

FILE S2: ANALYSIS OF THE DIPLOID MODEL

By assuming Hardy-Weinberg proportions at every time instance, which requires sufficiently weak evolutionary forces, the structure of the dynamical equations for the diploid model becomes the same as that for the haploid model, Eq. (1),

$$\begin{aligned}\dot{x}_1 &= x_1(w_1 - \bar{w} - m) - rD, & \dot{x}_2 &= x_2(w_2 - \bar{w} - m) + rD + m, \\ \dot{x}_3 &= x_3(w_3 - \bar{w} - m) + rD, & \dot{x}_4 &= x_4(w_4 - \bar{w} - m) - rD,\end{aligned}\tag{S.100}$$

but with the marginal fitness values

$$\begin{aligned}w_1 &= \beta x_2 + \alpha x_3 + (\alpha + \beta - \gamma_1)x_4, \\ w_2 &= \beta + \beta x_2 + (\alpha - \gamma_1)x_3 + (\alpha + \beta - \gamma_2)x_4, \\ w_3 &= \alpha + (\beta - \gamma_1)x_2 + \alpha x_3 + (\alpha + \beta - \gamma_3)x_4, \\ w_4 &= \alpha + \beta - \gamma_1 + (\beta + \gamma_1 - \gamma_2)x_2 + (\alpha + \gamma_1 - \gamma_3)x_3 + (\alpha + \beta + \gamma_1 - \gamma_4)x_4,\end{aligned}\tag{S.101}$$

and the mean fitness

$$\bar{w} = 2(\beta x_2 + \alpha x_3 + (\alpha + \beta - \gamma_1)x_4 - \gamma_1 x_2 x_3 + (\gamma_1 - \gamma_2)x_2 x_4 + (\gamma_1 - \gamma_3)x_3 x_4 + (\gamma_1 - \gamma_4/2)x_4^2).\tag{S.102}$$

For the special case  $\Gamma = (\gamma/2, \gamma, \gamma, 2\gamma)$  and in linkage equilibrium ( $x_1 x_4 = x_2 x_3$ ), we obtain  $\bar{w} = 2(\beta x_2 + \alpha x_3 + (\alpha + \beta - \gamma)x_4)$ . In this case, the dynamical equations for the two-dimensional system with  $p = x_3 + x_4$  and  $q = x_2 + x_4$  reduces precisely to the corresponding equations for the haploid model. For all other choices of epistasis parameters, the dynamics of the diploid model is much more complex. Therefore, our analytical results are incomplete. They are presented below and, in more extensive form, in the supplementary *Mathematica* OS.

### S.9 Existence and linear stability of boundary equilibria

For  $m = 0$ , all four monomorphic equilibria exist and stability conditions can readily be derived (see the *Mathematica* OS). We find the following conditions for asymptotic stability:

$$\mathbf{M}_1 : \quad \alpha < 0, \beta < 0, \text{ and } r > \alpha + \beta - \gamma_1,\tag{S.103a}$$

$$\mathbf{M}_2 : \quad \alpha < \gamma_2, \beta > 0, \text{ and } r > \alpha - \beta - \gamma_1,\tag{S.103b}$$

$$\mathbf{M}_3 : \quad \alpha > 0, \gamma_3 > \beta, \text{ and } r > \beta - \alpha - \gamma_1,\tag{S.103c}$$

$$\mathbf{M}_4 : \quad \alpha > \gamma_4 - \gamma_2, \beta > \gamma_4 - \gamma_3, \text{ and } r > \gamma_4 - \gamma_1 - \alpha - \beta.\tag{S.103d}$$

