GLOBAL STABILITY OF SPATIALLY HOMOGENEOUS EQUILIBRIA IN MIGRATION-SELECTION MODELS[*]

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Abstract. We investigate the evolution of the gene frequencies at a multiallelic locus under the joint action of migration and viability selection. The population is subdivided into finitely many panmictic colonies that exchange adult migrants independently of their genotype. If the selection pattern is the same in every colony and such that $\hat{p}$ is a globally asymptotically stable equilibrium under pure selection, then can migration change the (global) stability of $\hat{p}$? When $\hat{p}$ is a complete polymorphism, the answer is *no*, which means the ultimate state of the population is unaffected by geographical structure. However, if not every allele is present in $\hat{p}$, this problem remains largely open. In this paper we resolve the latter case for three alleles. The situation when the population occupies a finite continuous habitat of arbitrary dimensionality and shape is similar and also addressed.

1. Introduction. Migration-selection models are important in the study of the amount and pattern of genetic variation in geographically structured populations. The continuous-time models are complicated nonlinear, coupled, first-order ordinary differential equations (ODEs) if space is discrete; and semilinear, coupled, second-order parabolic differential equations (PDEs) if space is continuous. Biological interest and the mathematical challenge have inspired a substantial body of work in this field. Interested readers may consult the instructive and systematic review papers of Bürger [6], Lou, Nagylaki, and Ni [16], and Nagylaki and Lou [24] on this topic.

One of the core questions for migration-selection models is to inquire under what conditions genetic structure is independent of geographical structure. For uniform selection, Nagylaki and Lou conjectured that a globally stable equilibrium under pure selection retains its global stability when migration is turned on [22, 23]. If this conjecture is true, then observed spatial genetic variation in a population hints that selection might be nonuniform.

Below we briefly introduce and formulate the continuous-time, discrete-space migration-selection models. We state the conjecture and comment on previous work and our progress made on this conjecture.

Consider a single locus with alleles A_i, where $i \in N = \{1, 2, \ldots, n\}$. Let $p_{i,\alpha}$ be the frequency of allele A_i in deme α, where $\alpha \in D = \{1, 2, \ldots, d\}$. The notation Δ_n

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represents the simplex

$$(1.1) \qquad \Delta_n = \left\{ (q_1, q_2, \ldots, q_n) \in \mathbb{R}^n : q_i \geq 0, \sum_{i=1}^{n} q_i = 1 \right\}.$$

The vector $p^{(\alpha)} = (p_{1,\alpha}, \ldots, p_{n,\alpha}) \in \Delta_n$ collects the gene frequencies in deme α, and $p = (p^{(\alpha)})_{\alpha \in D} = (p_{i,\alpha}) \in \Delta_n^d$ is the full vector comprising gene frequencies of all alleles in all demes.

The selection coefficient (also known as the Malthusian fitness) of the genotype $A_i A_j$ in deme α is $r_{ij,\alpha}$. We do not distinguish paternal from maternal genes; therefore, $r_{ij,\alpha} = r_{ji,\alpha}$. The selection coefficient of allele A_i and the mean selection coefficient of the population in deme α are given, respectively, by

$$(1.2) \qquad r_{i,\alpha}(p^{(\alpha)}) = \sum_{j=1}^{n} r_{ij,\alpha} p_{j,\alpha}, \quad \bar{r}_\alpha(p^{(\alpha)}) = \sum_{i,j=1}^{n} r_{ij,\alpha} p_{i,\alpha} p_{j,\alpha}.$$

In deme α, under selection, the frequency vector $p^{(\alpha)}$ changes according to (see, e.g., [6, 22])

$$(1.3) \qquad \dot{p}_{i,\alpha} = p_{i,\alpha} \left[r_{i,\alpha}(p^{(\alpha)}) - \bar{r}_\alpha(p^{(\alpha)}) \right] := f_{i,\alpha}(p^{(\alpha)}),$$

in which the superior dot stands for d/dt.

If selection is uniform across demes, i.e., $r_{ij,\alpha} = r_{ij}$ for every $\alpha \in D$ and every $i, j \in N$, then in each deme selection is described by the same system of ODEs,

$$(1.4) \qquad \dot{p}_i = p_i \left[r_i(p) - \bar{r}(p) \right] := f_i(p),$$

where

$$(1.5) \qquad r_i(p) = \sum_{j=1}^{n} r_{ij} p_j, \quad \bar{r}(p) = \sum_{i,j=1}^{n} r_{ij} p_i p_j,$$

and $p = (p_i) \in \Delta_n$ signifies the gene frequencies subject to uniform selection. The context clearly distinguishes $p = (p_i)$ from the full vector $p = (p_{i,\alpha}) \in \Delta_n^d$.

Let the constants $\mu_{\alpha\beta} \geq 0$ (for $\alpha \neq \beta$) be the backward migration rates, i.e., $\mu_{\alpha\beta} dt$ is the probability that a randomly chosen individual/allele in deme α has arrived there recently (within time dt) from deme β. We write

$$(1.6) \qquad \mu_{\alpha\alpha} := - \sum_{\beta: \beta \neq \alpha} \mu_{\alpha\beta} < 0,$$

and call $M = (\mu_{\alpha\beta})$ the migration matrix.

Then the standard migration-selection model in continuous time is given by (see [22, eq. 2.21])

$$(1.7) \qquad \dot{p}_{i,\alpha} = \sum_{\beta=1}^{d} \mu_{\alpha\beta} p_{i,\beta} + f_{i,\alpha}(p^{(\alpha)}).$$

This system of ODEs is defined on Δ_n^d, which is forward invariant under (1.7) because of $\sum_{\beta=1}^{d} \mu_{\alpha\beta} = 0$ and $\sum_{i=1}^{n} f_{i,\alpha} = 0$ for every α. Moreover, by (1.3), (1.7), and the

fact that $r_{i,\alpha}$ and $\bar{r}_\alpha$ are uniformly bounded for $p^{(\alpha)} \in \Delta_n$, we obtain

$$(1.8) \qquad \dot{p}_{i,\alpha} = \sum_{\beta:\,\beta\neq\alpha} \mu_{\alpha\beta}p_{i,\beta} + \mu_{\alpha\alpha}p_{i,\alpha} + p_{i,\alpha}\left[r_{i,\alpha}(p^{(\alpha)}) - \bar{r}_\alpha(p^{(\alpha)})\right]$$

$$\geq \mu_{\alpha\alpha}p_{i,\alpha} + p_{i,\alpha}\left[r_{i,\alpha}(p^{(\alpha)}) - \bar{r}_\alpha(p^{(\alpha)})\right]$$

$$\geq -cp_{i,\alpha}\,,$$

where c is a positive constant. Hence, $p_{i,\alpha}(t) \geq p_{i,\alpha}(0)e^{-ct}$, and therefore,

$$(1.9) \qquad\qquad p_{i,\alpha}(0) > 0 \;\Rightarrow\; p_{i,\alpha}(t) > 0 \text{ for every } t > 0\,.$$

The model with migration and uniform selection reads

$$(1.10) \qquad\qquad \dot{p}_{i,\alpha} = \sum_{\beta=1}^{d} \mu_{\alpha\beta}p_{i,\beta} + p_{i,\alpha}\left[r_i(p^{(\alpha)}) - \bar{r}(p^{(\alpha)})\right]\,.$$

For (1.10) Nagylaki and Lou [22, Remark 5.8] conjectured the following.

CONJECTURE. *If (1.4) has a globally asymptotically stable equilibrium $\hat{p} \in \Delta_n$, then for (1.10) the spatially homogeneous state with $p^{(\alpha)} = \hat{p}$ for every $\alpha \in D$ is globally asymptotically stable.*

Here $\hat{p} \in \Delta_n$ is *globally asymptotically stable* (g.a.s.) for (1.4) if it is asymptotically stable and its basin of attraction contains $\mathring{\Delta}_n$ (the relative interior of the simplex), and similarly for an equilibrium of (1.10) on Δ_n^d.

For interior $\hat{p} \in \mathring{\Delta}_n$ this is proven by Nagylaki and Lou [22, Thms. 5.6 and 5.9] under some mild additional assumptions. See also Remark 2.4 and Corollary 2.5 below. For $\hat{p}$ on the boundary of Δ_n this conjecture is largely open except for $n = 2$ alleles.

In the case of $n = 2$ alleles, the condition for (1.4) to have a globally stable equilibrium at, e.g., vertex 1 of Δ_2 (i.e., $(p_1, p_2) = (1, 0)$) is $r_{22} \leq r_{12} \leq r_{11}$ with at least one inequality strict (see, e.g., [6, p. 890]). For (1.10), we see from $\sum_{\beta=1}^{d} \mu_{\alpha\beta} = 0$ that every positive spatially homogeneous solution $(p_{1,\alpha}, p_{2,\alpha}) = (u, 1-u)$ satisfies

$$(1.11) \qquad\qquad \dot{u} = u(1-u)[(r_{12} - r_{22})(1-u) + (r_{11} - r_{12})u]\,,$$

whence u increases to 1. Then the global convergence of any positive solution of (1.10) to vertex 1 follows from the monotonicity of the flow. See also [22, Thm. 3.5].

In the multiple-allele case $n \geq 3$, both (1.4) and (1.10) are nonlinear, coupled systems of differential equations; the complication of the dynamics increases dramatically due to the lack of monotonicity. The aim of this paper is to prove the above conjecture for $n = 3$ alleles under the generic assumption that all the equilibria of (1.4) are regular (see Remark 2.9).

