

Here, we derive the possible equilibrium and bifurcation structures of the haploid model (Section *The haploid model*). Our main results are formulated and proved in Section S.7. The supplementary *Mathematica* notebook will be useful in checking several of the results presented below. It also contains interactive gadgets to visualize these results.

The results derived in this Online Supplement are not merely auxiliary to those presented in the main text, but they complement and extend previous studies of two-locus haploid models. Theorem S.2 characterizes the equilibrium structure of the diallelic haploid two-locus model with arbitrary selection (and no migration) for the cases that are not covered by the analyses of FELDMAN (1971) and RUTSCHMAN (1994). These are the cases when an internal equilibrium exists and two boundary equilibria are asymptotically stable. However, in contrast to their analyses, ours is performed for the continuous-time model. This not only facilitates some computations but in particular enables the application of the index theory of continuous dynamical systems. Index theorems are a powerful tool that, to our knowledge, has not been used in the population genetic literature so far. Except for non-generic, degenerate cases, Theorems S.4 and S.5 characterize all equilibrium and bifurcation patterns for the haploid two-locus continent-island model with negative epistatic selection. In particular, they extend the main mathematical result of BÜRGER and AKERMAN (2011), who derived these patterns for nonepistatic selection.

For easier reference, we state the basic differential equations describing the haplotype dynamics:

$$\dot{x}_1 = x_1[-\alpha(x_3 + x_4) - \beta(x_2 + x_4) + \gamma x_4] - rD - mx_1, \quad (\text{S.1a})$$

$$\dot{x}_2 = x_2[-\alpha(x_3 + x_4) + \beta(x_1 + x_3) + \gamma x_4] + rD + m(1 - x_2), \quad (\text{S.1b})$$

$$\dot{x}_3 = x_3[\alpha(x_1 + x_2) - \beta(x_2 + x_4) + \gamma x_4] + rD - mx_3, \quad (\text{S.1c})$$

$$\dot{x}_4 = x_4[\alpha(x_1 + x_2) + \beta(x_1 + x_3) - \gamma(x_1 + x_2 + x_3)] - rD - mx_4. \quad (\text{S.1d})$$

This is a dynamical system on the simplex $S_4 = \{(x_1, x_2, x_3, x_4) : x_i \geq 0 \forall i \text{ and } \sum_i x_i = 1\}$ which constitutes our state space. We always assume $m \geq 0$, $r \geq 0$, and $\gamma \geq 0$.

For many purposes, it will be convenient to describe the dynamics in terms of the allele frequencies $p_A = x_3 + x_4$, $p_B = x_2 + x_4$, and the measure D of linkage disequilibrium (LD). Deviating from the main text, we use the notation $p = p_A$ and $q = p_B$ throughout this Online Supplement. Then the dynamical equations read

$$\dot{p} = \alpha p(1-p) - \gamma(1-p)(pq+D) + \beta D - mp, \quad (\text{S.2a})$$

$$\dot{q} = \beta q(1-q) - \gamma(1-q)(pq+D) + \alpha D + m(1-q), \quad (\text{S.2b})$$

$$\begin{aligned} \dot{D} = & [\alpha(1-2p) + \beta(1-2q)]D - \gamma[(1-p)(1-q) - D](pq+D) \\ & - rD - m[p(1-q) + D]. \end{aligned} \quad (\text{S.2c})$$

We recall that D has to satisfy

$$-\min[pq, (1-p)(1-q)] \leq D \leq \min[p(1-q), (1-p)q]. \quad (\text{S.3})$$

S.1 Existence and linear stability of boundary equilibria

We denote the monomorphic equilibria $x_i = 1$ by \mathbf{M}_i . If $m = 0$, then all monomorphic equilibria exist. However, if $\alpha > 0$ and $\gamma > \beta$, the conditions most relevant for this investigation (see (S.24) below), \mathbf{M}_1 and \mathbf{M}_4 are always unstable.

If $m > 0$, then only \mathbf{M}_2 (fixation of the continental type) is an equilibrium. The eigenvalues of (the Jacobian of (S.1) at) \mathbf{M}_2 are

$$-\beta - m, \alpha - \gamma - m, \alpha - \beta - m - r. \quad (\text{S.4})$$

Hence, \mathbf{M}_2 is asymptotically stable if

$$m > \max[-\beta, \alpha - \gamma, \alpha - \beta - r], \quad (\text{S.5})$$

i.e., if (A.3) holds.

If $m = 0$, the eigenvalues of \mathbf{M}_3 are

$$-\alpha, \beta - \gamma, -\alpha + \beta - r. \quad (\text{S.6})$$

Hence, \mathbf{M}_3 is asymptotically stable if $\alpha > 0$, $\gamma > \beta$, and $r > \beta - \alpha$.

Next, there may exist two equilibria at which one locus is polymorphic and the other is fixed. The equilibrium \mathbf{S}_A has the coordinates $(p, q, D) = (1 - \frac{m}{\alpha - \gamma}, 1, 0)$ and is admissible if and only if $m < \alpha - \gamma$. Its eigenvalues are

$$-\alpha + \gamma + m, \frac{1}{2} \left[-(\alpha + r) + 2(\gamma - \beta) \pm \sqrt{(\alpha + r)^2 + \frac{4\alpha r m}{\gamma - \alpha}} \right]. \quad (\text{S.7})$$

Hence, \mathbf{S}_A is asymptotically stable if

$$\gamma < \alpha + \beta \quad \text{and} \quad \frac{(\alpha - \gamma)(\gamma - \beta)}{\alpha} \left(1 + \frac{\alpha + \beta - \gamma}{r} \right) < m < \alpha - \gamma, \quad (\text{S.8})$$

which requires $r > \gamma - \beta$.

The equilibrium \mathbf{S}_B has coordinates the $(0, -\frac{m}{\beta}, 0)$ and is admissible if and only if $m < -\beta$. Its eigenvalues are

$$\beta + m, \frac{1}{2} \left[-(\gamma - \beta + r) + 2\alpha \pm \sqrt{(\gamma - \beta + r)^2 + \frac{4(\gamma - \beta)rm}{\beta}} \right]. \quad (\text{S.9})$$

Hence, \mathbf{S}_B is asymptotically stable if

$$\gamma > \alpha + \beta \quad \text{and} \quad \frac{-\beta\alpha}{\gamma - \beta} \left(1 + \frac{\gamma - \beta - \alpha}{r} \right) < m < -\beta, \quad (\text{S.10})$$

which requires $r > \alpha$.

In the following lemma, we collect a few simple but important observations that follow from the above analysis.

Lemma S.1. *1. For given $m > 0$, at most one of the boundary equilibria \mathbf{M}_2 , \mathbf{S}_A , or \mathbf{S}_B can be stable. Their asymptotic stability conditions are given by (S.5), (S.8), or (S.10), respectively.*

2. \mathbf{M}_2 is asymptotically stable if m is sufficiently large. If \mathbf{M}_2 is asymptotically stable, then \mathbf{S}_A and \mathbf{S}_B are not admissible.

3. As a function of m , boundary equilibria change stability at most once. If a change in stability occurs, then it is from unstable to stable (as m increases).

Finally, if $r = 0$, there is a fully polymorphic equilibrium \mathbf{R}_0 on the edge $x_1 = x_4 = 0$ of S_4 . Thus, only the island and the continental haplotypes are present. It satisfies $p = x_3$, $q = x_2$, $D = -pq$, and $p + q = 1$. The coordinates (p, q, D) of \mathbf{R}_0 are

$$\left(1 - \frac{m}{\alpha - \beta}, \frac{m}{\alpha - \beta}, \frac{m^2}{(\alpha - \beta)^2} - \frac{m}{\alpha - \beta} \right). \quad (\text{S.11})$$

The eigenvalues are

$$-\alpha, \beta - \gamma, -\alpha + \beta + m. \quad (\text{S.12})$$

This equilibrium exists and is asymptotically stable if and only if

$$m < \alpha - \beta \quad (\text{S.13})$$

holds; cf. (8).

S.2 Global stability properties of boundary equilibria

In the following we prove global asymptotic stability of boundary equilibria for various sets of parameters by applying the theory of Lyapunov functions (e.g. LASALLE 1976, in particular, Theorem 6.4 and Corollary 6.5). By global asymptotic stability of an equilibrium we mean that every trajectory, such that initially all alleles are present, converges to this equilibrium. By (S.5), (S.8), and (S.10), there is at most one asymptotically stable boundary equilibrium for any given set of parameters. Hence, convergence of all trajectories to the boundary is sufficient for demonstrating global stability. Because global convergence to the boundary precludes the existence of an internal equilibrium, these results yield the necessary conditions for a stable DMI (i.e., a stable internal equilibrium) in the section *Necessary conditions for stable DMIs*.

S.2.1 Proof of the necessary conditions $\alpha > 0$ and $\beta < \gamma$

We define

$$Y = \frac{x_1 + x_3}{x_3 + x_4} = \frac{1 - q}{p}, \quad (\text{S.14})$$

where we assume $x_3 + x_4 > 0$. Differentiating Y with respect to t and using (S.1), we obtain

$$\dot{Y} = -\frac{(\beta - \gamma)x_4(x_1 + x_3) + \alpha x_1(x_3 + x_4)}{(x_3 + x_4)^2}. \quad (\text{S.15})$$

We infer immediately that

$$\dot{Y} \leq 0 \quad \text{if} \quad \alpha > 0 \text{ and } \beta \geq \gamma, \quad (\text{S.16a})$$

$$\dot{Y} \geq 0 \quad \text{if} \quad \alpha \leq 0 \text{ and } \beta < \gamma, \quad (\text{S.16b})$$

and the inequalities for \dot{Y} are strict in the interior of S_4 . Therefore, $q(t) \rightarrow 1$ as $t \rightarrow \infty$ if (S.16a) applies. It is an easy, but not necessary, exercise to show that \mathbf{S}_A is globally asymptotically stable if $\alpha > \gamma$ and \mathbf{M}_2 is globally asymptotically stable if $\alpha \leq \gamma$ (see also below). If (S.16b) applies, then $p(t) \rightarrow 0$, and either \mathbf{M}_2 (if (S.5) holds) or \mathbf{S}_B (otherwise) is globally asymptotically stable.

