial x = \varepsilon^{-\alpha}\partial/\partial\xi$, $\partial/\partial y = \varepsilon^{-\alpha}\partial/\partial\eta$, $\partial^2/\partial x^2 = \varepsilon^{-2\alpha}\partial^2/\partial\xi^2$, $\partial^2/\partial y^2 = \varepsilon^{-2\alpha}\partial^2/\partial\eta^2$, and $x - y = \varepsilon^\alpha(\xi - \eta)$. Substituting into Eq. 16, one finds that all terms have the same order in ε if $\alpha = 2$ and that to the dominant order this equation can be approximated as

$$\xi\frac{\partial^2 u}{\partial \xi^2} + \eta\frac{\partial^2 u}{\partial \eta^2} + \left[(s_1 - m)\xi + m\eta\right]\frac{\partial u}{\partial \xi} + \left[m\xi + (s_2 - m)\eta\right]\frac{\partial u}{\partial \eta} = 0 \tag{17}$$



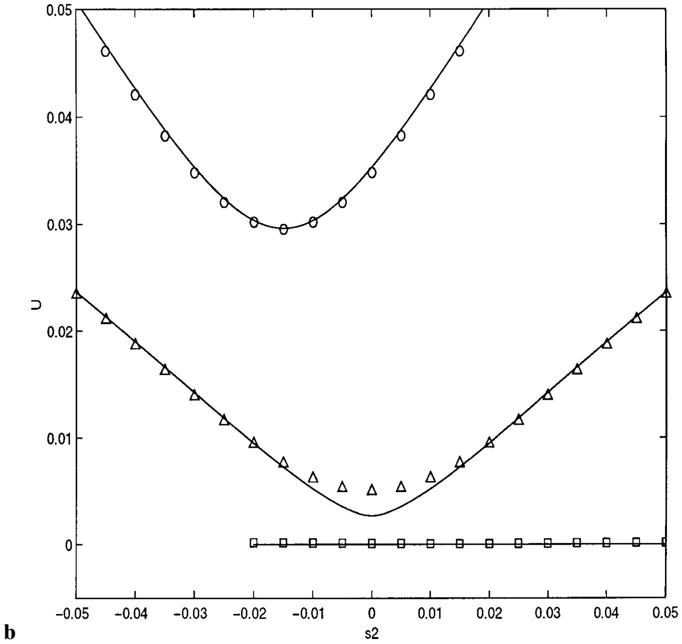


Fig. 5. Probability of fixation of allele **A** for different values of s_2. Numerical solutions are given by symbols: *circles*, allele **A** is advantageous on average with $s_1 + s_2 = 0.02$; *triangles*, allele **A** is neutral on average with $s_1 + s_2 = 0$; *squares*, allele **A** is deleterious on average with $s_1 + s_2 = -0.02$. The corresponding analytical approximations are given by *solid lines*. **a** $m = 0.0005$; **b** $m = 0.005$; **c** $m = 0.05$

We will use the *Ansatz*

$$u = c_1 + c_2 \exp(-a\xi - b\eta) \tag{18}$$

where coefficients $a > 0$ and $b > 0$ are chosen to satisfy Eq. 17 and coefficients c_1 and c_2 are chosen to satisfy the boundary conditions. Substituting this *Ansatz* into Eq. 17, one finds the equality

$$\begin{aligned} \exp(-a\xi - b\eta)\big[&\xi(a^2 - as_1 + am - bm) \\ &+ \eta(b^2 - bs_2 + bm - am)\big] = 0 \end{aligned} \tag{19}$$

This result shows that a and b must be positive roots of the system of nonlinear algebraic equations:

$$a^2 - as_1 + m(a - b) = 0 \tag{20a}$$

$$b^2 - bs_2 + m(b - a) = 0 \tag{20b}$$

Matching boundary conditions at $x = y = 0$ and $x = y = 1$, one finds that

$$c_1 + c_2 = 0,\ c_1 + c_2 \exp(-4N(a + b)) = 1$$

leading to solution 7.

Deterministic equilibrium (0, 0) is stable. If the parameters are such that the deterministic equilibrium (0, 0) is stable, then the boundary layer is located in a neighborhood of the point (1, 1) (see Fig. 4b). In this case the appropriate variable change is $x = 1 - \varepsilon^{\alpha}\xi$, $y = 1 - \varepsilon^{\alpha}\eta$ with $\alpha = 2$. Note that $\partial/\partial x = -\varepsilon^{-\alpha}\partial/\partial\xi$, $\partial/\partial y = -\varepsilon^{-\alpha}\partial/\partial\eta$, $\partial^2/\partial x^2 = \varepsilon^{-2\alpha}\partial^2/\partial\xi^2$, $\partial^2/\partial y^2 = \varepsilon^{-2\alpha}\partial^2/\partial\eta^2$, and $x - y = -\varepsilon^{\alpha}(\xi - \eta)$. The derivations leading to the approximate solution 9 are analogous to those already considered, with the difference that the sign of the second terms in Eq. 20 changes to the opposite.

