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Two-Locus Two-Allele Dynamics in the Weak-Selection Limit

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CONTENTS

1. DISCRETE-TIME MODEL

The model presented here is the standard two-locus two-allele discrete-time model, as described first by Lewontin and Kojima (1960). We assume a randomly mating diploid population with discrete generations and big enough population size to ignore effects of random genetic drift.
Let A_1, A_2 be the alleles on the A locus and B_1, B_2 the alleles on the B locus. Let the frequencies of the four gametes $A_1B_1, A_2B_1, A_1B_2, A_2B_2$ be x_1, x_2, x_3, x_4, respectively, with $\sum_{i=1}^{4} x_i = 1$. We denote the viability of an individual with genotype ij by w_{ij}, where $w_{ij} = w_{ji}$ and $w_{14} = w_{23}$. By assuming Hardy-Weinberg proportions the frequency of this genotype is $x_i x_j$. Define the linkage disequilibrium

$$D = x_1 x_4 - x_2 x_3,$$

and the frequency p of the allele A_1 and q of the allele B_1,

$$p = x_1 + x_3, \;\; q = x_1 + x_2. \tag{1.1}$$

Then, we have

$$\begin{aligned} x_1 &= pq + D \\ x_2 &= (1-p)q - D \\ x_3 &= p(1-q) - D \\ x_4 &= (1-p)(1-q) + D. \end{aligned} \tag{1.2}$$

Finally, denote the recombination probability by r.

	A_1A_1	A_1A_2	A_2A_2
B_1B_1	w_{11}	w_{12}	w_{22}
B_1B_2	w_{13}	w_{14}	w_{24}
B_2B_2	w_{33}	w_{34}	w_{44}

Tab. 1.1: Fitness scheme

The evolution of this system is described by

$$x_i' = \frac{x_i w_i \pm w_{14} r D}{\overline{w}} \text{ for } i = 1, 2, 3, 4 \tag{1.3}$$

where the sign is negative for $i = 1, 4$ and positive for $i = 2, 3$. The marginal mean fitness of gamete i is

$$w_i = \sum_{j=1}^{4} w_{ij} x_j,$$

and the mean fitness of the population is

$$\overline{w} = \sum_{j=1}^{4} w_j x_j.$$

The marginal or induced mean fitnesses at the A locus are the quantities that would be observed if only that locus were studied. They are computed as

$$\begin{aligned} w_{A_1A_1} &= (w_{11}x_1^2 + 2w_{13}x_1x_3 + w_{33}x_3^2)/(x_1+x_3)^2 \\ w_{A_1A_2} &= (w_{12}x_1x_2 + 2w_{14}x_1x_4 + w_{34}x_3x_4)/(x_1+x_3)(x_2+x_4) \\ w_{A_2A_2} &= (w_{22}x_3^2 + 2w_{24}x_2x_4 + w_{44}x_4^2)/(x_2+x_4)^2, \end{aligned} \tag{1.4}$$

with similar relations holding for the marginal fitnesses at the B locus.
Another important notion is that of additive epistasis e_i. It is given by $e_i = w_{1i} - w_{2i} - w_{3i} + w_{4i}$ for $i = 1, 2, 3, 4$. The way it is defined here, was first used in this context by Bodmer and Felsenstein (1967). If one assumes non-epistasis and sets $e_i = 0$, the model gets simpler. This is often used in the literature.
The only property known about this model in full generality is that the maximum possible number of equilibria is $2^4 - 1 = 15$, if there are no continua. This was conjectured by Feldman and Karlin and proven by Altenberg (2010). Eight of those are boundary equilibria and therefore seven internal equilibria are possible, as shown by Feldman and Karlin (1970) with a symmetric viability matrix.

2. THE WEAK-SELECTION LIMIT

To determine the dynamics for two loci and two alleles under weak selection, we follow the work of Nagylaki et al. (1999) and let $w_{ij} = 1 + sm_{ij}$ for every i, j. For the case of no selection, $s = 0$, the system (1.3) simplifies to

$$x_i' = x_i \pm rD \text{ for } i = 1, 2, 3, 4. \tag{2.1}$$

For the evolution of the linkage disequilibrium

$$D' = x_1'x_4' - x_2'x_3' = (1-r)D \tag{2.2}$$

holds. Thus D converges to zero if $r > 0$. Hence the linkage-equilibrium manifold, also called the Wright manifold, $\Lambda_0 = \{x : D = 0\}$ is invariant and globally attracting at a uniform geometric rate. For small $s > 0$ (weak selection), the theory of normally hyperbolic manifolds (Fenichel (1971); or Hirsch et al. (1977)) implies the existence of a smooth invariant manifold Λ_s close to Λ_0, which is globally attracting at a geometric rate for (1.3). Thus, on Λ_s, and more generally, for any initial values, after a long time, the linkage disequilibrium D is $O(s)$. (For more on this, including proofs, see Nagylaki (1992)).

We define the marginal fitness m_i in terms of p and q as

$$m_i = m_{i1}pq + m_{i2}(1-p)q + m_{i3}p(1-q) + m_{i4}(1-p)(1-q)$$

and the mean fitness $\overline{m}$ of the population by

$$\overline{m} = m_1pq + m_2(1-p)q + m_3p(1-q) + m_4(1-p)(1-q).$$

Thus we can write $w_i = 1 + sm_i + sD(m_{i1} - m_{i2} - m_{i3} + m_{i4}) = 1 + sm_i + O(s^2)$ and $\overline{w} = 1 + s\overline{m} + sD(m_1 - m_2 - m_3 + m_4) = 1 + s\overline{m} + O(s^2)$.

This implies that the recursion relations for the gene frequencies can be written as

$$p' = x_1' + x_3' = \frac{x_1w_1 - w_{14}rD + x_3w_3 + w_{14}rD}{\overline{w}}. \tag{2.3}$$

After sufficiently long time, we can invoke (1.2), $w_{ij} = 1 + sm_{ij}$ and $D = O(s)$ and this leads, up to order s, to

$$\begin{aligned}
p' =& \frac{(pq + D)(1 + sm_1) + (p(1-q) - D)(1 + sm_3)}{1 + s\overline{m}} && (2.4)\\
=& \frac{pq + D + spqm_1 + p(1-q) - D + sp(1-q)m_3 + O(s^2)}{1 + s\overline{m}}\\
=& p\frac{1 + s\overline{m} - s\overline{m} + s(qm_1 + (1-q)m_3)}{1 + s\overline{m}} + O(s^2)\\
=& p + sp\frac{qm_1 + (1-q)m_3 - \overline{m}}{1 + s\overline{m}} + O(s^2)\\
=& p + sp(1-p)\frac{q(m_1 - m_2) + (1-q)(m_3 - m_4)}{1 + s\overline{m}} + O(s^2). && (2.5)
\end{aligned}$$

We can now approximate the discrete model (2.5) by a continuous model under the assumption of weak selection. We rescale time according to $t = \lfloor \tau/s \rfloor$, where $\lfloor\rfloor$ denotes the Gauss bracket. Then

s may be interpreted as generation length and for $p(t)$ satisfying the difference equation (2.5) we write $\pi(\tau) = p(t)$. Then we obtain formally

$$\frac{d\pi}{d\tau} = \lim_{s\downarrow 0} \frac{1}{s}[\pi(\tau+s) - \pi(\tau)] = \lim_{s\downarrow 0} \frac{1}{s}[p(t+1) - p(t)].$$

Ignoring higher order terms in s, we get from (2.5)

$$p(t+1) - p(t) = sp(1-p)\frac{q(m_1 - m_2) + (1-q)(m_3 - m_4)}{1 + s\overline{m}}.$$

Therefore $\dot{\pi} = \pi(1-\pi)[q(m_1 - m_2) + (1-q)(m_3 - m_4)]$.
By doing the same with q and replacing π again with p, we get the system

$$\begin{aligned} \dot{p} &= p(1-p)[q(m_1 - m_2) + (1-q)(m_3 - m_4)], \\ \dot{q} &= q(1-q)[p(m_1 - m_3) + (1-p)(m_2 - m_4)]. \end{aligned} \tag{2.6}$$

System (2.6) is called the *weak-selection limit* of (1.3). The map (1.3), restricted on Λ_s, behaves like a first order numerical discretization procedure for the differential equation (2.6), with step size s, whereas (2.5) is essentially the Euler scheme for (2.6). Additionally Theorem 3.1 of Nagylaki et al. (1999) applies and states that if each equilibrium of (2.6) is regular, then each solution $\mathbf{x}(t)$ of (1.3) converges to a fixed point of (1.3) as $t \to \infty$. $\mathbf{x}(t)$ denotes the vector of all genotype frequencies x_i at time t.
In a continuous-time model, the (malthusian) fitness m_{ij} of a genotype ij can be interpreted as its birth rate minus its death rate.
One can write marginal fitness, mean fitness and the dynamics of the continuous system in form of matrices and vectors in the following way:

$$\begin{pmatrix} m_1 & m_2 \\ m_3 & m_4 \end{pmatrix} = \begin{pmatrix} q & 1-q & 0 \\ 0 & q & 1-q \end{pmatrix} \begin{pmatrix} m_{11} & m_{12} & m_{22} \\ m_{13} & m_{14} & m_{24} \\ m_{33} & m_{34} & m_{44} \end{pmatrix} \begin{pmatrix} p & 0 \\ 1-p & p \\ 0 & 1-p \end{pmatrix}, \tag{2.7a}$$

$$\overline{m} = \begin{pmatrix} q, & 1-q \end{pmatrix} \begin{pmatrix} m_1 & m_2 \\ m_3 & m_4 \end{pmatrix} \begin{pmatrix} p \\ 1-p \end{pmatrix}, \tag{2.7b}$$

$$\dot{p} = p(1-p) \begin{pmatrix} q, & 1-q \end{pmatrix} \begin{pmatrix} m_1 & m_2 \\ m_3 & m_4 \end{pmatrix} \begin{pmatrix} 1 \\ -1 \end{pmatrix}, \tag{2.7c}$$

$$\dot{q} = q(1-q) \begin{pmatrix} 1, & -1 \end{pmatrix} \begin{pmatrix} m_1 & m_2 \\ m_3 & m_4 \end{pmatrix} \begin{pmatrix} p \\ 1-p \end{pmatrix}. \tag{2.7d}$$

The marginal fitnesses at the A and B locus (1.4) are much simpler in terms of allele frequencies rather than genotype frequencies. The marginal fitnesses at the A locus become:

$$m_{A_1A_1} = m_{11}q^2 + 2m_{13}q(1-q) + m_{33}(1-q)^2, \tag{2.8a}$$

$$m_{A_1A_2} = m_{12}q^2 + 2m_{14}q(1-q) + m_{34}(1-q)^2, \tag{2.8b}$$

$$m_{A_2A_2} = m_{22}q^2 + 2m_{24}q(1-q) + m_{44}(1-q)^2, \tag{2.8c}$$

or in matrix notation:

$$\begin{pmatrix} m_{A_1A_1}, & m_{A_1A_2}, & m_{A_2A_2} \end{pmatrix} = \begin{pmatrix} q, & 1-q \end{pmatrix} \begin{pmatrix} q & 1-q & 0 \\ 0 & q & 1-q \end{pmatrix} \begin{pmatrix} m_{11} & m_{12} & m_{22} \\ m_{13} & m_{14} & m_{24} \\ m_{33} & m_{34} & m_{44} \end{pmatrix}.$$

Similar at the B locus:

$$m_{B_1B_1} = m_{11}p^2 + 2m_{12}p(1-p) + m_{22}(1-p)^2, \tag{2.9a}$$

$$m_{B_1B_2} = m_{13}p^2 + 2m_{14}p(1-p) + m_{24}(1-p)^2, \tag{2.9b}$$

$$m_{B_2B_2} = m_{33}p^2 + 2m_{34}p(1-p) + m_{44}(1-p)^2, \tag{2.9c}$$

again in matrix notation:

$$\begin{pmatrix} m_{B_1B_1} \\ m_{B_1B_2} \\ m_{B_2B_2} \end{pmatrix} = \begin{pmatrix} m_{11} & m_{12} & m_{22} \\ m_{13} & m_{14} & m_{24} \\ m_{33} & m_{34} & m_{44} \end{pmatrix} \begin{pmatrix} p & 0 \\ 1-p & p \\ 0 & 1-p \end{pmatrix} \begin{pmatrix} p \\ 1-p \end{pmatrix}. \tag{2.9d}$$

This shows the two alternative representations of $\overline{m}$:

$$\overline{m} = p^2 m_{A_1A_1} + 2p(1-p)m_{A_1A_2} + (1-p)^2 m_{A_2A_2} = q^2 m_{B_1B_1} + 2q(1-q)m_{B_1B_2} + (1-q)m_{B_2B_2} \tag{2.10}$$

With equations (2.10) it is easy to compute $\frac{\partial \overline{m}}{\partial p}$ and $\frac{\partial \overline{m}}{\partial q}$, since the marginal allele frequencies do only depend on one of the two variables.

$$\frac{1}{2}\frac{\partial \overline{m}}{\partial p} = p m_{A_1A_1} + (1-2p)m_{A_1A_2} + (p-1)m_{A_2A_2} = q(m_1 - m_2) + (1-q)(m_3 - m_4) \tag{2.11a}$$

$$\frac{1}{2}\frac{\partial \overline{m}}{\partial q} = q m_{B_1B_1} + (1-2q)m_{B_1B_2} + (q-1)m_{B_2B_2} = p(m_1 - m_3) + (1-p)(m_2 - m_4) \tag{2.11b}$$

Form this we see

$$\dot{p} = p(1-p)\frac{1}{2}\frac{\partial \overline{m}}{\partial p} \tag{2.12a}$$

$$\dot{q} = q(1-q)\frac{1}{2}\frac{\partial \overline{m}}{\partial q}. \tag{2.12b}$$

This looks like a gradient system with positive prefactors and one calls this a Shahshahani gradient system (see Shahshahani (1979) and Hofbauer and Sigmund (1998) for more on this). Using the equations (2.12), one can easily compute the time derivative of the mean fitness

$$\begin{aligned} \dot{\overline{m}} = \frac{\partial \overline{m}}{\partial p}\dot{p} + \frac{\partial \overline{m}}{\partial q}\dot{q} &= 2p(1-p)[q(m_1 - m_2) + (1-q)(m_3 - m_4)]^2 \\ &+ 2q(1-q)[p(m_1 - m_3) + (1-p)(m_2 - m_4)]^2 \geq 0 \,\forall p, q \in [0,1], \end{aligned} \tag{2.13}$$

with equality only at the equilibria. Therefore $\overline{m}$ is a strict Lyapunov function for our system (2.6). This shows that the ω-limit of every solution of (2.6) consists of equilibria. This excludes complex behaviour such as limit cycles or chaos as proven by Nagylaki et al. (1999) for arbitrary number of loci and alleles.

We say the A locus exhibits induced or marginal overdominance if the inequalities

$$m_{A_1A_2} > m_{A_1A_1} \text{ and } m_{A_1A_2} > m_{A_2A_2} \tag{2.14}$$

hold for all $p, q \in [0,1]$. If one reverses both inequality signs, then one speaks of induced or marginal underdominance. A similar relation can be defined at the B locus. This terminology was introduced by Bodmer and Felsenstein (1967).

In contrast to that, we define the term "overdominance at the margins" or "overdominance on the boundary" by the relations

$$\begin{gathered} m_{ij} > m_{ii} \text{ and } m_{ij} > m_{jj} \\ \forall (i,j) \in \{(1,2),(1,3),(2,4),(3,4)\}. \end{gathered} \tag{2.15}$$

This is the starting point for our investigation of the behaviour of the dynamics (2.6).

3. ANALYSING THE DIFFERENTIAL EQUATIONS

3.1 General results and derivations

We start this section by writing out (2.6) in detail:

$$\begin{aligned}\dot{p} = p(1-p)[q^2(p(m_{11}-m_{12}) + (1-p)(m_{12}-m_{22})) + (1-q)^2(p(m_{33}-m_{34})+ \\ + (1-p)(m_{34}-m_{44})) + 2q(1-q)(p(m_{13}-m_{14}) + (1-p)(m_{14}-m_{24}))]\end{aligned} \tag{3.1a}$$

$$\begin{aligned}\dot{q} = q(1-q)[p^2(q(m_{11}-m_{13}) + (1-q)(m_{13}-m_{33})) + (1-p)^2(q(m_{22}-m_{24})+ \\ + (1-q)(m_{24}-m_{44})) + 2p(1-p)(q(m_{12}-m_{14}) + (1-q)(m_{14}-m_{34}))]\end{aligned} \tag{3.1b}$$

This is a dynamical system in two dimensions with nine free parameters. Since p and q denote the frequencies of alleles A_1 and B_1, their values have to be between 0 and 1 to be biologically reasonable. Thus the dynamics lives on the unit square, where p is the horizontal axis pointing leftwards and q the vertical one pointing upwards, such that the entry m_{44} of the fitness scheme in table 1.1 corresponds to the lower right corner $C_4 = (0,0)$ of the unit square. This is reasonable, since m_{44} is the viability parameter of a genotype in which neither allele A_1, nor B_1 is present.
The right hand side is of degree three in p and two in q for the first equation (3.1a) and the other way round for (3.1b). We want to study the equilibria of the system. To do so one has to find the isoclines of the equations. There are three for (3.1a):

$$p = 0, \; p = 1 \tag{3.2}$$

and

$$\begin{aligned}p = [(m_{12}-m_{22})q^2 + 2(m_{14}-m_{24})q(1-q) + (m_{34}-m_{44})(1-q)^2]/ \\ [(2m_{12}-m_{11}-m_{22})q^2 + 2(2m_{14}-m_{13}-m_{24})q(1-q) + (2m_{34}-m_{33}-m_{44})(1-q)^2]\end{aligned} \tag{3.3}$$

and three for (3.1b):

$$q = 0, \; q = 1 \tag{3.4}$$

and

$$\begin{aligned}q = [(m_{13}-m_{33})p^2 + 2(m_{14}-m_{34})p(1-p) + (m_{24}-m_{44})(1-p)^2]/ \\ [(2m_{13}-m_{11}-m_{33})p^2 + 2(2m_{14}-m_{12}-m_{34})p(1-p) + (2m_{24}-m_{22}-m_{44})(1-p)^2].\end{aligned} \tag{3.5}$$

We can write (3.3) and (3.5) in the simpler form

$$p = f(q) = \frac{m_{A_1A_2} - m_{A_2A_2}}{2m_{A_1A_2} - m_{A_1A_1} - m_{A_2A_2}}, \tag{3.6a}$$

$$q = g(p) = \frac{m_{B_1B_2} - m_{B_2B_2}}{2m_{B_1B_2} - m_{B_1B_1} - m_{B_2B_2}} \tag{3.6b}$$

by using (2.8).
From (3.2) and (3.4) we can conclude that all four corners $C_i, \; i = 1,2,3,4$ of the unit square are equilibria. Their stability properties are easy to calculate and to interprete.

	first eigenvalue	second eigenvalue
$C_4 = (0,0)$	$m_{34} - m_{44}$	$m_{24} - m_{44}$
$C_3 = (1,0)$	$m_{34} - m_{33}$	$m_{13} - m_{33}$
$C_2 = (0,1)$	$m_{12} - m_{22}$	$m_{24} - m_{22}$
$C_1 = (1,1)$	$m_{12} - m_{11}$	$m_{13} - m_{11}$

Tab. 3.1: Eigenvalues of the corner equilibria, where the eigenvector to the first eigenvalue is parallel to the p-axis and the other one to the q-axis.

From standard local stability theory, we know that each of them is asymptotically stable and saturated (explained in a minute), if both eigenvalues are negative. Those are given in table 3.1. Evaluating (3.6a) and (3.6b) at $p, q = 0$ and $p, q = 1$ yields the equilibria

(3.7a) $$C_{34}: \ p = \frac{m_{34} - m_{44}}{2m_{34} - m_{33} - m_{44}} \text{ at } q = 0$$

(3.7b) $$C_{12}: \ p = \frac{m_{12} - m_{22}}{2m_{12} - m_{11} - m_{22}} \text{ at } q = 1$$

(3.7c) $$C_{24}: \ q = \frac{m_{24} - m_{44}}{2m_{24} - m_{22} - m_{44}} \text{ at } p = 0$$

(3.7d) $$C_{13}: \ q = \frac{m_{13} - m_{33}}{2m_{13} - m_{11} - m_{33}} \text{ at } p = 1.$$

Such an equilibrium is admissible if and only if its heterozygous fitness value is greater or smaller than both its neighbouring homozygous fitness values. This is exactly the definition of over- resp. underdominance at the margins as defined in (2.15). For example, C_{34} is admissible whenever $(m_{34} - m_{44})(m_{34} - m_{33}) \geq 0$ and similar for the other C_{ij}'s. Since the p-axis points leftwards, we have a correspondence between the fitness scheme in table 1.1 and the unit square, such that we can easily read off the name of the boundary equilibria (C with the same index as the corresponding fitness parameter, only one number for the corner and two for the edge-equilibria) and the eigenvalues of the corner equilibria and the fitness parameters corresponding to the admissibility of C_{ij}.

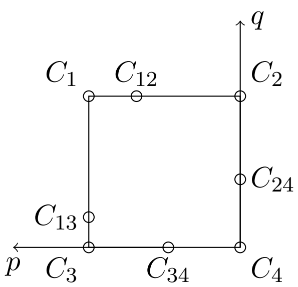


Fig. 3.1: The state space with all boundary equilibria admissible

To determine stability and/or saturation, one has to compute the Jacobi matrix of (2.6) and the sign of each of its two eigenvalues, at C_{ij}.
An equilibrium is called linearly stable or sink, iff both eigenvalues of the Jacobi matrix at the equilibrium are negative. It is called fully unstable or source, iff both are positive. An equilibrium is a saddlepoint, iff the eigenvalues have different sign.
For a boundary equilibrium the Jacobi matrix has a special form, since it is in block form and in particular for this two-dimensional setting in triangular form. The diagonal element in the row of the zero entry is the so called *external eigenvalue* and the other one the *internal eigenvalue*, since one can read off the eigenvalues of a triangular matrix directly from the diagonal. The sign

of the internal eigenvalue describes the flow around the equilibrium within the boundary and the sign of the external eigenvalue the flow around the equilibrium transversal to the boundary. If the external eigenvalue is nonpositive, the equilibrium is called *saturated* or *externally stable* (see Hofbauer and Sigmund (1998)). It can be interpreted as follows: the allele missing on this edge cannot invade into the population near this boundary equilibrium.
If we first compute the Jacobian on each of the edges, not yet at the C_{ij} itself, we see that the external eigenvalues are determined by the marginal fitnesses at the two loci:

$$\lambda_{34} = m_{B_1B_2} - m_{B_2B_2} \tag{3.8a}$$
$$\lambda_{12} = m_{B_1B_2} - m_{B_1B_1} \tag{3.8b}$$
$$\lambda_{24} = m_{A_1A_2} - m_{A_2A_2} \tag{3.8c}$$
$$\lambda_{13} = m_{A_1A_2} - m_{A_1A_1}. \tag{3.8d}$$

Here λ_{ij} is the external eigenvalue at the boundary on which C_{ij} sits. On each edge of the unit square exactly one allele is missing and the marginal fitnesses at the locus from where it is missing, define the external eigenvalue.
The eigenvalue λ_{ij} evaluated at the corresponding C_{ij} is

$$\begin{aligned}\hat\lambda_{34} =&\frac{1}{\xi_{34}^2}[(m_{13}-m_{33})(m_{34}-m_{44})^2+2(m_{14}-m_{34})(m_{34}-m_{44})(m_{34}-m_{33})+\\ &+(m_{24}-m_{44})(m_{34}-m_{33})^2],\end{aligned} \tag{3.9a}$$
$$\begin{aligned}\hat\lambda_{12} =&\frac{1}{\xi_{12}^2}[(m_{13}-m_{11})(m_{12}-m_{22})^2+2(m_{14}-m_{12})(m_{12}-m_{22})(m_{12}-m_{11})+\\ &+(m_{24}-m_{22})(m_{12}-m_{11})^2],\end{aligned} \tag{3.9b}$$
$$\begin{aligned}\hat\lambda_{24} =&\frac{1}{\xi_{24}^2}[(m_{12}-m_{22})(m_{24}-m_{44})^2+2(m_{14}-m_{24})(m_{24}-m_{44})(m_{24}-m_{22})+\\ &+(m_{34}-m_{44})(m_{24}-m_{22})^2],\end{aligned} \tag{3.9c}$$
$$\begin{aligned}\hat\lambda_{13} =&\frac{1}{\xi_{13}^2}[(m_{12}-m_{11})(m_{13}-m_{33})^2+2(m_{14}-m_{13})(m_{13}-m_{33})(m_{13}-m_{11})+\\ &+(m_{34}-m_{33})(m_{13}-m_{11})^2],\end{aligned} \tag{3.9d}$$

where $\xi_{ij} = 2m_{ij} - m_{ii} - m_{jj}$, $\forall (i,j) \in \{(1,2),(1,3),(2,4),(3,4)\}$. The sign of $\hat\lambda_{ij}$ determines whether C_{ij} is saturated or not. Since the m_{14} shows up in each eigenvalue at the same position, for suitable large $|m_{14}|$ the external eigenvalues have all the same sign as m_{14}. The internal eigenvalues μ_{ij} of the Jacobian at C_{ij} are listed here:

$$\mu_{34} = \frac{(m_{34}-m_{33})(m_{34}-m_{44})}{m_{33}-2m_{34}+m_{44}} \tag{3.10a}$$
$$\mu_{12} = \frac{(m_{12}-m_{11})(m_{12}-m_{22})}{m_{11}-2m_{12}+m_{22}} \tag{3.10b}$$
$$\mu_{24} = \frac{(m_{24}-m_{22})(m_{24}-m_{44})}{m_{22}-2m_{24}+m_{44}} \tag{3.10c}$$
$$\mu_{13} = \frac{(m_{13}-m_{11})(m_{13}-m_{33})}{m_{11}-2m_{13}+m_{33}} \tag{3.10d}$$

If C_{ij} is admissible, then the numerator of the corresponding μ_{ij} is positive, while the sign of the denominator is the opposite of the sign of one of the factors of the numerators. If the boundary, on which the corresponding C_{ij} sits, is in overdominance (attention: this means overdominance on the boundary in the sense of (2.15)), then μ_{ij} is negative and the corresponding C_{ij} is internally stable. The factors of the numerator however are each an eigenvalue of the Jacobi matrix of the neighbouring corner equilibria. If both neighbouring corner equilibria have a negative eigenvalue in direction of the C_{ij}, it follows that the μ_{ij} is positive and the other way round. Additionally we

see that for different sign of the eigenvalues of the neighbouring corner equilibria, the equilibrium of this edge is not admissible.
So we have seen that there are up to eight equilibria on the boundary of the unit square, if we ignore the degenerate cases, where a whole edge consists of infinitely many equilibria and those are ignored throughout this thesis.
The question is how many are inside of the unit square? The following theorem on the upper bound sheds a first light on this problem.

Theorem 1. *There are at most* 5 *equilibria for* (3.1) *with* $p, q \in (0, 1)$, *except for the degenerate case of a continuum of equilibria.*

Proof. To determine the interior equlibria we have to compute the intersection of the two isoclines (3.6a) and (3.6b). Thus we have to solve the fixed point equation

$$p = f(g(p)). \tag{3.11}$$

$f(q)$ and $g(p)$ have the same form in terms of the degree of the numerator and denominator which is two. So by inserting one equation into the other we have the rational function $f(g(p))$ with numerator and denominator both polynomial of degree 4. Therefore one sees that we have to compute the zeros of a polynomial of degree 5 for the determination of the intersection points. By the fundamental theorem of algebra, we conclude that there are at most 5 intersection points. □

There is no explicit formula for the zeroes of a polynomial of degree higher than 4 and therefore we have to try otherwise in order to derive useful results.
One thing we can do is to compute the Jacobian of interior points:

Lemma 1. *Let us define* $m_A = m_{A_1A_1} + m_{A_2A_2} - 2m_{A_1A_2}$, $m_B = m_{B_1B_1} + m_{B_2B_2} - 2m_{B_1B_2}$ *and* $\hat{m} = m_1 - m_2 - m_3 + m_4$, *then the Jacobi matrix at any point in the interior of the unit square is given by*

$$J_{int} = \begin{pmatrix} p(1-p)m_A & 2p(1-p)\hat{m} \\ 2q(1-q)\hat{m} & q(1-q)m_B \end{pmatrix} \tag{3.12}$$

and its eigenvalues are real.

