Invariant manifolds of Competitive Selection-Recombination dynamics ☆

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Abstract

We study the two-locus-two-allele (TLTA) Selection-Recombination model from population genetics and establish explicit bounds on the TLTA model parameters for an invariant manifold to exist. Our method for proving existence of the invariant manifold relies on two key ingredients: (i) monotone systems theory (backwards in time) and (ii) a phase space volume that decreases under the model dynamics. To demonstrate our results we consider the effect of a modifier gene β on a primary locus α and derive easily testable conditions for the existence of the invariant manifold.

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1. Introduction

In diploids, during meiosis, genetic material is occasionally exchanged between the duplicated chromosomes due to a crossover among the maternal and paternal chromosomes, and the result is new combinations of genes in the resulting gametes. This phenomenon is called *recombination* (see for example, [1, 2, 3]), and it leads to genetic variation among the resulting offspring in which genotypes may appear in the gametes that were not possible by exact duplication of the parental chromosomes [4, 5].

In the absence of selection, or other genetic forces, such as mutation or migration, recombination is a 'shuffling' action that leads ultimately to *linkage equilibrium* where the frequency of gamete genotypes is simply the product of the frequencies of the alleles contributing to that genotype. In allele frequency space this linkage equilibrium defines a manifold known as the Wright manifold which we denote by Σ_W. When only recombination acts the Wright manifold is invariant, globally attracting, and analytic. It turns out that the Wright manifold is also invariant when selection acts, *provided* that fitnesses are additive, so that there is no epistasis, and recombination may

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or may not be present. The geometry behind these facts was examined by Akin in his monograph [5].

In the case of weak selection, when the linkage disequilibrium on the invariant manifold is small and changes slowly, the manifold is known as the *Quasilinkage Equilibrium manifold* (QLE). A number of authors have discussed the existence of the QLE when selection is small [6, 7, 8, 9], and also the implications for the asymptotic distribution of gametes [5]. Particularly relevant is [9] where the authors employ the theory of normally hyperbolic manifolds to show existence of the QLE manifold in a discrete-time multilocus selection-recombination model for small selection intensity. However, it is not known how far the QLE manifold persists when selection increases, nor when the strength of recombination diminishes.

Here we are able to provide an improved understanding of persistence of an invariant manifold in the classical continuous-time two-locus, two-allele selection-recombination model [10] via a new approach that uses monotone systems theory. Using our approach we obtain explicit estimates for parameter values for which the manifold persists in a standard modifier gene model [11, 12, 13].

When there is no selection, our key observation is that the recombination only model is actually a *competitive system* relative to an order induced by a polyhedral cone. In itself, this offers no more insight when recombination is the only genetic force in action because explicit forms for the evolving gamete frequencies are possible, and the invariant manifold is precisely the Wright manifold. However, when selection is included that is sufficiently weak relative to recombination, the model remains competitive for the same polyhedral cone. Then the work of Hirsch [14], Takáč [15], and others, suggests that the selection-recombination model should possess a codimension-one Lipschitz invariant manifold. This manifold is precisely the Wright manifold when the fitnesses are additive [16]. When fitnesses are not additive, provided that recombination remains strong relative to selection, the model remains competitive, and we use this to establish existence of a codimension-one Lipschitz invariant manifold. Moreover, we use that the volume of phase space is contracting under the model flow to show that the identified codimension-one invariant manifold is actually globally attracting.

On the invariant manifold the dynamics can be written entirely in terms of the allele frequencies, and from these allele frequencies all other genetically interesting quantities can be calculated (since in building the model it is assumed that the Hardy-Weinberg law holds). If the attraction to the manifold is rapid then after a short transient the dynamics on the manifold is a good approximation of the true dynamics. To show the true versatility of the dynamics on the invariant manifold, it is necessary to show exponential attraction and asymptotic completeness of the dynamics, i.e. that each orbit in phase space is shadowed by an orbit in the invariant manifold to which it is exponentially attracted in time (i.e. the manifold is an inertial manifold). We do not establish that here, but merely the weaker condition that the invariant manifold is globally attracting.

When recombination is absent the resulting dynamics is gradient-like for the Shahshahani metric introduced in [17], as well as identical to that of the continuous-time replicator dynamics with symmetric fitness matrix [5, 4] and then the fundamental theorem of natural selection is valid: fitness is increasing along an orbit of gametic frequencies.

When recombination is present, and fitnesses are additive, mean fitness increases [16, 5, 4].

If the recombination rate is small, and epistasis is present, generically orbits will also increase mean fitness. However, as recombination increases, it becomes more difficult to predict long-term outcomes as recombination can work either with or against selection. When recombination works against selection sufficient recombination can cause fitness to decrease. In fact, it is known [18, 19, 20] that for some selection-recombination scenarios there are stable limit cycles, which indicates that mean fitness does not always increase, and moreover nor does any Lyapunov function that might be a generalisation of mean fitness [5].

2. The two-locus two-allele (TLTA) model

Suppose both loci α and β come with two alleles: A, a for the locus α and B, b for the locus β. Hence there are four possible gametes ab, Ab, aB and AB; these haploid genotypes will be denoted by G_1, G_2, G_3, G_4, whose frequencies at the zygote stage (i.e. immediately after fertilisation) are $\mathbb{P}(ab) = x_1$, $\mathbb{P}(Ab) = x_2$, $\mathbb{P}(aB) = x_3$ and $\mathbb{P}(AB) = x_4$ respectively (we follow the notation of [4]). Here $\mathbb{P}(G_i)$ denotes the present frequency of the gamete G_i in an effectively infinite population of the 4 gametes G_1, G_2, G_3, G_4.

We let W_{ij} denote the probability of survival from the zygote stage to adulthood for an individual resulting from a G_i-sperm fertilising a G_j-egg. If the genotypes of the gametes from each parent is swapped, we expect the fitness to stay the same; thus we assume $W_{ij} = W_{ji}$ $i, j = 1, 2, 3, 4$. We also assume the *absence of position effect*, i.e. $W_{14} = W_{23} = \theta$ [8], since the full diploid genotype of an individual obtained through combination of G_1 and G_4 gametes is identical to that of an individual resulting from G_2 and G_3 gametes instead, namely Aa/Bb [4]. It is possible to fix $\theta = 1$ without loss of generality [21, 4, 8]; however we will not do so here. A derivation of the model (2.2) is given in [21].

We use $\mathbb{R} = (-\infty, +\infty)$ and $\mathbb{R}_+ = [0, +\infty)$.

The fitness matrix is the following symmetric matrix:

$$W = \begin{pmatrix} W_{11} & W_{12} & W_{13} & \theta \\ W_{12} & W_{22} & \theta & W_{24} \\ W_{13} & \theta & W_{33} & W_{34} \\ \theta & W_{24} & W_{34} & W_{44} \end{pmatrix}, \tag{2.1}$$

and the governing equations for the selection-recombination model for $t \in \mathbb{R}_+$ are

$$\dot{x}_i = f_i(\mathbf{x}) = x_i(m_i - \bar{m}) + \varepsilon_i r\theta D, \qquad i = 1, 2, 3, 4. \tag{2.2}$$

Here $m_i = (W\mathbf{x})_i$ represents the fitness of G_i, while $\bar{m} = \mathbf{x}^\top W\mathbf{x}$ is the mean fitness in the gamete pool of the population and $D = x_1x_4 - x_2x_3$. Also included are the recombination rate $0 \leq r \leq \frac{1}{2}$ and $\varepsilon_i = -1, 1, 1, -1$. When $r = 0$ we say that the model is one of selection only, or that recombination is absent. The system (2.2) defines a dynamical system on the unit probability simplex Δ_4 (the phase space) defined by

$$\Delta_4 = \left\{ (x_1, x_2, x_3, x_4) \in \mathbb{R}^4 : x_i \geq 0, \ \sum_{i=1}^{4} x_i = 1 \right\}. \tag{2.3}$$

We will denote the vertices of Δ_4 by $\mathbf{e_1} = (1,0,0,0)$, $\mathbf{e_2} = (0,1,0,0)$, $\mathbf{e_3} = (0,0,1,0)$ and $\mathbf{e_4} = (0,0,0,1)$. Moreover, for each $i, j \in I_4$, each edge connecting vertex $\mathbf{e_i}$ with $\mathbf{e_j}$ will be denoted by E_{ij}. The linkage disequilibrium coefficient $D = x_1x_4 - x_2x_3$ is a measure of the statistical dependence between the two loci α and β. Using $\mathbb{P}(a)$ to denote the frequency of allele a, $\mathbb{P}(ab)$ the frequency of genotype ab, and so on, then [4] D takes the form

$$D = \mathbb{P}(ab) - \mathbb{P}(a)\mathbb{P}(b).$$

Hence $D = 0$ if and only if

$$\mathbb{P}(ab) = \mathbb{P}(a)\mathbb{P}(b),$$

with similar results also holding for each of Ab, aB and AB. When $D = 0$ the population is said to be in linkage equilibrium. The 2−dimensional manifold defined by linkage equilibrium $D = 0$ is known as the Wright Manifold and we denote it by Σ_W (see, for example, Chapter 18 of [4]).

The linchpin of this paper is a 2−dimensional invariant manifold (i.e. codimension-one) to which all orbits are attracted, and which will be denoted by Σ_M. When fitnesses are additive and $r > 0$, $\Sigma_M = \Sigma_W$ [4]. Our numerical evidence so far suggests that Σ_M exists for a large range of values of the recombination rate r and fitnesses W. However, the existence of an invariant manifold has not previously been shown other than for weak selection (relative to r), weak epistasis [9], or additive fitnesses, or strong recombination, in the discrete-time case and it is not clear how persistence of Σ_M depends on the recombination rate r and the fitnesses W.

To begin the study of (2.2) it is first convenient to follow other authors [11, 12] and change dynamical variables via $\Phi : \Delta_4 \to \mathbb{R}^3_+$

$$\mathbf{x} \mapsto \mathbf{u} = (u, v, q) = \Phi(\mathbf{x}) := (x_1 + x_2, x_1 + x_3, x_1 + x_4)\,. \tag{2.4}$$

The mapping Φ has continuous inverse

$$\Phi^{-1}(\mathbf{u}) = \frac{1}{2}\,(u + v + q - 1, u - v - q + 1, -u + v - q + 1, -u - v + q + 1)\,. \tag{2.5}$$

Φ maps Δ_4 onto a tetrahedron $\Delta = \Phi(\Delta_4) \subset \mathbb{R}^3_+$ given by

$$\Delta = \mathrm{Conv}\,\{\tilde{\mathbf{e}}_\mathbf{1}, \tilde{\mathbf{e}}_\mathbf{2}, \tilde{\mathbf{e}}_\mathbf{3}, \tilde{\mathbf{e}}_\mathbf{4}\}\,, \tag{2.6}$$

where $\tilde{\mathbf{e}}_\mathbf{i} = \Phi(\mathbf{e_i})$, so that $\tilde{\mathbf{e}}_\mathbf{1} = (1,1,1)$, $\tilde{\mathbf{e}}_\mathbf{2} = (1,0,0)$, $\tilde{\mathbf{e}}_\mathbf{3} = (0,1,0)$, $\tilde{\mathbf{e}}_\mathbf{4} = (0,0,1)$, and Conv S denotes the convex hull of a set S.

