Autocatalytic Networks with Translation

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Abstract

We consider the kinetics of an autocatalytic reaction network in which replication and catalytic action is separated by a translation step. We find that the behavior of such a system is closely related to second order replicator equations, which describe the kinetic of autocatalytic reaction networks in which the replicators act also as catalysts. In fact, the qualitative dynamics seems to be described almost entirely be the second order reaction rates of the replication step. For two species we recover the qualitative dynamics of the replicator equations. Larger networks show some deviations, however. A hypercyclic system consisting of three interacting species can converge towards a stable limit cycle in contrast to the replicator equation case. A singular perturbation analysis shows that the replication translation system reduces to a second order replicator equation if translation is fast. The influence of mutations on replication translation networks is also very similar to the behavior of selection-mutation equations.

1. Introduction

A variety of self-replicating chemical systems have been constructed and investigated experimentally in the past 25 years since Spiegelman's [46] *in vitro* serial transfer experiments on Qβ. The dynamics of this model-system, which contains a protein enzyme as part of the "environment", was subsequently studied in great details by Manfred Eigen and his collaborators [4, 5, 6, 3]. Catalytic activity of RNA for a variety of reactions has been discovered [7, 8, 22, 60], including a limited capacity for replication and self-replication [9, 10]. Artificial molecules that self-replicate in a protein-free environment have been synthesized, for instance, by Orgel [34], Rebek [45, 17, 36], and von Kiedrowski [58]. All these findings add to the credibility of an "RNA world" as one of the crucial stages in prebiotic evolution [19].

In parallel to these advances in *template chemistry* a mathematical theory of molecular evolution has been developed, based on a series of pioneering papers by M. Eigen and P. Schuster [11, 12, 13, 14]. Ignoring the molecular details one considers the dynamics of *replicators* as a auto-catalytic "chemical" reactions of the form

$$(A) + I \rightarrow 2I + (W),$$

where I is the replicator, (A) denotes the energy-rich building material for replicators and (W) indicates that the formation of the replicator will in general produce low-energy "waste".

One of the central questions in any theory of molecular evolution concerns the behavior of a collection of competing (or otherwise interacting) species of replicators $I_1, \ldots, I_n$. While the replication of polynucleotides is in reality an overwhelmingly complicated process involving a huge number of intermediates it nevertheless has turned out that it is sensible to focus on the over-all replication reaction. In other words, one can treat the replicators as "atomic" entities, and encapsulate their chemical details into a small set of reaction rate constants [16]. The system of interacting replicators is thus completely described by the concentrations (or relative frequencies) x_k of the different species I_k. In its most condensed form the logics of the RNA world is thus captured in the *autocatalytic reaction network*

$$I_k + I_l \longrightarrow 2I_k + I_l \qquad\qquad k,l = 1,\ldots,n.$$

The dynamical system associated with the above reaction scheme is now termed *replicator equation* [41]:

$$\dot{x}_k = x_k \left(\sum_{j=1}^{n} a_{kj} x_j - \sum_{i,j} a_{ij} x_i x_j \right) . \tag{$\mathcal{R}$}$$

Originally developed as a model of prebiotic evolution, replicator equations have been encountered since then in many different fields: populations genetics, mathematical ecology (where they occur disguised as Lotka-Volterra equations [28]), economics, or laser physics. Their properties have been the subject of hundreds of research papers by many research groups, most prominently among them J. Hofbauer, P. Schuster, and K. Sigmund in Vienna. The results of the first decade of investigation are compiled in the book [31].

Self-replication on molecular level was clearly the crucial invention at the origin of life. Almost equally important was the invention of translation and the genetic code. In this contribution we will *not* be concerned with the question why translation was invented, or how a RNA replicator that has invented translation would conquer the RNA world [21, 44]. We have a much less ambitious agenda here: We consider a reaction system that contains a number of different replicator species which all produce a gene product that carries the enzymatic activity. Our main question is the following: Is the picture of the selection dynamics that has emerged from the studies of autocatalytic reaction networks still valid once the catalytic activity has shifted to translation products?