Next, we define

$$X = \frac{x_1 + x_3}{x_1 + x_2} = \frac{1 - q}{1 - p}, \quad (\text{S.17})$$

where $x_1 + x_2 > 0$, and obtain

$$\dot{X} = -\frac{m(x_1 + x_3) + \beta x_2(x_1 + x_3) - \alpha x_3(x_1 + x_2)}{(x_1 + x_2)^2}. \quad (\text{S.18})$$

We conclude that

$$\dot{X} \leq 0 \quad \text{if} \quad \alpha < 0 \text{ and } \beta \geq 0, \quad (\text{S.19})$$

and $\dot{X} < 0$ in the interior of S_4 . Therefore, $q(t) \rightarrow 1$ as $t \rightarrow \infty$. Combining (S.16a), (S.16b), and (S.19) completes the proof that (2), i.e., $\alpha > 0$ and $\gamma > \beta$, is a necessary condition for the existence of a DMI.

S.2.2 Global convergence to \mathbf{M}_2

Assume $\alpha > 0$ and $\gamma > \beta$. Because

$$\begin{aligned} \dot{x}_2 &= x_2[\beta(x_1 + x_3) + \gamma x_4 - \alpha(x_3 + x_4) - r x_3] + m(x_1 + x_3 + x_4) + r x_1 x_4 \\ &\geq x_2[(m + \beta)x_1 + (m + \beta - \alpha - r)x_3 + (m - \alpha + \gamma)x_4], \end{aligned} \quad (\text{S.20})$$

global convergence to \mathbf{M}_2 follows at once if $m > \max[-\beta, \alpha - \gamma, \alpha - \beta + r] = \alpha - \beta + r$. This implies (3) and (4a). Hence, \mathbf{M}_2 is globally asymptotically stable for every m if $r < \beta - \alpha$.

S.2.3 Proof of (4b) and (4c)

Assume $\alpha > 0$ and $\gamma > \beta$. We first prove that $m \geq \max[\alpha - \beta, \frac{1}{4}\alpha]$ implies $\dot{X} \leq 0$, i.e., $q(t) \rightarrow 1$ as $t \rightarrow \infty$. Indeed, the denominator of $-\dot{X}$ in (S.18) satisfies

$$\begin{aligned} &m(x_1 + x_3) + \beta x_2(x_1 + x_3) - \alpha x_3(x_1 + x_2) \\ &= m x_1(x_1 + x_3 + x_4) + m x_3(x_1 + x_3 + x_4) - \alpha x_1 x_3 + x_1 x_2(m + \beta) + x_2 x_3(m + \beta - \alpha) \\ &\geq m(x_1 + x_3)^2 - \alpha x_1 x_3 + x_1 x_2(m + \beta) + x_2 x_3(m + \beta - \alpha) \geq 0 \end{aligned} \quad (\text{S.21})$$

if $m \geq \max[\alpha - \beta, \frac{1}{4}\alpha, -\beta]$. This proves $m_{\max}^+ \leq \max[\alpha - \beta, \frac{1}{4}\alpha]$ because $\alpha - \beta > -\beta$. The other inequality, (4c), follows analogously by using the Lyapunov function $(x_3 + x_4)/(x_2 + x_4)$ or by employing the model symmetry noted below (A.6), i.e., $\alpha \rightarrow \gamma - \beta$ and $\beta \rightarrow \gamma - \alpha$.

S.2.4 Internal equilibria exhibit negative linkage disequilibrium

We prove that every trajectory eventually enters the region $D \leq 0$ and remains there. Convergence to $D = 0$ occurs if and only if at least one allele is eventually lost. Thus, every internal equilibrium satisfies $D < 0$.

To prove these statements, we define

$$Z = \frac{x_2 x_3}{x_1 x_4}, \quad (\text{S.22})$$

where $x_1 > 0$ and $x_4 > 0$ is assumed. We note that $Z = 1$ if and only if $D = 0$, and $Z < 1$ if and only if $D > 0$. Then

$$\dot{Z} = x_1 x_3 x_4 (m + \gamma x_2) + r D (x_1 x_2 x_3 + x_2 x_3 x_4 + x_1 x_2 x_4 + x_1 x_3 x_4). \quad (\text{S.23})$$

We observe that $\dot{Z} \geq 0$ holds whenever $D \geq 0$. In addition, it follows immediately that $\dot{Z} > 0$ if $rD > 0$ and $x_2 + x_3 > 0$. If $x_2 + x_3 = 0$ and $x_1 x_4 > 0$, then $\dot{x}_1 + \dot{x}_4 < 0$ if $r + m > 0$. Hence, all trajectories leave $D > 0$ if $r > 0$. If $rD = 0$, then $\dot{Z} = 0$ only if $x_3 = 0$ or if $m = 0$ and $\gamma x_2 = 0$. Thus, our result follows by investigating (i) the dynamics on $x_3 = 0$ if $r = 0$, (ii) the dynamics on $x_2 = 0$ if $m = r = 0$, and (iii) the case $m = \gamma = 0$. We leave the simple first two cases to the reader. The third case is also not difficult and follows immediately from Section 3.4.1 in BÜRGER and AKERMAN (2011).

We conclude that at any equilibrium satisfying $D = 0$, one or both loci are fixed.

For the rest of this Online Supplement, we assume

$$\alpha > 0 \text{ and } \gamma > \beta \text{ and } r > \beta - \alpha, \quad (\text{S.24})$$

because we have proved that internal equilibria can exist only if (S.24) is satisfied. We note that (S.24) holds if and only if \mathbf{M}_3 (island haplotype fixed) is linearly stable in the absence of migration; cf. (S.6).

S.3 Calculating the internal equilibria

We derive a cubic equation from which the coordinate p of an internal equilibrium (p, q, D) can be obtained. Given p , the coordinates q and D can be computed from relative simple explicit formulas. Using these results, we show that at most three internal equilibria can exist.

By solving $\dot{p} = 0$, we find that, for given p and q , and if $p \neq 1 - \beta/\gamma$, the value of LD at equilibrium is

$$D = D(p, q) = p \frac{m + (1 - p)(\gamma q - \alpha)}{\beta - \gamma + \gamma p}. \quad (\text{S.25})$$

Substituting this into (S.2b), assuming $\beta \neq 0$, and solving $\dot{q} = 0$ for q , we obtain

$$q_{1,2}(p) = \frac{1}{2} \left[\left(1 - \frac{m}{\beta} \right) \pm \sqrt{Q} \right] \quad (\text{S.26})$$

where

$$Q = \left(1 + \frac{m}{\beta} \right)^2 - \frac{4\alpha m p}{\beta(\gamma - \beta)} - \frac{4\alpha(\gamma - \alpha)}{\beta(\gamma - \beta)} p(1 - p) \quad (\text{S.27})$$

needs to be nonnegative to yield an admissible equilibrium. Finally, we substitute $q = q_1(p)$ and $D = D(p, q_1(p))$ into (S.2c) and obtain that any equilibrium value p must be a solution of the equation

$$(\gamma - \beta)A(p) - \sqrt{Q}B(p) = 0, \quad (\text{S.28})$$

where

$$\begin{aligned} A(p) = & (\gamma - \beta) \{ \beta [(\alpha - r)(\gamma - 2\alpha) + \gamma(\alpha - \beta)] + [\beta(\gamma + \beta - 2\alpha) + r(2\beta - \gamma)]m + \beta m^2 \} \\ & + \{ \beta [2\alpha(2\gamma - 3\beta)(\gamma - \alpha) - \beta\gamma(\gamma - \beta)] - (2\gamma - \beta)(2\alpha - \gamma)r \\ & + [2\alpha\beta(\gamma - 2\beta) - \beta\gamma(\gamma - \beta) + \gamma(2\gamma - 3\beta)r]m \} p \\ & - [2\alpha\beta(\gamma - \alpha)(\gamma - 2\beta) + \beta\gamma(\gamma - 2\alpha)r + \gamma^2 r m] p^2, \end{aligned} \quad (\text{S.29a})$$

$$\begin{aligned} B(p) = & (\gamma - \beta)[-2\alpha\beta + \gamma(\beta + r) + \beta m] \\ & + [2\alpha\beta(\gamma - \beta) - \beta\gamma(\gamma - \beta) + r(\beta - 2\gamma)]p + \gamma^2 r p^2. \end{aligned} \quad (\text{S.29b})$$

If we substitute $q = q_2(p)$ and $D = D(p, q_2(p))$ into (S.2c), we obtain

$$(\gamma - \beta)A(p) + \sqrt{Q}B(p) = 0, \quad (\text{S.30})$$

instead of (S.28). If $A(p) = B(p) = 0$, then for given α , β , γ , and r , only one value of m can give rise to an internal equilibrium. We ignore this case here, but will encounter it further below. Otherwise, a solution p of (S.28) cannot be a solution of (S.30), and vice versa. Hence, for a solution p , only one of $q_1(p)$ or $q_2(p)$ can give rise to an admissible internal equilibrium. In fact,

$$\begin{aligned} & \text{if } A(p) \text{ and } B(p) \text{ have the same sign, only } q_1(p) \text{ can be admissible;} \\ & \text{if } A(p) \text{ and } B(p) \text{ have opposite signs, only } q_2(p) \text{ can be admissible.} \end{aligned} \quad (\text{S.31})$$

Therefore, solutions p of (S.28) or (S.30) satisfy

$$\begin{aligned} 0 = & (\gamma - \beta)^2 A(p)^2 - Q B(p)^2 \\ = & \frac{4\beta}{\gamma - \beta} (\beta - \gamma + \gamma p)^2 [m + (\gamma - \alpha)(1 - p)] P(p), \end{aligned} \quad (\text{S.32})$$

where

$$\begin{aligned} P(p) = & (\gamma - \beta)(m + r + \beta - \alpha)[\alpha\beta(\alpha + \beta - \gamma - r) - mr(\gamma - \beta)] \\ & + \{ \alpha\beta(\alpha - \beta)(\gamma - \beta)(\alpha + \beta - \gamma) + \alpha(\gamma - \beta)[3\beta(\gamma - 2\alpha) + m(4\beta - \gamma)]r \\ & + [\alpha(\gamma^2 + \beta\gamma - \beta^2) + \gamma(\gamma - \beta)m]r^2 \} p \\ & - 2\alpha r [\beta(\gamma - \beta)(\gamma - 2\alpha) + \gamma^2 r] p^2 + \alpha\gamma^2 r^2 p^3. \end{aligned} \quad (\text{S.33})$$

Because $p = 1 - \beta/\gamma$ never gives an equilibrium of (S.2) and $p = 1 - m/(\gamma - \alpha)$ can give rise only to a single-locus polymorphism, any internal equilibrium value p must satisfy $P(p) = 0$. It is easy to find parameter values such that P has three zeros in $(0, 1)$ (e.g., $\alpha = 1$, $\beta = 1.5$, $\gamma = 4$, $r = 2$, $m = 0.4$). Apparently, only two can give rise to an equilibrium (and this will be proved further below).

