Heteroclinic Cycles and Segregation Distortion

Bärbel M.R. Stadler

[a]Institut für Mathematik, Universität Wien, Austria

Mailing Address:
Institut für Mathematik der Universität Wien
Biomathematik Gruppe
Boltzmanngasse 9, A-1090 Wien, Austria
Phone: [43] 1 31367 4009 Fax: [43] 1 3106347

Abstract

Segregation Distorters are genetic elements that disturb the meiotic segregation of heterozygous genotypes. The corresponding genes are "ultra-selfish" in that they force their own spreading in the population without contributing positively to the fitness of the organisms carrying them. We consider here autosomal two-locus drive systems consisting of a "killer locus" and a "target locus". The diploid population dynamics is approximated by a game dynamical model leading to replicator equations. We investigate in detail the dynamics of the SD-system of *Drosophila melanogaster* and the competition of two killer alleles at the same gene locus. We show that heteroclinic cycles are a common type of attractors in models of segregation distortion systems, while they rarely occur in models with Mendelian segregation.

1. Introduction

Meiotic drive is the violation of the Mendelian rules of meiotic division. The mechanisms responsible for this phenomenon cause one member of a pair of heterozygous alleles or heteromorphic chromosomes to be transmitted to progeny in excess of the Mendelian proportion of 50%. The term "meiotic drive" for this phenomenon was coined by Sandler and Novitski [32]. Genetic elements that exhibit the phenomenon of meiotic drive are also known as *Segregation Distorters* [27]. They can be viewed as "ultra-selfish genes" since they not only show a tendency to increase in frequency without increasing the fitness of the organism harboring them, but the active element ("killer") achieves this increase by actively promoting the destruction of its allelic alternative(s) [8].

The effectivity of the drive mechanism is measured by the *distortion strength* ξ which is defined as the proportion of distorter alleles (chromosomes) among all viable alleles (chromosomes) transmitted into progeny. Thus $\xi = 1/2$ corresponds to Mendelian segregation, while $\xi = 1$ indicates complete distortion, i.e., all zygotes containing the "killer" produce only gametes that also carry the "killer" allele. The examples listed in table 1 show that meiotic drive systems in nature can act at all different levels of the distortion strength, from a slight bias to complete killing.

There are two classes of meiotic drive systems: *autosomal* and *sex-linked* segregation distorters. The latter are responsible for deviations of the sex ratio from 1/2. Both genetic systems occur in a wide range of organisms; table 1 lists a few examples. A comparison of a number of drive systems can be found in the review [27]. In this contribution we will restrict our attention to autosomal drive.

An early example of a segregation distorter system was found in several species of commensal mice, in particular in *mus domesticus* and *mus musculus* [10]. In these species, chromosome 17 carries an

Table 1. Some Examples of Segregation Distorters in Nature.

Organism	Genetic Element	ξ	Ref.
Sex Ration Distortion			
Lemming, *Myopus schisticolor*	X-Chromosome	0.8	[13]
African Butterflies, Genera *Danaus, Acrea*	W-Chromosome	1.0	[6]
Mosquito: *Aedes aegyptii*	X-Chromosome	0.6*	[41]
Drosophila: subgroups *affinis* and *obscura*	X-Chromosome (SR)	†	[3]
Nasonia	PSR	?	[40]
Autosomal Segregation Distortion			
Fungi, e.g. *Neurospora*	Spore Killer (Sk)	1.0	[38]
Mouse	t-haplotype (Chr. 17)	$0.9 - 1.0$	[35]
Drosophila *melanogaster*	SD-locus	0.95	[17]
Siberian Mouse	Chromosome 1	0.85	[1]
Maize	B Chromosome		[22]

*up to 1.0 in laboratory populations.
†many different subgenera with different distortion ratios.

array of inversions called TRD ("transmission ratio distortion") which comprises roughly 1.2% of the total mouse genome. Chromosomes carrying TRD have been termed t-haplotypes. Heterozygous t/+ males transmit predominately t-bearing sperm [35]. Segregation distorter chromosomes (SD) were discovered in 1956 in a natural population of *drosophila melanogaster* by Y. Hiraizumi [19]. In males, they violate the Mendelian rule of segregation. Males heterozygous for *SD* produce progeny among which at least $\xi = 95\%$ carry *SD*. The mechanism of distortion causes a large fraction of the sperms of the genetically normal homologue to be dysfunctional.

The population dynamics of species with meiotic drive systems have received considerable interest [7, 8, 12, 18, 23]. Almost all of this analysis has been concerned with the stability of polymorphism and questions of invadability of equilibria. In this contribution we will focus on the abundance of *heteroclinic cycles* in these models. A heteroclinic cycle is a cyclic arrangement of saddle points together with connecting orbits such that each orbit has one saddle point as its α-limit and the next one as its ω-limit. Heteroclinic cycles have not been very popular as ω-limits in biological models. Nevertheless they have been found in a number of simple models. We mention a few examples here.

A simple though rather artificial class of three-species models with circulant interaction matrices allows for heteroclinic cycles. The best-known example is the May-Leonard [28] model for cyclic competition, see e.g., [34, 31]. The assumptions behind this special Lotka-Volterra system are so artificial that it is unlikely that we could ever find them "in the field".

The Battle of the Sexes is an example of an asymmetric game due to Dawkins [9] modeling the conflict between males and females concerning their respective shares in parental investment [21, p.139f]. In Dawkin's original model the phase portrait consists of a continuum of periodic orbits surrounding a unique equilibrium in the interior of the square. Modifications of this model can lead to both an asymptotically stable and a repelling heteroclinic cycle [33, 16].

Heteroclinic cycles are abundant in hypercycle-like cooperation models [11, 2]. However, they are repelling in all these systems. Gaunersdorfer [14, 15] has investigated heteroclinic orbits in replicator equations, focusing on the time-averages of the orbits. Heteroclinic cycles in the iterated *prisoners' dilemma* have been discussed by Nowak and Sigmund [30].

In sect 2 we shall discuss the SD system in *drosophila melanogaster*. We adopt the game dynamical approach put forward by Haig and Grafen [18] because a complete analysis of the population dynamics in terms of individual alleles becomes too messy. In sect 3 we shall investigate the competition of two different killer alleles at the same locus. We shall see that in all these models heteroclinic cycles play a predominant role. Throughout this contribution we will always assume overlapping generations, that is, we will consider differential equations rather than (discrete time) difference equations, although the latter are more common in population genetics literature. The reason is mostly mathematical tractability.

2. Game Dynamics for Meiotic Drive Systems

In order to construct a model of the population dynamics of a meiotic drive system one needs to take into account that the species have in general two sexes. Thus the *Two Sex Equation* [21, p.266]

$$\begin{aligned} \dot{x}_k &= x_k(My)_k + (xM)_k y_k - 2x_k\bar{m} \\ \dot{y}_k &= x_k(Fy)_k + (xF)_k y_k - 2y_k\bar{f} \end{aligned} \tag{1}$$

is the appropriate dynamical system. Here x_k and y_k denote the frequencies of the male and female gametes, respectively. The entry m_{ij} of the matrix M is composed of the fertility $\tilde{m}_{ij}$ of a male

with genotype $i \times j$ and the proportion ξ_{ij} of functional gametes carrying allele i among all the sperm produced by a $i \times j$ male. Correspondingly, f_{ij} is composed of the fertility of a $i \times j$ female and the proportion η_{ij} of gametes carrying allele i among all eggs produced by the $i \times j$ female. For convenience one sets

$$m_{ij} = 2\xi_{ij}\tilde{m}_{ij} \qquad \text{and} \qquad f_{ij} = 2\eta_{ij}\tilde{f}_{ij}\,.$$

Not much is known in general on this system for more than $n = 2$ alleles. For special cases see [24, 25].

2.1. Segregation Distorter in Drosophila Melanogaster

The "Segregation Distorter" system in *Drosophila* comprises a two-locus system of meiotic drive. On the killer locus alleles S (Killer) and $+$ (Non-Killer) are possible, while on the target locus, alleles R (Resistant) and $+$ (Non-Resistant) can be found. The resulting four gametic types are $++$, $+R$, $S+$, SR. With this notation, SR is the genotype of the segregation distorter. Naturally occurring SR chromosomes usually carry a strong enhancer of distortion near the tip of the right arm of the chromosome and polygenic enhancers distributed along the whole right arm. In *drosophila melanogaster* segregation distortion occurs only in males, while recombination occurs only in females.

Since the distorting effect occurs only in males, the system reduces to a special case of the Two Sex Equation. It can then be shown [36] that the dynamics is closely related to a second order replicator equation, at least as far as the stability of the fixed points is concerned. It is justified, therefore, to approximate the population dynamics by the following ansatz for the frequencies x_k of the individual chromosome types:

$$\dot{x}_k = x_k[(Wx)_k - (x, Wx)] \tag{2}$$

where the entries of the matrix W are the effective fitnesses in male flies. We shall now discuss the entries w_{ij}, $i = 1, \ldots 4$ in detail:

The effective fitness $w_{ij} \stackrel{\text{def}}{=} 2\xi_{ij}u_{ij}$ of i in a pairing with j is composed of the relative fertility u_{ij} of $i \times j$ and the segregation ratio ξ_{ij}. Clearly we have $u_{ij} = u_{ji}$ and $\xi ij + \xi ji = 1$. Consequently fair segregation, i.e., $\xi_{ij} = \xi_{ji} = 1/2$ implies $w_{ij} = w_{ji}$. The following discussion follows [7].