2. The Model

We consider a system of n species $I_1, \ldots, I_n$ of replicators or genotypes and their translation products $T_1, \ldots, T_n$. For sake of definiteness, we may consider the genotypes as nucleic acids and the translation products as proteins in same later stage of prebiotic evolution [40]. The replication processes involve translation products T_j of the genotype I_j as catalysts:

$$(A) + I_k + T_j \xrightarrow{a'_{kj}} 2I_k + T_j + (W)$$

for all combinations $1 \leq k, j \leq n$. The rates of these reactions are $a'_{kj}[(A)]\,[I_k]\,[T_j]$, i.e. we assume mass action kinetics. Since there are no convincing models for the kinetics of translation in a prebiotic setting we make the most simple choice:

$$(B) + I_k \xrightarrow{w'_k} T_k + I_k$$

with rate $w'_k[(B)][I_k]$. We assume that the genotypes I_k and the translation products are different types of biopolymers, thus the concentrations of the monomers $[(A)]$ and $[(B)]$ are independent from each other. Consequently we will assume that the two types of polymers are subject to different degradation or removal reactions. In the mathematical model the latter are described by outflows $[T_k]\Phi^T$ and $[I_K]\Phi$, respectively.

Thus the dynamical system considered here reads in its most general form

$$\begin{aligned}
\frac{d}{dt}[I_k] &= [I_k]\left\{\sum_{j=1}^{n} a'_{kj}[(A)]\,[T_j] - \Phi\right\} \\
\frac{d}{dt}[T_k] &= w'_k[(B)]\,[I_k] - [T_k]\Phi^T
\end{aligned}$$

Note that we are still missing equations governing the concentrations of the monomers $[(A)]$ and $[(B)]$, and that we have not yet specified the functions Φ and Φ^T which describe the removal processes. It is convenient to consider these as "boundary conditions" under which the replication-translation process takes place. Three types of boundary conditions have been discussed in the literature:

(1) *Constant Organization* assumes (i) that the monomer concentrations are buffered and thus constant in time, and (ii) that the total concentration of the different polymer types is kept

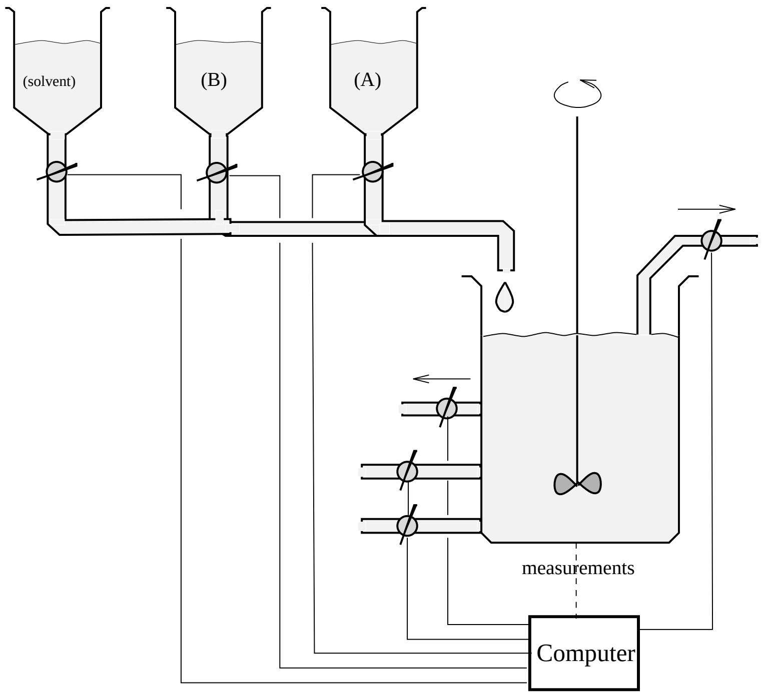

Figure 1: The hypothetical Evolution Reactor is a kind of dialysis reactor with walls impermeable to polynucleotides and polypeptides. The in-flow of monomers keeps the reaction mixture away from equilibrium. It is adjusted such that the the concentrations of the monomers occur in excess in the reactor, i.e., the monomer concentrations do not change significantly over time. The out-flow of polynucleotides and poly-peptides through two different diaphragms is controlled such that total concentration of both types of polymers is kept at constant levels. While this type of evolution reactor will not be easy to realize in practice it establishes boundary conditions for replication-translation systems that lead to mathematically tractable dynamical systems.