Proof. For the Jacobi matrix, one needs to compute the four derivatives $\frac{\partial \dot{p}}{\partial p}, \frac{\partial \dot{p}}{\partial q}, \frac{\partial \dot{q}}{\partial p}, \frac{\partial \dot{q}}{\partial q}$ restricted to the interior. This restriction means that the terms $q(m_1 - m_2) + (1-q)(m_3 - m_4)$ and $p(m_1 - m_3) + (1-p)(m_2 - m_4)$ are equal to zero after taking the derivative. For $\frac{\partial \dot{p}}{\partial p}$ this yields:

$$\begin{aligned}\frac{\partial \dot{p}}{\partial p} &= (1-2p)(q(m_1 - m_2) + (1-q)(m_3 - m_4)) + p(1-p)\frac{\partial}{\partial p}(q(m_1 - m_2) + (1-q)(m_3 - m_4)) \\ &= p(1-p)\frac{\partial}{\partial p}(q(m_1 - m_2) + (1-q)(m_3 - m_4)) = \\ &= p(1-p)m_A.\end{aligned}$$

The last step is simple algebra. For $\frac{\partial \dot{p}}{\partial q}$ we compute:

$$\begin{aligned}\frac{\partial \dot{p}}{\partial q} &= p(1-p)\frac{\partial \begin{pmatrix} q, & 1-q \end{pmatrix} \begin{pmatrix} m_1 & m_2 \\ m_3 & m_4 \end{pmatrix} \begin{pmatrix} 1 \\ -1 \end{pmatrix}}{\partial q} \\ &= p(1-p)[\begin{pmatrix} 1, & -1 \end{pmatrix} \begin{pmatrix} m_1 & m_2 \\ m_3 & m_4 \end{pmatrix} \begin{pmatrix} 1 \\ -1 \end{pmatrix} + \begin{pmatrix} q, & 1-q \end{pmatrix} \frac{\partial \begin{pmatrix} m_1 & m_2 \\ m_3 & m_4 \end{pmatrix}}{\partial q} \begin{pmatrix} 1 \\ -1 \end{pmatrix}] \\ &= p(1-p)[(m_1 - m_2 - m_3 + m_4) + \begin{pmatrix} q, & 1-q \end{pmatrix} \begin{pmatrix} 1 & -1 & 0 \\ 0 & 1 & -1 \end{pmatrix} M \begin{pmatrix} p & 0 \\ 1-p & p \\ 0 & 1-p \end{pmatrix} \begin{pmatrix} 1 \\ -1 \end{pmatrix}] \\ &= 2p(1-p)\hat{m}.\end{aligned}$$

We used the matrix representation derived in (2.7c) for computing the derivative. The other derivatives are computed the same way.
Next we compute the discriminant, which is the square of the trace minus four times the determinant:

$$\begin{aligned} &p^2(1-p)^2m_A^2 + 2pq(1-p)(1-q)m_Am_B + q^2(1-q)^2m_B^2 - 4pq(1-p)(1-q)[m_Am_B - 4\hat{m}^2] \\ =&(p(1-p)m_A - q(1-q)m_B)^2 + 16pq(1-p)(1-q)\hat{m}^2 \end{aligned}$$

The outcome is a sum of two squares and for $p, q \in [0,1]$, the discriminant is positive. Thus there cannot be complex eigenvalues. □

This lemma will prove itself very helpful in the later chapters together with the following

Proposition 1 (planar Routh-Hurwitz criterion)**.** *A planar equilibrium $\hat{x}$ is a*

- *saddlepoint* $\Leftrightarrow \det J_{\hat{x}} < 0$,
- *sink* $\Leftrightarrow \det J_{\hat{x}} > 0$ *and* $\mathrm{tr}(J_{\hat{x}}) < 0$,
- *source* $\Leftrightarrow \det J_{\hat{x}} > 0$ *and* $\mathrm{tr}(J_{\hat{x}}) > 0$.

Proof. in every ordinary differential equations text book. □

Another way to analyse the dynamics further will be employed in the next section.

3.2 The flow on the boundary

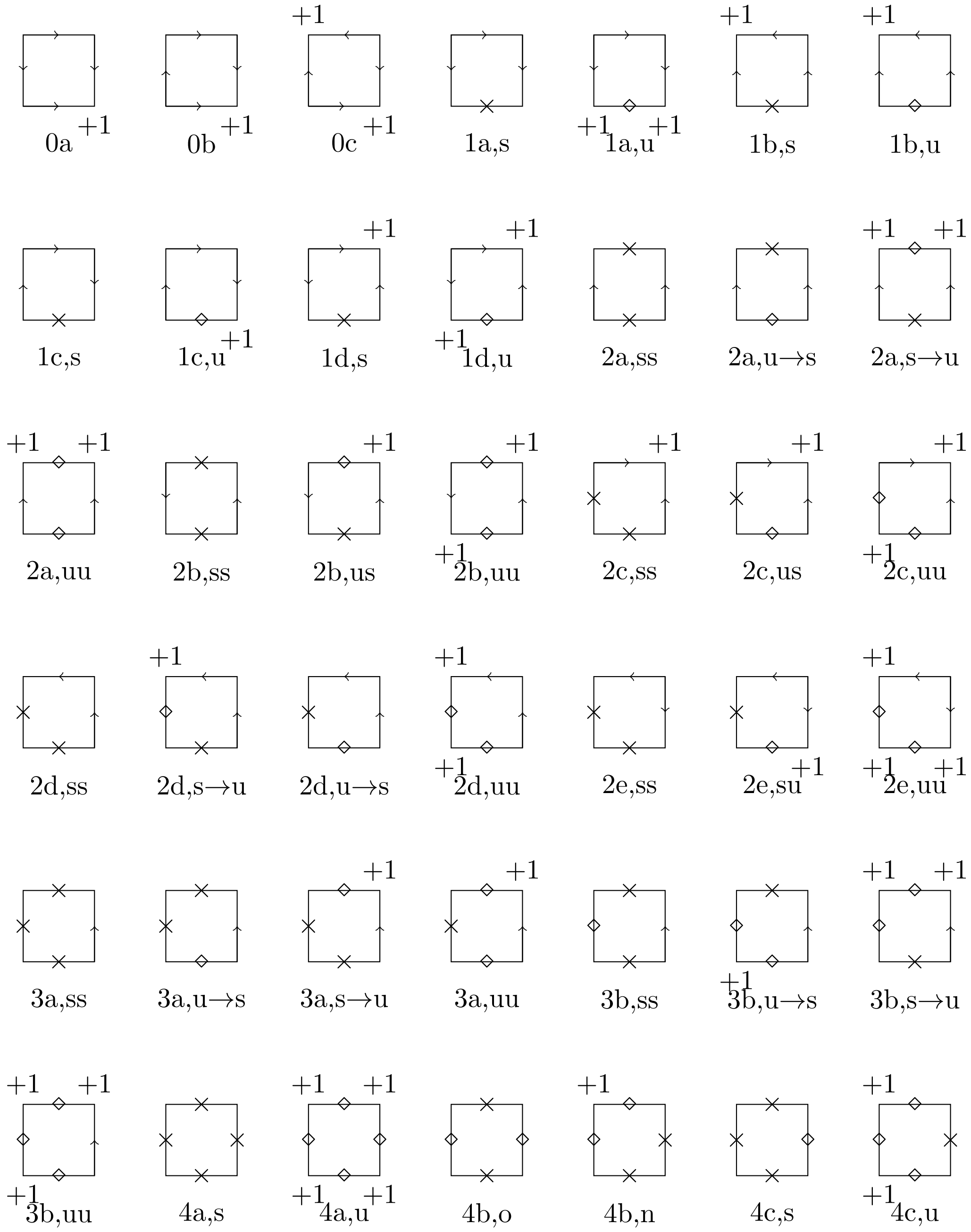


Fig. 3.2: All 42 possible boundary flows. The symbol $\times$ shows the meeting of two arrow tips, for an internally stable fixed point on the edge and symbol $\diamond$ shows two fins of arrows that go apart, for an internally unstable one, while an arrow on the edge represents the flow in absence of an equilibrium there. If the flow on the two neighbouring edges of a corner point to the corner, then this corner-equilibrium is asymptotically stable and hence saturated with index $+1$. The case numbering follows the following rules:

- The number represents the number of fixed points on the edges of this case
- The letter orders the different flows with the same number of boundary fixed points.
- s and u stand for internally stable resp. unstable edge-equilibria.
- If needed, an arrow from s to u, or reversed, represents the boundary flow direction from the one to the other edge-equilibrium.
- Exception is in 4b, where o (n) stands for opposing (neighbouring) equilibria with same internal stability.

First we determine all possible flows on the boundary. As mentioned before, on each side of the square there can be at most one fixed point. It can be internally stable or internally unstable. As it can be seen in figure 3.2 there are 42 different (up to symmetry operations like rotations and reflections of the square) boundary flows possible.
To reduce the number of possible boundary cases further, we search fig. 3.2 for flow reversals. This means, we reverse all arrows and stable equilibria get completely unstable and reversed. If we do this with each of the 42 cases, we notice that 10 are invariant (0a, 0b, 0c, 2a,u→ s, 2a,s→ u, 2b,us, 2d,s→ u, 2d,u→s, 4b,o, 4b,n), this means a reversed flow results in the same phase portrait. For the other 32 cases always two are the flow reversed pictures of each other and can therefore be seen as one case. Thus we are left with 26 cases if we take flow reversals into account.

3.3 Extending the boundary flow

In the next step, we extend the flow to a neighbourhood of the boundary. The following special version of an index theorem by Hofbauer (1990) will be useful.

Theorem 2. *For the system of differential equations* (3.1) *with* $p, q \in [0,1]$*, the following holds: If there are only finitely many saturated equilibria, then:*

$$\sum_{\overline{x}\ \text{saturated}} \operatorname{ind}(\overline{x}) = +1$$

holds.

Proof. For the proof, we refer to Hofbauer (1990). □

A short reminder on saturation on the square (assuming that there are no zero eigenvalues):

- A corner equilibrium is saturated if and only if both eigenvalues are negative.
- An edge-equilibrium is saturated if and only if the external eigenvalue is negative.
- An internal equilibrium is per definition always saturated.

Assume the Jacobi matrix at the equilibrium $\overline{x}$ has no eigenvalues equal zero and k positive eigenvalues. Then the point is called regular and the index for a regular point $\overline{x}$ is defined by

$$\operatorname{ind}(\overline{x}) = \operatorname{sgn}(\det(-J(\overline{x}))) = (-1)^k.$$

It follows that a point in the plane with index -1 has to be a saddle point, because stable points (sinks) and completely unstable points (sources) have an even number of positive eigenvalues.
We now compute the sum of the indices of the saturated boundary equilibria for each case and call this number the *boundary index sum* δ. Since the sign of the external eigenvalue of the C_{ij} isn't fully determined by the boundary flow alone, we have several case distinctions for C_{ij} being saturated, if it exists. Fig. 3.3 gives an example for the case distinction for the boundary flow class $1a, s$.
Ordering the 42 cases with respect to the boundary index sum, we see that δ could range from -2 to $+4$, with 1 case with $\delta = -2$, 10 with $\delta = -1$, 32 cases where $\delta = 0$, 41 where $\delta = +1$, 34 where $\delta = +2$, 12 where it is $\delta = +3$ and finally 2 cases with $\delta = +4$. This gives a total of 132 different possible cases. If we do the same counting with the 26 flow reversal classes, we get 80 different cases with respect to the value of δ. Note that flow reversal does not change the number and the index of internal equilibria. Therefore, δ is also not changed, because the sum of the internal indices plus δ is always 1 according to theorem 2.
If all saturated points are regular, then their number has to be odd. Therefore for the cases with an odd boundary index sum there has to be an even number of equilibria in the interior, because every internal equilibrium is saturated, but at most 4, since it is the biggest even number below

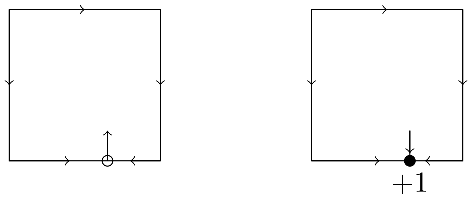


Fig. 3.3: Boundary flow class $1a, s$ with different sign of the external eigenvalue at the edge-equilibrium. On the left the edge-equilibrium is a saddle and non saturated, while on the right hand side the edge-equilibrium is asymptotically stable and saturated with index $+1$. Therefore for the left picture $\delta = 0$ and for the right one $\delta = +1$. For the left picture there must be at least one internal equilibrium. Since mean fitness must have a maximum on the state space, there has to be a stable interior equilibrium. But in general, the full flow in the interior of the square can not be deduced from this.

the maximum of 5 internal fixed points. Similarly for the boundary index sum being even, there can be $1, 3$ or 5 equilibria in the interior, except the case of $\delta = +4$ and $\delta = -2$, where at least three internal fixed points have to exists.
Until now the case distinctions where only formal. Nothing was said about the existence of each particular case in our model. The next subsections tells us more about it.

3.3.1 Some impossibilities

The case of $\delta = -2$ would lead to at least three simultaneously stable or repelling internal equilibria and therefore very interesting. In fact with a little algebra it can be shown that this is impossible and the same holds for some cases with $\delta = -1$.

Theorem 3. *For case $4b, o$, $\delta = -2$ is not possible.*
For the cases $4b, o$; $3b, ss$; $3a, uu$ and $2a, u \to s$, $\delta = -1$ is not possible.
The case $4b, o$, $\delta = 0$, with two neighbouring edge-equilibria saturated and the other two not, is not possible.

Proof. The proof works similar for all claims. We show it only once for $4b, o$ and $\delta = -2$:
As figure 3.2 shows in the case $4b, o$, there are four equilibria on the boundary edges. The upper (C_{12}) and the lower (C_{34}) one are internally stable, while the two others (C_{24}, C_{13}) are internal unstable. We assume that C_{34}, C_{12} are not saturated, while the other two are. This gives $\delta = -2$. Next we compute the conditions for this situation for the viability parameters. $\hat{\lambda}_{34}$ and $\hat{\lambda}_{12}$ are positive:

$$\begin{aligned}
&(m_{13} - m_{33})(m_{34} - m_{44})^2 + 2(m_{14} - m_{34})(m_{34} - m_{44})(m_{34} - m_{33}) + \\
&+(m_{24} - m_{44})(m_{34} - m_{33})^2 > 0, \\
&(m_{13} - m_{11})(m_{12} - m_{22})^2 + 2(m_{14} - m_{12})(m_{12} - m_{22})(m_{12} - m_{11}) + \\
&+(m_{24} - m_{22})(m_{12} - m_{11})^2 > 0,
\end{aligned} \tag{3.13}$$

whereas $\hat{\lambda}_{24}$ and $\hat{\lambda}_{13}$ are negative:

$$\begin{aligned}
&(m_{12} - m_{22})(m_{24} - m_{44})^2 + 2(m_{14} - m_{24})(m_{24} - m_{44})(m_{24} - m_{22}) + \\
&+(m_{34} - m_{44})(m_{24} - m_{22})^2 < 0, \\
&(m_{12} - m_{11})(m_{13} - m_{33})^2 + 2(m_{14} - m_{13})(m_{13} - m_{33})(m_{13} - m_{11}) + \\
&+(m_{34} - m_{33})(m_{13} - m_{11})^2 < 0.
\end{aligned} \tag{3.14}$$

In the last inequalities, the prefactor $\frac{1}{\xi_{ij}^2}$ was left away, because it is always positive and has thus no influence on the sign of the external eigenvalue. For $\hat{\lambda}_{34}$ and $\hat{\lambda}_{12}$ the first and the third term are negative as can be easily seen by the correspondence of the picture with the viability-matrix. This implies a positive second term, otherwise the eigenvalue would be negative for all choices of the parameters. For $\hat{\lambda}_{24}$ and $\hat{\lambda}_{13}$ the signs of the first and third terms are positive and this implies a negative second term. This gives us the following relation:

$$m_{12}, m_{34} < m_{14} < m_{24}, m_{13} \tag{3.15}$$

From the boundary flow of $4b, o$ one can read off the relations

$$m_{24} < m_{12}, m_{34} \text{ and } m_{13} < m_{12}, m_{34}. \tag{3.16}$$

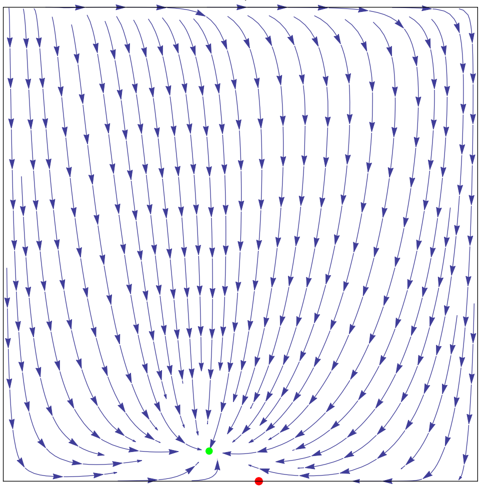
Therefore we have a contradiction. □

3.3.2 Some existence proofs with CAS

By now we have proven the non-existence of several cases. In this section we will show the existence of most of the other cases. We will do so by showing fitness-matrices found with the Mathematica built-in functions RandomReals and FindInstance. Then they are visualised by the built-in command StreamPlot. The plots contain not only the StreamPlot, but also the boundary equilibria depicted by a red dot and, if existing, internal equilibria marked by a green dot. It is roughly true that if the matrix has a 0 in the m_{14}, then it was found with FindInstance, otherwise with RandomReals. We were able to realize all possible boundary flow classes for $\delta \geq 1$. For $\delta = 0$ only 16 out of 19 possible were found and for $\delta = -1$ none could be found, but not all their impossibility could be proven like Theorem 3. Their existence remains an open problem, see sect. 3.4. Some cases are shown multiple times, because of different numbers of internal equilibria or several ways of saturation to reach the same boundary sum. An example for the first type is case $4a, s$ with $\delta = 4$ where 3 and 5 internal equilibria are depicted. An example for the second type is case $2d, u \to s$ and $\delta = 0$ with both edge-equilibria either saturated or not. A special type is case $4b, o$ and $\delta = 0$, where the two different ways of saturation to reach $\delta = 0$ are in fact time reversals of each other. In two pictures the saturation can not be seen clearly from the picture alone and so the corresponding external eigenvalue was added. For the boundary flow classes without edge-equilibria, 0a, 0b and 0c, it is clear that they exist and therefore only examples of them with a non-trivial number of internal equilibria are shown.

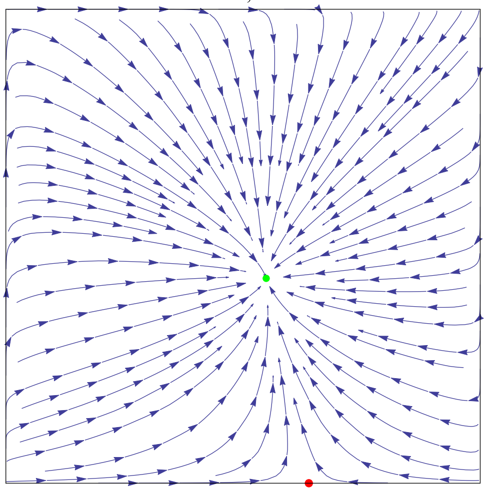
Fig. 3.4: $\delta = 0$

1a,s



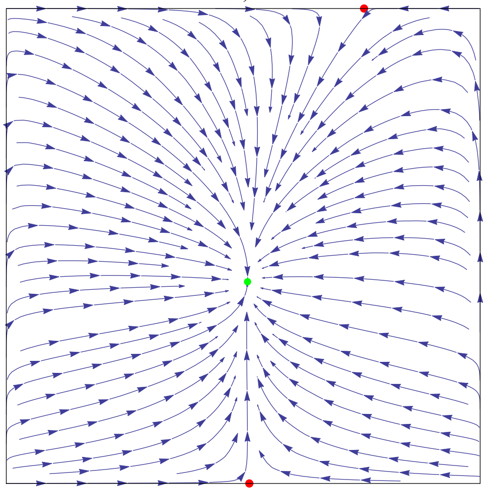
$$M=\begin{pmatrix} 0.0323153 & 0.0649948 & 0.472828 \\ 1.53771 & 2.15986 & 1.20255 \\ 1.64775 & 1.68729 & 1.65343 \end{pmatrix}$$

1c,s



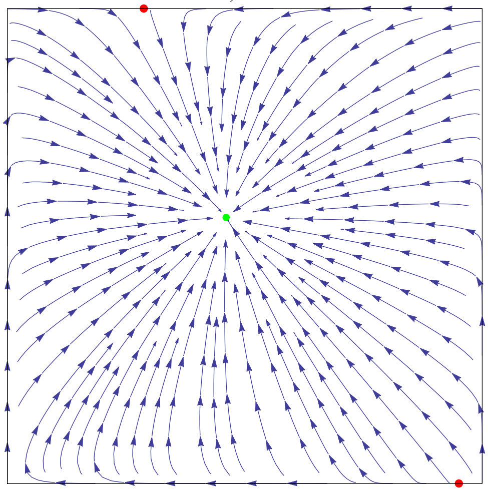
$$M=\begin{pmatrix} -414 & -397.5 & -396 \\ -438.5 & 0 & -390.625 \\ -445 & -300 & -382 \end{pmatrix}$$

2a,ss



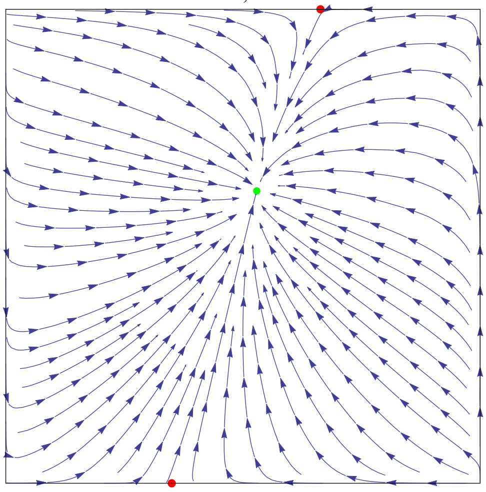
$$M=\begin{pmatrix} 0.377096 & 1.21407 & 0.942469 \\ 0.222758 & 5.63022 & 0.192432 \\ 0.0504174 & 2.79706 & 0.188251 \end{pmatrix}$$

2a,u->s



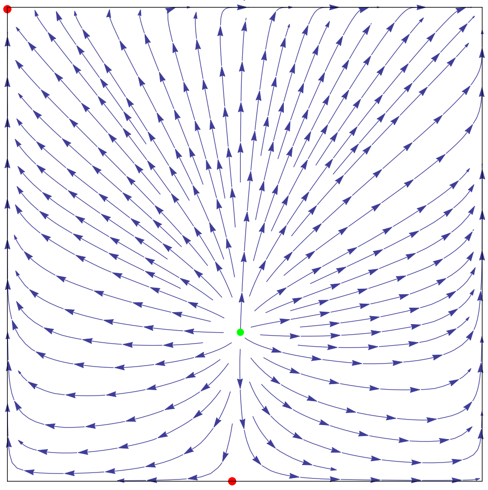
$$M=\begin{pmatrix} 0.323861 & 0.464196 & 0.116047 \\ 0.27942 & 2.54059 & 0.0932053 \\ 0.203503 & 0.0153935 & 0.0251142 \end{pmatrix}$$

2b,ss



$$M=\begin{pmatrix} 0.0265268 & 3.17954 & 1.57967 \\ 0.201144 & 8.51372 & 0.277673 \\ 0.490441 & 0.945811 & 0.099476 \end{pmatrix}$$

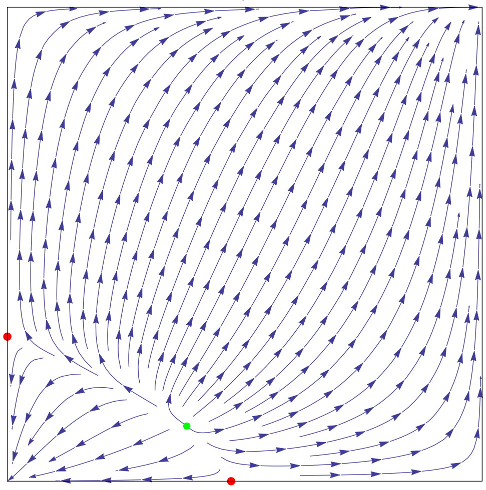
2c,us



$$M=\begin{pmatrix} 412.3 & 417.67 & 421 \\ 412.55 & 0 & 418.129 \\ 350 & 252 & 361 \end{pmatrix};\lambda_{13}=8101.51$$

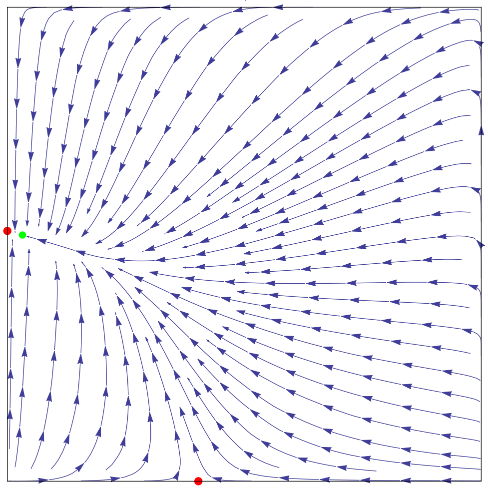
Fig. 3.5: $\delta = 0$ cont.

