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A Two-Locus Model of Migration and Stabilizing Selection

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Abstract

This diploma thesis studies the dynamics of a diallelic two-locus model under migration between two demes. The contributions of the loci to the genotypic value are purely additive and we assume quadratic stabilizing selection with an arbitrary optimum.

In Chapter 1 we introduce the notation and the basic equations (1.13) of the general selection-migration model with recombination. Furthermore, in Section 1.2 we explain additive quantitative traits. In Section 1.3 we define quadratic stabilizing selection.

As it is not possible to solve the complete system, we choose three different approaches. The first two are limiting cases, i.e., weak migration and weak selection. Therefore, we first assume one evolutionary force to be missing, i.e., Chapter 2 and Section 4.1, and then derive the limiting case.

The case of no migration is well studied, therefore most of Chapter 2 is a collection of existing results. It is important to note that if the double heterozygote is the fittest, the dynamics can be analyzed completely, cf. Section 2.1. Otherwise, (Section 2.2), we need the assumption of linkage equilibrium. In Chapter 3 we deduce the case of weak migration as a perturbation of the case of no migration.

For the case of no selection, treated in Section 4.1, we introduce the basic notation and deduce a general conclusion. In Section 4.2 we derive the limiting case of weak selection and compute all equilibria.

Our final approach is to study a special migration structure, namely the Levene model, in Chapter 5. For analytical results we assume linkage equilibrium. Finally, we also study the Levene model numerically.

In the Appendix, the interested reader finds the *Matlab* source code used for the numerical analysis of the Levene model.

Deutsche Zusammenfassung

In dieser Diplomarbeit wird die Dynamik eines diallelischen Zwei-Lokus-Modells unter Migration, Rekombination und quadratischer stabilisierender Selektion untersucht. Hierbei beeinflussen die beiden Loci den Genotypwert rein additiv und das Optimum der gewählten Fitnessfunktion ist beliebig.

In Kapitel 1 werden sowohl die zugrunde liegende Notation, als auch die Gleichungen des allgemeinen Selektions-Migrations-Modells unter Rekombination eingeführt. Das Modell wird durch die Einführung des additiven kontinuierlichen Merkmals in Abschnitt 1.2, sowie der quadratischen stabilisierenden Selektion in Abschnitt 1.3 vollständig aufgebaut.

Um das so entstandene komplexe Gleichungssystem zu lösen werden drei verschiedene Ansätze gewählt. Für die ersten zwei betrachten wir jeweils den Grenzfall, dass entweder Migration oder Selektion schwach ist. Für jeden der beiden Ansätze wird das System jeweils unter der Annahme untersucht, dass eine der evolutionären Kräfte vollständig fehlt, siehe Kapitel 2 und Abschnitt 4.1, um dann den Grenzfall herzuleiten.

Der in Kapitel 2 betrachtete Fall ohne Migration wurde bereits intensiv untersucht, daher stellt dieses Kapitel vor allem eine Zusammenfassung schon vorhandener Resultate dar. Für den Fall, dass der doppelt heterozygote Genotyp der fitteste ist, kann die gesamte Dynamik untersucht werden, siehe Abschnitt 2.1. Wird diese Annahme nicht getroffen muss man zusätzlich voraussetzen, dass sich das System im Kopplungsgleichgewicht befindet. In Kapitel 3 wird der Grenzfall der schwachen Migration als Störung des Systems ohne Migration behandelt.

In Kapitel 4 wird der Fall der schwachen Selektion betrachtet. Dafür wird in Abschnitt 4.1 das allgemeine Model ohne Selektion untersucht und die benötigte Notation eingeführt. In Abschnitt 4.2 wird der schwache Selektionsgrenzwert hergeleitet und alle Gleichgewichte so wie deren Stabilitätseigenschaften berechnet.

Als dritter Ansatz wird abschließend in Kapitel 5 eine spezielle Migrationsstruktur, das Levene Modell, gewählt. Um analytische Ergebnisse erhalten zu können muss das Kopplungsgleichgewicht vorausgesetzt werden. Schließlich wird das Levene Modell nummerisch untersucht.

Im Appendix findet der/die interessierte LeserIn den *Matlab*-Code, der für die nummerische Untersuchung des Levene Modells verwendet wurde.

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0 Introduction

This diploma thesis is written in the field of mathematical population genetics. This field is concerned with the evolution of the genetic structure of populations under the influence of evolutionary forces. These forces include, for instance, selection, recombination, mutation, or migration.

One of the biggest questions is how to maintain genetic variation in a population. Therefore, our main interest is, whether there exists a stable fully polymorphic equilibrium, i.e., none of the alleles becomes extinct.

The relationship between phenotype and fitness can often be described by one of three modes of selection (Futuyma, 2005, p. 270). They are directional selection, stabilizing selection and disruptive selection. In the following, we discuss the case of quadratic stabilizing selection. In the general case of an arbitrary position of the fitness optimum, the internal equilibria can not be computed explicitly. Even worse, for the biologically relevant case of weak selection, the internal equilibrium is never stable.

Furthermore, we assume a geographically structured population. Note that, from a mathematical point of view, migration is a powerful mechanism to establish polymorphisms. In a nutshell, this can be explained in the following way: Consider isolated populations, each of them at a different equilibrium. Introducing weak migration, the subpopulations blend and all the alleles present in the entire population may exist in each subpopulation.

We are not going to explain basic concepts of population genetics, as we assume them to be known. We expect the reader to understand the basic population-genetic terms and equations, as well as basic biomathematical concepts, especially dynamical systems. For the population-genetic background we refer the reader to Bürger (2000), for the theory of dynamical systems to Hofbauer and Sigmund (1998).

Instead of introducing the biological background, we refere to Futuyma (2005) and Bürger (2000).

Our approach is therefore the following. Outright, we jump into the basic notation. We briefly define the required equations, and then directly start to investigate them.

1 The Setting

1.1 The basic model

Let us introduce the basic notation that is needed for the model. We consider a diploid population with discrete, non-overlapping generations. The two sexes are assumed to be equivalent with respect to our assumptions on genetics, migration and selection; hence they need not be distinguished. Selection acts in each deme through different viabilities, which are constant in time. After selection, recombination occurs and adults migrate, their migration rate is only deme dependent, not genotype dependent. In each deme random mating of migrated adults is assumed, therefore offspring are in Hardy-Weinberg proportions (Bürger, 2000, p. 46).

The set of all demes is denoted by K and we refer to single demes using Greek letters. The number of demes is denoted by $\Gamma = |K|$. The genetic system consists of two loci with two alleles. We call the alleles at the first locus A_1 and A_2 and at the second locus B_1 and B_2. The relative frequencies of the four gametes A_1B_1, A_1B_2, A_2B_1 and A_2B_2 in deme α are denoted by $x_{1,\alpha}$, $x_{2,\alpha}$, $x_{3,\alpha}$ and $x_{4,\alpha}$. We denote the set of gametes by $I = \{1, 2, 3, 4\}$, single gametes by i, j. The allele frequencies of A_1, A_2, B_1 and B_2 in deme α are

$$p^{(1)}_{1,\alpha} = x_{1,\alpha} + x_{2,\alpha},\ p^{(1)}_{2,\alpha} = x_{3,\alpha} + x_{4,\alpha},\ p^{(2)}_{1,\alpha} = x_{1,\alpha} + x_{3,\alpha},\ p^{(2)}_{2,\alpha} = x_{2,\alpha} + x_{4,\alpha}, \tag{1.1}$$

the superscript denotes the locus.

When convenient, we will use the following simplified notation of allele frequencies: $p^{(1)}_{\alpha} = p^{(1)}_{1,\alpha}$ and $p^{(2)}_{\alpha} = p^{(2)}_{1,\alpha}$, which is sufficient to describe allele frequencies when there are only two alleles per locus.
We will use the following vector notation

$$x_i = (x_{i,1}, ..., x_{i,\Gamma})^T \in \mathbb{R}^{\Gamma}, \tag{1.2a}$$

$$x_{(\alpha)} = (x_{1,\alpha}, ..., x_{4,\alpha})^T \in \Delta_4, \tag{1.2b}$$

$$x = \left(x^T_{(1)}, ..., x^T_{(\Gamma)}\right) \in \Delta^{\Gamma}_4, \tag{1.2c}$$

with

$$\Delta_k = \{z \in \mathbb{R}^k : z_i \geq 0\ \forall i \in \{1, \ldots, k\}, \sum_i z_i = 1\}, \tag{1.3}$$

being the four dimensional simplex and Δ^{Γ}_4 being the Γ-fold cartesian product of the four dimensional simplex.

The fitness of a zygote consisting of gametes i and j in deme α is denoted by $w_{ij,\alpha} = w_{ji,\alpha}$. This leads to a 4×4 matrix for every deme, but as we assume no

position effect, i.e., $w_{23,\alpha} = w_{14,\alpha}$, we can express it by a 3×3 matrix of the single locus genotypes:

$$\begin{array}{c} \\ A_1A_1 \\ A_1A_2 \\ A_2A_2 \end{array} \begin{array}{c} \begin{array}{ccc} B_1B_1 & B_1B_2 & B_2B_2 \end{array} \\ \begin{pmatrix} w_{11,\alpha} & w_{12,\alpha} & w_{22,\alpha} \\ w_{13,\alpha} & w_{14,\alpha} & w_{24,\alpha} \\ w_{33,\alpha} & w_{34,\alpha} & w_{44,\alpha} \end{pmatrix} \end{array}. \tag{1.4}$$

Next, we define the marginal fitness of a gamete i in deme α

$$w_{i,\alpha} = \sum_{j=1}^{4} w_{ij,\alpha} x_{j,\alpha}, \tag{1.5}$$

and the mean fitness of the population in deme α

$$\overline{w}_\alpha = \sum_{i,j} w_{ij,\alpha} x_{i,\alpha} x_{j,\alpha} = \sum_i w_{i,\alpha} x_{i,\alpha}. \tag{1.6}$$

Sums without ranges indicate summation over all admissible indices, for example (1.5) reads as $\sum_j w_{ij,\alpha} x_{j,\alpha}$.

Remember that we assume the following life cycle: selection, recombination and then migration. The frequency of the genotype ij after selection is given by (Bürger, 2000, p. 30)

$$x_{i,\alpha} x_{j,\alpha} w_{ij,\alpha} / \overline{w}_\alpha. \tag{1.7}$$

Next, r is the probability of a recombination event, i.e., an individual with genotype A_iB_j/A_kB_l produces a gamete A_iB_l or A_kB_j. If $r = 0$, the two loci are called completely linked and may be treated as a single locus. If $r = \frac{1}{2}$ they are called unlinked. In this case, all gametes are produced with the same frequency $\frac{1}{4}$. Hence, the recombination rate satisfies $0 \leq r \leq \frac{1}{2}$.

Thus, the fraction of gametes ij and kl after recombination is given by $\frac{1}{2}(1-r)$, and, that of gametes il and kj equals $\frac{1}{2}r$. Now, combining selection and recombination, we obtain the following formula (Bürger, 2000, p. 47):

$$\overline{w}_\alpha x^*_{i,\alpha} = x_{i,\alpha} w_{i,\alpha} - \eta_i r w_{14,\alpha} D_\alpha, \tag{1.8}$$

where $\eta_1 = \eta_4 = 1$, $\eta_2 = \eta_3 = -1$ and $D_\alpha = x_{1,\alpha} x_{4,\alpha} - x_{2,\alpha} x_{3,\alpha}$ denotes linkage disequilibrium.

To derive (1.8) one has to calculate all probabilities for all the genotypes to produce one of the four gametes and plug them into (1.7).

Let

$$\Lambda_\alpha = \left\{ x_{(\alpha)} : D_\alpha = 0 \right\}, \tag{1.9}$$

denote the linkage-equilibrium manifold, or Wright manifold, in deme α and let

$$\Lambda = \left\{ x : D_\alpha \left(x_{(\alpha)} \right) = 0, \forall \alpha \in K \right\}, \tag{1.10}$$

denote global linkage equilibrium. Note that (1.8) shows that on the linkage-equilibrium manifold recombination alone does not change the gamete frequencies. This is especially important, as the boundary of Δ_4 is invariant under selection. Hence, only the four edges for which $D_\alpha = 0$ holds are invariant, and, therefore can contain fixed points of the system.

The probability for an individual in deme α to have migrated from deme β is denoted by $m_{\alpha\beta}$. Obviously, the $\Gamma \times \Gamma$ backwards migration matrix $M = (m_{\alpha\beta})$ is stochastic, i.e.,

$$m_{\alpha\beta} \geq 0 \; \forall \alpha, \beta \in K \text{ and } \sum_{\beta \in K} m_{\alpha\beta} = 1 \; \forall \alpha \in K. \tag{1.11}$$

We assume that M is constant. For many results we are also going to need the assumption that the backward migration matrix is ergodic, i.e., irreducible and aperiodic.

If we do so, there exists a principal left eigenvector $\mu \in \text{int}\Delta_\Gamma$ such that

$$\mu^T M = \mu^T. \tag{1.12}$$

The eigenvector μ is the unique stationary distribution of the Markov chain with transition matrix M (Bürger, 2009, p. 946).

The gamete frequencies after migration are given by

$$x'_{i,\alpha} = \sum_\beta m_{\alpha\beta} x^*_{i,\beta}, \; i \in I, \alpha \in K. \tag{1.13a}$$

Together with

$$x^*_{i,\alpha} = \frac{(x_{i,\alpha} w_{i,\alpha} - \eta_i r w_{14,\alpha} D_\alpha)}{\overline{W}_\alpha}, \tag{1.13b}$$

this fully describes the dynamics of the gamete frequencies in our population.

Furthermore, for the limiting cases that we discuss later, we will need the assumption that all equilibria are hyperbolic. An equilibrium of a system of difference equations is hyperbolic, if the Jacobian at the equilibrium has no eigenvalues of modulus one. In a compact set, there can be at most finitely many hyperbolic equilibria.

1.2 Additive quantitative traits

Next, we assume a quantitative trait, to which the loci contribute additively. A quantitative trait is a phenotypic character that can be measured on a metric scale, such as height or body mass. As we assume that the loci contribute additively to the genotypic value, we assume no epistasis. Epistasis refers to the presence of interaction between genes at different loci. If, in a multilocus model the gametic contribution to a character can not be split up into the effects of the single loci, epistasis is said to occur. Note that the notion of epistasis is a very broad one, as the character can be, for example, the genotypic value or fitness. Obviously, in our case we talk about the genotypic level; on the fitness level, the model is not free of epistasis.

The contributions in deme α of the alleles A_1, A_2, B_1 and B_2 to the trait are $-\frac{1}{2}\gamma_{1,\alpha}$, $\frac{1}{2}\gamma_{1,\alpha}$, $-\frac{1}{2}\gamma_{2,\alpha}$ and $\frac{1}{2}\gamma_{2,\alpha}$. Therefore the contributions of the four gametes A_1B_1, A_1B_2,

A_2B_1 and A_2B_2 in deme α are $-\frac{1}{2}(\gamma_{1,\alpha}+\gamma_{2,\alpha})$, $-\frac{1}{2}(\gamma_{1,\alpha}-\gamma_{2,\alpha})$, $\frac{1}{2}(\gamma_{1,\alpha}-\gamma_{2,\alpha})$ and $\frac{1}{2}(\gamma_{1,\alpha}+\gamma_{2,\alpha})$. If we assume that dominance is absent, i.e., the genotypic value of a zygote can be decomposed additively into the genotypic contributions of the gametes forming the zygote, than the resulting genotypic values (G_{ij}) are given by

$$\begin{array}{c} \\ A_1A_1 \\ A_1A_2 \\ A_2A_2 \end{array} \begin{array}{c} \begin{array}{ccc} B_1B_1 & B_1B_2 & B_2B_2 \end{array} \\ \begin{pmatrix} -\gamma_{1,\alpha}-\gamma_{2,\alpha} & -\gamma_{1,\alpha} & -\gamma_{1,\alpha}+\gamma_{2,\alpha} \\ -\gamma_{2,\alpha} & 0 & \gamma_{2,\alpha} \\ \gamma_{1,\alpha}-\gamma_{2,\alpha} & \gamma_{1,\alpha} & \gamma_{1,\alpha}+\gamma_{2,\alpha} \end{pmatrix} \end{array}. \tag{1.14}$$

We assume $\gamma_{1,\alpha} \geq \gamma_{2,\alpha} > 0 \ \forall \alpha \in K$ and refer to these loci as major and minor. We call $\gamma_{1,\alpha}$ and $\gamma_{2,\alpha}$ the effects of the loci, or the allelic effect.

Let us introduce the mean genotypic value in deme α and the total genetic variance in deme α:

$$\overline{G}_\alpha = \sum_{i,j} P_{ij,\alpha} G_{ij,\alpha}, \tag{1.15a}$$

$$\sigma^2_{G,\alpha} = \sum_{i,j} P_{ij,\alpha} g^2_{ij,\alpha}, \tag{1.15b}$$

where $G_{ij,\alpha}$ is the genotypic value, $P_{ij,\alpha}$ is the frequency and $g_{ij,\alpha}$ is the average excess of genotype ij in deme α. The average excess is defined as:

$$g_{ij,\alpha} = G_{ij,\alpha} - \overline{G}_\alpha. \tag{1.16}$$

As we calculate the mean genotypic value and total genetic variance before selection, the system is in Hardy-Weinberg equilibrium, i.e., $P_{ij,\alpha} = x_{i,\alpha}x_{j,\alpha}$. Furthermore, as we assume no dominance, it is sufficient to calculate these values among gametes and multiply them by two. The mean haploid genotypic value in deme α is:

$$\overline{G}_{h,\alpha} = \frac{1}{2}(\gamma_{1,\alpha}+\gamma_{2,\alpha})(x_{4,\alpha}-x_{1,\alpha}) + \frac{1}{2}(\gamma_{1,\alpha}-\gamma_{2,\alpha})(x_{3,\alpha}-x_{2,\alpha}). \tag{1.17}$$

Therefore, the total genetic variance is

$$\sigma^2_\alpha = E[\gamma^2_\alpha] + \gamma_{1,\alpha}\gamma_{2,\alpha}(x_{1,\alpha}+x_{4,\alpha}-x_{2,\alpha}-x_{3,\alpha}) \tag{1.18}$$

$$- \frac{1}{2}[(\gamma_{1,\alpha}+\gamma_{2,\alpha})(x_{4,\alpha}-x_{1,\alpha}) + (\gamma_{1,\alpha}-\gamma_{2,\alpha})(x_{3,\alpha}-x_{2,\alpha})]^2, \tag{1.19}$$

where

$$E[\gamma^2_\alpha] = \frac{1}{2}(\gamma^2_{1,\alpha}+\gamma^2_{2,\alpha}) \tag{1.20}$$

is the average of the squared effects of the loci.

In the classical theory, the total genetic variance is decomposed into an additive part, the additive genetic variance, and into a residual component, which incorporates dominance and epistasis (Bürger, 2000, p. 59). As the residual component equals zero under the assumptions of no dominance and no epistasis, in our model, the total genetic variance is equivalent to the additive genetic variance. We therefore refer to it as genetic variance.

Furthermore, we have to introduce the genetic variance of the whole population, as in general, the genetic variance will vary between demes. It is simply given as the weighted arithmetic mean of the genetic variances, where the weights equal the relative deme sizes. Therefore, in most cases it is the arithmetic mean, as demes are equaly sized. One important exception is the Levene model, where the migration rates are given by the deme sizes. But, as the Levene model exhibits a panmictic population, there is no difference of the genetic compositions between demes. Therefore, the genetic variance is deme independent. Furthermore, for the numerical evaluation, we define the variance of a subpopulation to be the weighted arithmetic mean of the genetic variances at the equilibria, weight by the relative size of the basin of attraction.

To complete our model we have to define a fitness function that acts on the genotypic values. We assume quadratic stabilizing selection in every deme.

1.3 Quadratic stabilizing selection

Quadratic stabilizing selection was first introduced by Wright (1935). For quadratic stabilizing selection the fitness function is given by:

$$w_\alpha(G) = 1 - s(O_\alpha - G)^2, \tag{1.21}$$

where O_α denotes the optimum in deme α.

Of course, s has to be small enough, i.e., $s \leq \frac{1}{(\gamma_{1,\alpha}+\gamma_{2,\alpha}+|O_\alpha|)^2}$, so that $w_\alpha(G) \geq 0$ holds for all α, and for all admissible G, i.e., $G \in (-\gamma_{1,\alpha} - \gamma_{2,\alpha}, \gamma_{1,\alpha} + \gamma_{2,\alpha})$. Therefore, our fitness matrix is given by

$$\begin{array}{c} \\ A_1A_1 \\ A_1A_2 \\ A_2A_2 \end{array} \begin{array}{c} \begin{array}{ccc} B_1B_1 & B_1B_2 & B_2B_2 \end{array} \\ \begin{pmatrix} 1 - s\left(\gamma_{1,\alpha} + \gamma_{2,\alpha} + O_\alpha\right)^2 & 1 - s\left(\gamma_{1,\alpha} + O_\alpha\right)^2 & 1 - s\left(\gamma_{1,\alpha} - \gamma_{2,\alpha} + O_\alpha\right)^2 \\ 1 - s\left(\gamma_{2,\alpha} + O_\alpha\right)^2 & 1 - sO_\alpha^2 & 1 - s\left(-\gamma_{2,\alpha} + O_\alpha\right)^2 \\ 1 - s\left(-\gamma_{1,\alpha} + \gamma_{2,\alpha} + O_\alpha\right)^2 & 1 - s\left(-\gamma_{1,\alpha} + O_\alpha\right)^2 & 1 - s\left(-\gamma_{1,\alpha} - \gamma_{2,\alpha} + O_\alpha\right)^2 \end{pmatrix} \end{array} \tag{1.22}$$

Note that Figure 1.1 shows that the value $\gamma_{2,\alpha} = \frac{\gamma_{1,\alpha}}{2}$ is going to be of special interest, as for this value the ordering of the zygotes changes. Furthermore, for $|O_\alpha| \geq \gamma_{1,\alpha}+\gamma_{2,\alpha}$ our model is equivalent to the model of directional selection (Bürger, 2000, p. 214).