constant in time. These conditions can in principle be enforced in a sophisticated *evolution reactor* as the one shown in figure 1. It will be convenient to use the effective rate constants

$$a_{kj} \stackrel{\text{def}}{=} [(A)]a'_{kj} \qquad \text{and} \qquad w_k \stackrel{\text{def}}{=} [(B)]w'_k \,.$$

A further simplification is achieved by switching to relative coordinates

$$x_k \stackrel{\text{def}}{=} [I_k]\Big/\sum_j [I_j] \qquad \text{and} \qquad t_k \stackrel{\text{def}}{=} [T_k]\Big/\sum_j [T_j]\,.$$

As simple calculation then shows that

$$\Phi = \sum_{i,j} x_i a_{ij} t_j \qquad \text{and} \qquad \Phi^T = \sum_i w_i x_i \;.$$

In matrix notation we obtain thus

$$\dot{x}_k = x_k\left[(At)_k - \langle x, At\rangle\right] \qquad\qquad \dot{t}_k = w_k x_k - t_k\langle w, x\rangle \qquad\qquad (CO)$$

The state space of this model is the direct sum of the two $(n-1)$-dimensional simplices corresponding to the coordinates x_k, $k=1,\dots n$, and t_k, $k=1,\dots n$, respectively.

(2) The *Continuously Stirred Flow Reactor* (CSTR) is the most convenient experimental setting. A constant flow of rate r through the system carries the monomers with concentrations a_0 and b_0 and removes monomers and polymers at the same flow rate r proportional to their concentration. Using conservation of mass one immediately finds the dynamical equations for the concentrations of the monomers $a \stackrel{\text{def}}{=} [(A)]$ and $b \stackrel{\text{def}}{=} [(B)]$. In order to simplify the notation we use $y_k \stackrel{\text{def}}{=} [I_k]$ and $u_k = [T_k]$.

$$\begin{aligned} \dot{y}_k &= y_k\left[a(A'u)_j - r\right] \\ \dot{u}_k &= w'_k b y_k - r u_k \\ \dot{a} &= -a\langle y, A'u\rangle + r(a_0 - a) \\ \dot{b} &= -b\langle w', y\rangle + r(b_0 - b) \end{aligned} \tag{CSTR}$$

The state of the system is described by a vector $(y,u,a,b) \in \mathbb{R}^n_+ \oplus \mathbb{R}^n_+ \oplus \mathbb{R}_+ \oplus \mathbb{R}_+$.

(3) We assume that there is no flux of material into or out of the system. The system is kept away from thermodynamic equilibrium by means of an energy consuming *regeneration reaction* that produces active monomers from the degradation products of the polymers. While not very realistic for an experimental approach this type of boundary condition is very useful for the study of pattern formation processes as it leads to meaningful reaction- diffusion models [59, 54, 25]. In spatially homogeneous models we obtain equations similar to the CSTR discussed above. The rate constants of the degradation reactions are d_k and d^T_k, respectively. Conservation of mass ensures that $[(A)] + \sum_k [I_k] = a_0$ and $[(B)] + \sum_k [T_k] = b_0$.

$$\begin{aligned} \dot{y}_k &= y_k\left[a(A'u)_j - d_k\right] \\ \dot{u}_k &= w'_k b y_k - d^T_k \\ \dot{a} &= -a\langle y, A'u\rangle + \langle d, y\rangle \\ \dot{b} &= -b\langle w', y\rangle + \langle d^T, u\rangle \end{aligned} \tag{REG}$$

The state space is the direct sum $S_{n+1} \oplus S_{n+1}$ of two n-dimensional simplices.

Since all three dynamical systems describe the same chemical reaction system, although under quite different boundary conditions it is not surprising that their dynamics is quite similar. Constant organization is by far the most tractable case. We will therefore give a complete derivation of our results only for this case. Results for the CSTR and the regeneration system are often very similar to the CO case. The details can be found in [23]. It has been observed quite often that the dynamics of replication systems in a CSTR or in a model with regeneration reaction(s) become very similar to the constant organization case when the flow rate r (or the reaction rates for the regeneration steps) become small. A singular perturbation treatment of this effect can be found in [24]. For a partial result see [42].