Remark 1. *Other coordinate changes are possible, for example the nonlinear change of coordinates $\mathbf{x} \mapsto \mathbf{u} = (u, v, D)$. This has the advantage that the Wright manifold is flat, but now the new coordinates may not be not ideal for the detection of monotonicity (backwards in time) in the dynamics (to be discussed in section 5 below).*

In the new coordinates (2.2) becomes

$$\dot{\mathbf{u}} = \mathbf{F}(\mathbf{u}), \tag{2.7}$$

and the new phase space is Δ. $\mathbf{F} = (U, V, Q)$ are cubic multivariate polynomials of u, v, q and are given explicitly in Appendix A. It is the system (2.7) that forms the focus of our study here, although occasionally we will revert back to (2.2).

Figure 1 shows examples of dynamics of the TLTA model in the old and new coordinates. The Wright manifold is shown in (a) for simplex coordinates $\mathbf{x}$ and (b) the Wright manifold is shown in the new tetrahedral coordinates $\mathbf{u}$. Notice that in (b), the new coordinates allow the manifold to be written as the graph of a function over $[0,1]^2$. (The manifold can also be written as the graph of a function in (a), but the construction is somewhat clumsy). In (c), (d) we also show an example of the TLTA model with positive recombination rate. Here we see that the invariant manifold is a perturbation of the Wright manifold (see [9] for an analysis of this perturbation as the QLE manifold for a discrete-time multilocus model using the method of normal hyperbolicity).

Remark 2. *For small values of $r > 0$, an attempt at numerically computing Σ_M using the NDSolve function of Mathematica leads to a numerically unstable solution. The computed solution is also numerically divergent, which hints that Σ_M may not exist for such values of r where selection dominates; an example is presented in Appendix B.*

3. Main result and method

Our objective is to establish explicit parameter value ranges of recombination rate r and selection W in the TLTA model that guarantee the existence of a globally attracting invariant manifold.

Here we establish:

Theorem 3.1 (Existence of a globally attracting invariant manifold). *Suppose that the TLTA model (2.2) is competitive (relative to a polyhedral cone) and that a suitable phase space measure decreases under the flow of (2.2). Then there exists a Lipschitz invariant manifold that globally attracts all initial polymorphisms.*

Our method is to first establish conditions for the TLTA model (2.7) to be a competitive system (see section 5 for information on competitive systems). This will be achieved by showing that there is a proper polyhedral cone K_M with dual cone K_M^* such that (2.7) is a K_M^*−monotone system when time runs backwards. In establishing this, it is particularly fortuitous that the boundary of the graph of the Wright manifold in (u, v, q) coordinates is invariant under the TLTA dynamics. The invariant boundary then provides fixed Dirichlet boundary conditions for a computation of the invariant manifold as the limit $\phi^*(\cdot)$ of a time-dependent solution $\phi(\cdot, t)$ of a quasilinear partial differential equation (see equation (4.2) below). The global existence in time of $\phi(\cdot, t)$ and convergence to a Lipschitz limit is guaranteed by K_M^*−monotonicity of (2.7) backwards in time, which ensures confinement of the normal of the graph of $\phi(\cdot, t)$ to K_M.

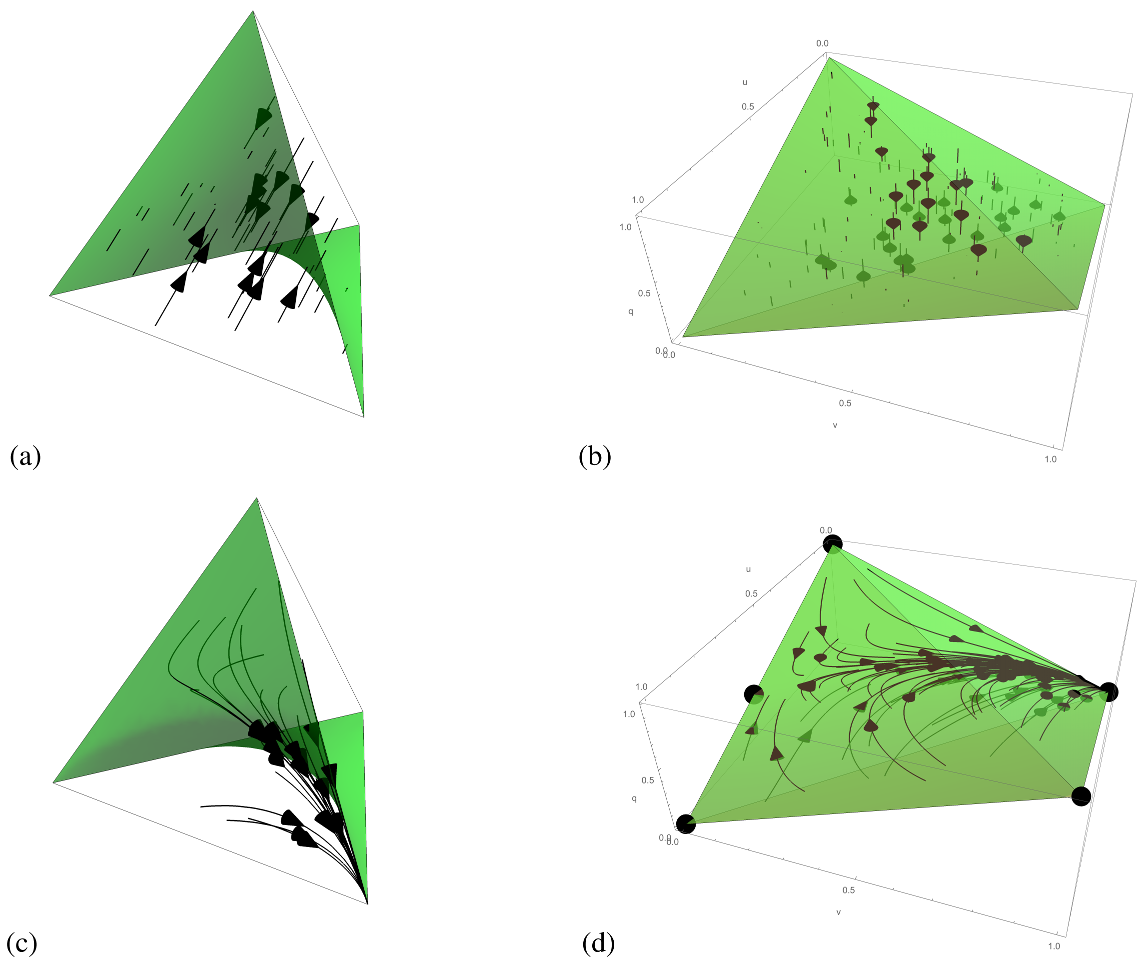

Figure 1: (a) The Wright manifold (additive fitnesses) in $\mathbf{x}$ coordinates. (b) The Wright manifold in (u, v, q) coordinates. (c) The invariant manifold $(r > 0)$ in $\mathbf{x}$ coordinates. (d) The invariant manifold $(r > 0)$ in (u, v, q) coordinates. (Parameters chosen: $W_{11} = 0.1$, $W_{12} = 0.3$, $W_{13} = 0.75$, $W_{22} = 0.9$, $W_{24} = 1.7$, $W_{33} = 3.0$, $W_{34} = 2.$, $W_{44} = 0.3$, $\theta = 1.$, $r = 0.3$)

4. Evolution of Lipschitz surfaces

We will use $C_\gamma([0,1]^2)$ to denote the space of Lipschitz functions on $[0,1]^2$ with Lipschitz constant γ. Define the space of functions

$$B = \{\phi \in C_1([0,1]^2) : \operatorname{graph}\phi \subset \Delta,\ \partial \operatorname{graph}\phi = \tilde{E}_{12} \cup \tilde{E}_{13} \cup \tilde{E}_{42} \cup \tilde{E}_{43},\ N\operatorname{graph}\phi \subset K_M\}, \quad (4.1)$$

where ∂S denotes the (relative) boundary of a surface S and $N(S)$ denotes the normal bundle of S. The set B is nonempty as it contains $(u,v) \mapsto 1-u-v+2uv$. Also, $\tilde{E}_{ij} = \Phi(E_{ij})$. All functions in B have the same Lipschitz constant one, hence B is a uniformly equicontinuous family of functions, and their graph is always contained in Δ so all function in B are bounded. Hence by the Arzelà-Ascoli Theorem, B is compact. Thus every infinite sequence of elements in B has a subsequence that converges uniformly to a Lipschitz function in B. Our constructions will mostly involve sequences C^1 function in B, and the limit function may only be differentiable almost everywhere.

Let a smooth $\phi_0 \in B$ be given. Typically we will take ϕ_0 to correspond to the Wright manifold. Then $S_0 = \operatorname{graph}\phi_0$ is a connected and compact Lipschitz surface which is mapped diffeomorphically onto a new surface S_t by the flow of (2.7) and S_t is the graph of a function $\phi_t : [0,1]^2 \to \mathbb{R}$ for small enough t. Let $\phi(u,v,t) = \phi_t(u,v)$. Then similar to [22], we use a partial differential equation to track the time evolution of the function $\phi : [0,1]^2 \times [0,\tau_0) \to \mathbb{R}_+ = [0,\infty)$ with the initial condition $\phi(u,v,0) = \phi_0(u,v) \in B$. Here, τ_0 is the maximal time of existence of ϕ as a classical solution in B of the first order partial differential equation

$$\frac{\partial \phi}{\partial t} = Q(u,v,\phi) - U(u,v,\phi)\frac{\partial \phi}{\partial u} - V(u,v,\phi)\frac{\partial \phi}{\partial v}, \quad (u,v) \in (0,1)^2, t > 0, \qquad (4.2)$$

with smooth initial data $\phi_0 \in B$.

Boundary conditions are also required that are consistent with the invariance of the edges $\tilde{E}_{42}$, $\tilde{E}_{12}$, $\tilde{E}_{13}$ and $\tilde{E}_{43}$:

$$\phi(u,0,t) = 1-u, \qquad \text{i.e. } \mathbb{P}(B) = 0, \qquad (4.3)$$
$$\phi(1,v,t) = v, \qquad \text{i.e. } \mathbb{P}(a) = 0, \qquad (4.4)$$
$$\phi(u,1,t) = u, \qquad \text{i.e. } \mathbb{P}(b) = 0, \qquad (4.5)$$
$$\phi(0,v,t) = 1-v, \qquad \text{i.e. } \mathbb{P}(A) = 0. \qquad (4.6)$$

All four edges being invariant indicates that for all $t > 0$

$$\partial \operatorname{graph}\phi_t = \partial \operatorname{graph}\phi_0 = \tilde{E}_{12} \cup \tilde{E}_{13} \cup \tilde{E}_{42} \cup \tilde{E}_{43}. \qquad (4.7)$$

But Δ is also forward invariant, hence, $\operatorname{graph}\phi_t \subset \Delta$ for all $t \in [0,\tau_0)$.