Now, we can compute the marginal fitness of the gametes in deme α,

$$\begin{aligned} w_{1,\alpha} = 1 - s[&O_\alpha^2 + (x_{1,\alpha} + x_{2,\alpha})\,\gamma_{1,\alpha}^2 + (x_{1,\alpha} + x_{3,\alpha})\,\gamma_{2,\alpha}^2 \\ &+ 2O_\alpha\gamma_{1,\alpha}\,(x_{1,\alpha} + x_{2,\alpha}) + 2O_\alpha\gamma_{2,\alpha}\,(x_{1,\alpha} + x_{3,\alpha}) \\ &+ 2x_{1,\alpha}\gamma_{1,\alpha}\gamma_{2,\alpha}], \end{aligned} \tag{1.23a}$$

$$\begin{aligned} w_{2,\alpha} = 1 - s[&O_\alpha^2 + (x_{1,\alpha} + x_{2,\alpha})\,\gamma_{1,\alpha}^2 + (x_{2,\alpha} + x_{4,\alpha})\,\gamma_{2,\alpha}^2 \\ &+ 2O_\alpha\gamma_{1,\alpha}\,(x_{1,\alpha} + x_{2,\alpha}) - 2O_\alpha\gamma_{2,\alpha}\,(x_{2,\alpha} + x_{4,\alpha}) \\ &- 2x_{2,\alpha}\gamma_{1,\alpha}\gamma_{2,\alpha}], \end{aligned} \tag{1.23b}$$

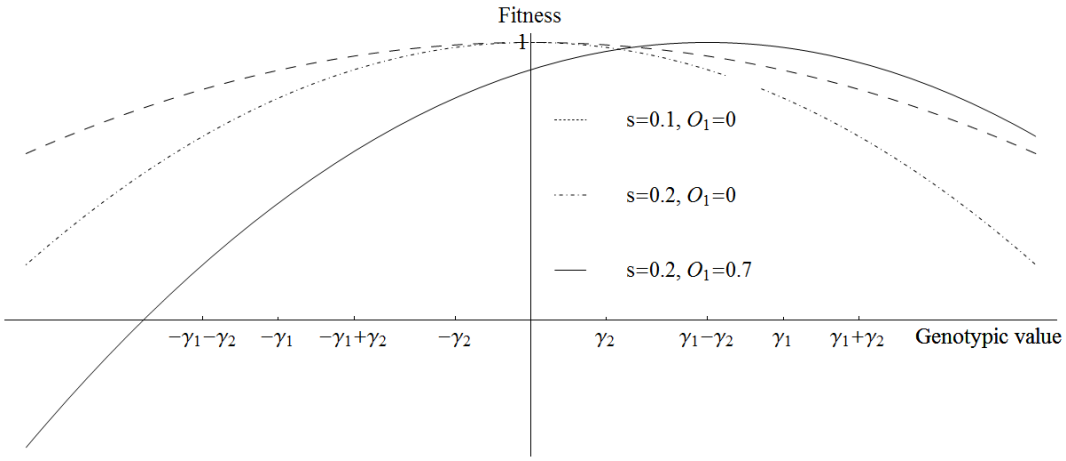


Figure 1.1: Three different fitness functions are plotted against the genotypic values for $\gamma_2 = 0.3$ and $\gamma_1 = 1$. The deme index was dropped for reasons of legibility. It is important to note that the value $\gamma_2 = \frac{\gamma_1}{2}$ is of special interest, as for this value the ordering of the zygotes changes.

$$\begin{aligned} w_{3,\alpha} = 1 - s[&O_\alpha^2 + (x_{1,\alpha} + x_{3,\alpha})\,\gamma_{2,\alpha}^2 + (x_{3,\alpha} + x_{4,\alpha})\,\gamma_{1,\alpha}^2 \\ &+ 2O_\alpha\gamma_{2,\alpha}\,(x_{1,\alpha} + x_{3,\alpha}) - 2O_\alpha\gamma_{1,\alpha}\,(x_{3,\alpha} + x_{4,\alpha}) \\ &- 2x_{3,\alpha}\gamma_{1,\alpha}\gamma_{2,\alpha}], \end{aligned} \tag{1.23c}$$

$$\begin{aligned} w_{4,\alpha} = 1 - s[&O_\alpha^2 + (x_{2,\alpha} + x_{4,\alpha})\,\gamma_{2,\alpha}^2 + (x_{3,\alpha} + x_{4,\alpha})\,\gamma_{1,\alpha}^2 \\ &- 2O_\alpha\gamma_{2,\alpha}\,(x_{2,\alpha} + x_{4,\alpha}) - 2O_\alpha\gamma_{1,\alpha}\,(x_{3,\alpha} + x_{4,\alpha}) \\ &+ 2x_{4,\alpha}\gamma_{1,\alpha}\gamma_{2,\alpha}], \end{aligned} \tag{1.23d}$$

and the mean fitness of the population in deme α,

$$\begin{aligned} \overline{W}_\alpha =1 - s[&O_\alpha^2 + (x_{1,\alpha} + x_{2,\alpha})^2\left(\gamma_{1,\alpha}^2 + 2O_\alpha\gamma_{1,\alpha}\right) + (x_{1,\alpha} + x_{3,\alpha})^2\left(\gamma_{2,\alpha}^2 + 2O_\alpha\gamma_{2,\alpha}\right) \\ &+ (x_{2,\alpha} + x_{4,\alpha})^2\left(\gamma_{2,\alpha}^2 - 2O_\alpha\gamma_{2,\alpha}\right) + (x_{3,\alpha} + x_{4,\alpha})^2\left(\gamma_{1,\alpha}^2 - 2O_\alpha\gamma_{1,\alpha}\right) \\ &- 2\gamma_{1,\alpha}\gamma_{2,\alpha}\left(x_{1,\alpha}^2 - x_{2,\alpha}^2 - x_{3,\alpha}^2 + x_{4,\alpha}^2\right)]. \end{aligned} \tag{1.24}$$

Clearly, the problem of finding fixed points of our system is, that (1.8) exhibits polynomials of third degree. Thus, to find fixed points we have to impose additional assumptions to simplify the system.

Looking at the equations for the marginal and the mean fitness, the first noticeable simplification is to set $O_\alpha = 0$.

Another simplification is to assume linkage equilibrium. Under this assumption, the

allele frequencies are sufficient to calculate the gamete frequencies, as

$$\begin{aligned} x_{1,\alpha} &= x_{1,\alpha} - x_{1,\alpha}x_{4,\alpha} + x_{2,\alpha}x_{3,\alpha} = x_{1,\alpha}\left(1 - x_{4,\alpha}\right) + x_{2,\alpha}x_{3,\alpha} \\ &= x_{1,\alpha}\left(x_{1,\alpha} + x_{2,\alpha} + x_{3,\alpha}\right) + x_{2,\alpha}x_{3,\alpha} = \left(x_{1,\alpha} + x_{2,\alpha}\right)\left(x_{1,\alpha} + x_{3,\alpha}\right) \\ &= p_\alpha^{(1)} p_\alpha^{(2)}, \end{aligned} \tag{1.25}$$

holds. The other gamete frequencies can be calculated analogously.

Furthermore, restrictions to our migration pattern will lead to further simplifications.

2 No Migration

In the case of no migration the model is already well studied, especially for $O = 0$, i.e., if the double heterozygote is the fittest. The following chapter is a collection of the existing results with special attention to the genetic variation maintained in the system. We are therefore especially interested in the questions of whether there exists a stable internal equilibrium and to what extent genetic variance at stable equilibria can be maintained. For simplicity,we drop the deme index in the following sections.

2.1 The symmetric viability model, $O = 0$

If $O = 0$, as we have seen before, the system simplifies a lot. It was studied by Hastings (1987), who analyzed the case of equal allelic effects. Furthermore, Gavrilets and Hastings (1993) and Gavrilets and Hastings (1994) derived all equilibria and studied them extensively. Throughout this section, we follow Bürger (2000, pp. 204). Proofs for the stability conditions of the calculated equilibria may be found in Bürger and Gimmelfarb (1999).

The fitness matrix (1.22) reduces to

$$\begin{array}{c} \\ A_1A_1 \\ A_1A_2 \\ A_2A_2 \end{array} \begin{array}{c} \begin{array}{ccc} B_1B_1 & B_1B_2 & B_2B_2 \end{array} \\ \begin{pmatrix} 1-s\left(\gamma_1+\gamma_2\right)^2 & 1-s\gamma_1^2 & 1-s\left(\gamma_1-\gamma_2\right)^2 \\ 1-s\gamma_2^2 & 1 & 1-s\gamma_2^2 \\ 1-s\left(-\gamma_1+\gamma_2\right)^2 & 1-s\gamma_1^2 & 1-s\left(-\gamma_1-\gamma_2\right)^2 \end{pmatrix} \end{array}. \tag{2.1}$$

Note that the double heterozygote is the fittest. Obviously, one can rewrite this matrix as

$$\begin{array}{c} \\ A_1A_1 \\ A_1A_2 \\ A_2A_2 \end{array} \begin{array}{c} \begin{array}{ccc} B_1B_1 & B_1B_2 & B_2B_2 \end{array} \\ \begin{pmatrix} 1-d & 1-b & 1-a \\ 1-c & 1 & 1-c \\ 1-a & 1-b & 1-d \end{pmatrix} \end{array}, \tag{2.2}$$

where

$$a = s(\gamma_1-\gamma_2)^2,\ b = s\gamma_1^2,\ c = s\gamma_2^2,\ d = s(\gamma_1+\gamma_2)^2. \tag{2.3}$$

This is exactly the symmetric viability model, which is already well understood. For example Bodmer and Felsenstein (1967, pp. 244) and Karlin and Feldman (1970) extensively analyzed this model.

2.1.1 Equilibria

There are up to nine equilibria. Obviously there are the four corner equilibria, which always exist. We denote them by E_1, E_2, E_3 and E_4. The index i denotes fixation of

the ith gamete. Only two of them can be stable, namely

$$E_2 : \hat{x}_2 = 1, \hat{x}_1 = \hat{x}_3 = \hat{x}_4 = 0, \tag{2.4}$$

$$E_3 : \hat{x}_3 = 1, \hat{x}_1 = \hat{x}_2 = \hat{x}_4 = 0, \tag{2.5}$$

which correspond to the fixation of A_1B_2 and A_2B_1.

Next, we derive the edge equilibria. They are denoted by E_5, E_6, E_7 and E_8 and correspond to the fixation of the allele A_1, B_1, A_2 and B_2 respectively. We easily derive, using *Mathematica* (Wolfram, 1994), that only the two edge equilibria with the major locus polymorphic can exist. They are given by

$$E_6 : \hat{x}_2 = \hat{x}_4 = 0, \hat{x}_1 = \frac{1}{2} - \frac{\gamma_2}{\gamma_1}, \hat{x}_3 = \frac{1}{2} + \frac{\gamma_2}{\gamma_1} \text{ and} \tag{2.6}$$

$$E_8 : \hat{x}_1 = \hat{x}_3 = 0, \hat{x}_2 = \frac{1}{2} + \frac{\gamma_2}{\gamma_1}, \hat{x}_4 = \frac{1}{2} - \frac{\gamma_2}{\gamma_1}. \tag{2.7}$$

They are in the simplex, if

$$\gamma_1 > 2\gamma_2 \tag{2.8}$$

holds.

As only the part of the boundary of Δ_4 that is in linkage equilibrium is invariant under the dynamics, there exist no equilibria in the interior of the 2-dimensional boundary simplices.

Finally, according to Bürger (2000, p. 205), there may exist three internal equilibria. The first one, denoted by E_9, is symmetric, i.e.,

$$\hat{x}_1 = \hat{x}_4, \hat{x}_2 = \hat{x}_3, \tag{2.9}$$

and exists always. The two other internal equilibria, E_{10} and E_{11}, are not symmetric and exist if and only if

$$r_1 \leq r \leq r_2, \tag{2.10}$$

where

$$r_1 = \frac{1}{3}s(\gamma_1^2 + \gamma_2^2) + \frac{2}{3}s\sqrt{\gamma_1^4 - \gamma_1^2\gamma_2^2 + \gamma_2^4}, \tag{2.11}$$

$$r_2 = \min\{s(\gamma_1 - \gamma_2)^2, \frac{1}{3}s(\gamma_1^2 - \gamma_2^2)\}. \tag{2.12}$$

The complete formulas for the internal equilibria are quite long, and, as for us it is enough to note their existence, and later their stability conditions, we refer the interested reader to Bürger (2000, p. 205).

2.1.2 Stability

The two monomorphic equilibria E_2 and E_3 are stable, if

$$\gamma_1 \leq 2\gamma_2 \text{ and } r \geq r_2, \tag{2.13}$$

as is easily seen by linearization and calculation of the eigenvalues of the Jacobian at the equilibrium. For stability, the eigenvalues have to be of modulus smaller than one.

The one-locus polymorphic equilibria E_8 and E_6 are stable, if they exist and

$$r \geq \frac{1}{3}s(\gamma_1^2 - \gamma_2^2) \tag{2.14}$$

holds. Again, this is computed using the eigenvalues of the Jacobian at the equilibria. Using (2.8) and (2.12), this reads as

$$\gamma_1 > 2\gamma_2 \text{ and } \ r \geq r_2. \tag{2.15}$$

This means that whenever $r > r_2$ holds, there are precisely two stable equilibria on the boundary of S_4. These are either the two monomorphic equilibria, or those two with one locus polymorphic.

The polymorphic unsymmetric equilibria E_{10} and E_{11} are stable whenever they exist, so whenever (2.10) holds. Finally, the symmetric internal equilibrium E_9, which always exists, is stable if

$$r \leq r_1 \tag{2.16}$$

holds. Let us now investigate these conditions for increasing r.

For $0 < r < r_1$, E_9 is asymptotically stable, the other two internal equilibria do not exist yet. Once r reaches the first critical value r_1, a bifurcation event occurs, i.e., the internal equilibrium splits into three equilibria, loosing its stability to the two new equilibria E_{10} and E_{11}. As r increases, the fully polymorphic unsymmetric equilibria E_{10} and E_{11} move towards the boundary of the simplex. They converge to E_6 and E_8 if they exist, i.e., $\gamma_1 > 2\gamma_2$. Otherwise, they converge to E_3 and E_2. The corner equilibria become stable, as the equilibria leaving the simplex coincide with them.

Note, that in this model, at most two stable equilibria can coexist.

2.2 Arbitrary position of the optimum

Without the assumption of $O = 0$, the system gets quite complicated. Especially, to obtain the position and the stability properties of internal equilibria, we need further assumptions. Hastings and Hom (1990) analyzed the model neglecting linkage disequilibrium and assuming weak selection.

2.2.1 Equilibria on the boundary of Δ_4 and their stability

Again, there exist the four monomorphic equilibria. But now all four of them can be stable, not more than two simultaneously. The stability conditions are as follows:
$E_1 = (1, 0, 0, 0)$:

$$O < -(\gamma_1 + \frac{\gamma_2}{2}), \tag{2.17a}$$

$$rw_{14} > s[(\gamma_1 + \gamma_2)^2 + 2O(\gamma_1 + \gamma_2)], \tag{2.17b}$$

$E_2 = (0, 1, 0, 0)$:

$$\frac{\gamma_2}{2} - \gamma_1 < O < -\frac{\gamma_1}{2} + \gamma_2, \tag{2.18a}$$

$$rw_{14} > s[(\gamma_1 - \gamma_2)^2 + 2O(\gamma_1 - \gamma_2)], \tag{2.18b}$$

$E_3 = (0, 0, 1, 0)$:

$$\frac{\gamma_1}{2} - \gamma_2 < O < \gamma_1 - \frac{\gamma_2}{2}, \tag{2.19a}$$

$$rw_{14} > s[(\gamma_1 - \gamma_2)^2 - 2O(\gamma_1 - \gamma_2)], \tag{2.19b}$$

$E_4 = (0, 0, 0, 1)$:

$$O > \gamma_1 + \frac{\gamma_2}{2}, \tag{2.20a}$$

$$rw_{14} > s[(\gamma_1 + \gamma_2)^2 - 2O(\gamma_1 + \gamma_2)]. \tag{2.20b}$$

Obviously, only E_2 and E_3 can be simultaneously stable if and only if

$$-(\gamma_2 - \frac{\gamma_1}{2}) < O < \gamma_2 - \frac{\gamma_1}{2} \tag{2.21}$$

holds. Note that $w_{14} = 1 - sO^2$ converges to one, if s converges to zero. Hence, if selection is relatively weak compared to recombination, i.e., $s \ll r$, the second stability conditions, i.e., (2.17b), (2.18b), (2.19b), (2.20b) respectively, always hold.

Furthermore, there exist four equilibria with one locus polymorphic and the other monomorphic. They are given by
$E_5 = (\hat{x}_1, \hat{x}_2, 0, 0)$ with

$$\hat{x}_1 = \frac{-2\gamma_1 + \gamma_2 - 2O}{2\gamma_2},\ \hat{x}_2 = 1 - \hat{x}_1, \tag{2.22a}$$

$E_6 = (\hat{x}_1, 0, \hat{x}_3, 0)$ with

$$\hat{x}_1 = \frac{\gamma_1 - 2\gamma_2 - 2O}{2\gamma_1},\ \hat{x}_3 = 1 - \hat{x}_1, \tag{2.22b}$$

$E_7 = (0, 0, \hat{x}_3, \hat{x}_4)$ with

$$\hat{x}_3 = \frac{2\gamma_1 + \gamma_2 - 2O}{2\gamma_2},\ \hat{x}_4 = 1 - \hat{x}_3, \tag{2.22c}$$

and $E_8 = (0, \hat{x}_2, 0, \hat{x}_4)$ with

$$\hat{x}_2 = \frac{\gamma_1 + 2\gamma_2 - 2O}{2\gamma_1},\ \hat{x}_4 = 1 - \hat{x}_2. \tag{2.22d}$$

For their existence one computes the following conditions:
$E_5 \in \Delta_4 \Leftrightarrow$

$$-\gamma_1 - \frac{\gamma_2}{2} < O < -\gamma_1 + \frac{\gamma_2}{2}, \tag{2.23a}$$

$E_6 \in \Delta_4 \Leftrightarrow$

$$-\gamma_2 - \frac{\gamma_1}{2} < O < -\gamma_2 + \frac{\gamma_1}{2}, \tag{2.23b}$$

$E_7 \in \Delta_4 \Leftrightarrow$

$$\gamma_1 - \frac{\gamma_2}{2} < O < \gamma_1 + \frac{\gamma_2}{2}, \tag{2.23c}$$

$E_8 \in \Delta_4 \Leftrightarrow$

$$\gamma_2 - \frac{\gamma_1}{2} < O < \gamma_2 + \frac{\gamma_1}{2}. \tag{2.23d}$$

As one can easily calculate, for every O only two of these equilibria can exist simultaneously. Existence of a stable internal equilibrium will be treated for the case of linkage equilibrium in Section 2.2.3.

2.2.2 The genetic variance at the equilibria on the boundary

Using the equation for the genetic variance (1.18), we easily calculate the genetic variance at the equilibria to be:

$$\sigma^2(E_i) = 0 \text{ for } i = 1, .., 4, \tag{2.24a}$$

$$\sigma^2(E_5) = \frac{\gamma_2^2}{2} - 2(\gamma_1 + O)^2, \tag{2.24b}$$

$$\sigma^2(E_6) = \frac{\gamma_1^2}{2} - 2(\gamma_2 + O)^2, \tag{2.24c}$$

$$\sigma^2(E_7) = \frac{\gamma_2^2}{2} - 2(\gamma_1 - O)^2, \tag{2.24d}$$

$$\sigma^2(E_8) = \frac{\gamma_1^2}{2} - 2(\gamma_2 - O)^2. \tag{2.24e}$$

Note that for the special case of $O = 0$, $\sigma^2(E_5) = \sigma^2(E_7)$ and $\sigma^2(E_6) = \sigma^2(E_8)$ hold. Therefore, whenever there are two stable boundary equilibria, they have the same genetic variance.

Furthermore, note the following: The genetic variance at the equilibria E_5, E_6, E_7 and E_8, attains its maximal value if $O = -\gamma_1$, $-\gamma_2$, γ_1, γ_2 respectively. This is always the center of the region of existence for the corresponding equilibrium. In this case the equilibrium is situated at the center of the edge. The genetic variance decreases symmetrically from its optimum and reaches zero once the equilibrium ceases to exist, i.e., becomes the corner equilibrium.

2.2.3 Linkage equilibrium

In the case of $O \neq 0$, we cannot find the internal equilibria without further assumptions. Assuming linkage equilibrium, as we have noted before, simplifies the model drastically, as we only have to consider allele frequencies, and, therefore reduce the system to two equations. All results of this section have already been deduced by Gavrilets and Hastings (1994).

