

AN INTRODUCTION TO MIGRATION-SELECTION PDE MODELS

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ABSTRACT. This expository article concerns a system of semilinear parabolic partial differential equations that describes the evolution of the gene frequencies at a single locus under the joint action of migration and selection. We shall review mathematical techniques suited for the models under investigation; discuss some of the main mathematical results, including most recent developments; and also propose some open problems.

1. Introduction. This expository article concerns partial differential equation (PDE) models that describe the evolution of the gene frequencies at a single locus under the joint action of migration and selection. The mathematical models are semilinear parabolic partial differential equations (for two alleles) and systems of semilinear parabolic equations (for three or more alleles). The main goals of this paper are to (i) review some mathematical techniques that are suited for these models; (ii) discuss some of the main mathematical results in this area, including recent developments; and (iii) propose and discuss some open problems. These notes are prepared for mathematically oriented readers who have background in differential equations and are interested in studying mathematical population genetics. We hope that these notes will serve the purpose of attracting some readers to work on this area.

This paper is based on a previous survey article [30] but with some significant differences: (i) The current article is completely focused on PDE models (continuous space and continuous time), whereas [30] is more extensive and also includes discrete models (discrete space and discrete time) and patch models (discrete space and continuous time). (ii) This paper includes a review of some mathematical techniques

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for these models, which are scattered in the literature. (iii) The present article includes some more recent developments in this area [17, 26, 27, 28, 31].

2. The mathematical models. We consider a single locus with alleles A_i , $1 \leq i \leq n$. Loosely speaking, an allele is a piece of DNA, and a locus is the location of a particular allele. For example, at the *ABO* locus for human blood type, there are three main alleles, denoted by A , B , and O . Correspondingly, there are six genotypes (AA , AB , AO , BB , BO , and OO) and four phenotypes (A , B , O , and AB). Note that the phenotype A includes two genotypes (AA and AO) and the phenotype B also includes two genotypes (BB and BO). We say that alleles A and B are dominant over allele O , or allele O is recessive to alleles A and B . The phenotype AB corresponds exactly to the genotype AB , and we say that alleles A and B are codominant. The concepts of complete dominance and no dominance will be defined precisely in the next subsection, when we introduce the selection coefficients of genotypes.

2.1. Discrete-time selection model. The main reference for this subsection is [24]. Let $P_i(t)$ denote the frequency of allele A_i in a population in generation t , where n denotes the number of alleles, and $i = 1, 2, \dots, n$, and $t \in \{0, 1, 2, \dots\}$.

Let the constant w_{ij} denote the fitness of genotype A_iA_j , where $1 \leq i, j \leq n$. Biologically, the fitness of a genotype is defined as the product of the survival probability from zygote to adult and the number of offspring. Here, we assume that there are no fertility differences and $w_{ij} = w_{ji} > 0$, i.e., we do not distinguish genotypes A_iA_j and A_jA_i .

Examples. (a) No-dominance series: $w_{ij} = s_i + s_j$ for every $i, j \in \{1, 2, \dots, n\}$. Thus, allelic fitnesses are additive. (b) Complete-dominance series: $w_{ij} = s_i$ for every $i, j \in \{1, 2, \dots, n\}$. Given any $i < j$, allele A_i is dominant over allele A_j , i.e., the phenotype is determined solely by A_i .

Let $w_i(t) = \sum_{j=1}^n w_{ij}P_j(t)$ denote the marginal fitness of allele A_i in generation t , and let $\bar{w}(t) = \sum_{j=1}^n w_jP_j$ denote the mean fitness of the population. Marginal fitness is the average fitness of all individuals that carry a copy of A_i .

The discrete-time selection model is given by

$$P_i(t+1) = \frac{w_i(t)}{\bar{w}(t)}P_i(t), \quad t \geq 0. \quad (2.1)$$

The model (2.1) looks simple, but is rather interesting, and we shall make a few comments. If some allele is not present in the population initially, it will never be present. Hence, without loss of generality, we simply assume that $P_i(0) > 0$ for every $i = 1, 2, \dots, n$. Then it follows from (2.1) that $P_i(t) > 0$ for every $i = 1, 2, \dots, n$ and $t \geq 1$.

(1) It always holds that $\sum_{i=1}^n P_i(t) = 1$ for $t \geq 1$. Indeed, from (2.1) we have

$$\sum_{i=1}^n P_i(t+1) = \sum_{i=1}^n \frac{w_i(t)P_i(t)}{\bar{w}(t)} = \frac{\bar{w}(t)}{\bar{w}(t)} = 1.$$

The definition of w_i and \bar{w} require the initial condition, $\sum_{i=1}^n P_i(0) = 1$, but this was not used in the preceding line.

(2) It always holds that $\bar{w}(t+1) \geq \bar{w}(t)$ for $t \geq 0$. This ensures that the average fitness of the population increases and less fit alleles will be eliminated. The following proof of the monotonicity of the average fitness is due to Kingman [11], who

refers to earlier proofs.

$$\begin{aligned}
\bar{w}(t+1) &= \sum_{i,j}^n w_{ij} P_i(t+1) P_j(t+1) \\
&= \sum_{i,j}^n w_{ij} \cdot \frac{w_i(t) P_i(t)}{\bar{w}(t)} \cdot \frac{w_j(t) P_j(t)}{\bar{w}(t)} \\
&= \frac{1}{\bar{w}^2} \sum_{i,j=1}^n w_{ij} P_i P_j w_i w_j \\
&= \frac{1}{\bar{w}^2} \sum_{i,j=1}^n w_{ij} P_i P_j \cdot \left(\sum_{l=1}^n w_{il} P_l \right) \cdot \frac{w_j + w_j}{2} \\
&= \frac{1}{\bar{w}^2} \sum_{i,j,l=1}^n w_{ij} w_{il} P_i P_j P_l \cdot \frac{w_j + w_j}{2} \\
&= \frac{1}{\bar{w}^2} \sum_{i,j,l=1}^n w_{ij} w_{il} P_i P_j P_l \cdot \frac{w_j + w_l}{2} \\
&\geq \frac{1}{\bar{w}^2} \sum_{i,j,l=1}^n w_{ij} w_{il} P_i P_j P_l \cdot \sqrt{w_j w_l} \\
&= \frac{1}{\bar{w}^2} \sum_{i=1}^n P_i \left[\sum_{j,l} w_{ij} w_{il} P_j P_l \cdot \sqrt{w_j w_l} \right] \\
&= \frac{1}{\bar{w}^2} \sum_{i=1}^n P_i \left[\sum_j w_{ij} P_j \cdot \sqrt{w_j} \right]^2 \\
&\geq \frac{1}{\bar{w}^2} \left(\sum_{i=1}^n P_i \left[\sum_j w_{ij} P_j \cdot \sqrt{w_j} \right] \right)^2 \quad (\text{Jensen's inequality}) \\
&= \frac{1}{\bar{w}^2} \left(\sum_{j=1}^n P_j \sqrt{w_j} \left[\sum_i w_{ij} P_i \right] \right)^2 \\
&= \frac{1}{\bar{w}^2} \left(\sum_{j=1}^n P_j w_j^{3/2} \right)^2 \\
&\geq \frac{1}{\bar{w}^2} \left(\sum_{j=1}^n P_j w_j \right)^3 \quad (\text{Jensen's inequality}) \\
&= \frac{1}{\bar{w}^2} \bar{w}^3 \\
&= \bar{w}(t).
\end{aligned}$$

The first inequality above is an equality if and only if w_i is independent of i for every i , which is precisely the necessary and sufficient condition for (2.1) to be at equilibrium.

(3) Given any initial data, $P(t) = (P_1(t), \dots, P_n(t))$ converges to some equilibrium as $t \rightarrow \infty$. This nontrivial result was established by Lyubich et al. [18, 19]. If the equilibria are isolated, Result 2 above immediately implies convergence of $P(t)$ as $t \rightarrow \infty$. The importance of the theorem of Lyubich et al. is that $P(t)$ still converges when there is a manifold of equilibria. The proof uses the monotonicity of $\bar{w}(t)$ and estimates of its single-generation change.

Remark 2.1. Suppose that $w_{ij} = s_i + s_j$, $1 \leq i, j \leq n$, and $s_1 > s_2 > \dots > s_n$. Then $\lim_{t \rightarrow \infty} P_1(t) = 1$ and $\lim_{t \rightarrow \infty} P_i(t) = 0$, $2 \leq i \leq n$. To see this, note that if $0 < P_1(t) < 1$, then $P_i(t) > 0$ for some $i > 1$, where $P_1(t+1) > P_1(t)$. Therefore, $P_1(t) \rightarrow 1$ as $t \rightarrow \infty$, which implies that $P_i(t) \rightarrow 0$ for every $i = 2, \dots, n$ as $t \rightarrow \infty$.

2.2. Continuous-time selection model. The main reference for this subsection is [24].

If we assume that selection is weak, i.e., $w_{ij} = 1 + \epsilon r_{ij}$, where ϵ is positive and sufficiently small, then

$$w_i = 1 + \epsilon \sum_j r_{ij} P_j$$

and

$$\bar{w} = 1 + \epsilon \sum_j r_{ij} P_i P_j.$$

Let $t = [\tau/\epsilon]$, i.e., the integer part of τ/ϵ . Set $q_i(\tau) = P_i(t)$. Then

$$\begin{aligned} \frac{q_i(\tau + \epsilon)}{q_i(\tau)} &= \frac{P_i(t+1)}{P_i(t)} \\ &= \frac{w_i(t)}{\bar{w}(t)} \\ &= \frac{1 + \epsilon \sum_j r_{ij} P_j}{1 + \epsilon \sum_{i,j} r_{ij} P_i P_j} \\ &= 1 + \epsilon \left(\sum_j r_{ij} q_j - \sum_{i,j} r_{ij} q_i q_j \right) + O(\epsilon^2) \end{aligned}$$

as $\epsilon \rightarrow 0$. Hence,

$$\frac{q_i(\tau + \epsilon) - q_i(\tau)}{\epsilon} = q_i \left(\sum_j r_{ij} q_j - \sum_{i,j} r_{ij} q_i q_j \right) + O(\epsilon).$$

Letting $\epsilon \rightarrow 0$ in the above equation, we obtain the continuous-time selection model for the evolution of the gene frequencies:

$$\frac{dq_i}{d\tau} = q_i \left(\sum_j r_{ij} q_j - \sum_{i,j} r_{ij} q_i q_j \right), \quad \tau > 0. \quad (2.2)$$

It is easy to show that $\bar{r} := \sum_{i,j} r_{ij} q_i q_j$ is monotone increasing in time. To this end, set $r_i = \sum_j r_{ij} q_j$. Note that $\bar{r} = \sum_i r_i q_i$. Then, using the symmetry of r_{ij} , we

obtain

$$\begin{aligned} \frac{d\bar{r}}{d\tau} &= 2 \sum_{i,j} r_{ij} q_j \frac{dq_i}{dt} \\ &= 2 \sum_i r_i q_i (r_i - \bar{r}) \\ &= 2 \sum_i q_i [(r_i - \bar{r}) + \bar{r}] (r_i - \bar{r}) \\ &= 2 \sum_i q_i (r_i - \bar{r})^2 \geq 0. \end{aligned}$$

From (2.2) we infer that equality holds if and only if the population is at equilibrium.