2c,uu



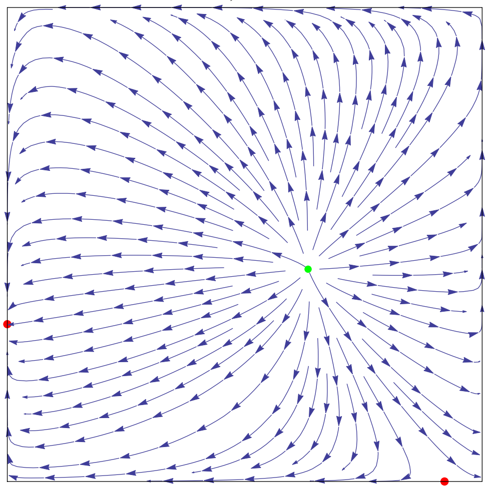
$$M=\begin{pmatrix} 2.45212 & 3.76488 & 4.64896 \\ 0.436638 & 0.323302 & 1.9026 \\ 1.32137 & 0.522794 & 1.41841 \end{pmatrix}$$

2d,ss



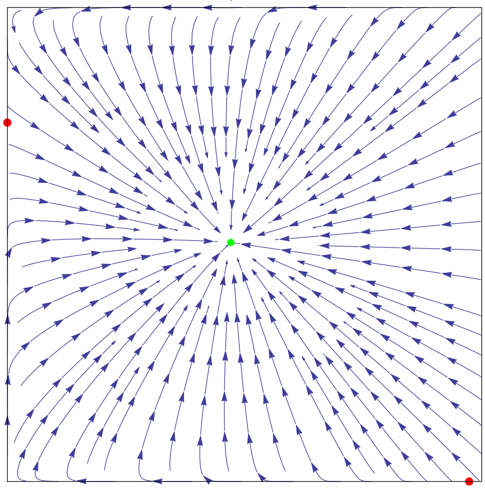
$$M=\begin{pmatrix} 2.50193 & 1.11185 & 0.538238 \\ 9.92284 & 9.63424 & 0.168344 \\ 1.61933 & 4.71494 & 0.131372 \end{pmatrix}$$

2d,u−>s



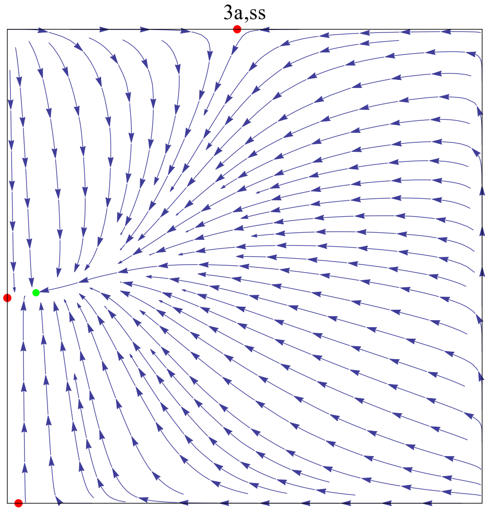
$$M=\begin{pmatrix} 0.786521 & 0.724035 & 0.246548 \\ 1.4194 & -2.74341 & 0.186821 \\ 1.10503 & 0.0745116 & 0.163191 \end{pmatrix}$$

2d,u−>s



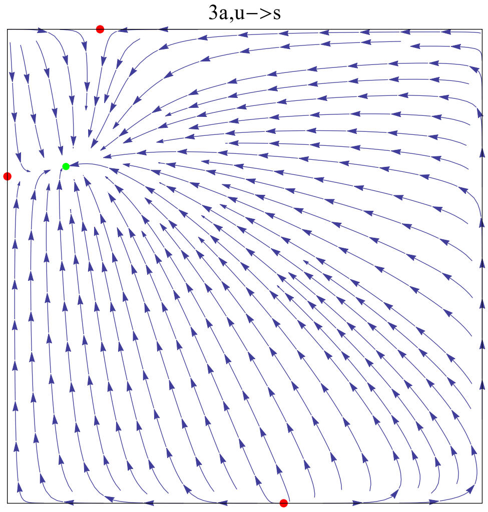
$$M=\begin{pmatrix} 0.123066 & 0.00510671 & 0.00399313 \\ 0.149437 & 2.19019 & 0.00201898 \\ 0.0672247 & -0.000642811 & 0.0011948 \end{pmatrix}$$

3a,ss



$$M=\begin{pmatrix} 1.72638 & 4.9758 & 1.51379 \\ 9.62099 & 9.0015 & 0.939638 \\ 3.58857 & 3.65718 & 0.821117 \end{pmatrix}$$

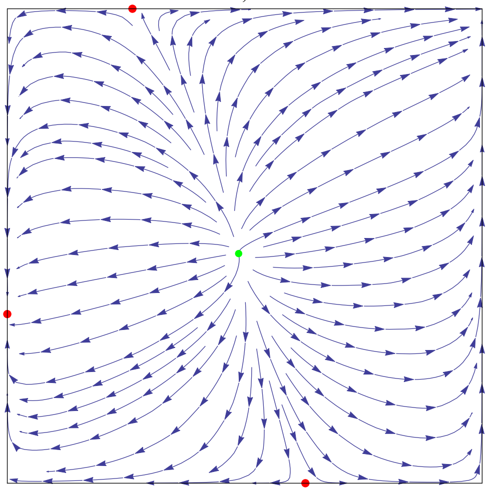
3a,u−>s



$$M=\begin{pmatrix} 0.477568 & 0.564708 & 0.205657 \\ 0.716508 & 0.782755 & 0.156553 \\ 0.185644 & 0.0597078 & 0.150184 \end{pmatrix}$$

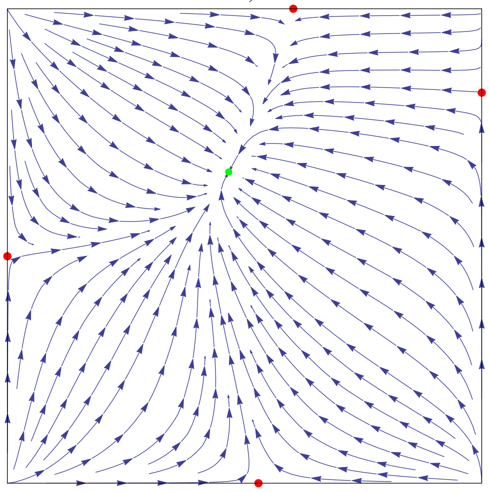
Fig. 3.6: $\delta = 0$ cont.

3a,uu



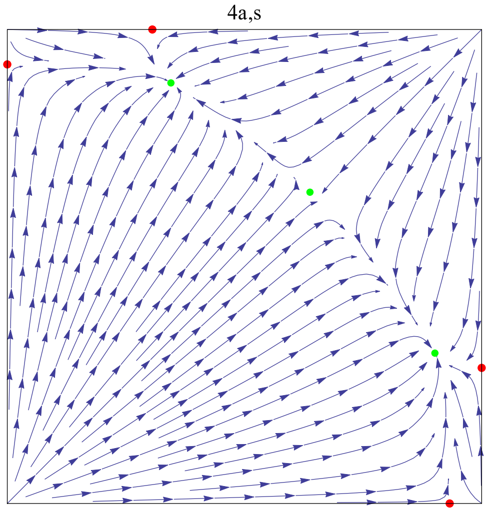
$$M=\begin{pmatrix} 326.8 & 281 & 409 \\ 394.5 & 0 & 394.8 \\ 357 & 287.6 & 328.75 \end{pmatrix}$$

4a,s



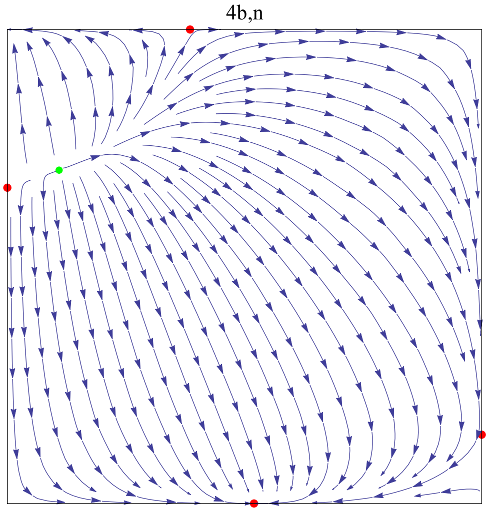
$$M=\begin{pmatrix} 0.23018 & 9.86024 & 3.51277 \\ 8.8571 & 8.85036 & 4.04543 \\ 0.946457 & 6.53766 & 1.56558 \end{pmatrix}$$

4a,s



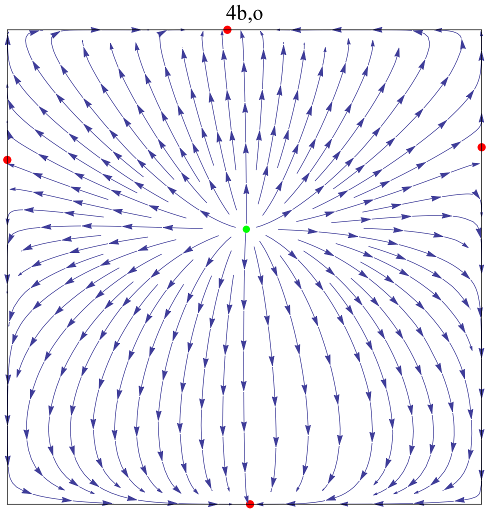
$$M=\begin{pmatrix} 3.71985 & 3.9997 & 3.36438 \\ 3.99999 & 4. & 3.99991 \\ 0.475323 & 3.99998 & 3.74519 \end{pmatrix}$$

4b,n



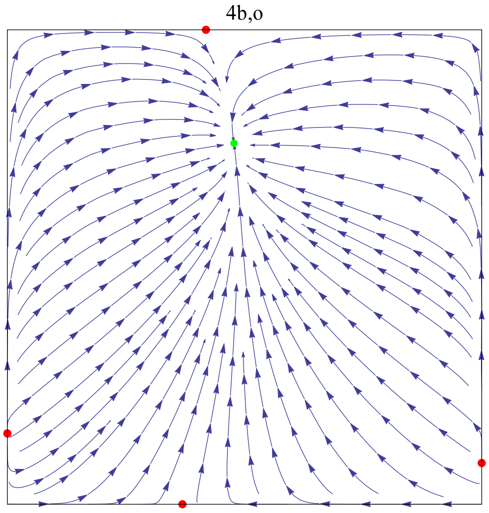
$$M=\begin{pmatrix} 118.7 & 83 & 140 \\ 18 & 0 & 246 \\ 219 & 336 & 228 \end{pmatrix}$$

4b,o



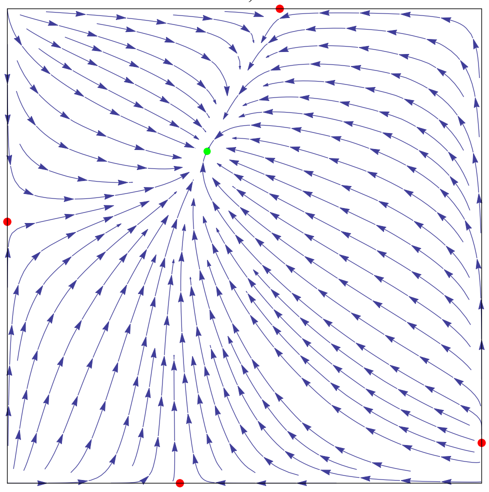
$$M=\begin{pmatrix} 0.490183 & 0.802586 & 0.441695 \\ 0.322959 & -6.41116 & 0.226789 \\ 0.765533 & 3.24926 & 0.880019 \end{pmatrix}$$

4b,o



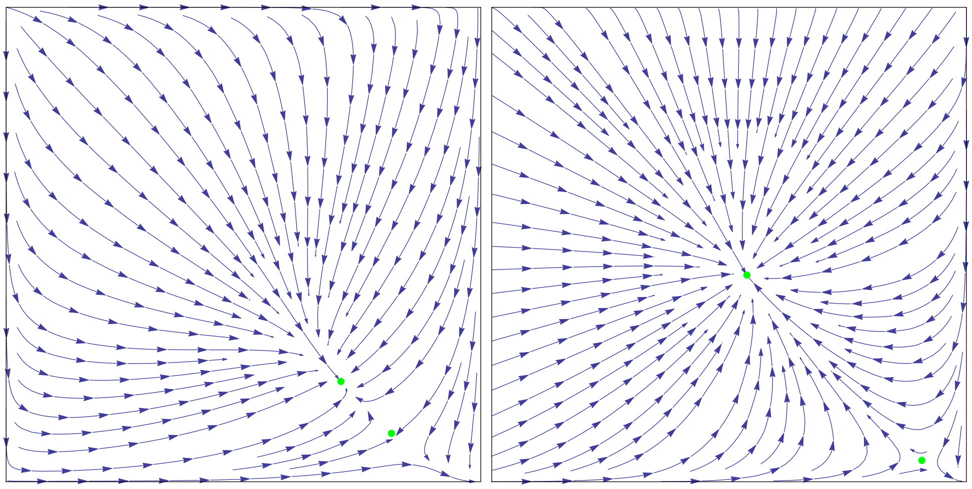
$$M=\begin{pmatrix} 3.70707 & 5.98452 & 2.82199 \\ 0.324941 & 12.2379 & 0.327161 \\ 0.918782 & 1.41833 & 0.564567 \end{pmatrix}$$

Fig. 3.7: $\delta = 0$ cont.



$$M=\begin{pmatrix} 1.782 & 5.11253 & 2.64484 \\ 3.99272 & 7.4198 & 0.33382 \\ 1.27985 & 2.25675 & 0.548636 \end{pmatrix}$$

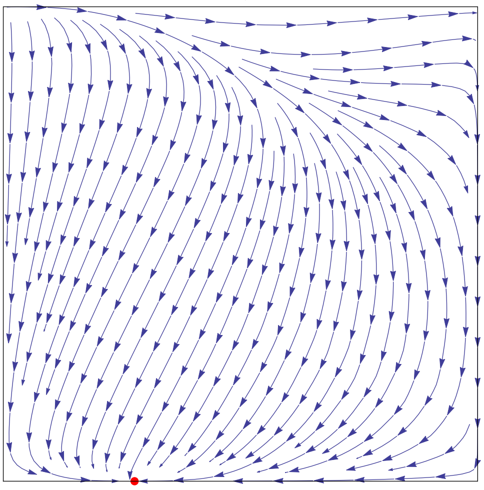
Fig. 3.8: $\delta = 1$



$$M=\begin{pmatrix} 0.25 & 0.5 & 0.53125 \\ 0.5 & 1.77 & 0.8125 \\ 0.625 & 1 & 1.0625 \end{pmatrix} \qquad M=\begin{pmatrix} 0.000108783 & 0.00181475 & 0.00183228 \\ 0.0000573344 & 0.35 & 0.00821327 \\ 0.0000340083 & 0.0436669 & 0.0679599 \end{pmatrix}$$

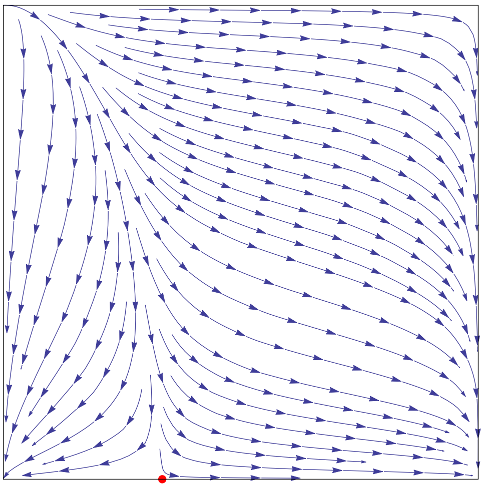
Fig. 3.9: $\delta = 1$ cont.

1a,s



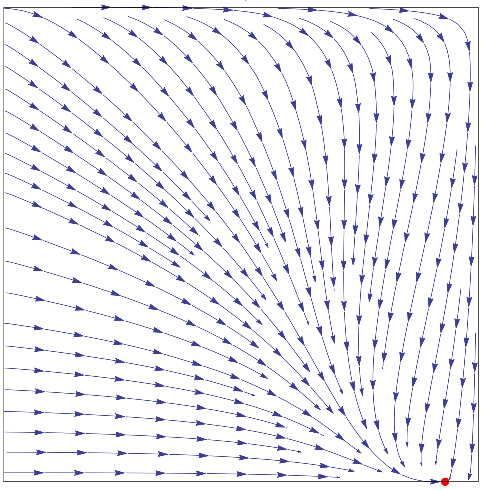
$$M=\begin{pmatrix} 32 & 80 & 105 \\ 206 & 0 & 105.5 \\ 206 & 250 & 135 \end{pmatrix}$$

1a,u



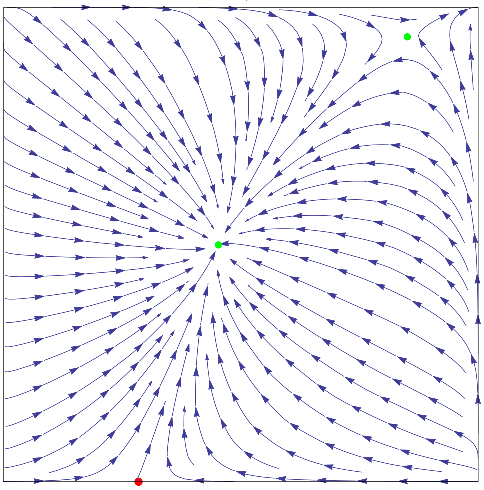
$$M=\begin{pmatrix} 12.2 & 22 & 93 \\ 43 & 0 & 134 \\ 93 & 9 & 176 \end{pmatrix}$$

1c,s



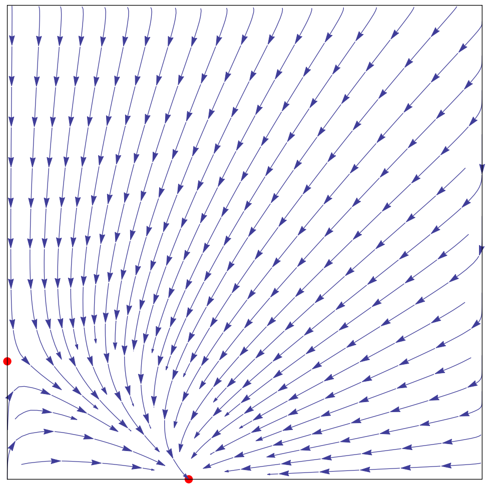
$$M=\begin{pmatrix} 0.0192022 & 0.132228 & 0.738807 \\ 0.010837 & 2.84441 & 0.914631 \\ 0.0108352 & 2.72528 & 2.52157 \end{pmatrix}$$

1d,s



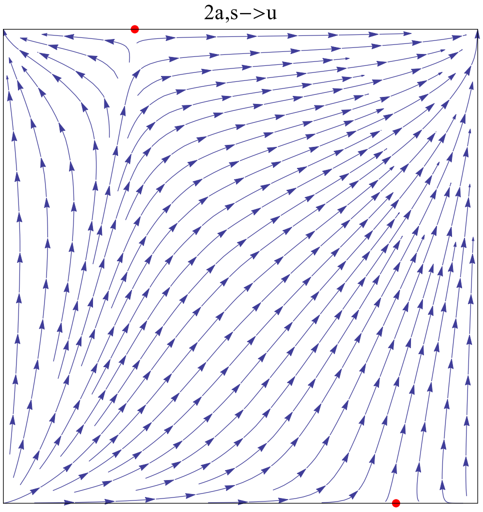
$$M=\begin{pmatrix} -4443 & -4405 & -3810 \\ -4428.88 & 0 & -5260 \\ -4405 & -3770 & -5370 \end{pmatrix}$$

2a,ss



$$M=\begin{pmatrix} -0.23146 & 0.004358 & 0.005506 \\ 11.5969 & 5.89 & 0.00786 \\ 7.679 & 19.3723 & 0.4654 \end{pmatrix}$$

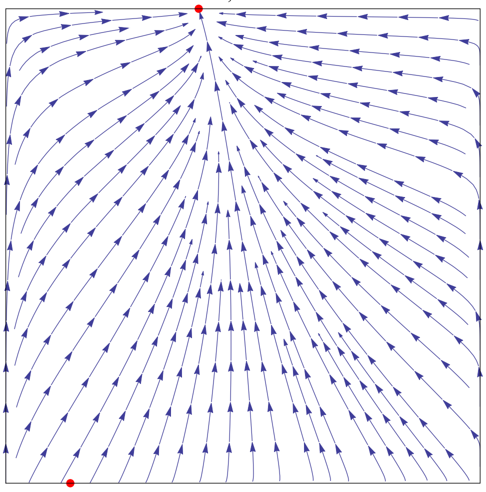
2a,s−>u



$$M=\begin{pmatrix} 910 & -1313 & 4487 \\ -343 & 0 & 1582 \\ -2163 & -749 & -1043 \end{pmatrix}$$

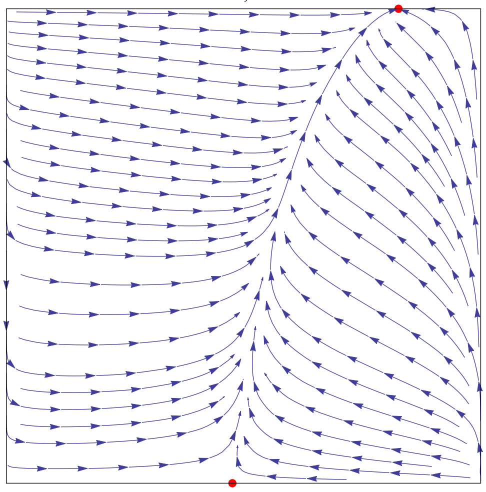
Fig. 3.10: $\delta = 1$ cont.

2a,u−>s



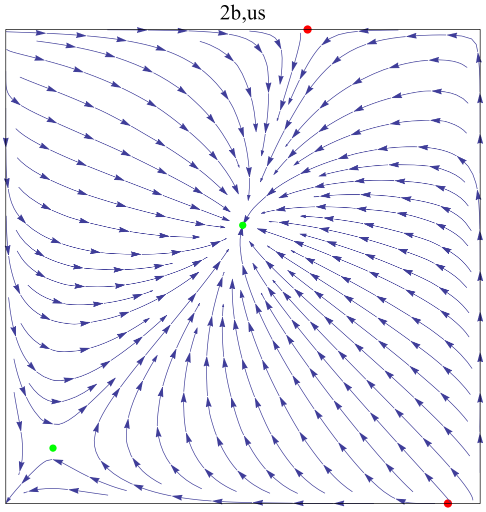
$$M=\begin{pmatrix} 1.08475 & 2.84449 & 0.277101 \\ 0.219578 & 2.80305 & 0.055769 \\ 0.0290646 & 0.0255685 & 0.0477743 \end{pmatrix}$$

2b,ss



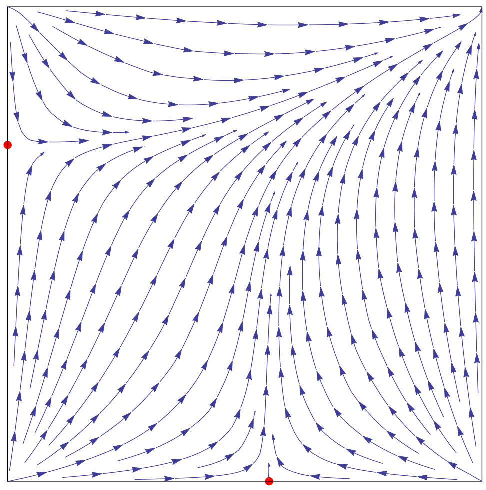
$$M=\begin{pmatrix} 0.0445964 & 5.81736 & 4.60708 \\ 0.190734 & 8.59607 & 1.51831 \\ 0.700582 & 6.34452 & 0.144421 \end{pmatrix}$$

2b,us



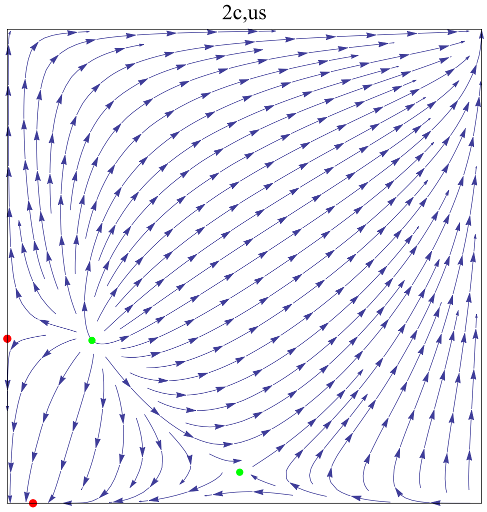
$$M=\begin{pmatrix} 0.103347 & 2.22347 & 1.01104 \\ 0.142385 & 7.53309 & 0.0627039 \\ 1.67414 & -0.112731 & 0.0175177 \end{pmatrix}$$

2c,ss



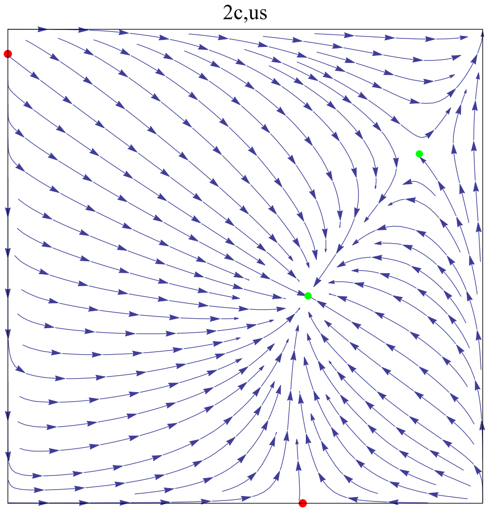
$$M=\begin{pmatrix} -33 & 14 & 28 \\ 36 & 0 & 24.25 \\ -132 & 18.6 & -104 \end{pmatrix}$$

2c,us



$$M=\begin{pmatrix} 1.16994 & 1.39718 & 4.14179 \\ 0.610676 & -0.251755 & 2.98162 \\ 0.90811 & 0.928984 & 0.565325 \end{pmatrix}$$

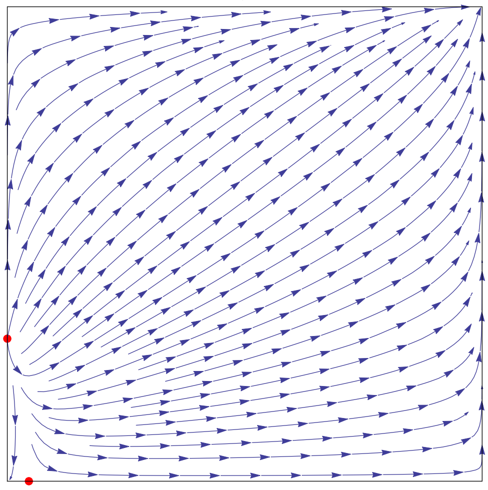
2c,us



$$M=\begin{pmatrix} 0.0215412 & 0.0902221 & 1.6179 \\ 0.00698545 & 3.45438 & 0.859089 \\ 0.271803 & 1.39792 & 0.710469 \end{pmatrix}$$

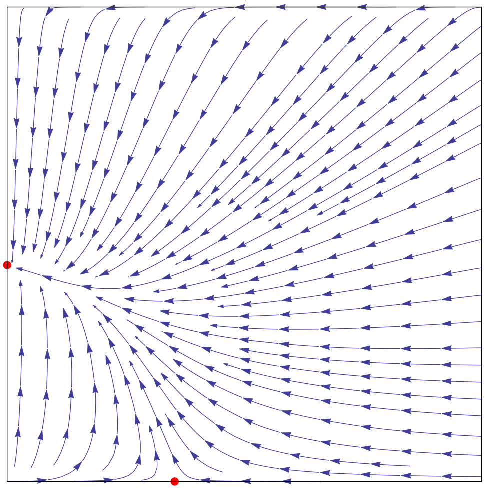
Fig. 3.11: $\delta = 1$ cont.

2c,uu



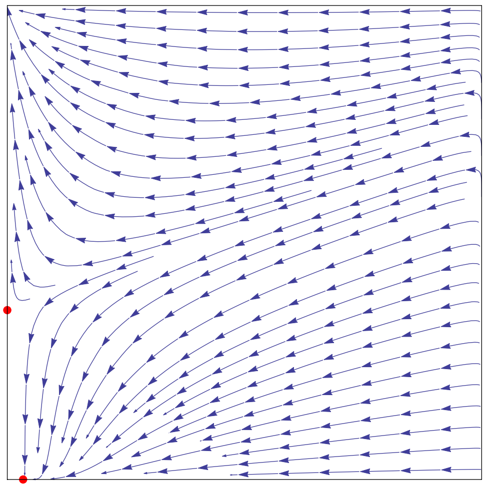
$$M=\begin{pmatrix} 1.64028 & 9.06174 & 9.43515 \\ 0.0947212 & 0.357491 & 8.42018 \\ 0.758407 & 0.439885 & 7.12443 \end{pmatrix}$$

2d,ss



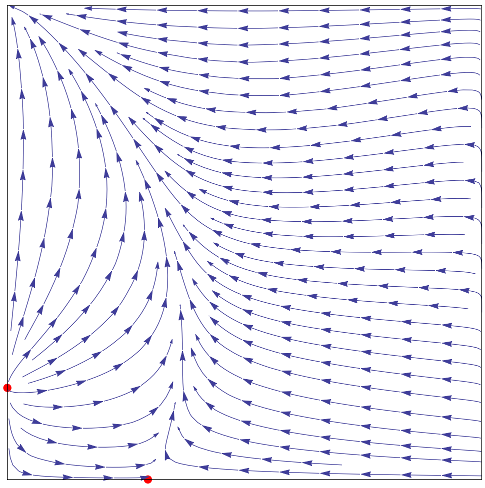
$$M=\begin{pmatrix} 0.371285 & 0.0465841 & 0.0126514 \\ 4.05023 & 3.1518 & 0.0101383 \\ 0.964459 & 2.11211 & 0.00998286 \end{pmatrix}$$

2d,s−>u



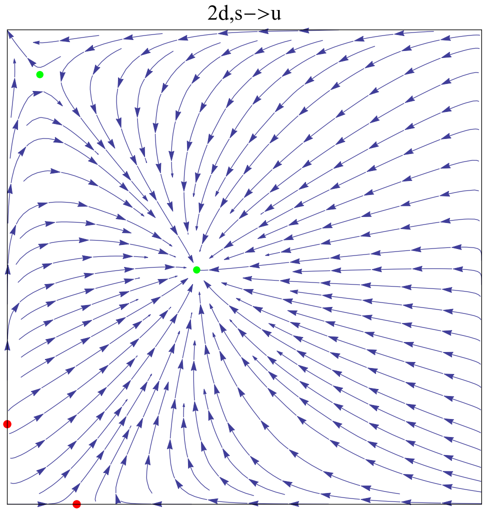
$$M=\begin{pmatrix} 3.47928 & 0.532403 & 0.0737026 \\ 1.2951 & 1.44741 & 0.0274743 \\ 2.50944 & 2.59893 & 0.00493055 \end{pmatrix}$$

2d,s−>u



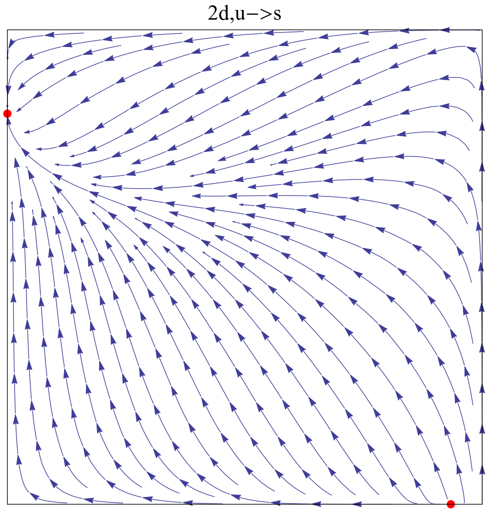
$$M=\begin{pmatrix} 8.57153 & 3.13766 & 0.246884 \\ 0.82276 & 7.48061 & 0.0383571 \\ 2.67991 & 4.60726 & 0.0297722 \end{pmatrix}$$

2d,s−>u



$$M=\begin{pmatrix} 2.72294 & 1.28833 & 0.167247 \\ 1.59251 & 9.56151 & 0.006396 \\ 1.82201 & 2.19892 & 0.00120147 \end{pmatrix}$$

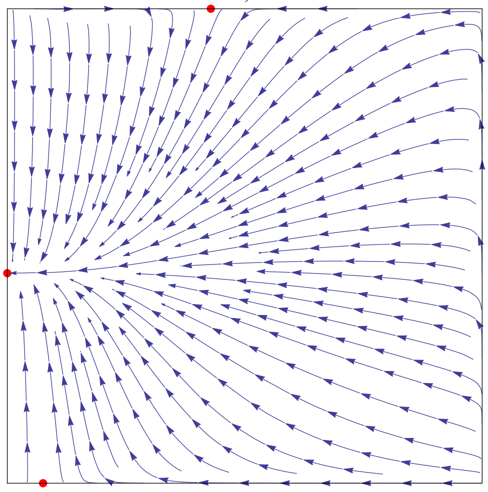
2d,u−>s



$$M=\begin{pmatrix} 3.51966 & 1.81264 & 1.70758 \\ 4.00642 & 5.23645 & 1.46447 \\ 1.73925 & 0.350719 & 0.44902 \end{pmatrix}$$

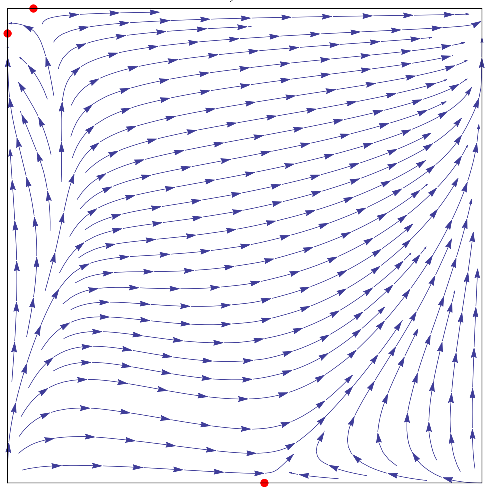
Fig. 3.12: $\delta = 1$ cont.