We now have a partial differential equation for the evolution of a surface $S_t := \operatorname{graph}(\phi(\cdot,\cdot,t))$. Since we wish to recover an invariant manifold as Σ_t in the limit as $t \to \infty$, we need that the solution $\phi(\cdot,\cdot,t) : [0,1]^2 \to \mathbb{R}$ exists globally in $t > 0$, and that it remains suitably regular, say uniformly Lipschitz. We will achieve this goal by showing that the normal bundle of S_t is contained in a proper convex cone for all $t \geq 0$. As we show in the next section, it turns out that keeping the normal bundle of the graph contained within a proper convex cone is intimately related to monotonicity properties of the flow of (2.7).

5. Competitive dynamics - a brief background

Before establishing when (2.2) is competitive, we give a brief background on continuous-time competitive systems. For simplicity we will present ideas in Euclidean space, although most of what we discuss in this subsection can be realised in a general Banach space (see, for example, [23]).

We recall that a set $K \subseteq \mathbb{R}^n$ is called a cone if $\mu K \subseteq K$ for all $\mu > 0$. A cone is said to be proper if it is closed, convex, has a non-empty interior and is pointed ($K \cap (-K) = \{\mathbf{0}\}$). A closed cone is polyhedral provided that it is the intersection of finitely many closed half spaces; one example is the orthant. The dual of K, is $K^* = \{\boldsymbol{\ell} \in (\mathbb{R}^n)^* : \boldsymbol{\ell} \cdot \mathbf{x} \geq 0 \quad \forall \mathbf{x} \in K\}$. If K and $F \subseteq K$ are pointed closed cones, we call F a face of K if [24]

$$\forall \mathbf{x} \in F \quad \mathbf{0} \leq_K \mathbf{y} \leq_K \mathbf{x} \quad \Rightarrow \quad \mathbf{y} \in F.$$

The face F is non-trivial if $F \neq \{\mathbf{0}\}$ and $F \neq K$. Given a proper cone K, we may define a partial order relation $\leq_K$ via $\mathbf{x} \leq_K \mathbf{y}$ if and only if $\mathbf{y} - \mathbf{x} \in K$. Similarly we say $\mathbf{x} <_K \mathbf{y}$ if and only if $\mathbf{x} \leq_K \mathbf{y}$ and $\mathbf{x} \neq \mathbf{y}$, while $\mathbf{x} \ll_K \mathbf{y}$ if and only if $\mathbf{y} - \mathbf{x} \in \text{int}K$, where $\text{int}K$ is the nonempty interior of K. A set $U \subset \mathbb{R}^n$ is said to be $p-$convex if whenever $\mathbf{x}, \mathbf{y} \in U$ and $\mathbf{x} < \mathbf{y}$ then $[\mathbf{x}, \mathbf{y}] := \{\mathbf{z} \in \mathbb{R}^n : \mathbf{x} < \mathbf{z} < \mathbf{y}\} \subseteq U$.

Let $U \subset \mathbb{R}^n$ be open and $p-$convex, and $\mathbf{H} : \mathbb{R}_+ \times U \to \mathbb{R}^n$ be continuously differentiable on $\mathbb{R}_+ \times U$. When K is a polyhedral cone (as in our application here) we say that the system

$$\dot{\mathbf{u}} = \mathbf{H}(t, \mathbf{u}) \tag{5.1}$$

is K-cooperative if for some $\alpha \in \mathbb{R}$ (possibly 0), $\alpha I + D\mathbf{H}(t, \mathbf{u})$ leaves the cone K invariant, i.e. $(\alpha I + D\mathbf{H}(t, \mathbf{u}))K \subseteq K$ for all $\mathbf{u} \in U$ and $t \in \mathbb{R}_+$ [23]. When $\mathbf{x}(0) \leq_K \mathbf{y}(0)$ and (5.1) is $K-$cooperative, $\mathbf{x}(t) \leq_K \mathbf{y}(t)$ for all $t \in \mathbb{R}_+$. Similarly we say that (5.1) is K-competitive if $\dot{\mathbf{u}} = -\mathbf{H}(t, \mathbf{u})$ is $K-$cooperative. When (5.1) is $K-$competitive, if $\mathbf{x}(t) \leq_K \mathbf{y}(t)$ for $t \in \mathbb{R}_+$ for which both exist, then $\mathbf{x}(s) \leq_K \mathbf{y}(s)$ for all $0 \leq s \leq t$.

A simple way of checking whether for some $\alpha \in \mathbb{R}$ that $(\alpha I + D\mathbf{H}(t, \mathbf{u}))K \subseteq K$ for all $\mathbf{u} \in U$ and $t \in \mathbb{R}_+$ is to note that $\mathbf{k} \in K \Leftrightarrow \boldsymbol{\ell} \cdot \mathbf{k} \geq 0$ for all $\boldsymbol{\ell} \in K^*$ and hence that when $\mathbf{k} \in K$, $(\alpha I + D\mathbf{H}(t, \mathbf{u}))\mathbf{k} \in K$ if and only if

$$\forall \mathbf{k} \in K, \boldsymbol{\ell} \in K^*, \quad \boldsymbol{\ell} \cdot (\alpha I + D\mathbf{H}(t, \mathbf{u}))\mathbf{k} \geq 0. \tag{5.2}$$

As this can also be written as

$$\forall \mathbf{k} \in K, \boldsymbol{\ell} \in K^*, \quad \mathbf{k} \cdot (\alpha I + D\mathbf{H}(t, \mathbf{u})^{\mathsf{T}})\boldsymbol{\ell} \geq 0$$

we conclude that $(\alpha I + D\mathbf{H}(t, \mathbf{u}))K \subset K$ if and only if $(\alpha I + D\mathbf{H}(t, \mathbf{u})^{\mathsf{T}})K^* \subset K^*$.

6. Conditions for the TLTA model to be competitive

Now return to equation (2.7) and assume that there is an $\alpha \in \mathbb{R}$ and proper (convex) polyhedral cone K such that $\alpha I - D\mathbf{F}K \subset K$, i.e. that the TLTA model (2.7) is competitive with respect to K.

We will relate the invariance of the polyhedral cone K for $\alpha I - D\mathbf{F}$ to properties of surfaces that evolve in $[0,1]^3$ under the flow ϕ_t generated by (2.7). Let S_0 be a compact connected smooth surface in $[0,1]^3$, and $S_t = \phi_t(S_0)$ be the image of S_0 under the flow map ϕ_t. As stated in [22], the governing equation for the time evolution of a vector $\mathbf{n}$ in the direction of the outward unit normal at $\mathbf{u}(\mathbf{t})$ (evolving under (2.7)) is

$$\dot{\mathbf{n}} = \left(\mathrm{Tr}\left(\mathrm{D}\mathbf{F}(\mathbf{u}(\mathrm{t}))\right)\mathrm{I} - \mathrm{D}\mathbf{F}(\mathbf{u}(\mathrm{t}))^{\top}\right)\mathbf{n}, \tag{6.1}$$

where $\mathbf{F} = (U, V, Q)$. (Note that $\mathbf{n}$ is not necessarily a unit vector.)

The condition for the normal bundle of S_t to remain inside a convex cone K for all time t is that $(\mathrm{Tr}\,(D\mathbf{F}(\mathbf{u}(t)))I - D\mathbf{F}(\mathbf{u}(t))^{\mathsf{T}})K \subset K$, or in other words $(\mathrm{Tr}\,(D\mathbf{F}(\mathbf{u}(t)))I - D\mathbf{F}(\mathbf{u}(t)))K^* \subset K^*$ which is the condition that the original dynamics with vector field $\mathbf{F}$ is K^*-competitive, i.e. competitive for the polyhedral cone K^* dual to K:

Lemma 6.1. *A cone K stays invariant under the flow of normal dynamics (6.1) if and only if the original dynamical system (2.7) is K^*-competitive.*

Returning to (2.7), at $t = 0$ the respective normals to $\Sigma_t = \phi_t(S_0)$ at the invariant vertices $\tilde{\mathbf{e}}_\mathbf{1}, \tilde{\mathbf{e}}_\mathbf{2}, \tilde{\mathbf{e}}_\mathbf{3}, \tilde{\mathbf{e}}_\mathbf{4}$ are

$$\mathbf{p}_1 = (-1, -1, 1) \tag{6.2}$$
$$\mathbf{p}_2 = (1, -1, 1) \tag{6.3}$$
$$\mathbf{p}_3 = (-1, 1, 1) \tag{6.4}$$
$$\mathbf{p}_4 = (1, 1, 1). \tag{6.5}$$

However, if we set $\mathbf{u}(t) = \tilde{\mathbf{e}}_\mathbf{1}$ and $\mathbf{n}(0) = \mathbf{p}_1$, it turns out that $\mathbf{p}_1$ is an eigenvector of $-D\mathbf{F}(\mathbf{u}(t))^{\top} + \mathrm{Tr}(\mathrm{D}\mathbf{F}(\mathbf{u}(\mathrm{t})))\mathrm{I}$. As a result, the right hand side of Equation (6.1) equals a constant multiple of $\mathbf{p}_1$ for all $t \geq 0$, indicating that the direction of $\mathbf{n}(t)$ matches that of $\mathbf{p}_1$ for all time at the vertex $\tilde{\mathbf{e}}_\mathbf{1}$. Similarly, for $i = 2, 3, 4$ also, $\mathbf{n}(t)$ always shares the same direction as $\mathbf{p_i}$ at $\tilde{\mathbf{e}}_\mathbf{i}$.

Thus let us generate a polyhedral cone K_M from the four linearly independent vectors $\mathbf{p}_1$, $\mathbf{p}_2$, $\mathbf{p}_3$ and $\mathbf{p}_4$:

$$K_M = \mathbb{R}_+\mathbf{p}_1 + \mathbb{R}_+\mathbf{p}_2 + \mathbb{R}_+\mathbf{p}_3 + \mathbb{R}_+\mathbf{p}_4.$$

Using the formulae for $\mathbf{p}_1, \mathbf{p}_2, \mathbf{p}_3$ and $\mathbf{p}_4$ given by (6.2) to (6.5), we have for the dual cone

$$K_M^* = \mathbb{R}_+\boldsymbol{\alpha}_1 + \mathbb{R}_+\boldsymbol{\alpha}_2 + \mathbb{R}_+\boldsymbol{\alpha}_3 + \mathbb{R}_+\boldsymbol{\alpha}_4,$$

where

$$\boldsymbol{\alpha}_1 = \mathbf{p}_1 \times \mathbf{p}_2 = 2(0,1,1) \tag{6.6}$$
$$\boldsymbol{\alpha}_2 = \mathbf{p}_2 \times \mathbf{p}_4 = 2(-1,0,1) \tag{6.7}$$
$$\boldsymbol{\alpha}_3 = \mathbf{p}_4 \times \mathbf{p}_3 = 2(0,-1,1) \tag{6.8}$$
$$\boldsymbol{\alpha}_4 = \mathbf{p}_3 \times \mathbf{p}_1 = 2(1,0,1), \tag{6.9}$$

although in what follows we drop the factors of 2 without loss of generality.