In section 2, we present the main tools: global stability results via quasiconcave Lyapunov functions. These allow us to give a unified derivation of several results of Nagylaki and Lou [22] under weaker conditions. Section 3 is devoted to the proof of the conjecture for three alleles through a case-by-case analysis. Finally, we treat a continuous-space analog (the PDE version) of these results in section 4.

2. The tools. We first recall the concept of a quasiconcave function; see [3].

Let C be a convex subset of some Euclidean space. A function $V : C \to \mathbb{R}$ is *quasiconcave* if, for every $x, y \in C$ and $\lambda \in [0, 1]$,

$$(2.1) \qquad\qquad V(\lambda x + (1-\lambda)y) \geq \min\{V(x), V(y)\}$$

holds. Equivalently, the superlevel sets $\{x \in C : V(x) \geq w\}$ are convex for each $w \in \mathbb{R}$. If C is a relatively open convex set [3] and the function $V : C \to \mathbb{R}$ is C^1, with derivative $V'(x)$ at each $x \in C$, then V is quasiconcave if and only if

$$(2.2) \qquad V(x) \leq V(y) \;\Rightarrow\; V'(x)(y - x) \geq 0 \quad \forall \; x, y \in C.$$

If V is C^2, then the following is also equivalent:

$$(2.3) \qquad \text{if } V'(x)z = 0, \text{ then } zV''(x)z \leq 0.$$

Remark 2.1. It is clear from (2.1) that a concave function is quasiconcave. It is also easy to see that a concave function satisfies (2.2): Since a concave function lies below its tangents

$$V(y) \leq V(x) + V'(x)(y - x),$$

it follows that

$$V'(x)y \geq V'(x)x - V(x) + V(y) \geq V'(x)x$$

whenever $V(y) \geq V(x)$.

However, the class of quasiconcave functions is much larger than the class of concave functions. For example, every monotone function $f : \mathbb{R} \to \mathbb{R}$ is quasiconcave. Moreover, if $f : \mathbb{R} \to \mathbb{R}$ is monotonically increasing and $V : C \to \mathbb{R}$ is concave, then $f \circ V$ is quasiconcave.

Our key tool is the following result on quasiconcave Lyapunov functions, which applies to the general migration-selection model (1.7). We define

$$f^{(\alpha)} = (f_{1,\alpha}, f_{2,\alpha}, \ldots, f_{n,\alpha})^T.$$

THEOREM 2.2. *Suppose there is a C^1 quasiconcave function $V : \mathring{\Delta}_n \to \mathbb{R}$ that is a Lyapunov function for* (1.3) *in each deme, i.e.,*

$$(2.4) \qquad \dot{V}(p^{(\alpha)}) = V'(p^{(\alpha)})f^{(\alpha)}(p^{(\alpha)}) \geq 0 \quad \text{for every } p^{(\alpha)} \in \mathring{\Delta}_n \text{ and } \alpha \in D.$$

Then $\underline{V}(p) := \min_\alpha V(p^{(\alpha)})$ is an increasing Lyapunov function for the spatial model (1.7).

Proof. For simplicity, we first assume that at some time $t > 0$,

$$(2.5) \qquad \underline{V}(p) = V(p^{(\alpha)}) < V(p^{(\beta)})$$

holds for some α and all β such that $\beta \neq \alpha$. Then by the continuity of V and p, (2.5) holds in a small time interval around t, and therefore,

$$(2.6) \qquad \begin{aligned} \underline{\dot{V}}(p) = \dot{V}(p^{(\alpha)}) &= V'(p^{(\alpha)})\dot{p}^{(\alpha)} \\ &= V'(p^{(\alpha)})f^{(\alpha)}(p^{(\alpha)}) + \sum_\beta \mu_{\alpha\beta} V'(p^{(\alpha)})p^{(\beta)} \\ &\geq 0 + \sum_\beta \mu_{\alpha\beta} V'(p^{(\alpha)})p^{(\alpha)} = 0. \end{aligned}$$

The inequality in (2.6) follows from (2.4), (2.5), and (2.2) with $x = p^{(\alpha)}$ and $y = p^{(\beta)}$.

Now if at some point the minimum is attained at more than one deme, then $\underline{V}(p)$ may not be differentiable but $t \mapsto \underline{V}(p(t))$ is still absolutely continuous and $\underline{\dot{V}}(p(t)) = \dot{V}(p^{(\alpha)}(t))$ holds for almost all t and all minimizing demes α. For details, see the appendix. Hence, $t \mapsto \underline{V}(p(t))$ is monotonically increasing. $\square$

From the above proof, for equality $\dot{\underline{V}}(p) = 0$, one needs the following two conditions for every α with $V(p^{(\alpha)}) = \min_\beta V(p^{(\beta)})$:

$$(2.7) \qquad V'(p^{(\alpha)})f^{(\alpha)}(p^{(\alpha)}) = 0\,,$$

$$(2.8) \qquad V'(p^{(\alpha)})(p^{(\beta)} - p^{(\alpha)}) = 0 \quad \text{for every } \beta \text{ with } \mu_{\alpha\beta} > 0\,.$$

In light of (2.7) and (2.8), we have the following results on $\underline{V}(p(t))$ being strictly increasing.

COROLLARY 2.3. *Suppose the following holds:*
(a) $\hat{p} \in \mathring{\Delta}_n$ *satisfies* $f_{i,\alpha}(\hat{p}) = 0$ *for every* $i \in N$ *and* $\alpha \in D$.
(b) *The assumption in Theorem 2.2 holds, and for every α equality in (2.4) is achieved if and only if $p^{(\alpha)} = \hat{p}$; and $\hat{p}$ is the unique maximizer of V in $\mathring{\Delta}_n$.*
Then for (1.7), $\dot{\underline{V}}(p(t)) \geq 0$ for almost all $t > 0$, and equality holds only when $p(t) = (\hat{p}, \hat{p}, \ldots, \hat{p})$. Hence, for $p(0) \in \mathring{\Delta}_n^d$ we conclude that $p(t) \to (\hat{p}, \hat{p}, \ldots, \hat{p})$ as $t \to \infty$.

Proof. Theorem 2.2 implies that every solution $p(t)$ of (1.7) satisfies $\dot{\underline{V}}(p(t)) \geq 0$ for almost all $t > 0$. By (2.7) and (2.8) and assumption (b), we see that $\dot{\underline{V}}(p(t)) = 0$ if and only if $p(t) = (\hat{p}, \hat{p}, \ldots, \hat{p})$.
Now, for $p(0) \in \mathring{\Delta}_n^d$, we know from (1.9) that $p(t) \in \mathring{\Delta}_n^d$ for every $t > 0$. Since $V(p)$ is bounded from above in $\mathring{\Delta}_n$ with a unique maximizer $\hat{p}$, we see that $\underline{V}(p(t)) \leq V(\hat{p})$ and equality holds only when $p(t) = (\hat{p}, \hat{p}, \ldots, \hat{p})$. Hence, since the ω-limit set of $p(t)$ is invariant and $\underline{V}$ is constant on it, we infer that it contains only $(\hat{p}, \hat{p}, \ldots, \hat{p})$. This proves that $p(t) \to (\hat{p}, \hat{p}, \ldots, \hat{p})$ as $t \to \infty$. $\square$

Remark 2.4. As a first application we rederive Theorems 5.6 and 5.9 in [22]. Note that the first theorem assumes positive migration rates and the second symmetric and irreducible migration. Here, we do not require these additional assumptions.

COROLLARY 2.5. *Suppose that the selection model (1.4) admits a g.a.s. interior equilibrium $\hat{p}$. Then for the corresponding uniform selection model with migration (1.10), the spatially homogeneous state $(\hat{p}, \hat{p}, \ldots, \hat{p})$ is globally asymptotically stable.*

Proof. For (1.4) the mean selection coefficient $\bar{r}(p)$ (defined in (1.5)) satisfies $\dot{\bar{r}}(p) \geq 0$ and equality holds if and only if p is at an equilibrium; see, e.g., [5, 16]. Moveover, if (1.4) admits an asymptotically stable interior equilibrium $\hat{p} \in \mathring{\Delta}_n$, then it is the unique interior equilibrium of (1.4) and $\bar{r} : \Delta_n \to \mathbb{R}$, as a function of p, is strictly concave, and $\hat{p}$ is the unique maximizer of $\bar{r}$ in Δ_n (see, e.g., [19, p. 62]). Hence, the conclusion of Corollary 2.5 follows from Corollary 2.3 by taking $V = \bar{r}$. $\square$

Remark 2.6. In [22, p. 34], under the assumption in Corollary 2.5, the Lyapunov function $V(p) = \sum_{i=1}^n \hat{p}_i \log p_i$ is used instead of $\bar{r}(p)$. In fact, for (1.4), $\dot{V}(p) = \bar{r}(\hat{p}) - \bar{r}(p) \geq 0$, and equality holds only when $p = \hat{p}$. Since this V is defined in terms of $\hat{p}$ and is independent of the selection coefficients r_{ij}, it can be applied even to nonuniform selection.