3a,ss



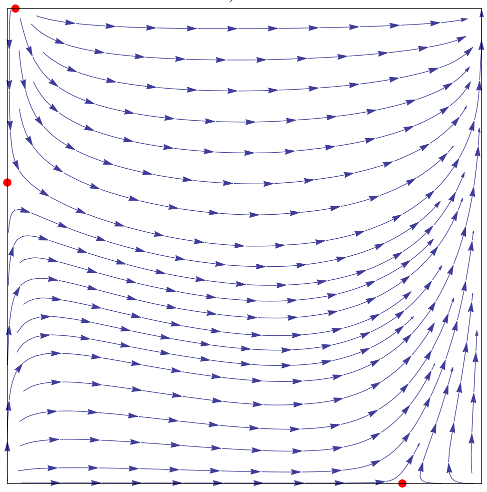
$$M=\begin{pmatrix} 0.999106 & 1.77025 & 0.742321 \\ 8.74046 & 7.31559 & 0.387676 \\ 2.59259 & 2.79859 & 0.270003 \end{pmatrix}$$

3a,s−>u



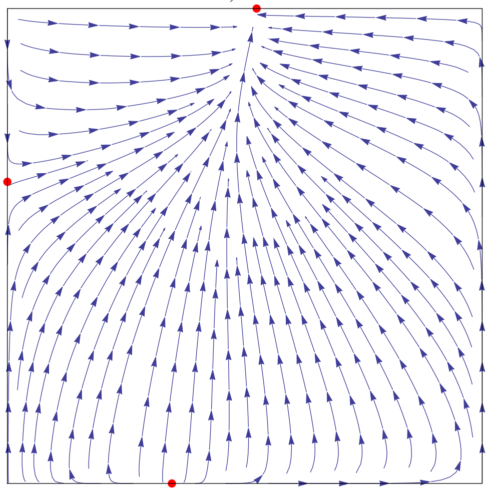
$$M=\begin{pmatrix} 2.32938 & 1.94408 & 8.62571 \\ 2.39975 & 0.174222 & 8.21394 \\ 1.13274 & 4.44686 & 1.63996 \end{pmatrix}$$

3a,s−>u



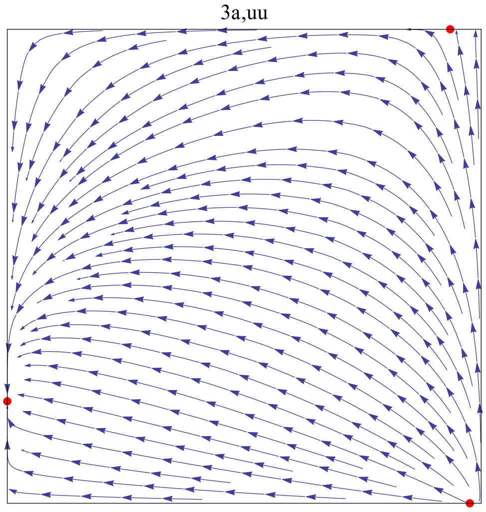
$$M=\begin{pmatrix} 0.171966 & 0.12 & 3.09897 \\ 0.345408 & 0.387823 & 2.26822 \\ 0.0452972 & 1.37285 & 1.10631 \end{pmatrix}$$

3a,u−>s



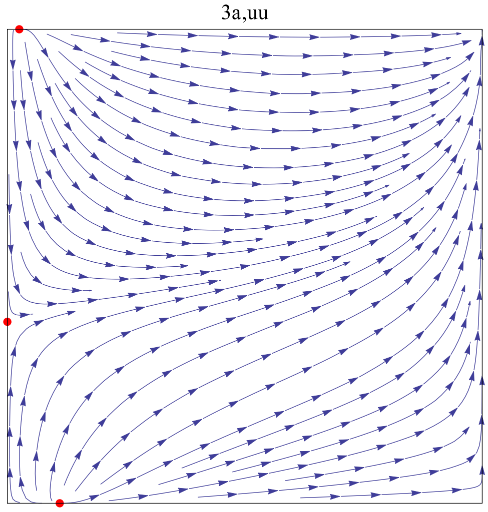
$$M=\begin{pmatrix} 0.146904 & 0.749293 & 0.204154 \\ 0.288683 & 0.709908 & 0.128345 \\ 0.0418685 & 0.000463392 & 0.078572 \end{pmatrix}$$

3a,uu



$$M=\begin{pmatrix} 4.31998 & 2.36709 & 2.50379 \\ 7.94756 & 4.62692 & 0.234265 \\ 6.95369 & -0.1 & 0.0736007 \end{pmatrix}$$

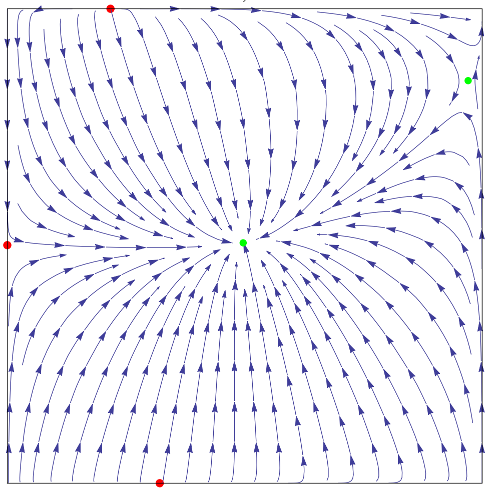
3a,uu



$$M=\begin{pmatrix} 0.273403 & 0.138255 & 5.37592 \\ 1.16956 & 2.26062 & 2.98494 \\ 0.613664 & 0.305122 & 2.79391 \end{pmatrix}$$

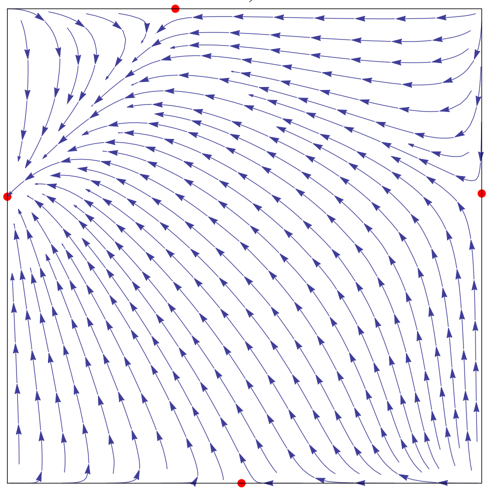
Fig. 3.13: $\delta = 1$ cont.

3a,uu



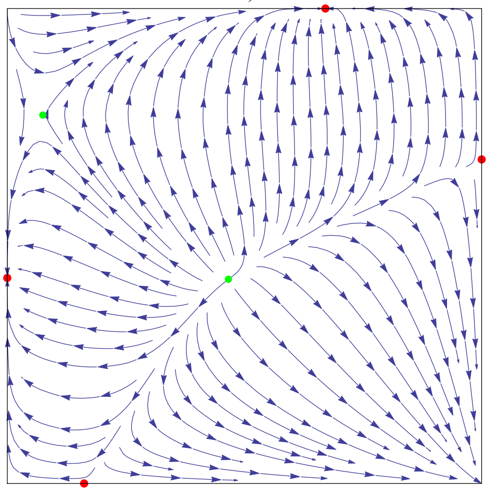
$$M=\begin{pmatrix} 0.775021 & 0.0512571 & 2.65736 \\ 3.54307 & 9.88334 & 2.4331 \\ 0.75588 & 0.635056 & 0.890652 \end{pmatrix}$$

4a,s



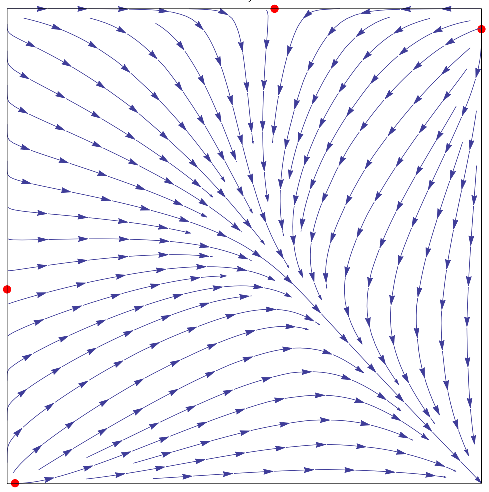
$$M=\begin{pmatrix} 3.52839 & 6.25672 & 1.28283 \\ 9.80833 & 1.83247 & 3.1664 \\ 0.234645 & 1.08446 & 0.212954 \end{pmatrix}$$

4b,n



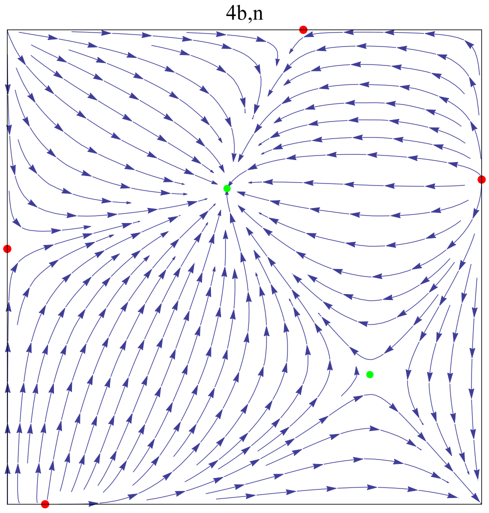
$$M=\begin{pmatrix} 1.86327 & 3.67487 & 2.78498 \\ 2.61867 & -0.374093 & 0.326833 \\ 2.04239 & 1.18843 & 5.60595 \end{pmatrix}$$

4b,n



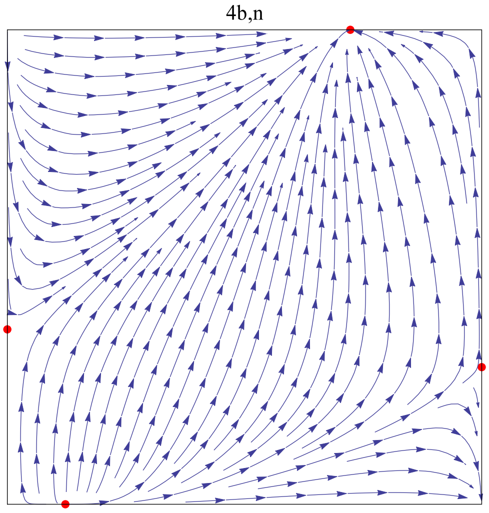
$$M=\begin{pmatrix} 0.204752 & 1.65458 & 0.533115 \\ 0.364685 & 9.62638 & 0.171312 \\ 0.254214 & 0.11595 & 8.22932 \end{pmatrix}$$

4b,n



$$M=\begin{pmatrix} 1.61197 & 6.07086 & 3.38519 \\ 5.13764 & 9.79049 & 0.51788 \\ 1.02832 & 0.487107 & 6.73299 \end{pmatrix}$$

4b,n



$$M=\begin{pmatrix} 0.491706 & 9.07916 & 5.78898 \\ 3.54549 & 3.80666 & 2.49715 \\ 1.7628 & 1.42709 & 3.83519 \end{pmatrix}$$

Fig. 3.14: $\delta = 1$ cont.

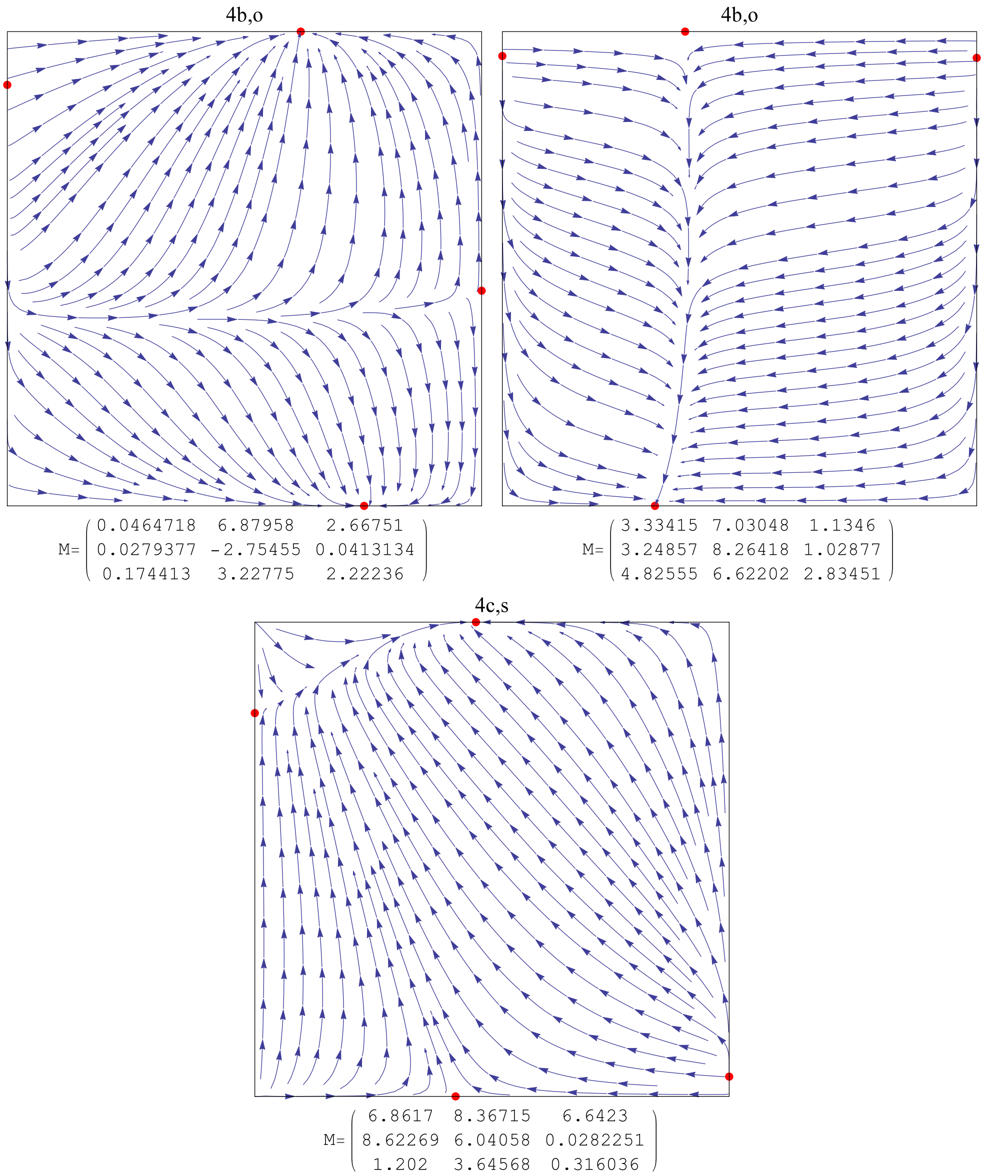
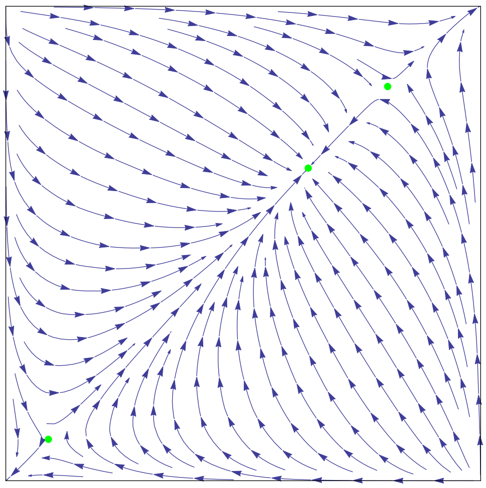


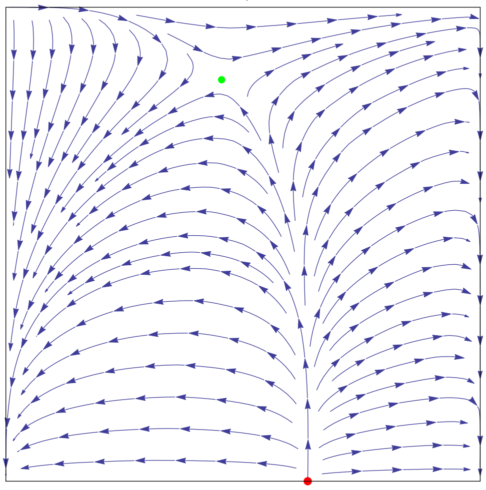
Fig. 3.15: $\delta = 2$

0c



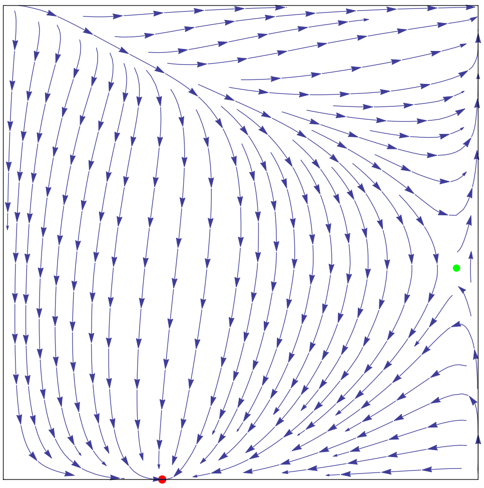
$$M=\begin{pmatrix} 0.08408 & 0.30918 & 0.444511 \\ 0.15602 & 0.9 & 0.26484 \\ 0.285497 & 0.162749 & 0.0642104 \end{pmatrix}$$

1a,u



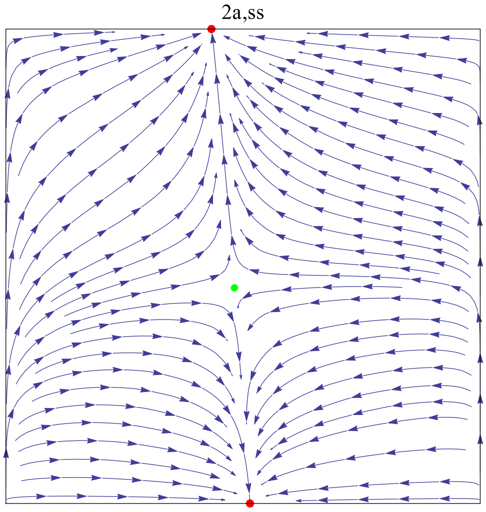
$$M=\begin{pmatrix} 17.8 & 27.3 & 36 \\ 69 & 0 & 37 \\ 120 & -55 & 45 \end{pmatrix}$$

1d,s



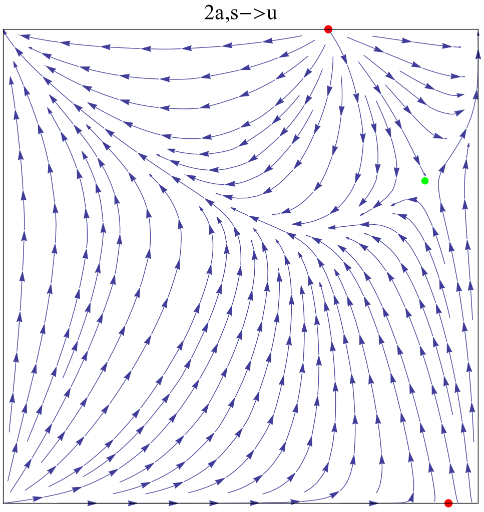
$$M=\begin{pmatrix} 54.9 & 59.8333 & 93 \\ 79.3333 & 0 & 90.375 \\ 156 & 239 & 74 \end{pmatrix}$$

2a,ss



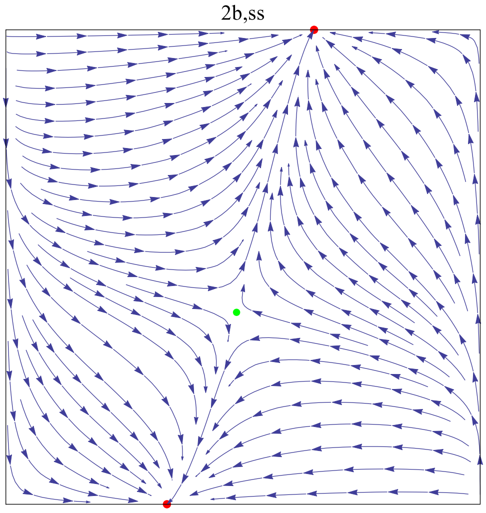
$$M=\begin{pmatrix} 1.65534 & 4.29408 & 0.843705 \\ 0.886685 & 2.16029 & 0.654414 \\ 0.0349149 & 4.97132 & 0.317541 \end{pmatrix}$$

2a,s−>u



$$M=\begin{pmatrix} 17.2 & -104.3 & -48.3 \\ -76.3 & 0. & -53.3 \\ -104.3 & -74.3 & -76.3 \end{pmatrix}$$

2b,ss



$$M=\begin{pmatrix} 0.197525 & 9.17717 & 4.33731 \\ 0.466055 & 4.67598 & 1.18013 \\ 3.65806 & 7.52248 & 0.00679562 \end{pmatrix}$$

Fig. 3.16: $\delta = 2$ cont.

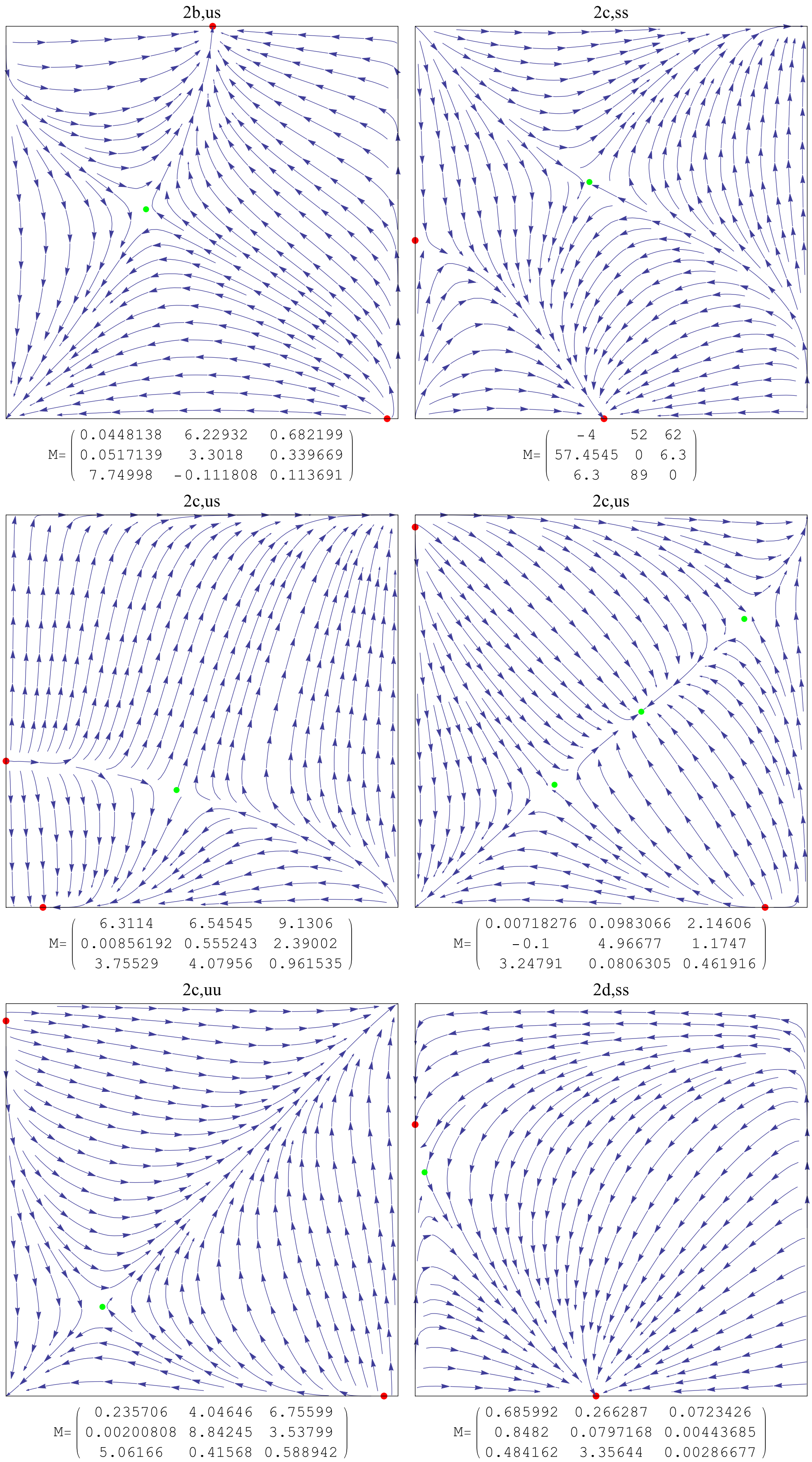


Fig. 3.17: $\delta = 2$ cont.