The aim is to show that the normal bundle of graph ϕ_{t} in equation (4.2) stays in a subset of K_M for all time $t \in [0,\infty)$. The required condition is

$$-\boldsymbol{\ell} \cdot D\mathbf{F}(\mathbf{u})^{\top}\mathbf{n} \geq 0 \text{ whenever } \boldsymbol{\ell} \in K_M^*, \mathbf{n} \in \partial K_M, \boldsymbol{\ell} \cdot \mathbf{n} = 0. \tag{6.10}$$

In fact, in (6.10) we may restrict ourselves to the generators $\alpha_{\mathbf{i}}$ for K_M:

$$-\boldsymbol{\alpha}_i \cdot D\mathbf{F}(\mathbf{u})^{\top}\mathbf{n} \geq 0 \text{ whenever } \mathbf{n} \in \partial K_M, \alpha_{\mathbf{i}} \cdot \mathbf{n} = 0, \quad i = 1,2,3,4. \tag{6.11}$$

Noting for example that, $\boldsymbol{\alpha}_1 \cdot \mathbf{n} = 0 \Rightarrow \mathbf{n} = \lambda_1\mathbf{p}_1 + \lambda_2\mathbf{p}_2$ for $\lambda_1 \geq 0, \lambda_2 \geq 0$ (and not both zero), and repeating for $\boldsymbol{\alpha}_j$, $j = 2,3,4$ we find that we require

$$-\boldsymbol{\alpha}_i \cdot D\mathbf{F}(\mathbf{u})^{\top}\mathbf{p}_j \geq 0 \; i,j = 1,2,3,4, \text{ with } i \neq j, \tag{6.12}$$

which gives eight sufficient conditions for the normal bundle of the graph of ϕ_t to remain within K_M for all $t > 0$:

$$\boldsymbol{\alpha}_1 \cdot D\mathbf{F}(\mathbf{u})^{\top}\mathbf{p}_1 = (\mathbf{p}_1 \times \mathbf{p}_2) \cdot D\mathbf{F}(\mathbf{u})^{\top}\mathbf{p}_1 \leq 0 \tag{6.13}$$
$$\boldsymbol{\alpha}_1 \cdot D\mathbf{F}(\mathbf{u})^{\top}\mathbf{p}_2 = (\mathbf{p}_1 \times \mathbf{p}_2) \cdot D\mathbf{F}(\mathbf{u})^{\top}\mathbf{p}_2 \leq 0 \tag{6.14}$$
$$\boldsymbol{\alpha}_2 \cdot D\mathbf{F}(\mathbf{u})^{\top}\mathbf{p}_2 = (\mathbf{p}_2 \times \mathbf{p}_4) \cdot D\mathbf{F}(\mathbf{u})^{\top}\mathbf{p}_2 \leq 0 \tag{6.15}$$
$$\boldsymbol{\alpha}_2 \cdot D\mathbf{F}(\mathbf{u})^{\top}\mathbf{p}_4 = (\mathbf{p}_2 \times \mathbf{p}_4) \cdot D\mathbf{F}(\mathbf{u})^{\top}\mathbf{p}_4 \leq 0 \tag{6.16}$$
$$\boldsymbol{\alpha}_3 \cdot D\mathbf{F}(\mathbf{u})^{\top}\mathbf{p}_4 = (\mathbf{p}_4 \times \mathbf{p}_3) \cdot D\mathbf{F}(\mathbf{u})^{\top}\mathbf{p}_4 \leq 0 \tag{6.17}$$
$$\boldsymbol{\alpha}_3 \cdot D\mathbf{F}(\mathbf{u})^{\top}\mathbf{p}_3 = (\mathbf{p}_4 \times \mathbf{p}_3) \cdot D\mathbf{F}(\mathbf{u})^{\top}\mathbf{p}_3 \leq 0 \tag{6.18}$$
$$\boldsymbol{\alpha}_4 \cdot D\mathbf{F}(\mathbf{u})^{\top}\mathbf{p}_3 = (\mathbf{p}_3 \times \mathbf{p}_1) \cdot D\mathbf{F}(\mathbf{u})^{\top}\mathbf{p}_3 \leq 0 \tag{6.19}$$
$$\boldsymbol{\alpha}_4 \cdot D\mathbf{F}(\mathbf{u})^{\top}\mathbf{p}_1 = (\mathbf{p}_3 \times \mathbf{p}_1) \cdot D\mathbf{F}(\mathbf{u})^{\top}\mathbf{p}_1 \leq 0. \tag{6.20}$$

Our other key ingredient is $D\mathbf{F}(\mathbf{u})^{\top}$ which, in the original $\mathbf{x} = (x_1, x_2, x_3, x_4)$ coordinates, takes on the following form

$$D\mathbf{F}(\mathbf{u}(\mathbf{x}))^{\top} = r\theta \begin{pmatrix} 0 & 0 & 2x_1 + 2x_3 - 1 \\ 0 & 0 & 2x_1 + 2x_2 - 1 \\ 0 & 0 & -1 \end{pmatrix} + M_S(\mathbf{x}), \tag{6.21}$$

where M_S is a matrix whose entries are quadratic polynomials of $\mathbf{x}$ and the fitnesses W. We do not give its explicit form here. However, we derive sufficient conditions for (6.13)-(6.20). For example, (6.13) reduces to

$$\begin{aligned}&2x_4\left[2x_2\left(W_{11}-2W_{12}+W_{22}\right)+2x_3\left(W_{11}-W_{12}-W_{13}+\theta\right)\right.\\&\left.+\ 2x_4\left(W_{11}-W_{12}-\theta+W_{24}\right)-2W_{11}+2W_{12}+\theta-W_{24}\right]-2\theta r(x_3+x_4)\leq 0.\end{aligned}$$

We divide throughout by 2 and define $\hat{r}=r\theta$, then rearrange to obtain

$$\begin{aligned}\hat{r}(x_3+x_4)\geq x_4&\left[2x_2\left(W_{11}-2W_{12}+W_{22}\right)+2x_3\left(W_{11}-W_{12}-W_{13}+\theta\right)\right.\\&\left.+\ 2x_4\left(W_{11}-W_{12}-\theta+W_{24}\right)-2W_{11}+2W_{12}+\theta-W_{24}\right].\end{aligned}$$

But $\hat{r}\geq 0$, and so $\hat{r}(x_3+x_4)\geq\hat{r}x_4$, hence it suffices to consider

$$\begin{aligned}\hat{r}x_4\geq x_4&\left[2x_2\left(W_{11}-2W_{12}+W_{22}\right)+2x_3\left(W_{11}-W_{12}-W_{13}+\theta\right)\right.\\&\left.+\ 2x_4\left(W_{11}-W_{12}-\theta+W_{24}\right)-2W_{11}+2W_{12}+\theta-W_{24}\right]\end{aligned}$$

or, rearranging,

$$\begin{aligned}0\geq x_4&\left[2x_2\left(W_{11}-2W_{12}+W_{22}\right)+2x_3\left(W_{11}-W_{12}-W_{13}+\theta\right)\right.\\&\left.+\ 2x_4\left(W_{11}-W_{12}-\theta+W_{24}\right)-2W_{11}+2W_{12}+\theta-W_{24}-\hat{r}\right]\end{aligned}$$

which is obviously true for $x_4=0$. Meanwhile, for $x_4>0$ we can divide throughout by x_4, which yields

$$\begin{aligned}0\geq\ &2x_2\left(W_{11}-2W_{12}+W_{22}\right)+2x_3\left(W_{11}-W_{12}-W_{13}+\theta\right)+2x_4\left(W_{11}-W_{12}-\theta+W_{24}\right)\\&-2W_{11}+2W_{12}+\theta-W_{24}-\hat{r}\\&=2x_2\left(W_{11}-2W_{12}+W_{22}\right)+2x_3\left(W_{11}-W_{12}-W_{13}+\theta\right)+2x_4\left(W_{11}-W_{12}-\theta+W_{24}\right)\\&+\left(-2W_{11}+2W_{12}+\theta-W_{24}-\hat{r}\right)\left(x_1+x_2+x_3+x_4\right),\end{aligned}$$

where the constant terms have been multiplied by $\sum_{i=1}^{4}x_i=1$. Finally, we can rearrange the previous inequality to obtain

$$\begin{aligned}&x_1\left(\hat{r}+2W_{11}-2W_{12}-\theta+W_{24}\right)+x_2\left(\hat{r}+2W_{12}-\theta-2W_{22}+W_{24}\right)\\&+x_3\left(\hat{r}+2W_{13}-3\theta+W_{24}\right)+x_4\left(\hat{r}+\theta-W_{24}\right)\geq 0.\end{aligned}\tag{6.22}$$

Repeating the entire procedure on each of (6.14) to (6.20) gives also

$$
\begin{aligned}
& x_1\,(\hat{r} - 2W_{11} + 2W_{12} + W_{13} - \theta) + x_2\,(\hat{r} - 2W_{12} + W_{13} - \theta + 2W_{22}) \\
& + x_3\,(\hat{r} - W_{13} + \theta) + x_4\,(\hat{r} + W_{13} - 3\theta + 2W_{24}) \geq 0 && (6.23) \\
& x_1\,(\hat{r} + 2W_{12} - 3\theta + W_{34}) + x_2\,(\hat{r} - \theta + 2W_{22} - 2W_{24} + W_{34}) \\
& + x_3\,(\hat{r} + \theta - W_{34}) + x_4\,(\hat{r} - \theta + 2W_{24} + W_{34} - 2W_{44}) \geq 0 && (6.24) \\
& x_1\,(\hat{r} - W_{12} + \theta) + x_2\,(\hat{r} + W_{12} - \theta - 2W_{22} + 2W_{24}) \\
& + x_3\,(\hat{r} + W_{12} - 3\theta + 2W_{34}) + x_4\,(\hat{r} + W_{12} - \theta - 2W_{24} + 2W_{44}) \geq 0 && (6.25) \\
& x_1\,(\hat{r} - W_{13} + \theta) + x_2\,(\hat{r} + W_{13} - 3\theta + 2W_{24}) \\
& + x_3\,(\hat{r} + W_{13} - \theta - 2W_{33} + 2W_{34}) + x_4\,(\hat{r} + W_{13} - \theta - 2W_{34} + 2W_{44}) \geq 0 && (6.26) \\
& x_1\,(\hat{r} + 2W_{13} - 3\theta + W_{24}) + x_2\,(\hat{r} + \theta - W_{24}) \\
& + x_3\,(\hat{r} - \theta + W_{24} + 2W_{33} - 2W_{34}) + x_4\,(\hat{r} - \theta + W_{24} + 2W_{34} - 2W_{44}) \geq 0 && (6.27) \\
& x_1\,(\hat{r} - 2W_{11} + W_{12} + 2W_{13} - \theta) + x_2\,(\hat{r} - W_{12} + \theta) \\
& + x_3\,(\hat{r} + W_{12} - 2W_{13} - \theta + 2W_{33}) + x_4\,(\hat{r} + W_{12} - 3\theta + 2W_{34}) \geq 0 && (6.28) \\
& x_1\,(\hat{r} + 2W_{11} - 2W_{13} - \theta + W_{34}) + x_2\,(\hat{r} + 2W_{12} - 3\theta + W_{34}) \\
& + x_3\,(\hat{r} + 2W_{13} - \theta - 2W_{33} + W_{34}) + x_4\,(\hat{r} + \theta - W_{34}) \geq 0, && (6.29)
\end{aligned}
$$

where $\hat{r} = r\theta$. Thus a sufficient condition for (2.7) to be K_M^*−competitive is that inequalities (6.23) to (6.29) hold for all $\mathbf{x} \in \Delta_4$. Each of the inequalities (6.23) to (6.29) represents one row in a matrix inequality of the form

$$M\mathbf{x} \geq \mathbf{0}, \qquad (6.30)$$

where M is an 8×4 matrix that depends on W and r. $M \geq \mathbf{0}$ (i.e. all entries of M are nonnegative) is a necessary and sufficient condition for (6.30) to hold, for all $\mathbf{x} \in \Delta_4$.