2.3. PDE models for migration-selection. The main reference for this section is [23].

Let $p_i(x, t)$ denote the frequency of allele A_i at location x and time t , where $x \in \Omega$, Ω is a bounded, open domain in \mathbb{R}^N with C^2 boundary $\partial\Omega$, and ν is the outward unit normal vector on $\partial\Omega$. Set $P(x, t) = (p_1(x, t), \dots, p_n(x, t))$. Let $r_{ij}(x)$ denote the selection coefficient of genotype $A_i A_j$;

$$r_i(x, P) = \sum_j r_{ij} p_j$$

is the marginal selection coefficient of allele A_i ; and

$$\bar{r}(x, P) = \sum_{i,j} r_{ij} p_i p_j$$

is the mean selection coefficient of the population. If we rescale from τ to t , the contribution of selection is given by

$$S_i(x, P) := \lambda p_i (r_i - \bar{r}),$$

where $\lambda > 0$ is the ratio of the selection intensity to that of migration. The PDE model for the evolution of the gene frequencies under the joint action of migration and selection is given by (see [23] for the derivation)

$$\begin{cases} \frac{\partial p_i}{\partial t} = \sum_{\alpha,\beta=1}^N V_{\alpha\beta}(x) \frac{\partial^2 p_i}{\partial x_\alpha \partial x_\beta} + b(x) \cdot \nabla p_i + S_i(x, P) & \text{in } \Omega \times (0, \infty), \\ \nu \cdot V \nabla p_i = 0 & \text{on } \partial\Omega \times (0, \infty), \\ p_i(x, 0) \geq 0, \quad p_i(x, 0) \not\equiv 0, \quad \sum_j p_j(x, 0) \equiv 1 & \text{in } \Omega. \end{cases} \tag{2.3}$$

Note that the vector b does not appear in the boundary condition. This is due to the fact that it is the density of individuals, not the frequency of A_i that disperses. The diffusion-coefficient matrix is positive definite for every $x \in \Omega$. We refer to [23] for more details.

If we assume that $V_{\alpha\beta} = \delta_{\alpha\beta}$ and $b = 0$, then (2.3) becomes

$$\begin{cases} \frac{\partial p_i}{\partial t} = \Delta p_i + S_i(x, P) & \text{in } \Omega \times (0, \infty), \\ \nu \cdot \nabla p_i = 0 & \text{on } \partial\Omega \times (0, \infty), \\ p_i(x, 0) \geq 0, \quad p_i(x, 0) \not\equiv 0, \quad \sum_j p_j(x, 0) \equiv 1 & \text{in } \Omega, \end{cases} \tag{2.4}$$

where Δ is the Laplace operator in the Euclidean space \mathbb{R}^N . If we further assume that r_{ij} , $V_{\alpha\beta}$, and b are Hölder-continuous in $\bar{\Omega}$ and the initial data $p_i(x, 0)$ are continuous in $\bar{\Omega}$, then (2.4) has a unique solution $P(x, t)$ that exists for all time, $p_i \in C(\bar{\Omega} \times [0, \infty)) \cap C^{2,1}(\bar{\Omega} \times (0, \infty))$, $p_i(x, t) \geq 0$, and $\sum_i p_i(x, t) \equiv 1$ for every $x \in \Omega$ and $t > 0$. To see the last assertion, observe that

$$\begin{cases} \frac{\partial}{\partial t} \left(\sum_i p_i \right) = \Delta \left(\sum_i p_i \right) + \lambda \bar{r} \left[1 - \left(\sum_i p_i \right) \right] & \text{in } \Omega \times (0, \infty), \\ \nu \cdot \nabla \left(\sum_i p_i \right) = 0 & \text{on } \partial\Omega \times (0, \infty), \\ \sum_i p_i(x, 0) \equiv 1. \end{cases} \tag{2.5}$$

By the uniqueness of the solutions of linear parabolic equations [6], $\sum_i p_i(x, t) \equiv 1$ for every $x \in \Omega$ and $t > 0$. By the maximum principle for parabolic equations [34], if $p_i(x, 0) \not\equiv 0$, then $p_i(x, t) > 0$ for every $x \in \Omega$ and $t > 0$. Hence, without loss of generality, we assume that $p_i(x, t) > 0$ for every i , $x \in \bar{\Omega}$, and $t \geq 0$.

In general, the dynamics of (2.4) are quite complex even for rather simple selection coefficients. To motivate our discussion, consider the case without dominance: $r_{ij}(x) = s_i(x) + s_j(x)$. Define

$$\begin{aligned} \Omega_+ &= \{x \in \Omega : s_1(x) > s_2(x) > \dots > s_n(x)\}, \\ \Omega_- &= \{x \in \Omega : s_1(x) < s_2(x) < \dots < s_n(x)\}, \\ \Omega_0 &= \{x \in \Omega : s_1(x) = s_2(x) = \dots = s_n(x)\}. \end{aligned}$$

Assume that $\Omega = \Omega_+ \cup \Omega_- \cup \Omega_0$ and consider the selection model

$$\frac{dp_i}{dt} = \lambda p_i \left(s_i - \sum_j s_j p_j \right), \quad t > 0, \quad p_i(x, 0) = p_0(x) > 0.$$

We established above that for each $x \in \Omega_+$,

$$\lim_{t \rightarrow \infty} p_i(x, t) = \begin{cases} 1, & i = 1, \\ 0, & 2 \leq i \leq n, \end{cases}$$

and for each $x \in \Omega_-$,

$$\lim_{t \rightarrow \infty} p_i(x, t) = \begin{cases} 1, & i = n, \\ 0, & 1 \leq i \leq n - 1. \end{cases}$$

We call alleles A_1 and A_n extreme alleles because they are the fittest alleles in Ω_+ and Ω_- , respectively. We call alleles A_i , $2 \leq i \leq n$, intermediate alleles because they are nowhere the fittest and nowhere the least fit in the habitat. If migration is present, the following two questions naturally arise. Can extreme alleles be maintained in the habitat? Can intermediate alleles be maintained? These are some of the principal questions that will be addressed in next two sections.

3. Migration-selection model for two alleles. For two alleles, since $p_2 = 1 - p_1$, therefore

$$S_1(x, P) = \lambda p_1 p_2 [(r_{11} - r_{12})p_1 + (r_{12} - r_{22})p_2].$$

The following four cases are of particular interest.

(a) No dominance: $r_{ij} = s_i + s_j$:

$$S_1(x, P) = \lambda(s_1 - s_2)p_1 p_2.$$

(b) Allele A_1 is dominant and A_2 is recessive: $r_{12} = r_{11}$:

$$S_1(x, P) = \lambda(r_{11} - r_{22})p_1p_2^2.$$

(c) Allele A_1 is recessive: $r_{12} = r_{22}$:

$$S_1(x, P) = \lambda(r_{11} - r_{22})p_1^2p_2.$$

(d) $r_{11}(x) = g(x)$, $r_{12}(x) = \kappa g(x)$, and $r_{22}(x) = -g(x)$:

$$S_1(x, P) = \lambda g(x)p_1p_2(1 + \kappa - 2\kappa p_1).$$

Since (a)–(c) are special cases of (d), it suffices to consider (d). If we abbreviate $p_1(x, t)$ as $p(x, t)$, we have the following model for two alleles:

$$\begin{cases} \frac{\partial p}{\partial t} = \Delta p + \lambda g(x)p(1 - p)(1 + \kappa - 2\kappa p) & \text{in } \Omega \times (0, \infty), \\ \nu \cdot \nabla p = 0 & \text{on } \partial\Omega \times (0, \infty), \\ 0 < p(x, 0) < 1 & \text{in } \bar{\Omega}. \end{cases} \tag{3.1}$$

3.1. No dominance. In this subsection we consider (3.1) with $\kappa = 0$, i.e.,

$$\begin{cases} \frac{\partial p}{\partial t} = \Delta p + \lambda g(x)p(1 - p) & \text{in } \Omega \times (0, \infty), \\ \nu \cdot \nabla p = 0 & \text{on } \partial\Omega \times (0, \infty), \\ 0 < p(x, 0) < 1 & \text{in } \bar{\Omega}. \end{cases} \tag{3.2}$$

For some of the earliest works concerning (3.2) and its variants (e.g., in unbounded habitats), see [5, 20, 21, 22]. It was demonstrated in [5] that the following linear eigenvalue problem with indefinite weight plays a crucial role in understanding the dynamics of (3.2):

$$\begin{cases} -\Delta\varphi = \lambda g(x)\varphi & \text{in } \Omega, \\ \frac{\partial\varphi}{\partial\nu} = 0 & \text{on } \partial\Omega, \quad \varphi > 0 & \text{in } \Omega. \end{cases} \tag{3.3}$$

We say that λ is a principal eigenvalue of (3.3) if (3.3) has a solution. Clearly, zero is always a principal eigenvalue of (3.3) with positive constants as its corresponding eigenfunctions. However, only positive principal eigenvalues of (3.3) are relevant in analyzing the dynamics of (3.2). In this connection, we have

Theorem 3.1. *Suppose that g is not identically zero. Then (3.3) has a positive eigenvalue if and only if g changes sign in Ω and*

$$\int_{\Omega} g(x) dx < 0.$$

Proof. We first establish necessity. If (3.3) has a positive eigenvalue with eigenfunction $\varphi > 0$ in Ω , then by the strong maximum principle for elliptic equations [34], we have $\varphi > 0$ in $\bar{\Omega}$. Hence, dividing (3.3) by φ and integrating the result in Ω , we obtain

$$\int_{\Omega} g dx = \frac{1}{\lambda} \int_{\Omega} \frac{-\Delta\varphi}{\varphi} dx = -\frac{1}{\lambda} \int_{\Omega} \frac{|\nabla\varphi|^2}{\varphi^2} dx < 0,$$

where the last inequality is strict because φ is not a constant function (if φ were a constant, then $g \equiv 0$, which contradicts our assumption). Furthermore, integrating (3.3) in Ω , we find $\int_{\Omega} g\varphi dx = 0$, which together with the positivity of φ , implies that g must change sign.