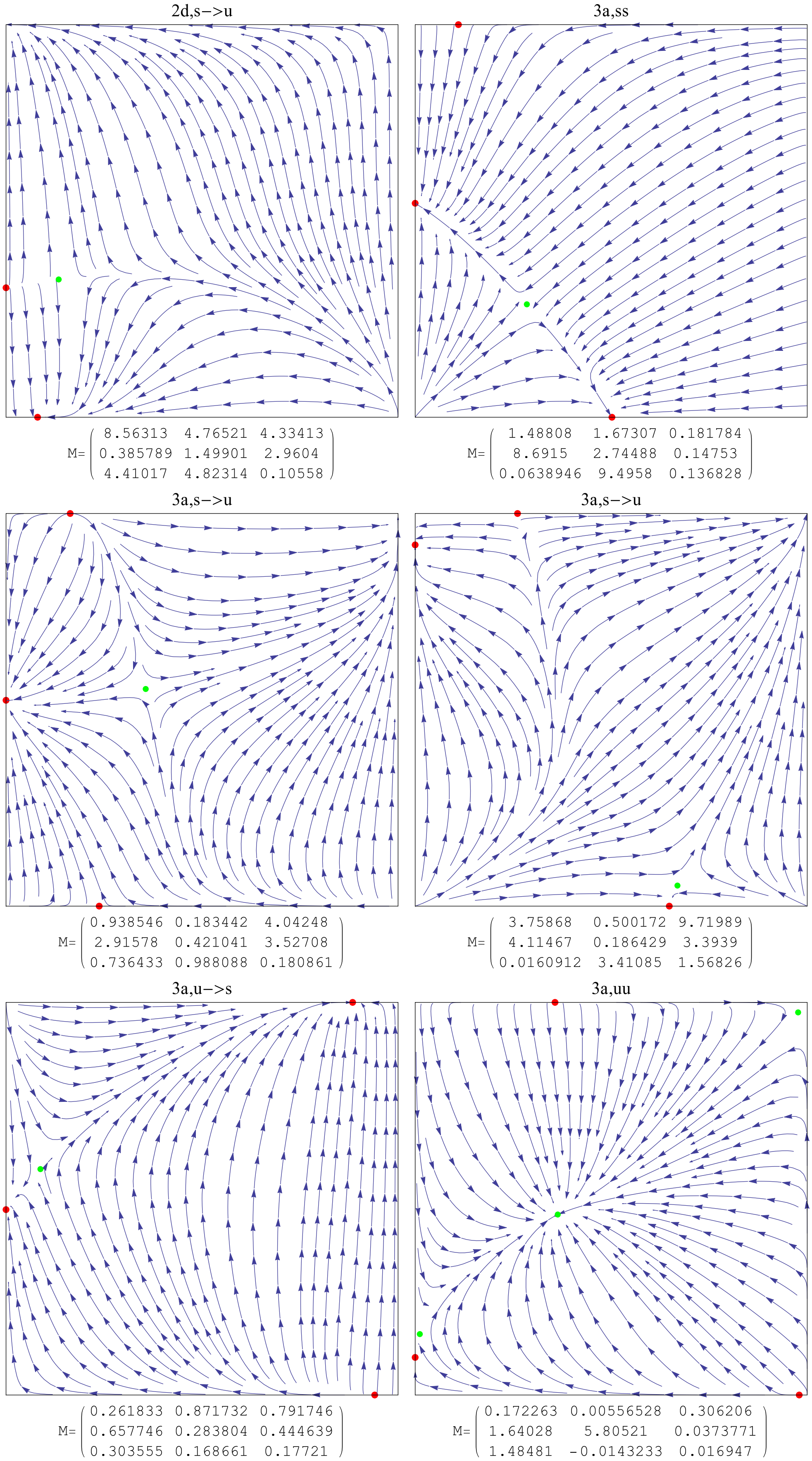
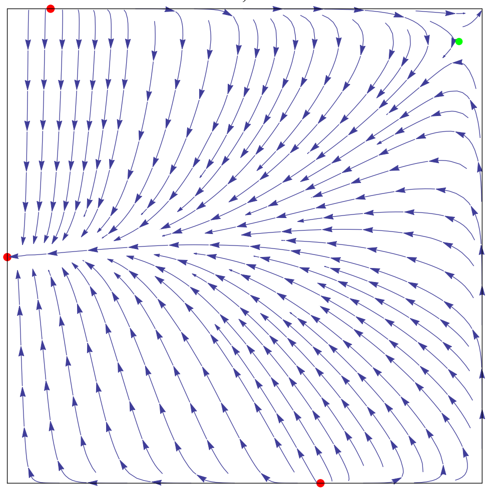


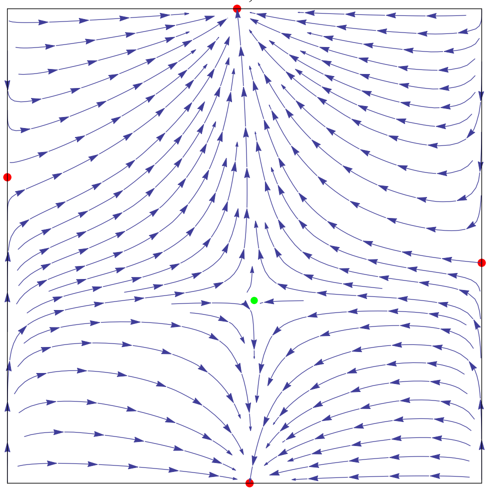
Fig. 3.18: $\delta = 2$ cont.

3a,uu



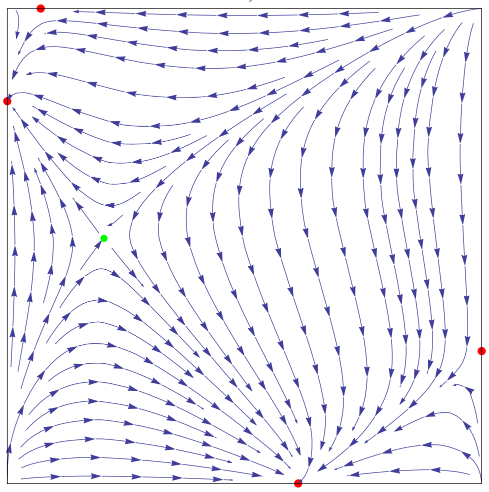
$$M=\begin{pmatrix} 0.601632 & 0.503357 & 1.48246 \\ 7.49323 & 7.39979 & 0.821889 \\ 1.21842 & 0.178787 & 0.71544 \end{pmatrix}$$

4a,s



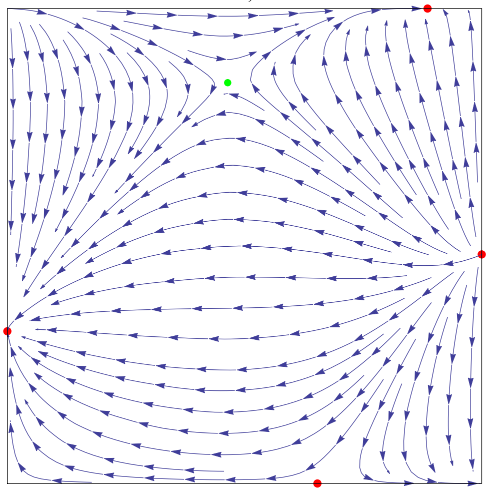
$$M=\begin{pmatrix} 1.19897 & 8.4131 & 0.730427 \\ 1.81232 & 1.40803 & 2.26886 \\ 0.698778 & 6.33371 & 0.93425 \end{pmatrix}$$

4a,s



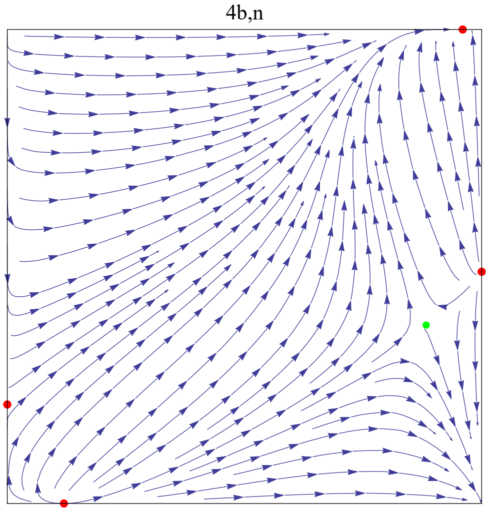
$$M=\begin{pmatrix} 71.7 & 78 & -5 \\ 90 & 0 & 127 \\ 14.5 & 181 & 76 \end{pmatrix}$$

4b,n



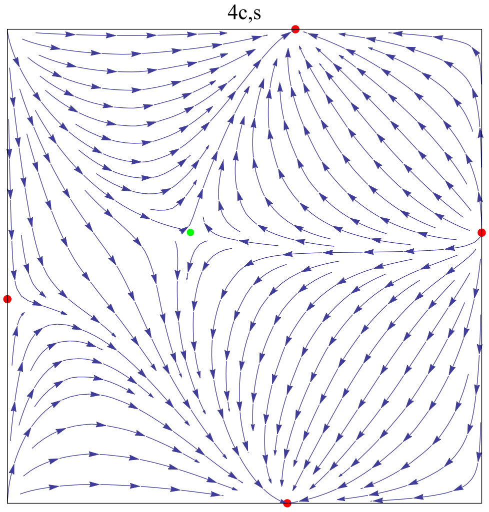
$$M=\begin{pmatrix} 2.58432 & 5.38461 & 5.0236 \\ 8.28549 & 3.67435 & 1.34528 \\ 5.5961 & 3.84198 & 4.77148 \end{pmatrix}$$

4b,n



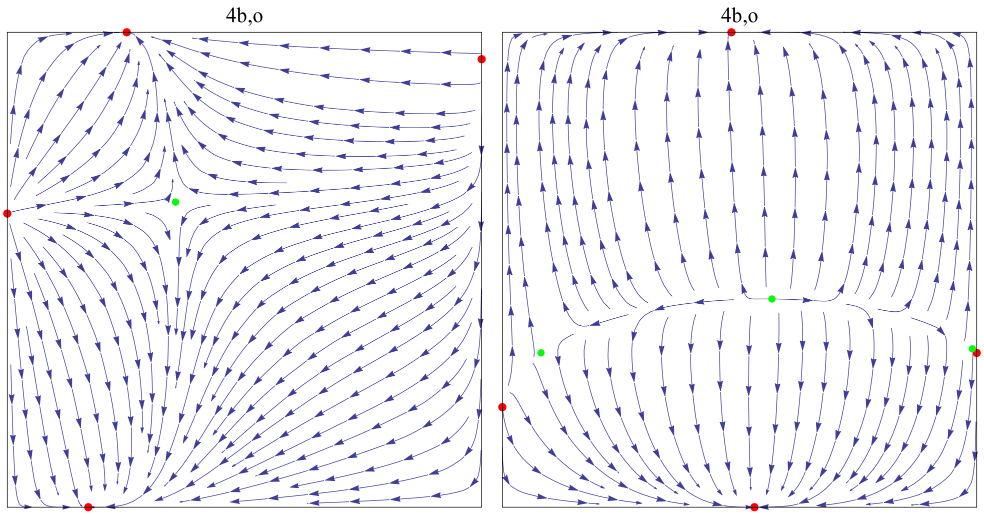
$$M=\begin{pmatrix} 1.06235 & 8.82782 & 8.50417 \\ 1.86937 & 9.56355 & 2.14686 \\ 1.6563 & 0.625869 & 8.2282 \end{pmatrix}$$

4c,s



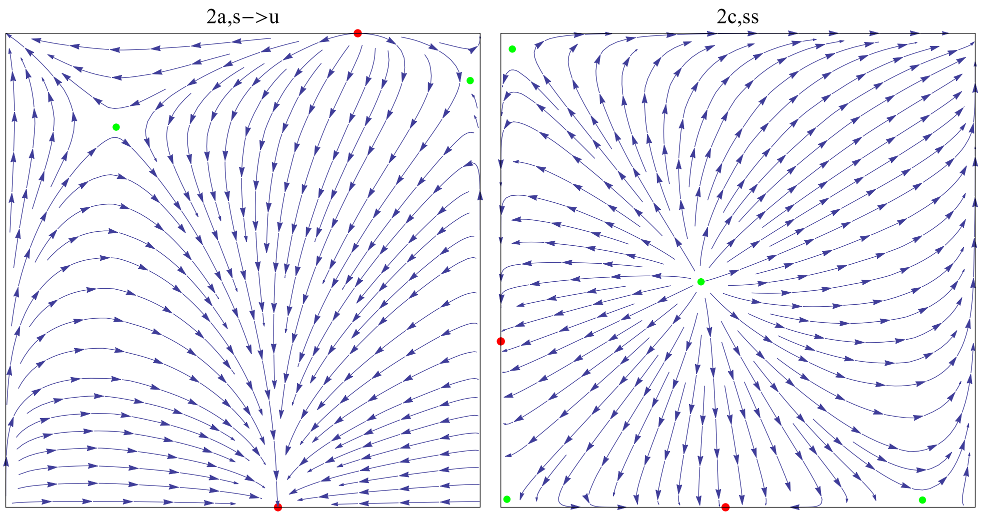
$$M=\begin{pmatrix} 2.40346 & 8.93419 & 4.70986 \\ 6.75472 & 2.47295 & 3.28295 \\ 3.46319 & 9.09201 & 5.18117 \end{pmatrix}$$

Fig. 3.19: $\delta = 2$ cont.



$$M=\begin{pmatrix} 5.40584 & 7.96434 & 0.361754 \\ 0.583323 & 5.77742 & 0.206816 \\ 8.39574 & 9.85165 & 2.78632 \end{pmatrix} \qquad M=\begin{pmatrix} 4.74877 & 6.57464 & 4.61983 \\ 0.836425 & -3.79184 & 0.262212 \\ 1.88102 & 5.92457 & 2.35869 \end{pmatrix}$$

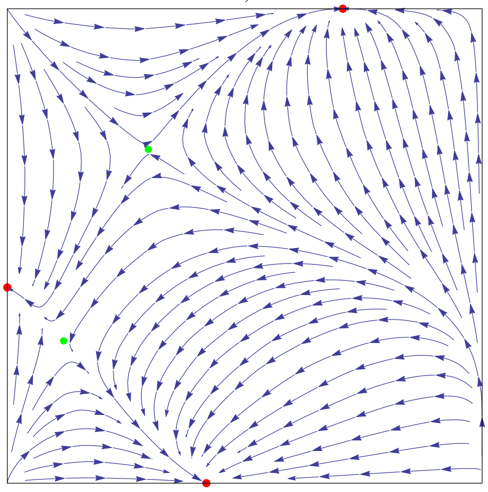
Fig. 3.20: $\delta = 3$



$$M=\begin{pmatrix} -12.5 & -35.5 & -27.5 \\ -37.5 & 0. & -29.2 \\ -65.5 & 70.5 & -30.5 \end{pmatrix} \qquad M=\begin{pmatrix} 25 & 26.6 & 33 \\ 26.3 & 0 & 32 \\ 25.6 & 26.5 & 25.5 \end{pmatrix}$$

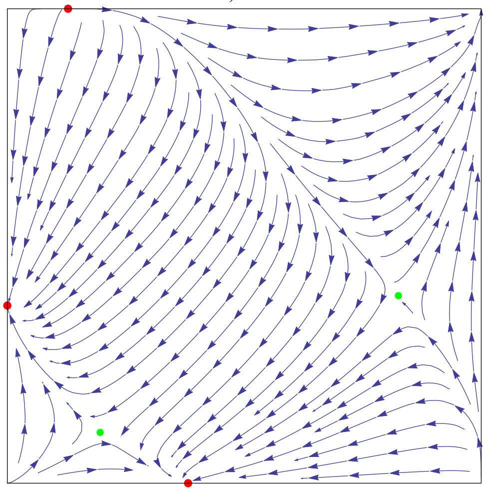
Fig. 3.21: $\delta = 3$ cont.

3a,ss



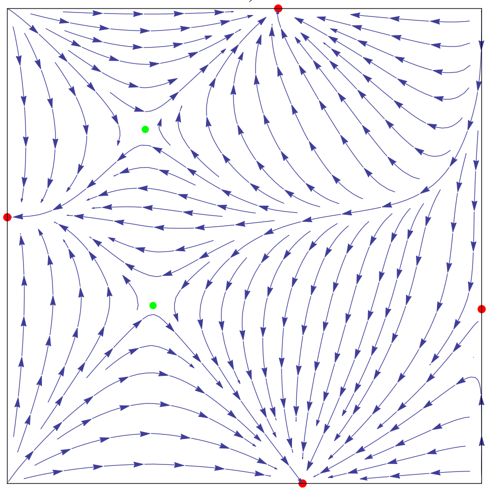
$$M=\begin{pmatrix} 33.3 & 173 & 115 \\ 160 & 0 & 27 \\ 71 & 206 & 19 \end{pmatrix}$$

3a,s->u



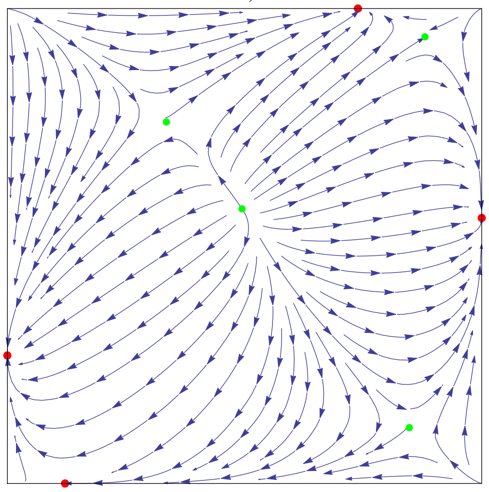
$$M=\begin{pmatrix} 1.8131 & 0.854687 & 7.37095 \\ 9.70305 & 0.348534 & 3.88148 \\ 4.98092 & 8.33096 & 2.89949 \end{pmatrix}$$

4a,s



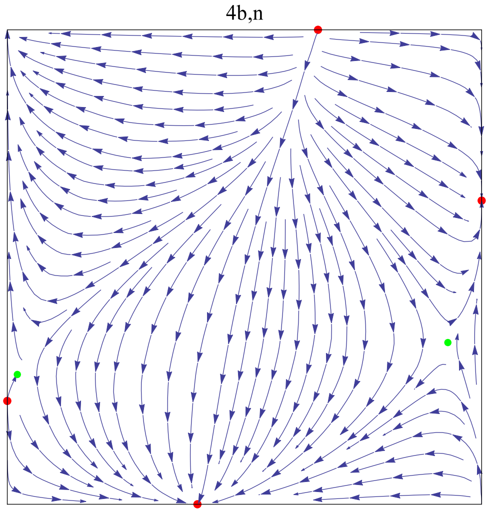
$$M=\begin{pmatrix} 2.6742 & 7.33143 & 3.83419 \\ 8.04945 & 0.7518 & 4.66265 \\ 1.19425 & 8.78787 & 4.18213 \end{pmatrix}$$

4a,s



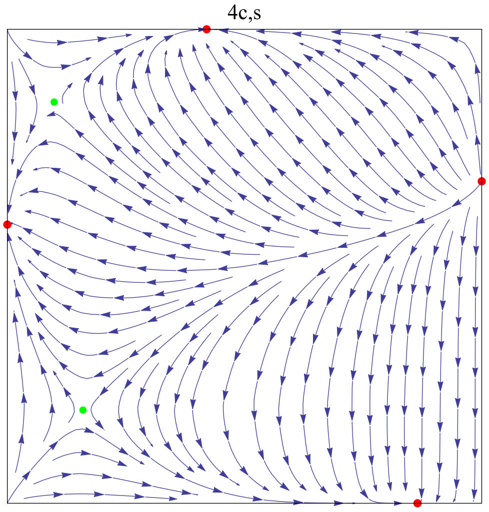
$$M=\begin{pmatrix} 3.06719 & 6.47953 & 5.27457 \\ 7.8991 & 0 & 6.97622 \\ 6.11636 & 6.32509 & 4.81863 \end{pmatrix};\lambda_{34}=0.162026$$

4b,n



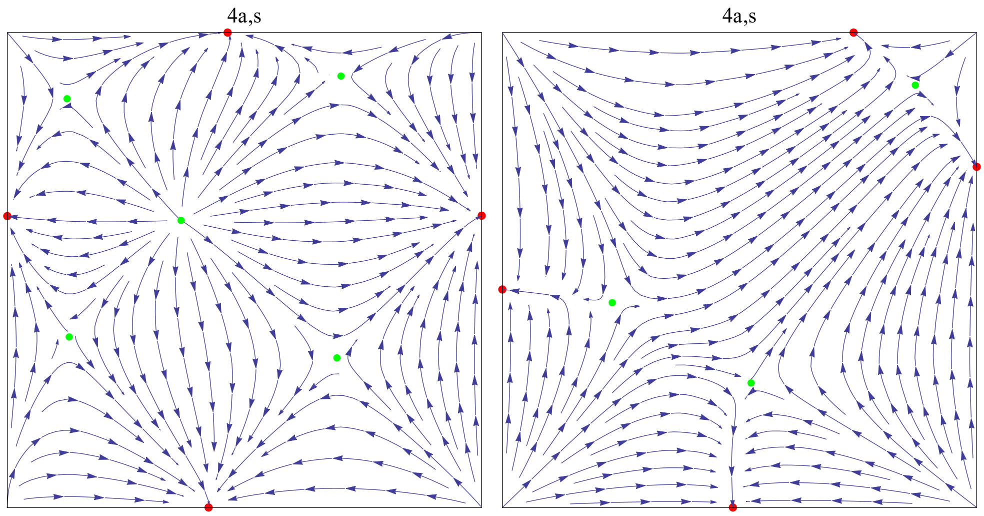
$$M=\begin{pmatrix} 186 & -19 & 89 \\ 89 & 0 & 116 \\ 116 & 213 & 68 \end{pmatrix}$$

4c,s



$$M=\begin{pmatrix} 128 & 199 & 101 \\ 177.2 & 0 & 33 \\ 107 & 190 & 177 \end{pmatrix}$$

Fig. 3.22: $\delta = 4$



$$M = \begin{pmatrix} 4.9658 & 6.46283 & 4.73625 \\ 6.43486 & 1.08881 & 9.02654 \\ 4.10269 & 9.45818 & 2.19322 \end{pmatrix} \qquad M = \begin{pmatrix} 0.9 & 115 & 75 \\ 117 & 0 & 115.4 \\ 18.5 & 115.4 & 12.9 \end{pmatrix}$$

3.4 Open Problems

There are several questions about the equilibria that are not answered in this thesis:

- Is there a boundary flow possible, such that $\delta = -1$ and can the open cases (2b,us, 2d,s$\rightarrow$ u, 3a,s$\rightarrow$ u) from $\delta = 0$ be realized?
- Are three simultaneously stable equilibria in the interior possible? (Two are seen in 4a,s and $\delta = 0$)
- Can every possible boundary flow have representations with a different number of internal equilibria?
- Is 4,as and $\delta = 4$ the only case with five internal equilibria?
- Can there be sources and sinks simultaneously in the interior?
- What is the largest possible number for stable equilibria? (internal and boundary; currently 5; formally possible: 4 on the boundary and three internal)

4. CONTINUOUS ISOCLINES IN [0,1]

In (2.14), the notion of marginal over- or underdominance was introduced. Now we want to outline why and try to derive some results for interior equilibria from those premisses.
Marginal overdominance at one of the loci means that the marginal fitness of the heterozygote is higher than the marginal fitness of both corresponding homozygotes. For marginal underdominance the inequality signs are the other way round. Thus for example marginal overdominance at the A locus will hold, if the inequalities

(4.1a) $$m_{A_1A_2} > m_{A_1A_1}$$

and

(4.1b) $$m_{A_1A_2} > m_{A_2A_2}$$

hold for the marginal fitness functions (2.8).
The two isoclines (3.6) are written in terms of the marginal fitnesses at the corresponding locus. The following theorem shows us that this is very useful.

Theorem 4. *The isocline $f(q)$ maps $[0,1]$ continuously to $(0,1)$ if and only if the A-locus is in either over-, or underdominance.*

Proof. ($\Rightarrow$): From $f(q)$ being a continuous rational function follows, that the denominator is nonzero for all $q \in [0,1]$. Second $f(q)$ is greater than 0 for all $q \in [0,1]$, therefore the numerator and the denominator are either both positive or both negative in this intervall. Finally $f(q)$ is smaller than 1, so $0 < 1 - f(q) = \frac{m_{A_1A_2} - m_{A_1A_1}}{2m_{A_1A_2} - m_{A_1A_1} - m_{A_2A_2}}$ and $m_{A_1A_2} - m_{A_1A_1}$ has the same sign as the denominator and the numerator before and this is the definition of over- or underdominance.

($\Leftarrow$): The inequalities in the definition of over- and underdominance are strict and therefore the numerator and the denominator of $f(q)$ have no zeroes in $[0,1]$ and additionally they have the same sign, so $f(q) > 0$. The absolute value of the denominator is greater than that of the numerator and it follows, that $f(q) < 1$ for $q \in [0,1]$. $\square$

Remark 1. *An analogous theorem holds for the isocline $g(p)$.*

This theorem implies that the graph of $f(q)$ enters the unit square at C_{34} and leaves it on the opposite side at C_{12}. The graph of $g(p)$ goes from C_{24} on the q-axis to C_{13} on the line parallel to the q-axis at $p = 1$. Both never cut nor touch the boundary except at their corresponding C_{ij}. In addition the theorem states that both graphs are continuous in the interior and therefore there has to be at least one intersection point of the two interior isoclines. An intersection point of isoclines always corresponds to an equilibrium of the ODE-system. Together with theorem 1 this yields the

Corollary 1. *Let the isoclines (3.6) be continuous maps from $[0,1]$ to $(0,1)$, then the number of internal equilibria is between 1 and 5, with both bounds possible.*

Proof. The upper bound was stated in theorem 1, the lower bound follows from theorem 4. $\square$

4.1 Both loci in marginal overdominance

In this section we first assume overdominance in both loci and see what we are able to conclude from it. After that we assume underdominance in both loci and will be able to infer the results from the overdominance case.
At first we will have a closer look at the boundary equilibria, which of course all eight exist in this case.
The relations defining marginal overdominance in both loci (see (2.8) and (4.1) for the A-locus) have to hold for all $p, q \in [0, 1]$ and therefore have to hold especially at 0 and 1. This yields the following relations of the parameters:

$$m_{12} > m_{11}, m_{22} \tag{4.2a}$$
$$m_{13} > m_{11}, m_{33} \tag{4.2b}$$
$$m_{24} > m_{22}, m_{44} \tag{4.2c}$$
$$m_{34} > m_{33}, m_{44}, \tag{4.2d}$$

or shorter: overdominance at each of the margins.
This is already the proof of

Lemma 2. *If locus A exhibits marginal overdominance, then there is overdominance on the boundaries $\{q = 0\}$ and $\{q = 1\}$.*

Note that only m_{14} is excluded in these relations (4.2). This suggests additional assumptions on m_{14} such that the converse of Lemma 2 is true. Indeed:

Proposition 2. *If and only if overdominance holds on the margins $\{q = 0\}$ and $\{q = 1\}$ and m_{14} fulfils both of the following conditions*

- $m_{14} > m_{24} - \sqrt{(m_{12} - m_{22})(m_{34} - m_{44})}$
- $m_{14} > m_{13} - \sqrt{(m_{12} - m_{11})(m_{34} - m_{33})}$,

then there is marginal overdominance at the A-locus.

To prove this and similar propositions, we show the following

Lemma 3.

$$ax^2 + 2bx(1 - x) + c(1 - x)^2 > 0,\ \forall x \in [0, 1] \Leftrightarrow a, c > 0 \text{ and } b > -\sqrt{ac}$$

Proof. If the left-hand side holds, it has to hold in particular for $x = 0$ and $x = 1$, which yields $a, c > 0$. Then we use the coordinate transformation $v = \frac{x}{1-x}$. Thus the condition on the left-hand side becomes

$$av^2 + 2bv + c > 0,\ \forall v > 0. \tag{4.3}$$

If $b > 0$, then (4.3) holds trivially. If $b < 0$, then we have to exclude zeroes on the positive axis. (4.3) is zero for $v_{1,2} = \frac{-b \pm \sqrt{b^2 - ac}}{a}$. If those solutions are real, then at least one of them is positive for negative b and therefore $b > -\sqrt{ac}$. This finishes the left-to-right direction and the observation that all computations are reversible, finishes the whole proof. □

Proof of proposition (2). Since $m_{A_1A_2} - m_{A_2A_2}$ and $m_{A_1A_2} - m_{A_1A_1}$ have the form as the left-hand side of lemma 3, we can use this lemma and by assigning a, b and c in the right way, we get exactly proposition 2. □

The analog theorem for the B-locus:

Proposition 3. *If and only if overdominance holds on the margins $\{p=0\}$ and $\{p=1\}$ and m_{14} fulfils both of the following conditions*

- $m_{14} > m_{12} - \sqrt{(m_{24}-m_{22})(m_{13}-m_{11})}$
- $m_{14} > m_{34} - \sqrt{(m_{24}-m_{44})(m_{13}-m_{33})}$,

then there is marginal overdominance at the B-locus.