In drosophila meiosis is fair in $++/++$ individuals, and their relative fertility is set to 1 by definition. Meiosis is also fair in $++/+R$ individuals but there is a viability cost for the resistance-allele R which is parameterized by $s_1 > 0$. In $+R/+R$ individuals the viability cost is $s_3 > s_1$. In a simplified model one may as well assume that the viability cost is additive, i.e., $s_3 = 2s_1$, as in the model of Haig and Grafen discussed later in this section. $S+$ and $++$ seem to behave equivalently in combination with SR, thus we set

$$w_{SR/S+} = w_{SR/++} \quad w_{S+/SR} = w_{++/SR}.$$

Unfair segregation occurs in $SR/++$, $SR/S+$, $SR/++$, $+R/S+$, and $+R/SR$ genotypes. In $SR/++$ individuals the gametes SR are produced in more than $\xi_{SR,++} = 95\%$ of all cases, the corresponding segregation ratio is denoted by k_1. In addition we assume a fertility loss s_2 for $SR/++$ males. Thus we have

$$w_{SR/++} = 2k_1(1-s_2) \qquad \stackrel{\text{def}}{=} 1 + K_2$$

$$w_{++/SR} = 2(1-k_1)(1-s_2) \stackrel{\text{def}}{=} 1 - K_1$$

and therefore $s_2 = (K_1 - K_2)/2$ and consequently $K_1 > K_2$ whenever $s_2 > 0$.

Naturally occurring $+R$ chromosomes are not completely insensitive to the strongly distorting SR chromosomes. In fact, $SR/+R$ males produce about 80% SR-bearing offspring. This segregation ratio is denoted by k_3. Assuming a viability cost $s_4 > 0$ we have

$$w_{+R/SR} = 2(1-k_3)(1-s_4) \stackrel{\text{def}}{=} 1 - K_5$$

$$w_{SR/+R} = 2k_3(1-s_4) \quad \stackrel{\text{def}}{=} 1 + K_6$$

As above we conclude that $K_5 > K_6$. We assume that $1 - s_5 < 1 - K_5 < 1 + K_6$, that is, the product of a $SR \times SR$ mating is less viable than the offsprings of a $SR \times +R$ mating. The segregation ratio of $+R/S+$ males is not known exactly, but it seems to be around 60% in favor of $+R$. This segregation ratio is denoted k_2, the corresponding viability cost is s_2.

The parameters $s_i > 0$ denote viability costs, therefore we will assume $s_i > 0$ for all i. It follows then from the above assumptions that $K_1 > K_2$, $K_5 > K_6$, and $K_4 > K_3$.

From the above assumptions Charlesworth and Hartl [7] have constructed the following matrix for male viabilities in their discrete-time model for the segregation distorter (*SD*) locus of *Drosophila Melanogaster*:

$++$	$+R$	$S+$	SR	
1	$1-s_1$	1	$2(1-k_1)(1-s_2)$ $=1-K_1$	$++$
$1-s_1$	$1-s_3$	$2k_2(1-s_2)$ $=1+K_3$	$2(1-k_3)(1-s_4)$ $=1-K_5$	$+R$
1	$2(1-k_2)(1-s_6)$ $=1-K_4$	1	$2(1-k_1)(1-s_2)$ $=1-K_1$	$S+$
$2k_1(1-s_2)$ $=1+K_2$	$2k_2(1-s_4)$ $=1+K_6$	$2k_1(1-s_2)$ $=1+K_2$	$1-s_5$	SR

2.2. Existence of Heteroclinic Cycles

Definition. An edge [XY] is directed from X to Y, in symbols [X→Y], if the omega-limit of every point except for X in [XY] is Y.

Lemma 1. Let $\lambda_Y(X)$ and $\lambda_X(Y)$ be the transversal eigenvectors at X and Y with eigenvectors in [XY]. Then [X→Y] if and only if $\lambda_Y(X) \geq 0$ and $\lambda_X(Y) \leq 0$ and at least one of them is non-zero.

Proof. This follows from the classification of replicator equations with $n = 2$ in [11]. ∎

Corollary. The n corner equilibria P_1, P_2, ..., P_n of S_n form a heteroclinic cycle $[P_1P_2 \ldots P_n]$ if and only if $[P_1 \to P_2]$, $[P_2 \to P_3]$, ..., $[P_{n-1} \to P_n]$, and $[P_n \to P_1]$.

In order to avoid degenerate cases we will henceforth assume that all eigenvalues $\lambda_P(Q)$ are non-zero in a heteroclinic cycle.

In the Charlesworh and Hartl model there are at most two heteroclinic 3-cycles. These lie either in the face $F_0 = [++/SR/+R]$ or in the face $F_1 = [+R/S+/SR]$. These heteroclinic cycles exist

for the following choices of parameters:

$$F_0: \quad K_3 < 0 < s_1 < s_3 < -K_6 < s_5 < K_1, \quad K_5 < s_5 < K_1, \quad 0 < K_2 < K_1, \quad K_4 < s_3\,.$$

$$F_1: \quad 0 < s_1 < s_3 < -K_6 < s_5 < K_1, \quad K_5 < s_5 < K_1, \quad 0 < K_2 < K_1$$

Hence both cycles exist whenever the first system of inequalities is fulfilled.

The edge $[++/S+]$ is a line of fixed points, thus there are no heteroclinic cycles in the faces $[++/+R/S+]$ and $[++/SR/S+]$. This follows immediately from the classification of all possible phase portraits of the replicator equation by Immanuel Bomze [4].

For the same reason there are only two possible 4-cycles left, namely:

$$++ \to SR \to S+ \to +R \quad \text{and} \quad ++ \to +R \to S+ \to SR$$

In the first case we require $s_5 > K_1$ for the expanding eigenvalue $SR \to S+$. However, the contracting eigenvalue $SR \to ++$ has to fulfill $s_5 < K_1$ in order to allow for the existence of a heteroclinic 4-cycle, thus this cycle never exists. The second case is the same cycle with the reverse direction; it does not exist for the very same reason. Consequently, there is no heteroclinic cycle involving all four pure genotypes in the Charlesworth-Hartl model.

2.3. Stability Concepts For Heteroclinic Cycles

The definitions given below are taken from [5]. They are based on the work of Ura [39] and Melbourne [29, 26].

Consider a flow on a subset $X \subseteq \mathbb{R}^n$.

Definition. Given any subset $N \subseteq X$, a closed invariant subset A of X is said to be *stable relative to the set* N or *stable in* N, if for every neighborhood U of A there is a neighborhood V of A, such that

$$\forall x \in V \cap N : x(t) \in U \forall t \geq 0.$$

A is said to be *asymptotically stable, relatively to* N, or *asymptotically stable in* N, if it is stable in N and there is a neighborhood V of A such that $\omega(x) \subset A \forall x \in V \cap N$, where $\omega(x)$ denotes as

usual the ω-limit of x.

In the context of this work we will say that a heteroclinic cycle A is *relatively (asymptotically) stable* if there exists a set N such that A is (asymptotically) stable in N and $N \cap \text{int}S_n \neq \emptyset$.

Definition. A closed invariant subset A of X, is *essentially asymptotically stable in* N if it is relatively asymptotically stable to a set N which satisfies

$$\lim_{\epsilon \to 0} \frac{\mu(B_\epsilon(A) \cap N)}{\mu(B_\epsilon(A)} = 1,$$

where $B_\epsilon(A) =: \{x \in X | dist(x, A) < \epsilon\}$ and μ is the Lebesgue measure.

In this work we will say that a heteroclinic cycle is essentially asymptotically stable if it is essentially asymptotically stable in S_n.

We will be concerned here only with heteroclinic cycles in S_3 and S_4. We shall make extensive use of results by Brannath [5] which will be outlined in the following. First we need some notations:

Let Γ be a heteroclinic cycle consisting of the fixed points P_k, $k = 1, 2, 3$ and their connecting orbits. Then we use the following notation:

e_k expanding (outgoing) eigenvalue at corner P_k;

$-c_k$ contracting (incoming) eigenvalue at corner P_k;

t_k transversal eigenvalue at corner P_k.

The stability of the heteroclinic cycle depends on the following 4 characteristic parameters:

$$\begin{aligned} \Pi_\Gamma &= \prod_{k=1}^{3} e_k - \prod_{k=1}^{3} c_k, \quad \text{and} \\ \Delta_k &= t_k e_{k+1} e_{k+2} + c_k t_{k+1} e_{k+2} + c_k c_{k+1} t_{k+2}, \end{aligned} \tag{3}$$

where indices are taken modulo 3. The following result is one of the main tools for the analysis of heteroclinic cycles in this work:

Theorem 1. [5, Proposition 3.1] Let Γ be a heteroclinic cycle connecting 3 corners in S_4. Suppose $\Pi < 0$ and $\Delta_k < 0$ for $k = 1, 2, 3$, then Γ is relatively asymptotically stable. Conversely, if $\Pi > 0$ or $\Delta_k > 0$ for one $k \in \{1, 2, 3\}$ then for each neighborhood U of Γ there exists a trajectory which eventually leaves U, i.e., Γ is unstable.