Hence it suffices to have $M \geq \mathbf{0}$ to ensure that the normal bundle of the graph of ϕ_t is a subset of K_M for all $t > 0$. The surfaces S_t are normal to vectors of the form $(n_1, n_2, 1)$, where $-1 \leq n_1, n_2 \leq 1$. Consequently, the Lipschitz constant can be bounded above by $\gamma = 1$, uniformly in $t > 0$, hence $\phi_t \in C_1([0, 1]^2)$.

We conclude that $M \geq \mathbf{0}$ is sufficient to have $\phi_t \in B$ when $\phi_0 \in B$.

7. Existence of a globally attracting invariant manifold Σ_M for the TLTA model

For convenience, let the initial condition for (4.2) be $\phi_0(u, v) = 1 - u - v + 2uv$; that is, suppose that graph $\phi_0 = \Sigma_W$. Then $\phi_0 \in B$. If we assume $M \geq \mathbf{0}$ holds, then the solution ϕ_t of (4.2) stays in B for all $t > 0$ if $\phi_0 \in B$. At $t = 0$, the outward normal to Σ_W is in the direction of $(-\nabla\phi_0, 1) = (1 - 2v, 1 - 2u, 1)$. Then $\boldsymbol{\alpha}_1 \cdot (1 - 2v, 1 - 2u, 1) = 4(1 - u) \geq 0$, and similarly for $\boldsymbol{\alpha}_i$ with $i = 2, 3, 4$. Hence $(-\nabla\phi_0(u, v), 1) \in K_M$ for all $(u, v) \in [0, 1]^2$. Therefore the normal bundle of the graph of ϕ_0 is indeed contained in K_M. Since B is compact, there exists a sequence of $t_1, t_2, \ldots$ with $t_k \to \infty$ as $k \to \infty$ and a function $\phi^* \in B$ such that $\phi_{t_k} \to \phi^*$ as $k \to \infty$. The problem now is to show that (i) graph ϕ^* is *invariant* under (2.7) and (ii) graph ϕ^* *globally attracts* all points in Δ. In fact, in our approach (i) will follow from (ii).

Take some arbitrary smooth function $\psi_0 \in B$ not equal to ϕ_0 and, as done with ϕ_0, define $\psi_t = \mathcal{L}_t\psi_0$, where $\psi_t = \psi(\cdot, \cdot, t)$ is the solution of the PDE (4.2) with initial data $\psi(u, v, 0) = \psi_0(u, v)$ for $(u, v) \in [0, 1]^2$. The surface graph ψ_{t} is the image of graph ψ_0 under the flow generated by (2.7). We will compare the two surfaces graph ψ_{t} and graph ϕ^* and our aim is to show that graph ψ_{t} tends to graph ϕ^* as $t \to \infty$ (say in the Hausdorff set metric) by first showing that the volume between the two surfaces goes to zero as $t \to \infty$.

To this end let

$$\operatorname{epi} f = \{(u, v, q) \in \mathbb{R}^3 : q \geq f(u, v)\}$$

denote the epigraph of a function f and define the set

$$G_t = (\operatorname{epi} \phi^*) \vartriangle (\operatorname{epi} \psi_{\mathrm{t}}), \tag{7.1}$$

where $\vartriangle$ denotes the symmetric difference between two sets. Informally speaking, G_t is the set of all points trapped between the graphs of ϕ^* and ψ_t. The volume of this Lebesgue measurable set G_t is

$$\operatorname{vol}(G_t) = \int_{G_t} \mathrm{d}\lambda_3, \tag{7.2}$$

where λ_3 denotes Lebesgue measure in $\mathbb{R}^3$. The Liouville formula states that [4]:

$$\frac{\mathrm{d}}{\mathrm{d}t}[\operatorname{vol}(G_t)] = \int_{G_t} \nabla_{\mathbf{u}} \cdot \mathbf{F} \, \mathrm{d}\lambda_3, \tag{7.3}$$

where $\nabla_{\mathbf{u}} = \left(\frac{\partial}{\partial u}, \frac{\partial}{\partial v}, \frac{\partial}{\partial q}\right)$. Hence $\nabla_{\mathbf{u}} \cdot \mathbf{F} < 0$ would suffice to show that $\operatorname{vol}(G_t)$ is decreasing in t. As the volume is also bounded below by zero, $\operatorname{vol}(G_t)$ will converge to some limit; in fact, $\lim_{t\to 0} \operatorname{vol}(G_t) = 0$ since $\nabla_{\mathbf{u}} \cdot \mathbf{F}$ is strictly negative.

Lemma 7.1. *Let* $\mathbf{f}(\mathbf{x})$ *denote the right hand side of (2.2) and* $\mathbf{F}$ *as in (2.7). Then*

$$\nabla_{\mathbf{u}} \cdot \mathbf{F} = \nabla_{\mathbf{x}} \cdot \mathbf{f}. \tag{7.4}$$

Proof. Let us set up two more mappings; the first one being the projection

$$(x_1, x_2, x_3, x_4) = \mathbf{x} \mapsto \Pi_4(\mathbf{x}) = (x_1, x_2, x_3).$$

Let $\Pi_4|_{\Delta_4}$ be Π_4 restricted to Δ_4. $\Pi_4|_{\Delta_4}$ is a diffeomorphism with inverse

$$\Pi_4|_{\Delta_4}^{-1}(\mathbf{x}') = (x_1, x_2, x_3, 1 - x_1 - x_2 - x_3),$$

where $\mathbf{x}' = (x_1, x_2, x_3)$. Then define the second diffeomorphism from $\Pi_4(\Delta_4)$ to Δ as follows:

$$\mathbf{x}' \mapsto \mathbf{u} = \Xi(\mathbf{x}') = (x_1 + x_2, x_1 + x_3, 1 - x_2 - x_3),$$

which has inverse

$$\Xi^{-1}(\mathbf{u}) = \frac{1}{2}(u + v + q - 1, u - v - q + 1, -u + v - q + 1).$$

Then $\Phi = \Xi \circ \Pi_4$ (or $\Phi^{-1} = \Pi_4^{-1} \circ \Xi^{-1}$).

In (x_1, x_2, x_3) coordinates with $x_4 = 1 - x_1 - x_2 - x_3$, the equations of motion (2.2) become

$$\dot{x}_i = g_i(x_1, x_2, x_3) = f_i(x_1, x_2, x_3, 1 - x_1 - x_2 - x_3), \quad i = 1, 2, 3. \tag{7.5}$$

Thus

$$\nabla_{\mathbf{x}'} \cdot \mathbf{g} = \sum_{i=1}^{3} \frac{\partial g_i}{\partial x_i} = \sum_{i=1}^{3} \frac{\partial f_i}{\partial x_i} - \sum_{i=1}^{3} \frac{\partial f_i}{\partial x_4} = \sum_{i=1}^{4} \frac{\partial f_i}{\partial x_i} - \sum_{i=1}^{4} \frac{\partial f_i}{\partial x_4} = \nabla_{\mathbf{x}} \cdot \mathbf{f} - \frac{\partial}{\partial x_4}\left(\sum_{i=1}^{4} f_i\right).$$

But $\sum_{i=1}^{4} f_i = 0$, so that

$$\nabla_{\mathbf{x}'} \cdot \mathbf{g} = \nabla_{\mathbf{x}} \cdot \mathbf{f}. \tag{7.6}$$

Meanwhile,

$$\mathbf{g}(\mathbf{x}') = (D\Xi(\mathbf{x}'))^{-1}\mathbf{F}(\Xi(\mathbf{x}')),$$

which is the definition of the systems (7.5) and $\dot{\mathbf{u}} = \mathbf{F}(\mathbf{u})$ being smoothly equivalent, with Ξ as the diffeomorphism [25]. However,

$$D\Xi(\mathbf{x}') = \begin{pmatrix} 1 & 1 & 0 \\ 1 & 0 & 1 \\ 0 & -1 & -1 \end{pmatrix} \quad \Rightarrow \quad (D\Xi(\mathbf{x}'))^{-1} = \frac{1}{2}\begin{pmatrix} 1 & 1 & 1 \\ 1 & -1 & -1 \\ -1 & 1 & -1 \end{pmatrix}$$

which are constant matrices. Also,

$$D\mathbf{g}(\mathbf{x}') = (D\Xi)^{-1} D(\mathbf{F}(\Xi(\mathbf{x}'))),$$

and the Chain Rule yields

$$D\mathbf{g}(\mathbf{x}') = (D\Xi)^{-1} D\mathbf{F}(\Xi(\mathbf{x}')) D\Xi. \tag{7.7}$$

But

$$\nabla_{\mathbf{x}'} \cdot \mathbf{g} = \mathrm{Tr}(D\mathbf{g}(\mathbf{x}')),$$

so by taking the trace on both sides of (7.7), we obtain

$$\begin{aligned} \nabla_{\mathbf{x}'} \cdot \mathbf{g} &= \mathrm{Tr}((D\Xi)^{-1} D\mathbf{F}(\Xi(\mathbf{x}')) D\Xi) \\ &= \mathrm{Tr}(D\mathbf{F}(\mathbf{u})) \\ &= \nabla_{\mathbf{u}} \cdot \mathbf{F}, \end{aligned}$$

and finally

$$\nabla_{\mathbf{u}} \cdot \mathbf{F} = \nabla_{\mathbf{x}'} \cdot \mathbf{g},$$

which, combined with (7.6), gives the desired result.

We conclude that it suffices to seek conditions for the right hand side of (7.4) to be negative to ensure the volume of G_t is decreasing.

Recall that a matrix A is said to be copositive if $\mathbf{x}^\top A\mathbf{x} \geq 0$ for $x > 0$.