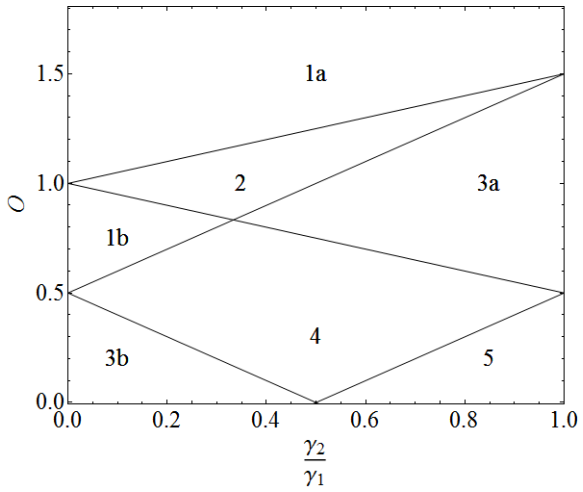


Figure 2.1: Regions of stability of the different equilibria under the assumption of linkage equilibrium. The following abbreviations are used for the regions of stability. 1a,1b: one monomorphic equilibrium (E_4, respectively E_3); 2: one equilibrium with one locus polymorphic (E_7); 3a,3b: two equilibria with one locus polymorphic (E_7, E_8 respectively E_6, E_8); 4: one monomorphic equilibrium and one equilibrium with one locus polymorphic (E_3, E_8); 5: two monomorphic equilibria (E_2, E_3).

As recombination drives the population towards linkage equilibrium and selection drives it away, our assumption is going to be valid if linkage is rather loose, i.e., r is close to $\frac{1}{2}$ and selection is weak, i.e., s is small.

Under the assumption of linkage equilibrium there are nine possible equilibria. We write them in the following form: $(p^{(1)}, p^{(2)})$.

Again, there are the four monomorphic equilibria, which have the same stability conditions as before except the second condition, since it is always fulfilled if $s \ll r$.

Next, there exist the same equilibria on the boundary as before. Their stability conditions coincide with their conditions of existence. We compute the internal equilibrium to be:

$$E_9 = (\frac{3\gamma_1 - 2O}{6\gamma_1}, \frac{3\gamma_2 - 2O}{6\gamma_2}) = (\frac{1}{2} - \frac{O}{3\gamma_1}, \frac{1}{2} - \frac{O}{3\gamma_2}). \tag{2.25}$$

Obviously, its conditions for existence are:

$$-\frac{3}{2}\gamma_2 < O < \frac{3}{2}\gamma_2, \tag{2.26a}$$

$$-\frac{3}{2}\gamma_1 < O < \frac{3}{2}\gamma_1. \tag{2.26b}$$

As we assumed $\gamma_1 \geq \gamma_2$, we only need the condition (2.26a). Linearizing at E_9, we compute the stability condition to be

$$|O| \in \left(\frac{3}{2}\gamma_2, \frac{3}{2}\sqrt{\frac{\gamma_1^2 + \gamma_2^2}{2}}\right). \tag{2.27}$$

Therefore, the internal equilibrium can never be stable.

3 Weak Migration

In this chapter we want to analyze the limiting case of weak migration. To do so, we start with two isolated panmictic populations, i.e., without migration. Then, we deduce the case of weak migration by disturbing the system without migration. The idea is the following: If in each deme there exists an equilibrium on the boundary of the simplex, and we introduce weak migration, the disturbed equilibria move into the simplex, provided the unperturbed are stable. Hence, an internal equilibrium may emerge, even if the unperturbed system had only boundary equilibria.. Under the assumption that all equilibria are hyperbolic, the perturbed equilibria have the same stability properties as the unperturbed. It is important to note that in contrast to the case of weak selection, with weak migration the unstable boundary equilibria may leave the simplex. Under the additional assumption of weak selection, it can be shown (Bürger, 2009, pp. 968), that every trajectory converges to an equilibrium that is close to linkage equilibrium.

As we try to keep the analysis as general as possible, we first only assume that all equilibria are hyperbolic.

3.1 Two isolated demes

If no migration occurs, obviously all combinations of equilibria of the subpopulations exist. In every deme, the dynamics are described by the selection-recombination equation

$$x_{i,\alpha}^{*} = \frac{(x_{i,\alpha}W_{i,\alpha} - \eta_i r W_{14,\alpha} D_\alpha)}{\overline{W}_\alpha}. \tag{3.1}$$

Furthermore, we assume that the only difference between the demes is the position of the fitness optimum. All other parameters, i.e., the selection coefficients, the allelic effects and the recombination rates, are therefore deme independent. We discuss the case of opposite fitness optima, i.e.,

$$O_2 = -O_1 =: -O. \tag{3.2}$$

This parameter combination is of special interest because of the following two reasons. First, it simplifies the model drastically. Second as we have seen before, without migration there exists no stable internal fixed point under the assumption of linkage equilibrium. But, as is well known, migration can lead to a stable polymorphism, if without migration every allele is fixed in at least one deme. Furthermore, as was shown before in (2.23) the parameter regions for fixation of an allele at one locus are symmetric around $O = 0$ in the following sense: If the first allele is fixed for O than

the second allele is fixed for $-O$. Therefore, to reach a stable polymorphism, setting $O_2 = -O_1$ is a promising choice.

The stable equilibria of this model, i.e., without migration, are all the combinations of stable equilibria in the two demes. Therefore, the number of equilibria increases exponentially with respect to the number of subpopulations (Γ). Recall that for one deme in linkage equilibrium there exist nine equilibria as was shown in Section 2.2.3. Hence, if we neglect linkage disequilibrium and assume two demes, there exist 9^2 equilibria. Clearly, we are not going to discuss all of them in detail.

Let us start with all combinations of equilibria that are monomorphic in one subpopulation. For simplicity, we introduce the following notation of the equilibria:

> *E_{kl} denotes the equilibrium of the metapopulation consisting of the equilibria E_k in the first deme and E_l in the second deme.* (3.3)

Note, that for $i, j \leq 4$, E_{ij} represents fixation of gamete i in deme one and fixation of gamete j in the second deme, so for example $E_{23} = (0, 1, 0, 0, 0, 0, 1, 0)^T$. Therefore, under the assumption of opposite optima, the stability conditions are symmetric in the following sense: Assume that for the equilibrium E_{kl} to be stable, O has to fulfill some stability conditions C_i. Then, E_{lk} is stable, if and only if $-O$ fulfilles the stability conditions C_i. Furthermore, we refer to E_{lk} as the reflected equilibrium of E_{kl}.

First, there exist the four monomorphic equilibria E_{11}, E_{22}, E_{33} andE_{44} in Δ_4^2.

Furthermore, there are eight equilibria for which exactly one locus is fixed. For E_{12}, E_{21}, E_{34} and E_{43} the first locus is fixed. For E_{12} and E_{21} at the first locus only the first allele is present, for E_{34} and E_{43} only the second. The four equilibria, for which the second locus is fixed, are E_{13}, E_{31}, E_{24} and E_{42}. Analougusly, for E_{13} and E_{31} the first allele at the second locus is fixed.

Finally, there are four equilibria that are fully polymorphic, namely E_{14}, E_{23}, E_{32} and E_{41}.

Under the assumption (3.2), using (2.17), (2.18), (2.19) and (2.20), one easily deduces that only six of these equilibria can be stable. Their stability conditions are the following:

E_{14}:

$$O < -(\gamma_1 + \frac{\gamma_2}{2}), \tag{3.4a}$$

$$rw_{14} > s((\gamma_1 + \gamma_2)^2 + 2O(\gamma_1 + \gamma_2)), \tag{3.4b}$$

E_{23}:

$$\frac{\gamma_2}{2} - \gamma_1 < O < -\frac{\gamma_1}{2} + \gamma_2, \tag{3.5a}$$

$$rw_{14} > s((\gamma_1 - \gamma_2)^2 + 2O(\gamma_1 - \gamma_2)), \tag{3.5b}$$

E_{32}:

$$\frac{\gamma_1}{2} - \gamma_2 < O < \gamma_1 - \frac{\gamma_2}{2}, \tag{3.6a}$$

$$rw_{14} > s((\gamma_1 - \gamma_2)^2 - 2O(\gamma_1 - \gamma_2)), \tag{3.6b}$$

E_{41}:

$$O > \gamma_1 + \frac{\gamma_2}{2}, \tag{3.7a}$$

$$rw_{14} > s((\gamma_1 + \gamma_2)^2 - 2O(\gamma_1 + \gamma_2)), \tag{3.7b}$$

E_{22}:

$$\frac{\gamma_1}{2} - \gamma_2 < O < -\frac{\gamma_1}{2} + \gamma_2, \tag{3.8a}$$

$$rw_{14} > s((\gamma_1 - \gamma_2)^2 + 2|O|(\gamma_1 - \gamma_2)), \tag{3.8b}$$

E_{33}:

$$\frac{\gamma_1}{2} - \gamma_2 < O < -\frac{\gamma_1}{2} + \gamma_2, \tag{3.9a}$$

$$rw_{14} > s((\gamma_1 - \gamma_2)^2 - 2|O|(\gamma_1 - \gamma_2)). \tag{3.9b}$$

Note, that $w_{14} = 1 - sO^2$ is deme independent for the case of opposite optima, therefore the deme index was dropped. Furthermore, w_{14} converges to 1 as the selection coefficient converges to 0, while the right hand side of the conditions constraining rw_{14} converges to 0. Hence, for weak selection, the second stability condition is always fulfilled. It is important to note, that four of these equilibria can be stable simultaneously. If $\gamma_2 > \frac{\gamma_1}{2}$ holds, the two equilibria E_{23} and E_{32} can coexist. If these two equilibria are stable, E_2 and E_3 have to be stable in every deme. Therefore, also the equilibria E_{22} and E_{33} must be stable. Furthermore, whenever E_{22} is stable, so is E_{33}.

The equilibria that are not monomorphic in every deme will be treated separately in Section 3.2.1.

3.2 Weak migration

To investigate weak migration we set

$$m_{\alpha\beta} = \delta_{\alpha\beta} + \epsilon a_{\alpha\beta}, \tag{3.10}$$

where ϵ measures the strength of migration. As our matrix is stochastic, we have

$$a_{\alpha\beta} \geq 0 \text{ for every } \alpha \neq \beta, \text{ and } \sum_{\beta} a_{\alpha\beta} = 0. \tag{3.11}$$

Therefore, in the case of two demes our migration matrix reads

$$M = \begin{pmatrix} 1 - \epsilon a_1 & \epsilon a_1 \\ \epsilon a_2 & 1 - \epsilon a_2 \end{pmatrix}. \tag{3.12}$$

For weak migration, due to Karlin and McGregor (1972, p. 231), the following important theorem holds:

Theorem 3.2.1. *Suppose that all equilibria of the model without migration, i.e.,*(3.1)*, are hyperbolic, the migration matrix and the recombination rate are fixed, and* $\epsilon > 0$ *is sufficiently small.*

Then, in the neighborhood of each asymptotically stable equilibrium of (3.1)*, there exists exactly one equilibrium point of the perturbed system, i.e.,* (1.13) *with* (3.10)*, and it is asymptotically stable. In the neighborhood of each unstable equilibrium of* (3.1)*, there exists exactly one equilibrium point of* (1.13) *with* (3.10)*, and it is unstable. In the neighborhood of each unstable boundary equilibrium of* (3.1)*, there exists at most one equilibrium point of* (1.13) *with* (3.10)*, and, if it exists, it is unstable.*

The above theorem is a special case of Theorem 4.4 in (Karlin and McGregor, 1972, p. 231). Therefore, its proof applies to our theorem.

Using Theorem 3.2.1, we will now derive the equilibrium structure of our model. We define E^{ϵ}_{kl} as the equilibrium of (1.13) where the migration matrix is given by (3.10), that corresponds to E_{kl}. Let us start with the unstable equilibria. First, there exist the two unstable monomorphic equilibria E^{ϵ}_{11} and E^{ϵ}_{44}. They obviously are not affected by migration, they therefore always exist and are unstable.

Next we discuss E^{ϵ}_{12}. As this equilibrium can never be stable, we have to check whether it leaves the simplex under weak migration. To compute the equilibria of the perturbed system, we assume that the small migration rates ϵa_1 and ϵa_2 introduce a perturbation of the equilibria. We therefore obtain that the perturbed equilibrium E^{ϵ}_{12} must be of the form

$$E^{\epsilon}_{12} = (1 - \epsilon y_1, \epsilon y_1, 0, 0, \epsilon z_1, 1 - \epsilon z_1, 0, 0)^T. \tag{3.13}$$

We can simplify the dynamics, i.e., (1.13) with (3.10), by developing into a Taylor series of first order in ϵ. Doing so, we obtain the simpler system:

$$y_1' = \frac{a_1(1 - (\gamma_1 + \gamma_2 + O)^2 s + (1 - (\gamma_1 + O)^2 s)y_1}{1 - (\gamma_1 + \gamma_2 + O)^2 s}, \tag{3.14a}$$

$$z_1' = \frac{a_2(1 - (-\gamma_1 + \gamma_2 + O)^2 s + (1 - (\gamma_1 - O)^2 s)z_1}{1 - (-\gamma_1 + \gamma_2 + O)^2 s}. \tag{3.14b}$$

The equilibria of this system are easily deduced using *Mathematica* and are given by:

$$\hat{y}_1 = \frac{a_1(1 - (\gamma_1 + \gamma_2 + O)^2 s)}{\gamma_2 s(-2\gamma_1 - \gamma_2 - 2O)}, \tag{3.15a}$$

$$\hat{z}_1 = \frac{a_2(1 - (-\gamma_1 + \gamma_2 + O)^2 s)}{\gamma_2 s(2\gamma_1 - \gamma_2 - 2O)}. \tag{3.15b}$$

As the numerators in (3.15) are products of a_i and a (positive) fitness value, they are always positive. Therefore, as γ_2 and s are always positive, $\hat{y}_1$ and $\hat{z}_1$ are positive, whenever

$$O < -\gamma_1 - \frac{\gamma_2}{2}, \text{ and} \tag{3.16a}$$

$$O < \gamma_1 - \frac{\gamma_2}{2} \tag{3.16b}$$

hold. Obviously, the first condition is sufficient, as it is a more restrictive condition than the second.

As was stated before, we immediately deduce the condition of existence for the unstable equilibrium E^{ϵ}_{21} by inserting $-O$ instead of O in (3.16a). The condition of existence therefore reads

$$O > \gamma_1 + \frac{\gamma_2}{2}. \tag{3.17}$$

In the following, we are not going to write the condition of existence for the reflected equilibria.

Next, we discuss the unstable equilibrium E^{ϵ}_{13}. Using the same ansatz as before, it is given by

$$E^{\epsilon}_{13} = (1 - \epsilon y_1, 0, \epsilon y_1, 0, \epsilon z_1, 0, 1 - \epsilon z_1, 0))^T, \tag{3.18}$$

and, we derive that

$$\hat{y}_1 = \frac{a_1(1 - (\gamma_1 + \gamma_2 + O)^2 s)}{\gamma_1 s(-\gamma_1 - 2\gamma_2 - 2O)}, \text{ and} \tag{3.19a}$$

$$\hat{z}_1 = \frac{a_2(1 - (\gamma_1 - \gamma_2 + O)^2 s)}{\gamma_1 s(-\gamma_1 + 2\gamma_2 - 2O)} \tag{3.19b}$$

must hold at equilibrium. Following the analog argumentation as for (3.15), we deduce the condition of existence:

$$O < -\gamma_2 - \frac{\gamma_1}{2}. \tag{3.20}$$

As is easily calculated, the perturbed unstable equilibrium E^{ϵ}_{24}, given by $(0, 1 - \epsilon y_1, 0, \epsilon y_1, 0, \epsilon z_1, 0, 1 - \epsilon z_1)^T$, exists, if

$$O < -\gamma_2 - \frac{\gamma_1}{2} \tag{3.21}$$

holds, which is fulfilled exactly whenever E^{ϵ}_{13} exists.

Finally, E^{ϵ}_{34} has the same condition of existence as E^{ϵ}_{12}.

Because of Theorem 3.2.1, the only stable equilibria of the perturbed system are the equilibria that had been stable without migration. Obviously, the two stable monomorphic equilibria E_{22} and E_{33} do not change under migration. They therefore always exist and are stable if the conditions (3.8) and (3.9) respectively, hold. Let us now investigate the other four stable equilibria.

As E_{14} consists of A_1B_1 in the first deme and A_2B_2 in the second deme, migration introduces all gametes in all demes. Hence, the perturbed equilibrium is of the form

$$E^{\epsilon}_{14} = (1 - \epsilon(y_1 + y_2 + y_3), \epsilon y_1, \epsilon y_2, \epsilon y_3, \epsilon z_1, \epsilon z_2, \epsilon z_3, 1 - \epsilon(z_1 + z_2 + z_3))^T. \tag{3.22}$$

We now simplify the dynamics by developing into a Taylor series of first order in ϵ. Doing so, we obtain the linearized system

$$y_1' = \frac{((1 - (\gamma_1 + O)^2 s)y_1 + r(1 - O^2 s)y_3}{1 - (\gamma_1 + 2\gamma_2 + O)^2 s}, \tag{3.23a}$$

$$y_2' = \frac{((1 - (\gamma_2 + O)^2 s)y_2 + r(1 - O^2 s)y_3}{1 - (\gamma_1 + 2\gamma_2 + O)^2 s}, \tag{3.23b}$$

$$y_3' = \frac{a_1(1-(\gamma_1+2\gamma_2+O)^2 s)+(1-r)(1-O^2 s)y_3}{1-(\gamma_1+2\gamma_2+O)^2 s}, \tag{3.23c}$$

$$z_1' = \frac{a_2(1-(\gamma_1+2\gamma_2+O)^2 s)+(1-r)(1-O^2 s)z_1}{1-(\gamma_1+2\gamma_2+O)^2 s}, \tag{3.23d}$$

$$z_2' = \frac{((1-(\gamma_2+O)^2 s)z_2+r(1-O^2 s)z_1}{1-(\gamma_1+2\gamma_2+O)^2 s}, \tag{3.23e}$$

$$z_3' = \frac{((1-(\gamma_1+O)^2 s)z_3+r(1-O^2 s)z_1}{1-(\gamma_1+2\gamma_2+O)^2 s}. \tag{3.23f}$$

The equilibria of this system are given by

$$\hat{y}_1 = \frac{a_1 r(1-O^2 s)(1-(\gamma_1+\gamma_2+O)^2 s)}{\gamma_2 s(-2\gamma_1-\gamma_2-2O)[r(1-O^2 s)-s[(\gamma_1+\gamma_2)^2+2O(\gamma_1+\gamma_2)]]}, \tag{3.24a}$$

$$\hat{y}_2 = \frac{a_1 r(1-O^2 s)(1-(\gamma_1+\gamma_2+O)^2 s)}{\gamma_1 s(-2\gamma_2-\gamma_1-2O)[r(1-O^2 s)-s[(\gamma_1+\gamma_2)^2+2O(\gamma_1+\gamma_2)]]}, \tag{3.24b}$$

$$\hat{y}_3 = \frac{a_1(1-(\gamma_1+\gamma_2+O)^2 s)}{r(1-O^2 s)-s[(\gamma_1+\gamma_2)^2+2O(\gamma_1+\gamma_2)]}, \tag{3.24c}$$

$$\hat{z}_1 = \frac{a_2(1-(\gamma_1+\gamma_2+O)^2 s)}{r(1-O^2 s)-s[(\gamma_1+\gamma_2)^2+2O(\gamma_1+\gamma_2)]}, \tag{3.24d}$$

$$\hat{z}_2 = \frac{a_2 r(1-O^2 s)(1-(\gamma_1+\gamma_2+O)^2 s)}{\gamma_1 s(-2\gamma_2-\gamma_1-2O)[r(1-O^2 s)-s[(\gamma_1+\gamma_2)^2+2O(\gamma_1+\gamma_2)]]}, \tag{3.24e}$$

$$\hat{z}_3 = \frac{a_2 r(1-O^2 s)(1-(\gamma_1+\gamma_2+O)^2 s)}{\gamma_2 s(-2\gamma_1-\gamma_2-2O)[r(1-O^2 s)-s[(\gamma_1+\gamma_2)^2+2O(\gamma_1+\gamma_2)]]}. \tag{3.24f}$$

Note, that as for the other equilibria, the numerators in (3.24) are products of positive parameters a_i and fitness values. Hence, they are always positive. Under the condition that E_{14} is stable, i.e., equations (3.4) hold, the denominator is also positive. Hence, all $\hat{y}_i$ and all $\hat{z}_i$ are positive. Therefore, as long as ϵ is small, the perturbed equilibrium E_{14}^{ϵ} exists and is stable. This is consistent with the theory, i.e., that the perturbed stable equilibria never leave the simplex.