On S_4, networks of more than one heteroclinic cycle are possible. The most important case for the work presented here consists of two heteroclinic 3-cycles Γ_1 and Γ_2, which necessarily have one edge of the simplex S_4 in common.

Let $\Gamma_1 := [F_1 \to F_2 \to F_3]$ and $\Gamma_2 := [F_1 \to F_2 \to F_4]$, i.e., the heteroclinic cycles share the edge $[F_1 \to F_2]$ and branch at the corner F_2. Generalizing the notation introduced above we label the eigenvalues at corner F_k of the cycle Γ_ℓ by $e_{k\ell}$, $c_{k\ell}$, and $t_{k\ell}$, for the unstable, stable and transversal directions, respectively. See figure 1.

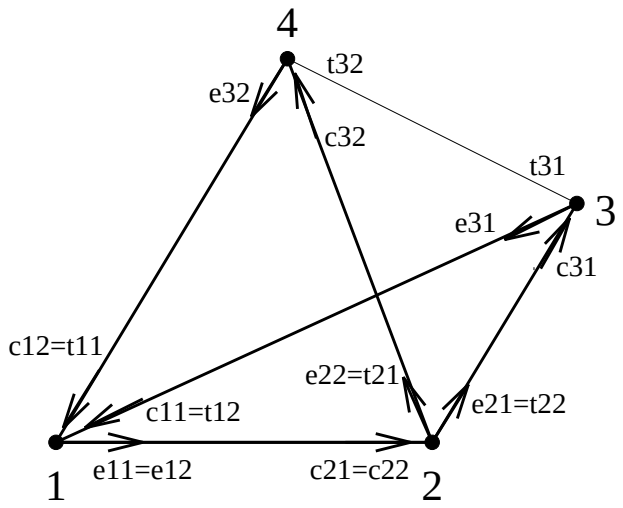


Figure 1: Notation for heteroclinic cycles on S_4.

The above theorem says that Γ_ℓ is relatively asymptotically stable if $\Pi_{\Gamma_\ell} < 0$ and each

$$\Delta_{k\ell} := t_{k,\ell} e_{(k+1),\ell} e_{(k+2),\ell} + c_{k,\ell} t_{(k+1),\ell} e_{(k+2),\ell} + c_{k,\ell} c_{(k+1),\ell} t_{(k+2),\ell} < 0,$$

where $k = 1, 2, 3$ is counted cyclically.

It is easy to check that $t_{1,l}, t_{3,l} < 0$ and $\Pi_{\Gamma_\ell} < 0$ implies

$$c_{3,\ell}\Delta_{1,\ell} < e_{3,\ell}\Delta_{3,\ell} \qquad \text{and} \qquad e_{2,\ell}\Delta_{2,\ell} < c_{2,\ell}\Delta_{3,\ell}.$$

Brannath [5] showed the following

Theorem 2. (i) Γ_ℓ is relatively asymptotically stable if and only if $\Delta_{k,\ell} < 0$ for all k.
(ii) If both Γ_1 and Γ_2 are relatively asymptotically stable then Γ_1 is essentially asymptotically stable if and only if $e_{21} > e_{22}$.

Result (ii) has a simple interpretation: If two heteroclinic cycles "compete" for stability the cycle with the larger expanding eigenvalue at the branching points "wins". It would be interesting to see if an analogous rule holds also in higher dimensions.

As for the 3-cycles discussed in the previous section it will be convenient to use e_k, $-c_k$, and t_k for the expanding, contracting and transversal eigenvalue at the corner k, respectively. If there is a heteroclinic 4-cycle [1234] involving the four corners of the simplex S_4 then lemma 2.1.2 implies that the interaction matrix is of the form

$$A = \begin{pmatrix} 0 & -c_2 & t_3 & e_4 \\ e_1 & 0 & -c_3 & t_4 \\ t_1 & e_2 & 0 & -c_4 \\ -c_1 & t_2 & e_3 & 0 \end{pmatrix} . \tag{4}$$

If all transversal eigenvalues are negative, $t_i < 0$, $i = 1, 2, 3, 4$, then the replicator network is termed *essentially hypercyclic* [21, p.187].

Theorem 3. [20] Suppose $\mathcal{R}$ on S_4 is essentially hypercyclic. Then the heteroclinic 4-cycle [1234] is asymptotically stable if

$$\Pi = e_1 e_2 e_3 e_4 - c_1 c_2 c_3 c_4 < 0$$

and unstable if $\Pi > 0$.

The situation becomes more involved when not all transversal eigenvalues are negative. If exactly one of the transversal directions is positive we obtain a network consisting of a 4-cycle and a 3-cycle forming a "short cut". This type of heteroclinic network will not occur in this work[1].

If two of the transversal eigenvalues are positive and the other two are negative we have two possibilities: either there is only the 4-cycle and both remaining edges contain a rest point (this case will not concern us here), or we have to deal with a network consisting of the 4-cycle and *two* 3-cycles. Brannath [5] has analyzed the latter case.

Theorem 4. [5] Let A be of the form given above and suppose $t_1, t_2 < 0$ and $t_3, t_4 > 0$. Assume, furthermore, that

$$\Delta_1(\Gamma_1) = -(c_1 e_2 t_2 + t_1 t_2 t_3 + t_1 c_2 e_3) > 0 \qquad \text{and}$$

$$\Delta_2(\Gamma_2) = -(c_2 e_3 t_4 + t_2 t_3 t_4 + t_2 c_2 e_4) > 0$$

[1]The stability of the 4-cycle is determined by an analogue of theorem 4 below [5]. One may simply omit the condition of Δ_i for the missing 3-cycle.

i.e., neither one of the two 3-cycles [123] and [234] is relatively asymptotically stable. Then the 4-cycle is relatively asymptotically stable if det $A > 0$ or if $\Pi < 0$. If both det $A < 0$ and $\Pi > 0$ then there is neighborhood U of the 4-cycle such that all trajectories beginning in $U \cap \text{int}S_4$ will eventually leave U.

Note that with the notation of figure 1 the 4-cycle is [1243] while the two 3-cycles are [123] and [124].

2.4. Stability of Heteroclinic Cycles in the CH Model

Theorem 5. Both heteroclinic cycles can be stable within their planes, but at most one of them can be relatively asymptotically stable.

Proof. A short calculation shows that the cycles are stable within their planes provided

$$K_2(s_5 - K_5)(s_3 - K_4) < K_3(s_3 + K_6)(K_1 - s_5) \text{ for } [+R/S+/SR], \text{and}$$

$$K_2(s_5 - K_5)(s_3 - s_1) < s_1(-s_3 - K_6)(K_1 - s_5) \text{ for } [++/SR/+R].$$

Assume for instance $K_4 > -K_3 > s_1$. Then the above inequalities can be rewritten as

$$K_2(s_5 - K_5)(s_3 - K_4) < K_2(s_5 - K_5)(s_3 - s_1)\,,$$

$$s_1(s_3 + K_6)(K_1 - s_5) < K_3(-s_3 - K_6)(K_1 - s_5)\,,$$

and we conclude immediately that stability of the heteroclinic cycle within $[++/SR/+R]$ implies stability of the cycle in $[+R/S+/SR]$.

Let us now turn to relative asymptotic stability. We have the following transversal eigenvectors:

$$\begin{array}{cccc} t_1 = 0 & t_2 = s_5 - K_1 < 0 & t_3 = s_3 - K_4 > 0 & [++/SR/+R] \\ t_1 = s_3 - s_1 > 0 & t_2 = 0 & t_3 = s_5 - K_1 < 0 & [+R/S+/SR] \end{array}$$

The conditions for relative asymptotical stability are therefore

$$\Delta_2([++/SR/+R]) = K_2(s_3 - K_4)(s_5 - K_1) - (s_5 - K_1)(s_3 - s_1)K_2 < 0$$

$$\Delta_3([+R/S+/SR]) = K_2(s_5 - K_1)(s_3 - s_1) - K_2(s_5 - K_1)(s_3 - K_4) < 0$$

Hence the heteroclinic cycle in $[++/SR/+R]$ is relatively asymptotically stable for $s_1 < K_4$, while the heteroclinic cycle in $[+R/S+/SR]$ is relatively asymptotically stable for $s_1 > K_4$, i.e., only one of them can be relatively asymptotically stable. ∎

Example. The heteroclinic cycle $[++/SR/+R]$ is relatively asymptotically stable for the following choice of parameters

$$K_1 = 3/5,\ K_2 = 1/2,\ K_3 = -33/100,\ K_4 = 34/100,\ K_5 = 4/10,$$

$$K_6 = -4/10,\ s_1 = 3/10,\ s_3 = 7/20,\ s_5 = 1/2.$$

In this case $[+R/S+/SR]$ is stable in its plane but not relatively asymptotically stable.