Compared with the haploid case, two additional boundary equilibria, denoted by  $\tilde{\mathbf{S}}_{\mathcal{A}}$  and  $\tilde{\mathbf{S}}_{\mathcal{B}}$ , can exist for the diploid model if  $m = 0$ . These equilibria exist if locus  $\mathcal{A}$  or  $\mathcal{B}$  are over- or underdominant when the derived allele ( $B$  or  $A$ ) at the other locus is fixed. They can be stable only in the case of overdominance. In particular, an overdominant equilibrium  $\tilde{\mathbf{S}}_{\mathcal{A}}$  with

coordinates  $p = (\gamma_4 - \gamma_2 - \alpha)/(\gamma_4 - 2\gamma_2)$  and  $q = 1$  exists if  $\gamma_2 < \alpha < \gamma_4 - \gamma_2$ . An overdominant boundary equilibrium  $\tilde{\mathbf{S}}_{\mathcal{B}}$  with  $p = 1$  and  $q = x_4 = (1 - x_3) = (\gamma_4 - \gamma_3 - \beta)/(\gamma_4 - 2\gamma_3)$  exists if  $\gamma_3 < \beta < \gamma_4 - \gamma_3$ . Note that overdominance is only a necessary, but not sufficient condition for stability of  $\tilde{\mathbf{S}}_{\mathcal{A}}$  or  $\tilde{\mathbf{S}}_{\mathcal{B}}$  in the full model. Sufficient conditions can be derived from the Jacobian (see the *Mathematica* OS) but result in complicated cubic equations for the eigenvalues.

If  $m > 0$ , boundary equilibria can exist only at the edges  $p = 0$  (implying  $x_3 = x_4 = D = 0$ ) or  $q = 1$  (i.e.,  $x_1 = x_3 = D = 0$ ) of the state space. The only monomorphic equilibrium to fulfill this condition is  $\mathbf{M}_2$  (fixation of the continental haplotype). For an arbitrary point on the edge  $x_3 = x_4 = 0$ , the eigenvalues of the Jacobian are as follows:

$$\begin{aligned} \lambda_1 &= \beta - 2\beta x_2 - m \\ \lambda_{2,3} &= \frac{1}{2} \left( \beta + 2\alpha - r - \gamma_1 - 2\beta x_2 - \gamma_2 x_2 - 2m \right. \\ &\quad \left. \pm \sqrt{(\beta - r - \gamma_1 + 2\gamma_1 x_2 - \gamma_2 x_2)^2 + 4r x_2 (\beta - \gamma_1 + 2\gamma_1 x_2 - \gamma_2 x_2)} \right) \end{aligned} \quad (\text{S.104})$$

Setting  $x_2 = 1$ , we obtain the stability conditions for  $\mathbf{M}_2$ :

$$m > \max[-\beta, \alpha - \beta - \gamma_1 - r, \alpha - \gamma_2]. \quad (\text{S.105})$$

As in the haploid case, these conditions correspond to the invasion criteria for the three other haplotypes,  $ab$ ,  $Ab$ , and  $AB$ . Additional boundary equilibria, with a single polymorphic locus, can exist if  $m > 0$ . In Section S.13 below, we analyze the stability of these equilibria for a particular choice of the epistasis parameters.

### S.10 Global stability of the boundary

Here, we derive sufficient conditions for global convergence to the boundary. Alternatively, these may be viewed as necessary conditions for the existence of a DMI (i.e., a stable internal equilibrium). The following assumptions on epistasis will be required:

$$0 \leq \gamma_1 \leq \min[\gamma_2, \gamma_3] \quad \text{and} \quad \max[\gamma_2, \gamma_3] \leq \gamma_4, \quad (\text{S.106})$$

$$\gamma_1 + \gamma_4 \geq \gamma_2 + \gamma_3. \quad (\text{S.107})$$

Clearly, the recessive and the co-dominant model with  $\Gamma_0 := (0, \gamma, \gamma, 2\gamma)$  and  $\Gamma_1 := (\gamma/2, \gamma, \gamma, 2\gamma)$  satisfy these assumptions. In addition, we shall need the following condition on the selection parameters:

$$\beta \geq \max[\gamma_2, \gamma_3, \gamma_4 - \gamma_1]. \quad (\text{S.108})$$

Throughout the following, we always assume (S.106). The results below hold whenever  $m \geq 0$  and  $r > 0$ .