Lemma 7.2. *When $r > 0$ the volume of G_t in (7.1) is strictly decreasing whenever the matrix $-W'$ given by $W'_{ij} = W_{ii} - 6W_{ij} - \sum_{k=1}^{4} W_{kj}$ is copositive.*

Proof. We compute

$$\begin{aligned}
\nabla_{\mathbf{x}} \cdot \mathbf{f} &= \sum_{i=1}^{4} [(m_i - \bar{m}) + x_i(W_{ii} - 2m_i)] - r\theta \\
&= \sum_{i=1}^{4} (W_{ii}x_i + m_i) - 6\bar{m} - r\theta \\
&< \sum_{i,j=1}^{4} W_{ii}x_i x_j + \sum_{k=1}^{4} m_k - 6\sum_{i,j=1}^{4} W_{ij}x_i x_j \\
&= \sum_{i,j=1}^{4} \left(W_{ii} - 6W_{ij}\right) x_i x_j + \sum_{k=1}^{4} m_k \\
&= \sum_{i,j=1}^{4} \left(W_{ii} - 6W_{ij}\right) x_i x_j + \sum_{j,k=1}^{4} W_{kj}x_j \\
&= \sum_{i,j=1}^{4} \left(W_{ii} - 6W_{ij}\right) x_i x_j + \sum_{i,j,k=1}^{4} W_{kj}x_i x_j \\
&= \sum_{i,j=1}^{4} \left(W_{ii} - 6W_{ij} + \sum_{k=1}^{4} W_{kj}\right) x_i x_j \\
&= \sum_{i,j=1}^{4} W'_{ij} x_i x_j.
\end{aligned} \tag{7.8}$$

So we arrive at the requirement $\mathbf{x}^\top W'\mathbf{x} \leq 0$ for $\mathbf{x} > 0$, where

$$W'_{ij} = W_{ii} - 6W_{ij} + \sum_{k=1}^{4} W_{kj}. \tag{7.9}$$

Hence the righthand side of (7.8) is negative if and only if the matrix $-W'$ is copositive.

Remark 3. *There are necessary and sufficient conditions for a 3×3 matrix being copositive [26], but no known counterpart for 4×4 matrices. For $-W'$ to be copositive, each 3×3 submatrix of $-W'$ would need to be copositive, but this would be cumbersome to check, and we will not pursue it here.*

Here we will use the sufficient condition: Verify that all components of W' are nonpositive, i.e.

$$W_{ii} \leq 6W_{ij} - \sum_{k=1}^{4} W_{kj} \quad \forall\, i, j = 1, 2, 3, 4. \tag{7.10}$$

Actually, it suffices to check only the largest component of W'.

Remark 4. *For variations on (7.10) we may also explore the existence of Dulac functions $\sigma : \Delta \to \mathbb{R}_+$ for which $\nabla_{\mathbf{u}} \cdot (\sigma \mathbf{F})$ is single signed in Δ.*

Remark 5. *The question arises: Are alternative ways of showing global convergence to the graph of ϕ^*? That is, are there methods that do not require an application of Liouville's theorem, and therefore do not require the inequality (7.10) in addition to $M \geq 0$ (6.30)? Consider, for example, the treatment of carrying simplices which are codimension-one invariant manifolds of competitive population models, where global attraction usually requires only mild additional conditions beyond competitiveness (see, for example, [27, 28, 29, 30]). In the continuous time case, in his seminal paper on carrying simplices [14], Hirsch merely adds to competition (that the per-capita growth function has all nonpositive entries) the stronger condition that at any nonzero equilibrium the per-capita growth function has all negative entries) (although as stated in [28], the proof is not complete and we are not aware of a published correction).*

Lemma 7.3. *Suppose that for the volume G_t defined by (7.1) we have $\lim_{t\to\infty} \mathrm{vol}(G_t) = 0$. Then ψ_t converges pointwise to ϕ^*.*

Proof. Suppose, for a contradiction that ψ_t does not converge pointwise to ϕ^*. Then $\exists\, u, v \in [0, 1]\ \ \exists\, \varepsilon > 0\ \ \forall c \exists t > c$ such that $|\psi_t(u, v) - \phi^*(u, v)| \geq 2\varepsilon$. We can fix $c = 0$. Moreover, $\psi_t(u, v) = \phi^*(u, v)$ for each of $u = 0, 1$ and $v = 0, 1$. Therefore we arrive at

$$\exists\, u, v \in (0, 1)\ \ \exists\, \varepsilon > 0\ \ \exists t > 0 \quad |\psi_t(u, v) - \phi^*(u, v)| \geq 2\varepsilon. \tag{7.11}$$

Define $\mathbf{p_c} = (u, v, \frac{1}{2}(\psi_t(u, v) + \phi^*(u, v)))$ and $\mathbf{p}_\pm = \mathbf{p_c} \pm (0, 0, l)$, where $l = \frac{1}{2}|\psi_t(u, v) - \phi^*(u, v)|$. Note that

$$\frac{1}{2}(\psi_t(u, v) + \phi^*(u, v)) \pm l = \psi_t(u, v) \quad \text{or} \quad \phi^*(u, v),$$

so in fact $\mathbf{p}_\pm = (u, v, q_\pm)$ where $q_+ = \max(\psi_t(u, v), \phi^*(u, v))$ and $q_- = \min(\psi_t(u, v), \phi^*(u, v))$.

We set $K_{\text{ice}} = \left\{\mathbf{x} \in \mathbb{R}^n : x_3 \geq \sqrt{x_1^2 + x_2^2}\right\}$ ('ice' for ice-cream cone), and define

$$\mathbf{p}_- + K_{\text{ice}} = \{\mathbf{p}_- + \mathbf{v} : \mathbf{v} \in K_{\text{ice}}\}, \quad \mathbf{p}_+ - K_{\text{ice}} = \{\mathbf{p}_+ - \mathbf{v} : \mathbf{v} \in K_{\text{ice}}\}.$$

and seek an open ball $B(\mathbf{p_c}, \rho)$ such that $B(\mathbf{p_c}, \rho) \subset \tilde{K} \subset G_t$ where $\tilde{K} = (\mathbf{p}_- + K_{\text{ice}}) \cap (\mathbf{p}_+ - K_{\text{ice}})$ and $\rho = \min_{\mathbf{v}\in\partial\tilde{K}} ||\mathbf{v} - \mathbf{p_c}||_2$, or by symmetry of $\mathbf{p}_- + K_{\text{ice}}$ and $\mathbf{p}_+ - K_{\text{ice}}$, $\rho = \min_{\mathbf{v}\in\partial(\mathbf{p}_- + K_{\text{ice}})} ||\mathbf{v} - \mathbf{p_c}||_2$.

Translating these sets by $(-\mathbf{p}_-)$ shifts $\mathbf{p}_-$ to the origin, while $\mathbf{p_c}$ and $\partial(\mathbf{p}_- + K_{\text{ice}})$ are shifted to $(0, 0, l)$ and K_{ice} respectively. Then

$$\rho = \min_{\mathbf{v}\in\partial K_{\text{ice}}} \|\mathbf{v} - (0, 0, l)\|_2. \tag{7.12}$$

Put $\mathbf{v} = (\tilde{u}, \tilde{v}, \tilde{q})$. Then (7.12) is solved by minimising

$$\tilde{u}^2 + \tilde{v}^2 + (\tilde{q} - l)^2, \tag{7.13}$$

subject to the constraint $\tilde{q}^2 = \tilde{u}^2 + \tilde{v}^2$, which we use to rewrite (7.13) in terms of $\tilde{q}$ only:

$$\tilde{q}^2 + (\tilde{q} - l)^2,$$

whose minimum occurs at $\tilde{q} = l/2$. Hence

$$\rho = \sqrt{\left(\frac{l}{2}\right)^2 + \left(-\frac{l}{2}\right)^2} = \frac{l}{\sqrt{2}},$$

but by (7.11), $l \geq \varepsilon$, so choose $\rho = \frac{\varepsilon}{\sqrt{2}}$. Hence $B(\mathbf{p_c}, \rho) \subset G_t$, and so for all $t > 0$:

$$\text{vol}(G_t) \geq \text{vol}(B(\mathbf{p}, r)) = \frac{4\pi}{3} r^3 = \frac{\pi\sqrt{2}}{3}\varepsilon^3 > 0,$$

yielding $\exists\, \varepsilon > 0\ \ \forall t > 0 \quad \text{vol}(G_t) \geq \frac{\pi\sqrt{2}}{3}\varepsilon^3$ which contradicts our earlier assumption that $\text{vol}(G_t)$ is decreasing and tends to 0 as $t \to \infty$.

We therefore conclude that for any smooth $\psi_0 \in B$, $\psi_t \to \phi^*$ pointwise on $[0, 1]^2$. However, for all $t > 0$, ψ_t is a (smooth) Lipschitz function, with Lipschitz constant at most 1, on the compact set $[0, 1]^2$, thus pointwise convergence is sufficient to ensure uniform convergence to ϕ^*. We set $\Sigma_M = \text{graph}\, \phi^*$.

To show global convergence of each point $(u_0, v_0, q_0) \in \Delta$ to Σ_M, we first show global convergence of each point $(u_0, v_0, q_0) \in \text{int}\Delta$ to Σ_M. We need a lemma to show that given $(u_0, v_0, q_0) \in \text{int}\Delta$, there exists a $\psi_0 \in B$ such that $q_0 = \psi_0(u_0, v_0))$, i.e. the interior point $(u_0, v_0, q_0) \in \text{graph}\, \psi_0$.

Lemma 7.4. *Given $(u_0, v_0, q_0) \in int\Delta$ there exists a $\psi \in B$ such that $\psi(u_0, v_0) = q_0$.*

Proof. Consider the following piecewise linear construction. Let $P = (u_0, v_0, s) \in \text{int}\Delta$ and S_1 be the convex hull of the 3 points $P, (1, 0, 0), (1, 1, 1)$, S_2 the convex hull of the points $P, (0, 1, 0), (1, 1, 1)$, S_3 the convex hull of $P, (0, 1, 0), (0, 0, 1)$ and S_4 the closed convex hull of $P, (1, 0, 0), (0, 0, 1)$. Take $\psi_0 : [0, 1]^2 \to [0, 1]$ to be the piecewise linear function whose graph is $\cup_{i=1}^4 S_i$. ψ_0 has constant gradient everywhere, except along lines that join (u_0, v_0) to a vertex of $[0, 1]^2$.

Consider, for example, the section S_1. The outward normal on S_1 is in the direction of $n_1 = (P - (1, 0, 0)) \times (P - (1, 1, 1)) = (s - v_0, u_0 - 1, 1 - u_0)$. We require that $n_1 \in K_M$, or equivalently that $L_i := \alpha_i \cdot n_1 \geq 0$ for all $i = 1, 2, 3, 4$ which leads to $L_1 \equiv 0$, $L_2 = 1 - s - u_0 + v_0 \geq 0$, $L_3 = 2(1 - u_0) \geq 0$ and $L_4 = 1 + s - u_0 - v_0 \geq 0$. Each point $P \in \text{int}\Delta$ can be written as $P = \mu_1(1, 0, 0) + \mu_2(0, 1, 0) + \mu_3(0, 0, 1) + \mu_4(1, 1, 1)$ where $\mu_1, \mu_2, \mu_3, \mu_4 > 0$ and $\sum_{i=1}^4 \mu_i = 1$. Then $L_2 > 0$ as $u_0 \in (0, 1)$ and $L_2 = 2\mu_2 > 0$, $L_3 = 2\mu_3 > 0$. Hence $n_1 \in K_M$. Similarly for the other sections S_2, S_3, S_4. Hence where the normal exists to the graph of ψ_0, it belongs to K_M.