The converse holds for instance for the following choice of parameters

$$K_1 = 3/5,\ K_2 = 1/10,\ K_3 = -2/10,\ K_4 = 1/20,\ K_5 = 4/10,$$

$$K_6 = -4/10,\ s_1 = 3/10,\ s_3 = 7/20,\ s_5 = 1/2.$$

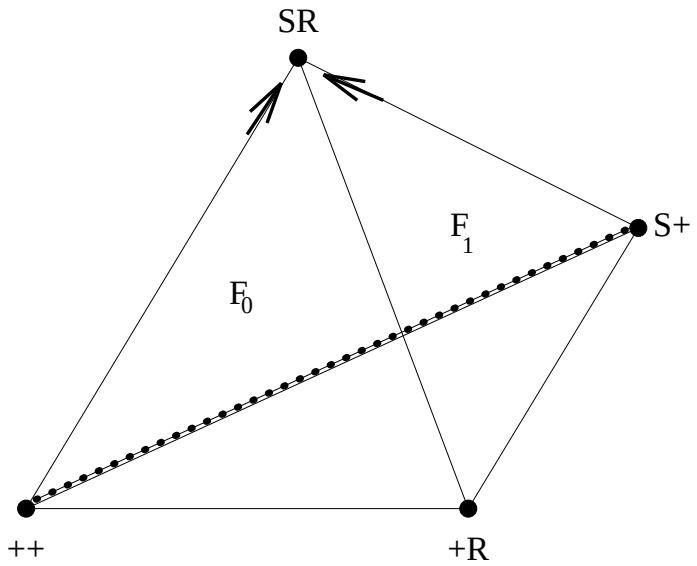


Figure 2: Heteroclinic cycles in the Charlesworth-Hartl model. The arrows indicate two eigenvalues at [SR] which are identical and hence prohibit the existence of a heteroclinic 4-cycle. Two heteroclinic 3-cycles are possible, in the faces F_0 (which corresponds to the model of Haig and Grafen discussed below) and F_1, see sect. 2.2.

2.5. Reduction to Three Species

Charlesworth and Hartl [7] argue that, *for biologically reasonable choice of the parameters*, all equilibria containing $S+$ either cannot exist or, if they exist, are unstable to the introduction of

new gametic types. This conclusion is based on the following analytical results for the discrete-time replicator equation with the above interaction matrix. It is not hard to check [36] that analogous results hold for the continuous time model investigated in this contribution:

(1) The $S+$ corner is unstable to SR if $K_2 > 0$ and unstable to $+R$ if $K_3 > 0$.

(2) A $S+/SR$ marginal equilibrium is unstable to the introduction of $+R$ if $K_2(K_1 - K_5) + K_3(s_5 - K_1) > 0$. Since $K_5 < s_5 < K_1$ are realistic parameter values and K_2 can be fairly close to K_3, the equilibrium will be unstable in most cases.

(3) An $S+/+R$ equilibrium is unstable to the introduction of $++$ if $K_4 > s_1$.

(4) An $S+/++$ equilibrium is unstable to SR if $K_2 > 0$.

(5) An equilibrium on the $S+/SR/+R$ face is unstable to the introduction of $++$ if $K_4 > s_1$.

(6) The existence of an equilibrium on the $S+/+R/++$ face would require $K_4 = s_1$.

(7) An equilibrium on the $S+/SR/++$ face exists if and only if $s_5 > K_1$ and $K_2 > 0$. It is unstable to $+R$ if

(a) $K_2(K_1 - K_5) + s_1(K_1 - s_5) > 0$ given that $K_3 > -s_1$, and

(b) $K_2(K_1 - K_5) - K_3(K_1 - s_5) > 0$ given that $K_3 < -s_1$,

(8) No equilibrium can exist within the $++/+R/S+/SR$ simplex, except for in the degenerate case $K_4 = s_1$, which is considered impossible.

(9) A stable $++/+R/SR$ equilibrium is stable to the introduction of $S+$ if $K_4 > s_1$.

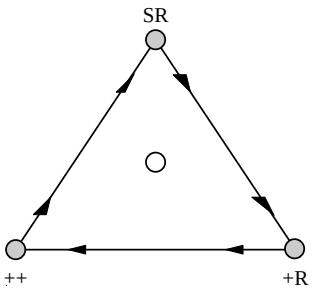


Figure 3: The heteroclinic cycle corresponding to the model of Haig and Grafen.

Result (8) implies that all trajectories of the continuous-time version of the Charlesworth-Hartl model converge to the boundary of the simplex. This is an immediate consequence of the *exclusion principle*, see, e.g., [21, p. 64]. Assuming that $S+$ is non-viable and can be neglected therefore, we

obtain the following three species model:

$$A = \begin{pmatrix} 1 & 1-s_1 & 1-K_1 & ++ \\ 1-s_1 & 1-s_3 & 1-K_5 & +R \\ 1+K_2 & 1+K_6 & 1-s_5 & SR \\ \\ ++ & +R & SR & \end{pmatrix} \tag{5}$$

Its game matrix reads:

$$A = \begin{pmatrix} 0 & s_3-s_1 & s_5-K_1 \\ -s_1 & 0 & s_5-K_5 \\ K_2 & s_3+K_6 & 0 \end{pmatrix}$$

As a consequence of the discussion in sect. 2.2. there is a heteroclinic cycle if and only if $0 < s_1 < s_3 < -K_6$, $K_5 < s_5 < K_1$, and $K_2 > 0$. It is stable provided $K_2(s_5 - K_5)(s_3 - s_1) < s_1(-s_3 - K_6)(K_1 - s_5)$.

2.6. The Model of Haig and Grafen

Haig and Grafen [18] proposed a simple model with heritable targets assuming two loci, which they called *Killer* locus and *Target* locus, whose wild-type alleles are *Non-Killer* and *Non-Resistant*, respectively. The idea is that an allele *Killer* can arise at the *Killer* locus that causes haploid products to die at the end of meiosis unless they carry an allele *Resistant* at the *Target* locus. The death of some haploid products is assumed to benefit the survivors in some way: either by the acquisition of resources from the dead haploids, or by reduction of competition for fertilizations. The possession of *Resistant* is assumed to impose a viability cost, as compared with its allele *Non-Resistant*. The model is based on an imaginary proti st life cycle, in which haploid organisms occasionally meet and fuse. There are three chromosome types in the populations: *Killer-Resistant* (K), *Non-Killer-Resistant* (R), and *Non-Killer-Non-Resistant* (N). The fourth type *Killer-Non-Resistant* kills itself during the meiosis that might have created it. A variation of the model relaxing the last assumption is discussed in the next section.

The detailed assumptions of Haig and Grafen's model are the following:

(1) There is a viablility cost w for each *Resistant* allele involved in the meiosis.

(2) There is a cost v for each unsuccessful attempt to kill.

(3) The gain in viability obtained by the driving allele *Killer* is j compared to a $N\times N$ mating.

(4) When two K mate, their relative viability is k.

(5) In $K\times N$ matings the drive is 100% successful, i.e., no *Non-Resistant* gametes survive.

(6) Drive does not occur in matings involving R.

Standardizing the fitness of $N\times N$ as 1 and bringing the interaction matrix to normal form one obtains the following game matrix:

$$A = \begin{pmatrix} 0 & w & -k \\ -w & 0 & 1-k-v-2w \\ j & -v & 0 \end{pmatrix} \tag{6}$$

where $j, k, v, w > 0$.

Table 2. Correspondence of the Haig-Grafen and the Charlesworth-Hartl models for the SD system in *Drosophila melanogaster*

Charlesworth-Hartl	Haig-Grafen
Genotypes	
$+/+$	$[NK/NR] = N$
$+/R$	$[NK/R] = R$
S/R	$[K/R] = K$
$S/+$	$[K/NR]$ lethal
Viabilities	
$w_{++/++} = 1$	$w_{NN} = 1$
$w_{++/+R} = 1 - s_1$	$w_{NR} = 1 - w$
$w_{+R/+R} = 1 - s_3 < 1 - s_1$	$w_{RR} = 1 - 2w$
$w_{SR/++} = 1 + K_2$	$w_{KN} = 1 + j$
$w_{++/SR} = 1 - K_1$	$w_{NK} = 0$
$w_{+R/SR} = 1 - K_5$	$w_{RK} = 1 - v - 2w$
$w_{SR/+R} = 1 + K_6$	$w_{KR} = w_{RK}$
$w_{SR/SR} = 1 - s_5$	$w_{KK} = k$
Realistic Values	
$w_{++/SR} < w_{SR/SR} < w_{+R/SR}$	$w_{NK} < w_{KK} < w_{RK}$

In the following the most important properties of this model are summarized as follows:

Lemma 2. There is a heteroclinic cycle if $k + v + 2w < 1$.

Proof. See Haig & Grafen [18]. ∎

Lemma 3. The heteroclinic cycle is stable if and only if

$$1 - v - 2w > k > \frac{j}{v + j}(1 - v - 2w) \, .$$

Proof. The heteroclinic cycle is stable if the interior equilibrium is unstable and *vice versa*, see, e.g., [4], [37]. The theorem follows now immediately from Appendix A in [18]. ∎

The model by Haig and Grafen is closely related to the earlier, and much more complicated model by Charlesworth and Hartl discussed in the previous sections, see table 2.