**Theorem S.6.** *Each of the following assumptions ensures that all trajectories converge to an equilibrium at the boundary of the state space  $S_4$ :*

$$(i) \quad \alpha \leq 0 \text{ and (S.107);} \quad (S.109)$$

$$(ii) \quad \alpha \geq 0 \text{ and (S.107) and (S.108);} \quad (S.110)$$

$$(iii) \quad m \geq \max[\frac{1}{4}\alpha, \alpha + \gamma_1 - \beta, \gamma_2 - \gamma_3] \text{ and (S.107).} \quad (S.111)$$

**Remark S.5.** In (i), assumption (S.107) is needed only for technical reasons. Without it, internal equilibria could be excluded, but not limit cycles or other complex attractors. Importantly, the proof shows that any internal equilibrium, hence every DMI, will be in negative linkage disequilibrium.

It is not difficult to show that the assumption (S.108) in (ii) can be replaced by the weaker assumption

$$\beta \geq \max[\gamma_2 - \alpha, \gamma_3, \gamma_4 - \gamma_3, \gamma_4 - \gamma_1 - \alpha]. \quad (S.112)$$

The proof is based on several lemmas.

**Lemma S.9.** *If  $m + \gamma_1 + \gamma_4 \geq \gamma_2 + \gamma_3$ , then every  $\omega$ -limit is contained in the set  $\{D \leq 0\}$ . Any internal  $\omega$ -limit points have to satisfy  $D < 0$ . In particular, the conclusions apply if  $m \geq 0$  and (S.107) hold.*

For the proof, define

$$Z = \frac{x_2 x_3}{x_1 x_4}. \quad (S.113)$$

Then the lemma follows from the identity

$$(x_1 x_4)^2 \dot{Z} = rD(x_1 x_2 x_3 + x_2 x_3 x_4 + x_1 x_2 x_4 + x_1 x_3 x_4) + x_1 x_3 x_4 \{m + x_2[x_2(\gamma_2 - \gamma_1) + x_3(\gamma_3 - \gamma_1) + x_4(\gamma_1 + \gamma_4 - \gamma_2 - \gamma_3)]\}. \quad (S.114)$$

**Lemma S.10.** *(i) Assume  $\alpha \leq 0$  and  $D \leq 0$ . Then  $(x_1/x_3) \geq 0$ , and the inequality is strict in the interior of the state space.*

This follows immediately from the identity

$$x_3^2 \left( \frac{x_1}{x_3} \right) \dot{\phantom{x_1}} = -\alpha x_1 x_3 - r(x_1 + x_3)D + x_1 x_3 [\gamma_1 x_2 + (\gamma_3 - \gamma_1)x_4], \quad (S.115)$$

**Lemma S.11.** (i) Assume  $\alpha \leq 0$  and  $D \geq 0$ . Then  $(x_2/x_4) \dot{\geq} 0$ , and the inequality is strict in the interior of the state space.

This follows immediately from the identity

$$x_4^2 \left( \frac{x_2}{x_4} \right) \dot{=} mx_4 + r(x_2 + x_4)D - \alpha x_2 x_4 + x_2 x_4 [\gamma_1 x_1 + \gamma_2 x_2 + (\gamma_3 - \gamma_1)x_3 + (\gamma_4 - \gamma_2)x_4]. \quad (\text{S.116})$$

**Lemma S.12.** Assume  $\alpha + \beta \geq \max[\gamma_2, \gamma_3, \gamma_4 - \gamma_1]$ . Then  $(x_1/x_4) \dot{\leq} 0$  if  $D(x_1 - x_4) \leq 0$  and the set  $\{x_1 \leq x_4\}$  is forward invariant.

The proof follows from the identity

$$x_4^2 \left( \frac{x_1}{x_4} \right) \dot{=} rD(x_1 - x_4) - x_1 x_4 [x_1(\alpha + \beta - \gamma_1) + x_2(\alpha + \beta - \gamma_2) + x_3(\alpha + \beta - \gamma_3) + x_4(\alpha + \beta - \gamma_4 + \gamma_1)]. \quad (\text{S.117})$$

**Lemma S.13.** Let

$$Y = \frac{x_1 + x_3}{x_3 + x_4}. \quad (\text{S.118})$$

Assume  $\alpha > 0$  and (S.108). Then  $\dot{Y} \leq 0$  on the set  $\{x_1 \leq x_4\}$ .