Now we smooth ψ_0. We consider $\phi(u, v, t) = 1 - u - v + 2uv + \sum_{k=0}^{\infty} A_k(\phi_0) \sin(k\pi u) \sin(k\pi v) e^{-2k^2\pi^2 t}$. Then ϕ satisfies the heat equation with Dirichlet boundary conditions equivalent to (4.3) - (4.6). Here the coefficients $A_k(\phi_0)$ are found from the initial condition $\phi_0(u, v) = \phi(u, v, 0)$. Now choose s in the interval $I = (q_0 - \delta, q_0 + \delta)$ for $\delta > 0$ small enough that $(u_0, v_0, s) \in \text{int}\Delta$ for all $s \in I$. For each $s \in I$, there is a smooth solution $\phi_s(\cdot, \cdot, t)$ that passes through (u_0, v_0, s) at $t = 0$. For $t = \epsilon > 0$ sufficiently small $q_0 \in \{\phi_s(u_0, v_0, \epsilon) : s \in I\}$. If $s_0 \in I$ is such that $q_0 = \phi_{s_0}(u_0, v_0, \epsilon)$ we set $\psi(u, v) = \phi_{s_0}(u, v, \epsilon)$. By construction ψ is smooth, satisfies the boundary conditions and $\psi(u_0, v_0) = q_0$. Lastly we must check that the normal bundle of the graph of ψ belongs to K_M, i.e. $\alpha_i \cdot (-\psi_u - \psi_v, 1) \geq 0$ for $(u, v) \in (0, 1)^2$ and $i = 1, 2, 3, 4$. This is not immediate from small perturbation arguments since $\alpha_1 \cdot n_1 \equiv 0$. However, we note that $\phi_u(\cdot, \cdot, t)$ satisfies $\frac{\partial \phi_u}{\partial t} = \Delta \phi_u$, and similarly for ϕ_v so that $\frac{\partial \zeta}{\partial t} = \Delta \zeta$ where $\zeta(u, v, t) = \ell \cdot (-\phi_u(u, v, t), -\phi_v(u, v, t), 1)$ for any constant $\ell \in K_M^*$. $\zeta(u, v, 0) \geq 0$ for all $(u, v) \in (0, 1)^2$ and $\ell \in K_M^*$, so since the semigroup of operators for the heat equation is positivity preserving, $\zeta(u, v, t) \geq 0$ for all $t \geq 0$ which shows that the normal bundle of the graph of ϕ is a subset of K_M for all $t \geq 0$. We conclude that $\psi \in B$.

Now consider points $(u_0, v_0, q_0) \in \partial\Delta$. Recall that $\mathbf{x} \in \partial\Delta_4$ if and only if $x_1 x_2 x_3 x_4 = 0$ and that $\Phi^{-1}(\partial\Delta) = \partial\Delta_4$. Suppose that $x_1 = 0$. Then $\dot{x}_1 = r\theta x_2 x_3 \geq 0$, and on the interior of the face where $x_1 = 0$ we have $\dot{x}_1 > 0$. Similarly we establish $\dot{x}_i > 0$ on the interior of the face of Δ_4 where $x_i = 0$ for $i = 1, 2, 3, 4$. Hence all points on the interior of the faces of Δ_4 move inwards under the TLTA flow (2.2). This implies that all points interior to faces of Δ move inwards under the flow (2.7). Next we must consider the edges of Δ_4 which map under Φ to the edges of Δ. For example, on $\tilde{E}_{14}$ we have $\dot{q} = x_1 m_1 + x_4 m_4 - \bar{m} - 2r\theta x_1 x_4 \leq 0$ with equality if and only if $x_1 = 1, x_4 = 0$ or $x_4 = 1, x_1 = 0$ and these two points are invariant vertices that belong to graph ϕ^*. Similarly, on $\tilde{E}_{23}$ we have $\dot{q} = 2r\theta x_2 x_3 \geq 0$ with equality if and only if $x_2 = 1, x_3 = 0$ or $x_2 = 0, x_3 = 1$ and again these are two vertices that belong to graph ϕ^*. Hence non-vertex points of boundary edges $\tilde{E}_{14}$ and $\tilde{E}_{23}$ move into the interior of Δ_4 under flow and hence points on $q = 1, u = v$ and $q = 0, v = 1 - u$ move inwards in Δ under the flow (2.7). Finally the remaining edges $\tilde{E}_{12}, \tilde{E}_{13}, \tilde{E}_{42}, \tilde{E}_{43}$ of Δ are invariant and belong to graph ϕ^* by (4.7).

We conclude that either $(u_0, v_0, q_0) \in \text{int}\Delta$, in which case lemma 7.4 immediately applies, or $(u_0, v_0, q_0) \in \partial\Delta$ and moves inwards under the flow (2.7) so that lemma 7.4 can then be applied, or $(u_0, v_0, q_0) \in \partial\Delta$ belongs to the invariant boundary $\partial\text{graph}\phi^* = \tilde{E}_{12} \cup \tilde{E}_{13} \cup \tilde{E}_{42} \cup \tilde{E}_{43}$. Hence for each $t > 0$, the point $(u(t), v(t), q(t))$ on the forward orbit through (u_0, v_0, q_0) under (2.7) will converge onto Σ_M because $\psi_t \to \phi^*$ uniformly.

To conclude, if we can find a suitable condition on r and W such that (7.10) holds and $M \geq 0$, then there exists a globally attracting Lipschitz invariant manifold Σ_M with (relative) boundary corresponding to the union of the four edges E_{12}, E_{13}, E_{42} and E_{43}. This establishes Theorem 3.1.

Remark 6. *It would be interesting to establish conditions on W and r for which* Σ_M *is a differentiable manifold. (A similar question was asked by Hirsch in the context of Carrying Simplices [14]). To the best of our knowledge the smoothness of a carrying simplex* on its interior *is currently an open problem). One possible approach might be to investigate when* Σ_M *is actually an inertial manifold, and employ the theory of Chow et. al. [31].*

Remark 7. *Our method* does not *show that* Σ_M *is asymptotically complete (i.e. we have not shown that for each* $(u_0, v_0, q_0) \in \Delta$ *there exists an orbit in* Σ_M *which 'shadows' the orbit through* (u_0, v_0, q_0)*). If* Σ_M *were an inertial manifold it would be asymptotically complete [32]. In the absence of selection (or for weak selection [9]), the Wright manifold* is *an inertial manifold, and so is asymptotically complete (as can be shown using explicit solutions when* $r > 0$ *and W is the zero matrix).*

8. An example: The modifier gene case of the TLTA model

The two-locus two-allele (TLTA) model has widely been used (for example, [12, 11, 13]) to investigate the effect of a modifier gene β on a primary locus α, in the context of Fisher's theory for the evolution of dominance [33]. In many cases the dynamics of the TLTA model is well-understood [12, 11, 13]. Our use of the modifier gene case of the TLTA model is not to provide new results on equilibria and their stability basins, but rather to demonstrate how our method works through a computable example. Using our method we can obtain explicit estimates on the range of recombination rates and selection coefficients for a 2−dimensional globally attracting invariant manifold to exist.

The fitness matrix for the TLTA model for the modifier gene scenario is:

$$W = \begin{pmatrix} 1-s & 1-hs & 1-s & 1-ks \\ 1-hs & 1 & 1-ks & 1 \\ 1-s & 1-ks & 1-s & 1 \\ 1-ks & 1 & 1 & 1 \end{pmatrix}. \tag{8.1}$$

Traditionally (see, for example, [34, 35, 36, 11, 13, 37]) these fitnesses are denoted as in Table 1. The parameter s is often called the "selection intensity" or "selection coefficient" [38, 13], while

	AA	Aa	aa
BB	1	1	$1-s$
Bb	1	$1-ks$	$1-s$
bb	1	$1-hs$	$1-s,$

Table 1: Table of fitnesses for the nine different diploid genotypes. Here $0 < s \leq 1$, $0 \leq k \leq h \leq \frac{1}{s}$ and $h \neq 0$ [11].

h and k are referred to as measures of "the influence of the dominance relations between alleles" [12]. In [38] s is interpreted as the recessive allele effect, while h (and k) is the heterozygote effect.

Our given range of values for h excludes the case of overdominance ($h < 0$). The idea of using s and h traces back to [39]; Wright's third parameter h' is used similarly to k, except the fitness of Aa/BB is $1 - ks$ instead of 1. The case with $k = 0$ is considered in [33, 40, 39, 41]. Later, Ewens assumed that modification depends on whether B occurs in a homozygote BB or a heterozygote Bb [35], which prompted him to include the third parameter k.

For this modifier gene example the matrix problem (6.30) leads to

$$M = \begin{pmatrix} \hat{r} + s(2h + k - 2) & \hat{r} + s(-2h + k) & \hat{r} + s(3k - 2) & \hat{r} - sk \\ \hat{r} + s(-2h + k + 1) & \hat{r} + s(2h + k - 1) & \hat{r} + s(-k + 1) & \hat{r} + s(3k - 1) \\ \hat{r} + s(-2h + 3k) & \hat{r} + sk & \hat{r} - sk & \hat{r} + sk \\ \hat{r} + s(h - k) & \hat{r} + s(-h + k) & \hat{r} + s(-h + 3k) & \hat{r} + s(-h + k) \\ \hat{r} + s(-k + 1) & \hat{r} + s(3k - 1) & \hat{r} + s(k + 1) & \hat{r} + s(k - 1) \\ \hat{r} + s(3k - 2) & \hat{r} - sk & \hat{r} + s(k - 2) & \hat{r} + sk \\ \hat{r} + s(-h + k) & \hat{r} + s(h - k) & \hat{r} + s(-h + k) & \hat{r} + s(-h + 3k) \\ \hat{r} + sk & \hat{r} + s(-2h + 3k) & \hat{r} + sk & \hat{r} - sk \end{pmatrix} \geq \mathbf{0}. \tag{8.2}$$

The condition $M \geq 0$ is equivalent to

$$\begin{aligned} \hat{r} \quad \geq \quad & s \max\{k, -k, 1 - k, -1 - k, h - k, k - h, h - 3k, 2h - 3k, 1 - 3k, 2 - 3k, \\ & 2 - k, 2h - k, 2h - k - 1, -2h - k + 1, 2 - 2h - k\}. \end{aligned} \tag{8.3}$$

As $k > 0$, we can eliminate any non-positive entries in the right hand side of (8.3), leading to

$$\hat{r} \geq s \max(k, 1 - k, h - k, h - 3k, 2h - 3k, 1 - 3k, 2 - 3k, 2 - k, 2h - k, 2h - k - 1, -2h - k + 1, 2 - 2h - k),$$

and, by inspection, we can narrow down the options to

$$\begin{aligned} \hat{r} &\geq s \max(k, h - k, 2 - k, 2h - k, 2 - 2h - k) \\ &= s \max(k, 2 - k, 2h - k). \end{aligned}$$

Moreover, since $h \geq k$,

$$2h - k = h + (h - k) \geq h \geq k,$$

leaving us with

$$\hat{r} \geq s \max(2 - k, 2h - k),$$

which can be summarised as

$$\hat{r} \geq s(2 \max(1, h) - k). \tag{8.4}$$

Next, we use (7.10) with Lemma 7.2 to obtain the condition for decreasing phase volume. Here, the largest components of W' is $i = 1, j = 1$ and $i = 2, j = 1$, which yield the conditions $-9 + 7s + hs + ks < 0$ and $-9 + 2s + 7hs + ks < 0$ respectively. These rearrange to $9 > s(7 + h + k)$ and $9 > s(2 + 7h + k)$, which can be rewritten as

$$9 > s(\max(7 + h, 2 + 7h) + k). \tag{8.5}$$

Combining this with (8.4), we obtain the following result:

Theorem 8.1. *Consider the TLTA model (2.2) with* W *given by (8.1). Then if* $0 \le s \le 1$ *and* $0 \le k \le h \le \frac{1}{s}$, $h > 0$, *(8.5) and*

$$r(1 - ks) \ge s\,(2\max(1, h) - k)\,, \tag{8.6}$$

all hold, there exists a Lipschitz invariant manifold that globally attracts all initial polymorphisms.