COROLLARY 2.7. *Suppose that $\hat{p} \in \mathring{\Delta}_n$ satisfies $f_{i,\alpha}(\hat{p}) = 0$ for every $i \in N$ and $\alpha \in D$ and is asymptotically stable with respect to (1.3) in each deme. Then for the corresponding migration-selection model (1.7), the spatially homogeneous state $(\hat{p}, \hat{p}, \ldots, \hat{p})$ is the globally asymptotically stable equilibrium.*

Proof. The conclusion follows from Corollary 2.3 and Remark 2.6 by taking the concave Lyapunov function $V(p) = \sum_i \hat{p}_i \log p_i$ with the unique maximizer $\hat{p}$ in $\mathring{\Delta}_n$. $\square$

If the g.a.s. equilibrium $\hat{p}$ lies on the boundary of Δ_n, i.e., $p \in \partial \Delta_n$, then (1.4) has no interior equilibrium. This situation has been characterized in [1] and [9, Thm. 4] as follows.

LEMMA 2.8. *If the selection equation* (1.4) *admits no interior equilibrium, then there are constants* $c_i \in \mathbb{R}$, *not all zero, such that*

$$(2.9) \qquad \sum_{i=1}^{n} c_i = 0 \quad and \quad \sum_{i=1}^{n} c_i r_i(p) > 0 \quad for \ every \ p \in \mathring{\Delta}_n .$$

Moreover, (2.9) *implies that for every interior solution* $p(t)$ *of* (1.4), $\sum_{i=1}^{n} c_i \log p_i(t)$ *is strictly increasing in* t, *and both the α-limit set and the ω-limit set of* $p(t)$ *are contained in* $\partial \Delta_n$.

Remark 2.9. If in Lemma 2.8, we assume in addition the following:
(A2.1) Every equilibrium of (1.4) is *regular*, i.e., the Jacobian matrix at every equilibrium has no zero eigenvalue.
Then we claim that the c_i's can be chosen such that the strict inequality in (2.9) holds on the whole Δ_n. To see this, we recall the proof of Theorem 4 in [9]: The convex set $C := \{(r_1(p), \ldots, r_n(p)) : \ p \in \mathring{\Delta}_n\} \subset \mathbb{R}^n$ is disjoint from the line $\ell := \{y \in \mathbb{R}^n : \ y_1 = \cdots = y_n\}$. Now, if every equilibrium is regular, then $\bar{C}$ (the closure of C) is disjoint from ℓ. For otherwise, there exists some $p \in \partial \Delta_n$ such that $r_i(p) = \bar{r}(p)$ for all i and $p_j = 0$ for at least one j. Clearly, such p is a boundary equilibrium of (1.4) and its eigenvalue in direction j is $r_j(p) - \bar{r}(p) = 0$, which violates the regularity of p. Then our claim follows from the separation theorem for two disjoint nonempty closed convex sets, with one of them compact.

Remark 2.10. Since all the eigenvalues of the Jacobian matrix at every equilibrium of (1.4) are real [12, 21], "regular" in (A2.1) implies "hyperbolic." Moreover, the assumption (A2.1) is generic [21, Appendix A].

Proposition 2.12, which is Theorem 3.5 in [22], extends Lemma 2.8 to the selection-migration model (1.7) in the crucial case that only one of the c_j's is negative. Here, we derive it as a consequence of Theorem 2.2. First, we prove the following lemma.

LEMMA 2.11. *The function* $V : (0, \infty)^n \to \mathbb{R}$, $V(x) = \sum_{i=1}^{n-1} q_i \log x_i - \log x_n$ *is quasiconcave if* q_i *for* $i = 1, \ldots, n-1$ *are nonnegative constants and* $\sum_{i=1}^{n-1} q_i = 1$.

Proof. Let $V(y) \geq V(x)$. Then

$$(2.10) \qquad \sum_{i=1}^{n-1} q_i \log \frac{y_i}{x_i} \geq \log \frac{y_n}{x_n}.$$

Since log is concave and strictly increasing, from (2.10) we get

$$(2.11) \qquad \sum_{i=1}^{n-1} q_i \frac{y_i}{x_i} \geq \frac{y_n}{x_n}.$$

Now $V'(x) = (\frac{q_1}{x_1}, \ldots, \frac{q_{n-1}}{x_{n-1}}, -\frac{1}{x_n})$ and (2.11) lead to

$$(2.12) \quad V'(x)(y - x) = \sum_{i=1}^{n-1} q_i \frac{y_i - x_i}{x_i} - \frac{y_n - x_n}{x_n} = \sum_{i=1}^{n-1} q_i \frac{y_i}{x_i} - \sum_{i=1}^{n-1} q_i - \frac{y_n}{x_n} + 1 \geq 0. \ \square$$

PROPOSITION 2.12. *Suppose there exists $q \in \Delta_n$ with $q_j = 0$ for some j such that*

$$(2.13) \qquad r_{j,\alpha}(p^{(\alpha)}) < \sum_i q_i r_{i,\alpha}(p^{(\alpha)}) \qquad \forall \, p^{(\alpha)} \in \Delta_n, \forall \, \alpha \in D \,.$$

Then along all interior solutions of (1.7), $\frac{\prod_i p_{i,\alpha}^{q_i}}{p_{j,\alpha}} \to \infty$ *for all α. Hence $p_{j,\alpha} \to 0$ for all α, i.e., allele A_j vanishes in all demes.*

Proof. The assumption (2.13) implies that $V(p) = \sum_i q_i \log p_i - \log p_j$ is a strictly increasing Lyapunov function for the selection equation (1.3) in each deme α; cf. Lemma 2.8:

$$(2.14) \qquad \dot{V}(p^{(\alpha)}) = \sum_i q_i r_{i,\alpha}(p^{(\alpha)}) - r_{j,\alpha}(p^{(\alpha)}) \geq c > 0 \,.$$

The positive lower bound $c > 0$ follows from (2.13) and the compactness of Δ_n. Hence $V(p^{(\alpha)}(t)) \to \infty$ along interior solutions of (1.3).

This function V is quasiconcave by Lemma 2.11. From Theorem 2.2 and (2.6) and (2.14), we conclude that $\underline{V}(p) = \min_\alpha V(p^{(\alpha)})$ is strictly increasing towards ∞ along interior solutions of (1.7). Therefore, $\min_\alpha \frac{\prod_i p_{i,\alpha}^{q_i}}{p_{j,\alpha}}$ is strictly increasing towards ∞. Since the numerator is bounded, $p_{j,\alpha} \to 0$ for every α. $\square$

Remark 2.13. From the proof of Proposition 2.12 we see that if a solution $p(t)$ of (1.7) satisfies

$$(2.15) \qquad \sum_i q_i r_{i,\alpha}(p^{(\alpha)}(t)) - r_{j,\alpha}(p^{(\alpha)}(t)) \geq c > 0$$

for every $\alpha \in D$ after some finite time, then for this solution we have $p_{j,\alpha} \to 0$ for every α, although (2.13) may not hold on the entire Δ_n.

Remark 2.14. If we relax condition (2.13) by requiring the strict inequality to hold only for those $p \in \Delta_n^d$ with $p_{j,\alpha} > 0$ for all α, and assume in addition that M is irreducible, then the conclusion $p_{j,\alpha} \to 0$ for every α still holds [22, Thm. 3.5].

Remark 2.15. If, in Lemma 2.8, more than one component of c is negative, then the Lyapunov function $\sum_{i=1}^n c_i \log p_i$ for (1.4) is no longer quasiconcave and we cannot apply Theorem 2.2.

3. Proof for three alleles. By Corollary 2.5, it is sufficient to prove the conjecture for $\hat{p} \in \partial \Delta_n$. We assume (A2.1) throughout this section. The classification of the three-allele selection equation (1.4) in [27, 28] tells us that there are five scenarios with a globally stable vertex and seven scenarios with a globally stable edge equilibrium. They are shown in Figure 1, where a large solid dot denotes a sink (asymptotically stable equilibrium), an open dot a source (repeller), and a small solid dot a saddle point. A dotted curve stands for a separatrix and a dashed curve for a typical orbit. Without loss of generality we label the left-lower, right-lower, and upper vertices by vertex 1, 2, and 3, respectively, and vertex i refers to the monomorphic equilibrium with A_i present. Notation E_{ij} for $i \neq j$ designates the edge equilibrium with alleles A_i and A_j present for (1.4). We use the same notation for the corresponding spatially homogeneous equilibria for (1.10).

Lemma 3.1(a),(b) was stated in [22, Remark 5.3] without a proof. We include a proof here following the idea in [22, Thm. 5.1] for the reader's convenience. Lemma 3.1(c) will be used in our later proofs.
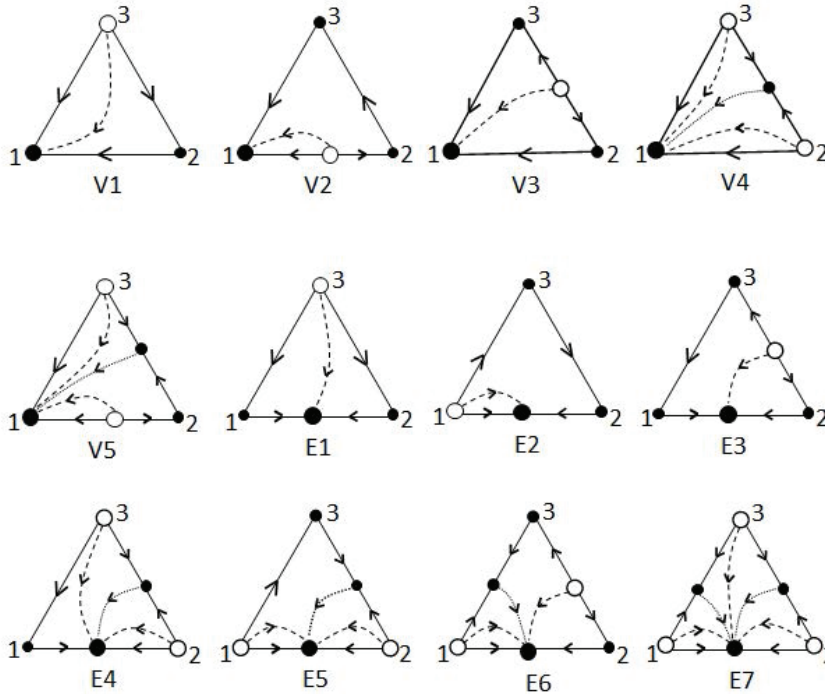
FIG. 1. *Three-allele selection patterns with a globally stable boundary equilibrium.*