3. Competition of Killers with Complete Distortion

3.1. The Model

Let us consider a model with two different Killer alleles K_1 and K_2. Then we have two alleles (R and $+$) at the target locus and three alleles ($+$, K_1, and K_2) at the killer locus. Thus there are six possible diploid genotypes. In order to reduce the model we make the following assumptions: (i) $+K_1$ and $+K_2$ are both lethal, and (ii) the two resistant genotypes RK_1 and RK_2 are (kinetically) indistinguishable and can hence be considered as single resistant genotype R. As in the model of Haig and Grafen $++$ is the sensitive genotype. The remaining two genotypes RK_1 and RK_2 are the two different killer strains K_1 and K_2, respectively. In order to reduce the number of free parameters we will assume additionally that the interaction with the resistant strain is the same for both killers. Thus we obtain the following game matrix:

	R	N	K_1	K_2
R	$1-2w$	$1-w$	$1-v-2w$	$1-v-2w$
N	$1-w$	1	0	0
K_1	$1-v-2w$	$1+j_1$	k_1	k
K_2	$1-v-2w$	$1+j_2$	k	k_2

In normal form this becomes

$$A = \begin{pmatrix} 0 & -w & 1-v-2w-k_1 & 1-v-2w-k_2 \\ w & 0 & -k_1 & -k_2 \\ -v & j_1 & 0 & k-k_2 \\ -v & j_2 & k-k_1 & 0 \end{pmatrix} \tag{7}$$

General Assumptions.

(i) All the parameters in the above equation game matrix are positive: $j_1, j_2, k, k_1, k_2, v, w > 0$.

(ii) Without loosing generality we assume $k_2 \leq k_1$; that is, the viability of a K_2/K_2 genotype is less or equal to the viability of a K_1/K_1 genotype.

(iii) Additionally we require that $k_1 < 1 - v - 2w$ if $k < k_1$ and
$(k^2 - k_1 k_2)/(2k - k_1 - k_2) < 1 - v - 2w)$ for $k > k_1, k_2$.
This condition guarantees that there is always a heteroclinic cycle in both the face $[RNK_1]$ and the face $[RNK_2]$.

We distinguish two cases:

(I) $k_2 < k < k_1$. Then there is no equilibrium on the $[K_1,K_2]$ edge. There are two heteroclinic cycles.

(II) $k_2 < k_1 < k$ or $k < k_2 < k_1$. Then there is an equilibrium F on the $[K_1,K_2]$ edge. In this case there are at least three heteroclinic cycles. We will prove this statement explicitly in the next section for a special case. In general it follows from [4, 37] that there are trajectories connecting $N \rightarrow F$ and $F \rightarrow R$, and hence we have the three heteroclinic orbits $[RNK_1]$, $[RNK_2]$, and $[RNF]$.

3.2. The Symmetric Case: $j_1 = j_2$

In this section we will restrict ourselves to $j_1 = j_2$. Biologically, this means that the killer alleles K_1 and K_2 differ only in their interactions with themselves and with one another, but not with the sensitive and resistant strains S and R, respectively. In the following subsection we will relax this condition and consider the general case.

3.2.1. Case I: Two Heteroclinic 3-Cycles

Let us assume that without loosing generality $k_2 \leq k \leq k_1$. Then there are two heteroclinic orbits, $[RNK_1]$ and $[RNK_2]$.

Theorem 6. (i) The heteroclinic cycle $[RNK_1]$ is relatively asymptotically stable under the general assumptions on the parameters if and only if $j(1 - v - 2w) < k_1$.

(ii) The heteroclinic cycle $[RNK_2]$ is never relatively asymptotically stable under the general assumptions on the parameters.

Proof. (i) The heteroclinic cycle $[RNK_1]$ is stable in its plane provided $j(1-v-2w)/(j+v) < k_1$. It is relatively asymptotically stable if in addition to the inequality above we have $\Delta_\ell(\Gamma_1) < 0$ for $\ell = 1,2,3$, i.e., if

$$(k-k_1)vw < 0, \quad j(1-v-2w) < k_1(j+v) + w(k_1-k), \quad (k-k_1)jw < 0.$$

The first and the third inequality follow immediately from $k_1 > k$, and the second one is weaker than the condition for stability in the plane.
The $[RNK_2]$ cycle is stable in its plane iff $j(1-v-2w) < k_2(j+v)$. For relative asymptotic stability we need in addition

$$jw(k-k_2) < 0, \quad vw(k-k_2) < 0, \quad j(1-v-2w) < k_2(j+v) + w(k_2-k).$$

The first two of these inequalities are never fulfilled since $k_2 < k$, thus $[RNK_2]$ is not relatively asymptotically stable in case I. ∎

In addition to the two 3-cycle three is also the 4-corner cycle [1243]. Since $\Delta_3(\Gamma_1) = (k-k_1)wj < 0$ we cannot use Brannath's results for determining whether [1243] can ever be relatively asymptotically stable. Numerical data suggest that it is never essentially asymptotically stable.

3.2.2. Case II: Three Heteroclinic 3-Cycles

Three heteroclinic cycles can occur if either $k_1, k_2 < k$ or $k_1, k_2 > k$. It is easy to check that

$$\dot{x}_3(k-k_1) - \dot{x}_4(k-k_2) = [x_3(k-k_1) - x_4(k-k_2)] \cdot [jx_1 - vx_2 - (xWx)],$$

and thus the plane $Z = \{x \in S_4 | x_4(k-k_2) = x_3(k-k_1)\}$ is invariant. The coordinates of the fixed point F on the $[K_1K_2]$ edge are

$$\hat{x}_1 = 0\,, \qquad \hat{x}_2 = 0\,, \qquad \hat{x}_3 = \frac{k-k_2}{2k-k_1-k_2}\,, \qquad \hat{x}_4 = \frac{k-k_1}{2k-k_1-k_2}\,. \tag{8}$$

The fixed point F lies in the invariant plane Z defined above.

It will be convenient to introduce the new coordinates

$$z = \frac{1}{N}[(k-k_1)x_3 + (k-k_2)x_4] \qquad \text{and} \qquad d = \frac{1}{N}[(k-k_1)x_3 - (k-k_2)x_4]\,,$$

where N is a suitable normalization such that $z = x_3 + x_4$ holds on Z, i.e., $[(k-k_1)x_3 + (k-k_2)x_4] = N(x_3+x_4)$. One finds explicitly $N = 2(k-k_1)(k-k_2)/(2k-k_1-k_2)$.

We obtain the following system of differential equations

$$\begin{aligned}
\dot{x}_1 &= x_1\left[-wx_2 + \frac{(1-v-2w-k_1)(k-k_2)+(1-v-2w-k_2)(k-k_1)}{2k-k_1-k_2}z + \right.\\
&\qquad \left. + \frac{(1-v-2w-k_1)(k-k_2)-(1-v-2w-k_2)(k-k_1)}{2k-k_1-k_2}d - (xWx)\right]\\
\dot{x}_2 &= x_2\left[wx_1 - \frac{k_1(k-k_2)+k_2(k-k_1)}{2k-k_1-k_2}z - \frac{k_1(k-k_2)-k_2(k-k_1)}{2k-k_1-k_2}d - (xWx)\right] \qquad (9)\\
\dot{z} &= z\left[-vx_1 + jx_2 + \frac{(k-k_1)(k-k_2)}{2k-k_1-k_2}z - (xWx)\right] - \frac{(k-k_1)(k-k_2)}{2k-k_1-k_2}d^2\\
\dot{d} &= d[-vx_1 + jx_2 - (xWx)]
\end{aligned}$$

It is easy to see that this reduces to a 3-species replicator equation for $d = 0$, i.e., on the invariant plane Z.

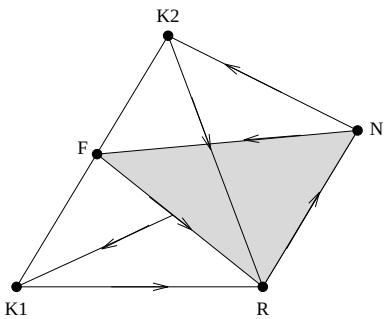


Figure 4: The invariant plane containing the equilibrium F also contains a heteroclinic 3-cycle.

The game matrix for the system $[RNF]$ reads:

$$Q = \begin{pmatrix} 0 & -w & (1-v-2w)+(k_1k_2-k^2)/(2k-k_1-k_2) \\ w & 0 & (k_1k_2-k^2)/(2k-k_1-k_2) \\ -v & j & 0 \end{pmatrix} \qquad (10)$$

Let us denote the corresponding heteroclinic cycle $[RNF]$ by Γ_F. It is stable in its plane iff $\Pi_{\Gamma_F} < 0$. There are two cases to distinguish:

(i) $k_2 < k_1 < k$, therefore $2k - k_1 - k_2 > 0$, and

(ii) $k_1 > k_2 > k$, therefore $2k - k_1 - k_2 < 0$.

Theorem 7. The heteroclinic cycle $[RNF]$ is stable in its plane iff $k_2 < k_1 < k$ and

$$\frac{j}{j+v}(1-v-2w) < \frac{k^2-k_1k_2}{2k-k_1-k_2}. \tag{11}$$

Then it is also relatively asymptotically stable in S_4.