For sufficiency, define

$$\lambda_1(g) := \inf_{\psi \in \mathcal{S}} \frac{\int_{\Omega} |\nabla \psi|^2 dx}{\int_{\Omega} g \psi^2 dx},$$

where the set \mathcal{S} is given by $\mathcal{S} = \{\psi \in W^{1,2}(\Omega) : \int_{\Omega} g \psi^2 dx > 0\}$. Since g changes sign, the set \mathcal{S} is nonempty. Since $\int_{\Omega} g dx < 0$, therefore $\lambda_1(g)$ is strictly positive. One can further show that $\lambda_1(g)$ is attained by some function $\psi > 0$ in Ω , and that ψ satisfies

$$\Delta \psi + \lambda_1(g)g\psi = 0 \quad \text{in } \Omega$$

and $\partial\psi/\partial\nu = 0$. □

The complete proof of Theorem 3.1 can be found in [2, 3, 9], and its generalization appears in [37].

It is known that if the principal eigenvalue $\lambda_1(g)$ exists, it is simple and its corresponding eigenfunction can be chosen positive in $\bar{\Omega}$. Moreover, if λ is a positive eigenvalue of (3.3), then $\lambda \geq \lambda_1(g)$. Hence, in the literature $\lambda_1(g)$ is sometimes called the smallest positive eigenvalue of (3.3).

Theorem 3.2. *Suppose that $\int_{\Omega} g dx < 0$ and g changes sign in Ω . If $\lambda \leq \lambda_1(g)$, the equilibrium $p \equiv 0$ of (3.2) is globally asymptotically stable, provided that the initial data are nonnegative and not identically zero. If $\lambda > \lambda_1(g)$, then (3.2) has a unique positive equilibrium satisfying $p^* < 1$ in $\bar{\Omega}$, which is globally asymptotically stable.*

Remark 3.3. Suppose that g changes sign in Ω . If $\int_{\Omega} g dx \geq 0$, the dynamics of (3.2) is also completely determined: (i) If $\int_{\Omega} g dx = 0$, then for every $\lambda > 0$, the problem (3.2) has a unique nontrivial equilibrium, which is globally asymptotically stable. (ii) If $\int_{\Omega} g dx > 0$, there exists $\lambda^* > 0$ such that if $0 < \lambda \leq \lambda^*$, then $p \equiv 1$ is globally asymptotically stable, and if $\lambda > \lambda^*$, then (3.2) has a unique nontrivial equilibrium, which is globally asymptotically stable.

In the following, we discuss some of the main steps in the proof of Theorem 3.2.

3.1.1. *Local stability of the equilibrium $p \equiv 0$.* Let σ_1 denote the smallest eigenvalue of

$$\begin{cases} -\Delta \varphi - \lambda g(x)\varphi = \sigma \varphi & \text{in } \Omega, \\ \frac{\partial \varphi}{\partial \nu} = 0 & \text{on } \partial \Omega. \end{cases} \tag{3.4}$$

It is well known that $p \equiv 0$ is stable (in the Lyapunov sense) if $\sigma_1 > 0$ and unstable if $\sigma_1 < 0$. We claim that

$$\sigma_1 \begin{cases} > 0 & \text{if } 0 < \lambda < \lambda_1(g), \\ = 0 & \text{if } \lambda = \lambda_1(g), \\ < 0 & \text{if } \lambda > \lambda_1(g). \end{cases} \tag{3.5}$$

As a consequence of (3.5), the equilibrium $p = 0$ is stable if $0 < \lambda < \lambda_1(g)$ and unstable if $\lambda > \lambda_1(g)$. This local-stability result was first established by Fleming [5]. Here we present a different proof based on the following lemma.

Lemma 3.4. *Suppose that g is a nonconstant function. Then $\sigma_1(\lambda)$ is strictly concave downward.*

Since $\sigma_1(0) = \sigma_1(\lambda_1(g)) = 0$, therefore (3.5) follows directly from Lemma 3.4.

Lemma 3.4 is related to more general results of Kato about the convexity of the spectral radius of bounded linear operators with respect to some parameters [10].

Next, we present two different proofs of Lemma 3.4.

First proof. By the variational characterization of $\sigma_1(\lambda)$, for any $\lambda \neq \bar{\lambda}$,

$$\begin{aligned} & \sigma_1\left(\frac{\lambda + \bar{\lambda}}{2}\right) \\ &= \inf_{\{\psi \in H^1, \int_{\Omega} \psi^2 = 1\}} \int_{\Omega} \left[|\nabla \psi|^2 - \frac{\lambda + \bar{\lambda}}{2} g \psi^2 \right] dx \\ &= \inf_{\{\psi \in H^1, \int_{\Omega} \psi^2 = 1\}} \left[\frac{1}{2} \int_{\Omega} (|\nabla \psi|^2 - \lambda g \psi^2) dx + \frac{1}{2} \int_{\Omega} (|\nabla \psi|^2 - \bar{\lambda} g \psi^2) dx \right] \\ &> \frac{1}{2} \inf_{\{\psi \in H^1, \int_{\Omega} \psi^2 = 1\}} \int_{\Omega} (|\nabla \psi|^2 - \lambda g \psi^2) dx + \frac{1}{2} \inf_{\{\psi \in H^1, \int_{\Omega} \psi^2 = 1\}} \int_{\Omega} (|\nabla \psi|^2 - \bar{\lambda} g \psi^2) dx \\ &= \frac{1}{2} [\sigma_1(\lambda) + \sigma_1(\bar{\lambda})], \end{aligned}$$

where the inequality is strict because the eigenfunctions of $\sigma_1(\lambda)$ and $\sigma_1(\bar{\lambda})$ are linearly independent. The above proof is adopted from [32].

Second proof. This proof is in [9]; since it is based on the maximum principle, it works for general second-order elliptic operators. Let φ_{λ} denote the eigenfunction of $\sigma_1(\lambda)$ uniquely determined by $\max_{\bar{\Omega}} \varphi_{\lambda} = 1$, i.e.,

$$\Delta \varphi_{\lambda} + \lambda g \varphi_{\lambda} = -\sigma_1(\lambda) \varphi_{\lambda}.$$

Then φ_{λ} satisfies

$$\Delta(\ln \varphi_{\lambda}) + |\nabla \ln \varphi_{\lambda}|^2 + \lambda g = -\sigma_1(\lambda).$$

Similarly,

$$\Delta(\ln \varphi_{\bar{\lambda}}) + |\nabla \ln \varphi_{\bar{\lambda}}|^2 + \bar{\lambda} g = -\sigma_1(\bar{\lambda})$$

and

$$\Delta(\ln \varphi_{(\lambda+\bar{\lambda})/2}) + |\nabla \ln \varphi_{(\lambda+\bar{\lambda})/2}|^2 + \frac{\lambda + \bar{\lambda}}{2} g = -\sigma_1\left(\frac{\lambda + \bar{\lambda}}{2}\right).$$

Combining these equations, we obtain

$$\begin{aligned} & \Delta\left(\frac{\ln \varphi_{\lambda} + \ln \varphi_{\bar{\lambda}}}{2} - \ln \varphi_{(\lambda+\bar{\lambda})/2}\right) + \frac{|\nabla \ln \varphi_{\lambda}|^2 + |\nabla \ln \varphi_{\bar{\lambda}}|^2}{2} - |\nabla \ln \varphi_{(\lambda+\bar{\lambda})/2}|^2 \\ &= \sigma_1\left(\frac{\lambda + \bar{\lambda}}{2}\right) - \frac{\sigma_1(\lambda) + \sigma_1(\bar{\lambda})}{2}. \end{aligned}$$

Set

$$w = \frac{\ln \varphi_{\lambda} + \ln \varphi_{\bar{\lambda}}}{2} - \ln \varphi_{(\lambda+\bar{\lambda})/2}.$$

Then

$$\begin{aligned} & \frac{|\nabla \ln \varphi_{\lambda}|^2 + |\nabla \ln \varphi_{\bar{\lambda}}|^2}{2} - |\nabla \ln \varphi_{(\lambda+\bar{\lambda})/2}|^2 \\ &= \left| \frac{\nabla \ln \varphi_{\lambda} + \nabla \ln \varphi_{\bar{\lambda}}}{2} \right|^2 + \left| \frac{\nabla \ln \varphi_{\lambda} - \nabla \ln \varphi_{\bar{\lambda}}}{2} \right|^2 - |\nabla \ln \varphi_{(\lambda+\bar{\lambda})/2}|^2 \\ &= b \cdot \nabla w + \left| \frac{\nabla \ln \varphi_{\lambda} - \nabla \ln \varphi_{\bar{\lambda}}}{2} \right|^2, \end{aligned}$$

where

$$b = \frac{1}{2}(\nabla \ln \varphi_\lambda + \nabla \ln \varphi_{\bar{\lambda}}) + \nabla \ln \varphi_{(\lambda+\bar{\lambda})/2}.$$

Hence, w satisfies

$$\begin{cases} \Delta w + b \cdot \nabla w + \left| \frac{\nabla \ln \varphi_\lambda - \nabla \ln \varphi_{\bar{\lambda}}}{2} \right|^2 = \sigma_1 \left(\frac{\lambda + \bar{\lambda}}{2} \right) - \frac{\sigma_1(\lambda) + \sigma_1(\bar{\lambda})}{2} & \text{in } \Omega, \\ \frac{\partial w}{\partial \nu} = 0 & \text{on } \partial\Omega. \end{cases}$$

If $\sigma_1(\frac{\lambda+\bar{\lambda}}{2}) - \frac{\sigma_1(\lambda)+\sigma_1(\bar{\lambda})}{2} \leq 0$, then by the strong maximum principle [34], the function w must be equal to some constant and

$$\left| \frac{\nabla \ln \varphi_\lambda - \nabla \ln \varphi_{\bar{\lambda}}}{2} \right|^2 \equiv 0,$$

which implies that $\varphi_\lambda/\varphi_{\bar{\lambda}}$ is equal to some constant. This is a contradiction. \square

3.1.2. Existence of a nontrivial equilibrium. We apply the supersolution and subsolution method to show that if $\lambda > \lambda_1(g)$, then (3.2) has at least one nontrivial equilibrium p^* , i.e., p^* satisfies $0 < p^* < 1$ in $\bar{\Omega}$. Since $\int_\Omega g \, dx < 0$, from the last two subsections we see that the equilibrium $p \equiv 1$ is unstable for every $\lambda > 0$ and $p \equiv 0$ is unstable for every $\lambda > \lambda_1(g)$.