The case $\beta = 0$ can be treated separately and is much simpler because $q(p)$ is uniquely determined. In particular, the value p of an internal equilibrium has to satisfy $P(p) = 0$. If $p = 1 - \frac{\beta}{\gamma}$, we necessarily have $r = \frac{\gamma(\alpha-\beta)(\alpha+\beta-\gamma)}{(\gamma-2\alpha)(\gamma-2\beta)}$. Then $q = \alpha/\gamma$ is uniquely determined and $D = -\frac{\alpha(\gamma-\alpha)(\alpha+\beta-\gamma)}{(\gamma-2\alpha)(\gamma-2\beta)}$. This equilibrium may be admissible or not.

Remark S.1. In the absence of epistasis ($\gamma = 0$) there can be at most two internal equilibria. Their coordinates are obtained from a quadratic equation in p . The admissibility conditions are given by simple formulas (BÜRGER and AKERMAN 2011).

We can summarize these findings as follows.

Theorem S.1. *The haploid dynamics (S.2) can have at most three internal equilibria. The coordinate \hat{p} of an internal equilibrium $(\hat{p}, \hat{q}, \hat{D})$ is a zero of the polynomial P given by (S.33). For given \hat{p} with $P(\hat{p}) = 0$, only one of $q_1(\hat{p})$ or $q_2(\hat{p})$ (S.26) can yield an equilibrium value \hat{q} . \hat{D} is calculated from \hat{p} and \hat{q} by (S.25). This procedure yields an internal equilibrium if and only if $0 < \hat{p} < 1$, $0 < \hat{q} < 1$, and $-\min[\hat{p}\hat{q}, (1 - \hat{p})(1 - \hat{q})] \leq \hat{D} < 0$ hold. If $\gamma = 0$, there are at most two internal equilibria.*

For several important limiting cases, explicit expressions for the internal equilibria are obtained below (see Sections S.6 and S.8).

S.4 Critical m at which two internal equilibria may bifurcate

A bifurcation of two internal equilibria can occur if and only if $P(p^*) = 0$, where $p^* \in (0, 1)$ is a critical point of P , i.e., $P'(p^*) = 0$. There are at most two such critical points, and they are given by

$$p_{1,2}^* = \frac{1}{3\alpha\gamma^2r} \left\{ 2\alpha[\beta(\gamma - 2\alpha)(\gamma - \beta) + \gamma^2r] \pm \sqrt{R} \right\}, \quad (\text{S.34a})$$

where

$$\begin{aligned} R = & \alpha^2 \{ -\beta(\gamma - \beta) [16\alpha\beta(\gamma - \alpha)(\gamma - \beta) + \gamma^2(3\alpha^2 + \beta^2) - \gamma^3(3\alpha + \beta)] \\ & - \beta\gamma^2(\gamma - \beta)(\gamma - 2\alpha)r + \gamma^2(3\beta^2 - 3\beta\gamma + \gamma^2)r^2 \} \\ & - 3mr\alpha\gamma^2(\gamma - \beta)[4\alpha\beta + \gamma(r - \alpha)] \end{aligned} \quad (\text{S.34b})$$

Solving either $P(p_1^*) = 0$ or $P(p_2^*) = 0$ for m , we obtain after some straightforward manipulations that the critical value m^* must be a solution of the following quartic equation:

$$[\alpha\beta(2\beta - \gamma)(\alpha + \beta - \gamma + r) + \gamma(\gamma - \beta)rm]^2[-\psi_1 + 2\psi_2rm + 27\alpha\gamma^2(\gamma - \beta)r^2m^2] = 0, \quad (\text{S.35a})$$

where

$$\psi_1 = \alpha(\gamma - \beta)(\alpha - \beta + r)^2[4\alpha\beta(\gamma - \alpha)(\gamma - \beta) + \gamma^2r^2], \quad (\text{S.35b})$$

$$\begin{aligned} \psi_2 = & 2\alpha^2(\gamma - \beta)^2(9\beta\gamma - 8\alpha\beta - \alpha\gamma) + 3\alpha\gamma(\gamma - \beta)(3\beta\gamma - 2\alpha\beta - \alpha\gamma)r \\ & + 3\alpha\gamma^2(\gamma - \beta)r^2 + 2\gamma^3r^3. \end{aligned} \quad (\text{S.35c})$$

The zero $m = m_0$ arising from the first (linear) factor in (S.35a) does not give a valid bifurcation point for internal equilibria for the following reason. The corresponding critical value p_0 (which, depending on the parameters, can be p_1^* or p_2^*) is a double solution of $P(p)$ and has the property that $A(p_0) = B(p_0) = 0$. However, $P(p)$ was derived from (S.28) and (S.30) by squaring. Differentiating $(\gamma - \beta)A(p) \pm \sqrt{Q}B(p)$ with respect to p and evaluating at (p_0, m_0) , we infer from the Implicit Function Theorem that p is uniquely determined by m in a small neighborhood of m_0 unless r assumes one of two specific values. One of them leads to boundary equilibrium (thus not to an internal bifurcation). If we denote the other by $r_0 (= \beta[\alpha(\gamma - 4\beta) + \beta(\gamma - \beta)]/[\gamma(3\beta - \gamma)])$, then $p_0 = p_1 = p_2$ holds at m_0 . Although there is a bifurcation of three values p , only one of the resulting three branches gives rise to an admissible equilibrium.

The second (quadratic) factor in (S.35a) provides two potential solutions. However, because $\psi_1 \geq 0$, one is negative. Therefore, the critical value we are looking for is given by

$$\begin{aligned} m^* &= \frac{1}{27\alpha\gamma^2(\gamma - \beta)r} \left(-\psi_2 + \sqrt{\psi_2^2 + 27\alpha\gamma^2(\gamma - \beta)\psi_1} \right) \\ &= \frac{1}{27\alpha\gamma^2(\gamma - \beta)r} \left\{ -\psi_2 + 2 \left[\alpha^2(\gamma - \beta)^2 + 3\alpha\beta(\gamma - \beta)(\gamma - \alpha) + \alpha\gamma(\gamma - \beta)r + \gamma^2r^2 \right]^{3/2} \right\}. \end{aligned} \quad (\text{S.36})$$

At this value, two equilibria with non-zero allele frequencies collide and annihilate each other. Thus, m^* is the critical value at which a saddle-node bifurcation occurs. This gives an admissible bifurcation if both equilibria are internal (hence admissible) for either $m < m^*$ or $m > m^*$.

If $p_1^* = p_2^*$, i.e., if $R = 0$, a pitchfork bifurcation could occur at m^* . As a function of α , β , and γ , the condition $p_1^* = p_2^*$ can be satisfied at m^* only for three different values of r , of which at most two can be positive. It can be shown that at each of these values, one of the emerging zeros of $P(p)$ does not give rise to an admissible equilibrium (because $D > 0$ there). Thus, only a saddle-node bifurcation can occur.

We obtain the following series expansions for m^* . If $\beta < 0$ and γ is small, then

$$m^* = \frac{(\alpha - \beta + r)^2}{8r} + \frac{\gamma(\alpha - \beta - 3r)(\alpha - \beta + r)^2}{64\alpha\beta r} + O(\gamma^2). \quad (\text{S.37})$$

If $\gamma = 0$, this reduces to the expression given in BÜRGER and AKERMAN (2011).

If r is large, the following quasi-linkage-equilibrium (QLE) approximation is obtained:

$$m^* = \frac{\alpha(\gamma - \beta)}{4\gamma} \left(1 - \frac{4\beta\gamma - 3\alpha\beta - \alpha\gamma}{2\gamma r} \right) + O\left(\frac{1}{r^2}\right). \quad (\text{S.38})$$

S.5 The haploid two-locus selection model in the absence of migration

We assume $m = 0$. From Section S.3, we obtain the following properties of internal equilibria (p, q, D) . The LD is given by

$$D = D(p, q) = p(1 - p) \frac{\gamma q - \alpha}{\beta - \gamma + \gamma p}, \quad (\text{S.39})$$

where $p \neq 1 - \beta/\gamma$; cf. (S.25). For admissibility, we need

$$\max[-pq, -(1 - p)(1 - q)] < D < 0. \quad (\text{S.40})$$

For given p and if $\beta \neq 0$, the coordinate q of an internal equilibrium can assume only one of the following forms:

$$q_{1,2}(p) = \frac{1}{2} \left(1 \pm \sqrt{1 - \frac{4\alpha(\gamma - \alpha)p(1 - p)}{\beta(\gamma - \beta)}} \right). \quad (\text{S.41})$$

By Theorem S.1, for given p , at most one of $q_1 = q_1(p)$ or $q_2 = q_2(p)$ can give rise to an equilibrium.

Our goal here is to prove the following theorem:

Theorem S.2. *Suppose (S.24) and $m = 0$.*

1. *The haploid dynamics (S.2) admits at most one internal equilibrium.*
2. *Depending on the parameters, the internal equilibrium is given by either $(p, q_1(p), D(p, q_1(p)))$ or $(p, q_2(p), D(p, q_2(p)))$, where p is one of p_1 or p_2 in (S.45), and $q_i(p)$ and $D(p, q_i(p))$ are given by (S.41) and (S.39), respectively.*
3. *An internal equilibrium exists if and only if both \mathbf{M}_2 and \mathbf{M}_3 are asymptotically stable. This is the case if and only if*

$$\gamma > \alpha \text{ and } \beta > 0 \text{ and } r > \alpha - \beta. \quad (\text{S.42})$$

4. The internal equilibrium is unstable whenever it exists.

5. If (S.42) does not hold, then \mathbf{M}_3 is globally asymptotically stable.

This theorem complements the results derived by FELDMAN (1971) and RUTSCHMAN (1994) on the discrete-time dynamics of the haploid two-locus selection model. Rutschman proved global convergence to a boundary equilibrium for all parameter combinations for which no internal equilibrium exists. If transformed to the parameters used by Rutschman, condition (S.42) yields precisely the cases not covered by Rutschman's Theorem 14. Because our model is formulated in continuous time, the internal equilibrium can be determined by solving quadratic equations. This is instrumental for our proof.