The proof follows from the identity

$$(x_3 + x_4)^2 \dot{Y} = -\alpha x_1(x_3 + x_4) + \gamma_1 x_2 x_3(x_1 - x_4) - x_4 [x_1^2(\beta - \gamma_1) + x_2(x_1 + x_3)(\beta - \gamma_2) + x_3(2x_1 + x_3)(\beta - \gamma_3) + x_1 x_4(\beta - \gamma_4 + \gamma_1) + x_3 x_4(\beta - \gamma_4 + \gamma_3)]. \quad (\text{S.119})$$

**Lemma S.14.** Assume  $m \geq \max[\alpha - \beta, \gamma_2 - \gamma_3]$ . Then  $(x_2/x_3) \dot{\geq} 0$  holds on the forward-invariant set  $\{x_2 \geq x_3\} \cap \{D \leq 0\}$ .

The proof follows from the identity

$$x_3^2 \left( \frac{x_2}{x_3} \right) \dot{=} -rD(x_2 - x_3) + \gamma_1 x_2 x_3(x_2 - x_3) + mx_3(x_1 + x_3) + mx_3 x_4(x_1 + x_3 + x_4) + (m - \alpha + \beta)x_2 x_3 + (m + \gamma_3 - \gamma_2)x_2 x_3 x_4. \quad (\text{S.120})$$

**Lemma S.15.** Let

$$X = \frac{x_1 + x_3}{x_1 + x_2}. \quad (\text{S.121})$$

Assume  $\alpha > 0$  and  $m \geq \max[\frac{1}{4}\alpha, \alpha + \gamma_1 - \beta, \gamma_2 - \gamma_3]$ . Then  $\dot{X} \leq 0$  on the set  $\{x_3 \geq x_2\}$ .

This statement follows from the identity

$$(x_1 + x_2)^2 \dot{X} = -m(x_1 + x_3)^2 + \alpha x_1 x_3 - (m - \alpha - \gamma_1 x_3 + \beta) x_2 x_3 - (m + \beta) x_1 x_2 \\ - (m - \gamma_2 + \gamma_3) x_2 x_4 (x_1 + x_3) + \gamma_1 x_2^2 x_3^2 + (\gamma_3 - \gamma_1) x_1 x_4 (x_3 - x_2) \quad (\text{S.122})$$

because  $-m(x_1 + x_3)^2 + \alpha x_1 x_3 \leq -\frac{1}{4}\alpha[(x_1 + x_3)^2 - 4x_1 x_3] = -\frac{1}{4}\alpha(x_1 - x_3)^2 \leq 0$ .

*Proof of Theorem S.6.* (i) We start by noting that, because we assume  $r > 0$ , the only positive-invariant subsets of the boundary are the four edges of the simplex corresponding to fixation of one of the alleles. On these edges, convergence to equilibrium occurs always. Hence, it is sufficient to consider the fate of solutions starting in the interior of the state space.

The first statement follows immediately from Lemmas S.10 and S.11. For the second statement, Lemma S.9 guarantees that every  $\omega$ -limit is contained in the positive-invariant set  $\{D \leq 0\}$ , whence Lemma S.10 yields the result.

(ii) By Lemma S.9, it is sufficient to show that there are no  $\omega$ -limit points satisfying  $D < 0$ . Because  $\{D \leq 0\}$  is forward invariant, Lemma S.12 shows that all trajectories in  $\{x_1 \geq x_4\} \cap \{D \leq 0\}$  enter the region  $\{x_1 \leq x_4\} \cap \{D \leq 0\}$  and remain there. Now Lemma S.13 yields the result.

(iii) By Lemma S.9, it is sufficient to show that there are no  $\omega$ -limit points satisfying  $D < 0$ . Application of Lemmas S.14 and S.15 yields the assertion.  $\square$

**Remark S.6.** The following simple results can also be proved:

1. If (S.107) and  $\alpha + \beta \geq \max[\gamma_2, \gamma_3, \gamma_4 - \gamma_1]$  hold, then any DMI (if it exists) satisfies  $D < 0$  and  $x_1 \leq x_4$ .