Subsolution. Let φ_λ denote the eigenfunction of $\sigma_1(\lambda)$ uniquely determined by $\max_{\bar{\Omega}} \varphi_\lambda = 1$. Note that $\sigma_1(\lambda) < 0$ when $\lambda > \lambda_1(g)$. Set $\underline{p} = \epsilon \varphi_\lambda$, where $\epsilon > 0$ is to be determined. Hence,

$$\Delta \underline{p} + \lambda g \underline{p}(1 - \underline{p}) = \Delta(\epsilon \varphi_\lambda) + \lambda g \epsilon \varphi_\lambda(1 - \epsilon \varphi_\lambda) = \epsilon \varphi_\lambda(-\sigma_1 - \epsilon \lambda g \varphi_\lambda) > 0,$$

where the inequality holds if $0 < \epsilon < -\sigma_1(\lambda)/(\lambda \|g\|_\infty)$.

Supersolution. Let ψ_λ denote the eigenfunction of the smallest eigenvalue (denoted as σ_1) of the following linear eigenvalue problem, where ψ_λ is uniquely determined by $\max_{\bar{\Omega}} \psi_\lambda = 1$:

$$\Delta \psi - \lambda g \psi = -\sigma \psi \quad \text{in } \Omega, \quad \frac{\partial \psi}{\partial \nu} = 0 \quad \text{on } \partial\Omega.$$

Note that $\sigma_1 < 0$ for every $\lambda > 0$, since

$$\int_\Omega \sigma_1 \, dx = - \int_\Omega \frac{\Delta \psi_\lambda}{\psi_\lambda} \, dx + \lambda \int_\Omega g \, dx = - \int_\Omega \frac{|\nabla \psi_\lambda|^2}{\psi_\lambda^2} \, dx + \lambda \int_\Omega g \, dx < 0.$$

Set $\bar{p} = 1 - \epsilon \psi_\lambda$. As in the construction of the subsolution, we can show that

$$\Delta \bar{p} + \lambda g \bar{p}(1 - \bar{p}) = \epsilon \psi_\lambda(\sigma_1 - \epsilon \lambda g \psi_\lambda) < 0$$

in Ω , where the inequality holds if $0 < \epsilon < -\sigma_1/(\lambda \|g\|_\infty)$.

By the supersolution and subsolution method [3], for any $\lambda > \lambda_1(g)$, the problem (3.2) has at least one equilibrium p^* satisfying $\underline{p} < p^* < \bar{p}$ in Ω .

3.1.3. Uniqueness of the nontrivial equilibrium. The problem of the uniqueness of the nontrivial equilibrium of (3.2) was settled by Henry [8]. The main ingredient of his proof is the following nondegeneracy result for any nontrivial equilibrium of (3.2).

Lemma 3.5. *Any equilibrium p^* of (3.2) satisfying $0 < p^* < 1$ is asymptotically stable; in particular, it is nondegenerate.*

We present two different proofs of this important result:

First proof. This proof is given in [1]. The linearized stability of p^* is determined by the sign of the smallest eigenvalue (denoted as σ_1) of

$$\Delta\psi + \lambda g(1 - 2p^*)\psi = -\sigma\psi \quad \text{in } \Omega, \quad \frac{\partial\psi}{\partial\nu} = 0 \quad \text{on } \partial\Omega.$$

Let $\psi_1 > 0$ denote an eigenfunction of σ_1 , i.e.,

$$\Delta\psi_1 + \lambda g(1 - 2p^*)\psi_1 = -\sigma_1\psi_1.$$

Multiplying the above equation by $f(p^*) = p^*(1 - p^*)$ and integrating the result in Ω , we obtain

$$-\int_{\Omega} (1 - 2p^*)\nabla p^* \cdot \nabla\psi_1 \, dx + \lambda \int_{\Omega} g(1 - 2p^*)p^*(1 - p^*)\psi_1 \, dx = -\sigma_1 \int_{\Omega} p^*(1 - p^*)\psi_1 \, dx. \tag{3.6}$$

Recalling (3.2) and multiplying the equation of p^* by $(1 - 2p^*)\psi_1$ and integrating the result in Ω , we find

$$2 \int_{\Omega} \psi_1 |\nabla p^*|^2 \, dx - \int_{\Omega} (1 - 2p^*)\nabla p^* \cdot \nabla\psi_1 \, dx + \lambda \int_{\Omega} g(1 - 2p^*)p^*(1 - p^*)\psi_1 \, dx = 0. \tag{3.7}$$

By (3.6) and (3.7) we have

$$\sigma_1 \int_{\Omega} p^*(1 - p^*)\psi_1 \, dx = 2 \int_{\Omega} \psi_1 |\nabla p^*|^2 \, dx > 0,$$

where the inequality is strict, since $\psi_1 > 0$ in Ω and p^* is nonconstant. Hence, $\sigma_1 > 0$. □

Second proof. This proof is due to Henry [8], and it works for general second-order elliptic operators. Let $\phi_1 > 0$ denote an eigenfunction of σ_1 , i.e.,

$$\Delta\phi_1 + \lambda g(1 - 2p^*)\phi_1 = -\sigma_1\phi_1 \quad \text{in } \Omega, \quad \frac{\partial\phi_1}{\partial\nu} = 0 \quad \text{on } \partial\Omega.$$

Set $\psi = \phi_1/f(p^*)$. Then ψ satisfies

$$\begin{cases} \Delta\psi + 2\frac{1 - 2p^*}{p^*(1 - p^*)}\nabla p^* \cdot \nabla\psi = (2|\nabla p^*|^2 - \sigma_1)\psi & \text{in } \Omega, \\ \frac{\partial\psi}{\partial\nu} = 0 & \text{on } \partial\Omega. \end{cases}$$

We argue by contradiction. Suppose that $\sigma_1 \leq 0$. Let $\psi(x_0) = \max_{\Omega} \psi$. If $x_0 \in \Omega$, then by the strong maximum principle [34], the eigenfunction ψ must be equal to some constant. This implies that $|\nabla p^*|^2 = 0$, i.e., p^* is a constant, which is a contradiction. Hence, the maximum of ψ can only be attained on the boundary $\partial\Omega$. By the Hopf Boundary Lemma [34], we have $\partial\psi/\partial\nu(x_0) > 0$, which contradicts the boundary condition on ψ . □

The uniqueness of the nontrivial equilibrium of (3.2) follows from Lemma 3.5: Since both trivial equilibria $p \equiv 0$ and $p \equiv 1$ are isolated, the construction of the supersolution \bar{p} and subsolution \underline{p} implies for sufficiently small ϵ that all nontrivial equilibria must lie between \underline{p} and \bar{p} . It is well known that the total (Leray-Schauder) degree of nontrivial equilibria between a supersolution and a subsolution is equal to one (see, e.g., the proof of Theorem 2.1 in [17]). Hence, the total degree of

all nontrivial equilibria is equal to one. By Lemma 3.5, each nontrivial equilibrium is linearly stable, so it must be isolated and have Leray-Schauder degree one. Therefore, (3.2) has at most one nontrivial equilibrium.

The uniqueness of the nontrivial equilibrium of (3.2) can also be proved by the bifurcation method and the implicit function theorem (it suffices to show that all nontrivial equilibria are nondegenerate). For details, see Proposition 2.4 of [13].

3.1.4. *An application of the stability of the nontrivial equilibrium.* Let p^* denote the unique nontrivial equilibrium of (3.2), when it exists. Since it is nondegenerate, it is a smooth function of λ .

Lemma 3.6. *For $\lambda > \lambda_1(g)$, i.e., when p^* exists, $\|\nabla p^*\|_{L^2(\Omega)}$ is a strictly monotone increasing function of λ .*

Since λ is inversely proportional to the migration rate, Lemma 3.6 implies that increasing the migration rate will make the cline distribution less steep. A more general result is in [12].