3. Fixed Points

Despite the fairly complicated form of our reaction scheme it is not difficult to compute the coordinates of all equilibria. Let us begin with interior equilibria, that is, with rest points at which all species occur with non-zero concentration. We shall use the notation $\mathbf{1}$ for the vector with entries 1.

Theorem 1. *Consider the reaction translation model under constant organization. Then there is a unique interior equilibrium $(\hat{x}, \hat{t}) \in int(S_n \oplus S_n)$ if and only if $A^{-1}\mathbf{1}$ is either strictly positive or strictly negative.*

Proof. Suppose A is invertible and $(\hat{x}, \hat{t})$ is a fixed point of (CO). An explicit computation shows

$$\hat{x}_k = \frac{(A^{-1}\mathbf{1})_k}{w_k \sum_{i=1}^{n} \frac{1}{w_i}(A^{-1}\mathbf{1})_i} \qquad \text{and} \qquad \hat{t}_k = \frac{(A^{-1}\mathbf{1})_k}{\langle \mathbf{1}, A^{-1}\mathbf{1}\rangle}\,.$$

Thus $\hat{t} \in \operatorname{int} S_n$ if and only if $(A^{-1}\mathbf{1})_k$ has the same sign for all k. Then $\hat{x}_k > 0$ as well since the coefficients w_k are all strictly positive by assumption. ∎

Remark. If there is an isolated interior equilibrium, then A is invertible and $(A^{-1}\mathbf{1})_k$ has the same sign for all k. Furthermore there are at most two isolated interior rest points for CSTR.

The expression for the x-coordinates of the interior rest point above strongly suggests to introduce the matrix

$$B \stackrel{\text{def}}{=} A\text{diag}[w].$$

With this definition we may write

$$\hat{x} = \frac{1}{\langle \mathbf{1}, B^{-1}\mathbf{1}\rangle} B^{-1}\mathbf{1} \qquad \text{and} \qquad \hat{t} = \frac{1}{\langle \mathbf{1}, A^{-1}\mathbf{1}\rangle} A^{-1}\mathbf{1}$$

for the location of the interior equilibrium.

On the boundary of the state space at least one coordinate is zero. It is useful to observe that equilibria on the boundary have a particular form:

Lemma 1. *Suppose all translation rates are non-zero and let $\xi = (\hat{x}, \hat{t})$ be a rest point. Then $\hat{x}_k = 0$ if and only if $\hat{t}_k = 0$.*

Proof. Suppose $\hat{x}_k = 0$. Then $\dot{t}_k = -t_k\langle w, x\rangle$, where the scalar product $\langle w, x\rangle > 0$ by assumption. Thus $\hat{t}_k = 0$. Now suppose $\hat{t}_k = 0$. This implies $0 = w_k\hat{x}_k$ and thus $\hat{x}_k$ must vanish. ∎

If some of the w_k are zero, parts of be boundary consist entirely of fixed points. We will not consider these degenerate cases any further. The non-zero coordinates of ξ can be obtained by restricting the dynamical system to the variables that do not vanish in ξ, i.e., to a smaller system of the type (RT). The theorem above can therefore be applied also to the non-zero part of a rest point ξ on the boundary of the state space. All isolated rest points of (RT) are thus obtained as the interior rest points of (RT) restricted to a subset $K \subset \{1, \dots, n\}$ of the n replicating species.