Proof. The condition for stability in the plane is simply $\Pi_{\Gamma_F} < 0$.

In order to determine the stability within S_4 we need to consider the Jacobian of the differential equation (2) for $d = 0$. All entries in the last row are 0, except the entry for $\frac{\partial \dot{d}}{\partial d}$ which is the transversal eigenvalue for a point in the face $[RNF]$. We have explicitly

$$\frac{\partial \dot{d}}{\partial d}|_{x_1=1} = -v\,, \qquad \frac{\partial \dot{d}}{\partial d}|_{x_2=1} = j\,, \qquad \frac{\partial \dot{d}}{\partial d}|_{z=1} = -\frac{(k-k_1)(k-k_2)}{2k-k_1-k_2}.$$

Therefore the relevant transversal eigenvalues are

$$t_1 = -v\,, \qquad t_2 = j\,, \qquad t_3 = -(k-k_2)(k-k_1)/(2k-k_1-k_2)\,.$$

Now we can apply Brannath's results [5, p. 25]:

Since $t_1 < 0$ and $t_3 < 0$ we have $e_3\Delta_3 > c_3\Delta_1$ and $c_2\Delta_3 > e_2\Delta_2$. Thus $\Delta_3 < 0$ implies already $\Delta_1, \Delta_2 < 0$, i.e., we have relative asymptotic stability iff

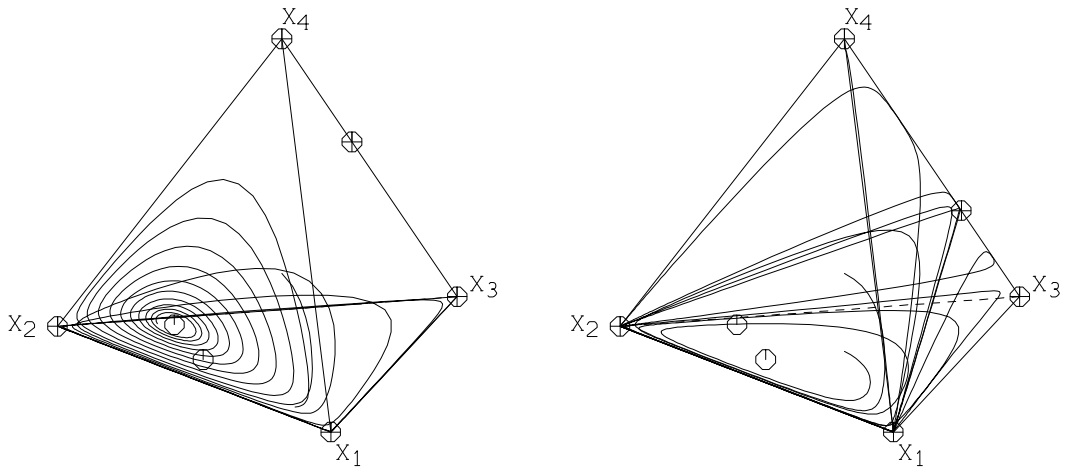
$$\Delta_3 = -\frac{(k-k_1)(k-k_2)}{2k-k_1-k_2} < 0$$

This inequality holds whenever $k_2 < k_1 < k$, i.e., in case (i). ∎

Remark. All three cycles Γ_1, Γ_2, Γ_F are stable within their respective planes if

$$k_2 < k_1 < k \qquad \text{and} \qquad j(1-v-2w) < k_2(j+v), \tag{12}$$

because $k_2 = \min\{k_1, k_2, (k^2-k_1k_2)/(2k-k_1-k_2)\}$. Brannath's results imply immediately that neither Γ_1 nor Γ_2 can be asymptotically stable in this case.



a **b**

Figure 5: **a)** Both Γ_1 and Γ_2 is stable.
Parameters: $v{=}w{=}1/10, k_1{=}7/20, k_2{=}6/20, k{=}1/5, j{=}1/20$.
b) In this case Γ_F is stable. Three trajectories, one in the invariant plane Z, and one starting below and above this plane, respectively, are shown.
Parameters: $v{=}w{=}1/10, k_1{=}7/20, k_2{=}6/20, k{=}8/20, j{=}1/20$.

It follows immediately from the proof of the above theorem that Γ_F cannot be relatively asymptotically stable in case (ii). In fact, the following result follows immediately from Brannath's conditions:

Lemma 4. Suppose $k_1 > k_2 > k$. Then the heteroclinic cycles Γ_1 and Γ_2 are relatively asymptotically stable whenever they are stable in their respective planes, i.e., iff

$$j(1-v-2w) < k_1(j+v) \quad \text{for } \Gamma_1 \qquad \text{and} \qquad j(1-v-2w) < k_2(j+v) \quad \text{for } \Gamma_2 \,.$$

Remark. Neither Γ_1 nor Γ_2 is essentially asymptotically stable w.r.t. S_4 since the invariant plane Z cuts the respective basins of attraction into two pieces, both with non-zero measure. In particular, the two cycles both attract a part of the neighborhood of the RN-edge with non-zero measure.

In case that both Γ_1 and Γ_2 are relatively asymptotically stable we find that

$$\omega\{x \in \mathrm{int}S_n | d > 0\} = \Gamma_1 \qquad \text{and} \qquad \omega\{x \in \mathrm{int}S_n | d < 0\} = \Gamma_2 \,.$$

3.3. The Asymmetric Case: $j_1 \neq j_2$

We have the following game matrix:

$$A = \begin{pmatrix} 0 & -w & 1-v-2w-k_1 & 1-v-2w-k_2 \\ w & 0 & -k_1 & -k_2 \\ -v & j_1 & 0 & k-k_2 \\ -v & j_2 & k-k_1 & 0 \end{pmatrix} \tag{13}$$

We assume $w, v, k, k_1, k_2, j_1, j_2, 1-v-2w-k_1, 1-v-2w-k_2 > 0$. In this more general case with $j_1 \neq j_2$ we cannot derive an equation for an invariant manifold corresponding to Z above.

3.3.1. Case 1: System without equilibrium on the K_1/K_2-edge

In this case we have $k_1 > k > k_2$. Again we assume without loosing generality that $k_1 > k_2$. In this case we have two heteroclinic cycles Γ_1 and Γ_2. One easily checks that the following propositions follow immediately from Brannath's formulae:

If (i) $j_1 > j_2$ then Γ_2 is never relatively asymptotically stable, and Γ_1 is essentially asymptotically stable if it is relatively asymptotically stable, i.e., iff

$$\frac{j}{j+v}(1-v-2w) < k_1 \quad \text{and} \quad \frac{kwj_1}{wj_1 + v(j_1 - j_2)} < k_1 \,.$$

If (ii) $j_1 < j_2$ stability of Γ_1 in its plane follows from stability of Γ_2 in its plane. If Γ_2 is relatively asymptotically stable, then it is already essentially asymptotically stable.

3.3.2. Case 2: System with equilibrium on K_1/K_2-edge

Let us first consider the dynamics on the face $[RK_1K_2]$; we have explicitly

$$\begin{aligned} \dot{x}_1 &= x_1[(1-v-2w-k_1)x_3 + (1-v-2w-k_2)x_4 - (xWx)] \\ \dot{x}_3 &= x_3[-vx_1 + (k-k_2)x_4 - (xWx)] \\ \dot{x}_4 &= x_4[-vx_1 + (k-k_1)x_3 - (xWx)] \end{aligned} \tag{14}$$

These equations are the same as in the symmetric case $j_1 = j_2$, since neither j_1 nor j_2 appears in them. We can thus rewrite them in terms of z and d, knowing that $L = \{d = 0\} \cap [RK_1K_2]$, the

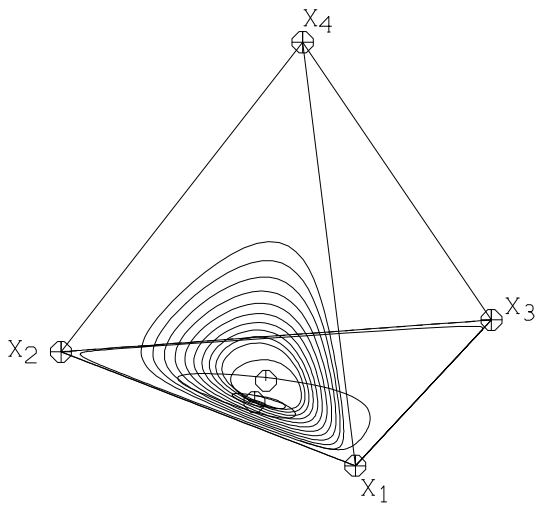


Figure 6: Example for (ii). Both Γ_1 and Γ_2 are relatively asymptotically stable. Only the Γ_2, the cycle in the front face, is essentially asymptotically stable. The parameter values are

$$v = w = 1/10, \quad k_1 = 3/5, \quad k = 8/15, \quad k_2 = 1/2, \quad j_1 = 1/20, \quad j_2 = 1/5\,.$$

straight line connecting the fixed points R and F is invariant. On L the dynamics reduces to a replicator equation with game matrix

$$A^* = \begin{pmatrix} 0 & 1 - v - 2w + (k_1k_2 - k^2)/(2k - k_1 - k_2) \\ -v & 0 \end{pmatrix}.$$

A necessary and sufficient condition for the existence of an equilibrium on the line $L = [RF]$ is that A^*_{12} and A^*_{21} have the same sign. $A^*_{21} < 0$ then implies instability. Thus there is an equilibrium on the line $L = [RF]$ iff $(1 - v - 2w) < (k^2 - k_1k_2)/(2k - k_1 - k_2)$. It is always unstable. Furthermore, one easily checks that $\dfrac{\partial \dot{x}_2}{\partial x_2}|_{x_1=1} = w > 0$, i.e., R is unstable with respect to the introduction of N.