Proof. Differentiating the equation of p^* with respect to λ , we have

$$\Delta \left(\frac{\partial p^*}{\partial \lambda} \right) + gp^*(1-p^*) + \lambda(1-2p^*) \frac{\partial p^*}{\partial \lambda} = 0 \quad \text{in } \Omega. \quad (3.8)$$

Note that $\frac{\partial p^*}{\partial \lambda}$ also satisfies the no-flux boundary condition

$$\frac{\partial}{\partial \nu} \left(\frac{\partial p^*}{\partial \lambda} \right) = 0 \quad \text{on } \partial\Omega. \quad (3.9)$$

Multiplying equation (3.8) by $\frac{\partial p^*}{\partial \lambda}$, integrating the result in Ω , and invoking (3.9) and the equation of p^* , we have

$$\begin{aligned} & \int_{\Omega} \left[\left| \nabla \frac{\partial p^*}{\partial \lambda} \right|^2 - \lambda(1-2p^*) \left(\frac{\partial p^*}{\partial \lambda} \right)^2 \right] dx \\ &= \int_{\Omega} gp^*(1-p^*) \frac{\partial p^*}{\partial \lambda} dx \\ &= -\frac{1}{\lambda} \int_{\Omega} (\Delta p^*) \frac{\partial p^*}{\partial \lambda} dx \\ &= \frac{1}{\lambda} \int_{\Omega} \nabla p^* \cdot \nabla \left(\frac{\partial p^*}{\partial \lambda} \right) dx \\ &= \frac{1}{2\lambda} \frac{d}{d\lambda} \int_{\Omega} |\nabla p^*|^2 dx. \end{aligned} \quad (3.10)$$

Since p^* is linearly stable, for any $\varphi \in W^{1,2}(\Omega)$,

$$\int_{\Omega} [|\nabla \varphi|^2 - \lambda(1-2p^*)\varphi^2] dx \geq 0,$$

where the inequality is strict for every $\varphi \neq 0$. By (3.8) we see that $\frac{\partial p^*}{\partial \lambda} \neq 0$. Hence,

$$\int_{\Omega} \left[\left| \nabla \frac{\partial p^*}{\partial \lambda} \right|^2 - \lambda(1-2p^*) \left(\frac{\partial p^*}{\partial \lambda} \right)^2 \right] dx > 0.$$

Therefore, (3.10) reveals that

$$\frac{d}{d\lambda} \int_{\Omega} |\nabla p^*|^2 dx > 0.$$

This completes the proof. □

3.2. Complete dominance. The main references for this subsection are [17, 31].

Recall that if allele A_1 is recessive,

$$S_1(x, P) = \lambda p_1^2(1 - p_1).$$

In this subsection we focus on the following scalar equation

$$\begin{cases} \frac{\partial p}{\partial t} = \Delta p + \lambda g(x)p^2(1 - p) & \text{in } \Omega \times (0, \infty), \\ \nu \cdot \nabla p = 0 & \text{on } \partial\Omega \times (0, \infty), \\ 0 < p(x, 0) < 1 & \text{in } \bar{\Omega}. \end{cases} \tag{3.11}$$

An immediate difficulty arises in trying to apply standard methods such as that of the supersolution and subsolution. Namely, the equilibrium $p \equiv 0$ of (3.11) is degenerate. It turns out that the stability of $p \equiv 0$ is completely determined by the sign of $\int_{\Omega} g \, dx$, and the dynamics of (3.11) is much more complicated and interesting than that of (3.2), where there is no dominance.

3.2.1. *Existence of a nontrivial equilibrium.* To illustrate the main idea, we consider the case $\int_{\Omega} g \, dx = 0$.

Theorem 3.7. *Suppose that g changes sign and $\int_{\Omega} g \, dx = 0$.*

- (i) *For every $\lambda > 0$, the problem (3.11) has at least one stable nontrivial equilibrium.*
- (ii) *As $\lambda \rightarrow 0+$, any sequence of nontrivial equilibria of (3.11) has a subsequence converging to $2/3$ in $C^2(\bar{\Omega})$.*
- (iii) *As $\lambda \rightarrow \infty$, $p^* \rightarrow 1$ uniformly on any compact subset of $\bar{\Omega}_+ \setminus \partial\Omega_+ \cap \bar{\Omega}$ and $p^* \rightarrow 0$ uniformly on any compact subset of $\bar{\Omega}_- \setminus \partial\Omega_- \cap \bar{\Omega}$, where $\Omega_+ = \{x \in \Omega : g(x) > 0\}$ and $\Omega_- = \{x \in \Omega : g(x) < 0\}$.*

The complete proof of Theorem 3.7 is given in [31]. Here we present

Proof of part (i). Since the magnitude of λ is irrelevant, without loss of generality we assume that $\lambda = 1$. Define the scalar function

$$F(p) = \begin{cases} 0 & \text{if } p < 0, \\ \int_0^p s^2(1 - s) \, ds & \text{if } 0 \leq p \leq 1, \\ \int_0^1 s^2(1 - s) \, ds & \text{if } p > 1 \end{cases}$$

and the functional J by

$$J(\varphi) = \int_{\Omega} \left[\frac{1}{2} |\nabla \varphi|^2 - g(x)F(\varphi) \right] dx, \quad \varphi \in W^{1,2}(\Omega).$$

It is not difficult to show that J has a global minimizer p^* ; furthermore, $0 \leq p^* \leq 1$. It remains to show that neither $p \equiv 0$ nor $p \equiv 1$ is a global minimizer. Since $J(0) = J(1) = 0$, it suffices to construct some test function of the form $C + \epsilon\varphi$ such that $J(C + \epsilon\varphi) < 0$, where $C \in (0, 1)$ is a constant, $\varphi > 0$, and $\epsilon > 0$ is sufficiently

small. First, choose $\varphi > 0$ and $\varphi \in C^1(\bar{\Omega})$ such that $\int_{\Omega} g\varphi \, dx > 0$. Then

$$\begin{aligned} J(C + \epsilon\varphi) &= \int_{\Omega} \left[\frac{\epsilon^2}{2} |\nabla\varphi|^2 - g(x)F(C + \epsilon\varphi) \right] dx \\ &= \int_{\Omega} \left\{ \frac{\epsilon^2}{2} |\nabla\varphi|^2 - g(x) [F(C) + C^2(1-C)\epsilon\varphi + O(\epsilon^2)] \right\} dx \\ &= -\epsilon C^2(1-C) \int_{\Omega} g\varphi \, dx + O(\epsilon^2) < 0, \end{aligned}$$

provided that $\epsilon > 0$ is sufficiently small. Note that C can be chosen as any positive constant less than one. \square

We shall give a different proof of part (i) by using the local stability of $p \equiv 0$ and $p \equiv 1$, which is the focus of the next subsection.

3.2.2. *Stability of $p \equiv 0$.* The main reference for this subsection is [17].

Theorem 3.8. *Suppose that g changes sign in Ω .*

- (i) *If $\int_{\Omega} g \, dx \geq 0$, then $p \equiv 0$ is unstable for every $\lambda > 0$.*
- (ii) *If $\int_{\Omega} g \, dx < 0$, then $p \equiv 0$ is stable for every $\lambda > 0$.*

Thus, the sign of $\int_{\Omega} g \, dx$ completely determines the stability of $p \equiv 0$. In particular, if $\int_{\Omega} g \, dx = 0$ and g changes sign, then both $p \equiv 0$ and $p \equiv 1$ are unstable, which implies that (3.11) has at least one stable nontrivial equilibrium for every $\lambda > 0$. This yields another proof of part (i) of Theorem 3.7. We now present the proof of part (i) of Theorem 3.8 and refer the proof of part (ii) to [17].

(a) $\int_{\Omega} g \, dx > 0$. In this case, we argue by contradiction. Suppose that $p \equiv 0$ is stable, i.e., for any $\epsilon > 0$, there exists $\delta = \delta(\epsilon) > 0$ such that if $0 < p(x, 0) < \delta$ in Ω , then $0 < p(x, t) < \epsilon$ for every $x \in \Omega$ and $t > 0$. Dividing the equation of $p(x, t)$ by p^2 and integrating the result in Ω , we obtain

$$\begin{aligned} \int_{\Omega} \frac{p_t}{p^2} \, dx &= \int_{\Omega} \frac{\Delta p}{p^2} \, dx + \lambda \left[\int_{\Omega} g \, dx - \int_{\Omega} gp \, dx \right] \\ &= 2 \int_{\Omega} \frac{|\nabla p|^2}{p^3} \, dx + \lambda \left[\int_{\Omega} g \, dx - \int_{\Omega} gp \, dx \right] \\ &\geq \lambda \left[\int_{\Omega} g \, dx - \int_{\Omega} gp \, dx \right] \\ &\geq \lambda \left[\int_{\Omega} g \, dx - \epsilon \int_{\Omega} |g| \, dx \right] \\ &\geq \frac{\lambda}{2} \int_{\Omega} g \, dx, \end{aligned}$$

where the last inequality holds if $\epsilon \leq \int_{\Omega} g \, dx / (2 \int_{\Omega} |g| \, dx)$. Then

$$\frac{d}{dt} \int_{\Omega} \frac{-1}{p} \, dx = \int_{\Omega} \frac{p_t}{p^2} \, dx \geq \frac{\lambda}{2} \int_{\Omega} g \, dx.$$

Integrating the above inequality in $(0, t)$, we get

$$\int_{\Omega} \frac{dx}{p(x, 0)} - \int_{\Omega} \frac{dx}{p(x, t)} \geq \frac{\lambda t}{2} \int_{\Omega} g \, dx.$$

In particular,

$$\int_{\Omega} \frac{dx}{p(x, 0)} \geq \frac{\lambda t}{2} \int_{\Omega} g \, dx \rightarrow \infty$$

as $t \rightarrow \infty$, which is a contradiction.

(b) $\int_{\Omega} g \, dx = 0$. This case is much more subtle than (a). We first demonstrate that $p \equiv 0$ is an isolated equilibrium. If it is not, then there exists a sequence of solutions $p_n \in (0, 1)$ such that $\|p_n\|_{\infty} \rightarrow 0$ as $n \rightarrow \infty$. Recall that p_n satisfies

$$\Delta p_n + \lambda g(x) p_n^2 (1 - p_n) = 0.$$

Dividing the above equation by $p_n^2 (1 - p_n)$, integrating the result in Ω , and using the assumption that $\int_{\Omega} g \, dx = 0$, we find

$$\int_{\Omega} |\nabla p_n|^2 \frac{2 - 3p_n}{p_n^3 (1 - p_n)^2} \, dx = 0,$$

which is contradiction because $2 - 3p_n > 0$ for sufficiently large n .