Using the same method as before, one computes that for the perturbed equilibrium

$$E_{23}^{\epsilon} = (\epsilon y_1, 1-\epsilon(y_1+y_2+y_3), \epsilon y_2, \epsilon y_3, \epsilon z_1, \epsilon z_2, 1-\epsilon(z_1+z_2+z_3), \epsilon z_3)^T, \tag{3.25}$$

the equilibria of the approximated system are given by

$$\hat{y}_1 = \frac{a_1 r(1-O^2 s)(1-(\gamma_1-\gamma_2+O)^2 s)}{\gamma_2 s(2\gamma_1-\gamma_2+2O)[r(1-O^2 s)-s[(\gamma_1-\gamma_2)^2+2O(\gamma_1-\gamma_2)]]}, \tag{3.26a}$$

$$\hat{y}_2 = \frac{a_1(1-(\gamma_1-\gamma_2+O)^2 s)}{r(1-O^2 s)-s[(\gamma_1-\gamma_2)^2+2O(\gamma_1-\gamma_2)]}, \tag{3.26b}$$

$$\hat{y}_3 = \frac{a_1 r(1-O^2 s)(1-(\gamma_1-\gamma_2+O)^2 s)}{\gamma_1 s(2\gamma_2-\gamma_1-2O)[r(1-O^2 s)-s[(\gamma_1-\gamma_2)^2+2O(\gamma_1-\gamma_2)]]}, \tag{3.26c}$$

$$\hat{z}_1 = \frac{a_2 r(1-O^2 s)(1-(\gamma_1-\gamma_2+O)^2 s)}{\gamma_1 s(2\gamma_2-\gamma_1-2O)[r(1-O^2 s)-s[(\gamma_1-\gamma_2)^2+2O(\gamma_1-\gamma_2)]]}, \tag{3.26d}$$

$$\hat{z}_2 = \frac{a_2(1-(\gamma_1-\gamma_2+O)^2 s)}{r(1-O^2 s)-s[(\gamma_1-\gamma_2)^2+2O(\gamma_1-\gamma_2)]}, \tag{3.26e}$$

$$\hat{z}_3 = \frac{a_2 r(1-O^2 s)(1-(\gamma_1-\gamma_2+O)^2 s)}{\gamma_2 s(2\gamma_1-\gamma_2+2O)[r(1-O^2 s)-s[(\gamma_1-\gamma_2)^2+2O(\gamma_1-\gamma_2)]]}. \tag{3.26f}$$

As for E_{14}^{ϵ}, the equilibrium E_{23}^{ϵ} is in the simplex and stable whenever E_{23} is stable and ϵ is small. As stated before, the equilibria are symmetric. Therefore, the perturbed equilibria E_{32}^{ϵ} and E_{41}^{ϵ} are in the simplex and stable whenever their unperturbed version is stable and ϵ is small.

The genetic variance at equilibrium can be calculated easily using (1.18). As it equals 0 for the monomorphic equilibria of the subpopulations, and, because the genetic variance is positive in the simplex, by increasing ϵ the genetic variance has to increase. To be precise, one calculates the genetic variance to be a polynomial of second degree in ϵ, where the constant term equals zero, the genetic variance of the unperturbed system, while the linear term has positive sign.

Furthermore, using (3.22), (3.25) respectively, we compute that the equilibria are in weak linkage disequilibrium, i.e., $D_\alpha = \mathcal{O}(\epsilon)$. To be precise, for E_{14}^{ϵ} the following holds:

$$\hat{D}_1 = \epsilon\hat{y}_3 + \mathcal{O}(\epsilon^2) \text{ and } \hat{D}_2 = \epsilon\hat{z}_1 + \mathcal{O}(\epsilon^2). \tag{3.27}$$

Similar results hold for the other three equilibria. Since all $\hat{y}_i$ and $\hat{z}_i$ are positive, as was stated above, linkage disequilibrium is positive for E_{14}^{ϵ} and E_{41}^{ϵ} and negative for E_{23}^{ϵ} and E_{32}^{ϵ}. This can be explained as follows. As D_α only equals zero on the boundaries of the simplex and on the Wright manifold, and, because the Wright manifold separates the simplex into two connected regions, D_α has to be positive for one region and negative for the other. We easily observe that E_{14}^{ϵ} and E_{41}^{ϵ} lie in one region, whereas the other two equilibria lie in the other.

Because of the ansatz we used for the equilibria, the equilibrium mean fitnesses in the demes are given by polynomials of second degree in ϵ. The mean fitnesses at the equilibria are easily calculated. As the formulas are very long, we collect the most import characteristics. Again, the constant term is equal to the mean fitness without migration. Furthermore, one calculates that the term that is linear in ϵ is negative whenever the equilibrium is stable. Therefore, for these equilibria weak migration reduces the mean fitness. This is also known as migration load, i.e., the reduction of mean fitness due to maladapted genes carried by migrated individuals.

3.2.1 Weak selection and strong recombination

Under the additional assumption of weak selection a much stronger result holds. We define weak selection by

$$w_{ij,\alpha} = 1 + \epsilon r_{ij,\alpha}, \tag{3.28}$$

where $\epsilon > 0$ is sufficiently small and $|r_{ij,\alpha}| \leq 1$. Note, that this is the same ϵ as in (3.12). Then, due to Bürger (2009, p. 969), the following theorem holds:

Theorem 3.2.2. *Suppose that* (3.28) *holds in addition to the conditions of Theorem 3.2.1. Then in addition to the results of Theorem 3.2.1, the following holds:*

Every solution of (1.13) *converges to the quasi-linkage equilibrium manifold Λ_ϵ, on which linkage disequilibria are of order ϵ.*

For arbitrary position of the fitness optima only nine different equilibria can exist in each subpopulation, as was shown in Section 2.2.3. Therefore, a total of 81 different equilibria exist. Furthermore, the stability conditions simplify. In the following we restrict our analysis to the stable equilibria that are fully polymorphic.

Besides the four stable fully polymorphic equilibria that we found in the general case, there are eight more, which are stable fully polymorphic equilibria; namely E^ϵ_{57}, E^ϵ_{58}, E^ϵ_{67}, E^ϵ_{68} and their reflected ones. Their stability conditions are the following:
For E^ϵ_{57}:

$$-\gamma_1 - \frac{\gamma_2}{2} < O < -\gamma_1 + \frac{\gamma_2}{2}, \tag{3.29}$$

and for E^ϵ_{68}:

$$-\gamma_2 - \frac{\gamma_1}{2} < O < -\gamma_2 + \frac{\gamma_1}{2}. \tag{3.30}$$

The two equilibria E^ϵ_{58} and E^ϵ_{67} have the same condition of existence:

$$-\gamma_2 - \frac{\gamma_1}{2} < O < -\gamma_1 + \frac{\gamma_2}{2}. \tag{3.31}$$

Therefore, they always exist simultaneously. Furthermore, it is important to note, that whenever condition (3.31) is fulfilled, so are (3.29) and(3.30). Hence, when (3.31) holds, four stable and fully polymorphic equilibria exist simultaneously. It is important to note that for the left hand side of (3.31) to be smaller than the right hand side, $\gamma_2 > \frac{\gamma_1}{3}$ has to hold.

These four simultaneously existing stable internal equilibria have also been verified numerically, but no full numerical analysis was done. Our data showed that even for $\epsilon a_1 = \epsilon a_2 = 0.005$ the gamete frequencies at the equilibria exceed 10^{-1}.

4 Weak Selection

In a multilocus system, in which recombination is the only evolutionary force, it can be shown (Bürger, 2000, pp. 57) that linkage disequilibria decay to zero at a geometric rate. Following Bürger (2009) we extend this result to the case including migration. Furthermore, we show that without selection spatial homogeneity is quickly approached.

Next, we work out the weak-selection limit explicitly. We state the result of Bürger (2009, p. 958), showing that weak selection is a perturbation of the weak-selection limit. The perturbed version has the same stability conditions, all equilibria are in quasi linkage equilibrium and, furthermore, for the limit case, the mean fitness is a Lyapunov function, hence all trajectories converge to an equilibrium point. We then apply these results to our model. It is shown that no stable polymorphic equilibrium can exist, a fact that without migration is already known, cf. Section 2.2.3. For strong migration the population rapidly reaches spatial homogeneity. Therefore, the model is equivalent to a panmictic population with a properly averaged fitness function.

4.1 Absence of selection

We shall use the following notation:

$$e = (1, ..., 1)^T \in \mathbb{R}^\Gamma, \tag{4.1a}$$

$$p^{(n)} = (p_1^{(n)}, ..., p_\Gamma^{(n)})^T \in \mathbb{R}^\Gamma, \tag{4.1b}$$

$$p_{(\alpha)} = (p_\alpha^{(1)}, p_\alpha^{(2)})^T \in \mathbb{R}^2, \tag{4.1c}$$

$$p = (p_1^T, ..., p_\Gamma^T) \in \mathbb{R}^{2\Gamma}, \tag{4.1d}$$

where $n \in \{1, 2\}$, and $\alpha \in G$. Remember the notation: $p_\alpha^{(n)} = p_{1,\alpha}^{(n)}$, which is sufficient information as $p_{2,\alpha}^{(n)} = 1 - p_{1,\alpha}^{(n)}$ holds.

We average the allele frequencies and the gamete frequencies with respect to μ, the positive left eigenvector of M corresponding to the eigenvalue $\lambda = 1$.

$$P_n = \mu^T p^{(n)}, \quad P = (P_1, P_2)^T \in \mathbb{R}^2, \tag{4.2a}$$

$$X_i = \mu^T x_i, \quad X = (X_1, X_2, X_3, X_4)^T \in \mathbb{R}^4. \tag{4.2b}$$

Next, we define the allele frequency and the gamete frequency deviations, q and y, from the averaged frequencies P and X

$$q_\alpha^{(n)} = p_\alpha^{(n)} - P_n, \tag{4.3a}$$

$$q^{(n)} = p^{(n)} - P_n e \in \mathbb{R}^{\Gamma}, \tag{4.3b}$$
$$q = (q^{(1)}, q^{(2)})^T \in \mathbb{R}^{2\Gamma}, \tag{4.3c}$$
$$y_{i,\alpha} = x_{i,\alpha} - X_i, \tag{4.3d}$$
$$y_i = x_i - X_i e \in \mathbb{R}^{\Gamma}, \tag{4.3e}$$
$$y = (y_1, y_2, y_3, y_4) \in \mathbb{R}^{4\Gamma}, \tag{4.3f}$$

where $n \in \{1, 2\}$, $\alpha \in G$ and $i \in I$, the set of gametes. Therefore, q and y measure spatial heterogeneity or diversity. If $q = 0$ ($y = 0$), the allelic (gametic) distribution is spatially homogeneous.

The assumption of no selection, i.e., $w_{ij,\alpha} = 1$, simplifies the dynamics of (1.13) to

$$x'_{i,\alpha} = \sum_{\beta} m_{\alpha\beta}(x_{i,\beta} - D_{i,\beta}(x)), \tag{4.4a}$$

with

$$D_{i,\alpha}(x) = \eta_i r(x_{1,\alpha}x_{4,\alpha} - x_{2,\alpha}x_{3,\alpha}). \tag{4.4b}$$

If we use vector notation, (4.4) reads as

$$x_i{}' = M(x_i - D_i(x)), \tag{4.5a}$$

with

$$D_i(x) = (D_{i,1}(x), ..., D_{i,\Gamma}(x)). \tag{4.5b}$$

For the allele frequencies, (4.5) reduces to

$$p_{i,\alpha}^{(n)\prime} = M(p_{i,\alpha}^{(n)}), \tag{4.6}$$

since the allele frequencies are invariant under recombination. Therefore, using (1.12) the dynamics of the averaged allele frequencies are

$$P_n{}' = \mu^T p^{(n)\prime} = \mu^T M p^{(n)} = \mu^T p^{(n)} = P_n. \tag{4.7}$$

Hence, the averaged allele frequencies are invariant under the dynamics, i.e., constant in time, and we can write

$$P_n(t) = P_n(0). \tag{4.8}$$

Using (4.6) and (4.8) we get

$$q^{(n)}(t) = p^{(n)}(t) - P_n(0)e = M^t p^{(n)}(0) - e\mu^T p^{(n)}(0). \tag{4.9}$$

As is stated in (Bürger, 2009, pp. 946) the following theorem holds

Theorem 4.1.1. *Let M be ergodic, with the largest non unit eigenvalue λ_1. Then for every κ with*

$$|\lambda_1| < \kappa < 1, \tag{4.10}$$

there exists a c_z independent of t such that

$$\left\| M^t z - e\mu^T z \right\| \leq c_z \kappa^t, \tag{4.11}$$

holds.

From Theorem 4.1.1 we obtain

$$\left\|q^{(n)}(t)\right\| \leq c_n \kappa^t, \tag{4.12}$$

for every κ and every n, where c_n are appropriate constants. Therefore the allele frequencies $p_\alpha^{(n)}$ converge geometrically at least as fast as κ^t to the constant averaged allele frequencies P_n.

The following theorem is known from Bürger (2009, pp. 949)

Theorem 4.1.2. *Suppose that* (4.5) *holds and M is ergodic. Then, the manifold*

$$\Psi_0 = \left\{x \in \Delta_I^\Gamma : D(x) = 0 \text{ and } q = 0\right\} \tag{4.13}$$

is invariant under (4.5) *and globally attracting at a geometric rate. Furthermore every point of Ψ_0 is an equilibrium point. Thus, linkage equilibrium and spatial homogeneity are quickly approached under recombination and (ergodic) migration.*

The proof is found in Bürger (2009) for the much more general case of multiple multiallelic loci. Hence, without migration, all trajectories converge at a geometric rate to the manifold Ψ_0, on which global linkage equilibrium holds and alleles are identical across demes.

4.2 Weak Selection

We want to investigate the case of strong migration, strong recombination and weak selection. We therefore set

$$w_{ij,\alpha} = 1 + \epsilon r_{ij,\alpha}, \tag{4.14}$$

where $\epsilon > 0$ is sufficiently small and $|r_{ij,\alpha}| \leq 1$. We assume fixed migration rates and a fixed recombination rate, so that fitness differences are small compared to them. From (4.14) it follows that:

$$w_{i,\alpha}(x_{(\alpha)}) = 1 + \epsilon r_{i,\alpha}(x_{(\alpha)}), \quad \overline{w}_\alpha(x_{(\alpha)}) = 1 + \epsilon \overline{r}_\alpha(x_{(\alpha)}), \tag{4.15}$$

with

$$r_{i,\alpha}(x_{(\alpha)}) = \sum_j r_{ij,\alpha} x_{j,\alpha}, \quad \overline{r}_\alpha(x_{(\alpha)}) = \sum_{i,j} r_{ij,\alpha} x_{i,\alpha} x_{j,\alpha}, \tag{4.16}$$

the fitness deviation of the gamete i and of the subpopulation in deme α.

On the linkage equilibrium manifold $\Lambda_{0,\alpha}$, they can be rewritten as

$$r_{i,\alpha}(x(p_{(\alpha)})) = \sum_j r_{ij,\alpha} \prod_k p_{j_k,\alpha}^{(k)}, \tag{4.17a}$$

$$r_{i_n,\alpha}^{(n)}(x(p_{(\alpha)})) = \sum_{i|i_n} r_{i,\alpha}(x(p_{(\alpha)})) \prod_{k:k\neq n} p_{i_k,\alpha}^{(k)}, \tag{4.17b}$$

$$\overline{r}_\alpha(x(p_{(\alpha)})) = \sum_i r_{i,\alpha}(x(p_{(\alpha)})) \prod_k p_{i_k,\alpha}^{(k)}, \tag{4.17c}$$

with

$$x(p_{(\alpha)}) = \left(p_{1,\alpha}^{(1)} p_{1,\alpha}^{(2,)}, p_{1,\alpha}^{(1)} p_{2,\alpha}^{(2)}, p_{2,\alpha}^{(1)} p_{1,\alpha}^{(2)}, p_{2,\alpha}^{(1)} p_{2,\alpha}^{(2)}\right)^T \tag{4.18}$$

being the function mapping the allele frequencies to the gamete frequencies. In the following, we write $f(p_{(\alpha)})$ as an abbreviation of $f(x(p_{(\alpha)}))$. To understand the subscript of $p_{j_k,\alpha}^{(k)}$, note that when we defined $x_{i,\alpha}$, the i actually was a multi-index. So $i = (i_1, i_2)$ denotes the gamete $A_{i_1}B_{i_2}$. In $\sum_{i|i_n}$, the sum runs over all multi-indices i with the nth component fixed as i_n. Next, we average the fitness deviations of genotype ij, gamete i, allele i_n at locus n, and of the entire population with respect to μ:

$$w_{ij} = \sum_\alpha \mu_\alpha r_{ij,\alpha}, \tag{4.19a}$$

$$w_i(P) = \sum_j w_{ij} \prod_k P_{j_k}^{(k)} = \sum_\alpha \mu_\alpha r_{i,\alpha}(x(P)), \tag{4.19b}$$

$$w_{i_n}^{(n)}(P) = \sum_{i|i_n} w_i(P) \prod_{k\neq n} P_{i_k}^{(k)} = \sum_\alpha \mu_\alpha r_{i_n,\alpha}^{(n)}(x(P)), \tag{4.19c}$$

$$\overline{w}(P) = \sum_i w_i(P) \prod_k P_{i_k}^{(k)} = \sum_\alpha \mu_\alpha \overline{r}_\alpha(x(P)). \tag{4.19d}$$

Note that with selection, the averaged allele frequencies are not constant in time any more, as it is the case without selection where (4.8) holds. Instead of x, we use P, q and D to analyze (1.13). For $\overline{w}(P)$, we obtain the alternative representations:

$$\overline{w}(P) = \sum_n \sum_{i_n} w_{i_n}^{(n)}(P) P_{i_n}^{(n)} \tag{4.19e}$$

$$= \sum_{i,j} w_{ij} \left(\prod_n P_{i_n}^{(n)}\right)\left(\prod_k P_{j_k}^{(k)}\right). \tag{4.19f}$$

Furthermore, for the mean fitness the following holds:

$$\frac{d\overline{w}(P)}{dP_{i_n}^{(n)}} = 2w_{i_n}^{(n)}(P). \tag{4.20}$$

As will be justified by the following theorem, we call the system of differential equations

$$\frac{dP_n}{dt} = P_n\left[w_1^{(n)}(P) - \overline{w}(P)\right], \tag{4.21a}$$

$$D = 0, \quad q = 0, \tag{4.21b}$$

the *weak-selection limit* of (1.13). Because of

$$\frac{d\overline{w}}{dt} = 2\sum_n \sum_{i_n} P_{i_n}^{(n)}\left[w_{i_n}^{(n)} - \overline{w}(P)\right]^2 \geq 0, \tag{4.22}$$

for weak selection, mean fitness is nondecreasing along solutions of (4.21), i.e., the mean fitness is a Lyapunov function. To be precise, it is only constant for equilibria of

(4.21), i.e., it is a strict Lyapunov function. Hence, all trajectories converge, therefore no complicated dynamics, such as cycling, can occur. The following theorem is known from Bürger (2009, p. 958), the proof may also be found there.