We assume $\beta > 0$ because otherwise $q(t) \rightarrow 0$ as $t \rightarrow \infty$ if $m = 0$ (this follows because $\dot{q} < 0$ on $D < 0$ in this case, and we already know that all solutions eventually reach $D \leq 0$ and remain there). In addition, for $m > 0$ we showed that internal equilibria can exist only if $\alpha > 0$ and $\gamma > \beta$. Because with $m = 0$ we have the additional model symmetry of exchangeable α and β , we may assume

$$\gamma > \alpha \geq \beta > 0. \quad (\text{S.43})$$

We need four lemmas to prove the above theorem.

Lemma S.2. *The coordinate p of an equilibrium is a zero of the polynomial*

$$P(p) = \gamma^2 r^2 p^2 - r[2\beta(\gamma - \beta)(\gamma - 2\alpha) + r\gamma^2]p + \beta(\gamma - \beta)(\alpha - \beta - r)(\alpha + \beta - \gamma - r). \quad (\text{S.44})$$

If $r > 0$, the two zeros of P are given by

$$p_{1,2} = \frac{1}{2} + \frac{\gamma - 2\alpha}{r} \frac{\beta}{\gamma} \left(1 - \frac{\beta}{\gamma}\right) \pm \frac{1}{2} \left(1 - \frac{2\beta}{\gamma}\right) \sqrt{1 + \frac{4\alpha(\gamma - \alpha)}{r^2} \frac{\beta}{\gamma} \left(1 - \frac{\beta}{\gamma}\right)} \quad (\text{S.45})$$

and satisfy

$$|p_1 - p_2| = \left(1 - \frac{2\beta}{\gamma}\right) \sqrt{1 + \frac{4\alpha(\gamma - \alpha)}{r^2} \frac{\beta}{\gamma} \left(1 - \frac{\beta}{\gamma}\right)} > \left|1 - \frac{2\beta}{\gamma}\right|. \quad (\text{S.46})$$

The minimum value of P is

$$P(p_{\min}) = \frac{-(\gamma - 2\beta)^2}{4\gamma^2} [4\alpha\beta(\gamma - \alpha)(\gamma - \beta) + \gamma^2 r^2] < 0, \quad (\text{S.47})$$

where

$$p_{\min} = \frac{1}{2} + \frac{1}{r} \frac{\beta}{\gamma} \left(1 - \frac{\beta}{\gamma}\right) (\gamma - 2\alpha). \quad (\text{S.48})$$

In addition, we have

$$P\left(\frac{\beta}{\gamma}\right) = \beta \left(1 - \frac{\beta}{\gamma}\right) [(\alpha - \beta)(\alpha + \beta - \gamma)\gamma + (\gamma - 2\alpha)(\gamma - 2\beta)r] \quad (\text{S.49a})$$

and

$$P\left(1 - \frac{\beta}{\gamma}\right) = \beta\left(1 - \frac{\beta}{\gamma}\right) [(\alpha - \beta)(\alpha + \beta - \gamma)\gamma - (\gamma - 2\alpha)(\gamma - 2\beta)r]. \quad (\text{S.49b})$$

Proof. The expression $P(p)$ follows from (S.33) because $m = 0$. The other statements are derived readily. \square

An immediate consequence of (S.44) is that no internal equilibrium exists if $r = 0$ and at most one if $\gamma = 0$.

Lemma S.3. (i) $(p, q_1(p))$ can give rise to an internal equilibrium if and only if

$$\tilde{A}(p) = (\gamma - \beta)[(\alpha - r)(\gamma - 2\alpha) + \gamma(\alpha - \beta)] + [2\alpha(\gamma - \alpha)(2\beta - \gamma) + r\gamma(\gamma - 2\alpha)]p \quad (\text{S.50})$$

and

$$\tilde{B}(p) = -(\gamma - \beta)[\beta(\gamma - 2\alpha) + \gamma r] + r\gamma^2 p \quad (\text{S.51})$$

have opposite signs. Otherwise, $(p, q_2(p))$ may give rise to an internal equilibrium.

(ii) Assume (S.43). If p_1 and p_2 are the two zeros of $P(p)$, then $\tilde{B}(p_1)\tilde{B}(p_2) < 0$. Hence, $\tilde{B}(p)$ changes sign between p_1 and p_2 . Because $\alpha > \beta$, we have $\tilde{A}(p_1)\tilde{A}(p_2) > 0$ for every $r > 0$ if and only if $\gamma \leq \alpha + \beta$. Hence, in this case, $\tilde{A}(p)$ does not change sign between p_1 and p_2 .

(iii) Assume (S.43). If $\gamma \leq \alpha + \beta$ and P has two zeros in $(0, 1)$, at most one of them can give rise to an admissible internal equilibrium $(p, q_1, D(p, q_1))$.

Proof. (i) Since $m = 0$, we obtain from (S.29) $A(p) = \beta(1 - p)\tilde{A}(p)$ and $B(p) = -(1 - p)\tilde{B}(p)$, which, on account of (S.31), proves (i).

(ii) These statements follow because

$$\tilde{A}(p_1) = \frac{\gamma - 2\beta}{2\gamma^2 r} \left[\phi_1 + \phi_2 \sqrt{4\alpha\beta(\gamma - \alpha)(\gamma - \beta) + \gamma^2 r^2} \right], \quad (\text{S.52a})$$

$$\tilde{A}(p_2) = \frac{\gamma - 2\beta}{2\gamma^2 r} \left[\phi_1 - \phi_2 \sqrt{4\alpha\beta(\gamma - \alpha)(\gamma - \beta) + \gamma^2 r^2} \right], \quad (\text{S.52b})$$

and

$$\tilde{B}(p_1) = \frac{\gamma - 2\beta}{2} \left[-\gamma r + \sqrt{4\alpha\beta(\gamma - \alpha)(\gamma - \beta) + \gamma^2 r^2} \right], \quad (\text{S.53a})$$

$$\tilde{B}(p_2) = \frac{\gamma - 2\beta}{2} \left[-\gamma r - \sqrt{4\alpha\beta(\gamma - \alpha)(\gamma - \beta) + \gamma^2 r^2} \right], \quad (\text{S.53b})$$

where

$$\phi_1 = 4\alpha\beta(\gamma - \beta)(\gamma - \alpha)(2\alpha - \gamma) + 2\alpha\gamma(\gamma - \alpha)(\gamma - 2\beta)r + \gamma^2(2\alpha - \gamma)r^2, \quad (\text{S.54a})$$

$$\phi_2 = 2\alpha(\gamma - \alpha)(2\beta - \gamma) + r\gamma(\gamma - 2\alpha), \quad (\text{S.54b})$$

and

$$\begin{aligned} & \phi_1^2 - \phi_2^2[4\alpha\beta(\gamma - \alpha)(\gamma - \beta) + \gamma^2r^2] \\ &= 4\alpha\beta\gamma^2(\gamma - \alpha)(\gamma - \beta)[4\alpha(\alpha - \beta)(\gamma - \alpha)(\alpha + \beta - \gamma) + (2\alpha - \gamma)^2r^2] > 0 \end{aligned} \quad (\text{S.55})$$

if $\alpha + \beta > \gamma$.

(iii) This is an immediate consequence of (i) and (ii). \square

Lemma S.4. *Under the assumption (S.43), $(p, q_1, D(p, q_1))$ can be an admissible internal equilibrium only if one of the following three conditions is satisfied:*

$$\gamma \geq 2\alpha \quad \text{and} \quad p < 1 - \frac{\beta}{\gamma}, \quad (\text{S.56a})$$

or

$$\gamma < 2\alpha \quad \text{and} \quad p < \min \left[\frac{\beta}{\gamma}, 1 - \frac{\beta}{\gamma} \right], \quad (\text{S.56b})$$

or

$$\gamma < 2\beta \quad \text{and} \quad 1 - \frac{\beta}{\gamma} < p < \frac{\beta}{\gamma}. \quad (\text{S.56c})$$

Proof. We utilize the fact that an internal admissible equilibrium has to satisfy (S.40), where $D = D(p, q_1)$ is given by (S.39). We consider two cases.

Case 1. $p < 1 - \frac{\beta}{\gamma}$. Then $D < 0$ if and only if $\gamma q_1 > \alpha$, which is satisfied if and only if one of the following conditions holds:

$$\gamma \geq 2\alpha, \quad (\text{S.57a})$$

$$\gamma < 2\alpha \quad \text{and} \quad p(1 - p) < \frac{\beta}{\gamma} \left(1 - \frac{\beta}{\gamma} \right). \quad (\text{S.57b})$$

Because $p < 1 - \frac{\beta}{\gamma}$, (S.57b) is equivalent to (S.56b). Thus, each of (S.56a) or (S.56b) is necessary for admissibility of an equilibrium with $p < 1 - \frac{\beta}{\gamma}$.

Case 2. $p > 1 - \frac{\beta}{\gamma}$. Then $D < 0$ if and only if $\gamma q_1 < \alpha$, which is satisfied if and only if

$$\gamma < 2\alpha \quad \text{and} \quad 1 - \frac{\beta}{\gamma} < p < \frac{\beta}{\gamma}. \quad (\text{S.58})$$

Clearly, this requires $\gamma < 2\beta$. Hence, (S.58) can be replaced by (S.56c).

We recall from Section S.3 that if $p = 1 - \beta/\gamma$, there exists at most one internal equilibrium. \square

Lemma S.5. *Under the assumption (S.43), $(p, q_2, D(p, q_2))$ can be an admissible internal equilibrium only if*

$$\gamma > 2\alpha \tag{S.59}$$

and

$$\frac{\beta}{\gamma} < p \leq 1 - \frac{\beta}{\gamma} \tag{S.60}$$

hold.

Proof. Case 1. $p < 1 - \frac{\beta}{\gamma}$. Then $D < 0$ if and only if $\gamma q_2 > \alpha$, which can be satisfied only if (S.59) and (S.60) hold.