Proof. The proof is again a application of lemma 3. □

From those relations of the viability parameters above, we will infer the possible boundary flows, when both loci are in marginal overdominance. From (4.2) one can easily analyse stability of the corner equilibria. Their eigenvalues are given in table 3.1, and they are all positive under the premisses of marginal overdominance at both loci. This means that all four corner equilibria are repellors, what corresponds to the behaviour of corner equilibria in the one dimensional overdominance case.
The external eigenvalues on the boundary λ_{ij} have just the form of what defines marginal overdominance (see (3.8)). This yields $\lambda_{ij} > 0$, $\forall (i,j) \in \{(1,2),(1,3),(2,4),(3,4)\}$, $\forall p,q \in [0,1]$. Since this holds for all $p,q \in [0,1]$, the external eigenvalues $\hat{\lambda}_{ij}$ of the C_{ij} are all positive, and therefore none of those equilibria is saturated. This is case 4a,s from fig. 3.2, without saturated boundary equilibria and hence $\delta = 0$.
For marginal overdominance in both loci, the μ_{ij} are all negative, therefore each of the C_{ij} is a saddle point by attracting orbits on the boundary and repelling them into the unit square.
For each boundary edge alone we have the same behaviour as in the one dimensional overdominance case: Both corner equilibria are unstable and the interior equilibrium is admissible and stable (internally).
From theorem 2 about the sum of the indices of saturated fixed points follows that we have at least one interior equilibrium, because there are no saturated fixed points on the boundary. To determine the stability properties of internal equilibria Lemma 1 does the job.
The Routh Hourwitz criterion (proposition 1) for dimension two tells us, that the sign of the determinant of the Jacobi matrix at an equilibrium shows us, if it is a saddle or not. The sign of the trace, on the other hand, is different for a sink or a source. The trace of any equilibrium in the interior of the unit square has the form $p(1-p)m_A + q(1-q)m_B$ and for marginal overdominance (see (4.1)) in both loci, this is negative. Therefore any equilibria that are no saddles have to be completely stable (sinks). So, if there is only one interior equilibrium, this has to have index $+1$ by the index theorem and is therefore no saddle. Thus we obtain it has to be a sink and attracts all orbits, is so called globally asymptotically stable. If all interior restpoints are regular, their number has to be odd. Therefore we can exclude the case of 2 and 4 interior equilibria. For 3 internal equilibria there has to be one saddlepoint and two attracting points. For 5 internal equilibria there have to be two saddles and three attracting points. Let us summarize these results in the following

Theorem 5. *Let both loci be in marginal overdominance. This implies the following*

- *The boundary flow is like case $4a,s$ in fig. 3.2.*
- *None of the eight admissible boundary equilibria is saturated, therefore $\delta = 0$.*
- *Either one, three or five equilibria exist in the interior.*
- *Internal equilibria are either saddles or sinks.*
- *Sinks are the local maxima of $\overline{m}$.*
- *If exactly one internal equilibrium exists, this is globally asymptotically stable.*
- *If exactly three internal equilibria exist, two are sinks and one is a saddle.*

- *If exactly five internal equilibria exist, three are sinks and two are saddles.*

The construction of numerical examples for the different number of internal equilibria turned out to be rather difficult. It wasn't possible for me to find parameters which yield 5 internal fixed points. For 3 only a few could be obtained, but most of the time only one interior fixed point was found.
Thus it remains an open problem, if there could be a maximum of three simultaneously stable equilibria in the marginal overdominance in both loci case. This is for now all we can say about the marginal overdominance in both loci case, so we turn to the fully underdominant case.

4.2 Both loci in marginal underdominance

As in the overdominance case, we start by looking closer at the boundary equilibria. The conditions for marginal underdominance in both loci have to hold for all $p, q \in [0,1]$ and thus for $p = 0, 1$ and $q = 0, 1$. From this we get the relations (4.2) reversed.

$$m_{12} < m_{11}, m_{22} \tag{4.4a}$$
$$m_{13} < m_{11}, m_{33} \tag{4.4b}$$
$$m_{24} < m_{22}, m_{44} \tag{4.4c}$$
$$m_{34} < m_{33}, m_{44} \tag{4.4d}$$

This shows that the underdominance equivalent of Lemma 2 holds and also the underdominance equivalent of Theorems 2 and 3 are true after we prove the following

Lemma 4.

$$ax^2 + 2bx(1-x) + c(1-x)^2 < 0,\ \forall x \in [0,1] \Leftrightarrow a, c < 0 \text{ and } b < \sqrt{ac}$$

Proof. The argument goes the same way as in the proof of lemma 3. For $b < 0$ everything is clear and for $b > 0$, $b < \sqrt{ac}$ follows in the same way as before. □

Proposition 4 (underdominance equivalent of prop. 2)**.** *If and only if underdominance holds on the margins $\{q = 0\}$ and $\{q = 1\}$ and m_{14} fulfils both of the following conditions*

- $m_{14} < m_{24} + \sqrt{(m_{12} - m_{22})(m_{34} - m_{44})}$
- $m_{14} < m_{13} + \sqrt{(m_{12} - m_{11})(m_{34} - m_{33})}$,

then there is marginal underdominance at the A-locus.

Proposition 5 (underdominance equivalent of prop. 3)**.** *If and only if underdominance holds on the margins $\{p = 0\}$ and $\{p = 1\}$ and m_{14} fulfils both of the following conditions*

- $m_{14} < m_{12} + \sqrt{(m_{24} - m_{22})(m_{13} - m_{11})}$
- $m_{14} < m_{34} + \sqrt{(m_{24} - m_{44})(m_{13} - m_{33})}$,

then there is marginal underdominance at the B-locus.

Proof. Both proofs are simple applications of lemma 4. □

The eigenvalues of the four corners are written in table 3.1 and we easily see, that all four corner equilibria are stable and for corner equilibria this means saturated too. Each of it has index +1. For the C_{ij} we can conclude that their external eigenvalue is negative for each of them. Therefore they are all saturated. To determine their index one has to compute the second eigenvalue of each C_{ij}. This has already been done in (3.10) and we can conclude that each such eigenvalue is positive. This means each C_{ij} is a saturated saddle point and has index -1. It follows that $\delta = 0$. This is case $4a, u$ from fig. 3.2 with all boundary equilibria saturated. As this is the flow reversed case of $4as$, with $\delta = 0$ in both cases, the results can be directly inferred from the analysis of the fully overdominant case above, with points that were sinks above are now sources and non-saturated boundary equilibria are now saturated. For exactly one internal fixed point, the state space is divided into four regions by the isoclines and each of those contains a corner equilibrium which attracts all orbits from its region. Thus the summarizing theorem for the marginal underdominance in both loci case can be inferred from Theorem 5.

Theorem 6. *Let both loci be in marginal underdominance. This implies the following*

- *The boundary flow is like case* $4a, u$ *in fig. 3.2.*
- *All of the eight admissible boundary equilibria are saturated.*
- *The four corner equilibria have index* $+1$ *and the four equilibria on the edges* -1*, therefore* $\delta = 0$*.*
- *Either one, three or five equilibria exist in the interior.*
- *Internal equilibria are either saddles or sources.*
- *Sources are the local minimas of* $\overline{m}$
- *If exactly one internal equilibrium exists, the isoclines divide the state space into four regions, which are the basins of attraction of the corresponding corner equilibrium.*
- *If exactly three internal equilibria exist, two are sources and one is a saddle.*
- *If exactly five internal equilibria exist, three are sources and two are saddles.*

4.3 Marginal overdominance and marginal underdominance in one locus each

Without loss of generality, we assume marginal overdominance in the A locus and marginal underdominance in the B locus. Evaluation of the corresponding relations at $0, 1$ give the following parameter relations:

$$m_{12} > m_{11} > m_{13} \tag{4.5a}$$
$$m_{12} > m_{22} > m_{24} \tag{4.5b}$$
$$m_{34} > m_{33} > m_{13} \tag{4.5c}$$
$$m_{34} > m_{44} > m_{24} \tag{4.5d}$$

This is the same as in the case $4b, o$ from fig. 3.2. We obtain the parameter relations equivalent to marginal overdominance at the A-locus and marginal underdominance at the B-locus, by combining proposition 2 and proposition 5. In the previous section we had one sided restrictions on m_{14}, whereas here it is bounded from above and below by

$$\begin{gathered} m_{24} - \sqrt{(m_{12} - m_{22})(m_{34} - m_{44})},\ m_{13} - \sqrt{(m_{12} - m_{11})(m_{34} - m_{33})} \\ < m_{14} < \\ m_{12} + \sqrt{(m_{24} - m_{22})(m_{13} - m_{11})},\ m_{34} + \sqrt{(m_{24} - m_{44})(m_{13} - m_{33})}. \end{gathered} \tag{4.6}$$

The eigenvalues of the four corner equilibria are described in table 3.1. In this case now the Jacobian of each of the equilibria has one positive and one negative eigenvalue. Thus they are all saddles and not saturated.
With the premisses stated above we see, that $\lambda_{12}, \lambda_{34} < 0$ and $\lambda_{24}, \lambda_{13} > 0$ (3.8), thus C_{12}, C_{34} are both saturated and C_{13}, C_{24} not. We are now interested in the sign of μ_{34} and μ_{12}. They are given

in (3.10) and both negative with the fitness parameters given in (4.5). This means, that C_{12}, C_{34} are saturated and stable and have index $+1$.
By applying the index theorem for saturated equilibria, we obtain that for one inner equilibrium, this has to be a saddle, in order to have index -1, for three in the interior, two have to be saddle and one stable or unstable and eventually for five internal equilibria three have to be saddles and two stable or unstable.
But in this case one can obtain even more by looking again at the Jacobi matrix for an arbitrary internal equilibrium as was given in Lemma 1.

$$J_{int} = \begin{pmatrix} p(1-p)m_A & 2p(1-p)\hat{m} \\ 2q(1-q)\hat{m} & q(1-q)m_B \end{pmatrix} \tag{4.7}$$

The determinant of this internal 2×2 Jacobi matrix is the product of the two eigenvalues. Thus if the determinant is negative, the eigenvalues have different signs. This is exactly the case for the marginal overdominance in one locus and marginal underdominance in the other locus case, as the determinant is given by $pq(1-p)(1-q)[m_A m_B - 4\hat{m}^2]$. m_A is smaller than zero if the A locus is in marginal overdominance and the m_B is greater than zero if the B locus is in marginal underdominance. Thus we have $negative - positive = negative$ for all $p, q \in [0, 1]$. This means every internal equilibrium point is a saddlepoint and thus has index -1. It attracts only the orbits from the two non-saturated edge equilibria and the orbits above the attractive subspace of the saddlepoint converge to the asymptotically stable edge equilibrium that lies in this region.
From our analysis we did before, this rules out the case of three or five internal equilibria, since at least one of them would need to have index $+1$ and this was excluded by the determinant of the inner Jacobi matrix and the consequences we drew out of it.
Thus we have proven the following

Theorem 7. *For marginal overdominance in one locus and marginal underdominance in the other locus, there are eight boundary equilibria, of which two are sinks, two are sources and four are saddlepoints. In addition, there is a unique internal equilibrium, which is a saddlepoint.*

It may be interesting to note that if, in the case $4b, o$ with $\delta = 2$, the condition of marginal overdominance in one and marginal underdominance in the second locus is not fulfilled, then more than one internal equilibrium are possible. This can be seen in fig. 3.19 in section 3.3.2. The plot of case $4b, o$ with $\delta = 2$ with three internal equilibria violates condition (4.6), while the other one doesn't.

5. LINEAR ISOCLINES

After the restriction to continuous isoclines we now present another simplification in terms of the isoclines.
In this section, we set some of the parameters in a way that we end up with linear isoclines. This simplifies the system of differential equations and allows us to compare ours with the system used by Schuster et al. (1981) to study the evolution of two strategies in animal contests between two populations. An additional interesting property is the fact that three other well known models, such as the additive viability model, the haploid dynamics and a model presented in Gavrilets (1992), are special cases of the one derived in this chapter.
If we order the differential equations of (3.1) by the monomials 1, p, q, pq, p^2, q^2, p^2q and q^2p, when they exist, the first things to note are that the p^2q-term in the first equations is the same as the q^2p-term in the second and the pq-term of one equation is the same as the p^2- or q^2-term in the other equation. This suggests that an elimination of these terms reduce both equations simultaneously. Thus we get

$$\begin{aligned}\dot{p} =& \frac{1}{2}p(1-p)[q(m_{11}-m_{22}-m_{33}+m_{44})+2(m_{34}-m_{44})+2p(m_{33}-2m_{34}+m_{44})]\\ \dot{q} =& \frac{1}{2}q(1-q)[p(m_{11}-m_{22}-m_{33}+m_{44})+2(m_{24}-m_{44})+2q(m_{22}-2m_{24}+m_{44})],\end{aligned} \tag{5.1}$$

a significantly simpler system. The elimination was done by assuming the following relations:

$$\begin{aligned}4m_{14}-2m_{13}-2m_{24} &= 2m_{12}-m_{11}-m_{22}+2m_{34}-m_{33}-m_{44}\\ 2m_{12}-m_{11}-m_{22} &= 2m_{34}-m_{33}-m_{44}\\ 2m_{13}-m_{11}-m_{33} &= 2m_{24}-m_{22}-m_{44}.\end{aligned} \tag{5.2}$$

The first relation sets the epistasis term $e_1-e_2-e_3+e_4=0$, while the other two ensure that the term $2m_{ij}-m_{ii}-m_{jj}$ is the same for opposing margins. Together, those parameter elimination lead to the fact that the epistasis parameter $e_i=\frac{1}{4}(m_{11}-m_{22}-m_{33}+m_{44})$ $\forall i=1,2,3,4$. This term is exactly a quarter of the interaction term with the other species c.

	A_1A_1	A_1A_2	A_2A_2
B_1B_1	$2a+b+2(c+d)+f$	$a+c+2d+f$	$2d+f$
B_1B_2	$2a+b+c+d$	$a+\frac{c}{2}+d$	d
B_2B_2	$2a+b$	a	0

Tab. 5.1: Fitness scheme to get the representation in five parameters from Schuster et al. (1981).

If we set the viability matrix as that in table 5.1, we get a similar representation of the system as in Schuster et al. (1981):

$$\begin{aligned}\dot{p} =& p(1-p)(a+bp+cq)\\ \dot{q} =& q(1-q)(d+cp+fq),\end{aligned} \tag{5.3}$$

with the only deviation being that the interaction term with the other species is the same, whereas Schuster et al. (1981) allow two different interaction terms. This is important, since it rules out the boundary flow being cyclic, which can occur in the setting of Schuster et al. (1981).

For the dynamics that can occur in such a system, they have already characterized all, but in four cases the flow on the boundary together with the position of the isoclines does not fully determine the flow in the interior of the square and limit cycles can occur. Since we have a Lyapunov function in our general system, we have one here too: $\overline{m} = fq^2 + bp^2 + 2cpq + 2dq + 2ap$ is again a generalized potential function. This rules out the occurrence of limit cycles.
Because of the second and third equation of (5.2), the denominator of μ_{12} (μ_{13}) is the same as of μ_{34} (μ_{24}). Thus, if the two opposite edge-equilibria exist, then the sign of their internal eigenvalues is the same and therefore their internal stability. This rules out 7 of 26 boundary flows, with flow reversal taken into account, described in fig. 3.2. The isoclines in this chapter are simple lines and have at most one intersection point. This rules out boundary flows with boundary index sum $\delta = -2, -1, 3, 4$. Transferring the results from Schuster et al. (1981) to our terminology and a special look at the four, more difficult, cases, leads to a full classification of the phase portraits for all 19 possible boundary flows.
6 boundary flow classes can have $\delta = 0$, namely $1c, s$, $2b, ss$, $2d, ss$, $2e, ss (= 2c, uu$ reversed), $3a, ss$ and $4a, s$. The internal equilibrium in all those classes is a global attractor.
16 boundary flow classes can have $\delta = 1$, which excludes the existence of an internal equilibrium. This set of classes includes all 19 possible, except $0c$(since $\delta = +2$ always), $4a, s$ and $4b, o$. For the latter two, this follows from the position of the isoclines.
Finally 8 boundary flow classes can have $\delta = 2$, namely $0c$, $1d, s$, $2b, ss$, $2c, us$, $2c, ss$, $2d, s \to u$, $3a, uu$ and $4b, o$. This implies that in all those cases, the internal equilibrium is a saddle.
Altogether we have 30 different structurally stable flows on the square, a slightly reduced number in comparison to the 36 conjectured by Schuster et al. (1981). For the flows with $\delta = +1, +2$ we have the same results, as can be seen by comparison with the figures 4 and 5 of Schuster et al. (1981). In the same work a Hopf-bifurcation could happen for the boundary-flows $1c, s$ and $2b, ss$ and $\delta = 0$, but this is excluded here.
The three aforementioned special cases will be analysed next. They arise from this model here, by applying different constraints to the parameters a, b, c, d and f.
If we set $a = d$ and $b = f$, the system reduces to one analysed by Gavrilets (1992), where the loci have the same effect on the fitness parameter. It will be further employed in sect. 5.1.
If we set the epistasis parameter $c = 0$ in the system (5.3), the system reduces to that derived in sect. 5.2, which is also called a no-epistasis model.
If we set $b = f = 0$ in the system (5.3), we reach a system without dominance as derived in sect. 5.3.

5.1 Viability matrix introduced by Gavrilets

For the study of multilocus systems, one tries to find the simplest models, where the results that can be derived are, however, not trivial. Such a class of models was introduced by Zhivotovsky and Gavrilets (1992), for which they claim that it is the simplest additive-kind model-class with epistasis and dominance. It can describe multilocus scenarios, where each of the loci contains two alleles.
In a subsequent paper, Gavrilets (1992) applies this model for two loci and assumes that both loci effect the fitness values equally. This results in the viability matrix shown in table 5.2.

	A_1A_1	A_1A_2	A_2A_2
B_1B_1	$4u + 4v + 8w$	$3u + 2v + 4w$	$2u + 2v$
B_1B_2	$3u + 2v + 4w$	$2u + 2w$	u
B_2B_2	$2u + 2v$	u	0

Tab. 5.2: Fitness scheme as defined by Gavrilets (1992)

This viability matrix W is symmetric in the sense that $W = W^T$. This comes from the fact that the two loci have equal effects. If we plug this matrix into the system (3.1),we get:

$$\begin{aligned} \dot{p} &= p(1-p)[u + 2vp + 4wq], \\ \dot{q} &= q(1-q)[u + 2vq + 4wp], \end{aligned} \tag{5.4}$$

which is exactly system (5.3) with $a = d = u$, $b = f = 2v$ and $c = 4w$.
Because of the symmetry, the phase portrait of this system is symmetric with respect to the line $q = p$, this means not only that, for example, C_{34} and C_{24} are symmetric, if they exist, but also that the flow around them is the same. This is an important additional property to those already inherited from (5.3).
This implies that from the 19 possible boundary flow classes for (5.3), only 5 ($0a$, $0c$, $2c, ss$, $2e, ss$ and $4a, s$) have this additional property. For four of those classes, δ is already unique in (5.3) and thus only the case $2e, ss$ needs slightly more attention. It is however easily seen that this case can have $\delta = 0, 2$, but not $\delta = 1$ due to symmetry. $\delta = 0$ holds if and only if $v^2 - 4w^2 > 0$.
Together, we have

- two cases, $0a$ and $2c, ss$, where all orbits are attracted by a globally asymptotic stable corner equilibrium,
- two classes, $0c$ and $2e, ss$ (under the right conditions), where we have two attracting corner equilibria separated by a saddle in the interior of the state space,
- and two classes, $2e, ss$ (under the right conditions) and $4a, s$, where we have a globally asymptotic stable equilibrium in the interior of the state space.

If we set $v = 0$, we get a symmetric haploid model. The standard one will be analysed in sect. 5.3. On the other hand, if we set $w = 0$, we get a symmetric additive model. The standard additive viability model will be analysed in the following section.

5.2 Additive viability model

In the discrete-time model, only special cases for the viability matrix are considered, because of the complexity of the resulting formulas. The most popular ones are, in increasing complexity, the additive, multiplicative and symmetric viability model. The first two are without epistasis, in contrast to the latter. The names of the first two come from the fact that the fitness of genotypes are determined additively/multiplicatively from fitnesses at individual loci. In the weak-selection limit however, it turns out that the additive and multiplicative model coincide, which is definitely not true for arbitrary selection. From those three, we will first treat the additive one, as it can be seen of a special case of linear-isoclines system (5.3).
For the additive model we assign each genotype A_iA_j and B_kB_l a own parameter, and for the A- and B-locus combined we take the sum of their parameters. This is also called the no epistasis fitness scheme. This results in table 5.3.

	A_1A_1	A_1A_2	A_2A_2
B_1B_1	$a_1 + b_1$	$a_2 + b_1$	$a_3 + b_1$
B_1B_2	$a_1 + b_2$	$a_2 + b_2$	$a_3 + b_2$
B_2B_2	$a_1 + b_3$	$a_2 + b_3$	$a_3 + b_3$

Tab. 5.3: Additive fitness scheme per diploid genotype

This reduces the system (3.1) to

$$\begin{aligned} \dot{p} &= p(1-p)[a_2 - a_3 + p(a_1 - 2a_2 + a_3)] \\ \dot{q} &= q(1-q)[b_2 - b_3 + q(b_1 - 2b_2 + b_3)], \end{aligned} \tag{5.5}$$

a very simple form. The nontrivial isoclines are given by the constant lines

$$
\begin{aligned}
p &= \frac{a_3 - a_2}{a_1 - 2a_2 + a_3} \\
q &= \frac{b_3 - b_2}{b_1 - 2b_2 + b_3}.
\end{aligned} \tag{5.6}
$$

Both are constant lines parallel to one of the axes. The first is inside the unit square if and only if $\mathrm{sgn}(a_3 - a_2) = \mathrm{sgn}(a_1 - a_2)$ and the same holds for the second (with a_i changed to b_i). This is the same condition that holds for the admissibility of the C_{ij} in the general model. The flow on opposite sides of the square has to be the same, since it is determined by the ordering of the three parameters of one locus.

For both isoclines outside the unit square, this yields only the case $0a$ of Fig.3.2, with exactly one of the corner equilibria stable and thus attracting all orbits.

For one of the isoclines inside of the square w.l.o.g $\mathrm{sgn}(a_3 - a_2) = \mathrm{sgn}(a_1 - a_2)$ and $\mathrm{sgn}(b_3 - b_2) > 0 > \mathrm{sgn}(b_1 - b_2)$, we get for the internal eigenvalues at C_{34}, C_{12}: $\mu_{34} = \mu_{12}$. The external eigenvalues simplify to $\hat{\lambda}_{34} = b_2 - b_3$ and $\hat{\lambda}_{12} = b_2 - b_1$, therefore C_{34} is saturated, while C_{12} is not. The flow on the q-axis goes downwards, on the parallel side too. This is equivalent to case $2a, ss$ for $\mu_{34} > 0$ and $2a, uu$ for $\mu_{34} < 0$. In both cases C_{34} is saturated and this leads to boundary index sum of $+1$, what could have implied from the index theorem (theorem 2), since there can't be an interior fixed point. For C_{34} being fully stable, all orbits converge to it, for it being internal unstable, the isocline separates the square in two parts, where each orbit in each of the parts goes to the corner equilibrium neighbouring C_{34} and contained in the right part.

If both isoclines are inside the square, there can be three distinct cases. Both $a_1 - 2a_2 + a_3$ and $b_1 - 2b_2 + b_3$ are positive or negative, or they have opposite sign. If the sign is negative, we can speak of marginal overdominance, whereas for positive sign it is called marginal underdominance, since $m_{A_1A_1} - 2m_{A_1A_2} + m_{A_2A_2} = a_1 - 2a_2 + a_3$ in this setting. For both loci in marginal overdominance none of the boundary equilibria is saturated (numerator of the isocline has to be negative too and the external eigenvalue is the negative numerator, thus positive) and the internal one is therefore globally asymptotic stable. For the full underdominance case all eight boundary equilibria are saturated and the interior is a repellor. The isoclines separate the state space into four parts which each contains a stable corner equilibria, which attracts therefore all orbits contained in its part.

If one locus is in marginal overdominance while the other in marginal underdominance, then the internally stable boundary equilibria are saturated too. This gives a boundary index sum of $+2$, therefore we need a saddle in the interior and since there is only one internal fixed point, this has to be the saddle. The two saturated boundary equilibria attract all orbits lying in their halfplane separated by the isocline connecting the internal unstable ones. For general over- or underdominance, see sect. 4.3.

Thus we have characterized all flows that can occur for the special case of additive fitness scheme. The same has been achieved for the additive model with arbitrary strong selection. It has also at most one internal equilibrium which coincides with the one derived above. The stability pattern in the weak selection additive model and in the general one are also the same, because the mean fitness is non-decreasing in both.

This is not true for the general multiplicative viability model, as here two additional equilibria can exist and mean fitness can be decreasing near a stable equilibrium. Thus global convergence is an open problem here. For more on the cases with arbitrary s see Bürger (2000) chapter II.1.1-2.

5.3 The haploid two-locus two-allele model

One of the first to treat the two-locus two-allele haploid model was Felsenstein (1965). Further investigation was conducted by Feldman (1971), Rutschman (1994) and completed by Bank et al. (2012). From those it is known that at most one internal equilibrium can exist. If we take their dynamics and derive the weak-selection limit, we end up with the following system of ODE's:

$$\begin{aligned}\dot{p} =& p(1-p)(v_3 - v_4 + q(v_1 - v_2 - v_3 + v_4))\\ \dot{q} =& q(1-q)(v_2 - v_4 + p(v_1 - v_2 - v_3 + v_4)),\end{aligned} \tag{5.7}$$

where the fitness matrix V is given by:

	A_1	A_2
B_1	v_1	v_2
B_2	v_3	v_4

Tab. 5.4: Haploid fitness scheme

By comparing system (5.7) to (5.3), one can directly see that setting $b = f = 0$ in (5.3) gives the former.
Using the fitness parameter per genotype in the haploid model and assuming additivity between them, we get the fitness scheme as seen in table (5.5). This is a fitness scheme which exhibits no dominance. Applying this in the system (3.1), we get exactly the equations given in (5.7).

	A_1A_1	A_1A_2	A_2A_2
B_1B_1	$2v_1$	$v_1 + v_2$	$2v_2$
B_1B_2	$v_1 + v_3$	$\frac{v_1+v_2+v_3+v_4}{2}$	$v_2 + v_4$
B_2B_2	$2v_3$	$v_3 + v_4$	$2v_4$

Tab. 5.5: Additive fitness scheme per haploid genotype

It turns out that this dynamic plays a role in the conflict of the sexes as described in Schuster and Sigmund (1981) and is in fact the replicator equation for 2×2 games. Again the only difference is the equality of the interacting terms. Without it there can be infinitely many periodic orbits, but here, due to the existence of a Lyapunov function, this cannot be the case. As shown in Schuster and Sigmund (1981) and Bank et al. (2012), if the internal equilibrium exists, but no limit cycles, as it is the case here, then it is a saddlepoint and two diametrical monomorphic equilibria are sinks. This is exactly boundary flow class $0c$, while for the other two possible classes $0a$ and $0b$ no internal equilibria exist and all orbits converge to one of the corner equilibrium, which is therefore globally asymptotically stable. No other boundary flows can exist due to the fact that $v_i + v_j$ is always intermediate between $2v_i$ and $2v_j$ and thus no edge-equilibria can exist.
Another aspect of the weak-selection limit in the haploid model, is that (5.7) can be written as

$$\begin{aligned}\dot{p_i} =& p_i((V^T\mathbf{q})_i - \mathbf{p}V^T\mathbf{q})\\ \dot{q_i} =& q_i((V\mathbf{p})_i - \mathbf{q}V\mathbf{p}),\end{aligned} \tag{5.8}$$

where $\mathbf{p}$ is the vector of the allele frequencies on locus A and $\mathbf{q}$ the same for locus B. One can expand the model to more than two alleles per locus and the dynamic can still be written in the presented form (5.8), which in fact is the replicator dynamic for partnership games as described in Hofbauer and Sigmund (1998). One important aspect of partnership games is the existence of the potential $\mathbf{p}V\mathbf{q} = \overline{m}$, which is the same as for the general weak-selection limit.