Theorem 4.2.1. *Suppose that* (1.13) *and* (4.14) *hold, M is ergodic, all equilibria of* (4.21) *are hyperbolic, the migration matrix and the recombination rate are fixed, and $\epsilon > 0$ is sufficiently small.*

1. *The set of equilibria $\Xi_0 \subset \Delta_I^\Gamma$ of* (4.21) *contains only isolated points, as does the set of equilibria $\Xi_\epsilon \subset \Delta_I^\Gamma$. As $\epsilon \to 0$, each equilibrium in Ξ_ϵ converges to the corresponding equilibrium in Ξ_0 .*

2. *In the neighborhood of each equilibrium in Ξ_0, there exists exactly one equilibrium point in Ξ_ϵ. The stability of each equilibrium in Ξ_ϵ is the same as that of the corresponding equilibrium in Ξ_0; i.e., each pair is either asymptotically stable or unstable.*

3. *Every solution $p(t)$ of* (1.13) *converges to one of the equilibrium points in Ξ_ϵ.*

For two loci and two alleles we obtain:

$$\begin{aligned} w_1^{(1)}(P) =& P_1[P_2^2 w_{11} + 2P_2(1-P_2)w_{12} + (1-P_2)^2 w_{22}] \\ &+ (1-P_1)[P_2^2 w_{13} + 2P_2(1-P_2)w_{14} + (1-P_2)^2 w_{24}], \end{aligned} \tag{4.23a}$$

$$\begin{aligned} w_2^{(1)}(P) =& P_1[P_2^2 w_{13} + 2P_2(1-P_2)w_{14} + (1-P_2)^2 w_{24}] \\ &+ (1-P_1)[P_2^2 w_{33} + 2P_2(1-P_2)w_{34} + (1-P_2)^2 w_{44}], \end{aligned} \tag{4.23b}$$

$$\begin{aligned} w_1^{(2)}(P) =& P_2[P_1^2 w_{11} + 2P_1(1-P_1)w_{13} + (1-P_1)^2 w_{33}] \\ &+ (1-P_2)[P_1^2 w_{12} + 2P_1(1-P_1)w_{14} + (1-P_1)^2 w_{34}], \end{aligned} \tag{4.23c}$$

$$\begin{aligned} w_2^{(2)}(P) =& P_2[P_1^2 w_{21} + 2P_1(1-P_1)w_{14} + (1-P_1)^2 w_{43}] \\ &+ (1-P_2)[P_1^2 w_{22} + 2P_1(1-P_1)w_{24} + (1-P_1)^2 w_{44}], \end{aligned} \tag{4.23d}$$

and

$$\overline{w}(P) = P_1 w_1^{(1)} + (1-P_1) w_2^{(1)} \tag{4.24a}$$

$$\begin{aligned} =& P_1^2[P_2^2 w_{11} + 2P_2(1-P_2)w_{12} + (1-P_2)^2 w_{22}] \\ &+ 2P_1(1-P_1)[P_2^2 w_{13} + 2P_2(1-P_2)w_{14} + (1-P_2)^2 w_{24}] \\ &+ (1-P_1)^2[P_2^2 w_{33} + 2P_2(1-P_2)w_{34} + (1-P_2)^2 w_{44}] \end{aligned} \tag{4.24b}$$

$$= P_2 w_1^{(2)} + (1-P_2) w_2^{(2)} \tag{4.24c}$$

Therefore we obtain:

$$\begin{aligned} w_1^{(n)}(P) - \overline{w}(P) &= w_1^{(n)}(P) - \left(P_n w_1^{(n)} + (1-P_n) w_2^{(n)}\right) \\ &= (1-P_n)\left(w_1^{(n)}(P) - w_2^{(n)}(P)\right), \end{aligned} \tag{4.25}$$

hence (4.21) becomes

$$\frac{dP_n}{dt} = P_n\,(1-P_n)\left[w_1^{(n)}(P) - w_2^{(n)}(P)\right], \tag{4.26a}$$

$$D = 0, \quad q = 0. \tag{4.26b}$$

4.3 Application to our model

4.3.1 Two demes

First, for the migration matrix

$$M = \begin{pmatrix} 1-u & u \\ v & 1-v \end{pmatrix}, \tag{4.27}$$

we get the left leading eigenvector corresponding to the eigenvalue $\lambda = 1$

$$\mu = (\frac{v}{u+v}, \frac{u}{u+v})^T. \tag{4.28}$$

Furthermore, note that for small s the fitness of quadratic stabilizing selection already has the form of (4.14), if we denote the selection coefficient as ϵ. Plugging the fitness values given by 1.22 into (4.26) we obtain:

$$\begin{aligned}\frac{dP_1}{dt} = \frac{P_1\,(1-P_1)}{u+v}[&\gamma_{1,2}u(\gamma_{1,2}(1-2P_1) + 2\gamma_{2,2}(1-2P_2) - 2O_2) \\ &+ \gamma_{1,1}v(\gamma_{1,1}(1-2P_1) + 2\gamma_{2,1}(1-2P_2) - 2O_1)],\end{aligned} \tag{4.29a}$$

$$\begin{aligned}\frac{dP_2}{dt} = \frac{P_2\,(1-P_2)}{u+v}[&\gamma_{2,2}u(\gamma_{2,2}(1-2P_2) + 2\gamma_{1,2}(1-2P_1) - 2O_2) \\ &+ \gamma_{2,1}v(\gamma_{2,1}(1-2P_2) + 2\gamma_{1,1}(1-2P_1) - 2O_1)].\end{aligned} \tag{4.29b}$$

We can simplify (4.29) by introducing the following parameters:

$$\widetilde{\sigma}_1 := \frac{\gamma_{1,2}^2 u + \gamma_{1,1}^2 v}{u+v}, \tag{4.30a}$$

$$\widetilde{\sigma}_2 := \frac{\gamma_{2,2}^2 u + \gamma_{2,1}^2 v}{u+v}, \tag{4.30b}$$

$$\widetilde{\sigma} := \frac{2\gamma_{1,2}\gamma_{2,2}u + 2\gamma_{1,1}\gamma_{2,1}v}{u+v}, \tag{4.30c}$$

$$\widetilde{\kappa}_1 := \frac{2\gamma_{1,2}O_2 u + 2\gamma_{1,1}O_1 v}{u+v}, \tag{4.30d}$$

$$\widetilde{\kappa}_2 := \frac{2\gamma_{2,2}O_2 u + 2\gamma_{2,1}O_1 v}{u+v}. \tag{4.30e}$$

Note that $\widetilde{\sigma}_i$ and $\widetilde{\sigma}$ are always positive, while $\widetilde{\kappa}_1$ and $\widetilde{\kappa}_2$ can be negative and even have different signs. Because $\gamma_{2,\alpha} \leq \gamma_{1,\alpha}$ the following inequalities,

$$\widetilde{\sigma}_1 \geq \widetilde{\sigma}_2 \geq 0, \tag{4.31a}$$

$$\widetilde{\sigma} > \widetilde{\sigma}_2, \tag{4.31b}$$

always hold. Then the weak-selection limit (4.29) can be written as:

$$\frac{dP_1}{dt} = P_1(1-P_1)[\widetilde{\sigma}_1(1-2P_1) + \widetilde{\sigma}(1-2P_2) - \widetilde{\kappa}_1], \tag{4.32a}$$

$$\frac{dP_2}{dt} = P_2(1-P_2)[\widetilde{\sigma}_2(1-2P_2) + \widetilde{\sigma}(1-2P_1) - \widetilde{\kappa}_2]. \tag{4.32b}$$

Next, as $\widetilde{\sigma}$ is always positive, we can divide (4.32) by $\widetilde{\sigma}$ without changing the dynamics. The new parameters are written without the tilde, e.g., $\sigma_1 = \frac{\widetilde{\sigma}_1}{\widetilde{\sigma}}$. Therefore, the weak-selection limit reduces to

$$\frac{dP_1}{dt} = P_1(1-P_1)[\sigma_1(1-2P_1) + (1-2P_2) - \kappa_1], \tag{4.33a}$$

$$\frac{dP_2}{dt} = P_2(1-P_2)[\sigma_2(1-2P_2) + (1-2P_1) - \kappa_2], \tag{4.33b}$$

which is now only dependent on four parameters. The inequalities in (4.31) change to

$$\sigma_1 \geq \sigma_2 \geq 0, \tag{4.34a}$$

$$1 > \sigma_2. \tag{4.34b}$$

Obviously, there exist the four monomorphic equilibria

$$E_1 = (1,1), \tag{4.35a}$$

$$E_2 = (1,0), \tag{4.35b}$$

$$E_3 = (0,1), \tag{4.35c}$$

$$E_4 = (0,0). \tag{4.35d}$$

Next, there are four equilibria with one locus polymorphic and the other one fixed
$E_5 = (1, \hat{p}_2)$, with

$$\hat{p}_2 = \frac{1}{2} - \frac{\kappa_2 + 1}{2\sigma_2}, \tag{4.36a}$$

$E_6 = (\hat{p}_1, 1)$, with

$$\hat{p}_1 = \frac{1}{2} - \frac{\kappa_1 + 1}{2\sigma_1}, \tag{4.36b}$$

$E_7 = (0, \hat{p}_2)$, with

$$\hat{p}_2 = \frac{1}{2} - \frac{\kappa_2 - 1}{2\sigma_2}, \tag{4.36c}$$

$E_8 = (\hat{p}_1, 0)$, with

$$\hat{p}_1 = \frac{1}{2} - \frac{\kappa_1 - 1}{2\sigma_1}, \tag{4.36d}$$

and we also obtain one internal equilibrium
$E_9 = (\hat{p}_1, \hat{p}_2)$, with

$$\hat{p}_1 = \frac{1}{2} - \frac{\kappa_2 - \kappa_1\sigma_2}{2(1 - \sigma_1\sigma_2)}, \tag{4.37a}$$

$$\hat{p}_2 = \frac{1}{2} - \frac{\kappa_1 - \kappa_2\sigma_1}{2(1 - \sigma_1\sigma_2)}. \tag{4.37b}$$

For the existence, i.e., allele frequencies between zero and one, we obtain the following conditions:
For E_5

$$\sigma_2 - 1 \geq \kappa_2 \geq -\sigma_2 - 1, \tag{4.38a}$$

for E_6

$$\sigma_1 - 1 \geq \kappa_1 \geq -\sigma_1 - 1, \tag{4.38b}$$

for E_7

$$\sigma_2 + 1 \geq \kappa_2 \geq -\sigma_2 + 1, \tag{4.38c}$$

and for E_8

$$\sigma_1 + 1 \geq \kappa_1 \geq -\sigma_1 + 1. \tag{4.38d}$$

E_9 exists if

$$|\kappa_1\sigma_2 - \kappa_2| \leq |1 - \sigma_1\sigma_2| \text{ and } |\kappa_2\sigma_1 - \kappa_1| \leq |1 - \sigma_1\sigma_2| \tag{4.38e}$$

holds. For the stability conditions we linearize the system of differential equations and check the sign of the determinant and the trace of the Jacobian. The equilibria are stable, if the following conditions hold:
For E_1

$$\kappa_1 < -1 - \sigma_1 \text{ and } \kappa_2 < -1 - \sigma_2, \tag{4.39a}$$

for E_2

$$\kappa_1 < 1 - \sigma_1 \text{ and } \kappa_2 > \sigma_2 - 1, \tag{4.39b}$$

for E_3

$$\kappa_1 > \sigma_1 - 1 \text{ and } \kappa_2 < 1 - \sigma_2, \tag{4.39c}$$

for E_4

$$\kappa_1 > 1 + \sigma_1, \text{and } \kappa_2 > 1 + \sigma_2. \tag{4.39d}$$

For the equilibria with one locus polymorphic, we compute the stability conditions to be:
For E_5

$$\kappa_1 < 1 - \sigma_1 \text{ and } -1 + \kappa_1\sigma_2 + \sigma_1\sigma_2 < \kappa_2, \tag{4.40a}$$

for E_6

$$\kappa_2 < 1 - \sigma_2 \text{ and } -1 + \kappa_2\sigma_1 + \sigma_1\sigma_2 < \kappa_1, \tag{4.40b}$$

for E_7

$$-1 + \sigma_1 < \kappa_1 \text{ and } \kappa_2 < 1 + \kappa_1\sigma_2 - \sigma_1\sigma_2, \tag{4.40c}$$

and for E_8

$$-1+\sigma_2<\kappa_2 \text{ and } \kappa_1<1+\kappa_2\sigma_1-\sigma_1\sigma_2. \tag{4.40d}$$

Note, that the second condition can be stronger than the condition of existence. This is the case if $-1-\sigma_1<\kappa_1$, $-1-\sigma_2<\kappa_2$, $\kappa_1<1+\sigma_1$ or $\kappa_2<1+\sigma_2$ holds for E_5, E_6, E_7 and E_8 respectively.

Let us check whether the internal equilibrium E_9 can be stable. To do this, note that the conditions for existence can be rewritten into:

$$\kappa_1\in(\kappa_2\sigma_1+1-\sigma_1\sigma_2;\kappa_2\sigma_1-1+\sigma_1\sigma_2)\,, \tag{4.41a}$$

$$\kappa_1\in\left(\frac{\kappa_2+1-\sigma_1\sigma_2}{\sigma_2};\frac{\kappa_2-1+\sigma_1\sigma_2}{\sigma_2}\right). \tag{4.41b}$$

In general, this notation is not correct as $-1+\sigma_1\sigma_2>0$ does not have to hold. Hence, the endpoints of the intervals could be interchanged. But as we will see, this is the only case where stability of the internal equilibrium could be reached. For stability of the equilibrium Det >0 has to hold for the Jacobian. The determinant is a polynomial of fourth degree in κ_1, which has its four zeros exactly at the endpoints of the intervals of existence. Furthermore, it has the sign of $(\sigma_1\sigma_2-1)$. Obviously, if the intersection of two real intervals is non empty, it has to be the interval between the two endpoints that lie in between the other two endpoints. Therefore, whenever the internal equilibrium exists, κ_1 has to be between the two zeros of the determinant that lie between the other two zeros. Therefore, for the determinant two be positive when the equilibrium exists, the sign of the leading term has to be positive. Hence, $\sigma_1\sigma_2>1$ is a necessary condition for the existence of a stable polymorphism. Plugging (4.30) into this condition we get:

$$(\gamma_{1,2}^2u+\gamma_{1,1}^2v)(\gamma_{2,2}^2u+\gamma_{2,1}^2v)>2(\gamma_{1,2}\gamma_{2,2}u+\gamma_{1,1}\gamma_{2,1}v). \tag{4.42}$$

But as all parameters are positive and less or equal to one, this condition can never be fulfilled. Hence, whenever the internal equilibrium exists it is unstable.

Obviously, the conditions for the existence and stability of the equilibria on the boundary need further explanations. Especially we would want to rewrite them into conditions for the unweighted parameters, i.e., the allelic effects, the migration rates and the fitness optima. Without further assumptions this does not provide simple conditions. Let us therefore investigate a special case.

4.3.2 Deme-independent allelic effects

If we assume that the allelic effects are deme independent, the only deme dependent parameter left is the position of the fitness optima. The weighted parameters (4.30) therefore simplify to:

$$\widetilde{\sigma}_1=\gamma_1^2, \tag{4.43a}$$

$$\widetilde{\sigma}_2=\gamma_2^2, \tag{4.43b}$$

$$\widetilde{\sigma}=2\gamma_1\gamma_2, \tag{4.43c}$$

$$\widetilde{\kappa}_1 = 2\gamma_1 \frac{O_2 u + O_1 v}{u+v}, \tag{4.43d}$$

$$\widetilde{\kappa}_2 = 2\gamma_2 \frac{O_2 u + O_1 v}{u+v}. \tag{4.43e}$$

Hence, we get the new parameters

$$\sigma_1 = \frac{\gamma_1}{2\gamma_2}, \tag{4.44a}$$

$$\sigma_2 = \frac{\gamma_2}{2\gamma_1}, \tag{4.44b}$$

$$\kappa_1 = \frac{1}{\gamma_2} \frac{O_2 u + O_1 v}{u+v}, \tag{4.44c}$$

$$\kappa_2 = \frac{1}{\gamma_1} \frac{O_2 u + O_1 v}{u+v}. \tag{4.44d}$$

Introducing the new parameter $\bar{O} = \frac{O_2 u + O_1 v}{u+v}$ and plugging all this into the conditions of existence (4.38), they reduce to exactly the conditions of existence for the case of no migration, where O is replaced by $\bar{O}$. The monomorphic equilibria also have the same stability conditions, i.e., equations (2.17a), (2.18a), (2.19a), (2.20a) respectively. Recall, that the second condition of stability for the monomorphic equilibria without migration, i.e., (2.17b), (2.18b), (2.19b), (2.20b) respectively, is always fulfilled for weak selection. If the equilibria on the boundary exist, the first stability condition is always fulfilled. The second stability condition is fulfilled for the equilibria E_5 and E_7 if they exist. For E_6 and E_8 the stability condition is more restricting than the condition for existence. Combining them they read as: For E_6

$$-\frac{3}{2}\gamma_2 < \bar{O} < -\gamma_2 + \frac{\gamma_1}{2}, \tag{4.45a}$$

and for E_8

$$\gamma_2 - \frac{\gamma_1}{2} < \bar{O} < \frac{3}{2}\gamma_2. \tag{4.45b}$$

The internal equilibrium can never be stable, as was stated before.

Furthermore, as the equilibria are simply the equilibria without migration with properly averaged parameters, the genetic variance is the same. So for example $\sigma^2(E_8) = \frac{\gamma_1^2}{2} - 2(\gamma_2 - \bar{O})^2$. As $\bar{O} = \frac{O_2 u + O_1 v}{u+v}$ holds, we see that no simple conclusions can be drawn, as how the migration rates influence the genetic variance.

We have shown, that under weak selection compared to migration, at most two stable equilibria can coexist. They can be polymorphic at one locus, but no stable full polymorphism exists. The only difference to the case of no migration and linkage equilibrium is, that the stability conditions for E_6 and E_8 are slightly more stringent. Therefore, a parameter region exists, for which E_6 or E_8 is the only stable equilibrium. In Section 2.2.3 the only stable equilibria with one locus polymorphic that could exist individually, were E_5 and E_7.

5 The Levene Model

The model was first formulated by H. Levene in (Levene, 1953). The basic assumption is that migration is independent of the deme of origin. It follows that,

$$\exists c_\beta : \; m_{\alpha\beta} = c_\beta \; \forall \alpha, \beta \text{ and} \tag{5.1a}$$

$$\sum_\beta c_\beta = 1, \tag{5.1b}$$

hold, under the assumption of soft selection, i.e., selection does not change the relative deme size. After one round of migration the gamete frequencies are deme independent since

$$x'_{i,\alpha} = \sum_\beta m_{\alpha\beta} x^*_{i,\beta} = \sum_\beta c_\beta x^*_{i,\beta} \tag{5.2}$$

is independent of α.

The classical interpretation of this result is that after intrademic selection there is random mating in the entire population.

Note that for two demes the migration matrix simplifies to:

$$M = \begin{pmatrix} c & 1-c \\ c & 1-c \end{pmatrix}, \tag{5.3}$$

where c is the relative size of the first deme. Furthermore, note that by the scale transformation of dividing $\gamma_{1,\alpha}$, $\gamma_{2,\alpha}$ and O_α by $\gamma_{1,\alpha}$ and multiplying s with $\gamma^2_{1,\alpha}$, (1.22) does not change. Therefore, without loss of generality, we set $\gamma_{1,\alpha} = 1$. We use the following notation for the effects of the minor loci

$$\gamma_1 := \gamma_{2,1} \text{ and } \gamma_2 := \gamma_{2,2}. \tag{5.4}$$

5.1 Analytical results under linkage equilibrium

To achieve analytical results we neglect linkage disequilibrium. This is a valid assumption if recombination is strong compared to selection.

Remember, that under linkage equilibrium the allele frequencies are sufficient to describe the dynamics. As they are deme independent we drop the deme index and use the following notation for the equilibria:

$$(p_1, p_2) = (p^{(1)}_\alpha, p^{(2)}_\alpha) = (p^{(1)}_{1,\alpha}, p^{(2)}_{1,\alpha}) \tag{5.5}$$

Since we assume that s is small, it is valid to develop the equations (1.13) of the dynamic into a Taylor series around $s = 0$. Doing so, the dynamics simplify to

$$\begin{aligned} p_1' =& p_1 + sp_1(1-p_1) \\ & \cdot[1 - 2p_1 + 2(\gamma_1 c + \gamma_2(1-c)) \\ & - 2(O_1 c + O_2(1-c)) - 4p_2(\gamma_1 c + \gamma_2(1-c))], \end{aligned} \tag{5.6a}$$

$$\begin{aligned} p_2' =& p_2 + sp_2(1-p_2) \\ & \cdot[-2p_2(\gamma_1^2 c + \gamma_2^2(1-c)) + 2(\gamma_1 c + \gamma_2(1-c)) - (\gamma_1^2 c + \gamma_2^2(1-c)) \\ & - 2(\gamma_1 O_1 c + \gamma_2 O_2(1-c)) - 4p_1(\gamma_1 c + \gamma_2(1-c))]. \end{aligned} \tag{5.6b}$$

In this very general case, we can find nine equilibria, the four corner equilibria, four equilibria on the boundary of Δ_4 and one internal equilibrium. Without loss of generality we can assume $\gamma_1 \leq \gamma_2$. As the case of $\gamma_1 = \gamma_2$ is much simpler, we treat it separately in Section 5.1.1. Let us introduce the weighted parameters

$$O = O_1 c + O_2(1-c), \tag{5.7a}$$

$$\overline{O} = \gamma_1 O_1 c + \gamma_2 O_2(1-c), \tag{5.7b}$$

$$\gamma = \gamma_1 c + \gamma_2(1-c), \tag{5.7c}$$

$$\overline{\gamma^2} = \gamma_1^2 c + \gamma_2^2(1-c). \tag{5.7d}$$

Then (5.6) simplifies to:

$$p_1' = p_1 + sp_1(1-p_1)(1 - 2p_1 + 2\gamma - 2O - 4p_2\gamma), \tag{5.8a}$$

$$p_2' = p_2 + sp_2(1-p_2)(\overline{\gamma^2} - 2p_2\overline{\gamma^2} + 2\gamma - 2\overline{O} - 4p_1\gamma). \tag{5.8b}$$

The four corner equilibria are denoted by

$$E_1 = (1,1), \tag{5.9a}$$

$$E_2 = (1,0), \tag{5.9b}$$

$$E_3 = (0,1), \tag{5.9c}$$

$$E_4 = (0,0), \tag{5.9d}$$

and the equilibria with one locus polymorphic are given by

$$E_5 = (1, \frac{-2\gamma + \overline{\gamma^2} - 2\overline{O}}{2\overline{\gamma^2}}), \tag{5.9e}$$

$$E_6 = (\frac{1}{2} - \gamma - O, 1), \tag{5.9f}$$

$$E_7 = (0, \frac{2\gamma + \overline{\gamma^2} - 2\overline{O}}{2\overline{\gamma^2}}) \text{ and} \tag{5.9g}$$

$$E_8 = (\frac{1}{2} + \gamma - O, 0). \tag{5.9h}$$

Finally, there exists one internal equilibrium. First, note that the internal equilibria are the solutions of:

$$p_2 = -\frac{1}{2\gamma}p_1 + \frac{1 + 2\gamma - 2O}{4\gamma},$$
$$p_2 = -\frac{2\gamma}{\overline{\overline{\gamma^2}}}p_1 + \frac{\overline{\gamma^2} + 2\gamma - 2\overline{O}}{2\overline{\gamma^2}}.$$

Therefore, there exists a unique solution if

$$\frac{1}{2\gamma} \neq \frac{2\gamma}{\overline{\overline{\gamma^2}}},$$

holds, which is equivalent to $\gamma_i \neq 0$ for $i = 1, 2$. This equilibrium is given by:

$$E_9 = (\frac{4\gamma^2 - \overline{\gamma^2} + 2\overline{\gamma^2}O - 4\gamma\overline{O}}{2(4\gamma^2 - \overline{\gamma^2})}, \frac{4\gamma^2 - \overline{\gamma^2} + 2\overline{O} - 4\gamma O}{2(4\gamma^2 - \overline{\gamma^2})}). \tag{5.9j}$$

For the existence of the equilibria, we obtain the following conditions:
For E_5:

$$-\gamma - \frac{1}{2}\overline{\gamma^2} < \overline{O} < -\gamma + \frac{1}{2}\overline{\gamma^2}, \tag{5.10a}$$

for E_6:

$$-\gamma - \frac{1}{2} < O < -\gamma + \frac{1}{2}, \tag{5.10b}$$

for E_7:

$$\gamma - \frac{1}{2}\overline{\gamma^2} < \overline{O} < \gamma + \frac{1}{2}\overline{\gamma^2}, \tag{5.10c}$$

for E_8:

$$\gamma - \frac{1}{2} < O < \gamma + \frac{1}{2}, \tag{5.10d}$$

and for E_9:

$$-2\gamma^2 + \frac{1}{2}\overline{\gamma^2} < \overline{O} - 2\gamma O < 2\gamma^2 - \frac{1}{2}\overline{\gamma^2}, \tag{5.10e}$$

together with

$$-2\gamma^2 + \frac{1}{2}\overline{\gamma^2} < O\overline{\gamma^2} - 2\gamma\overline{O} < 2\gamma^2 - \frac{1}{2}\overline{\gamma^2}. \tag{5.10f}$$

By linearization and computation of the eigenvalues we derive the stability conditions of the equilibria. The monomorphic equilibria are asymptotically stable if the following conditions hold:
For E_1:

$$O < -\frac{1}{2} - \gamma \text{ and} \tag{5.11a}$$
$$\overline{O} < -\frac{1}{2}\overline{\gamma^2} - \gamma, \tag{5.11b}$$

for E_2:

$$O < -\frac{1}{2} + \gamma \text{ and} \tag{5.11c}$$

$$\overline{O} > \frac{1}{2}\overline{\gamma^2} - \gamma, \tag{5.11d}$$

for E_3:

$$O > \frac{1}{2} - \gamma \text{ and} \tag{5.11e}$$

$$\overline{O} < \gamma - \frac{1}{2}\overline{\gamma^2}, \tag{5.11f}$$

for E_4:

$$O > \frac{1}{2} + \gamma \text{ and} \tag{5.11g}$$

$$\overline{O} > \frac{1}{2}\overline{\gamma^2} + \gamma. \tag{5.11h}$$

The equilibria with one locus polymorphic are asymptotically stable in $[0,1]^2$ if they exist, i.e., if (5.10) holds, and the following conditions are fulfilled:
For E_5:

$$2\overline{\gamma^2}O - 4\gamma\overline{O} < 4\gamma^2 - \overline{\gamma^2}, \tag{5.12a}$$

for E_6:

$$\overline{O} - 2\gamma O < 2\gamma^2 - \frac{1}{2}\overline{\gamma^2}, \tag{5.12b}$$

for E_7:

$$2\overline{\gamma^2}O - 4\gamma\overline{O} > -4\gamma^2 + \overline{\gamma^2}, \tag{5.12c}$$

for E_8:

$$\overline{O} - 2\gamma O > -2\gamma^2 + \frac{1}{2}\overline{\gamma^2}. \tag{5.12d}$$

In this very general case, the stability conditions for the internal equilibrium could not be deduced.