LEMMA 3.1. *Suppose that $\hat{p}$ is an equilibrium of (1.4). Then the following conclusions hold.*

(a) *If $\hat{p}$ is linearly stable for (1.4), then it is also linearly stable for (1.10).*

(b) *If $\hat{p}$ is linearly unstable for (1.4), then it is also linearly unstable for (1.10).*

(c) *If $\hat{p}$ is a monomorphic, linearly repelling equilibrium of (1.4), then it repels every interior obit of (1.10) sufficiently close to it. More precisely, e.g., if $\hat{p}$ is the vertex 1, then there exists $\delta > 0$ such that for every positive solution of (1.10), $\min_\alpha\{1 - p_{1,\alpha}\}$ is strictly increasing as long as $\min_\alpha\{1 - p_{1,\alpha}\} \leq \delta$.*

Proof. We first prove parts (a) and (b). The Jacobian matrix of (1.10) at $\hat{p}$ reads

$$(3.1) \qquad\qquad J = M \otimes I_n + I_d \otimes \Gamma,$$

where M is the migration matrix, Γ is the Jacobian matrix of (1.4) at $\hat{p}$, I_n and I_d are identity matrices, and $\otimes$ signifies the Kronecker product. Let $\mu_1, \ldots, \mu_d$ and $\lambda_1, \ldots, \lambda_n$ be the eigenvalues of M and Γ, respectively (listed according to multiplicity).

On the one hand, we see from (1.6) that the row sums of M are zero, i.e., zero is an eigenvalue of M with eigenvector $(1, \ldots, 1)^T \in \mathbb{R}^d$. Since $\mu_{\alpha\beta} \geq 0$ for every $\alpha \neq \beta$, there exists $c > 0$ such that $M + cI_d$ is a nonnegative matrix. Applying the Perron–Frobenius theorem, one sees that the spectral bound $\sigma(M)$ (i.e., the maximum real part of eigenvalues) of M is an eigenvalue. Moreover, $\sigma(M)$ has to be zero here, since no other eigenvalue of M can have a positive eigenvector. Thus, all the eigenvalues of M have nonpositive real part.

On the other hand, in light of $\sum_{i=1}^n f_i(p) = 0$ for every $p \in \Delta_n$, we see that

$-\bar{r}$ is an eigenvalue of Γ with a left eigenvector $(1, \ldots, 1) \in \mathbb{R}^n$, which is not in the tangent space of Δ_n. Therefore, this eigenvalue $-\bar{r}$ is irrelevant to the stability of $\hat{p}$ with respect to the dynamics on Δ_n. Since all the eigenvalues of Γ are real [12, 21], we order the other $n-1$ eigenvalues (whose eigenvectors are in the tangent space of Δ_n) as $\lambda_1 \geq \cdots \geq \lambda_{n-1}$.

Hence, since by (3.1) the (relevant) eigenvalues of J are

$$(3.2) \qquad \mu_\alpha + \lambda_i \quad \text{for} \ \alpha = 1, \ldots, d \ \text{and} \ i = 1, \ldots, n-1$$

[29, Thm. 4.8], we see that if $\hat{p}$ is linearly stable (unstable) for (1.4), i.e, $\lambda_1 < 0$ ($\lambda_1 > 0$), then it is also linearly stable (unstable) for (1.10). This proves parts (a) and (b).

Next, we prove part (c). We take vertex 1 as an example. The eigenvalues of Γ at vertex 1 are $r_{1i} - r_{11}$ for $i = 2, 3, \ldots, n$. Since we assume that vertex 1 is linearly repelling, we know $r_{1i} - r_{11} > 0$ for $i = 2, 3, \ldots, n$. We will apply Theorem 2.2 with $V(p) = 1 - p_1$, which is linear and thus quasiconcave.

Recalling (1.4) and (1.5), we know

$$(3.3) \qquad \dot{V}(p) = V'(p)f(p) = -f_1(p) = p_1(\bar{r} - r_1)$$

$$= p_1 \sum_{i=1}^n (r_i - r_1)p_i$$

$$= p_1 \sum_{i=2}^n \left[(r_{i1} - r_{11})p_1 + \sum_{j=2}^n (r_{ij} - r_{1j})p_j\right]p_i$$

$$\geq p_1 \sum_{i=2}^n \left[Ap_1 - B(1 - p_1)\right]p_i$$

$$= p_1(1 - p_1)\left[p_1 A - (1 - p_1)B\right],$$

where $A = \min_{2 \leq i \leq n}(r_{i1} - r_{11}) > 0$ and $B = \max_{2 \leq i,j \leq n}|r_{ij} - r_{1j}| > 0$.

We infer from (3.3) that if we choose some $\delta \in (0, A/(A + B))$, then $\dot{V}(p) > 0$ as long as $0 < 1 - p_1 \leq \delta$. Thus, from Theorem 2.2 and (2.6), we conclude that for positive solutions of (1.10), the function $\underline{V}(p) = \min_\alpha\{1 - p_{1,\alpha}\}$ is strictly increasing as long as $\underline{V}(p) \leq \delta$. This proves part (c). □

In each case the key to proving that every positive solution of (1.10) converges to $\hat{p}$, is to show that $p_{j,\alpha}(t) \to 0$ as $t \to \infty$ for every j such that $\hat{p}_j = 0$ and every α. For this, by Proposition 2.12, we need to verify only (2.13). This is sufficient for the vertex cases, whereas for the edge cases we need to show further that the ω-limit set of every positive solution contains only $\hat{p}$. We present the cases in order of increasing difficulty.

3.1. Case V3. This case is defined by the fitness relations

$$(3.4) \qquad r_{11} > r_{12} > r_{22}, \quad r_{11} > r_{13} > r_{33}, \quad \text{and} \quad r_{22}, r_{33} > r_{23}.$$

This implies $r_{1i} > r_{2i}$ and $r_{1i} > r_{3i}$ for all i. Therefore, from (1.5) we infer that $r_1 > r_2$ and $r_1 > r_3$ on Δ_3, and by Proposition 2.12, both p_2 and p_3 vanish in each deme as $t \to \infty$. Hence vertex 1 is globally asymptotically stable for (1.10).

3.2. Case V1. This case is defined by the fitness relations

$$(3.5) \qquad r_{11} > r_{12} > r_{22} > r_{23} > r_{33} \quad \text{and} \quad r_{11} > r_{13} > r_{33}.$$

Allele A_1 is always strictly fitter than A_3, i.e., $r_{1i} > r_{3i}$ for all i. Hence $r_1 > r_3$ on Δ_3, and by Proposition 2.12, p_3 vanishes in each deme in the limit. Once p_3 is sufficiently small, we have $r_1 > r_2$, and thus p_2 vanishes in all demes eventually; see Remark 2.13. This demonstrates the global asymptotic stability of vertex 1 for (1.10).

3.3. Case V2. This case is defined by the fitness relations

$$(3.6) \qquad r_{11}, r_{22} > r_{12} \quad \text{and} \quad r_{11} > r_{13} > r_{33} > r_{23} > r_{22}.$$

Then we have $r_{3i} > r_{2i}$ for all i, i.e., $r_3 > r_2$ for all $p \in \Delta_3$, and hence $p_2 \to 0$. Once p_2 is sufficiently small, we have $r_1 > r_3$, and therefore by Remark 2.13, $p_3 \to 0$ in each deme. This shows that $p_1 \to 1$ in each deme.

3.4. Case V5. This case is defined by the fitness relations

$$(3.7) \qquad r_{11}, r_{22} > r_{12}, \quad r_{11} > r_{13} > r_{33}, \quad \text{and} \quad r_{23} > r_{22}, r_{33}.$$

The additional information that there is no interior equilibrium, the assumption (A2.1), Lemma 2.8, and Remark 2.9 guarantee the existence of $c_i \in \mathbb{R}$ for $i = 1, 2, 3$, not all zero, such that $\sum_{i=1}^3 c_i = 0$ and $\sum_{i=1}^3 c_i r_i(p) > 0$ holds for all $p \in \Delta_3$. The sign of the c_i can be determined in the following way.

LEMMA 3.2. *Suppose that for $n = 3$ the selection equation (1.4) has no interior equilibrium and (A2.1) holds. Let $c_i \in \mathbb{R}$ for $i = 1, 2, 3$ be as in Remark 2.9. For $\{i, j, k\} = \{1, 2, 3\}$, if the edge equilibrium E_{ij} exists and λ_k designates its eigenvalue in direction k, then $\lambda_k c_k > 0$.*

Proof. At $p = E_{ij}$ we have $r_i(p) = r_j(p) = \bar{r}(p)$ and $\lambda_k = r_k(p) - \bar{r}(p)$. Hence

$$0 < c_i r_i(p) + c_j r_j(p) + c_k r_k(p) = (c_i + c_j)\bar{r} + c_k(\bar{r} + \lambda_k) = c_k \lambda_k. \qquad \square$$

Now from the fact that vertex 1 is globally asymptotically stable for (1.4) we infer that $\lambda_1 > 0$, since $\lambda_1 = 0$ is excluded by assumption (A2.1) and $\lambda_1 < 0$ would imply that E_{23} attracts at least one interior solution. Similarly, $\lambda_3 > 0$. Then Lemma 3.2 shows that $c_1 > 0$ and $c_3 > 0$. Hence $c_2 = -c_1 - c_3 < 0$, and we can apply Proposition 2.12 with $q_1 = -c_1/c_2$ and $q_3 = -c_3/c_2$ to show that $p_2 \to 0$ in each deme. Once p_2 is sufficiently small, we have $r_1 > r_3$ and subsequently $p_3 \to 0$ by Remark 2.13.