9. Discussion

The purpose of this paper has been to show that explicit parameter ranges for selection coefficients and recombination rates ranges can be found for the classic two-locus, two-allele continuous-time selection-recombination model to possess a globally attracting invariant manifold. We achieved this by determining those parameter ranges and coordinates for which the model could be written as a competitive system for a polyhedral cone. This competitive system is a monotone system backwards in time.

To the best of our knowledge this is a novel approach to the study of selection-recombination models and it paves the way for a fresh look at the global dynamics of the TLTA continuous-time selection-recombination model via monotone systems theory. In particular, it might be possible to study the periodic orbits found by Akin [18, 19] via suitable refinements [42, 43] of the Poincaré-Bendixson theory developed for monotone system in [44] and the orbital stability methods of Russell Smith [45].

The QLE manifold was studied for discrete-time multilocus systems in [9], and an obvious question is whether there is a convex cone for which the model studied there is competitive. In [9] results are based upon small selection or weak epistasis, but it is not clear how strong selection or weak epistasis can be relative to recombination for the invariant manifold to persist from the Wright manifold. The identification of a cone for which the discrete-time multilocus system is competitive would provide bounds on selection coefficients and recombination rates for the invariant manifold to exist. Certainly the discrete-time TLTA model could be studied using the same framework introduced here, but adapted to discrete time steps.

Typically the identification of a globally attracting invariant manifold in a finite-dimensional system enables reduction of the dimension of the dynamical system. In our case the reduction in dimension is one and all limit sets belong to the surface Σ_M. However, the smoothness properties of Σ_M are not known. To write the asymptotic dynamics on Σ_M, we would ideally like Σ_M to be at least of class C^1, so that the standard tools of dynamical systems on differentiable manifolds, such as linear stability analysis, bifurcation theory, and so on, can be applied. If the study of the smoothness of the codimension-one carrying simplex of continuous- and discrete-time competitive population models is indicative [46, 47, 48, 49, 50], and bearing in mind that our boundary conditions of Σ_M are particularly simple, we might expect that when the TLTA model is K_M^*−competitive for some polyhedral cone K_M, Σ_M is generically C^1, but this remains an interesting open problem.

Finally, as mentioned above, if the full power of the invariant manifold Σ_M is to be harnessed, global attraction to Σ_M has to be improved to exponential attraction and asymptotic completeness of the dynamics (2.7). By establishing asymptotic completeness, from a practical point of view it means that after a short transient, the dynamics on Σ_M is a good approximation of the full dynamics.

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Appendix A. The selection-recombination model in (u, v, q) coordinates

The equations of motion for $\dot{u}$, $\dot{v}$, and $\dot{q}$ are:

$$
\begin{aligned}
\dot{u} = \frac{1}{4}\{ & W_{11} - 2W_{12} - W_{13} + W_{22} + W_{42} + v(2q(W_{11} - 2W_{12} + W_{22}) - 2(W_{11} - 2W_{12} + W_{22} + W_{42} - \theta)) \\
& + v^2(W_{11} - 2W_{12} + W_{13} + W_{22} + W_{42} - 2\theta) - 2q(W_{11} - 2W_{12} - W_{13} + W_{22} + \theta) \\
& + q^2(W_{11} - 2W_{12} - W_{13} + W_{22} - W_{42} + 2\theta) \\
& + u\,[-3W_{11} + 2W_{12} + 4W_{13} + W_{22} - W_{33} - 2W_{42} - 2W_{43} - W_{44} + 2\theta \\
& + v(-2q(W_{11} - 2W_{12} + W_{22} - W_{33} + 2W_{43} - W_{44}) + 2(2W_{11} - 2W_{12} - W_{33} + 2W_{42} + W_{44} - 2\theta)) \\
& + q^2(-W_{11} + 2W_{12} + 2W_{13} - W_{22} - W_{33} + 2w_{42} + 2W_{43} - W_{44} - 4\theta) \\
& + 2q(2W_{11} - 2W_{12} - 3W_{13} + W_{33} + W_{42} - W_{44} + 2\theta) \\
& + v^2(-W_{11} + 2W_{12} - 2W_{13} - W_{22} - W_{33} - 2W_{42} + 2W_{43} - W_{44} + 4\theta)\Big] \\
& + u^2\,[3W_{11} + 2W_{12} - 5W_{13} - W_{22} + 2W_{33} - W_{42} + 4W_{43} + 2W_{44} - 6\theta \\
& - 2\,(W_{11} - 2W_{13} - W_{22} + W_{33} + 2W_{42} - W_{44})\,q - 2v\,(W_{11} - W_{22} - W_{33} + W_{44})] \\
& + u^3(-W_{11} - 2W_{12} + 2W_{13} - W_{22} - W_{33} + 2W_{42} - 2W_{43} - W_{44} + 4\theta)\},
\end{aligned}
$$

$$
\begin{aligned}
\dot{v} = \frac{1}{4}\{ & W_{11} - W_{12} - 2W_{13} + W_{33} + W_{43} \\
& + u(2\,(-W_{11} + 2W_{13} - W_{33} - W_{43} + \theta) + 2q\,(W_{11} - 2W_{13} + W_{33})) \\
& + u^2(W_{11} + W_{12} - 2W_{13} + W_{33} + W_{43} - 2\theta) \\
& - 2q(W_{11} - W_{12} - 2W_{13} + W_{33} + \theta) + q^2(W_{11} - W_{12} - 2W_{13} + W_{33} - W_{43} + 2\theta) \\
& + v\,[-3W_{11} + 4W_{12} + 2W_{13} - W_{22} + W_{33} - 2W_{42} - 2W_{43} - W_{44} + 2\theta \\
& + u(-2q\,(W_{11} - 2W_{13} - W_{22} + W_{33} + 2W_{42} - W_{44}) + 2(2W_{11} - 2W_{13} - W_{22} + 2W_{43} + W_{44} - 2\theta)) \\
& + q^2(-W_{11} + 2W_{12} + 2W_{13} - W_{22} - W_{33} + 2W_{42} + 2W_{43} - W_{44} - 4\theta) \\
& + 2q(2W_{11} - 3W_{12} - 2W_{13} + W_{22} + W_{43} - W_{44} + 2\theta) \\
& + u^2\,(-W_{11} - 2W_{12} + 2W_{13} - W_{22} - W_{33} + 2W_{42} - 2W_{43} - W_{44} + 4\theta)] \\
& + v^2\,[3W_{11} - 5W_{12} + 2W_{13} + 2W_{22} - W_{33} + 4W_{42} - W_{43} + 2W_{44} - 6\theta \\
& -2q(W_{11} - 2W_{12} + W_{22} - W_{33} + 2W_{43} - W_{44}) - 2u(W_{11} - W_{22} - W_{33} + W_{44})] \\
& + v^3(-W_{11} + 2W_{12} - 2W_{13} - W_{22} - W_{33} - 2W_{42} + 2W_{43} - W_{44} + 4\theta)\},
\end{aligned}
$$

$$
\begin{aligned}
\dot{q} = \frac{1}{4}\{ & W_{11} - W_{12} - W_{13} + W_{42} + W_{43} + W_{44} - 2\theta \\
& + u(-2(W_{11} - W_{13} + W_{43} + W_{44} - 2\theta) + 2v(W_{11} + W_{44} - 2\theta)) \\
& + u^2(W_{11} + W_{12} - W_{13} - W_{42} + W_{43} + W_{44} - 2\theta) \\
& - 2v(W_{11} - W_{12} + W_{42} + W_{44} - 2\theta) + v^2(W_{11} - W_{12} + W_{13} + W_{42} - W_{43} + W_{44} - 2\theta) \\
& + q\,[-3W_{11} + 4W_{12} + 4W_{13} - W_{22} - W_{33} - 2W_{42} - 2W_{43} + W_{44} \\
& + u(-2v(W_{11} - W_{22} - W_{33} + W_{44}) + 2(2W_{11} - 3W_{13} - W_{22} + W_{33} + W_{42} + 2W_{43} - 2\theta)) \\
& + u^2(-W_{11} - 2W_{12} + 2W_{13} - W_{22} - W_{33} + 2W_{42} - 2W_{43} - W_{44} + 4\theta) \\
& + 2v(2W_{11} - 3W_{12} + W_{22} - W_{33} + 2W_{42} + W_{43} - 2\theta) \\
& + v^2(-W_{11} + 2W_{12} - 2W_{13} - W_{22} - W_{33} - 2W_{42} + 2W_{43} - W_{44} + 4\theta)\Big] \\
& + q^2\,[3W_{11} - 5W_{12} - 5W_{13} + 2W_{22} + 2W_{33} - W_{42} - W_{43} - W_{44} + 6\theta \\
& - 2u(W_{11} - 2W_{13} - W_{22} + W_{33} + 2W_{42} - W_{44}) - 2v(W_{11} - 2W_{12} + W_{22} - W_{33} + 2W_{43} - W_{44})] \\
& + q^3(-W_{11} + 2W_{12} + 2W_{13} - W_{22} - W_{33} + 2W_{42} + 2W_{43} - W_{44} - 4\theta)\} \\
& + r(1 - q - u - v + 2uv).
\end{aligned}
$$

Appendix B. Example of the model without an invariant manifold Σ_M

For the following values of the fitnesses and recombination rate

$$W = \begin{pmatrix} 0.1 & 0.3 & 20 & 1 \\ 0.3 & 0.9 & 1 & 10 \\ 20 & 1 & 1.3 & 2 \\ 1 & 10 & 2 & 0.5 \end{pmatrix}, \qquad r = \frac{1}{19}, \tag{B.1}$$

the invariant manifold Σ_M cannot be numerically found; perhaps it does not even exist for these values of the parameters. A lot of numerical instabilities are present which oscillate about $q = 0$.