2. If (S.107) and  $\alpha + \beta \leq \min[\gamma_2, \gamma_3, \gamma_4 - \gamma_1]$  hold, then any DMI (if it exists) satisfies  $D < 0$  and  $x_1 \geq x_4$ .

Under the assumption of linkage equilibrium, the dynamical equation for  $p$  can be written as

$$\dot{p} = p \left( \alpha - m - \alpha p - q(1-p) [2\gamma_1(1-q)(1-p) + \gamma_2 q(1-p) \\ + 2(\gamma_3 - \gamma_1)p(1-q) + (\gamma_4 - \gamma_2)pq] \right). \quad (\text{S.123})$$

We thus see that  $p$  is a Lyapunov function and  $p(t) \rightarrow 0$  as  $t \rightarrow \infty$  if  $\gamma_4 \geq \gamma_2$ ,  $\gamma_3 \geq \gamma_1$ , and  $m > \alpha$  (here it is not necessary to assume (S.106), (S.107), or (S.108)).

### S.11 Tight linkage

Arguments analogous to those in Section S.8.1 yield that, if  $r = 0$ ,

$$V = V(x_1, x_2, x_3, x_4) = \frac{1}{2}\bar{w} + m \ln x_2 \quad (\text{S.124})$$

is a Lyapunov function, whence the dynamics is gradient-like. Again, the proof of Theorem 2.3 in NAGYLAKI *et al.* (1999) applies and shows that for sufficiently small  $r$  every trajectory converges to an equilibrium point (provided every equilibrium of the unperturbed system is hyperbolic). For small  $r$ , the asymptotically stable equilibria are obtained by perturbation of the asymptotically stable equilibria for  $r = 0$ . In particular, if there is a unique asymptotically stable equilibrium for  $r = 0$ , then its perturbation is globally asymptotically stable for sufficiently small  $r$ . It is worth emphasizing that this holds for arbitrary fitness assignments (such that all equilibria are hyperbolic).

### S.12 Internal equilibria: Weak migration

In addition to our results from Lyapunov functions, we obtain conditions for the existence of a DMI under weak migration from perturbation arguments. On the one hand, the existence of a stable equilibrium with positive frequency of the island haplotype ( $x_3 > 0$ ) for  $m = 0$  implies the existence of a DMI for sufficiently small  $m > 0$ . On the other hand, if a stable equilibrium with  $x_3 > 0$  does not exist if  $m = 0$ , a DMI cannot be maintained for small  $m$ .

Extensive computer simulations confirm that there are always uniquely defined maximum rates of gene flow,  $m_{\max}^{\pm}$ , which separate the domains in which a locally or globally stable DMI exists (if  $m < m_{\max}^{\pm}$ ) from the region in which a DMI does not exist ( $m > m_{\max}^{\pm}$ ). We note that although this conjecture is highly plausible, we do not have a rigorous proof beyond the cases treated in the previous section. These arguments imply that  $m_{\max}^+ > 0$  if there is a stable equilibrium with  $x_3 > 0$  for  $m = 0$ , and  $m_{\max}^+ = 0$ , otherwise. Similarly, we can conclude that  $m_{\max}^- > 0$  if the only stable equilibrium for  $m = 0$  is one with  $x_3 > 0$ .

Our numerical analysis of the diploid model (see the *Mathematica* OS) indicates that for  $m = 0$  there are no stable equilibria in the interior of the state space. As we have seen above, two boundary equilibria with  $x_3 > 0$  may exist if  $m = 0$ : the monomorphic equilibrium  $\mathbf{M}_3$  and the single-locus polymorphism  $\tilde{\mathbf{S}}_{\mathcal{B}}$ . A necessary condition for the asymptotic stability of at least one of these boundary equilibria is

$$\beta < \max[\gamma_3, \gamma_4 - \gamma_3]. \quad (\text{S.125})$$

Given our numerical evidence, this translates into a necessary condition for a stable DMI (hence, for  $m_{\max}^+ > 0$ ) with weak migration. We note that this condition is slightly more stringent than the negation of (S.108). In addition, we already know from Theorem S.6 that  $\alpha > 0$  is another necessary condition.