The coordinates of the equilibrium F on the $[K_1K_2]$-edge are given by

$$\hat{x}_1 = 0, \quad \hat{x}_2 = 0, \quad \hat{x}_3 = \frac{k - k_2}{2k - k_1 - k_2}, \quad \hat{x}_4 = \frac{k - k_1}{2k - k_1 - k_2}. \tag{15}$$

There is no invariant plane for general $x_2 \neq 0$; As in the symmetric case, however, we can have three heteroclinic orbits.

Theorem 8. There is a heteroclinic cycle Γ_F=NRF if Γ_1, Γ_2 and F exist.

Table 3. Stability of Heteroclinic Cycles in the Asymmetric Case.

Case	Γ_1	Γ_2	$\Gamma_1 \wedge \Gamma_2$
$k_1 > k_2 > k$ $j_1 > j_2$	s.i.p. $\Longrightarrow$ e.a.s.	(r.a.s.)	
$k_1 > k_2 > k$ $j_1 < j_2$	(r.a.s.)	s.i.p. $\Longrightarrow$ e.a.s (r.a.s)	Γ_2 s.i.p. $\Longrightarrow$ Γ_1 s.i.p. (both r.a.s)
$k > k_1 > k_2$ $j_1 > j_2$	r.a.s. $\Longrightarrow$ e.a.s	(s.i.p.) never r.a.s.	
$k > k_1 > k_2$ $j_1 < j_2$	(s.i.p.) never r.a.s.	(r.a.s)	Γ_2 r.a.s. $\Longrightarrow$ Γ_1 s.i.p.
$k_1 > k > k_2$ $j_1 > j_2$	r.a.s. $\Longrightarrow$ e.a.s.	(s.i.p.) never r.a.s.	
$k_1 > k > k_2$ $j_1 < j_2$	(r.a.s)	s.i.p. $\Longrightarrow$ e.a.s.	Γ_2 s.i.p. $\Longrightarrow$ Γ_1 s.i.p.

s.i.p., r.a.s., and e.a.s. means "stable within its plane", "relatively asymptotically stable", and "essentially asymptotically stable", respectively. Entries in parentheses indicate the existence of parameters such that the heteroclinic cycle has a certain stability property.

Proof. The transversal eigenvalues of F are

$$\lambda_1^{(F)} = \frac{\partial \dot{x}_1}{\partial x_1}|_F = \frac{(1-v-2w-k_1)(k-k_2)}{2k-k_1-k_2} + \frac{(1-v-2w-k_2)(k-k_1)}{2k-k_1-k_2}$$
$$\lambda_2^{(F)} = \frac{\partial \dot{x}_2}{\partial x_2}|_F = -\frac{k_1(k-k_2)}{2k-k_1-k_2} - \frac{k_2(k-k_1)}{2k-k_1-k_2}$$

The existence of Γ_1 and Γ_2 implies $(1-v-2w-k_1) > 0$ and $(1-v-2w-k_2) > 0$. The existence of F implies that k, k_1, k_2 fulfill one of the relations (i) through (iv), and hence the fractions $(k-k_j)/(2k-k_1-k_2)$, $j = 1, 2$ are positive. The classification of all possible phase-portraits of the 3-species replicator equation [4, 37] implies now that there are orbits connecting $N \rightarrow F$ and $F \rightarrow R$, respectively. The remaining connection $R \rightarrow N$ is shared with both Γ_1 and Γ_2. ∎

Recall that $k_1 > k_2$. We may distinguish four different sub-cases depending on the relative magnitudes of k, k_1, and k_2.

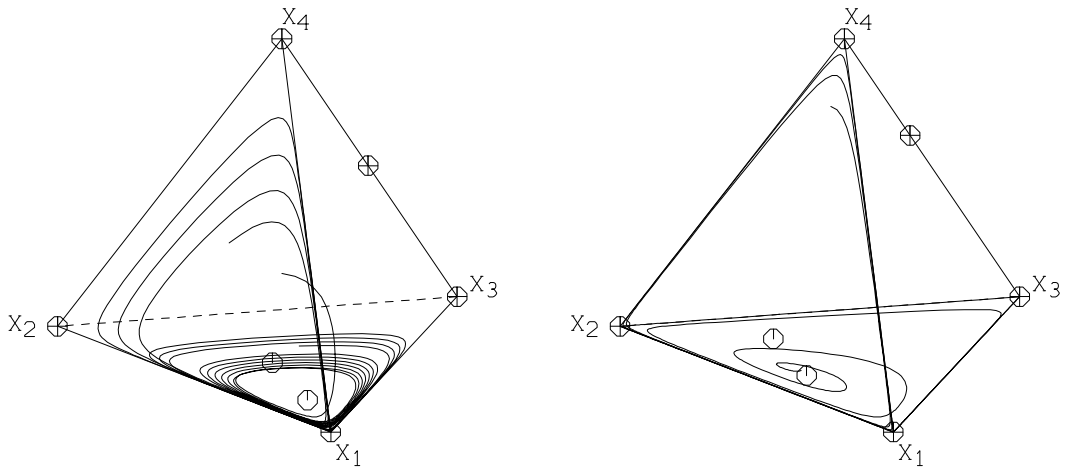
(i) $k_1 > k_2 > k$, $j_1 > j_2$

(ii) $k_1 > k_2 > k$, $j_1 < j_2$

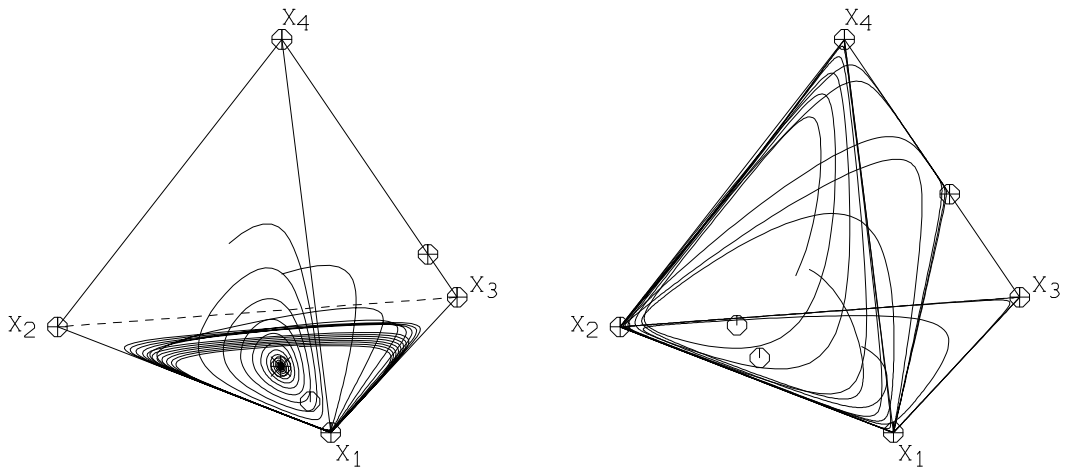
(iii) $k > k_1 > k_2$, $j_1 > j_2$

(iv) $k > k_1 > k_2$, $j_1 < j_2$

In the cases (iii) and (iv) we have also two 4-cycles involving F apart from the three 3-cycles, namely $[RNK_1F]$, $[RNK_2F]$. A numerical example in which one of them is stable is given in



Case i **Case ii**



Case iii **Case iv**

Figure 7: Examples to section 3.3.2. Parameter values are given in the text. Equilibrium points are indicated by circles. The interior equilibrium is omitted for clarity.

Case i: Both cycles are relatively asymptotically stable. Only Γ_1 (bottom face) is essentially asymptotically stable. $v{=}w{=}1/10,\quad k_1{=}6/10,\ k_2{=}7/12,\ k{=}1/12,\ j_1{=}1/2,\ j_2{=}1/3$.

Case ii: Both cycles are relatively asymptotically stable. Only Γ_2 (front face) is essentially asymptotically stable. $v{=}w{=}1/10,\quad k_1{=}6/10,\ k_2{=}4/10,\ k{=}2/20,\ j_1{=}1/15,\ j_2{=}1/10$.

Case iii: Γ_2 is unstable in its plane (front plane) while Γ_1 (bottom plane) is relatively asymptotically stable. $v{=}w{=}1/10,\quad k_1{=}3/5,\ k{=}5/8,\ k_2{=}1/2,\ j_1{=}55/100,\ j_2{=}1/2$.