Note, how similar the equilibria and their conditions for existence and stability are to the ones in Section 2.2. This is because the Levene model with weak soft selection can be viewed as random mating in the entire population after selection is properly averaged over demes, as was shown by Nagylak (2009, p. 201). Next, let us apply this to our model.

Recall, that for weak selection we set (4.14)

$$w_{ij,\alpha} = 1 + \epsilon r_{ij,\alpha}, \tag{5.13}$$

where $\epsilon > 0$ is sufficiently small. The principal left eigenvector μ of (5.3) is given by $\mu = (c, 1-c)^T$. The averaged fitness is the following:

$$w_{ij} = 1 + \epsilon \sum_{\beta} \mu_\beta r_{ij,\beta}. \tag{5.14}$$

Using this fitness in the selection-recombination system (1.13b) and assuming linkage equilibrium, we obtain the same equilibria as above. If terms of order $\mathcal{O}(\epsilon^2)$ are neglected, the stability conditions of the boundary equilibria can be computed explicitly. They are the same as (5.12).

To make the model even easier and to deduce the stability conditions of the internal equilibrium we set $\gamma_1 = \gamma_2$. Doing so, the genotypic value is deme independent. The only difference between the demes is the position of the optimum.

5.1.1 Deme-independent allelic effects

If we set $\gamma_1 = \gamma_2$, the combined parameters from (5.7c) and (5.7d) reduce to $\gamma = \gamma_2$ and $\overline{\gamma^2} = \gamma_2^2$.

Therefore, the four equilibria with one locus polymorphic are:

$$E_5 = (1, \frac{-2 + \gamma_2 - 2O}{2\gamma_2}), \tag{5.15a}$$

$$E_6 = (\frac{1 - 2\gamma_2 - 2O}{2}, 1), \tag{5.15b}$$

$$E_7 = (0, \frac{2 + \gamma_2 - 2O}{2\gamma_2}), \tag{5.15c}$$

$$E_8 = (\frac{1 + 2\gamma_2 - 2O}{2}, 0). \tag{5.15d}$$

Since they are exactly the same equilibria as in the case of no migration, cf. Chapter 2, they have the same conditions of existence. Therefore (2.23) must hold. Also the genetic variance at the equilibria is the same, hence, (2.24) holds. Note, that the only difference to Chapter 2 is the different meaning of O. Here, O is the weighted fitness optimum (5.7a). As the dynamics are different, so are the conditions of stability. Combined with (2.23) they are:
For E_5:

$$-1 - \frac{1}{2}\gamma_2 < O < -1 + \frac{1}{2}\gamma_2, \tag{5.16a}$$

for E_6:

$$-\frac{3}{2}\gamma_2 < O < -\gamma_2 + \frac{1}{2}, \tag{5.16b}$$

for E_7:

$$1 - \frac{1}{2}\gamma_2 < O < 1 + \frac{1}{2}\gamma_2, \tag{5.16c}$$

for E_8:

$$\gamma_2 - \frac{1}{2} < O < \frac{3}{2}\gamma_2. \tag{5.16d}$$

The equilibrium with both loci polymorphic is given by

$$E_9 = (\frac{1}{2} - \frac{O}{3}, \frac{1}{2} - \frac{O}{3\gamma_2}), \tag{5.17}$$

again the same as without migration (2.25). Therefore, for existence $|O| < \frac{3}{2}\gamma_2$ must hold. The eigenvalues of the internal equilibrium are given by:

$$\lambda_{1,2} = 1 - s\frac{b \pm \sqrt{b^2 + 12(9\gamma_2^2 - 4O^2)(9 - 4O^2)}}{36}, \tag{5.18}$$

with $b = 9 + 9\gamma_2^2 - 8O^2$. Therefore, the equilibrium is stable if and only if

$$\frac{3}{2}\gamma_2 < |O| < \frac{3}{2} \tag{5.19}$$

holds, as we assumed $\gamma_2 \leq 1$. Otherwise, $|\lambda_1| > 1$ and $|\lambda_2| < 1$ holds if s is small enough. Hence, the internal equilibrium is a saddle point whenever it exists.

It is important to note that this is exactly the same result as the result for the weak-selection limit with deme-independent allelic effects , cf. Section 4.3.2.

5.2 Numerical results

In the following we simulate the full dynamics (1.13), and compare the results with the analytical results under the assumption of linkage equilibrium.

First, let us recapitulate the assumptions we make. As we discuss the Levene model with two demes, we only have one parameter c for migration, the (relative) size of the first deme. The migration rates are therefore given by c and $1 - c$. Next, as we assume linkage equilibrium, we fix the recombination rate at $\frac{1}{2}$ throughout this section. Furthermore, we assume the effects of the loci to be deme independent. Therefore, we only have one parameter left, $0 \leq \gamma_2 \leq 1$, as without loss of generality we set $\gamma_{1,\alpha} = 1$.

5.2.1 The unstable internal equilibrium

For the numerical analysis of the unstable internal equilibrium, the full system of equations (1.13) using the migration matrix (5.3) was solved by employing NSolve in *Mathematica*. The positions of the fitness optima were varied from -1 to 1 using a step size of 0.1, the allelic effect γ_2 was set to $\frac{1}{4}$, $\frac{1}{2}$ and $\frac{3}{4}$ respectively. The deme size was between 0 and $\frac{1}{2}$ as the model is symmetric around $c = \frac{1}{2}$. As stated before, the recombination rate was fixed, while the selection coefficient was varied between 0 and 0.2.

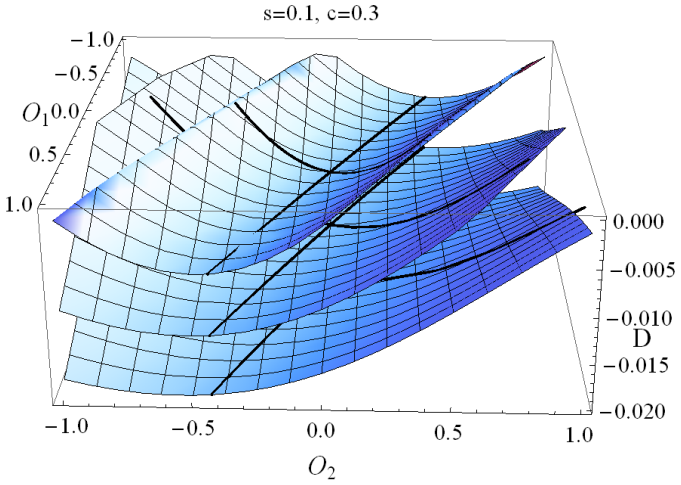


Figure 5.1: The value of linkage disequilibrium D for the internal equilibrium as a function of the position of the fitness optima for three different values of γ_2. The top manifold is for $\gamma_2 = 0.25$, the middle one for $\gamma_2 = 0.5$ and the bottom one for $\gamma_2 = 0.75$. The lines represent $O_2 = -\frac{c}{1-c}O_1$ and $O_2 = \frac{1-c}{c}O_1$.

Throughout the analysis of the internal equilibrium, two hyperplanes in the parameter space are of special interest, namely the hyperplanes g_1 and g_2 defined by

$$g_1 : O_2 = \frac{1-c}{c}O_1, \tag{5.20a}$$

$$g_2 : O_2 = -\frac{c}{1-c}O_1. \tag{5.20b}$$

In Figure 5.1 the value of linkage disequilibrium at the unstable internal equilibrium is plotted as a function of the position of the fitness optima while the other parameters are fixed. The three manifolds are for three different allelic effects, namely $\gamma_2 = 0.25$ for the upper manifold, $\gamma_2 = 0.5$ for the middle one, and $\gamma_2 = 0.75$ for the bottom manifold. First, note that the manifolds cease to exist once the value of disequilibrium reaches 0. This is not due to the axes range used for the plot, but rather due to the following: For our parameter set, when linkage disequilibrium reaches zero, this is the moment when the internal equilibrium leaves the interior of the simplex and therefore ceases to exist. Hence, also the parameter region for which the internal equilibrium exists is depicted in Figure 5.1. Setting for example $\gamma_2 = 0.25$, i.e., looking at the top manifold in Figure 5.1, the fitness optima, for which the manifold exists, are exactly the parameters for which the internal equilibrium exists. Furthermore, the plot shows why the set of parameters g_1 and g_2 are important: along g_2 the value of linkage disequilibrium stays nearly constant, while along g_1 it changes most, i.e., its absolute value decreases rapidly until it reaches zero. Furthermore, note that for g_2 the analytically calculated equilibria (5.15) and (5.17), are constant in O_1.

When we talk about moving along g_1 or g_2 respectively, we mean the following: O_1 increases from -1 to 1 while O_2 fulfills (5.20a) or (5.20b) respectively, and all the

other parameters are fixed.

To gain further understanding, let us consider the position of the equilibria in the (p_1, p_2)-plane, i.e., the plane of the frequencies of the alleles A_1 and B_1. In Figure 5.2 all the equilibria are plotted for $O_2 = -O_1$ and O_1 increases from 0 to 1 in ten steps. The other parameters are fixed at $c = 0.3$ and $s = 0.15$. The numerically found equilibria are marked with x_i, where x_i is an equilibrium found for $O_1 = \frac{i}{10}$. The approximation is depicted as a red line. In Figure 5.2(a), the allelic effect is $\gamma_2 = 0.25$. Besides the corner equilibria there exist one polymorphic equilibrium and two equilibria, $E_6 = (\hat{x}, 1)$ and $E_8 = (\hat{x}, 0)$, with the major locus polymorphic. By increasing O_1, E_8 moves to the corner equilibrium $E_2 = (1, 0)$, while the internal equilibrium moves towards E_6. In Figure 5.2(b) and Figure 5.2(c) the allelic effect of the minor locus is $\gamma_2 = 0.5$ and $\gamma_2 = 0.75$, respectively. For these two values of γ_2 the second equilibrium with one locus polymorphic does not exist any longer.

In Figure 5.3 the equilibria are plotted for the two extreme cases, i.e., moving along g_1 and g_2 respectively. They are extreme cases because along these lines linkage disequilibrium either changes most or stays nearly constant. As was stated above, moving along g_2, the analytically calculated approximation for the equilibria stay constant and the numerically calculated equilibria change their position only slightly, as one sees in Figure 5.3(b). Moving along g_1, i.e., Figure 5.3(a) the internal fixed point rapidly moves to the edge and also the edge equilibria move rapidly. Note, that in Figure 5.3(a) we used a different notation for the equilibria. Here, x_i denotes the numerically calculated internal equilibrium, while y_i denotes the numerical equilibrium with the second locus polymorphic and z_i denotes the numerical equilibrium with the first locus polymorphic. For $O_1 = 0$, there exists one internal equilibrium $E_9 = (0.5, 0.5)$, in addition to the always existing corner equilibria . As O_1 increases, this equilibrium moves to the edge on which $p_2 = 0$ holds, and an edge equilibrium, $E_8 = (\hat{x}, 0)$, starts to exist. As the internal equilibrium reaches the edge and leaves the plane via E_8, a second edge equilibrium, E_7, for which $p_1 = 0$ holds, starts to exist. Increasing O_1 further, the two edge equilibria rapidly move towards $E_4 = (0, 0)$. Once they reach it, there only exist the corner equilibria until two new edge equilibria, E_6 and E_5 emerge from $E_1 = (1, 1)$ and move away from it. That also yields further understanding of Figure 5.1. Moving along g_1 the equilibria rapidly move towards the edge of the plane where linkage disequilibrium equals 0. On the other hand, moving along g_2, the internal equilibrium stays nearly constant, therefore always exists and linkage disequilibrium stays nearly constant.

Furthermore, increasing s increases the absolute value of disequilibrium, as is shown in Figure 5.4. Here, s is increased from 0 to 0.2 in 20 steps, while the other parameters are fixed. Figure 5.4(a) shows that increasing γ_2 increases the absolute value of disequilibrium, Figure 5.4(b) shows the same fact for the deme size. To be precise the absolute value of disequilibrium grows as the deme size does until $c = 0.5$. If the deme size increases further the absolute value of disequilibrium decreases again as one sees in Figure 5.5.

In Figure 5.4, the value of linkage disequilibrium is nearly linear in s, but Figure 5.5 shows that this is not true if $O \neq 0$.

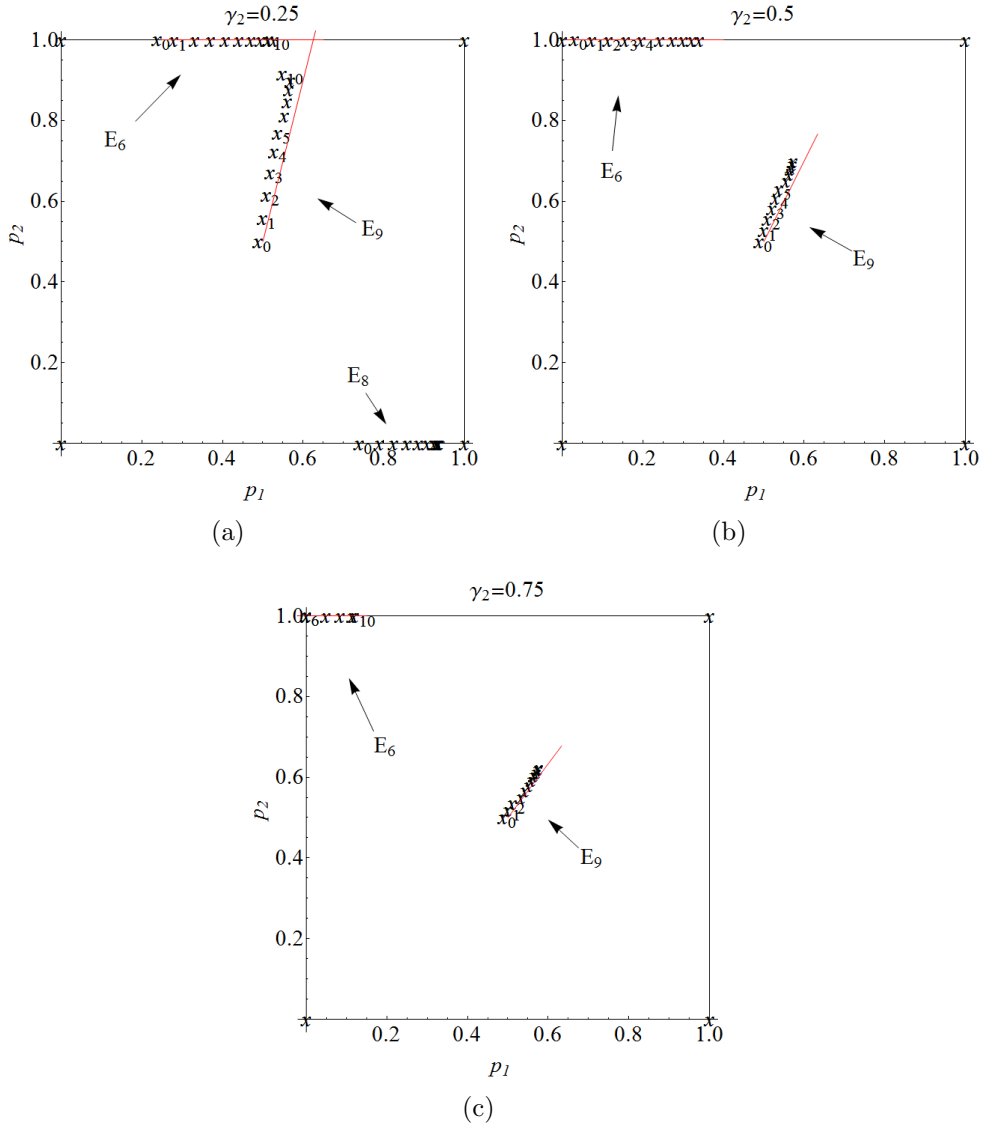
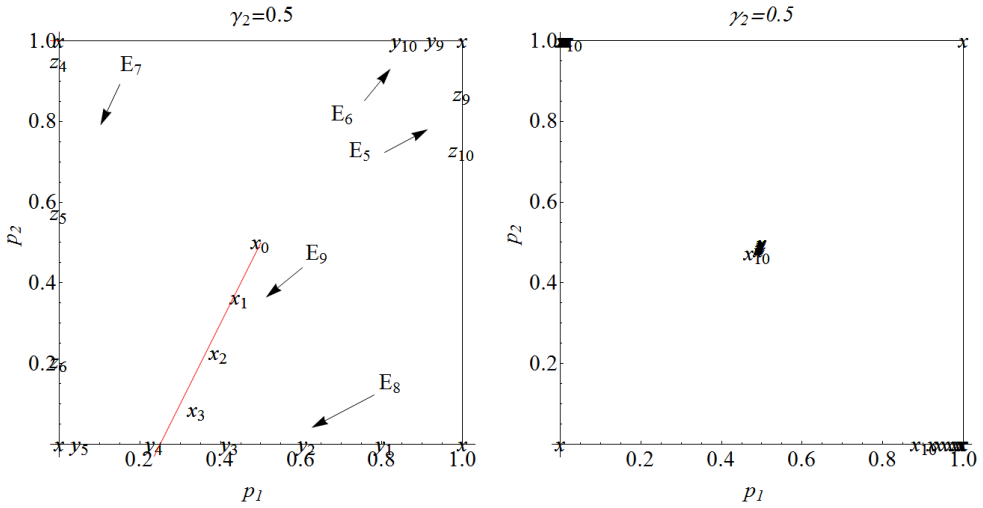
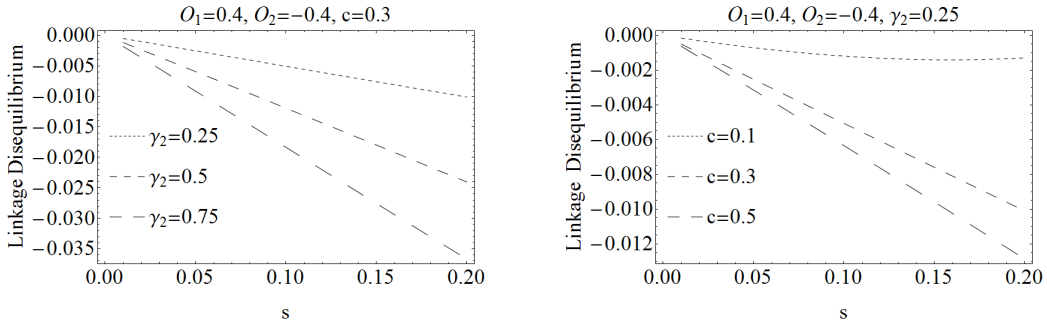


Figure 5.2: Position of the numerically calculated fixed points (x_i) and the analytically calculated ones (red line), as O_1 increases from 0 to 1 in ten steps while $O_2 = -O_1$. Thus, each x_i represents a fixed point for $O_1 = \frac{i}{10}$. By increasing O_1 the internal equilibrium moves to the boundary. The allelic effect γ_2 is given by 0.25, 0.5 and 0.75 in (a), (b), and (c), respectively. The parameters s and c are fixed; $s = 0.15$, $c = 0.3$.