The stability analysis of the rest points will turn out to be very complicated in general. It is fairly easy, however, to determine the stability of a boundary equilibrium ξ against introduction of species which are not present in ξ. The corresponding directions are called *transversal* [31]. To this end it will be convenient to temporarily rearrange the order of the coordinates such that

$$\xi = (x_1, t_1; x_2, t_2; \dots; x_n, t_n)$$

and $\hat{x}_i = \hat{t}_i = 0$ for $1 \le i \le m$. The entries of the Jacobian matrix in the first $2m$ rows and columns are readily computed:

$$\begin{aligned}
\frac{\partial \dot{x}_k}{\partial x_\ell}(\xi) &= \delta_{kl}[(A\hat{t})_k - \langle \hat{x}, A\hat{t}\rangle] + 0 \stackrel{\text{def}}{=} L_k(\xi)\delta_{kl} \\
\frac{\partial \dot{x}_k}{\partial t_\ell}(\xi) &= 0 \\
\frac{\partial \dot{t}_k}{\partial x_\ell}(\xi) &= \delta_{kl} w_k \\
\frac{\partial \dot{t}_k}{\partial t_\ell}(\xi) &= -\langle w, \hat{x}\rangle
\end{aligned}$$

Consequently the Jacobian $\partial\mathrm{RT}(\xi)$ is of the form

$$\left(\begin{array}{cccccc}
\begin{pmatrix} L_1(\xi) & 0 \\ w_1 & \langle w,\hat{x}\rangle \end{pmatrix} & \mathbf{0} & \cdots & \mathbf{0} & \begin{array}{cccc} 0 & 0 & \ldots & 0 \\ 0 & & & 0 \end{array} \\
\mathbf{0} & \begin{pmatrix} L_2(\xi) & 0 \\ w_2 & \langle w,\hat{x}\rangle \end{pmatrix} & & \mathbf{0} & \begin{array}{cccc} 0 & & & 0 \\ 0 & & & 0 \end{array} \\
\vdots & & \ddots & & \vdots \\
\mathbf{0} & \mathbf{0} & \cdots & \begin{pmatrix} L_m(\xi) & 0 \\ w_m & \langle w,\hat{x}\rangle \end{pmatrix} & \begin{array}{cccc} 0 & & & 0 \\ 0 & 0 & \ldots & 0 \end{array} \\
 & \mathbf{X} & & & \mathbf{Y}
\end{array}\right)$$

where the $2(n-m)\times 2m$ block $\mathbf{X}$ is irrelevant for the stability of ξ and $\mathbf{Y}$ is the $2(n-m)\times 2(n-m)$ Jacobian matrix of (RT) restricted to the species that do not vanish in the equilibrium ξ. The eigenvalues corresponding to the transversal direction k are now easily computed from the 2×2-blocks. We find explicitly

$$\lambda_k^{(1)} = L_k(\xi) \quad \text{and} \quad \lambda_k^{(2)} = -\langle w,\hat{x}\rangle \le 0.$$

Assuming as usual $\langle w,\hat{x}\rangle \neq 0$ we have $\hat{t} = \frac{1}{\langle w,\hat{x}\rangle}\mathrm{diag}[w]\,\hat{x}$ and thus

$$\lambda_k^{(1)} = \frac{1}{\langle w,\hat{x}\rangle}\left[(A\mathrm{diag}\,[w]\,\hat{x})_k - \langle \hat{x}, A\mathrm{diag}\,[w]\,\hat{x}\rangle\right] = \frac{1}{\langle w,\hat{x}\rangle}\left[(B\hat{x})_k - \langle \hat{x}, B\hat{x}\rangle\right] .$$

Following [29, 31] we will say that a rest point ξ of (RT) is *saturated* if all eigenvalues belonging to the transversal directions are non-positive. The above considerations can then be summarized as

Theorem 2. *Let $\xi = (\hat{x},\hat{t})$ be a boundary equilibrium of a replication translation model for which A is invertible and $w_k > 0$ for all k. Then ξ is a saturated equilibrium if and only if $\hat{x}$ is saturated equilibrium of the second order replicator equation with interaction matrix $B = A\mathrm{diag}[w]$, i.e., if and only if*

$$\tilde{\lambda}_k(\xi) \stackrel{\mathrm{def}}{=} (B\hat{x})_k - \langle \hat{x}, B\hat{x}\rangle \le 0 \quad \textit{for all } k \textit{ with } \hat{x}_k = 0.$$

The matrix $B = A\mathrm{diag}[w]$ occurs both in the explicit expression for the x-coordinates of an interior rest point and in the expression for the transversal eigenvalues of a boundary equilibrium. In both cases our result match the situation in a second order replicator equation with B as interaction matrix. We will see in the following sections that this relation between (RT) and replicator equations is even deeper.