Case 2. $p > 1 - \frac{\beta}{\gamma}$. Then $D < 0$ if and only if $\gamma q_2 < \alpha$, which can be satisfied only if $p > \max\left[\frac{\beta}{\gamma}, 1 - \frac{\beta}{\gamma}\right]$. Admissibility of an internal equilibrium also requires $D(p, q_2) > -pq_2$. A straightforward calculation shows that, because $p > 1 - \frac{\beta}{\gamma}$, this can hold only if $\alpha < \beta$, i.e., if assumption (S.43) is violated. \square

Remark S.2. For convenience, we briefly recapitulate the following index theorem (Theorem 2 in HOFBAUER 1990) which will play a decisive role in the proof of Theorem S.2. For every dissipative semiflow on \mathbb{R}_+^n such that all fixed points are regular, the sum of their indices equals +1. To apply this theorem, we note that system (S.1) satisfies the assumptions. (Here, we assume $m \geq 0$, because this remark will also be needed below when treating the case $m > 0$.) (S.1) is obviously well defined on \mathbb{R}_+^4 , \mathbb{R}_+^4 is forward invariant under (S.1) (i.e., if $x_i = 0$, then $\dot{x}_i \geq 0$), and S_4 is globally attracting in \mathbb{R}_+^4 under a modification of (S.1) that does not change the dynamics on S_4 . To show the latter, we note that adding a sufficiently large positive constant κ to each of the gametic fitnesses w_i does not change the dynamics on S_4 , but implies

$$\frac{d}{dt} \left(\sum_i x_i \right) = \left(1 - \sum_i x_i \right) [m + \kappa x_1 + (\beta + \kappa)x_2 + (\alpha + \kappa)x_3 + (\alpha + \beta - \gamma + \kappa)x_4] < 0 \tag{S.61}$$

if and only if $\sum_i x_i > 1$ and $\frac{d}{dt} (\sum_i x_i) > 0$ if and only if $\sum_i x_i < 1$.

In our case, the index of an equilibrium is $(-1)^m$, where m is the number of negative eigenvalues (they are always real). An internal equilibrium is always saturated. If it is asymptotically stable, it has index 1. Equilibria on the boundary of the simplex are saturated if and only if they are externally stable. This is the case if and only if no gamete that is missing at the equilibrium can invade. Because S_4 is attracting within \mathbb{R}_+^4 , the index of an asymptotically stable (hence, saturated) boundary equilibrium is 1.

Now we are ready to prove the theorem.

Proof of Theorem S.2. 1. and 2. We assume (S.43). By Theorem S.1, for given p , only one of $q_1(p)$ or $q_2(p)$ can give rise to an equilibrium. By Lemma S.4, $q_1(p)$ may give rise to an internal equilibrium if either of the conditions (S.56a), (S.56b), or (S.56c) is satisfied. By Lemma S.5, $q_2(p)$ may give rise to an equilibrium if (S.59) and (S.60) are satisfied.

If $\gamma \geq 2\alpha$, (S.49b) shows that $P(1 - \beta/\gamma) < 0$ and Lemma S.2 implies that one zero of P is greater than $1 - \beta/\gamma$. Hence, by (S.56a), only the zero of P which satisfies $p < 1 - \beta/\gamma$ can give rise to an admissible equilibrium $(p, q_1, D(p, q_1))$. By Lemma S.5, (S.59) and (S.60), only the zero $p < 1 - \beta/\gamma$ can give rise to an admissible equilibrium $(p, q_2, D(p, q_2))$. However, we already know that at most one of $q_1(p)$ or $q_2(p)$ can yield an equilibrium.

If $\gamma < 2\alpha$, then Lemmas S.4 and S.5 imply that only q_1 can give rise to an equilibrium. This requires that (S.56b) or (S.56c) apply. If (S.56c) applies, (S.46) shows that at most one zero of P can satisfy this condition. If (S.56b) applies and $\gamma \leq \alpha + \beta$, we conclude from Lemma S.3 (iii) that at most one zero can give rise to an equilibrium. If $\alpha + \beta < \gamma < 2\alpha$, then (S.49a) yields $P(\frac{\beta}{\gamma}) < 0$, whence one zero of P is bigger than $\frac{\beta}{\gamma}$, in contradiction to (S.56b). This finishes the proof of the first statement and shows that an internal equilibrium can exist only if (S.42) is satisfied.

3. and 4. It remains to prove that the internal equilibrium exists if (S.42) holds and that it is unstable. This follows readily from the index theorem of HOFBAUER (1990); see Remark S.2. In our model, the only boundary equilibria are the four monomorphic states. M_1 and M_4 are never saturated because they are unstable within S_4 . M_2 and M_3 are saturated if and only if they are asymptotically stable within S_4 . Then, we have $\text{ind}(M_2) = \text{ind}(M_3) = 1$. Hence there must exist an internal equilibrium with index -1. Such an equilibrium cannot be stable.

Because M_2 and M_3 are both asymptotically stable if and only if (S.42) holds, statements 3 and 4 are proved.

5. Let us first assume $\beta \leq 0$. Then (S.18) implies $\dot{X} \geq 0$ if $p < 1$, and $\dot{X} = 0$ only if $x_3 = 0$. Because $\dot{x}_3 > 0$ on $x_3 = 0$ except on the invariant edges $p = 0$ or $q = 1$, we infer $p(t) \rightarrow 1$. If $p = 1$, then $\dot{x}_3 = x_3(1 - x_3)(\gamma - \beta)$ yields the assertion.

Now assume $\beta > 0$. A simple calculation shows that

$$\dot{x}_3 + \dot{x}_4 = \alpha x_1 x_3 + (\alpha - \beta) x_2 x_3 + (\alpha - \gamma) x_2 x_4 + (\alpha + \beta - \gamma) x_1 x_4 \geq 0 \quad (\text{S.62})$$

if $\alpha \geq \gamma (> \beta)$, and equality holds at most at edges of S_4 . From this, it is an easy exercise to prove convergence of M_3 .

Finally, assume $\beta > 0$, $\gamma > \alpha$, and $r < \alpha - \beta$, which requires $\alpha > \beta$. Then global convergence to \mathbf{M}_3 follows from the inequality

$$\dot{x}_3 = \alpha x_1 x_3 + (\alpha - \beta)x_1 x_4 + (\gamma - \beta)x_3 x_4 - (\alpha - \beta - r)D \geq 0, \quad (\text{S.63})$$

which holds if $D \leq 0$ (as is sufficient; see Section S.2.4), and a simple investigation of the dynamics on the edges of S_4 . \square

S.6 Weak migration

With the aid of perturbation theoretical methods, we can derive the equilibrium and stability structure of our model for weak migration from the model without migration. Theorem 4.4 of KARLIN and MCGREGOR (1972b) implies that every equilibrium that is asymptotically stable for $m = 0$, persists for sufficiently small $m > 0$ and remains asymptotically stable. Stable equilibria on the boundary may move into the interior of the state space. Equilibria that are unstable if $m = 0$ remain unstable if $m > 0$. However, unstable equilibria at the boundary may leave the state space as m becomes positive. Application of this theorem requires that all equilibria in the unperturbed system are hyperbolic, i.e., they have no eigenvalues with zero real part. Theorem 5.4 in BÜRGER (2009) ensures global asymptotic stability of the perturbed equilibrium, at least if γ and m are small enough.

For our model these perturbation results in conjunction with Theorem S.2 and Lemma S.1 immediately yield the following result.

Theorem S.3. *If $m > 0$ is sufficiently small, the following equilibrium configurations can occur.*

1. *If (S.42) holds, there exists one unstable internal equilibrium, one asymptotically stable internal equilibrium (the perturbation of \mathbf{M}_3), and \mathbf{M}_2 is asymptotically stable. Neither \mathbf{S}_A nor \mathbf{S}_B is admissible.*

2. *Otherwise, i.e., if $\gamma < \alpha$ or $\beta < 0$ or $r < \alpha - \beta$, the perturbation of the equilibrium \mathbf{M}_3 is globally asymptotically stable (at least if γ is small). The equilibrium \mathbf{M}_2 is unstable, and the equilibria \mathbf{S}_A and \mathbf{S}_B may be admissible. If \mathbf{S}_A or \mathbf{S}_B is admissible, it is unstable.*

The coordinates of the internal equilibria can be determined explicitly to first order in m . The coordinates (p, q, D) of the stable equilibrium (\mathbf{I}_{DMI}) are

$$\left(1 - \frac{m(\alpha + r)}{\alpha(\alpha - \beta + r)}, \frac{m(\gamma - \beta + r)}{(\gamma - \beta)(\alpha - \beta + r)}, -\frac{m}{\alpha - \beta + r} \right). \quad (\text{S.64})$$

S.7 The complete equilibrium and stability structure

Now we are in the position to prove our main results about the equilibrium and bifurcation structure. We continue to assume (S.24), because we have already shown that otherwise an internal equilibrium (a DMI) cannot exist and global convergence to a boundary equilibrium occurs (Section S.2). Throughout, we always consider bifurcations as a function of (increasing) m .

We define

$$m_{\mathcal{A}} = \frac{(\alpha - \gamma)(\gamma - \beta)}{\alpha} \left(1 + \frac{\alpha + \beta - \gamma}{r} \right), \quad (\text{S.65a})$$

$$m_{\mathcal{B}} = \frac{-\beta\alpha}{\gamma - \beta} \left(1 + \frac{\gamma - \beta - \alpha}{r} \right), \quad (\text{S.65b})$$

$$m_2 = \alpha - \beta - r \quad (\text{S.65c})$$

and note that $m_{\mathcal{A}}$, $m_{\mathcal{B}}$, and m_2 are the critical values of m above which $\mathbf{S}_{\mathcal{A}}$, $\mathbf{S}_{\mathcal{B}}$, and \mathbf{M}_2 , respectively, are asymptotically stable provided they are admissible (Section S.1). We also recall the definitions of m^* (S.36) and of

$$m_{\max}^- = \begin{cases} m_{\mathcal{A}} & \text{if } \gamma < \min[\alpha, \alpha + \beta, \beta + r], \\ m_{\mathcal{B}} & \text{if } \gamma \geq \alpha + \beta = \min[\alpha, \alpha + \beta, \beta + r], \\ m_2 & \text{if } \gamma \geq \alpha + \beta = \min[\alpha, \alpha + \beta, \beta + r]; \end{cases} \quad (\text{S.66a})$$

$$\quad \quad \quad (\text{S.66b})$$

$$\quad \quad \quad (\text{S.66c})$$

cf. Appendix A.2.

Theorem S.4. *The following three types of bifurcation patterns can occur:*

Type 1.

- If $0 < m < m^*$, there exist two internal equilibria; one is asymptotically stable (\mathbf{I}_{DMI}), the other (\mathbf{I}_0) is unstable. The monomorphic equilibrium \mathbf{M}_2 is asymptotically stable.
- At $m = m^*$, the two internal equilibria collide and annihilate each other by a saddle-node bifurcation.
- If $m > m^*$, \mathbf{M}_2 is the only equilibrium; it is asymptotically stable and, presumably, globally stable.