(a) $O_2 = \frac{(1-c)}{c} O_1$ (b) $O_2 = -\frac{c}{(1-c)} O_1$

Figure 5.3: Position of the numerically calculated fixed points (x_i, y_i, z_i) and the analytically calculated ones (red line) as O_1 increases from 0 to 1 in ten steps while $O_2 = \frac{(1-c)}{c} O_1$, and $O_2 = -\frac{c}{(1-c)} O - 1$ in (a), and (b), respectively. Thus, each x_i, y_i, and z_i represents a fixed point for $O_1 = \frac{i}{10}$. In the first case x_i denotes the internal equilibrium, while y_i denotes an equilibrium with the second locus polymorphic and z_i denotes an equilibrium with the first locus polymorphic. In this case the internal equilibrium moves rapidly to the boundary while in the second case the equilibria stay nearly constant. The parameters s and c are fixed; $s = 0.15$, $c = 0.3$.



(a) (b)

Figure 5.4: The value of linkage disequilibrium at the internal equilibrium plotted as a function of the selection coefficient s. In the first graphic three different allelic effects are plotted and in the second graphic three different migration rates.

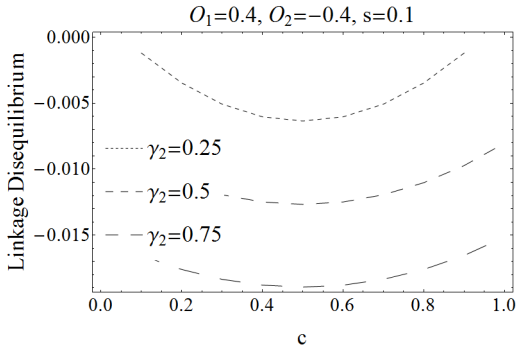


Figure 5.5: The value of linkage disequilibrium at the internal equilibrium plotted as a function of the deme size. The other parameters are fixed. As one sees, disequilibrium is symmetric around $c = \frac{1}{2}$.

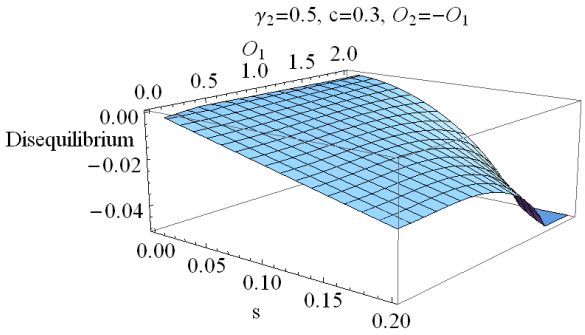


Figure 5.6: The linkage disequilibrium value at the internal equilibrium plotted as a function of the selection coefficient and the fitness optimum O_1. The position of the second fitness optimum is $O_2 = -O_1$ and the migration rate is fixed at $c = 0.3$. Although for small O_1 disequilibrium is nearly linear in s, this obviously does not hold for large O_1 .

O_1	0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
γ_2=0.25											
E_6	0.5	0.417	0.286	0.226	0.143	0.083	0.036	0.024	0	0	0
E_8	0.5	0.583	0.714	0.774	0.857	0.917	0.964	0.976	1	1	1
γ_2=0.5											
E_6	0.5	0.488	0.417	0.369	0.369	0.345	0.321	0.286	0.262	0.214	0.25
E_8	0.5	0	0	0	0	0	0	0	0	0	0
E_2	0	0.522	0.583	0.631	0.631	0.655	0.679	0.714	0.738	0.786	0.75
γ_2=0.75											
E_2	0.5	0.536	0.536	0.56	0.571	0.583	0.583	0.571	0.583	0.595	0.595
E_3	0.5	0.464	0.464	0.44	0.429	0.417	0	0	0	0	0
E_6	0	0	0	0	0	0	0.417	0.429	0.417	0.405	0.405

Table 5.1: Relative size of the basin of attraction of the stable equilibria for the case of opposite fitness optima, i.e., $O_2 = -O_1$. The allelic effect is deme independent and set at the three different values $\frac{1}{4}$, $\frac{1}{2}$ and $\frac{3}{4}$ respectively. The other parameters are fixed at $c = 0.3$, $s = 0.15$ and $r = 0.5$.

5.2.2 The stable equilibria

Next, let us analyze the stable equilibria. For the calculation of the stable fixed points a grid of starting points was laid over the simplex. The grid had a mesh size of 0.1 and was than disturbed by adding a random number between $-\frac{1}{30}$ and $\frac{1}{30}$. Grid points on the boundary of the simplex were excluded, as the only interesting part of the boundary is the one in linkage equilibrium, where the dynamics are known. The system of equations (1.13) together with the migration matrix (5.3) was iterated for these starting points. Once the gamete frequencies were fixed for the first eight decimal places, we assumed to have found a stable fixed point. Furthermore, for each stable fixed point, the converging trajectories were counted, thus allowing to estimate the relative size of the basins of attraction of the equilibria. Further above we discussed three special cases of the position of the fitness optima. Let us now discuss the stable equilibria in these cases.

The first special case is the case of opposite fitness optima. The optimum O_1 increases from 0 to 1 in ten steps, while the other parameters are fixed at $c = 0.3$, $s = 0.15$ and $r = 0.5$. The allelic effect γ_2 is set $\frac{1}{4}$, $\frac{1}{2}$ and $\frac{3}{4}$ respectively. In the first case, i.e., $\gamma_2 = \frac{1}{4}$, for $O_1 = 0$ the two equilibria with the major locus polymorphic, i.e., E_6 and E_8, are stable. As Table 5.1 shows, by increasing O_1, the basin of attraction of E_8 increases until it is globally attracting. An exact value can not be given, as we used finitely many starting points. As Figure 5.2 shows, by increasing O_1, the unstable internal equilibrium E_9 moves towards E_6. The closer it gets to E_6, the smaller its basin of attraction becomes, as is depicted in Figure 5.7. Since the internal equilibrium is a saddle point, there exist two trajectories that converge to it. These two trajectories dissect the plane into two connected regions, the basins of attraction of the stable equilibria. Therefore, the basin of attraction of E_6 exists until the internal equilibrium reaches the boundary. Our data lacks this information, since we used a grid of finitely many starting points, which we disturbed by random numbers. The generated starting points cannot have allele frequencies less than 0.14. Hence, once E_9

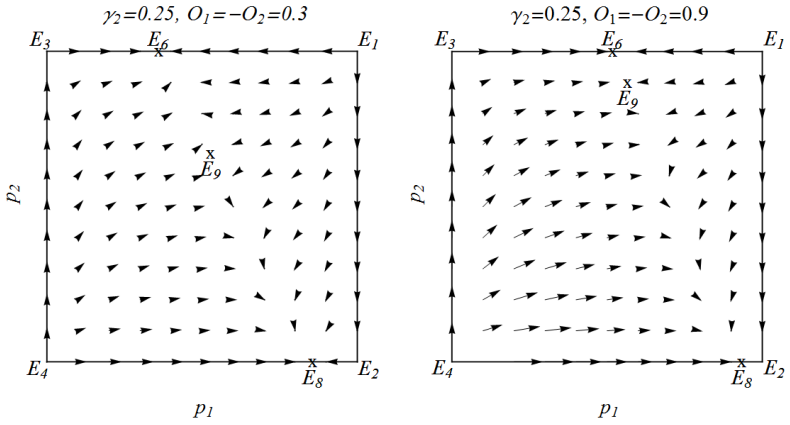


Figure 5.7: Two phase portraits for the Levene model with unlinked loci and opposite fitness optima. Note that for the second phase portrait, for reasons of continuity, there has to exist an area between E_6 and E_9 for which all points converge to E_6. The parameters s and c are fixed; $s = 0.15$, $c = 0.3$.

is close enough to the boundary, there are no starting points in the basin of attraction of E_6.

In the second case, i.e., $\gamma_2 = 0.5$, for $O_1 = 0$, the two stable equilibria with the major locus polymorphic exist. Increasing O_1, E_8 moves into the stable vertex E_2. Increasing O_1 further, again decreases the basin of attraction of E_6 and increases the basin of E_2. The fact that from $O_1 = 0.9$ to $O_1 = 1$ the relative size of the basin of attraction of E_6 increases, is an effect of randomization. Repeated runs of the program showed the expected behavior, i.e., in general the size of the basin of attraction of E_6 decreases, except for some disturbances.

In the last case, i.e., $\gamma_2 = 0.75$, for small O_1 there exist the two stable vertices E_2 and E_3. Once the equilibrium E_6 starts to exist it is stable together with E_2. The basins of attraction are quite similar in size, but the area that is attracted by E_2 is slightly smaller, as the unstable internal equilibrium moves slightly towards it.

Next, we study the two special cases that were treated above in Figure 5.3. Again, O_1 was increased from 0 to 1 in ten steps, while the other parameters where fixed at $c = 0.3$, $r = 0.5$, $s = 0.15$ and $\gamma_2 = 0.5$. In the first case $O_2 = \frac{(1-c)}{c} O_1$ is fulfilled, which, as was stated before, leads to a very rapid change of the equilibrium structure. As Table 5.2 shows, for $O_1 = 0$ there exist the two stable equilibria with the major locus polymorphic. By increasing O_1, the equilibrium E_6 moves into the vertex E_3. This vertex is stable together with E_8, until the unstable internal equilibrium reaches E_8 and a new globally attracting equilibrium E_7 starts to exist. In Figure 5.8 we illustrate this change. In Figure 5.8(a) the phase portrait of our model is shown, before the internal equilibrium ceases to exists. In Figure 5.8(b) the internal equilibrium does not exist any longer. Instead, the globally attracting equilibrium E_7 can be seen in the upper left corner. Once the quickly moving equilibrium E_7 reaches E_4, the vertex is stable. Next, at about $O_1 = 0.8$, a new stable equilibrium starts to exist via E_1.

O_1	0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
$O_2=\frac{1-c}{c}O_1$											
E_8	0.488	0.333	0.155	0.012	0	0	0	0	0	0	0
E_6	0.512	0	0	0	0	0	0	0	0	0	0
E_3	0	0.667	0.845	0.988	0	0	0	0	0	0	0
E_7	0	0	0	0	1	1	1	0	0	0	0
E_4	0	0	0	0	0	0	0	1	0.929	0.774	0.619
E_1	0	0	0	0	0	0	0	0	0.071	0	0
E_5	0	0	0	0	0	0	0	0	0	0.226	0.381
$O_2=-\frac{c}{1-c}O_1$											
E_8	0.488	0.5	0.488	0.5	0.524	0.512	0.488	0.488	0.476	0.452	0.452
E_6	0.512	0.5	0.512	0.5	0.476	0.488	0.512	0.512	0.524	0.548	0.548

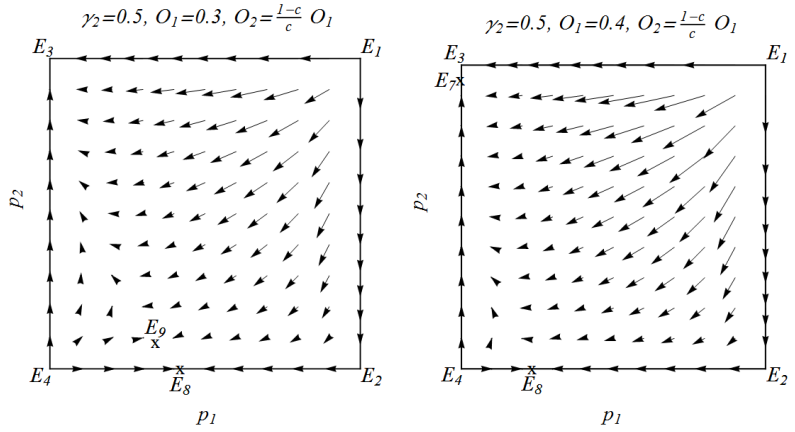
Table 5.2: The table shows the relative size of the basin of attraction for the stable equilibria for the two extreme cases $O_2 = \frac{(1-c)}{c}O_1$ and $O_2 = -\frac{c}{1-c}O_1$. In the first case by increasing O_1 the dynamic changes a lot, while in the second case the dynamic stays nearly constant.

Finally, in the case of $O_2 = -\frac{c}{1-c}O_1$, the dynamics stay nearly constant, there exist two stable equilibria E_6 and E_8. The relative size of the basin of attraction stays nearly constant, changes are because of the random starting points.

5.3 Influence of the recombination rate

We now want to analyze the stable equilibria for the Levene model with an arbitrary recombination rate. To minimize the number of parameters let us assume that the allelic effects are deme independent. To determine the stable equilibria we iterate the full dynamic (1.13) together with the migration matrix (5.3), on 84 starting points. Once the gamete frequencies are fixed for the first eight decimal places the so found point is called a stable fixed point. Recall, that for the Levene model, after one round of migration the gametic frequencies are deme independent. Therefore, we can choose the same starting points in both demes. For the initial values we used a grid on the simplex with a mesh size of 0.1, which was then disturbed by adding random numbers between $-\frac{1}{30}$ and $\frac{1}{30}$. Starting points on the boundary of the simplex were ignored. The allelic effect of the minor locus, γ_2, was set $\frac{1}{4}$, $\frac{1}{2}$, $\frac{3}{4}$ and 1.

As was shown in Section 5.1, under the assumption of weak selection and strong recombination, there exists no stable internal equilibrium. On the other hand, as stated above, in the case of no migration and if the double heterozygote is the fittest, i.e., $O = 0$, there exists an upper bound of the recombination rate, given by (2.16), so that for equal or weaker recombination there always exists a stable internal equilibrium. Because of reasons of continuity, it is plausible to try to find such an upper bound for the recombination rate, in dependence of the position of the fitness optima. We found this upper bound by increasing the recombination rate from 0, until the internal equilibrium ceased to exist. The used step size was 0.002. This upper bound is depicted in Figure 5.9. For the data, the remaining parameters were set at $s = 0.1$, $c = 0.3$ and for Figure 5.9(a): $\gamma_2 = 0.25$, for Figure 5.9(c): $\gamma_2 = 0.5$ and for Figure 5.9(e):



(a) (b)

Figure 5.8: Two phase portraits for the Levene model with unlinked loci. The allelic effect is $\gamma_2 = 0.5$. The fitness optima are at the ratio of $\frac{1-c}{c}$. By changing the optimum, the dynamics change drastically. The other parameters are $s = 0.15$ and $c = 0.3$.

$\gamma_2 = 0.75$. The case of equal allelic effects, i.e., $\gamma_2 = 1$, was also studied, but for this case there never exists an internal equilibrium. As in the previous section the parameter combination $O_2 = -\frac{c}{1-c}O_1$ is of special interest. Along this line are the maximal recombination rates resulting in a stable internal equilibrium. Furthermore, in the direction of g_2 the upper bound of the recombination rate stays nearly constant.

Next, we are interested in the existence of a globally attracting equilibrium. Again, we find an upper bound of the recombination rate, so that as long as the recombination rate lies below it, there always exists a globally attracting equilibrium. This upper bound was found analogously to that for the stable internal equilibrium. As this upper bound is bigger, we used a step size of 0.02. The upper bound of the recombination rate is depicted in Figure 5.9(b), Figure 5.9(d) and Figure 5.9(f). For the case of equal allelic effects, there never exists a globally stable equilibrium.

Let us now fix the recombination rate at $r = 0.001$. In the cases $\gamma_2 = 0.25$, 0.5, and 0.75 there exists a globally stable equilibrium as can be seen in Figure 5.9. Since, for the case of $\gamma_2 = 1$ the equilibria are not globally attracting, we computed the weighted average of the values of interest. We weighted by the amount of trajectories converging to the equilibrium.

For the stable equilibria, there are three more interesting values: linkage disequilibrium, the mean fitness and the (total) genetic variance.

In Figure 5.10, the value of linkage disequilibrium at equilibrium is depicted. The regions where the equilibrium is in linkage equilibrium, are the regions for which no internal equilibrium exists. Equilibria on the boundary of the simplex are always in linkage equilibrium.

Since the mean fitness depends on the fitness function, it is not deme independent.

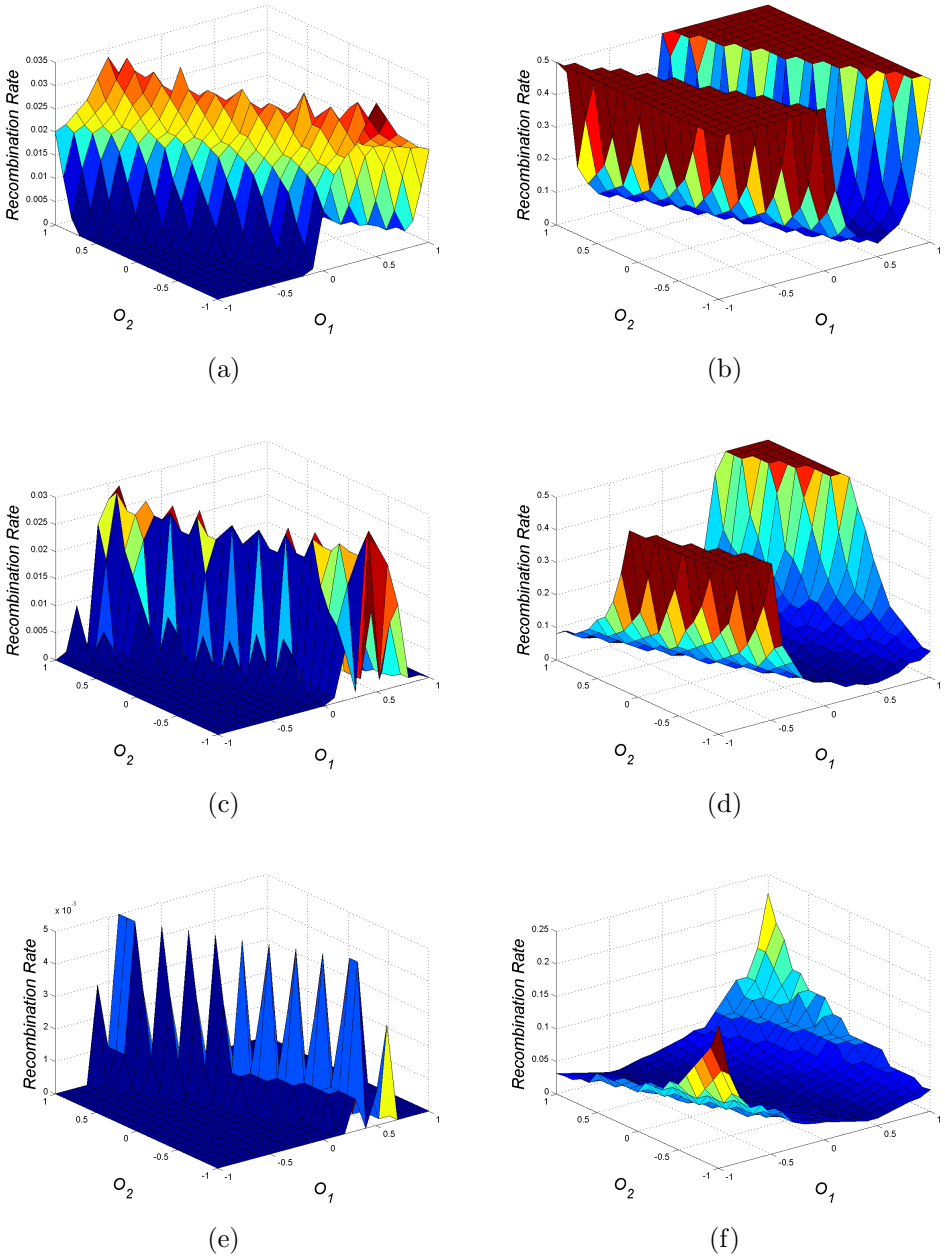


Figure 5.9: In the left column, the upper bound of the recombination rate, resulting in the existence of an internal equilibrium, is plotted as a function of O_1 and O_2. In the right column, the maximal recombination rate for which a globally attracting (not necessarily internal) equilibrium exists, is plotted against the fitness optima in the demes. The allelic effect is for (a) and (b) $\gamma_2 = 0.25$, for (c) and (d) $\gamma_2 = 0.5$ and for (e) and (f) $\gamma_2 = 0.75$. The other parameters are fixed at $s = 0.1$ and $c = 0.3$. Note that the maxima/minima are along g_2, i.e., $O_2 = -\frac{c}{1-c}O_1$.