Deterministic equilibrium (p_1^*, p_2^*) is stable. Let the parameter values guarantee the existence of a polymorphic equilibrium. We expect the solution of Eq. 16 to have two boundary layers [in the neighborhoods of the points (0, 0) and (1, 1), respectively] similar to those considered above and to be close to a constant for other values of x and y (see Fig. 4c). If $s_1 = -s_2$, then from the symmetry it follows that the constant must be equal to 1/2, leading to the approximate solution 11. If $s_1 \neq -s_2$, then the constant must be close to 0 or 1 depending on whether $s_1 + s_2$ is negative or positive, leading to approximate solutions 7 and 9.

Figure 5 shows that the approximate solutions are rather precise.

References

Barton NH (1993) The probability of fixation of a favoured allele in a subdivided population. Genet Res 62:149–157

Bell G (1997) Selection. The mechanism of evolution. Chapman and Hall, New York

Cherry JL (1998) Should we expect substitution rate to depend on population size? Genetics 150:911–919

Cooper VS, Lenski RE (2000) The population genetics of ecological specialization in evolving *Escherichia coli* populations. Nature (Lond) 407:736–739

Coyne JA, Barton NH, Turelli M (1997) A critique of Sewall Wright's shifting balance theory of evolution. Evolution 51:643–671

Coyne JA, Barton NH, Turelli M (1998) Is Wright's shifting balance process important in evolution? Evolution 54:306–317

Crow JF, Kimura M (1970) An introduction to population genetic theory. Harper and Row, New York

Dempster ER (1955) Maintenance of genetic heterogeneity. Cold Spring Harbor Symp Quant Biol 20:25–32

Eldredge N (1995) Reinventing Darwin. The great debate at the high table of evolutionary theory. Wiley, New York

Eldredge N (2002) The sloshing bucket: how the physical realm controls evolution. In: Crutchfield J, Schuster P (eds) Towards a comprehensive dynamics of evolution: exploring the interplay of selection, neutrality, accident, and function. Oxford University Press, New York (in press)

Eldredge N, Gould SJ (1974) Reply to Hecht. Evol Biol 7:303–308

Felsenstein J (1976) The theoretical population genetics of variable selection and migration. Annu Rev Genet 10:253–280

Futuyma DJ (1987) On the role of species in anagenesis. Am Nat 130:465–473

Futuyma DJ, Moreno G (1988) The evolution of ecological specialization. Annu Rev Ecol Syst 19:207–233

Gaston KJ (1994) Rarity. Chapman and Hall, London

Gaston KJ (1996) Species-range-size distributions: patterns, mechanisms and implications. Trends Ecol Evol 11:197–201

Gaston KJ (1998) Species-range size distributions: products of speciation, extinction and transformation. Philos Trans R Soc Lond B 353:219–230

Gavrilets S (1996) On phase three of the shifting-balance theory. Evolution 50:1034–1041

Gavrilets S (2000) Waiting time to parapatic speciation. Proc R Soc Lond B 267:2483–2492

Gillespie JH (1999) The role of population size in molecular evolution. Theor Popul Biol 55:145–156

Gillespie JH (2001) Is the population size of a species relevant to its evolution? Evolution 55:2161–2169

Grasman J, van Henwaarden OA (1999) Asymptotic methods for the Fokker–Plank equation and the exit problem in applications. Springer, Berlin

Hedrick PW (1986) Genetic polymorphism in heterogeneous environments: a decade later. Annu Rev Ecol Syst 17:536–566

Hedrick PW, Givenan ME, Ewing EP (1976) Genetic polymorphism in heterogeneous environments. Annu Rev Ecol Syst 7:1–32

Karlin S (1982) Classification of selection-migration structures and conditions for a protected polymorphism. Evol Bio 14:61–204

Kevorkian J, Cole JD (1996) Multiple scale and singular perturbation methods. Springer, Verlag, New York

Kimura M (1983) The neutral theory of molecular evolution. Cambridge University Press, New York

Lande R (1979) Effective deme size during long-term evolution estimated from rates of chromosomal rearrangement. Evolution 33:234–251

Levene H (1953) Genetic equilibrium when more than one ecological niche is available. Am Nat 87:331–333

Maruyama T (1970) On the fixation probability of mutant genes in a subdivided population. Genet Res 15:221–225

Mitton JB (1997) Selection in natural populations. Oxford University Press, Oxford

Nagylaki T (1980) The strong migration limit in geographically structured populations. J Math Biol 9:101–114

Ohta T (1972) Population size and rate of evolution. J Mol Evol 1:305–314

Pollak E (1966) On the survival of a gene in a subdivided population. J App Probabil 3:142–155

Pollak E (1972) Some effects of two types of migration on the survival of a gene. Biometrics 28:385–400

Slatkin M (1981) Fixation probabilities and fixation times in a subdivided population. Evolution 35:477–488

Stratton DA, Bennington CC (1998) Fine-grained spatial and temporal variation in selection does not maintain genetic variation in *Erigeron annuus*. Evolution 52:678–691

Tachida H, Iizuka M (1991) Fixation probability in spatially changing environments. Genet Res 58:243–251

Van Tienderen PH (1991) Evolution of generalists and specialists in a spatially heterogeneous environments. Evolution 45:1317–1331

Wade MJ, Goodnight CJ (1998) The theories of Fisher and Wright in the context of metapopulations: when nature does many small experiments. Evolution 52:1537–1553