Type 2. There exists a critical migration rate \tilde{m} satisfying $0 < \tilde{m} < m^*$ such that:

- If $0 < m < \tilde{m}$, there is a unique internal equilibrium (\mathbf{I}_{DMI}). It is asymptotically stable and, presumably, globally stable.
- At $m = \tilde{m}$, an unstable equilibrium (\mathbf{I}_0) enters the state space by an exchange-of-stability bifurcation with a boundary equilibrium.
- If $\tilde{m} < m < m^*$, there are two internal equilibria, one asymptotically stable (\mathbf{I}_{DMI}), the other unstable (\mathbf{I}_0), and one of the boundary equilibria is asymptotically stable.
- At $m = m^*$, the two internal equilibria merge and annihilate each other by a saddle-node bifurcation.
- If $m > m^*$, a boundary equilibrium asymptotically stable and, presumably, globally stable.

Type 3.

- If $0 < m < m_{\text{max}}^-$, a unique internal equilibrium (\mathbf{I}_{DMI}) exists. It is asymptotically stable and, presumably, globally stable.
- At $m = m_{\text{max}}^-$, \mathbf{I}_{DMI} leaves the state space through a boundary equilibrium by an exchange-of-stability bifurcation.
- If $m > m_{\text{max}}^-$, a boundary equilibrium is asymptotically stable and, presumably, globally stable.

Remark S.3. 1. Each of the bifurcation patterns of Type 2 and 3 include several subcases because the equilibria \mathbf{S}_A and \mathbf{M}_2 or \mathbf{S}_B and \mathbf{M}_2 may merge and thereby exchange stability. This may occur below or above m^* . If such a bifurcation occurs, then it is always \mathbf{M}_2 that becomes stable, and \mathbf{S}_A or \mathbf{S}_B leave the state space through \mathbf{M}_2 .

2. The conjectures about global asymptotic stability of a boundary equilibrium if $m > m^*$ (Type 1 or Type 2) or if $m > m_{\text{max}}^-$ (Type 3) are supported by extensive numerical iterations which provided no incidence of limit cycles or complex attractors. Global stability of \mathbf{M}_2 has been proved if $m > m_2$ (Section S.2.2).

3. The conjectures about global stability of the internal equilibrium in patterns of Type 2 and Type 3 are supported by extensive numerical iterations. For sufficiently small m and γ , they follow from Theorem 5.4 in BÜRGER (2009). For tight linkage and independent loci, limit cycles and complex attractors are excluded in Sections S.8.1 and S.8.2.

Proof of Theorem S.4. Theorem S.3 provides all equilibrium configurations for small m . Lemma S.1 provides control over the boundary equilibria. As m increases, they can vanish but not emerge. They can also become asymptotically stable as m increases. For sufficiently large m , there is always a globally asymptotically stable boundary equilibrium. By Theorem S.1, the

number of internal equilibria is at most three. In addition, internal equilibria can emerge or vanish only either by a saddle-node bifurcation (Section S.4) or because an equilibrium enters or leaves S_4 through one of boundary equilibria, when an exchange of stability occurs. A bifurcation involving the two internal equilibria can occur at most at one value of m , namely at m^* (S.36). An exchange-of-stability bifurcation can occur only at the values $m_{\mathcal{A}}$, $m_{\mathcal{B}}$, or m_2 . If it occurs, then the respective boundary equilibrium is asymptotically stable for every larger m for which it is admissible. By the index theorem of HOFBAUER (1990), cf. Remark S.2, the sum of the indices of all saturated equilibria equals 1.

If Case 1 of Theorem S.3 applies, then \mathbf{M}_2 is asymptotically stable for every $m > 0$, and it is the only boundary equilibrium. Hence, its index is 1. The index of the stable internal equilibrium is also 1. Because the sum of the indices of the internal equilibria must be 0, the index of the unstable equilibrium is -1. Because at most one bifurcation involving the two internal equilibria can occur and because for large m , \mathbf{M}_2 is globally asymptotically stable, the bifurcation must be of saddle-node type in which the equilibria collide and annihilate each other (but do not emerge). In principle, the internal equilibria could also leave S_4 through a boundary equilibrium (in this case, it must be \mathbf{M}_2). However, by the index theorem, they can do so only simultaneously. This occurs if and only if $m^* = m_2$, which is a non-generic degenerate case. Because the sum of indices of the internal equilibria must be zero, no equilibrium can enter the state space. These considerations settle the bifurcation pattern of Type 1.

If Case 2 of Theorem S.3 applies, then, for small m , the boundary equilibria are unstable, hence not saturated, and do not contribute to the sum of indices. Since then the indices of internal equilibria must sum up to 1, the only possible bifurcation that does not entail the stability of a boundary equilibrium would be a pitch-fork bifurcation of the internal equilibrium which, by Section S.4, does not occur. (Indeed, because m^* is the only value at which a bifurcation among internal equilibria can occur, and because for large m a boundary equilibrium is globally asymptotically stable, the three equilibria emerging by a pitchfork bifurcation would have to leave the state space through boundary equilibria. This, however, cannot occur, as follows easily from the results about linear stability in Section S.1.) Thus, any further bifurcations involve a boundary equilibrium. There are two possibilities.

(i) An equilibrium enters S_4 at some value \tilde{m} (which can only be one of $m_{\mathcal{A}}$, $m_{\mathcal{B}}$, or m_2) through one of the unstable boundary equilibria by an exchange-of-stability bifurcation. If $m > \tilde{m}$, there is one asymptotically stable boundary equilibrium, an unstable internal equilibrium (the one that entered S_4), and one asymptotically stable internal equilibrium. Now a reasoning analogous to that applied above to Case 1 of Theorem S.3 establishes the bifurcation pattern of Type 2.

(ii) The internal equilibrium leaves S_4 by exchange of stability through one of the boundary equilibria at m_{\max}^- . This becomes asymptotically stable then and, presumably, globally

stable. At larger values of m no equilibrium can enter S_4 through one of the (other) unstable boundary equilibria, because this would either lead to two simultaneously stable boundary equilibria, which is impossible (Lemma S.1), or this had to occur at the same value at which the hitherto stable boundary equilibrium merges with \mathbf{M}_2 and leaves the state space. This, too, is impossible because the sum of the indices of the new stable boundary equilibrium and the new unstable internal equilibrium would be zero. Thus, we have established the bifurcation pattern of Type 3 and excluded all other possibilities. \square

Our final goal is to assign the respective parameter combinations to the three bifurcation patterns determined above. As in Appendix A.3, we distinguish four selection scenarios:

Selection scenario 1: $0 < \alpha < \beta < \gamma$

Selection scenario 2: $0 < \beta < \alpha < \gamma$

Selection scenario 3: $\gamma - \alpha < 0 < \gamma - \beta < \alpha$

Selection scenario 4: $\beta < 0 < \alpha < \gamma - \beta$

From Appendix A.2, we recall the following definitions

$$r_{\mathcal{A}} = (\gamma - \alpha) \frac{3(\gamma - \beta) - \alpha}{2\gamma - \alpha}, \quad (\text{S.67a})$$

$$r_{\mathcal{B}} = \beta \frac{3\alpha + \beta - \gamma}{\beta + \gamma}, \quad (\text{S.67b})$$

$$r_2 = \frac{3\alpha(\gamma - \beta) - \sqrt{\alpha(\gamma - \beta)(4\beta\gamma + 5\alpha\gamma - 9\alpha\beta)}}{2\gamma}. \quad (\text{S.67c})$$

Now we define

$$f_2(r) = \alpha(\beta - \alpha)(\gamma - \beta) + 3\alpha(\gamma - \beta)r - \gamma r^2. \quad (\text{S.68})$$

Then r_2 is the smaller of the two zeros of f_2 (provided they are real).

We note the following properties of f_2 and r_2 :

- (i) $f_2(0) < 0$ if and only if $\alpha > \beta$;
- (ii) f_2 is concave and assumes its maximum at $r_{2,\max} = \frac{3}{2}\alpha(1 - \frac{\beta}{\gamma}) > 0$. The larger of the two zeros of f_2 is always greater (or equal) than α ;
- (iii) $f_2(r) < 0$ for every r if and only if $4\beta\gamma + 5\alpha\gamma - 9\alpha\beta < 0$;
- (iv) r_2 is real if and only if $4\beta\gamma + 5\alpha\gamma - 9\alpha\beta \geq 0$, and $r_2 > 0$ if, in addition, $\alpha > \beta$.

We define

$$r_2^* = \begin{cases} r_2 & \text{if } r_2 \text{ is real,} \\ \min[\alpha, \gamma - \beta] & \text{otherwise.} \end{cases} \quad (\text{S.69})$$

In selection scenarios 1 and 2, r_2 is always real. If r_2 is not real, we have $r_2^* = \beta - \gamma$ in selection scenario 3, and $r_2^* = \alpha$ in scenario 4. An important observation is that in selection scenario 4

$$r_2^* < \alpha \quad \text{if and only if} \quad \gamma(\alpha + \beta) > \beta(2\alpha + \beta). \quad (\text{S.70})$$

Lemma S.6. *Assume selection scenario 4, i.e., $\beta < 0$ and $\gamma > \alpha + \beta$.*

1) *An unstable internal equilibrium enters the state space through \mathbf{M}_2 at $m = m_2$ (and exists if $m = m_2 + \epsilon$, $\epsilon > 0$ small) if*

$$r \leq \alpha \quad \text{and} \quad f_2(r) > 0 \quad (\text{S.71})$$

or, equivalently, if

$$r_2^* < r \leq \alpha. \quad (\text{S.72})$$

2) *The stable internal equilibrium leaves the state space through \mathbf{M}_2 at $m = m_2$ if*

$$r \leq \alpha \quad \text{and} \quad f_2(r) \leq 0 \quad (\text{S.73})$$

or, equivalently, if

$$r \leq \min[\alpha, r_2^*]. \quad (\text{S.74})$$

Proof. The lemma follows from studying the perturbation of \mathbf{M}_2 near m_2 . To obtain D to first order in ϵ , one has to derive p and q up to second order in ϵ .