Sufficient conditions for  $m_{\max}^+ > 0$  can, in principle, be derived from a full linear stability analysis of  $\mathbf{M}_3$  and  $\tilde{\mathbf{S}}_{\mathcal{B}}$  for  $m = 0$ . In general, however, the conditions for the stability of  $\tilde{\mathbf{S}}_{\mathcal{B}}$  are not transparent. For the special case of independent loci ( $r \rightarrow \infty$ ), we find that  $\tilde{\mathbf{S}}_{\mathcal{B}}$  is stable if and only if  $\gamma_3 < \beta < \gamma_4 - \gamma_3$  and  $\alpha > \alpha^*$ , where

$$\alpha^* = \frac{(\beta - \gamma_3)[2(\gamma_3 - \gamma_1)(\gamma_4 - \gamma_3 - \beta) + (\beta - \gamma_3)(\gamma_4 - \gamma_2)]}{(\gamma_4 - 2\gamma_3)^2}. \quad (\text{S.126})$$

Note that  $\alpha^* > 0$  if  $\gamma_3 < \beta < \gamma_4 - \gamma_3$ .

If we exclude overdominance at the locus  $\mathcal{B}$  (and, hence,  $\tilde{\mathbf{S}}_{\mathcal{B}}$  can not be stable) further analytical results can be derived. In particular, for weak migration, any stable DMI must be a perturbation of the island equilibrium  $\mathbf{M}_3$ . A perturbation analysis to first order in  $m$  yields the coordinates  $\{x_1, x_2, x_3\}$  of  $\mathbf{PM}_3$ :

$$\mathbf{PM}_3 : \left\{ \frac{mr}{\alpha(r + \alpha - \beta + \gamma_1)}, \frac{m}{r + \alpha - \beta + \gamma_1}, 1 - \frac{m(r\alpha + (r + \alpha)(\gamma_3 - \beta))}{\alpha(r + \alpha - \beta + \gamma_1)(\gamma_3 - \beta)} \right\}. \quad (\text{S.127})$$

The coordinate  $x_3$  measures the level of population differentiation which is analyzed further in the main text.

For all our analytical and numerical derivations, we have assumed that the epistasis coefficients are non-decreasing with the number of  $A/B$  conflicts, i.e.,  $0 \leq \gamma_1 \leq \min[\gamma_2, \gamma_3]$  and  $\max[\gamma_2, \gamma_3] \leq \gamma_4$ . This condition is essential for our results. Additional internal equilibria can be found for other choices of the  $\gamma_i$ . In particular, we found numerically that stable internal equilibria are possible for  $\alpha = \beta = 0$  (and even for  $\alpha < 0$ ) if  $\gamma_1 \ll \min[\gamma_3, \gamma_4]$  (for examples see the *Mathematica* OS).

### S.13 Stability conditions for the recessive and the co-dominant model

Here, we consider the diploid model with the simplified epistasis scheme  $\Gamma = (\gamma_1, \gamma, \gamma, 2\gamma)$ . Obviously, both the recessive model with  $\Gamma_0 = (0, \gamma, \gamma, 2\gamma)$  and the co-dominant model with  $\Gamma_1 = (\gamma/2, \gamma, \gamma, 2\gamma)$  follow this scheme. In the following lemma, we collect some important consequences for this choice of the epistasis parameters. They all follow from our above analysis and elementary calculations.

**Lemma S.16.** *Elementary facts for the diploid model with  $\Gamma = (\gamma_1, \gamma, \gamma, 2\gamma)$ .*

1. *Overdominance or underdominance of single loci does not occur.*
2. *The model is symmetric under the exchange of the haplotypes  $ab$  and  $AB$ . As in the haploid case, this symmetry is reflected by an invariance of the model under the transformation  $\alpha \rightarrow \gamma - \beta$  and  $\beta \rightarrow \gamma - \alpha$ .*

3.  $\alpha > 0$  and  $\gamma > \beta$  are necessary conditions for the existence of a DMI.