Surprisingly, case V4 is the hardest vertex case and it is similar to case E4. Therefore, we treat it after case E4 at the end of this section.

3.5. Case E1. This case is defined by the fitness relations

$$(3.8) \qquad r_{12} > r_{11}, r_{22}, \quad r_{11} > r_{13} > r_{33}, \quad \text{and} \quad r_{22} > r_{23} > r_{33}.$$

In this case both $r_1 > r_3$ and $r_2 > r_3$ hold on Δ_3, and hence $p_3 \to 0$ in every deme. Therefore, the ω-limit set of any orbit, except vertex 3, is contained in the two-allele subsystem $p_3 = 0$.

In order to show that every interior orbit converges to $E_{12} = (\hat{p}, \hat{p}, \ldots, \hat{p})$, where $\hat{p} = (\hat{p}_1, \hat{p}_2, 0)$, we consider the function $V(p) = \sum_{i=1}^2 \hat{p}_i \log p_i$ for $p \in \Delta_3$. Note that $V = -\infty$ when $p_1 = 0$ or $p_2 = 0$, V has a unique maximum for $p \in \Delta_3$ at $\hat{p}$, and $\dot{V}(p) = \hat{p} \cdot Rp - p \cdot Rp$, where $R = (r_{ij})$ is the selection matrix.

On the one hand, by Remark 2.6 (for $n = 2$), $\dot{V}(p) > 0$ on the edge $p_3 = 0$, except at $\hat{p}$. On the other hand, as explained in [10, p. 288], since $\hat{p}$ is globally asymptotically stable for (1.4), we see that $\hat{p} \cdot R\hat{p} > p \cdot Rp$ for all $p \in \Delta_3$ and $p \neq \hat{p}$, and hence replacing

p by $2p - \hat{p}$ we conclude that $\hat{p} \cdot Rp > p \cdot Rp$ for p close to $\hat{p}$ (such that $2p - \hat{p} \in \Delta_3$). Thus, $\dot{V}(p) > 0$ holds in a pointed neighborhood of $\hat{p}$ in Δ_3.

Hence, for small p_3, $\dot{V}(p) \geq 0$ holds, with $\dot{V} = 0$ only at $\hat{p}$. Since V is concave with a unique maximizer $\hat{p}$ in Δ_3, and $p_3(t) \to 0$ as $t \to \infty$, we conclude by a similar argument as in the proof of Corollary 2.3 that for every $p(0) \in \mathring{\Delta}_3^d$, eventually $\underline{V}(p) = \min_\alpha V(p^\alpha)$ is a strictly increasing Lyapunov function for (1.10) and $\omega(p(0)) = \{(\hat{p}, \hat{p}, \ldots, \hat{p})\}$, i.e., $p(t) \to E_{12}$ as $t \to \infty$.

Remark 3.3. In fact, by [10, p. 288], the Lyapunov function $V(p) = \sum_i \hat{p}_i \log p_i$ works for a general asymptotically stable state $\hat{p}$ that supports k out of n alleles: $\dot{V}(p) > 0$ in an open neighborhood of the subsimplex Δ_k in which $\hat{p}$ is a relative interior point, except $\dot{V}(p) = 0$ at $\hat{p}$.

3.6. Case E2. This case is defined by the fitness relations

$$(3.9) \qquad r_{12} > r_{11}, r_{22}, \quad r_{33} > r_{13} > r_{11}, \quad \text{and} \quad r_{22} > r_{23} > r_{33}.$$

Here $r_2 > r_3$ holds on Δ_3, and hence $p_3(t) \to 0$ in every deme. Then $p(t) \to E_{12}$ as in case E1.

3.7. Case E3. This case is defined by the fitness relations

$$(3.10) \qquad r_{12} > r_{11}, r_{22}, \quad r_{11} > r_{13} > r_{33}, \quad \text{and} \quad r_{22}, r_{33} > r_{23}.$$

Here $r_1 > r_3$ holds on Δ_3, and hence $p_3(t) \to 0$ in every deme. Then $p(t) \to E_{12}$ as in case E1.

3.8. Case E5. This case is defined by the fitness relations

$$(3.11) \qquad r_{12} > r_{11}, r_{22}, \quad r_{33} > r_{13} > r_{11}, \quad \text{and} \quad r_{23} > r_{22}, r_{33}.$$

Because there is no interior equilibrium, by Lemma 2.8 and Remark 2.9 we find c_j for $i = 1, 2, 3$ such that $\sum_{j=1}^3 c_j r_j(p) > 0$ for all $p \in \Delta_3$, which at vertex 3 yields

$$(3.12) \qquad 0 < c_1 r_{13} + c_2 r_{23} + c_3 r_{33} = c_1(r_{13} - r_{33}) + c_2(r_{23} - r_{33}).$$

From Lemma 3.2 we infer that $c_1 > 0$ and $c_3 < 0$, whence (3.11) and (3.12) imply $c_2 > 0$. Therefore, Proposition 2.12 with $q_1 = -c_1/c_3$ and $q_2 = -c_2/c_3$ tells us that $p_3(t) \to 0$ in each deme. Then $p(t) \to E_{12}$ as in case E1.

3.9. Cases E6 and E7. Here there are three edge equilibria, and Lemma 3.2 implies $c_1 > 0$, $c_2 > 0$, and $c_3 < 0$. Hence, $p_3(t) \to 0$ in each deme, and $p(t) \to E_{12}$ as in case E1.

3.10. Case E4. This case is defined by the fitness relations

$$(3.13) \qquad r_{12} > r_{11}, r_{22}, \quad r_{11} > r_{13} > r_{33}, \quad \text{and} \quad r_{23} > r_{22}, r_{33}.$$

From (1.5) we know

$$(3.14) \qquad r_1 - r_3 = (r_{11} - r_{13})p_1 + (r_{12} - r_{23})p_2 + (r_{13} - r_{33})p_3.$$

Case 1. $r_{12} > r_{23}$.
From (3.13) and (3.14), we have $r_1 - r_3 > 0$ for every $p \in \Delta_3$. Hence, by Proposition 2.12, $p_3(t) \to 0$ in every deme, and then $p(t) \to E_{12}$ as in case E1.
Case 2. $r_{12} = r_{23}$.

We have $r_1 - r_3 = 0$ at vertex 2 and $r_1 - r_3 > 0$ elsewhere in Δ_3. Since vertex 2 is a repeller for (1.4), from Lemma 3.1(c) we see that any positive solution $p(t)$ of (1.10) will stay away from vertex 2. Therefore, $r_1(p(t)) - r_3(p(t)) > 0$ and is bounded away from zero, whence by Proposition 2.12 and Remark 2.13, $p_3(t) \to 0$ in every deme, and then $p(t) \to E_{12}$ as in case E1.

Case 3. $r_{12} < r_{23}$.

Since we have assumed that (1.4) has no interior equilibrium and only regular boundary equilibria, from Lemma 3.2 we find $c_1 > 0$ and $c_3 < 0$, and from Lemma 2.8 and Remark 2.9 we infer that (2.9) holds on the entire Δ_3. In particular, at the vertex 2,

$$(3.15) \qquad 0 < c_1 r_{12} + c_2 r_{22} + c_3 r_{23} = c_1(r_{12} - r_{23}) + c_2(r_{22} - r_{23}),$$

which shows $c_2 < 0$. Therefore, there is an $\alpha \in (0,1)$ such that

$$(3.16) \qquad r_1 > \alpha r_2 + (1-\alpha)r_3 \quad \text{on } \Delta_3,$$

whence we infer from Lemma 2.8 that the function $\frac{p_1}{p_2^\alpha p_3^{1-\alpha}}$ is an increasing Lyapunov function for (1.4). However, this function is not quasiconcave, and Theorem 2.2 does not help us here for the model with migration (see Remark 2.15). We have to proceed differently.

LEMMA 3.4. (i) *Suppose that* (1.4) *allows a linear (Lyapunov like) function* $H(p) = \sum_{i=1}^n a_i p_i$ *that satisfies*

$$(3.17) \qquad \dot{H}(p) = \sum_{i=1}^n a_i \dot{p}_i = \sum_{i=1}^n a_i f_i(p) > 0 \quad \text{whenever } H(p) \le 0 \text{ and } p \in \mathring{\Delta}_n.$$

Then for any positive solution $p(t) = (p_{i,\alpha}(t)) \in \mathring{\Delta}_n^d$ *of* (1.10), *the function* $\underline{H}(p) := \min_\alpha H(p^{(\alpha)}(t))$ *increases strictly as long as* $\underline{H}(p(t)) \le 0$.