Case iv: Both Γ_1 and Γ_2 are stable within their planes, but unstable against the forth direction. Numerically we find that the heteroclinic 4-cycle $[RNK_2F]$ is stable. $v{=}w{=}1/10, k_1{=}7/20, k{=}9/20, k_2{=}6/20, j_1{=}1/25, j_2{=}1/20$.

figure 8, case iv. Analytical criteria analogous to Brannath's results cannot be found because the parameters for the expanding direction at R cannot be determined analytically. Partial results on the stability properties of the three-cycles are listed below. An overview is compiled in table 3. They are all obtained by applying Brannath's formulae to the game matrix equ. (13) above. The details can be found in [36].

(i) Both cycles can be relatively asymptotically stable. If Γ_1 is stable within its plane then it is essentially asymptotically stable.

(ii) If Γ_2 is stable within its plane, then Γ_1 is also stable within its plane. Γ_2 is essentially asymptotically stable iff it is stable within its plane. Both heteroclinic cycles can be relatively asymptotically stable.

(iii) Γ_2 is never relatively asymptotically stable. Γ_1 can be relatively asymptotically stable.

(iv) If Γ_2 is stable within its plane, then Γ_1 is also stable within its plane. Γ_1 is never relatively asymptotically stable.

4. Conclusions

Heteroclinic orbits are a widespread type of attractor in models of biological processes. One finds that there is a wealth of heteroclinic cycles in various models of unfair segregation, at least in part even for biologically sensible choice of interaction parameters.

In this work a few dynamical systems of this type have been studied in detail. While all organisms exhibiting meiotic drive are of course diploid, and therefore should be described by the "two-sex" equation, it can be argued that 2nd order replicator equations are a sufficiently accurate model, as long as one is interested in stable fixed points and heteroclinic cycles on the boundary of the state space.

A two locus model for the SD complex in Drosophila melanogaster [7] shows two competing heteroclinic 3-cycles, one of which corresponds to the attracting heteroclinic cycle in the reduced game dynamical model by Haig and Grafen [18]. No 4-cycles can occur in these models and in some variants discussed here.

The competition of two different killer alleles at the same gene locus leads to a wealth of different qualitative dynamics, among which we have found stable heteroclinic 3-cycles and systems with

two such cycles. The model discussed here assumes that both killers behave equally against the non-killers and exhibit complete distortion. Brannath's formalism [5] has been used to study their stability properties. In addition a stable heteroclinic 4-cycle has been found in numerical simulations, which consists of three corner equilibria and a fixed point in the interior of an edge.

Acknowledgments

Extensive discussions with Karl Sigmund and Peter F. Stadler made this work possible. Special thanks to Christian Forst for his help with the figures. Part of this work was performed during visits to the Santa Fe Institute in 1993 and 1994.

References

[1] S. I. Agulnik, I. D. Sabantsev, and A. O. Ruvinsky. Effect of sperm genotype on chromatid segregation in female mice heterozygous for aberrant chromosome 1. *Genet. Res.*, 61:97–100, 1993.

[2] B. Aulbach and D. Flockerzi. The past in short hypercycles. *J. Math. Biol.*, 27:223–231, 1989.

[3] A. T. Beckenbach. Sex ratio polymorphism in Drosophila Pseudoobscura. *American Naturalist*, 137:340–343, 1991.

[4] I. M. Bomze. Lotka-Volterra equations and replicator dynamics: a two-dimensional classification. *Biol.Cybern.*, 48:201–211, 1983.

[5] W. Brannath. Heteroclinic networks on the tetrahedron. *Nonlinearity*, 7:1367–1384, 1994.

[6] A. O. Chanter and D. F. Owen. The inheritance and population genetics of sex ratio in the butterfly Acraea Encedon. *J. Zool.*, 166:363–383, 1972.

[7] B. Charlesworth and D. L. Hartl. Population dynamics of the segregation distorter polymorphism of *drosophila melanogaster*. *Genetics*, 89:171–192, 1978.

[8] J. F. Crow. The ultraselfish gene. *Genetics*, 118:389–391, 1988.

[9] R. Dawkins. *The Selfish Gene*. Oxford University Press, Oxford, UK, 1976.

[10] L. Dunn and J. Suckling. Studies of the genetic variability in wild populations of house mice. I. Analysis of seven alleles at locus T. *Genetics*, 41:344–352, 1956.

[11] M. Eigen and P. Schuster. *The Hypercycle*. Springer-Verlag, Berlin, 1979.

[12] M. W. Feldman and S. P. Otto. A comparative approach to the population-genetics theory of segregation distortion. *American Naturalist*, 138:443–456, 1991.

[13] K. Fredga, A. Gropp, H. Winking, and F. Frank. A hypothesis explaining the exceptional sex ratio in wood lemming (Myopus Schisticolor). *Hereditas*, 85:101–104, 1977.

[14] A. Gaunersdorfer. *Dynamics of Asymmetric Games and Heteroclinic Cycles*. PhD dissertation, Universität Wien, Inst. f. Mathematik, 1991.

[15] A. Gaunersdorfer. Time averages for heteroclinic attractors. *SIAM J. Appl. Math.*, 52:1476–1489, 1992.

[16] A. Gaunersdorfer, J. Hofbauer, and K. Sigmund. On the dynamics of asymmetric games. *Theor.Pop.Biol.*, 39:345, 1991.

[17] R. Greenberg-Temin, B. Genetzky, P. A. Powers, T. W. Lyttle, G. Pimpinelli, P. Dimitri, C.-I. Wu, and Y. Hiraizumi. Segregation distortion in Drosophila Melanogaster: Genetic and molecular analyses. *American Naturalist*, 137:287–331, 1991.

[18] D. Haig and A. Grafen. Genetic scrambling as a defence against meiotic drive. *J.Theor.Biol.*, 153:531–558, 1991.

[19] Y. Hiraizumi and J. F. Crow. Heterozygous effects on viability, fertility, rate of development, and longevity of Drosophila chromosomes that are lethal when homozygous. *Genetics*, 45:1071–1084, 1960.

[20] J. Hofbauer. Heteroclinic cycles on the simplex. In *Proc. Int. Conf. Nonlinear Oscillations*, Budapest, 1987. Janos Bolyai Math. Soc.

[21] J. Hofbauer and K. Sigmund. *The Theory of Evolution and Dynamical Systems*. Cambridge University Press, Cambridge UK, 1988.

[22] R. N. Jones. B-chromosome drive. *American Naturalist*, 137:430–442, 1991.

[23] S. Karlin. Some mathematical models of population genetics. *Amer. Math. Monthly*, 79:699–739, 1972.

[24] S. Karlin. Mathematical models, problems and controversies of evolutionary theory. *Bull. Amer. Math. Soc.*, 10:221–273, 1984.

[25] S. Karlin and S. Lessard. *Sex Ratio Evolution*, volume 22 of *Monographs in Population Biology*. Princeton University Press, Princeton, NJ, 1986.

[26] M. Krupa and I. Melbourne. Asymptotic stability of cycles in systems with symmetry. *Erg.Th.Dyn.Sys*, 1992. submitted.

[27] T. W. Lyttle. Segregation distorters. *Annu.Rev.Genet.*, 25:511–557, 1991.

[28] R. M. May and W. J. Leonard. Nonlinear aspects of competition between three species. *SIAM J.Appl.Math.*, 29:243–253, 1975.

[29] I. Melbourne. An example of a non-asymptotically stable attractor. *Nonlinearity*, 4:835–844, 1989.

[30] M. A. Nowak and K. Sigmund. Oscillations in the evolution of reciprocity. *J. Theor. Biol.*, 137:21–26, 1989.

[31] P. E. Phillipson, P. Schuster, and R. G. Johnston. An analytic study of the May-Leonard equations. *SIAM J.Appl.Math.*, 45:541–554, 1985.

[32] L. Sandler and E. Novitski. Meiotic drive as an evolutionary force. *Am.Nat.*, 41:105–110, 1957.

[33] P. Schuster, K. Sigmund, J. Hofbauer, R. Gottlieb, and P. Merz. Selfregulation of behaviour in animal societies iii: Games between two populations with self-interaction. *Biol.Cybern.*, 40:17–25, 1981.

[34] P. Schuster, K. Sigmund, and R. Wolff. On ω-limits for competition between three species. *SIAM J.Appl.Math.*, 37:49–54, 1979.

[35] L. M. Silver. Mouse t-haplotypes. *Annu. Rev. Genet.*, 19:179–208, 1985.

[36] B. M. R. Stadler. Segregation distortion and heteroclinic cycles. Master's thesis, University of Vienna, 1995.

[37] P. F. Stadler and P. Schuster. Dynamics of autocatalytic reaction networks I: Bifurcations, permanence and exclusion. *Bull.Math.Biol.*, 52:485–508, 1990.

[38] B. C. Turner and D. D. Perkins. Meiotic drive in Neurospora and other fungi. *American Naturalist*, 137:416–429, 1991.

[39] T. Ura. On the flow outside a closed invariant set; stability, relative stability, and saddle sets. *Contributions to Differential Equations*, 3(3):249–294, 1964.

[40] J. H. Werren. The paternal-sex-ratio chromosome of Nasonia. *American Naturalist*, 137:392–402, 1991.

[41] R. J. Wood and M. E. Newton. Sex ratio distortion caused by meiotic drive in mosquitos. *American Naturalist*, 137:379–391, 1991.