6. SYMMETRIC VIABILITY MODEL

As announced before, the symmetric viability model is most popular in studying two-locus two-allele dynamics for arbitrary strength of selection. This can be seen in Bodmer and Felsenstein (1967) chapter 6 and references therein. The fitness scheme is given in table 6.1.

	A_1A_1	A_1A_2	A_2A_2
B_1B_1	d	c	a
B_1B_2	b	0	b
B_2B_2	a	c	d

Tab. 6.1: Symmetric fitness scheme

This fitness scheme is centrosymmetric and not symmetric in the sense normally used for matrices. The name symmetric comes from the fact that you can interchange $A_1 \leftrightarrow A_2$ and $B_1 \leftrightarrow B_2$ simultaneously and get the same fitness matrix out.
We now reparametrize the fitness scheme in the way Nagylaki (1992) did, for better handling of the equations, according to table 6.2. The values of all parameters are elements of $\mathbb{R}$.

	A_1A_1	A_1A_2	A_2A_2
B_1B_1	$s+t+e_1$	t	$s+t+e_2$
B_1B_2	s	0	s
B_2B_2	$s+t+e_2$	t	$s+t+e_1$

Tab. 6.2: Symmetric fitness scheme reparametrized

This results in the system of equation

$$\dot{p} = p(1-p)(e_2(p-2pq+(-1+2p)q^2)+e_1(-(-1+q)^2+p(1+2(-1+q)q))+(-1+2p)s)$$

and

$$\dot{q} = q(1-q)(e_2(q+p(-p+2(-1+p)q))+e_1(-1+q+p(2-p+2(-1+p)q))+(-1+2q)t),$$

which is not very descriptive. So we introduce new parameter combinations to simplify the formulas (compare Nagylaki (1992)

$$l = e_1 + e_2, \; m = e_1 - e_2, \tag{6.1a}$$

$$r = e_1 + e_2 + 2s, \; u = e_1 + e_2 + 2t, \tag{6.1b}$$

$$r_1 = r + 2s, \; u_1 = u + 2t, \tag{6.1c}$$

$$\rho = r_1 u_1 - 4m^2, \tag{6.2}$$

$$\epsilon = \frac{r_1}{u_1} - \frac{r^2}{m^2}, \; \tilde{\epsilon} = \frac{u_1}{r_1} - \frac{u^2}{m^2} \tag{6.3}$$

Then the system reads:

$$\dot{p} = p(1-p)(-e_1 - s + 2e_1 q - lq^2 + p(r - 2l(1-q)q) \tag{6.4}$$

$$\dot{q} = q(1-q)(-e_1 - t + 2e_1 p - lp^2 + q(u - 2l(1-p)p) \tag{6.5}$$

From this one can directly read off the non-trivial isoclines

$$p = f(q) = \frac{e_1(1-q)^2 + e_2 q^2 + s}{r - 2l(1-q)q} \tag{6.6}$$

$$q = g(p) = \frac{e_1(1-p)^2 + e_2 p^2 + t}{u - 2l(1-p)p}. \tag{6.7}$$

The coordinates of the C_{ij} are given by:

$$\begin{aligned} C_{34} &: \left(\frac{e_1+s}{r}, 0\right) \\ C_{12} &: \left(\frac{e_2+s}{r}, 1\right) \\ C_{24} &: \left(0, \frac{e_1+t}{u}\right) \\ C_{13} &: \left(1, \frac{e_2+t}{u}\right) \end{aligned} \tag{6.8}$$

The non-zero coordinate of opposing C_{ij}'s sum up to one, therefore, one is admissible if and only if the other one is too. Their distance to $\frac{1}{2}$ is the same, but with opposite sign. If there is no fixed point on one of the sides, then the flow on this side is reversed to that on the opposite side. The reason of this is the point symmetry to the central point of the unit square $\left(\frac{1}{2}, \frac{1}{2}\right)$ =SE. This can be easily verified by checking that $f(1-q) + f(q) = 1$ (and the same for g), where $f(2x_0 - x) = 2y_0 - f(x)$ is the formula for checking that a function is point symmetric to (x_0, y_0). It also holds that the Jacobian at a point (p, q) is the same as at its symmetry point $(1-p, 1-q)$. This means that the flow around a point and around it's symmetric point is the same. Therefore we obtain that opposing C_{ij}'s have the same eigenvalues.
Another interesting way of seeing this symmetry, is by changing the coordinates of (6.4) according to

$$p = \frac{1}{2} + x, \;\; q = \frac{1}{2} + y. \tag{6.9}$$

This transforms the system (6.4) into one proportional to

$$\dot{x} = (1 - 4x^2)(r_1 x + 2my + 4lxy^2), \tag{6.10a}$$

$$\dot{y} = (1 - 4y^2)(u_1 y + 2mx + 4lyx^2), \tag{6.10b}$$

where $-\frac{1}{2} \leq x, y \leq \frac{1}{2}$. It is immediately clear, that the center $(0,0)$ is an equilibrium and the dynamics is point-symmetric about it, since the degrees of the monomials on the right-hand sides are odd.
The internal eigenvalues are:

$$\mu_{34} = \mu_{12} = \frac{(e_1+s)(e_2+s)}{r} \tag{6.11a}$$

$$\mu_{24} = \mu_{13} = \frac{(e_1+t)(e_2+t)}{u}. \tag{6.11b}$$

Since the opposing edge-equilibria are always simultaneously admissible, the numerators in equations (6.11) are always positive and the denominator is negative if and only if the corresponding equilibrium is internally stable.
Now comparing table 3.2 with those restrictions obtained in the last paragraph, we are left with the four cases 0c, 2b,ss, 4a,s and 4b,o. For the external eigenvalues, we get

$$\hat{\lambda}_{34} = \hat{\lambda}_{12} = -\frac{e_1 e_2 r_1 + l s^2}{r^2} - t = \frac{1}{4r^2}\left(m^2 r_1 - r^2 u_1\right) \tag{6.12a}$$

$$\hat{\lambda}_{24} = \hat{\lambda}_{13} = -\frac{e_1 e_2 u_1 + l t^2}{u^2} - s = \frac{1}{4u^2}\left(m^2 u_1 - u^2 r_1\right). \tag{6.12b}$$

Therefore for all four cases, the boundary index sum can be +2, for all but 0c it can be 0, for 4b,o it could be −2, but the impossibility of this was shown in theorem 3 and for case 4a,s it can be +4. Thus we have 8 distinct cases, while all might have 1 up to 5 internal equilibria.
Nagylaki (1992) (p. 337 f.) gives a family of symmetric viability matrices, which go, with increasing k, through the cases 0c and 2b,ss, both with one internal saddle, to 2b,ss with three internal equilibria to 2b,ss with one internal sink.
To specify the symmetric pairs of internal fixed points, we use (6.10).

Theorem 8. *For the symmetric viability model SE is always an equilibrium and the following pairs of equilibrium points can exist:*

$$y_{1,2} = \pm\sqrt{\frac{-r_1 - 2m\sqrt{\frac{r_1}{u_1}}}{4l}}, \quad x_{1,2} = \sqrt{\frac{u_1}{r_1}}y_{1,2}, \tag{6.13a}$$

$$y_{3,4} = \pm\sqrt{\frac{-r_1 + 2m\sqrt{\frac{r_1}{u_1}}}{4l}}, \quad x_{3,4} = -\sqrt{\frac{u_1}{r_1}}y_{3,4}. \tag{6.13b}$$

Additionally the following statements hold true:

- *If both isoclines have no poles, there can be two additional equilibria in the interior.*
- *If only one of the isoclines has poles, the symmetry point $\left(\frac{1}{2}, \frac{1}{2}\right) = SE$ is the only internal equilibrium.*
- *If both isoclines have poles, there can be at most four additional equilibria in the interior.*

Remark 2. *Note that if one pole (one internal equilibrium) exists, point-symmetry ensures the existence of a second pole (internal equilibrium), except they coincide at SE.*

We want to use some technical details that occur in the proof again later and so we first compute only the solutions and then prove a lemma from which the additional statements follow.

Proof. From (6.4) one can easily compute the zeroes of the denominator. For $lr_1 < 0$, $f(q)$ has two poles and for $lu_1 < 0$, $g(p)$ has two poles. Therefore for $\operatorname{sgn}(u_1) = \operatorname{sgn}(r_1) = \operatorname{sgn}(l)$ no isocline has poles, while for $\operatorname{sgn}(u_1) = \operatorname{sgn}(r_1) = -\operatorname{sgn}(l)$ all four poles exist. For exactly two poles to exist, only the sign of u_1 and r_1 have to differ.
The next step is to compute the x and y directly. We assume $x \neq 0$ or $y \neq 0$. From (6.10), we get

$$x = -\frac{2my}{r_1 + 4ly^2}, \; y = -\frac{2mx}{u_1 + 4lx^2}. \tag{6.14}$$

From this we see $x = 0$ if and only if $y = 0$, so we assume $xy \neq 0$. Now we are allowed to multiply the equations of (6.14) and divide then by xy. Eliminating x leads to

$$4m^2\frac{r_1}{u_1} = \left(r_1 + 4ly^2\right)^2. \tag{6.15}$$

Thus (6.15) has real solutions only if $\operatorname{sgn}(u_1) = \operatorname{sgn}(r_1)$, what proves the second of the additional statements.
Let this equality hold true for the following steps. Taking the square root and solving for y^2 leads to

$$y_{1,2}^2 = -\frac{r_1 + 2m\sqrt{\frac{r_1}{u_1}}}{4l}, \quad y_{3,4}^2 = -\frac{r_1 - 2m\sqrt{\frac{r_1}{u_1}}}{4l} \tag{6.16}$$

and assuming that those are positive gives the two pairs of solutions stated above.

Substituting (6.16) into (6.14) gives

$$x_{1,2} = \sqrt{\frac{u_1}{r_1}}y_{1,2}, \quad x_{3,4} = -\sqrt{\frac{u_1}{r_1}}y_{3,4}. \tag{6.17}$$

□

The following Lemma lists all conditions for the internal equilibria to be admissible.

Lemma 5. *The following table states the conditions for which the solutions* $y_{1,2}^2 = -\frac{r_1+2m\sqrt{\frac{r_1}{u_1}}}{4l}$, $y_{3,4}^2 = -\frac{r_1-2m\sqrt{\frac{r_1}{u_1}}}{4l}$ *and* $x_i^2 = \frac{u_1}{r_1}y_i^2$ *are inside of the unit square:*

	$0 < y_{1,2}^2$	$y_{1,2}^2 < \frac{1}{4}$	$0 < y_{3,4}^2$	$y_{3,4}^2 < \frac{1}{4}$
$0 < u_1 < r_1$:				
$l > 0$	$m < 0, \rho < 0$	$r > 0, \epsilon < 0$	$m > 0, \rho < 0$	$r > 0, \epsilon < 0$
$l < 0$	$m > 0$ or $m < 0, \rho > 0$	$r > 0, m < 0, \epsilon > 0$ or $r < 0, m > 0, \epsilon < 0$ or $r < 0, m < 0$	$m < 0$ or $m > 0, \rho > 0$	$r > 0, m > 0, \epsilon > 0$ or $r < 0, m > 0$ or $r < 0, m < 0, \epsilon < 0$
$0 < r_1 < u_1$:				
$l > 0$	$m < 0, \rho < 0$	$u > 0, \tilde{\epsilon} < 0$	$m > 0, \rho < 0$	$u > 0, \tilde{\epsilon} < 0$
$l < 0$	$m > 0$ or $m < 0, \rho > 0$	$u > 0, m < 0, \tilde{\epsilon} > 0$ or $u < 0, m > 0, \tilde{\epsilon} < 0$ or $u < 0, m < 0$	$m < 0$ or $m > 0, \rho > 0$	$u > 0, m > 0, \tilde{\epsilon} > 0$ or $u < 0, m > 0$ or $u < 0, m < 0, \tilde{\epsilon} < 0$
$0 > u_1 > r_1$:				
$l > 0$	$m < 0$ or $m > 0, \rho > 0$	$r > 0, m > 0$ or $r > 0, m < 0, \epsilon < 0$ or $r < 0, m > 0, \epsilon > 0$	$m < 0, \rho > 0$ or $m > 0$	$r > 0, m > 0, \epsilon < 0$ or $r > 0, m < 0$ or $r < 0, m < 0, \epsilon > 0$
$l < 0$	$m > 0, \rho < 0$	$r < 0, \epsilon < 0$	$m < 0, \rho < 0$	$r < 0, \epsilon < 0$
$0 > r_1 > u_1$:				
$l > 0$	$m < 0$ or $m > 0, \rho > 0$	$u > 0, m > 0$ or $u > 0, m < 0, \tilde{\epsilon} < 0$ or $u < 0, m > 0, \tilde{\epsilon} > 0$	$m < 0, \rho > 0$ or $m > 0$	$u > 0, m > 0, \tilde{\epsilon} < 0$ or $u > 0, m < 0$ or $u < 0, m < 0, \tilde{\epsilon} > 0$
$l < 0$	$m > 0, \rho < 0$	$u < 0, \tilde{\epsilon} < 0$	$m < 0, \rho < 0$	$u < 0, \tilde{\epsilon} < 0$

Tab. 6.3: The conditions for the inequalities in the top to hold, are given in the cells

Proof. The solutions can only be achieved, if $\operatorname{sgn}(u_1) = \operatorname{sgn}(r_1)$. Therefore let this hold from now on.
The single conditions can all be easily computed after one thinks about squaring and taking roots of inequalities. Therefore we show only parts of the computations.
Let us start with the upper left cell, where $0 < u_1 < r_1$ and $l > 0$ hold and let $0 < y_+^2$. Then positive r_1 multiplied with $\sqrt{\frac{u_1}{r_1}}$ gives $\sqrt{u_1 r_1}$. Therefore we get $0 < -\sqrt{u_1 r_1} - 2m$, which only holds for $m < 0$, since otherwise the right-hand side is always negative. Add $\sqrt{u_1 r_1}$ to the whole inequality and since both sides are then positive we are allowed to square the inequality and the sign stays the same. Subtracting $4m^2$ from both sides yields $\rho < 0$.
Let now be $\rho, m < 0$. Add $4m^2$ to $\rho < 0$ yields $r_1 u_1 < 4m^2$. When taking the square root of the inequality we use $m < 0$ and get $\sqrt{u_1 r_1} < -2m$. Subtract $\sqrt{u_1 r_1}$, multiply with $\sqrt{\frac{u_1}{r_1}}$ and divide by $4l > 0$ and you get $y_+^2 > 0$. If y^2 is positive so is x^2, since $\frac{u_1}{r_1} > 0$. All other calculations for $0 < y_\pm$ work in a similar way.
Next let us solve $y_+^2 < \frac{1}{4}$ under $0 < u_1 < r_1$ and $l > 0$, which means no poles. It's easy to see that

$l + r_1 = 2r$ and this yield the inequality $-m\sqrt{\frac{u_1}{r_1}} < r$. As the computation of $x_+^2 < \frac{1}{4}$ makes only sense if $y_+^2 > 0$, we get from a quick look at the table 6.3 that $m < 0$. This yields $r > 0$, because otherwise the inequality is false. Then dividing by $-m$ and squaring both positive sides, yields $\frac{r_1}{u_1} - \left(\frac{r}{m}\right)^2 = \epsilon < 0$.
Let now $\epsilon, m < 0,\ r > 0$. Add $\epsilon < 0$ with $\left(\frac{r}{m}\right)^2$ and while taking the root keep in mind that r/m is negative and therefore put a minus sign in front of it. Multiply both sides with $-2m$ and recall $2r = l + r_1$. Subtract both sides by r_1 and divide by $4l$ and you get $-\frac{r_1+2m\sqrt{\frac{u_1}{r_1}}}{4l} < \frac{1}{4}$, which was claimed. Since in this case $(0 < u_1 < r_1)$ $\frac{u_1}{r_1} < 1$ holds, $x^2 < y^2 < \frac{1}{4}$.
If we have four poles (this means $\operatorname{sgn}(l) = -\operatorname{sgn}(u_1)$), things get more technical, but however stay rather straightforward.
If u_1 and r_1 are interchanged, you have to show $0 < x^2 < \frac{1}{4}$ and for the conditions, this means interchange $r \to u$ and $\epsilon \to \tilde{\epsilon}$. □

Now we can finish the proof of theorem 8:

Proof. For the case of no poles, where l has the same sign as r_1, u_1, one can read off the table 6.3 that dependent on the sign of m only one of the $y_\pm^2$ is real. Thus only two additional fixed points can occur in the interior.
If both isoclines have two poles, there is the possibility of a parameter choice, where four fixed points can occur in the interior. This again can be seen by looking at table 6.3. This finishes the proof. □

Since l is a epistasis parameter, it pays for better intuition, to emphasise its connection to the number of poles.

Lemma 6. *For $l, s, t \neq 0$ the following holds true:*

- *$f(q)$ has exactly 2 poles if and only if $ls < 0$ and $\left|\frac{l}{2}\right| < |2s|$*
- *$g(p)$ has exactly 2 poles if and only if $lt < 0$ and $\left|\frac{l}{2}\right| < |2t|$*

$\frac{l}{2}$ can be interpreted as the arithmetic mean of epistasis and therefore it turns out that the isoclines only have poles, if the mean epistasis has opposite sign of the heterozygous fitness value and it's absolute value is simultaneously smaller than the absolute value of the doubled heterozygous fitness value. This connects the otherwise technical assumption of the existence of poles very closely with epistasis.

Proof. As was seen in the proof above $f(q)$ has poles if and only if $lr_1 < 0$. For $\operatorname{sgn}(l) = \operatorname{sgn}(s)$, $\operatorname{sgn}(r_1) = \operatorname{sgn}(l + 4s) = \operatorname{sgn}(s) = \operatorname{sgn}(l)$ and therefore $\operatorname{sgn}(lr_1) = \operatorname{sgn}(l)^2 > 0$ holds. Thus no poles for those ranges.
For $\operatorname{sgn}(l) = -\operatorname{sgn}(s) = +1$, the inequality reads $\frac{l}{2} < -2s$ and therefore $r_1 = l + 4s < 0$ and $lr_1 < 0$. For $\operatorname{sgn}(l) = -\operatorname{sgn}(s) = -1$, the inequality reads $-\frac{l}{2} < 2s$ and therefore $r_1 = l + 4s > 0$ and since $l < 0$, $lr_1 < 0$ holds. Thus $f(q)$ has in both cases two poles.

The other direction is also easy, if we consider first the case of $l > 0$, it $r_1 < 0$ and therefore $\frac{l}{2} < -2s$ follows from $lr_1 < 0$, what is the condition for having two poles. For negative l, $r_1 > 0$ and therefore $-\frac{l}{2} < 2s$. For the inequalities to hold, l and s have to have opposite signs and one can take absolute values to unite them in one inequality. □

As a next step towards a full characterization of all possible phase portraits in the centrosymmetric viability model, we need the following lemmas:

Lemma 7. *The following holds true:*

- *C_{34} and C_{12} are admissible* $\Leftrightarrow \left(\frac{r}{m}\right)^2 > 1$.

- *C_{24} and C_{13} are admissible* $\Leftrightarrow \left(\frac{u}{m}\right)^2 > 1$.

Proof. Using (6.9) we can equate the p-coordinate of C_{34} to $\frac{1}{2}+x$ and solve for x. We obtain $x = \frac{m}{2r}$. Since C_{34} is admissible, $-\frac{1}{2} < x < \frac{1}{2}$ holds. Multiplying by 2 and squaring the right side of the inequality, we find $\left(\frac{m}{r}\right)^2 < 1$ and by taking the reciprocal value, which changes the inequality sign, we get $\left(\frac{r}{m}\right)^2 > 1$.
For the other direction all steps made in the forward proof are reversed and one has to be careful by taking the square root of $\left(\frac{m}{r}\right)^2 < 1$, since the sign of 1 and of the inequality sign has to be changed if $\frac{m}{r} < 0$. C_{12} is admissible if and only if C_{34} is admissible. The proof of the second statement works in a similar way. ☐

Lemma 8. *Let* $\operatorname{sgn}(u_1) = \operatorname{sgn}(r_1)$*, then the following is true:*

- $\hat\lambda_{34} = \hat\lambda_{12} > 0 \Leftrightarrow \operatorname{sgn}(\epsilon) = \operatorname{sgn}(u_1)$
- $\hat\lambda_{24} = \hat\lambda_{13} > 0 \Leftrightarrow \operatorname{sgn}(\tilde\epsilon) = \operatorname{sgn}(u_1)$.

Proof. Let $\operatorname{sgn}(u_1) = -1$, then

$$\hat\lambda_{34} = \hat\lambda_{12} > 0 \Leftrightarrow m^2 r_1 - r^2 u_1 > 0 \Leftrightarrow \frac{r_1}{u_1} - \left(\frac{r}{m}\right)^2 < 0 \Leftrightarrow \epsilon < 0,$$
$$\hat\lambda_{24} = \hat\lambda_{13} > 0 \Leftrightarrow m^2 u_1 - u^2 r_1 > 0 \Leftrightarrow \frac{u_1}{r_1} - \left(\frac{u}{m}\right)^2 < 0 \Leftrightarrow \tilde\epsilon < 0.$$

For $\operatorname{sgn}(u_1) = +1$

$$\hat\lambda_{34} = \hat\lambda_{12} > 0 \Leftrightarrow m^2 r_1 - r^2 u_1 > 0 \Leftrightarrow \frac{r_1}{u_1} - \left(\frac{r}{m}\right)^2 > 0 \Leftrightarrow \epsilon > 0,$$
$$\hat\lambda_{24} = \hat\lambda_{13} > 0 \Leftrightarrow m^2 u_1 - u^2 r_1 > 0 \Leftrightarrow \frac{u_1}{r_1} - \left(\frac{u}{m}\right)^2 > 0 \Leftrightarrow \tilde\epsilon > 0$$

hold and prove the lemma. ☐

Lemma 9. *Let* $\operatorname{sgn}(u_1) = \operatorname{sgn}(r_1)$ *and* $\operatorname{sgn}(s-t) \neq 0$*, then the following implications hold:*

- *If* C_{34}, C_{12} *are admissible and* $\operatorname{sgn}(\hat\lambda_{34}) = \operatorname{sgn}(\hat\lambda_{12}) = -\operatorname{sgn}(s-t)$*, then* $\operatorname{sgn}(u_1) = \operatorname{sgn}(s-t)$
- *If* C_{24}, C_{13} *are admissible and* $\operatorname{sgn}(\hat\lambda_{24}) = \operatorname{sgn}(\hat\lambda_{13}) = \operatorname{sgn}(s-t)$*, then* $\operatorname{sgn}(u_1) = -\operatorname{sgn}(s-t)$.

Proof. Let $\operatorname{sgn}(s-t) = -1$, then $u_1 > r_1$ and

$$\text{for } \operatorname{sgn}(r_1) = +1 \Rightarrow \hat\lambda_{34} = \hat\lambda_{12} = m^2 r_1 - r^2 u_1 < r_1(m^2 - r^2) < 0 \tag{6.18}$$

and

$$\text{for } \operatorname{sgn}(u_1) = -1 \Rightarrow \hat\lambda_{24} = \hat\lambda_{13} = m^2 u_1 - u^2 r_1 > u_1(m^2 - u^2) > 0 \tag{6.19}$$

hold, since $(m^2 - r^2) = -4(e_1+s)(e_2+s) < 0$ for admissible C_{34}, C_{12} and $m^2 - u^2 = -4(e_1 + t)(e_2+t) < 0$ for admissible C_{24}, C_{13}. By negating (6.18), we get the claimed implications for $\operatorname{sgn}(s-t) = -1$ and for $\operatorname{sgn}(s-t) = +1$ a similar argument applies. ☐

After the lemmas about the boundary equilibria, let us state one about the center equilibrium SE.

Lemma 10.

$$\det J_{SE} = \frac{\rho}{16}, \tag{6.20}$$
$$\operatorname{tr}(J_{SE}) = \frac{r_1 + u_1}{8}. \tag{6.21}$$

Proof. Evaluation of the matrix given in lemma 1 with the reparametrized fitness parameters of the centrosymmetric viability model is:

$$J_{int} = \begin{pmatrix} p(1-p)(r-2l(q(1-q))) & 2p(1-p)(e_1+l(2pq-p-q)) \\ 2q(1-q)(e_1+l(2pq-p-q)) & q(1-q)(u-2l(p(1-p))) \end{pmatrix} \tag{6.22}$$

For the point $(\frac{1}{2}, \frac{1}{2})$ this simplifies to

$$J_{SE} = \frac{1}{4}\begin{pmatrix} \frac{r_1}{2} & m \\ m & \frac{u_1}{2}. \end{pmatrix} \tag{6.23}$$

The trace $\frac{r_1+u_1}{8}$ and the determinant $\frac{1}{4}\left(\frac{r_1u_1}{4} - m^2\right)$ can be easily computed from (6.23). □

By applying the Routh-Hourwitz criterion (proposition 1), the following corollary can be obtained directly.

Corollary 2. *If exactly one isocline has poles, then SE is unique in the interior and a saddlepoint and $\delta = 2$.*

Proof. If only one of the isoclines has poles, there is only one equilibrium in the interior and $\mathrm{sgn}(u_1) = -\mathrm{sgn}(r_1)$, as computed in the proof of theorem 8. SE is always an equilibrium in this framework and is always internal, therefore it is unique in the interior. The sign of the determinant of the Jacobian at SE is determined by $\rho = r_1u_1 - 4m^2 < 0$, since $\mathrm{sgn}(u_1r_1) = -1$ and thus SE is a saddlepoint by proposition 1. The index of a saddlepoint is -1 and in order to fulfil theorem 2 the boundary index sum has to be $+2$. □

Now we are ready to prove the main theorems of this section. Uniqueness and additional equilibria refers only to the interior of the unit square.

Theorem 9. *Let δ be the boundary index sum then the following holds true:*

1. *SE is unique in the interior if*
   (a) $\delta = 0$ *and* $\rho > 0$
   (b) $\delta = 2$ *and* $\rho < 0$
2. *Two additional equilibria exist if*
   (a) $\delta = 0$ *and* $\rho < 0$ *(sinks/sources)*
   (b) $\delta = 2$ *and* $\rho > 0$ *(saddles)*
   (c) $\delta = 4$ *and* $\rho < 0$ *(saddles)*
3. *Four additional saddlepoint equilibria exist if* $\delta = 4$ *and* $\rho > 0$.

Proof. Part 1 is harder to prove than the others.
That's why we start with the claim 2a. For $\rho < 0$ lemma 10 and proposition 1 ensure us that SE is a saddle and has therefore index -1. This excludes a unique interior equilibrium. To reach $\gamma = 1$, where γ denotes the total index sum, we need two additional equilibria with index $+1$. By assuming 5 internal equilibria, two more equilibria, whose indices sum up to zero, are needed. But then there a three additional equilibria with index $+1$ and one with index -1 and thus the symmetry doesn't hold any longer and hence we have a contradiction.
The proofs of the claims 2b, 2c and 3 work the same way.

For the proofs left, we will make use of the table of lemma 5. From $\rho < 0$ from claim 1b follows that SE is a saddle and has therefore an index of -1. The boundary index sum is 2 and in the case of only one equilibrium this sums up to one.
Assume that there are two additional equilibria in the interior. Their indices have to sum up to

zero and therefore one is a saddlepoint and the other one not. Because of the point symmetry of the dynamics this is impossible.
Now assume that there are four additional equilibria in the interior. The argument from above doesn't apply, because two of them are saddles and the other two are not. Four additional equilibria can only exist, if both isoclines have two poles. Therefore $\operatorname{sgn}(r_1) = \operatorname{sgn}(u_1) = -\operatorname{sgn}(l)$ holds. Comparison with the table of admissibility of the additional solutions allows this. For example assume $l < 0 < u_1 < r_1$, then y_+^2 is admissible for $m > 0$ or $m < 0$ and $\rho > 0$. y_-^2 on the other hand is admissible for $m < 0$ or $m > 0$ and $\rho > 0$. The conditions with $\rho > 0$ are not applicable because of the assumptions and m can't be greater and smaller than zero at the same time. For the other ranges of r_1 and u_1 similar arguments are used.