1) If $m = m_2 + \epsilon$ ($\epsilon > 0$), to leading order in ϵ , the perturbation analysis yields

$$p(\epsilon) = \frac{(\gamma - \beta)D(\epsilon)}{r - \gamma + \beta}, \quad q(\epsilon) = 1 - \frac{\alpha D(\epsilon)}{r - \alpha}, \quad D(\epsilon) = \epsilon \frac{-(r - \alpha)(r - \gamma + \beta)}{f_2(r)}. \quad (\text{S.75})$$

Because we know that $D(\epsilon) < 0$ holds at every equilibrium and because $\alpha < \gamma - \beta$, (S.71) follows. The equivalence of (S.71) and (S.72) follows easily from the properties of f_2 summarized above.

2) If $m = m_2 - \epsilon$ ($\epsilon > 0$), to leading order in ϵ , the perturbation analysis yields the same expressions for $p(\epsilon)$ and $q(\epsilon)$, and

$$D(\epsilon) = \epsilon \frac{(r - \alpha)(r - \gamma + \beta)}{f_2(r)}. \quad (\text{S.76})$$

Now, (S.73) and (S.74) follow as above. If $r = r_2$, then $f_2(r) = 0$. This case is degenerate because $m_2 = m^*$ and the outgoing and incoming equilibria collide at \mathbf{M}_2 and annihilate each other. \square

Lemma S.7. Assume selection scenario 2, i.e., $0 < \beta < \alpha < \gamma$.

1) An unstable internal equilibrium enters the state space through \mathbf{M}_2 at $m = m_2$ (and exists if $m = m_2 + \epsilon$, $\epsilon > 0$ small) if

$$r_2 < r < \alpha - \beta. \quad (\text{S.77})$$

2) The stable internal equilibrium leaves the state space through \mathbf{M}_2 at $m = m_2$ if

$$r \leq r_2. \quad (\text{S.78})$$

Proof. The proof is analogous to that of Lemma S.6 upon noting that $m_2 > 0$ if and only if $r < \alpha - \beta$, and that $\alpha - \beta < \min[\alpha, \gamma - \beta]$ holds. \square

Next, we define

$$f_B(r) = \beta(3\alpha + \beta - \gamma) - r(\beta + \gamma) \quad (\text{S.79})$$

and note that $f_B(r) = 0$ if and only if $r = r_B$. In addition, we have

$$r_B > \alpha \quad \text{if and only if} \quad \begin{cases} \gamma > -\beta \text{ and } \gamma(\alpha + \beta) < \beta(2\alpha + \beta), \text{ or} \\ \gamma < -\beta \text{ and } \gamma(\alpha + \beta) > \beta(2\alpha + \beta). \end{cases} \quad (\text{S.80})$$

In selection scenario 4, we obtain

$$r_2^* < \alpha \quad \text{if and only if} \quad \begin{cases} r_B < \alpha \text{ and } \gamma > -\beta, \text{ or} \\ r_B > \alpha \text{ and } \gamma < -\beta. \end{cases} \quad (\text{S.81})$$

If r_2 is real, this follows immediately from (S.70) and (S.80), or from the observation $f_2(\alpha) + \alpha f_B(\alpha) = 0$. Otherwise, it follows because $4\beta\gamma + 5\alpha\gamma - 9\alpha\beta < 0$ implies $\gamma(\alpha + \beta) < \beta(2\alpha + \beta)$.

Lemma S.8. Assume selection scenario 4, i.e., $\beta < 0$ and $\gamma > \alpha + \beta$.

1) An unstable internal equilibrium enters the state space through \mathbf{S}_B at $m = m_B$ (and exists for $m = m_B + \epsilon$, $\epsilon > 0$ small) if and only if

$$r > \alpha \quad \text{and} \quad f_B(r) < 0. \quad (\text{S.82})$$

This holds in precisely the following cases:

$$r > \max[\alpha, r_B] \text{ and } \gamma > -\beta, \quad (\text{S.83a})$$

$$\alpha < r < r_B \text{ and } \gamma < -\beta, \quad (\text{S.83b})$$

$$\alpha < r < \infty \text{ and } \gamma = -\beta < 3\alpha + \beta. \quad (\text{S.83c})$$

2) The stable internal equilibrium leaves the state space through \mathbf{S}_B at $m = m_B$ if and only if

$$r > \alpha \quad \text{and} \quad f_B(r) \geq 0. \quad (\text{S.84})$$

This holds in precisely the following cases:

$$r > \max[\alpha, r_B] \quad \text{and} \quad \gamma < -\beta, \quad (\text{S.85a})$$

$$r = r_B > \alpha, \quad (\text{S.85b})$$

$$\alpha < r < r_B \quad \text{and} \quad \gamma > -\beta, \quad (\text{S.85c})$$

$$\alpha < r < \infty \quad \text{and} \quad \gamma = -\beta \geq 3\alpha + \beta. \quad (\text{S.85d})$$

Proof. The lemma follows from studying the perturbation of \mathbf{S}_B near m_B . We recall from above (S.9) that \mathbf{S}_B is admissible for $m = m_B$ if and only if $m_B < -\beta$. Under the assumptions of the lemma, this reduces to $r > \alpha$.

1) If $m = m_B + \epsilon$ ($\epsilon > 0$), the perturbation analysis (for p and q terms of order ϵ^2 are required to obtain D to order ϵ) yields

$$p(\epsilon) = rD(\epsilon) \frac{\gamma - \beta}{\alpha(\alpha + \beta - \gamma)}, \quad D(\epsilon) = \epsilon \frac{(\alpha + \beta - \gamma)(\alpha - r)}{rf_B(r)}. \quad (\text{S.86})$$

$q(\epsilon)$ is needed only to get D . Because we know $D(\epsilon) < 0$ holds at every equilibrium, condition (S.82) follows. The particular cases follow easily by studying f_B .

The proof of 2) is analogous. The difference is that the perturbation analysis yields

$$D(\epsilon) = -\epsilon \frac{(\alpha + \beta - \gamma)(\alpha - r)}{rf_B(r)}. \quad (\text{S.87})$$

If $r = r_B$, then $f_B(r) = 0$. This case is degenerate because $m_B = m^*$ and the outgoing and incoming equilibria collide at \mathbf{S}_B and annihilate each other. \square

Theorem S.5. 1. *Bifurcation patterns of Type 1 occur in*

Selection scenario 1 if and only if $r > \beta - \alpha$;

Selection scenario 2 if and only if $r \geq \alpha - \beta$.

2. *Bifurcation patterns of Type 2 occur in*

Selection scenario 2 if and only if $r_2 < r < \alpha - \beta$;

Selection scenario 3 if and only if one of the following holds:

- (a) $r_2^* < r \leq \gamma - \beta$,
- (b) $r > \max[\gamma - \beta, r_{\mathcal{A}}]$ and $\gamma > \frac{1}{2}\alpha$,
- (c) $\gamma - \beta < r < \infty$ and $\gamma = \frac{1}{2}\alpha > 3\beta$,
- (d) $\gamma - \beta < r < r_{\mathcal{A}}$ and $\gamma < \frac{1}{2}\alpha$.

Selection scenario 4 if and only if one of the following holds:

- (a) $r_2^* < r \leq \alpha$,
- (b) $r > \max[\alpha, r_{\mathcal{B}}]$ and $\gamma > -\beta$,
- (c) $\alpha < r < \infty$ and $\gamma = -\beta < 3\alpha + \beta$,
- (d) $\alpha < r < r_{\mathcal{B}}$ and $\gamma < -\beta$.

3. Bifurcation patterns of Type 3 occur in

Selection scenario 2 if and only if $r \leq r_2$;

Selection scenario 3 if and only if one of the following holds:

- (a) $r \leq \min[\gamma - \beta, r_2^*]$,
- (b) $\gamma - \beta < r \leq r_{\mathcal{A}}$ and $\gamma > \frac{1}{2}\alpha$,
- (c) $\gamma - \beta < r < \infty$ and $\gamma = \frac{1}{2}\alpha < 3\beta$.
- (d) $r \geq \max[\gamma - \beta, r_{\mathcal{A}}]$ and $\gamma < \frac{1}{2}\alpha$.

Selection scenario 4 if and only if one of the following holds:

- (a) $r \leq \min[\alpha, r_2^*]$,
- (b) $\alpha < r \leq r_{\mathcal{B}}$ and $\gamma > -\beta$,
- (c) $\alpha < r < \infty$ and $\gamma = -\beta \geq 3\alpha + \beta$,
- (d) $r \geq \max[\alpha, r_{\mathcal{B}}]$ and $\gamma < -\beta$.

If $\gamma = 0$ and $\beta < -\alpha < 0$, which is subsumed in selection scenario 4(a), all possible

bifurcation diagrams are displayed in Figure 1 of BÜRGER and AKERMAN (2011). Each of the bifurcation patterns of Type 2 or 3 is governed by one of these bifurcation diagrams. Thus, the only fundamentally new bifurcation patterns that arise in the present, much more general model, are of Type 1.

Proof of Theorem S.5. 1. The statement about bifurcation patterns of Type 1 is an immediate consequence of condition (S.42) in Theorem S.2, (S.24), and Theorem S.4.

2. The statement about selection scenario 2 follows from Lemma S.7, that about scenario 4 from Lemmas S.6 and S.8 by employing (S.70), (S.80), and (S.81). The statements about selection scenario 3 follow from those about scenario 4 by the model symmetry noted below (A.6).

3. The statement about selection scenario 2 is a consequence of Lemma S.7, that about scenario 4 of Lemmas S.6 and S.8 together with (S.70), (S.80), and (S.81). The statements about scenario 3 follow from those about scenario 4 by the model symmetry. \square

Remark S.4. If, in selection scenario 4, $\gamma(\alpha + \beta) < \beta(2\alpha + \beta)$ and $\gamma < -\beta$ hold, then for every $r > 0$ a bifurcation pattern of Type 3 occurs, whence Type 2 (or Type 1) never occurs. These two conditions are satisfied whenever $-\beta > \max[2\alpha, \gamma]$. The first assertion follows immediately from Lemmas S.6 and S.8 by recalling (S.70), (S.79), and (S.80), the second is obvious.

Therefore, in the local-adaptation scenario with a slope-type fitness function, at most one internal equilibrium (which then is globally asymptotically stable) occurs whenever the selection intensity on the two loci differs by more of a factor of two. Thus, bistable equilibrium patterns can occur in the local adaptation scenario only if the selection strength on both loci is sufficiently similar and the recombination rate is about as strong as the selection intensity.