(ii) *Assume additionally that* $\min_{p \in \Delta_n} H(p) = H_m \le 0$ *and that there exists* $c > 0$ *such that for* (1.4),

$$(3.18) \quad \dot{H}(p) = \sum_{i=1}^n a_i \dot{p}_i = \sum_{i=1}^n a_i f_i(p) > 0 \quad \text{whenever } H_m < H(p) \le c \text{ and } p \in \Delta_n.$$

Then along any solution $p(t)$ *of* (1.10) *such that* $\underline{H}(p(0)) > H_m$, *we have* $\underline{H}(p(t)) > c$ *after finite time.*

Proof. (i) Note that the linear function H is concave and by (3.17) the strict inequality in (2.6) holds. Thus, it follows from the proof of Theorem 2.2 that $t \mapsto \underline{H}(p(t))$ increases strictly as long as $\underline{H}(p(t)) \le 0$.

(ii) Similarly to (i), we infer from (3.18) that for any solution $p(t)$ of (1.10) with $\underline{H}(p(0)) > H_m$, the function $\underline{H}(p(t))$ increases strictly as long as $H_m < \underline{H}(p(t)) \le c$.

We also observe that for (1.10), the set $\{p \in \Delta_n^d : \underline{H}(p) > c\}$ is forward invariant: If $\underline{H}(p(t)) = c$, then for every α such that $H(p^{(\alpha)}(t)) = c$, we have by the concavity of H and (2.6) and (3.18) that

$$(3.19) \qquad \dot{H}(p^{(\alpha)}(t)) \ge \sum_{i=1}^n a_i f_i(p^{(\alpha)}(t)) > 0.$$

Hence, if the conclusion that $\underline{H}(p(t)) > c$ after finite time does not hold, we must have $\underline{H}(p(t)) \le c$ for all $t > 0$. However, this together with the fact that

$\underline{H}(p(t))$ increases strictly as long as $H_m < \underline{H}(p(t)) \le c$ and the initial condition $\underline{H}(p(0)) > H_m$ would imply that

$$(3.20) \qquad \underline{H}(p(0)) < \underline{H}(p(t)) \le c \quad \text{for all } t > 0.$$

From (3.18), the continuity of f_i and H, and the compactness of $\{p \in \Delta_n : \underline{H}(p(0)) \le H(p) \le c\}$, we see that there exists $\varepsilon > 0$ such that

$$(3.21) \qquad \sum_{i=1}^{n} a_i f_i(p) \ge \varepsilon \quad \text{whenever } \underline{H}(p(0)) \le H(p) \le c.$$

Thus, recalling the proof of Theorem 2.2, from (2.6), (3.18), (3.20), (3.21), and the concavity of H, we see that for almost all $t > 0$ and all α such that $\underline{H}(p(t)) = H(p^{(\alpha)}(t))$,

$$(3.22) \qquad \underline{\dot{H}}(p(t)) = \dot{H}(p^{(\alpha)}) \ge \sum_{i=1}^{n} a_i f_i(p^{(\alpha)}) \ge \varepsilon,$$

whence $\underline{H}(p(t)) \to \infty$ as $t \to \infty$. This contradicts our assumption $\underline{H}(p(t)) \le c$ for all $t > 0$. Therefore, we must have $\underline{H}(p(t)) > c$ after finite time. $\qquad \square$

LEMMA 3.5. *Suppose that (1.4) has no interior equilibrium and (A2.1) holds, and that (3.13) and $r_{12} < r_{23}$ hold. Then for every positive solution $p(t) \in \overset{\circ}{\Delta}_3$ of (1.4), the difference $r_1(p(t)) - r_3(p(t))$ is strictly increasing in t as long as $r_1(p(t)) \le r_3(p(t))$.*

Proof. In view of (1.4) and (3.14), we deduce that

$$(3.23) \quad \dot{r}_1(p(t)) - \dot{r}_3(p(t))$$
$$= (r_{11} - r_{13})\dot{p}_1 + (r_{12} - r_{23})\dot{p}_2 + (r_{13} - r_{33})\dot{p}_3$$
$$= (r_{11} - r_{13})p_1(r_1 - \bar{r}) + (r_{12} - r_{23})p_2(r_2 - \bar{r})$$
$$\quad + (r_{13} - r_{33})p_3(r_3 - \bar{r})$$
$$= (r_{11} - r_{13})p_1(r_1 - \bar{r}) + (r_{12} - r_{23})p_2(r_1 - \bar{r} + r_2 - r_1)$$
$$\quad + (r_{13} - r_{33})p_3(r_1 - \bar{r} + r_3 - r_1)$$
$$= (r_1 - r_3)(r_1 - \bar{r}) + (r_{12} - r_{23})p_2(r_2 - r_1)$$
$$\quad + (r_{13} - r_{33})p_3(r_3 - r_1)$$
$$= (r_1 - r_3)[(r_1 - r_2)p_2 + (r_1 - r_3)p_3] + (r_{12} - r_{23})p_2(r_2 - r_1)$$
$$\quad + (r_{13} - r_{33})p_3(r_3 - r_1)$$
$$= (r_1 - r_2)p_2[(r_1 - r_3) + (r_{23} - r_{12})] + (r_1 - r_3)^2 p_3$$
$$\quad + (r_{13} - r_{33})p_3(r_3 - r_1)$$
$$= (r_1 - r_2)p_2[(r_{11} - r_{13})p_1 + (r_{23} - r_{12})(1 - p_2) + (r_{13} - r_{33})p_3]$$
$$\quad + (r_1 - r_3)^2 p_3 + (r_{13} - r_{33})p_3(r_3 - r_1).$$

If $r_1 \le r_3$, then the inequality (3.16) implies that $r_1 > r_2$. This and (3.13) inform us that for $p(t) \in \overset{\circ}{\Delta}_3$, the first term in the right-hand side of the last equality in (3.23) is positive and the last two terms are nonnegative. This proves the lemma. $\qquad \square$

Lemma 3.5 tells us that $H(p) = r_1(p) - r_3(p)$ satisfies (3.17). From (3.13) and (3.14) we see that $H_m = r_{12} - r_{23} < 0$, which is achieved only at vertex 2. We infer from (3.14) and (3.23) that $\dot{H}(p) > 0$ whenever $H_m < H(p) \le 0$. In particular,

$\dot{H}(p) > 0$ on $\{p \in \Delta_3 : H(p) = 0\}$. Then from the continuity of H and the compactness of $\{p \in \Delta_3 : H(p) = 0\}$, we infer that for sufficiently small $c > 0$, (3.18) holds.

It follows from Lemma 3.4(ii) that for any positive solution $p(t)$ of (1.10),

$$H(p^{(\alpha)}(t)) > c, \text{ i.e., } r_1(p^{(\alpha)}(t)) - r_3(p^{(\alpha)}(t)) \geq c > 0$$

for every α after finite time. Therefore, it follows from Proposition 2.12 and Remark 2.13 that $p_3(t) \to 0$ in each deme, and $p(t) \to E_{12}$ as in case E1.

3.11. Case V4. This case is defined by the fitness relations

$$(3.24) \qquad r_{11} > r_{12} > r_{22}, \quad r_{11} > r_{13} > r_{33}, \quad \text{and} \quad r_{23} > r_{22}, r_{33}.$$

From (1.5) we know

$$(3.25) \qquad r_1 - r_3 = (r_{11} - r_{13})p_1 + (r_{12} - r_{23})p_2 + (r_{13} - r_{33})p_3,$$
$$(3.26) \qquad r_1 - r_2 = (r_{11} - r_{12})p_1 + (r_{12} - r_{22})p_2 + (r_{13} - r_{23})p_3.$$

One can show that $p_3(t) \to 0$ in each deme as $t \to \infty$ in the exact same way as in case E4 above. Then since $r_{11} - r_{12} > 0$ and $r_{12} - r_{22} > 0$, we infer from (3.26) that regardless of the sign of $r_{13} - r_{23}$, there exists $\varepsilon > 0$ such that $r_1 - r_2 > \varepsilon$ if p_3 is sufficiently small. Therefore, by Remark 2.13, $p_2(t) \to 0$ in each deme as $t \to \infty$. This proves the global stability of vertex 1.

4. Continuous space. In case of a continuous habitat Ω, which is an open, connected, bounded set in $\mathbb{R}^d$ with smooth boundary $\partial\Omega$, the function $p_i(x,t)$ represents the frequency of allele A_i at position x and time t for $i = 1, \ldots, n$. Then the vector of allele frequencies is supposed to satisfy

$$(4.1) \qquad p(x,t) = (p_1(x,t), \ldots, p_n(x,t)) \in \Delta_n \text{ for every } x \in \bar{\Omega} \text{ and } t \geq 0.$$

Let the selection coefficient of the genotype $A_i A_j$ at location x be $r_{ij}(x)$ and assume $r_{ij}(x) = r_{ji}(x)$ as before. The selection coefficient of allele A_i and the mean selection coefficient of the population are given, respectively, by

$$(4.2) \qquad r_i(x,p) = \sum_{j=1}^{n} r_{ij}(x)p_j, \quad \bar{r}(x,p) = \sum_{i,j=1}^{n} r_{ij}(x)p_i p_j.$$

In analogy to (1.3), the contribution of selection to the change of allele frequencies is

$$(4.3) \qquad f_i(x,p) := p_i \left[r_i(x,p) - \bar{r}(x,p) \right].$$

The continuous-space analog of the discrete-space migration-selection model (1.7) is (see Nagylaki [17, 18, 20] and Fife [7])

$$(4.4a) \qquad \frac{\partial p_i}{\partial t} = L p_i + f_i(x,p) \quad \text{in } \Omega \times (0,\infty),$$

$$(4.4b) \qquad B p_i = 0 \qquad \qquad \text{on } \partial\Omega \times (0,\infty),$$

$$(4.4c) \qquad p(x,0) \in \Delta_n \qquad \qquad \text{for } x \in \bar{\Omega},$$

where

$$(4.5) \qquad L p_i = \sum_{\alpha,\beta=1}^{d} a_{\alpha\beta}(x)\frac{\partial^2 p_i}{\partial x_\alpha \partial x_\beta} + \sum_{\alpha=1}^{d} b_\alpha(x)\frac{\partial p_i}{\partial x_\alpha},$$

$$(4.6) \qquad B p_i = \nu^T A \nabla p_i.$$

Here, L describes migration, in which the matrix $A(x) := (a_{\alpha\beta}(x))$ is symmetric and positive definite for every $x \in \bar{\Omega}$, and every $a_{\alpha\beta}$, b_α belongs to $C^\theta(\bar{\Omega})$ $(0 < \theta < 1)$. In (4.6), at each $x \in \partial\Omega$, ν is the unit outward normal vector and ∇p_i signifies the gradient of p_i with respect to x. Therefore, since every $A(x)$ is positive definite, the boundary operator B is of Neumann co-normal type, and (4.4b) means that no individuals cross the boundary.