For claim 1a, $\gamma = +1$ as required by theorem 2, if SE is the only internal equilibrium. If we assume three internal equilibria, the indices of two new have to sum up to zero and due to symmetry this isn't possible. If we assume five internal equilibria, two poles for each of the isoclines exist and therefore $\operatorname{sgn}(r_1) = \operatorname{sgn}(u_1) = -\operatorname{sgn}(l)$ holds. A close examination of the table from lemma 5 shows that $\epsilon < 0$ or $\tilde{\epsilon} < 0$ follows, depending on ordering and sign of u_1 and r_1. $\delta = 0$ can only be achieved by cases $2b, ss, 4a, s$ and $4b, o$, which implies that C_{12} and C_{34} are admissible and internally stable. From internal stability, $r < 0$ follows directly.

In order to prove the result we have to treat all the cases separately. We start with the cases $4a, s$ and $4b, o$, where all equilibria are non-saturated. Thus $\operatorname{sgn}(\hat{\lambda}_{12}) = \operatorname{sgn}(\hat{\lambda}_{34}) = \operatorname{sgn}(\hat{\lambda}_{13}) = \operatorname{sgn}(\hat{\lambda}_{24}) = +1$ and lemma 8 gives us $\operatorname{sgn}(u_1) = \operatorname{sgn}(\epsilon) = -1$, or $\operatorname{sgn}(u_1) = \operatorname{sgn}(\tilde{\epsilon}) = -1$, depending on ordering of u_1 and r_1. For the one ordering $0 < r < u$ and for the other $0 < u < r$ follows from the table in lemma 5. This contradicts the internal stability of C_{12} and C_{34}.

Case $4b, o$ can achieve $\delta = 0$ in another way, with all equilibria saturated. Then lemma 8 states $\operatorname{sgn}(u_1) = -\operatorname{sgn}(\epsilon) = +1$, or $\operatorname{sgn}(u_1) = -\operatorname{sgn}(\tilde{\epsilon}) = +1$, depending on ordering of u_1 and r_1. This leads to $0 > u > r$ in the one ordering or $0 > r > u$ in the other ordering and both contradict the fact that $u > 0$ in case $4b, o$.

It remains the case $2b, ss$. From this boundary flow follows that $t > s$ and therefore, $u > r$ and $u_1 > r_1$. C_{12} and C_{34} are admissible and non saturated for $\delta = 0$. Thus $\operatorname{sgn}(\hat{\lambda}_{12}) = \operatorname{sgn}(\hat{\lambda}_{34}) = +1 = -\operatorname{sgn}(s-t)$. This is the condition for the first implication of lemma 9 and yields $\operatorname{sgn}(u_1) = \operatorname{sgn}(s-t) = -1$. Now we know exactly in which row of the table of lemma 5 we are and from there $0 < r < u$ follows, which again contradicts the internal stability of C_{12} and C_{34}.

All together, this shows that only for SE alone in the interior, the conditions $\delta = 0,\ \rho > 0$ and $\delta = 2,\ \rho < 0$ hold without contradictions. □

The essence of the theorem is that for given ρ and δ, the number of internal equilibria can be determined exactly. The reason of this lies definitely in the fact that SE is always an equilibrium and that the flow is symmetric to it. This allowed us to compute the position and admissibility of the other equilibria.
Nagylaki (1992) has already investigated the weak-selection limit of the two-locus two-allele dynamics with centrosymmetric viabilities, but he is particularly interested in stabilizing selection. This restricts the fitness matrix in such a way that for example the boundary flow class 4a,s can not occur and this excludes 5 internal equilibria to occur. Therefore, this chapter provides a generalization of the results in Nagylaki (1992).
An interesting thing here to note is the maximum number of stable internal equilibria, which can not exceed two. This is perhaps a good point to compare our results for weak selection with arbitrary selection in the symmetric viability model. For the latter the maximum number of internal equilibria was found by Feldman and Karlin (1970) to be seven, of which four can be simultaneously stable as shown by Hastings (1985). Three of the seven are the, first exclusively considered, so called symmetric equilibria with $x_1 = x_4$ and $x_2 = x_3$. In our context, where we can concentrate

on allele frequencies p, q, those conditions reduce to the fact $p = \frac{1}{2} = 1 - p$ and $q = \frac{1}{2} = 1 - q$ which is our symmetric equilibrium SE. In other words, the manifold, defined by $x_1 = x_4$ and $x_2 = x_3$ collapses in the weak-selection limit to one point. The three equilibria that could exist on it thus also are found in this one point. Thus the so called unsymmetric equilibria away from this manifold, first found by Feldman and Karlin (1970) roughly ten years after the three symmetric ones (see Lewontin and Kojima (1960)), correspond to our four additional internal equilibria away from SE.

Now it remains to show, which of the four, in this scenario possible, boundary flow classes attend which category of theorem 9.

A unique internal equilibrium can be reached in two different ways: Either $\delta = 0$ and $\operatorname{sgn}(\rho) = +1$, which can be achieved by all boundary flow classes, except 0c for the obvious reasons, or $\delta = 2$ and $\operatorname{sgn}(\rho) = -1$. The case of corollary 2 is a special case of the latter option. All boundary flow classes can admit $\delta = 2$ and $\operatorname{sgn}(\rho) = -1$ with only one of the isoclines having poles as well as otherwise. This distinction doesn't matter qualitatively as the the phase portraits are indistinguishable, with SE as a saddle separating the basins of attraction of the two sinks on the boundary (see fig. 6.2).

For the first of the two options for an unique internal equilibrium, SE has to be a sink, since 2b,ss 4a,s and 4b,o have $\delta = 0$, if all their edge-equilibria have positive external eigenvalues. Since 4b,o is invariant under flow reversal (this means the flow on the boundary after time reversal is the same, after rotation, as before), it has still $\delta = 0$ after flow reversal, but with another saturation pattern. As explained before flow reversal turns a sink into a source and that is happening here for SE (see fig. 6.1).

For three internal equilibria, two boundary flow classes can attain this while $\delta = 0$ (2b,ss and 4a,s, fig. 6.3) and since $\operatorname{sgn}(\rho) = -1$ in these cases, the two additional equilibria have to be either sources or sinks. In fact they are sinks for the same reason as before that the external eigenvalues are positive and therefore there has to be at least one sink in the interior and from symmetry, we conclude that the additional equilibria have to be sinks. Another way to have three internal equilibria is $\delta = 2$ and $\operatorname{sgn}(\rho) = +1$ (fig. 6.4) and this is possible for all four classes.

Only 4a,s can have $\delta = 4$ and ρ can be positive or negative. For $\operatorname{sgn}(\rho) = -1$ (fig. 6.5), there are three saddles in the interior and for positive ρ the additional interior fixed points are saddle points and SE is a source (see fig. 6.6), as it will be proven in the following lemma:

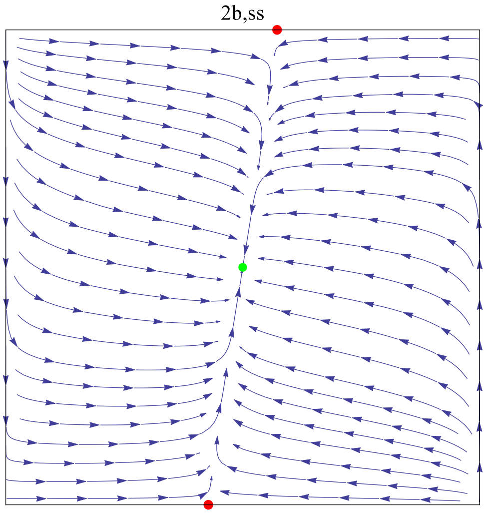
Lemma 11. *For $\delta = 4$ and $\operatorname{sgn}(\rho) = +1$, SE is a source.*

Proof. W.l.o.g. let $t > s$. From theorem 8, we know that both isoclines have two poles. Therefore $lu_1,\ lr_1 < 0$ and $\operatorname{sgn}(r_1) = \operatorname{sgn}(u_1)$. For $\delta = 4$, we need $\operatorname{sgn}(\hat{\lambda}_{34}) = \operatorname{sgn}(\hat{\lambda}_{12}) = \operatorname{sgn}(\hat{\lambda}_{24}) = \operatorname{sgn}(\hat{\lambda}_{13}) = -1$. Then the second statement of lemma 9 tells us that $\operatorname{sgn}(u_1) = -\operatorname{sgn}(s - t) = +1$. This means $l < 0 < r_1 < u_1$. Now the second statement of lemma 10 tells us that $\operatorname{tr}(J_{SE}) = \frac{r_1 + u_1}{8} > 0$. And together with $\operatorname{sgn}(\rho) = +1$ this means that SE is a source. □

Remember that all sources can be changed to sinks and reversed, if one makes a flow reversal. The boundary flow stays the same in cases 4b,o and 0c, but 2b,ss however, is then named 2b,uu and 4a,s turns into 4a,u.

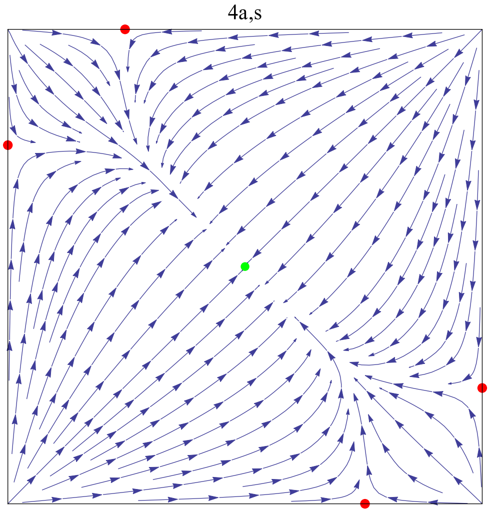
Fig. 6.1: $\delta = 0$, SE unique

2b,ss



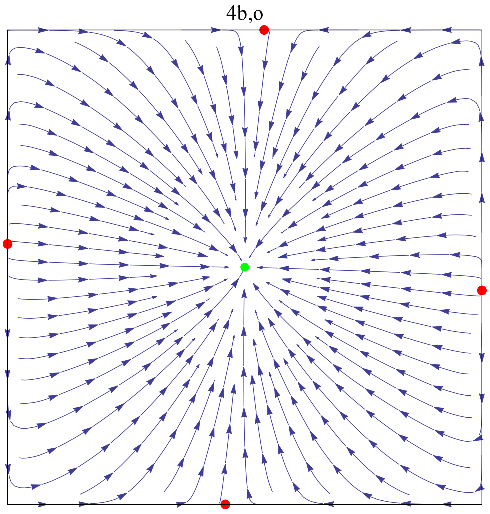
$$M=\begin{pmatrix} -\frac{83}{64} & -\frac{1}{8} & -1 \\ -\frac{65}{64} & 0 & -\frac{65}{64} \\ -1 & -\frac{1}{8} & -\frac{83}{64} \end{pmatrix}$$

4a,s



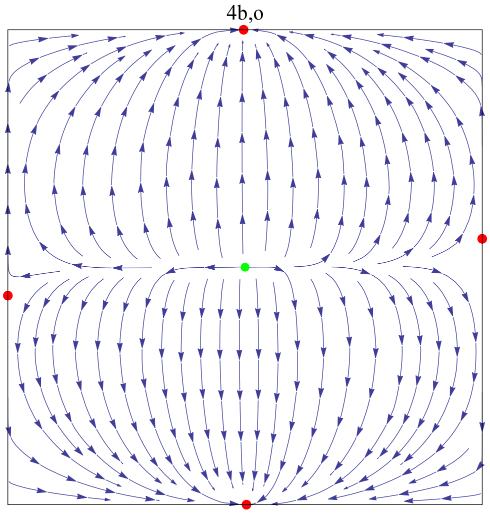
$$M=\begin{pmatrix} -\frac{87\,407}{262\,144} & -\frac{1}{128} & -1 \\ -\frac{1}{64} & 0 & -\frac{1}{64} \\ -1 & -\frac{1}{128} & -\frac{87\,407}{262\,144} \end{pmatrix}$$

4b,o



$$M=\begin{pmatrix} -311.25 & -303 & -310 \\ -317 & -200 & -317 \\ -310 & -303 & -311.25 \end{pmatrix}$$

4b,o



$$M=\begin{pmatrix} 968.6 & 1838 & 958 \\ 919 & -200 & 919 \\ 958 & 1838 & 968.6 \end{pmatrix}$$

Fig. 6.2: $\delta = 2$, SE unique

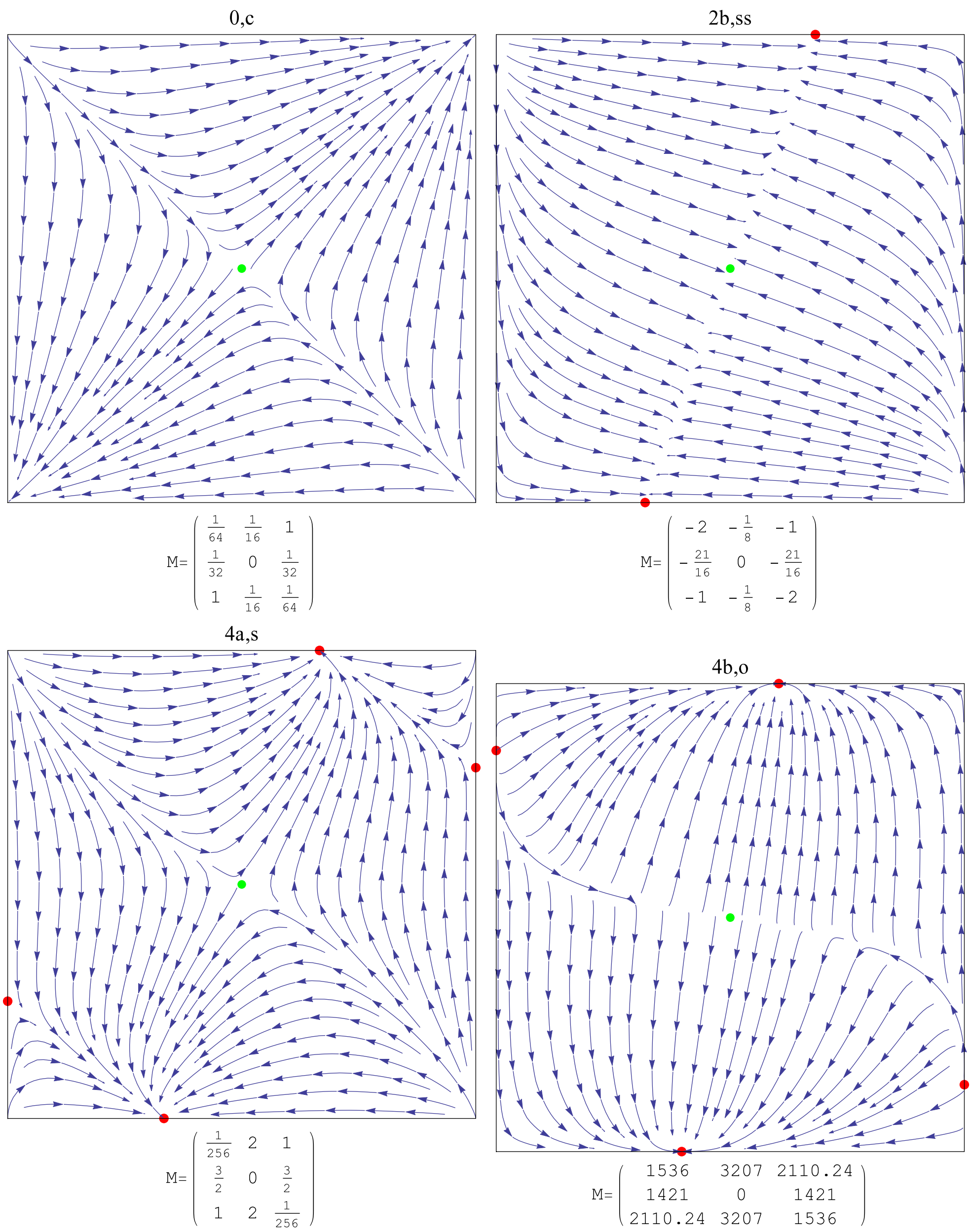


Fig. 6.3: $\delta = 0$, 3 internal equ.

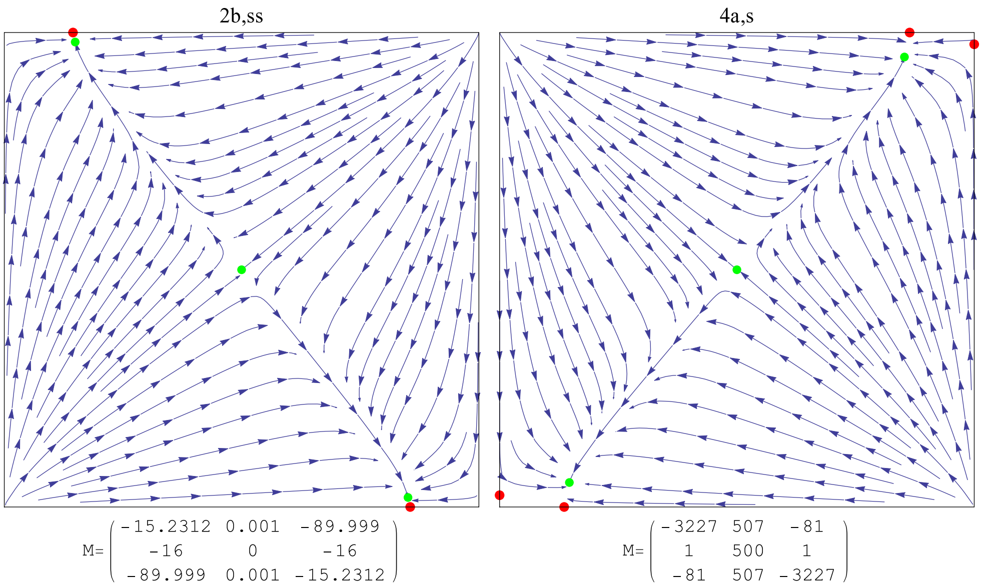


Fig. 6.4: $\delta = 2$, 3 internal equ.

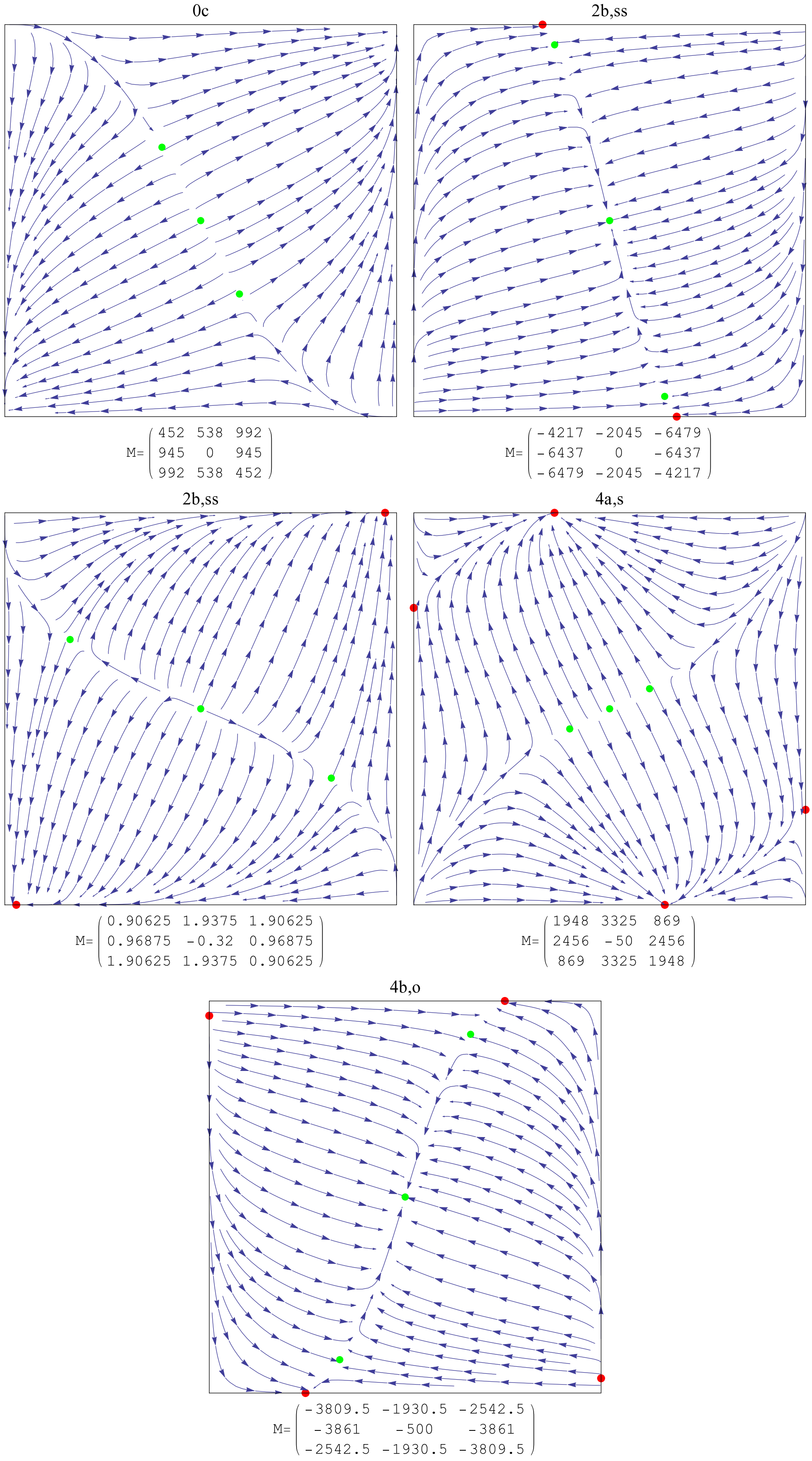
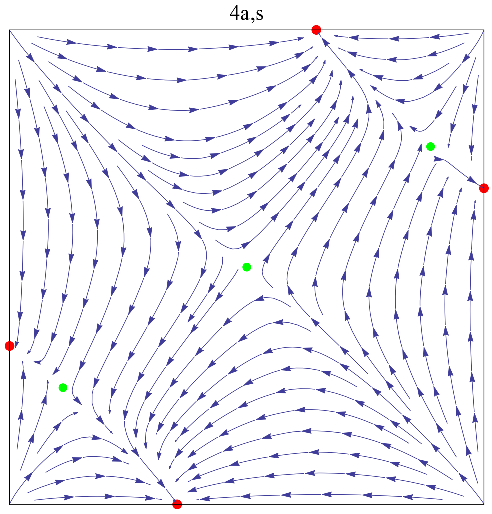
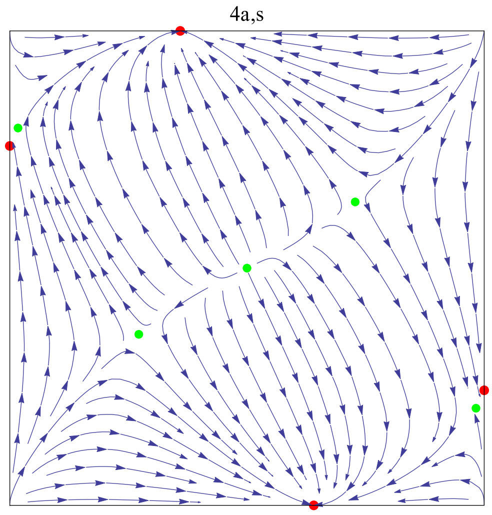


Fig. 6.5: $\delta = 4$, 3 internal equ.



$$M=\begin{pmatrix} \frac{1}{256} & 2.2 & 1 \\ 2 & 0 & 2 \\ 1 & 2.2 & \frac{1}{256} \end{pmatrix}$$

Fig. 6.6: $\delta = 4$, 5 internal equ.



$$M=\begin{pmatrix} 1948 & 3325 & 869 \\ 2456 & -500 & 2456 \\ 869 & 3325 & 1948 \end{pmatrix}$$

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Oct.09 - Jul.13	Bachelor Mathematics, University of Vienna Bachelor thesis 1: “Theorie der kollektiven Entscheidungen” Bachelor thesis 2: “Sperners Lemma bei fairer Teilung” Supervisor for both: Prof. Josef Hofbauer
Jul. 2000 - Jul.09	Adalbert Stifter Gymnasium Passau, Abitur

Languages

German, English, Java, Abap

Experiences

Aug.10/11, Sept.12	Software development company jb-x-group, developing Lifecycle-Management tools for colleges in SAP environment
Aug.09	AbiTUMath seminar in Kempten, Mathematics seminar offered by TU Munich for talented math students from Bavarian schools; topic: social choice theory

ABSTRACT

This Master's thesis studies the evolutionary dynamics of two diploid loci and two alleles under the assumption that the selection intensity is weak.
First the weak-selection limit is derived from the known classical equations. Then, we analyse this limit with different methods, in particular all possible flows on the boundary are characterized. Important is also an index-theorem of Hofbauer and the theory of saturated equilibria, which allows the extension of the characterization in terms of a boundary index sum. All in all 80 different classes can be formally found, but 5 of them turn out to be impossible with our parameters and for 69 parameter-collections were found that give the precise class. Thus for 6 classes it is not known yet if they exist or not.
In the second part of the thesis, various restrictions to the parameters are applied.
First of all, a condition is defined, for which the isoclines do not have poles and are thus continuous in the state space. The implications of this are analysed.
After this, assuming certain relations between the parameters leads to linear isoclines. The resulting equations are well known from evolutionary game theory. From this point, three other well known simpler models can be derived. The first is a generalized additive model with symmetry and epistasis. The second one is the well understood standard additive model. The third is the haploid two-locus two-allele dynamics and its connection to partnership games.
The final section deals with centrosymmetric fitness matrices. This class of selection matrices is also well studied, but not yet fully understood for arbitrary strength of selection. Here we show that the relation between epistasis and non-epistasis parameters plays an important role in this context, since it gives information about the maximum number of internal equilibria. More importantly, but also more technically, we give conditions under which one can tell exactly how many internal fixed points this system has and where they sit. Applying this knowledge enables us to characterize all possible phase portraits in this model.

ZUSAMMENFASSUNG

Diese Masterarbeit untersucht die evolutionären Dynamiken im Fall von zwei diploiden Loci und zwei Allelen unter der Annahme, dass die Selektionsintensität schwach ist.
Zuerst wird von den bekannten klassischen Gleichungen der Grenzfall für schwache Selektion hergeleitet. Dieser wird dann mit verschiedenen Methoden analysiert und unter anderem werden alle möglichen Flüsse am Rand des Zustandsraumes bestimmt. Wichtig sind dann ein Indextheorem von Hofbauer und die Theorie der saturierten Gleichgewichte, mit deren Hilfe eine erweiterte Fallunterscheidung der Randflüsse durch die Definition der Randindexsumme gemacht werden kann. 80 verschiedene Fälle wären formal möglich, aber für 5 davon wurde die Unmöglichkeit bewiesen und für 69 davon konnte die Existenz gezeigt werden. Also steht in 6 Fälle der Existenzbeweis noch aus.
Im zweiten Teil der Arbeit werden immer rigorosere Bedingungen an die Fitness Parameter gestellt. Zunächst werden Bedingungen definiert, die ausschließen, dass Isoklinen Polstellen haben und somit sicherstellen, dass die Isoklinen stetig sind. Das System wird unter diesen Bedingungen weiter untersucht.
Danach werden Parameter eliminiert, um lineare Isoklinen zu erhalten. Die daraus resultierenden Gleichungen sind aus der evolutionären Spieltheorie bekannt. Von diesen Gleichungen ausgehend, kann man 3 weitere bekannte Spezialfälle herleiten. Der erste, der dann behandelt wird, ist ein verallgemeinertes additives Model mit Symmetrien und Epistasis. Das zweite ist das wohlbekannte und sehr gut verstandene Standard-Modell mit additiver Fitness. Darauf folgt noch die Analyse des haploiden Models und dessen Zusammenhang zu Partnerschaftsspielen wird aufgezeigt.
Als Abschluss werden zentrosymmetrische Matrizen untersucht. Hier wird, unter der Annahme von schwacher Selektion, aufgezeigt, dass die Relation zwischen epistatischen und nicht-epistatischen Fitnessparametern wichtig ist. Ihr Verhältniss liefert eine leicht zu überprüfende Bedingung über die maximale Anzahl an inneren Gleichgewichten. Noch wichtigere aber auch technischere Bedingungen konnten gefunden werden, wo genau die einzelnen Gleichgewichte liegen und wann sie existieren. Mithilfe der genauen Position aller möglichen Gleichgewichte, konnten alle möglichen Flüsse, die auftreten können, charakterisiert werden.