In the absence of overdominance, we find that the boundary equilibria  $\mathbf{S}_A$  and  $\mathbf{S}_B$  exist under the same conditions and with the same coordinates as in the haploid case (Section S.1). The stability conditions are different, however. Evaluation of (S.104) at  $x_2 = -m/\beta$  leads to the stability conditions for  $\mathbf{S}_B$ . In analogy to (S.10), explicit bounds on the migration rate  $m$  can be derived, however, the expressions are lengthy. Due to the model symmetry, the stability conditions for the  $\mathbf{S}_A$  equilibrium can be obtained directly from the corresponding conditions for  $\mathbf{S}_B$ . For explicit results, we focus on the limiting cases with  $r = 0$  and  $r \rightarrow \infty$ . We always assume  $\alpha > 0$  and  $\gamma > \beta$ .

If  $r = 0$ , the equilibrium  $\mathbf{S}_B$  is asymptotically stable if and only if

$$-\beta > m > \max \left[ \frac{-\beta(\beta + 2\alpha - \gamma_1)}{\gamma}, \frac{-\beta \left( \alpha\gamma + \beta\gamma_1 - \gamma_1^2 + \sqrt{(\alpha\gamma + \beta\gamma_1 - \gamma_1^2)^2 - 4\alpha\gamma_1(\gamma - \gamma_1)(\beta + \alpha - \gamma_1)} \right)}{2\gamma_1(\gamma - \gamma_1)} \right]. \quad (\text{S.128})$$

For independent loci ( $r \rightarrow \infty$ ), and assuming  $\gamma \geq \gamma_1$ , the stability condition for  $\mathbf{S}_B$  can be expressed as

$$-\beta > m > \frac{-\beta \left( \beta - 2\gamma_1 + \sqrt{(2\gamma_1 - \beta)^2 + 4\alpha(\gamma - 2\gamma_1)} \right)}{2(\gamma - 2\gamma_1)}, \quad (\text{S.129})$$

For the recessive model, in which  $\gamma_1 = 0$ , we can summarize the stability conditions for the boundary equilibria as follows. If  $r = 0$ , condition (S.128) can never be fulfilled and the equilibria  $\mathbf{S}_A$  and  $\mathbf{S}_B$  are never stable. The monomorphic equilibrium  $\mathbf{M}_2$  is stable if and only if  $m > \alpha - \beta$ . For  $r \rightarrow \infty$ , the stability conditions for the three boundary equilibria are

$$\mathbf{M}_2 : \quad m > \max[-\beta, \alpha - \gamma], \quad (\text{S.130a})$$

$$\mathbf{S}_A : \quad \alpha - \gamma > m > (\alpha - \gamma) \frac{\gamma - \alpha + \sqrt{(\gamma - \alpha)^2 + 4\gamma(\gamma - \beta)}}{2\gamma}, \quad (\text{S.130b})$$

$$\mathbf{S}_B : \quad -\beta > m > -\beta \frac{\beta + \sqrt{\beta^2 + 4\alpha\gamma}}{2\gamma}. \quad (\text{S.130c})$$

For the co-dominant model, in which  $\gamma_1 = \gamma/2$ , we obtain for  $r = 0$ :



$$\mathbf{M}_2 : m > \max[-\beta, \alpha - \beta - \gamma/2, \alpha - \gamma], \quad (\text{S.131a})$$

$$\mathbf{S}_A : \alpha - \gamma > m > \frac{2(\gamma - \beta)(\alpha - \gamma)}{\gamma}, \quad (\text{S.131b})$$

$$\mathbf{S}_B : -\beta > m > \frac{-2\alpha\beta}{\gamma}. \quad (\text{S.131c})$$

As noted above, the dynamics of the co-dominant diploid model coincides with the haploid dynamics in the limit  $r \rightarrow \infty$ . Thus, also the stability conditions and maximum rates of gene flow coincide and can be taken from there (Eqs. (10)–(12) in the main text). Using our results for the stability of boundary equilibria for the recessive and the co-dominant model, the analytical results for the maximum rate of gene flow  $m_{\max}^-$  in the Section RESULTS: DIPLOID MODEL of the main text can easily be derived.

In addition, explicit results for  $m_{\max}^+$  for the co-dominant model with tight linkage can be deduced. Their derivation is provided in the supplementary *Mathematica* OS.

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