Next, we establish that for any $\delta > 0$, there exist some initial data $p(x, 0)$ satisfying $0 < p(x, 0) < \delta$ in Ω and a sequence t_n with $\lim_{n \rightarrow \infty} t_n = \infty$ such that

$$\max_{x \in \Omega} p(x, t_n) \geq \frac{1}{3}.$$

If so, then $p \equiv 0$ is unstable. As shown in the proof of part (i) of Theorem 3.7, there exists some $\varphi \in C^1(\bar{\Omega})$ such that for any constant $C \in (0, 1)$ and $\epsilon > 0$ sufficiently small,

$$J(C + \epsilon\varphi) < 0 = J(0).$$

Let $p(x, 0) = C + \epsilon\varphi$. Since the definition of J leads to

$$\frac{d}{dt} J(p(x, t)) = - \int_{\Omega} p_t^2 \, dx \leq 0$$

for every $t \geq 0$, we have

$$J(p(x, t)) \leq J(C + \epsilon\varphi) < 0 = J(0).$$

This implies that zero does not belong to the ω -limit set of (3.11) with initial data $p(x, 0) = C + \epsilon\varphi$. Hence, there exists some $t_n \rightarrow \infty$ as $n \rightarrow \infty$ such that $p(x, t_n) \rightarrow p^*(x)$ in $L^{\infty}(\Omega)$ with $p^* \geq 0$ and $p^* \not\equiv 0$. Since p^* is a nontrivial equilibrium and $p \equiv 0$ is the only equilibrium in the set $\{0 \leq p \leq 1, p \in C(\bar{\Omega}) : \|p\|_{\infty} < 2/3\}$, we must have that $\max_{x \in \Omega} p^*(x) \geq 2/3$. Hence, $\max_{x \in \Omega} p(x, t_n) \geq 1/3$ for large n . Note that for any given $\delta > 0$, we can choose $C = \delta/2$ and $\epsilon \leq \delta/(2\|\varphi\|_{\infty})$, so that $C + \epsilon\varphi \leq \delta$. Therefore, $p \equiv 0$ is unstable. \square

3.2.3. *Existence of two nontrivial equilibria.* Note that for sufficiently small $\lambda > 0$, the problem (3.11) has no nontrivial equilibrium if and only $\int_{\Omega} g \, dx \neq 0$ (Theorems 1.1 and 1.2 in [31]). What happens for sufficiently large λ ? It turns out that (3.11) can have at least two nontrivial equilibria, which is in strong contrast to the case (3.2) without dominance. The main reference for this subsection is [17].

Theorem 3.9. *Suppose that g changes sign and $\int_{\Omega} g \, dx < 0$. Then for sufficiently large λ , the problem (3.11) has at least two nontrivial equilibria, one stable and one unstable.*

We offer a sketch of the proof of Theorem 3.9. First, by constructing a supersolution and a subsolution, we can show that if g changes sign, then (3.11) has one stable nontrivial equilibrium, designated p^* . The existence of the second solution requires the condition $\int_{\Omega} g \, dx < 0$ to ensure that $p \equiv 0$ is locally stable from above and isolated. The existence of a further unstable nontrivial equilibrium between the two stable equilibria 0 and p^* follows from Theorem 6.1 of [9]. Indeed, both $p \equiv 0$ and the stable nontrivial equilibrium p^* are local minimizers of the energy functional J defined above, and the unstable equilibrium p_* corresponds to a saddle point of J .

3.3. Open problems. In this subsection, we discuss several open problems in migration-selection models for two alleles (cf. [13]).

3.3.1. *The effect of $\int_{\Omega} g \, dx$.* As we saw earlier, the sign of $\int_{\Omega} g \, dx$ plays an important role in determining the dynamics of (3.1). We consider

$$\begin{cases} \frac{\partial p}{\partial t} = \Delta p + \lambda g(x)f(p) & \text{in } \Omega \times (0, \infty), \\ \nu \cdot \nabla p = 0 & \text{on } \partial\Omega \times (0, \infty), \\ 0 < p(x, 0) < 1 & \text{in } \bar{\Omega}, \end{cases} \quad (3.12)$$

where $f \in C^1([0, 1])$, $f(0) = f(1) = 0$ and $f > 0$ in $(0, 1)$. The most important example of f is

$$f(p) = p(1-p)(1 + \kappa - 2\kappa p). \quad (3.13)$$

Henry [8] showed for $f''(p) \leq 0$ that (3.12) has at most one nontrivial equilibrium, which, if it exists, is globally asymptotically stable among initial data that are nonnegative and not identically zero. Note that his result does not restrict the sign of $\int_{\Omega} g \, dx$.

Conjecture. Suppose that $\int_{\Omega} g \, dx < 0$. If $f(p)/p$ is monotone decreasing in $(0, 1)$, then (3.12) has at most one nontrivial equilibrium, which, if it exists, is globally asymptotically stable.

Note that for f given by (3.13), we have $f''(p) \leq 0$ if and only if $-1/3 \leq \kappa \leq 1/3$, whereas $f(p)/p$ is monotone decreasing if and only if $-1/3 \leq \kappa \leq 1$. In particular, if this conjecture is true, it implies for (3.13) with $-1/3 \leq \kappa \leq 1$, that if $\int_{\Omega} g \, dx < 0$, then there exists some $\lambda_* > 0$ such that for $0 < \lambda \leq \lambda_*$, the equilibrium $p \equiv 0$ is globally asymptotically stable; if $\lambda > \lambda_*$, then (3.12) has a unique nontrivial equilibrium, which is globally asymptotically stable.

Conjecture. Suppose that $f(0) = f(1) = 0$, $f > 0$ in $(0, 1)$, and f has a unique critical point (which must be a global maximum) in $(0, 1)$. If $\int_{\Omega} g \, dx = 0$, then for every $\lambda > 0$, the problem (3.12) has a unique nontrivial equilibrium, which is globally asymptotically stable.

Note that for f given by (3.13), f has a unique critical point if and only $-1 \leq \kappa \leq 1$. In particular, if this conjecture is true, it implies that for (3.13) with $-1 \leq \kappa \leq 1$, if $\int_{\Omega} g \, dx = 0$, then for every $\lambda > 0$, the problem (3.12) has a unique nontrivial equilibrium, which is globally asymptotically stable.

Next, we consider complete dominance:

$$\begin{cases} \frac{\partial p}{\partial t} = \Delta p + \lambda g(x)p^2(1 - p) & \text{in } \Omega \times (0, \infty), \\ \nu \cdot \nabla p = 0 & \text{on } \partial\Omega \times (0, \infty), \\ 0 < p(x, 0) < 1 & \text{in } \bar{\Omega}. \end{cases} \tag{3.14}$$

The case $\int_{\Omega} g \, dx \geq 0$ was covered in the preceding two conjectures. (If the integral is positive, use $1 - p$.) For the case $\int_{\Omega} g \, dx < 0$, we have

Conjecture. Suppose that g changes sign and $\int_{\Omega} g \, dx < 0$.

(a) There exists some $\lambda^* > 0$ such that if $\lambda < \lambda^*$, then $p \equiv 0$ is globally asymptotically stable; for every $\lambda > \lambda^*$, the problem (3.14) has at least two nontrivial equilibria.

(b) For any λ , the problem (3.14) has at most one asymptotically stable nontrivial equilibrium.

(c) Let p^* denote any nontrivial equilibrium of (3.14). As $\lambda \rightarrow \infty$, passing to a subsequence if necessary, we have either $p^* \rightarrow 1$ in $\{x \in \Omega : g(x) > 0\}$ and $p^* \rightarrow 0$ in $\{x \in \Omega : g(x) < 0\}$, or $\lambda p^* \rightarrow w$, where w is a positive solution of

$$\begin{cases} \Delta w + g(x)w^2 = 0 & \text{in } \Omega, \\ \frac{\partial w}{\partial \nu} = 0 & \text{on } \partial\Omega. \end{cases} \tag{3.15}$$

It is of interest to estimate the threshold value λ^* in part (a) in terms of g and Ω .

One can see that if (3.15) has a positive solution, then g changes sign and $\int_{\Omega} g \, dx < 0$. When $N \leq 5$, by standard variational methods one can prove that the converse also holds. For $N \geq 6$, we do not know whether the assumptions that g changes sign and $\int_{\Omega} g \, dx < 0$ are sufficient to ensure that (3.15) has a positive solution.

Dancer [4] recently constructed some Ω and g such that (3.15) can have more than one solution. This suggests that the structure of the nontrivial equilibria of (3.14) can be complicated.

3.3.2. *General migration operators.* It would be interesting to see whether Theorem 3.8 can be generalized to the following model

$$\begin{cases} \mathcal{L}p + \lambda g(x)p^2(1 - p) = 0 & \text{in } \Omega, \\ \mathcal{B}p = 0 & \text{on } \partial\Omega, \end{cases} \tag{3.16}$$

where

$$\mathcal{L}p := \sum_{\alpha, \beta=1}^N V_{\alpha\beta} \frac{\partial^2 p}{\partial x_{\alpha} \partial x_{\beta}} + b \cdot \nabla p, \quad \mathcal{B}p := \nu \cdot V \nabla p.$$

Let $(\mathcal{L}^*, \mathcal{B}^*)$ denote the adjoint operator of $(\mathcal{L}, \mathcal{B})$, and let $\psi^* > 0$ be an eigenfunction of $(\mathcal{L}^*, \mathcal{B}^*)$ corresponding to the zero eigenvalue; see [36, 37] for more details. We have the following

Conjecture. Suppose that g changes sign in Ω .

(i) If $\int_{\Omega} g\psi^* \, dx \geq 0$, the equilibrium $p \equiv 0$ of (3.16) is unstable for every $\lambda > 0$.

(ii) If $\int_{\Omega} g\psi^* \, dx < 0$, the equilibrium $p \equiv 0$ of (3.16) is asymptotically stable for every $\lambda > 0$.

3.3.3. *Geographical barrier.* Much work remains to be done on the influence of ecological factors. Here we discuss some open problems concerning the effect of geographical barriers. The following model for a barrier at the origin was derived and examined in [23, 25]:

$$\begin{cases} \frac{\partial p}{\partial t} = p_{xx} + \lambda g(x)p(1-p), & x \in (-a_1, 0) \cup (0, a_2), t > 0, \\ p_x(0+, t) = p_x(0-, t) = \gamma [p(0+, t) - p(0-, t)], & t > 0, \\ p_x(-a_1, t) = p_x(a_2, t) = 0, & t > 0, \\ 0 \leq p(x, 0) \leq 1, & -a_1 \leq x \leq a_2, \end{cases} \quad (3.17)$$

where a_1, a_2 , and γ are positive constants. The parameter γ measures the transmissivity of the geographical barrier: if $\gamma = 0$, the barrier is impenetrable; as $\gamma \rightarrow \infty$, the barrier disappears. A general question is: how does γ affect the existence, stability, and profile of nontrivial equilibria of (3.17)?