S.8 Further limiting cases and perturbation results

S.8.1 Tight linkage

First, we treat the case $r = 0$. From Section S.1 we recall that the monomorphic equilibrium \mathbf{M}_2 is asymptotically stable if $m > \alpha - \beta$ (hence, whenever $\beta > \alpha$), and the polymorphic equilibrium \mathbf{R}_0 is asymptotically stable if $m < \alpha - \beta$. The single-locus polymorphisms \mathbf{S}_A and \mathbf{S}_B do not exist.

We infer global convergence to the (unique) asymptotically stable equilibrium because

$$V = V(x_1, x_2, x_3, x_4) = \bar{w} + m \ln x_2 \tag{S.88}$$

is a Lyapunov function on the state space S_4 (cf. PASSEKOV 1978; HOFBAUER 1985; BÜRGER and AKERMAN 2011). That V is a Lyapunov function follows from equations (2.13) - (2.16) on p. 103 in BÜRGER (2000) by taking into account that, here, selection acts on haploids and by observing that, if $r = 0$, the system (1) is formally equivalent to a one-locus selection-mutation model with four alleles and so-called house-of-cards mutation. To see this, set all mutation rates to types 1, 3, and 4 (gametes ab , Ab , AB) zero, and assume that each of types 1, 3, and 4 mutates to type 2 (aB) at rate m . Therefore (p. 103 in BÜRGER 2000), (1) is a generalized gradient system. This implies that every trajectory converges to an equilibrium.

As a consequence, for sufficiently small r , every trajectory in the perturbed system converges to an equilibrium provided all equilibria are hyperbolic if $r = 0$. Thus, in particular, (generic) global convergence to the unique stable equilibrium follows. The crucial point is that the above result for $r = 0$ implies that the chain-recurrent points of (1) are exactly the equilibria (Lemma 2.2 in NAGYLAKI *et al.* 1999). Therefore, the proof of Theorem 2.3 in NAGYLAKI *et al.* (1999) applies unaltered.

If linkage is tight, the coordinates of the (globally) stable internal equilibrium can be approximated by perturbing the equilibrium \mathbf{R}_0 (S.11). One obtains

$$\hat{p} = 1 - \frac{m}{\alpha - \beta} \left[1 + r \frac{\beta(\beta - \alpha) + m(\alpha + \beta)}{\alpha(\alpha - \beta)} \right] + O(r^2) \quad (\text{S.89a})$$

$$\hat{q} = \frac{m}{\alpha - \beta} \left[1 - r \frac{(\alpha + \beta - \gamma)(m + \beta - \alpha)}{\alpha(\alpha - \beta)(\gamma - \beta)} \right] + O(r^2) \quad (\text{S.89b})$$

$$\hat{D} = \frac{m}{\alpha - \beta} \left(1 - \frac{m}{\alpha - \beta} \right) \left[1 - r \frac{(\gamma - \beta)(\alpha - \beta) + m(\alpha + \beta - \gamma)}{\alpha(\alpha - \beta)(\gamma - \beta)} \right] + O(r^2). \quad (\text{S.89c})$$

S.8.2 Independent loci

Under the assumption of linkage equilibrium ($D = 0$), the dynamics (S.2) reduces to the much simpler, two-dimensional form

$$\dot{p} = p[\alpha(1 - p) - \gamma(1 - p)q - m], \quad (\text{S.90a})$$

$$\dot{q} = (1 - q)[\beta q - \gamma pq + m]. \quad (\text{S.90b})$$

The coordinates and local stability properties of the possible boundary equilibria (\mathbf{M}_2 , \mathbf{S}_A , \mathbf{S}_B) are obtained from Section S.1 by letting $r \rightarrow \infty$ (if necessary). There may exist up to two internal equilibria which can be determined explicitly:

$$\hat{p}^\pm = 1 - \frac{\gamma - \beta}{2\gamma}(1 \mp R), \quad \hat{q}^\pm = \frac{\alpha}{2\gamma}(1 \mp R), \quad (\text{S.91})$$

where

$$R = \sqrt{1 - \frac{4m\gamma}{\alpha(\gamma - \beta)}}. \quad (\text{S.92})$$

The equilibrium (\hat{p}^+, \hat{q}^+) corresponds to \mathbf{I}_{DMI} , (\hat{p}^-, \hat{q}^-) to \mathbf{I}_0 . The first one is asymptotically stable whenever it exists, the second one is unstable. It is easy to check directly, but also a straightforward consequence of Theorem S.4, that (\hat{p}^+, \hat{q}^+) is admissible if and only if

$$\text{selection scenario 1 or 2 applies and } m \leq m^*, \quad (\text{S.93a})$$

$$\text{selection scenario 3 applies and } m \leq \begin{cases} m_{\mathcal{A}} & \text{if } \gamma \leq \frac{1}{2}\alpha, \\ m^* & \text{if } \gamma > \frac{1}{2}\alpha, \end{cases} \quad (\text{S.93b})$$

$$\text{selection scenario 4 applies and } m \leq \begin{cases} m_{\mathcal{B}} & \text{if } \gamma \leq -\beta, \\ m^* & \text{if } \gamma > -\beta, \end{cases} \quad (\text{S.93c})$$

where we have $m_{\mathcal{A}} = (\alpha - \gamma)(\gamma - \beta)/\alpha$, $m_{\mathcal{B}} = -\alpha\beta/(\gamma - \beta)$, and $m^* = \frac{1}{4}\alpha(1 - \beta/\gamma)$.

(\hat{p}^-, \hat{q}^-) is admissible if and only if

$$\gamma > \max[\frac{1}{2}\alpha, -\beta] \text{ and } \max[m_{\mathcal{A}}, m_{\mathcal{B}}] < m < m^*. \quad (\text{S.94})$$

Then, and only then, both internal equilibria coexist. In this case, we have $\beta/\gamma < \hat{p}^- < \hat{p}^+ < 1$.

By the studying the nullclines of (S.90a), we can exclude the existence of periodic orbits. We have $\dot{p} = 0$ if and only if $p = 0$ or $q = K_A(p)$, where

$$K_A(p) = \frac{\alpha(1-p) - m}{\gamma(1-p)}, \quad (\text{S.95})$$

and we have $\dot{q} = 0$ if and only if $q = 1$ or $q = K_B(p)$, where

$$K_B(p) = \frac{m}{\gamma p - \beta}. \quad (\text{S.96})$$

The intersection points of K_A and K_B in the (open) square $(0, 1) \times (0, 1)$ are the internal equilibria. It is easy to check that both K_A and K_B are strictly monotone decreasing in p , that K_A is convex, and K_B is concave. Whether they intersect once or twice, the (two or three) areas between them are always positively invariant. This excludes the existence of periodic orbits because a periodic orbit has to enclose an equilibrium.

The domain of attraction of \mathbf{I}_{DMI} contains at least all initial conditions with $p > \hat{p}^+$ and $q < \hat{q}^+$. In particular, this includes the *island – continent*, *continent – continent* and *secondary contact* scenarios. In contrast, all points in the region $p < \hat{p}^+$ and $q > \hat{q}^+$ are outside of the

attraction domain and converge to a boundary equilibrium. This region includes the starting conditions for the *continent – island* and the *island – island* scenario.

From the coordinates of the equilibrium in terms of haplotype frequencies we obtain the level of population differentiation,

$$\hat{x}_3 = \frac{-\alpha\beta + \beta\gamma + \gamma^2}{2\gamma^2} + \frac{\alpha\beta - \beta\gamma + \gamma^2}{2\gamma^2} \sqrt{1 + \frac{4m\gamma}{\alpha\beta - \alpha\gamma}} - 2\frac{m}{\gamma}. \quad (\text{S.97})$$

In the limit of strong epistasis, $\gamma \rightarrow \infty$, this expression simplifies to

$$\hat{x}_3^* = \frac{1}{2} \left(1 + \sqrt{1 - \frac{4m}{\alpha}} \right). \quad (\text{S.98})$$

S.8.3 Strong recombination

By assuming that both selection and migration are weak relative to recombination, we can derive a quasi-linkage-equilibrium (QLE) approximation for the internal equilibria. Formally, we fix $r > 0$ and assume $\alpha = \epsilon a$, $\beta = \epsilon b$, $\gamma = \epsilon c$, and $m = \epsilon \mu$, where a , b , c , and μ are constants and $\epsilon \rightarrow 0$. It is straightforward to verify the results stated below by using an algebraic formula manipulation program (see the supporting online *Mathematica* notebook).

To first order in $1/r$, the coordinates of the two possible internal equilibria are

$$\hat{p}_\pm = 1 - \frac{\gamma - \beta}{2\gamma} (1 \mp R) \quad (\text{S.99a})$$

$$- \frac{\gamma - \beta}{2\gamma^2 r} \left[2\alpha\beta + \gamma(m - \beta) \pm R\alpha \frac{\beta(\gamma - \beta)(2\alpha - \gamma) + m\gamma(\gamma - 5\beta)}{4m\gamma - \alpha(\gamma - \beta)} \right]$$

$$\hat{q}_\pm = \frac{\alpha}{2\gamma} (1 \mp R) \quad (\text{S.99b})$$

$$+ \frac{\alpha}{2\gamma^2 r} \left[(\gamma - \alpha)(\gamma - 2\beta) + m\gamma \pm R(\gamma - \beta) \frac{\alpha(\gamma - \alpha)(\gamma - 2\beta) + m\gamma(5\alpha - 4\gamma)}{4m\gamma - \alpha(\gamma - \beta)} \right]$$

$$\hat{D}_\pm = - \frac{\alpha\beta(\gamma - \alpha)(\gamma - \beta)}{2\gamma^3 r} (1 \mp R) - \frac{m}{r} \left[1 - \frac{\beta}{\gamma} - \frac{\alpha}{2\gamma} \left(1 - \frac{3\beta}{\gamma} \right) \pm \frac{\alpha}{2\gamma} \left(1 - \frac{\beta}{\gamma} \right) R \right], \quad (\text{S.99c})$$

where we could return to the original parameters because they occur only as ratios. The stable equilibrium is $(\hat{p}_+, \hat{q}_+, \hat{D}_+)$. Because the QLE approximation is the result of a singular perturbation (BÜRGER 2009), it is necessary to develop \hat{p}_\pm and \hat{q}_\pm to order r^{-2} to obtain \hat{D}_\pm to order r^{-1} .

The QLE approximation (S.38) for m^* is readily obtained from (S.99) by solving $\hat{p}_+ = \hat{p}_-$ for m .