As explained in [13, p. 401], problem (4.4) has a unique classical solution that exists for all time $t > 0$ and (4.1) holds indeed. Moreover, by the strong maximum principle [25], if

$$(4.7) \qquad \int_\Omega p_i(x,0) \, dx > 0 \,,$$

then $p_i(x,t) > 0$ for every $x \in \bar{\Omega}$ and $t > 0$.

If selection is uniform over the habitat, then there exist constants $r_{ij} = r_{ji}$ for $i, j = 1, \ldots, n$ such that

$$(4.8) \qquad r_{ij}(x) = r_{ij} \quad \text{for every } x \in \bar{\Omega} \,.$$

The *conjecture for the PDE version* appears in [23, p. 792] and [16, p. 4370].

If the ODE system (1.4) *has a globally asymptotically stable equilibrium* $\hat{p} \in \Delta_n$, *then for the PDE system* (4.4) *with* (4.8) *where the constants* r_{ij} *are as in* (1.4), *the spatially homogeneous state* $\hat{p}(x) \equiv \hat{p}$ *on* $\bar{\Omega}$ *is globally asymptotically stable.*

Here $\hat{p}$ is *globally asymptotically stable* for (4.4) if it is asymptotically stable, and its basin of attraction contains all the initial data $p(x,0) \in C(\bar{\Omega}, \Delta_n)$ that satisfy (4.7) for every $i = 1, \ldots, n$.

For $\hat{p} \in \mathring{\Delta}_n$, the conjecture was settled by Hadeler [8, Thm. 1] for the Laplacian and by Nagylaki and Lou [23, Thm. 3.3] for general L. For $\hat{p} \in \partial\Delta_n$, it remains largely open. In the case of two alleles, the conjecture follows from the monotonicity of the flow (note that $p_1(x,t) \equiv u(t)$ satisfies (1.11)); see also [13, Thm. 3.1], [15, Appendix B].

The main aim of this section is to prove the above conjecture for $\hat{p} \in \partial\Delta_n$ with $n = 3$ as for the discrete-space case; the method used is also similar.

The following key proposition is a special case of [14, Thm. 1.1], [15, Appendix B]. It is the analog of Proposition 2.12.

PROPOSITION 4.1. *Suppose that there exists* $q \in \Delta_n$ *with* $q_j = 0$ *such that*

$$(4.9) \qquad r_j(x,p) < \sum_i q_i r_i(x,p) \quad \text{for every } p \in \Delta_n \text{ and } x \in \bar{\Omega} \,.$$

Then for every positive solution $p(x,t)$ *of* (4.4), $p_j(x,t) \to 0$ *uniformly in* x *as* $t \to \infty$.

In [14], the main ingredient in the proof of Proposition 4.1 is to show that for any positive solution $p(x,t)$ of (4.4), the function $\min_{x\in\bar{\Omega}} V(p(x,t))$, where $V(p) = \frac{1}{p_j} \prod_{i=1}^n p_i^{q_i}$, is strictly increasing. In fact, the assumption (4.9) implies that $V(p)$ is a quasiconcave Lyapunov function of (1.4) (see Remark 2.1 and Lemmas 2.8 and 2.11), and therefore, its monotonicity follows from the more general result below, which is the analog of Theorem 2.2.

THEOREM 4.2. *Suppose that there is a* C^2 *quasiconcave function* $V : \mathring{\Delta}_n \to \mathbb{R}$ *such that*

$$(4.10) \qquad V'(p)f(x,p) > 0 \quad \text{for every } p \in \mathring{\Delta}_n \text{ and } x \in \bar{\Omega},$$

where $V'(p)$ signifies the gradient (row) vector of V as a function of p and $f = (f_1, \ldots, f_n)^T$ is as in (4.3). Then for every positive solution $p(x,t)$ of (4.4), the function $\underline{V}(p)(t) := \min_{x \in \bar{\Omega}} V(p(x,t))$ is strictly increasing in t.

Proof. In light of (4.4) the function $(V \circ p)(x,t) := V(p(x,t))$ satisfies

$$(4.11\text{a}) \qquad \frac{\partial(V \circ p)}{\partial t} - L(V \circ p) = V'(p)f(x,p) - \sum_{\alpha,\beta=1}^{d} a_{\alpha\beta} \frac{\partial p}{\partial x_\alpha} V''(p) \left(\frac{\partial p}{\partial x_\beta}\right)^T$$

in $\Omega \times (0, \infty)$ and

$$(4.11\text{b}) \qquad\qquad\qquad B(V \circ p) = 0 \quad \text{on } \partial\Omega \times (0, \infty),$$

where $V''(p)$ denotes the Hessian matrix of V as a function of p, and $\frac{\partial p}{\partial x_\beta}$ stands for the vector $\left(\frac{\partial p_1}{\partial x_\beta}, \ldots, \frac{\partial p_n}{\partial x_\beta}\right)$.

We argue by contradiction: Suppose that for a positive solution $p(x,t)$ of (4.4),

$$(4.12) \qquad \min_{x \in \bar{\Omega}} V(p(x,t_2)) \leq \min_{x \in \bar{\Omega}} V(p(x,t_1)) \quad \text{for some } 0 \leq t_1 < t_2.$$

Then there exist $x^* \in \bar{\Omega}$ and $t^* \in (t_1, t_2]$ such that

$$(4.13) \qquad\qquad V(p(x^*, t^*)) = \min_{x \in \bar{\Omega},\ t \in [t_1,t_2]} V(p(x,t)).$$

There are two cases.

(a) $x^* \in \Omega$.

To derive a contradiction, we examine the sign of each term in (4.11a) at (x^*, t^*). Since $t^* \in (t_1, t_2]$, we see that $\frac{\partial(V \circ p)}{\partial t} \leq 0$. We infer from (4.5) and the positive definiteness of A that $-L(V \circ p) \leq 0$. Since A is symmetric, there exist vectors $w_\gamma = (w_{\gamma 1}, \ldots, w_{\gamma d})$ for $\gamma = 1, \ldots, d$, which are orthogonal to each other such that

$$(4.14) \qquad\qquad A = \sum_{\gamma=1}^{d} \lambda_\gamma w_\gamma^T w_\gamma, \quad \text{i.e., } a_{\alpha\beta} = \sum_{\gamma=1}^{d} \lambda_\gamma w_{\gamma\alpha} w_{\gamma\beta},$$

where λ_γ are the (real) eigenvalues of A. Moreover, all λ_γ are positive by the positive definiteness of A. Since $x^* \in \Omega$, the directional derivative $\nabla_w(V \circ p)$ with respect to the space variable x at (x^*, t^*) is zero along every direction $w \in \mathbb{R}^d$. In particular, we see that

$$(4.15) \qquad\qquad \nabla_{w_\gamma}(V \circ p) = V'(p)(\nabla_{w_\gamma} p)^T = 0 \quad \text{for every } \gamma,$$

whence the quasi-concavity of V and (2.3) and (4.14) inform us that

$$(4.16) \qquad \sum_{\alpha,\beta=1}^{d} a_{\alpha\beta} \frac{\partial p}{\partial x_\alpha} V''(p) \left(\frac{\partial p}{\partial x_\beta}\right)^T = \sum_{\gamma=1}^{d} \lambda_\gamma \nabla_{w_\gamma} p\, V''(p)(\nabla_{w_\gamma} p)^T \leq 0.$$

Hence at (x^*, t^*) the left-hand side of (4.11a) is nonpositive and by (4.10) and (4.16) the right-hand side is positive, which is a contradiction.

(b) $x^* \in \partial\Omega$.

Without loss of generality we may assume that

$$(4.17) \qquad V(p(x,t)) > V(p(x^*, t^*)) \quad \text{for every } x \in \Omega \text{ and } t \in (t_1, t_2],$$

for otherwise, if there exists some $(\tilde{x}^*, \tilde{t}^*) \in \Omega \times (t_1, t_2]$ at which V achieves its minimum on $\bar{\Omega} \times [t_1, t_2]$, we would get a contradiction as in case (a).