A related problem is to investigate the traveling-wave solutions of the model

$$\begin{cases} \frac{\partial p}{\partial t} = p_{xx} + \lambda g(x)p(1-p), & x \neq 0, t > 0, \\ p_x(0+, t) = p_x(0-, t) = \gamma [p(0+, t) - p(0-, t)], & t > 0, \\ 0 \leq p(x, 0) \leq 1. \end{cases} \quad (3.18)$$

Numerical results in [33] suggest that asymptotically the barrier delays the traveling wave by a time that is a decreasing function of γ . For sufficiently small γ , the delay appears to be a linear function of $\ln \gamma$.

4. Migration-selection model for multiple alleles.

4.1. **Uniform selection.** In this subsection we assume that all of the selection coefficients are constants. First, consider the system of ordinary differential equations for pure selection derived in Subsection 2.2:

$$\begin{cases} \frac{dp_i}{dt} = p_i \left(\sum_{j=1}^n r_{ij}p_j - \sum_{i,j=1}^n r_{ij}p_i p_j \right), & t > 0, \\ P(0) = (p_1(0), \dots, p_n(0)) \in S := \{P \in \mathbb{R}^n : p_i > 0, \sum_j p_j = 1\}. \end{cases} \quad (4.1)$$

Assumption. The system (4.1) has an equilibrium $\hat{P} \in S$ that is globally asymptotically stable for all initial data in S (see Section 4.3 in [24] for sufficient conditions).

Question. What conclusion can we draw about the dynamics of the corresponding migration-selection system of partial differential equations?

$$\begin{cases} \frac{\partial p_i}{\partial t} = \Delta p_i + p_i \left(\sum_{j=1}^n r_{ij}p_j - \sum_{i,j=1}^n r_{ij}p_i p_j \right), & x \in \Omega, t > 0, \\ \frac{\partial p_i}{\partial \nu} = 0 & x \in \partial\Omega, t > 0, \\ P(x, 0) \in S, & \forall x \in \Omega. \end{cases} \quad (4.2)$$

The following result is proved in [7].

Theorem 4.1. *The vector of gene frequencies $P(x, t) \rightarrow \hat{P}$ uniformly in x as $t \rightarrow \infty$.*

Theorem 4.1 implies that after a sufficiently long time, there is no indication of the initial spatial variation in gene frequencies. If $r_{ij} = r_{ij}(x)$, some spatial variation may be retained at equilibrium. The main ingredient in the proof of Theorem 4.1 is the demonstration that the mean fitness of the population, $\frac{1}{|\Omega|} \int_{\Omega} \bar{r}(P(x, t)) dx$, is monotone increasing in time, where \bar{r} is defined below (2.2). Our proof is adapted from [29], which allows general migration operators.

Proof. The first step is to show that our assumption implies for (4.1) that

$$\bar{r}(\hat{P}) \geq \bar{r}(P) \tag{4.3}$$

for every $P \in S$, and that equality holds if and only if $P = \hat{P}$. In Subsection 2.2 we showed that

$$\frac{d\bar{r}}{dt}(P(t)) \geq 0.$$

Next, let $P(t; P_0)$ denote the solution of (4.1) with initial data $P_0 \in S$. Since \hat{P} is globally asymptotically stable, $\lim_{t \rightarrow \infty} P(t; P_0) = \hat{P}$. By the monotonicity of $\bar{r}(P(t))$,

$$\bar{r}(P(t; P_0)) \geq \bar{r}(P_0)$$

for every $t \geq 0$. By letting $t \rightarrow \infty$ in the above inequality, we obtain (4.3).

Next, we prove for (4.2) that if $P(x, 0) \neq \hat{P}$, then

$$\min_{x \in \bar{\Omega}} \sum_{i=1}^n \hat{p}_i \ln p_i(x, t) \text{ is strictly increasing in } t. \tag{4.4}$$

To establish (4.4), set

$$f(x, t) = \sum_{i=1}^n \hat{p}_i \ln p_i(x, t).$$

Then f satisfies

$$\begin{cases} \frac{\partial f}{\partial t} = \Delta f + \sum_i \hat{p}_i |\nabla \ln p_i|^2 + [\bar{r}(\hat{P}) - \bar{r}(P)] & \text{in } \Omega \times (0, \infty), \\ \frac{\partial f}{\partial \nu} = 0 & \text{on } \partial\Omega \times (0, \infty). \end{cases} \tag{4.5}$$

Hence, (4.4) follows from the maximum principle [34] and (4.3).

The last step is to show that $\lim_{t \rightarrow \infty} P(x, t) = \hat{P}$ uniformly in $x \in \bar{\Omega}$. This follows from (4.4) and some compactness arguments that rely crucially on the *a priori* estimate in [35]:

$$\sup_{t \geq \delta} \|p_i(\cdot, t)\|_{C^{2,\alpha}(\bar{\Omega})} \leq C \tag{4.6}$$

for some $\alpha \in (0, 1)$ and some positive constant C that depend upon only on δ , Ω , and the initial data. □

4.2. No dominance. The main references for the rest of this paper are [13, 14, 15].

If we suppose that

$$r_{ij}(x) = s_i(x) + s_j(x), \quad 1 \leq i, j \leq n,$$

the gene frequency p_i for allele A_i satisfies

$$\begin{cases} \frac{\partial p_i}{\partial t} = \Delta p_i + \lambda p_i \left[s_i - \sum_{j=1}^n s_j p_j \right], & x \in \Omega, t > 0, \\ \frac{\partial p_i}{\partial \nu} = 0, & x \in \partial\Omega, t > 0. \end{cases} \quad (4.7)$$

4.2.1. *Elimination of allele.* A natural question is: When can we conclude that $\lim_{t \rightarrow \infty} p_i(x, t) = 0$ uniformly in x for some i ? That is, we seek sufficient conditions for the elimination of A_i . The following appears to be the first such result [13].

Theorem 4.2. *Suppose that*

- (a) *the selection difference $s_1 - s_n$ changes sign in Ω ;*
- (b) *there exists some $i \in \{2, \dots, n-1\}$ and $a_i \in (0, 1)$ such that*

$$s_i(x) \leq a_i s_1(x) + (1 - a_i) s_n(x) \quad \text{for all } x \in \Omega.$$

Then $\lim_{t \rightarrow \infty} p_i(x, t) = 0$ uniformly in x .

Example. Let $s_i = b_i g(x)$, where the function g changes sign in Ω . Assume that $b_1 > b_2 > \dots > b_n$. Then assumption (a) holds and assumption (b) in Theorem 4.2 can be satisfied by choosing

$$a_i = \frac{b_i - b_n}{b_1 - b_n}.$$

Recall that $\Omega_+ = \{x \in \Omega : g(x) > 0\}$ and $\Omega_- = \{x \in \Omega : g(x) < 0\}$. Then in Ω_+ , A_1 is the fittest allele and A_n is the least fit, and the opposite holds in Ω_- . We may call A_1 and A_n extreme alleles and A_i ($2 \leq i \leq n-1$) intermediate alleles. Theorem 4.2 implies that the intermediate alleles are eliminated. “The elimination of intermediate alleles can potentially provide a mechanism for sympatric speciation. Suppose that recurrent mutation introduces new alleles into the population, but at such a low rate that it need not be included in (4.2). If a new mutant is intermediate relative to the alleles already in the population, then it will be eliminated; if it is extreme, then it may survive and an intermediate allele will be eliminated. Thus, the difference between the selection coefficients of the alleles present is increasing, and if this reflects increasing phenotypic differentiation, then reproductive isolation may evolve” [13].

Proof. The proof of Theorem 4.2 is based on the construction of a Lyapunov functional. For any $i = 2, \dots, n-1$, set

$$u_i = \frac{p_1^{a_i} p_n^{1-a_i}}{p_i}.$$

Then u_i satisfies

$$\begin{aligned} \frac{\partial u_i}{\partial t} &= \Delta u_i + 2 \nabla \ln p_i \cdot \nabla u_i + \left\{ a_i(1 - a_i) \left| \nabla \ln \frac{p_1}{p_n} \right|^2 + [a_i s_1 + (1 - a_i) s_n - s_i] \right\} u_i \\ &\geq \Delta u_i + 2 \nabla \ln p_i \cdot \nabla u_i \end{aligned}$$

in $\Omega \times (0, \infty)$ and the no-flux boundary condition. We claim that $\min_{\bar{\Omega}} u_i(\cdot, t)$ is strictly increasing in t . To establish this assertion, we argue by contradiction. Suppose that there exist some t_1 and t_2 such that $0 \leq t_1 < t_2$ and $\min_{\bar{\Omega}} u_i(\cdot, t_1) \geq \min_{\bar{\Omega}} u_i(\cdot, t_2)$. Then there exists some $\bar{t} \in (t_1, t_2]$ such that $\min_{\bar{\Omega}} u_i(\cdot, \bar{t}) = \min_{\bar{\Omega} \times [t_1, t_2]} u_i$. By the strong maximum principle [34], the function u_i must be

equal to some positive constant in $\bar{\Omega} \times [t_1, t_2]$. This implies that $\nabla \ln \frac{p_1}{p_n} = 0$ in $\bar{\Omega} \times [t_1, t_2]$. Hence, $p_1(x, t)/p_n(x, t) = c(t)$ for some positive and continuously differentiable function $c(t)$. Substituting $p_1 = cp_n$ into the equation of p_1 yields

$$p_n \frac{dc}{dt} + c \frac{\partial p_n}{\partial t} = c_n \Delta p_n + \lambda c p_n \left(s_1 - \sum_{j=1}^n s_j p_j \right).$$

Together with the equation of p_n , this implies that

$$\frac{c'(t)}{c(t)} = \lambda(s_1 - s_n),$$

which is a contradiction, since $s_1 - s_n$ changes sign in Ω . By the monotonicity of $\min_{\bar{\Omega}} u(\cdot, t)$, the *a priori* estimate (4.6), and some compactness arguments [13], we can show that $p_i(x, t) \rightarrow 0$ uniformly in x as $t \rightarrow \infty$. \square

Similarly, we can demonstrate [14] that if there exist constants $a_j \geq 0, 1 \leq j \leq n$, such that $\sum_{j=1}^n a_j = 1$ and

$$s_1 \leq \sum_{j=1}^n a_j s_j, \quad s_1 \not\equiv \sum_{j=1}^n a_j s_j$$

in Ω , then $\lim_{t \rightarrow \infty} p_1(x, t) = 0$ uniformly in x . A natural question is whether this condition can be weakened and still ensure the elimination of allele A_1 . For sufficiently large λ , we can establish the sharper result [14]:

Theorem 4.3. *Suppose that $s_1(x) < \max_{1 \leq j \leq n} s_j(x)$ for every $x \in \bar{\Omega}$. If λ is sufficiently large, then $\lim_{t \rightarrow \infty} p_1(x, t) = 0$ uniformly in x .*

If the strict inequality $s_1 < \max_{1 \leq j \leq n} s_j$ is replaced by $s_1 \leq \max_{1 \leq j \leq n} s_j$ and $s_1 \not\equiv \max_{1 \leq j \leq n} s_j$, then the conclusion of Theorem 4.3 fails [14].