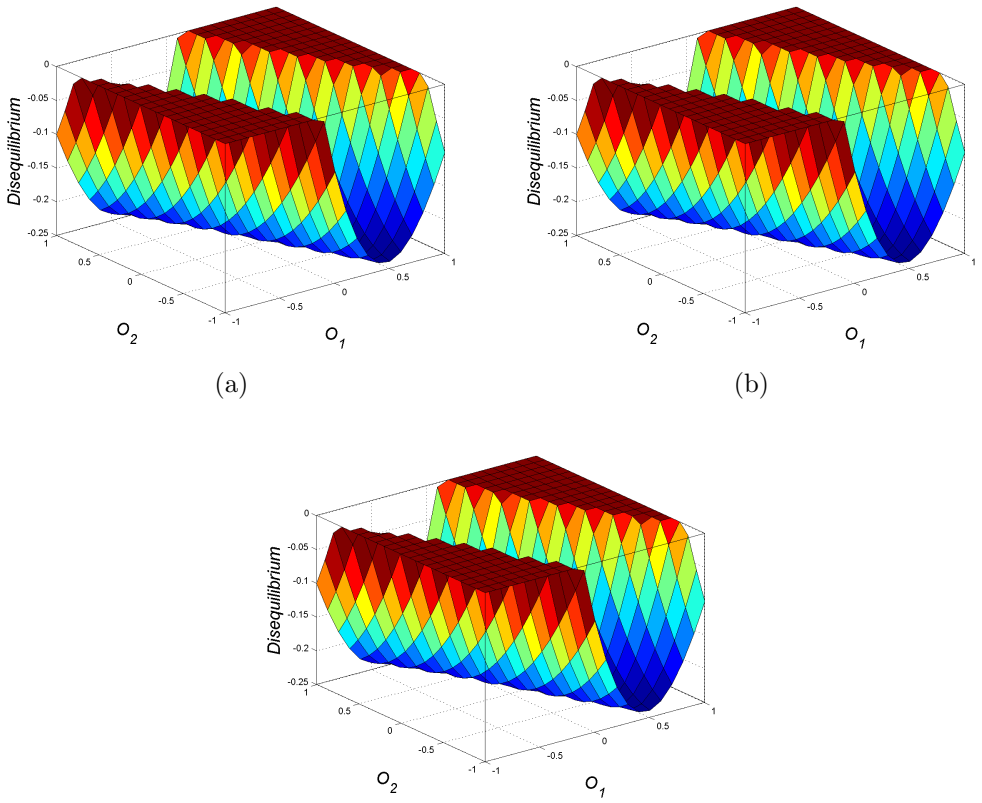


Figure 5.10: The value of linkage disequilibrium at the stable equilibrium is depicted for arbitrary position of the fitness optima and three different allelic effects. For (a) $\gamma_2 = 0.25$, for (b) $\gamma_2 = 0.5$ and for (c) $\gamma_2 = 0.75$ holds. The other parameters are fixed at $s = 0.1$, $c = 0.3$ and $r = 0.001$. For these parameter sets there always exists a globally attracting equilibrium. The regions for which linkage disequilibrium equals zero, correspond to the regions where no internal equilibrium exists. As for the case of $\gamma_2 = 1$ there never exists an internal equilibrium, the value of linkage disequilibrium at equilibrium equals zero.

Let us therefore introduce the weighted mean fitness of the total population,

$$\overline{W} = c\overline{W}_1 + (1-c)\overline{W}_2, \tag{5.21}$$

where $\overline{W}_\alpha$ is the mean fitness in deme α. As Figure 5.11 shows, the manifold of the mean fitness at equilibrium for different positions of the fitness optima may have one or two peaks. The minimum is along $O_1 = -O_2$, if $\gamma_2 \neq 1$. To be precise, this has to be formulated in the following way. Given the position of the fitness optimum O_1 in one deme, the mean fitness of the entire population gets minimized for $O_2 = -O_1$. This can be explained in the following way: For opposite fitness optima, in each deme the maximum of the fitness function gets shifted to one side, so would the equilibria in the case of isolated demes. Since for the Levene model the equilibria are deme independent, the resulting equilibrium is between these two fitness optima. Hence, the mean fitness is low.

Furthermore, we have to emphasize that the case of no migration, Chapter 2, is contained in our analysis. It is equivalent to the case of uniform selection. As we assumed the allelic effects to be deme independent, this is the case whenever $O_1 = O_2$ holds. From Figure 5.11 we see that the maxima of the mean fitness are on this line. By increasing the allelic effect of the minor locus, the two maxima move towards each other, until they finally coincide, since for weak recombination and no migration, only the two gametes A_1B_2 and A_2B_1 can exist as long as O is not to big. For small O they coexist, but the homozygous genotypes, i.e., $A_1A_1B_2B_2$ and $A_2A_2B_1B_1$ have very low fitness. By shifting the optimum towards the genotype value of one of these zygotes, the contained gamete gets fixed. Once the optimum reaches the zygotes genotypic value, i.e., $-1+\gamma_2$, $1-\gamma_2$ respectively, the mean fitness is maximized. Therefore, by increasing γ_2 the mean fitness optima move towards each other.

As was shown before, for our model, the total genetic variance coincides with the additive genetic variance. The genetic variance therefore is given by

$$\sigma^2 = \frac{1}{2}(1+\gamma_2^2) + \gamma_2(x_1 + x_4 - x_2 - x_3) \tag{5.22}$$

$$- \frac{1}{2}[(1+\gamma_2)(x_4 - x_1) + (1-\gamma_2)(x_3 - x_2)]^2. \tag{5.23}$$

The maximum of the genetic variance is $V_{\max} = \frac{1}{2}(1+\gamma_2^2)$. The ratio of the equilibrium genetic variance to $V_{\max}$ is depicted in Figure 5.12.

First, note that the manifold is constant in the direction of g_2, where g_2 was defined as the line for which $O_2 = -\frac{c}{1-c}O_1$ holds. In the direction of g_1 it is a polynomial of fourth degree in O_1. The local maximum along g_1 represents the high genetic variance at the fully polymorphic equilibrium. By increasing γ_2, the region of its existence contracts, until, for equal allelic effects of the loci, Figure 5.12(d), it vanishes as no fully polymorphic equilibrium exists. The region where the variance equals zero, is the parameter region for which only monomorphic equilibria exist. Finally, the genetic variance increases, if the positions of the fitness optima have the same sign, and both are large. The reason is, that for these parameters, the equilibria are polymorphic at one locus. Hence, the variance is positive.

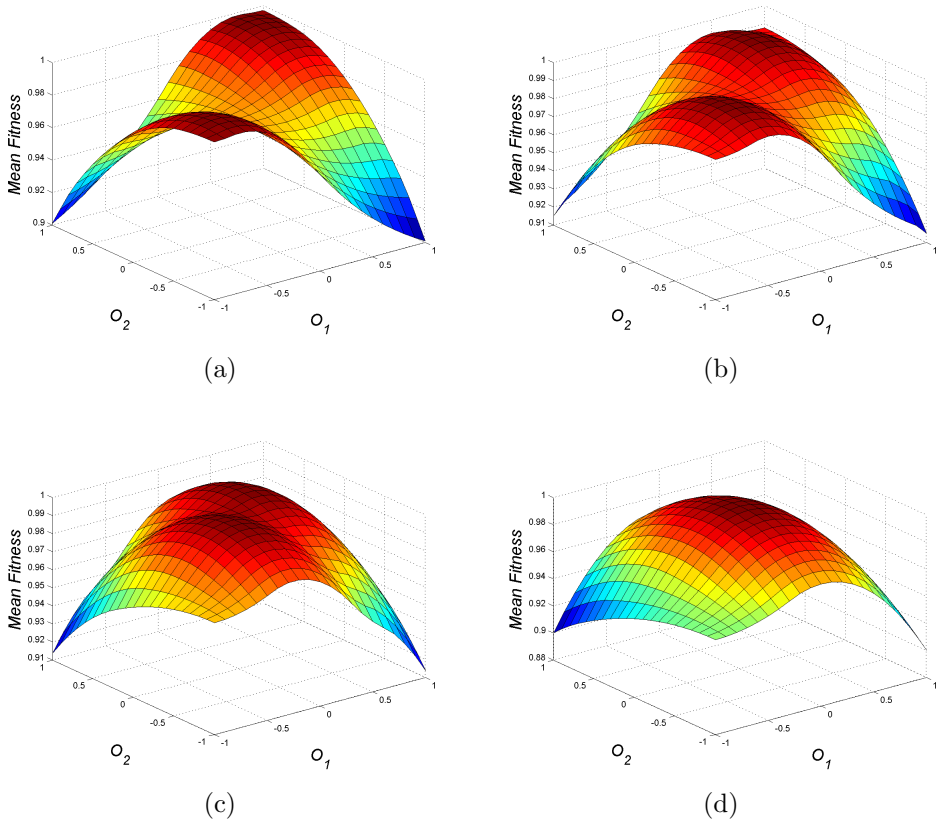


Figure 5.11: The weighted mean fitness of the population at equilibrium is depicted for different positions of the fitness optima. The four figures correspond to four different allelic effects of the minor locus: (a) $\gamma_2 = 0.25$, (b) $\gamma_2 = 0.5$, (c) $\gamma_2 = 0.75$ and (d) $\gamma_2 = 1$. The other parameters are fixed at $s = 0.1$, $c = 0.3$ and $r = 0.001$.

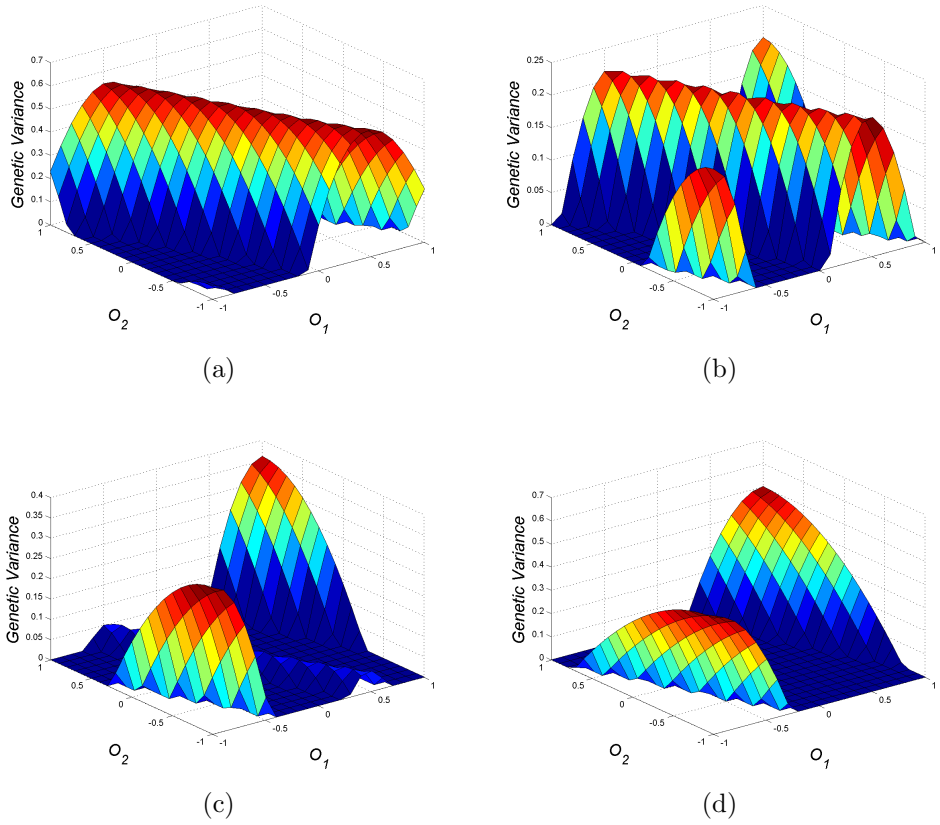


Figure 5.12: The ratio of the equilibrium genetic variance to the maximal genetic variance, $V_{\max} = \frac{1}{2}(1 + \gamma_2^2)$ is plotted for different positions of the fitness optima. The four figures correspond to four different allelic effects of the minor locus: (a) $\gamma_2 = 0.25$, (b) $\gamma_2 = 0.5$, (c) $\gamma_2 = 0.75$ and (d) $\gamma_2 = 1$. The other parameters are fixed at $s = 0.1$, $c = 0.3$ and $r = 0.001$.

6 Summary

In the first chapter, the basic mathematical model was defined. We stated the dynamical system (1.13) that describes the general model invoking selection, recombination and migration. Furthermore, in Section 1.3 we defined the fitness function, namely quadratic stabilizing fitness.

In Chapter 2 we collected the existing results for the model without migration. We distinguished between two cases. In the first one, the double heterozygote is the fittest. Under this assumption, all equilibria and their stability conditions can be computed. Furthermore, the stable fully polymorphic equilibria can be computed explicitly. Assuming that the fitness optimum is shifted, cf. Section 2.2, all the equilibria on the boundary can be derived. Neglecting linkage disequilibrium, the complete dynamics can be analyzed. For this case, no stable polymorphism exists.

Following Bürger (2009), we investigated the two limiting cases of weak migration and strong migration, i.e., weak selection, in the next two chapters.

In Chapter 3 we discussed the case of weak migration. For two isolated demes, we could fully describe the dynamics, under the assumption of linkage equilibrium. For twelve fully polymorphic equilibria we showed that they may be stable (but not simultaneously). Only four of them, i.e., the ones that originate purely from corner equilibria, could be computed explicitly. We also showed, that for these equilibria, weak migration reduces the mean fitness at equilibrium, while it increases the genetic variance at equilibrium.

The other stable fully polymorphic equilibria could not be computed explicitly, but parameter regions were found, for which four stable internal equilibria coexist. This was also verified numerically. Our data showed that for small migration rates, the gamete frequencies were much higher than expected.

For the case of weak selection in Chapter 4, we got qualitatively different results. If migration is very strong, differences of gamete frequencies between demes will be small. Therefore, the dynamics will be similar to the dynamics of a panmictic population with a properly averaged fitness. This is precisely the conclusion of Section 4.2. It was shown that strong migration between two demes under weak quadratic stabilizing selection can never lead to stable polymorphisms. Since the computed stability conditions of the equilibria are not easily interpreted, we also studied the case of deme independent allelic effects. We deduced all the equilibria. It turned out that they are equivalent to the equilibria of the panmictic case with a properly averaged position of the optimum. Also the stability conditions were derived, only for two equilibria they slightly differed from the conditions for a panmictic population. As for the panmictic model, at most two stable equilibria can coexist.

Finally, we discussed a special migration pattern, namely the Levene-model, in Chapter 5. To obtain analytical results we neglected linkage equilibrium. We therefore

assumed weak selection and strong recombination. As the Levene model with weak selection is an example for strong migration, this has to provide the same results as for the general case of strong migration. This was shown to be true. We also analyzed this case numerically. The conclusion is that for relatively strong selection the analytical results are still very good approximations. We then also analyzed the Levene model numerically for arbitrary recombination rates. We numerically established an upper bound for the recombination rate, sufficient for the existence of an internal equilibrium. Furthermore, we numerically found an upper bound for the recombination rate that ensures global convergence.

7 Appendix

7.1 Matlab source code

The following Matlab-code was used to compute the stable equilibria for a given set of parameters for the Levene model with two demes.

First, as after one round of migration the gamete frequencies are deme independent for the Levene model, we used the same starting points in both demes. To be able to use simple matrix multiplication we rewrote the frequencies into an 8-dimensional vector and the migration matrix into an 8×8 matrix of the proper form, which can be seen in the code in line 24:31. It is easily verified that this gives the correct result. Further redefinitions had to be done to be able to use this notation, but they should be self explaining.

The output of the program is a matrix, where every column represents a stable equilibrium. This vector is twelve-dimensional, the first entry is the number of trajectories that converged to it, than there are all the used parameters and the last four entries are the gamete frequencies, again only for one deme as they are deme independent.

```
1  %compute all the stable fixed points for the given parameter set:
2  %O1,O2=the two fitness optima
3  %s=the selection coefficient
4  %g1,g2=the effects of the minor locus in the demes
5  %c=the size of deme one
6  %r=the recombination rate
7  %n=reziproke value of the meshsize for the grid of starting points
8  function[w]=stablefixedpointslevene2(O1,O2,s,g1,g2,c,r,n)
9
10 w=ones(12,1);
11 counter=0;
12 eta=[1;-1;-1;1;1;-1;-1;1];
13 x1=zeros(8,2);
14
15 %produce a set of starting points
16 randpoints=randompoints(n);
17 [¬,m]=size(randpoints);
18
19 %define the migration rates
20 m1=1-c;
21 m2=c;
22
23 %define the migration matrix
24 mig=[1-m1,0,0,0,m1,0,0,0;
25     0,1-m1,0,0,0,m1,0,0;
```

```
    0,0,1-m1,0,0,0,m1,0;
    0,0,0,1-m1,0,0,0,m1;
    m2,0,0,0,1-m2,0,0,0;
    0,m2,0,0,0,1-m2,0,0;
    0,0,m2,0,0,0,1-m2,0;
    0,0,0,m2,0,0,0,1-m2];

%define the fitness matrix
fit=fitness(O1,O2,s,g1,g2);

%define the vector of the fitness value of the
%double heterozygote
w14(1:4,1)=fit(2,3);
w14(5:8,1)=fit(6,7);

%calculate all the equilibrium points and the number of
%trajectories that converge to them
for j=1:m
    x=randpoints(:,j);

    %iterate for a startingpoint x
    for i=1:1000000

        %compute the value of linkage disequilibrium, the
        %marginal fitnesses and the meanfitnesses of the demes
        disequilibrium=x(1)*x(4)-x(2)*x(3);
        marginalfitness=fit*x;
        x1(1:4,1)=x(1:4);
        x1(5:8,2)=x(5:8);
        meanfitness=x1' *marginalfitness;

        %compute the gamete frequencies after selection
        y1=(marginalfitness.*x-eta*(r*disequilibrium).*w14);
        y(1:4,1)=y1(1:4)/meanfitness(1);
        y(5:8,1)=y1(5:8)/meanfitness(2);

        %compute the frequencies after migration
        z=mig*y;

        %check if the change in one generation is small enough
        %to call it a fixed point....
        if abs(z-x)<10^(-8);
            v=z;

            %check if the fixed point is a new fixed point...
            b=checkifcontains(w,v,10^-4);

            %...if so, ad the stable point together with all
            %the parameters to the set of stable equilibria
            if  b==0;
                counter=counter+1;
                w(:,counter)=[1;O1;O2;s;g1;g2;c;r;v(1:4)];

                %...else ad one to the number of trajectories
```

```
80                  %that converge to that equilibrium
81              else w(1,b)=w(1,b)+1;
82              end
83              break;
84              %...else iterate it again
85          else x=z;
86          end
87      end
88  end
89  end
90
91  %produce the set of starting points, with meshsize 1/n before
92  %disturbing them with random numbers
93  function[a]=randompoints(n)
94  a=[];
95  for j=1:n-1
96      for k=1:n-j
97          for l=1:n-j-k
98              if k≠n
99                  if l≠n
100                     if (n-j-k-l)≠0
101                         %compute three random numbers between
102                         %-1/(3n) and 1/(3n)
103                         e=(1-2*rand(1))/(3*n);
104                         f=(1-2*rand(1))/(3*n);
105                         g=(1-2*rand(1))/(3*n);
106                         x1=j/n+e;
107                         x2=k/n+f;
108                         x3=l/n+g;
109                         x=...
110                         [x1;x2;x3;1-(x1+x2+x3);
111                          x1;x2;x3;1-(x1+x2+x3)];
112                         a=horzcat(a,x);
113                     end
114                 end
115             end
116         end
117     end
118 end
119 end
120
121 %define the fitness matrix
122 function[b]=fitness(O1,O2,s,g1,g2)
123 b=zeros(8,8);
124
125 b(1:4,1:4)=...
126     [1 - s*(O1 + 1 + g1)^2,1 - s* (O1 +1)^2,...
127     1 - s* (O1 + g1)^2, 1 - s *O1^2;
128     1 - s *(O1 + 1)^2,1 - s *(O1 + 1 - g1)^2,...
129     1 - s* O1^2, 1 - s* (O1 - g1)^2;
130     1 - s *(O1 + g1)^2, 1 - s* O1^2,...
131     1 - s *(O1 - 1 + g1)^2,1 - s *(O1 - 1)^2;
132     1 - s* O1^2, 1 - s *(O1 -g1)^2,...
133     1 - s *(O1 - 1)^2,1 - s *(O1 - 1 - g1)^2];
```

```
134
135 b(5:8,5:8)=...
136     [1 - s*(O2 + 1 + g2)^2,1 - s* (O2 +1)^2,...
137     1 - s* (O2 + g2)^2, 1 - s *O2^2;
138     1 - s *(O2 + 1)^2,1 - s *(O2 + 1 - g2)^2,...
139     1 - s* O2^2, 1 - s* (O2 - g2)^2;
140     1 - s *(O2 + g2)^2, 1 - s* O2^2,...
141     1 - s *(O2 - 1 + g2)^2,1 - s *(O2 - 1)^2;
142     1 - s* O2^2, 1 - s *(O2 -g2)^2,...
143     1 - s *(O2 - 1)^2,1 - s *(O2 - 1 - g2)^2;];
144
145 end
146
147 %checks for which column of w the distance to v is smaller
148 %than error, output=0 it is not close to any of the columns
149 function[a]=checkifcontains(w,v,error)
150
151 n=size(w);
152 b=[0;0;0;0];
153
154 %compute pointwise distance of v and all the columns of w
155 for j=1:n(2)
156     b(:,j)=abs(w(9:12,j)-v(1:4));
157 end
158
159 %check for each column if the distance is smaller than
160 %error
161 for i=1:n(2)
162     if b(:,i)<error;
163         %if so remember the column number
164         a=i;break;
165     else a=0;
166     end
167 end
168 end
```

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