We observe that $\nabla_w(V \circ p)$ is still zero along every direction w which is tangent to $\partial\Omega$ at x^*. This with the positive definiteness of A and (4.11b) implies that $\nabla_w(V \circ p) = 0$ for every $w \in \mathbb{R}^d$. Hence, (4.16) still holds at (x^*, t^*). Now since $V'(p(x^*, t^*))f(x^*, p(x^*, t^*)) > 0$, by the continuity of the involved functions, there exists a subregion of $\Omega \times (0, \infty)$, say, $E = \Omega_1 \times (t_1', t_2')$, such that $\bar{\Omega}_1 \setminus \{x^*\} \subset \Omega$, Ω_1 is smooth, $t_1 < t_1' < t^* < t_2'$, $\partial\Omega$ and $\partial\Omega_1$ are tangent at x^*, and

$$(4.18) \qquad \frac{\partial(V \circ p)}{\partial t} - L(V \circ p) \geq 0 \quad \text{in } E.$$

Hence from the Hopf boundary lemma [25, Thm. 6, p. 174] with $E_{t^*} = \{(x, t) \in E : t \leq t^*\}$, the fact that $V(p(x, t)) > V(p(x^*, t^*))$ for every $(x, t) \in E_{t^*}$ by (4.17), and the existence of a sphere required in this lemma by the smoothness of $\partial\Omega_1$, we infer that

$$(4.19) \qquad B(V \circ p) < 0 \quad \text{at } (x^*, t^*),$$

which contradicts (4.11b).

The contradictions prove the lemma. □

Remark 4.3. Similar to Remark 2.13, if a solution $p(x, t)$ of (4.4) satisfies

$$(4.20) \qquad \sum q_i r_i(x, p(x, t)) - r_j(x, p(x, t)) \geq c > 0$$

for every $x \in \bar{\Omega}$ after some finite time, then for this solution we have $p_j(x, t) \to 0$ uniformly in x as $t \to \infty$, although (4.9) may not hold on the entire Δ_n.

The following theorem of Nagylaki and Lou [23] deals with local stability of $\hat{p}$.

THEOREM 4.4. *Suppose that $\hat{p}$ is an equilibrium of* (1.4). *Then $\hat{p}$ is linearly stable (or linearly unstable) for* (1.4) *if and only if it is linearly stable (or linearly unstable) as a spatially homogeneous equilibrium of* (4.4).

Proof of the PDE version of the conjecture for $\hat{p} \in \partial\Delta_n$ with $n = 3$ under (A2.1). The local asymptotic stability of $\hat{p}$ follows from Theorem 4.4. To prove that any positive solution $p(x, t) \to \hat{p}$ as $t \to \infty$, we first demonstrate that $p_j(x, t) \to 0$ uniformly in x as $t \to \infty$ for every j such that $\hat{p}_j = 0$. By Proposition 4.1, we need only verify (4.9), which we already did in section 3 for each generic three-allele selection pattern that satisfies (A2.1). This suffices for all the vertex cases.

For the edge cases, suppose, for example, that A_3 is the allele absent from $\hat{p}$. Since $p_3(x, t) \to 0$ uniformly in x as $t \to \infty$, the ω-limit set of $p(x, t)$ is contained in the two-allele subsystem $p_3 = 0$.

In order to show that every positive solution $p(x, t)$ converges to $\hat{p}$, where $\hat{p} = (\hat{p}_1, \hat{p}_2, 0)$, we consider the function $V(p) = \sum_{i=1}^2 \hat{p}_i \log p_i$ as in section 3.5. We know that for small p_3, $\dot{V}(p) \geq 0$ holds, with $\dot{V} = 0$ only at $\hat{p}$, i.e., (4.10) holds as long as p_3 is small and $p \neq \hat{p}$. Since V is concave, and $p_3(x, t) \to 0$ uniformly in x as $t \to \infty$, we conclude from Theorem 4.2 that for (1.10), eventually, $\underline{V}(p)(t) := \min_{x \in \bar{\Omega}} V(p(x, t))$ is a strictly increasing Lyapunov function. Moreover, since $V(p)$ is bounded from above in Δ_3 with a unique maximizer $\hat{p}$, we see that $\underline{V}(p)(t) \leq V(\hat{p})$, and the equality holds only when $p(x, t) = \hat{p}$ for every $x \in \bar{\Omega}$. Hence, since the ω-limit set of $p(x, t)$ is invariant, on which $\underline{V}$ is constant, we infer that it contains only $\hat{p}$. This proves that $\hat{p}$ is g.a.s.

Thus, we have demonstrated that the PDE version of the conjecture for $\hat{p} \in \partial\Delta_n$ with $n = 3$ is true under the generic assumption (A2.1). ∎

Remark 4.5. In the case of two alleles, and if the less fit allele A_2 is dominant over A_1, i.e., $r_{12} = r_{22} < r_{11}$, substituting $p_1 = u$ and $p_2 = 1-u$, the selection term in (4.4a) is of the form $f(u) = ku^2(1-u)$ for $k > 0$. The equilibrium $u = 0$ is not regular, since its eigenvalue $r_{12} - r_{22}$ is 0. The equilibrium $u = 1$ is globally asymptotically stable for both (1.4) and (4.4), since every nonzero spatially homogeneous solution increases to $u = 1$ for both systems. Therefore, the conjecture still holds for this degenerate two-allele case.

However, if the domain is unbounded, e.g., $\mathbb{R}^d$, then for this degenerate two-allele migration-selection model, $u = 1$ is not always globally stable. Aronson and Weinberger [2, Corollary 3.2] showed the following interesting result: Suppose that $u(x, t) \not\equiv 0$ is a solution of

$$(4.21) \qquad \frac{\partial u}{\partial t} = \Delta u + f(u) \quad \text{in } \mathbb{R}^d.$$

If $d = 1$ or 2, then $\lim_{t \to \infty} u(x, t) = 1$ uniformly on bounded subsets of $\mathbb{R}^d$; but if $d \geq 3$ and $u(x, 0) \leq w(x)$ (which is some specified positive function) in $\mathbb{R}^d$, then $\lim_{t \to \infty} u(x, t) = 0$ uniformly in $\mathbb{R}^d$.

5. Discussion. We have proved the conjecture for three alleles where the globally stable equilibrium is either a monomorphism or a dimorphism. However, we restrict ourselves to generic selection matrices (that guarantee regular selection equilibria): Among the set of all 3×3 (symmetric) selection matrices, we ignore those from a subset of degenerate matrices that form a null set (in 6-dimensional space) that is contained in a finite union of co-dimension 1 manifolds [21]. In principle one could perform a complete analysis of the remaining cases, as they have been classified, e.g., in [4], but we refrain from this. The more interesting question is to decide the conjecture for more than three alleles. Obviously, the present case-by-case approach is not feasible for this; see the classification in [26].

More generally, we could ask similar questions for nonuniform selection: Question 1 concerns uniform g.a.s. equilibria, and Questions 2 and 3 deal with nonuniform g.a.s. equilibria.

QUESTION 1. *Suppose that $\hat{p} \in \Delta_n$ satisfies $f^{(\alpha)}(\hat{p}) = 0$, and is g.a.s. in each deme for (1.3). Then is the spatially homogeneous equilibrium $(\hat{p}, \hat{p}, \dots)$ globally asymptotically stable for (1.7) and (4.4)?*

If $\hat{p} \in \mathring{\Delta}_n$, this is answered positively in Corollary 2.7.

QUESTION 2. *Suppose that in every deme, selection (1.3) leads to a g.a.s. equilibrium. Will the combined dynamics with migration (1.7) lead to a g.a.s. equilibrium?*

The answer is no even for two alleles and two demes. See [11, Proposition 2.7 and Remarks 2.8 and 2.9] for counterexamples.

The following stronger assumption excludes these counterexamples.

QUESTION 3. *Suppose that in every deme, the mean selection coefficient $\bar{r}_\alpha$ is concave. Then the selection dynamics (1.3) has a g.a.s. equilibrium within each deme. Will the combined dynamics with migration, (1.7) or (4.4), lead to a g.a.s. equilibrium?*

For two alleles, this is shown in [11]. For $n \geq 3$ alleles, this is open.

Appendix. The following is a variant of the envelope theorem (also known as Danskin's lemma). Using $g_\alpha(t) = V(p^\alpha(t))$, the claim at the end of the proof of Theorem 2.2 follows.

LEMMA A.1. *Let $g_i : [a,b] \to \mathbb{R}$ for $i \in J$ (a finite set) be Lipschitz functions. Consider $\underline{g}(t) := \min_{i \in J} g_i(t)$ and $J(t) := \{i \in J : g_i(t) = \underline{g}(t)\}$. Then $\underline{g}$ is Lipschitz, and for almost all t: for all $i \in J(t)$, $\dot{\underline{g}}(t) = \dot{g}_i(t)$.*

Proof. Since g_i is Lipschitz, so is $\underline{g}$ as a composition of Lipschitz maps. Therefore, $\dot{\underline{g}}$ and $\dot{g}_i$ exist for $t \in [a,b] \setminus \mathcal{N}$ (with $\mathcal{N}$ a measure-zero set).

For $i \in J(t)$,

$$\text{(A.1)} \qquad \underline{g}(t) - \underline{g}(s) = g_i(t) - \underline{g}(s) \geq g_i(t) - g_i(s).$$

Thus, for $s \downarrow t$ we deduce from (A.1) that $\dot{\underline{g}}(t) \leq \dot{g}_i(t)$, while for $s \uparrow t$ we infer that $\dot{\underline{g}}(t) \geq \dot{g}_i(t)$. Hence for all $t \notin \mathcal{N}$ and all $i \in J(t)$,

$$\dot{\underline{g}}(t) = \dot{g}_i(t)$$

as claimed. $\square$

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