For sufficiently small λ , we can prove the following sharper result [15].

Theorem 4.4. *If*

$$\int_{\Omega} s_1 dx > \max_{2 \leq j \leq n} \int_{\Omega} s_j dx,$$

and λ is sufficiently small, then $\lim_{t \rightarrow \infty} p_1(x, t) = 1$ uniformly in x . In particular, $\lim_{t \rightarrow \infty} p_i(x, t) = 0$ uniformly in x for every $i \in \{2, \dots, n\}$.

It is natural to inquire whether allele A_n is eliminated if

$$\int_{\Omega} s_n dx < \max_{1 \leq j \leq n-1} \int_{\Omega} s_j dx.$$

If $\int_{\Omega} s_1 dx = \int_{\Omega} s_2 dx > \max_{3 \leq j \leq n} \int_{\Omega} s_j dx$, we do not yet know whether both alleles A_1 and A_2 can be maintained or alleles $A_j, 3 \leq j \leq n$, are eliminated.

4.2.2. Protection of an allele. We say that allele A_1 is protected if there exists some $\delta > 0$ such that for any initial data that are nonnegative and not identically zero, there exists some $t_1 > 0$ such that $p_1(x, t) \geq \delta$ for every $x \in \bar{\Omega}$ and $t \geq t_1$. Note that δ is assumed to be independent of the initial data but t_1 depends on them.

Theorem 4.5. [14] *If $s_1 - \max_{2 \leq i \leq n} s_i$ is positive somewhere in Ω , then for sufficiently large λ , allele A_1 is protected.*

The following result is a consequence of Theorem 4.5 and permanence theory [3].

Theorem 4.6. *If for each $i \in \{1, \dots, n\}$, the difference $s_i - \max_{1 \leq j \leq n, j \neq i} s_j$ is positive somewhere in Ω , then for sufficiently large λ , there exists at least one internal equilibrium.*

We do not know whether the internal equilibrium is unique and stable.

4.2.3. *Complex dynamics for three alleles.* The main reference for this subsection is [15]. In contrast to the diallelic case with no dominance, for intermediate λ the dynamics of the migration-selection model with three alleles and no dominance can be quite complex. This is probably not too surprising, because for such range of λ , the scales of migration and selection are comparable. In this subsection we consider a special case and assume that

$$s_1(x) = s_2(x) + \epsilon g(x), \quad s_3(x) = s_2(x) + h(x),$$

where $|\epsilon|$ is sufficiently small; i.e., allele A_1 is very similar to allele A_2 . Let $\theta = \theta(x; \lambda)$ denote the positive solution of

$$\begin{cases} \Delta\theta + \lambda h(x)\theta(1 - \theta) = 0 & \text{in } \Omega, \\ 0 < \theta < 1 & \text{in } \Omega, \\ \frac{\partial\theta}{\partial\nu} = 0 & \text{on } \partial\Omega. \end{cases}$$

Define

$$G(\lambda) = \int_{\Omega} g(x) [1 - \theta(x; \lambda)]^2 dx, \quad \lambda > 0.$$

Theorem 4.7. *Suppose that there exist $\lambda_1 < \dots < \lambda_l$ such that $G(\lambda_i) = 0$, $G'(\lambda_i) \neq 0$ for every $i = 1, \dots, l$, and $G(\lambda) \neq 0$ for $\lambda \notin \{\lambda_1, \dots, \lambda_l\}$. For any $\Lambda > \lambda_l$ and any sufficiently small $\epsilon > 0$, there exist $\lambda_1^\epsilon < \dots < \lambda_l^\epsilon$ and $\lambda_{1,\epsilon} < \dots < \lambda_{l,\epsilon}$ with $\lim_{\epsilon \rightarrow 0^+} \lambda_i^\epsilon = \lim_{\epsilon \rightarrow 0^+} \lambda_{i,\epsilon} = \lambda_i$ such that the following conclusions hold.*

- (a) *The 23-edge equilibrium changes stability at $\lambda = \lambda_1^\epsilon, \dots, \lambda_l^\epsilon$, and the 13-edge equilibrium changes stability at $\lambda = \lambda_{1,\epsilon}, \dots, \lambda_{l,\epsilon}$.*
- (b) *An internal equilibrium exists if $\min\{\lambda_i^\epsilon, \lambda_{i,\epsilon}\} < \lambda < \max\{\lambda_{i,\epsilon}, \lambda_i^\epsilon\}$ for at least one $i = 1, \dots, l$.*
- (c) *There exists some function g such that all internal equilibria are asymptotically stable, and there also exists some other function g such that they are all unstable.*

Theorem 4.7 shows that as λ increases, arbitrarily many changes of stability of the edge equilibria and corresponding appearance of an internal equilibrium can occur. Furthermore, it is shown in [15] that the conditions for protection or loss of an allele can both depend nonmonotonically on λ . None of these phenomena can occur in the diallelic case; see [15] for more details.

4.3. **Open problems.** There are many challenging mathematical problems for multiple alleles concerning the dynamics of (2.4).

4.3.1. *Uniform selection.* For uniform selection, a major unsolved problem concerns the situation when the globally stable equilibrium lies on the boundary of the simplex. More precisely, suppose that $\hat{P} \in \partial S$ is a globally asymptotically stable equilibrium of the ODE system (4.1). Is $\hat{P} \in \partial S$ also a globally asymptotically stable equilibrium of the PDE system (4.2) with constant selection coefficients? We do not even know how to rule out the existence of an internal equilibrium for the system (4.2) under this assumption.

4.3.2. *No dominance.* Recall that if there is no dominance, then $r_{ij} = s_i + s_j$, where $1 \leq i, j \leq n$. According to Theorem 4.6, if for each $i \in \{1, \dots, n\}$, the difference $s_i - \max_{j \neq i} s_j$ is positive somewhere in Ω , then for sufficiently large λ , the system (4.7) has an internal equilibrium. We conjecture that for sufficiently large λ , this equilibrium is unique and globally asymptotically stable.

4.3.3. *Complete-dominance series.* For the important complete-dominance series, $r_{ij}(x) = s_i(x)$ for $1 \leq i \leq j \leq n$ and $r_{ij} = r_{ji}$ for every $i, j = 1, 2, \dots, n$, very little is known about the dynamics of (2.4).

Conjecture. Suppose that $s_i(x) = a_i g(x)$, where $a_1 > \dots > a_n$ are constants and $g(x)$ changes sign. Then for every $i \in \{2, \dots, n-1\}$, the gene frequencies $p_i(x, t) \rightarrow 0$ uniformly in x as $t \rightarrow \infty$.

This conjecture, which is open even for $n = 3$, says that all of the intermediate alleles will be eliminated. However, we do not even know how to rule out the existence of an internal equilibrium.

4.3.4. *Migration-selection model with partial panmixia.* In a recent work [27], a PDE migration-selection model with partial panmixia at a single multiallelic locus was derived. The simplest version of this model can be written as

$$\begin{cases} \frac{\partial p_i}{\partial t} = \Delta p_i + B \left[\frac{1}{|\Omega|} \int_{\Omega} p_i dx - p_i \right] + S_i(x, P) & \text{in } \Omega \times (0, \infty), \\ \nu \cdot \nabla p_i = 0 & \text{on } \partial\Omega \times (0, \infty), \\ p_i(x, 0) \geq 0, \quad p_i(x, 0) \not\equiv 0, \quad \sum_i p_i(x, 0) \equiv 1 & \text{in } \Omega, \end{cases} \quad (4.8)$$

where $B > 0$ is the scaled panmictic rate; it measures the rate of long-distance migration. Some general results concerning the maintenance of two alleles were established in [16, 27]. For example, the minimal selection-migration ratio required to protect from loss the allele with the smaller average fitness was studied in [27]. In [16], previous analyses [27] on the maintenance of both alleles were extended from conservative to arbitrary migration and the uniqueness and global asymptotic stability of the nontrivial equilibrium were proved. For conservative migration, increasing the rate of panmixia makes it harder to maintain the allele with the smaller average fitness in the population [16].

In both [27] and [28], the effect of incorporating partial panmixia into diallelic single-locus clines maintained by migration and selection in an unbounded unidimensional habitat was investigated. The most interesting biological conclusion is that, in contrast to clines without panmixia, some genetic variability is maintained even at infinity: Suppose that $g(x) \rightarrow \pm\gamma_{\pm}$ as $x \rightarrow \pm\infty$, where $\gamma_{\pm} > 0$; the function $f(p)$ satisfies $f(0) = f(1) = 0$ and $f(p) > 0$ in $(0, 1)$; the solution $\hat{p}(x) \not\equiv 0, 1$ represents an equilibrium gene frequency; and $p_{\pm} = \lim_{x \rightarrow \pm\infty} \hat{p}(x)$. Then $0 < p_{\pm} < 1$ and the limiting equilibrium gene frequencies p_+ and p_- can be evaluated from the related two-colony model [27, 28]. There are many open problems concerning (4.8). A major question is to understand the difference between the dynamics of the migration-selection model (2.4) and that of (4.8).

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