In [52] it has been proposed to represent an autocatalytic network by a directed graph with colored edges. In complete analogy we introduce the same notation here: The vertices of the graph $\vec{\Gamma}(RT)$

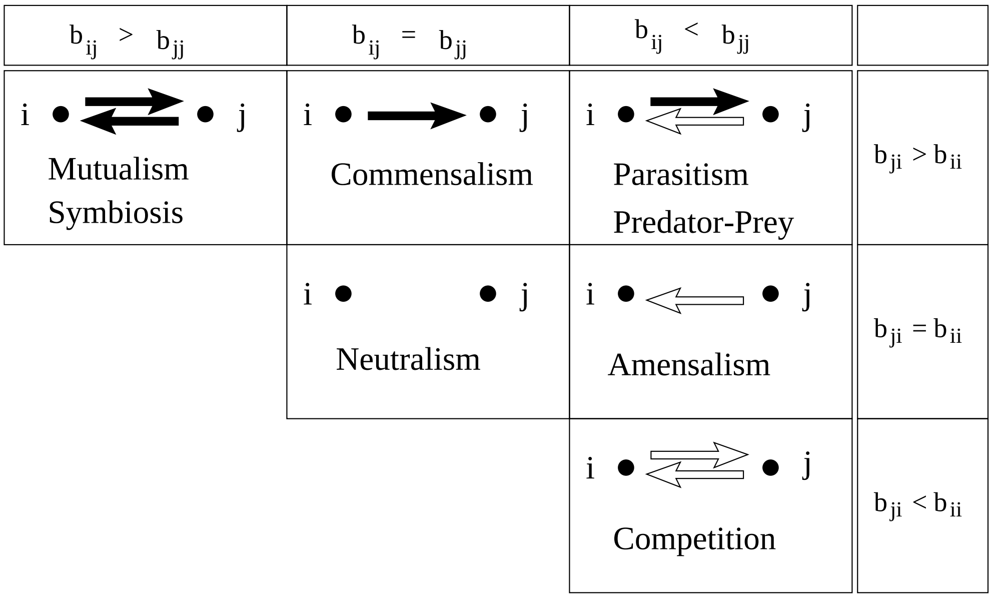

Figure 2: The different types of interaction: full arrows indicate $b_{ij} - b_{ii} > 0$, empty arrows $b_{ij} - b_{jj} < 0$.

associated with the reaction-translation model (RT) are the replicating species $I_1, \ldots, I_n$. There is a *"full"* arrow from j to i if $b_{ij} - b_{ii} = (a_{ij} - a_{jj})w_j > 0$, and there is a *"empty"* arrow from j to i if $b_{ij} - b_{jj} < 0$. As an example, look for the two-species model as follows. The six different graphs of this type on $n = 2$ vertices match the usual classification of ecological interactions between two species, see figure 2. In the following section we show that they also correspond in a very natural way to the classification of the dynamical behavior of the two-species replication-translation system, see figure 3.

4. Two Species

The special case $n = 2$ allows for a complete analysis of the dynamics under constant organization. We consider here the general two-species system with general selection matrix A with entries $a_{ij} > 0$ and and translation constants $(w_1, w_2) > 0$. It will be convenient to use the following abbreviations:

$$c_1 \stackrel{\text{def}}{=} a_{12} - a_{22}\,, \qquad c_2 \stackrel{\text{def}}{=} a_{21} - a_{11}\,.$$

The results of the previous section imply immediately that an interior equilibrium exists if and only if $c_1, c_2 > 0$ or $c_1, c_2 < 0$. The Jacobian of the interior rest point can be readily diagonalized with the help of `Mathematica`. One finds the two external eigenvalues

$$\lambda_1^{ext} = \frac{D}{2(c_1+c_2)} \qquad \text{and} \qquad \lambda_2^{ext} = -\frac{w_1 w_2 (c_1+c_2)}{c_1 w_2 + c_2 w_1}$$

which do not influence the dynamical behavior on $S_2 \oplus S_2$. Both are negative whenever there is an interior rest point. The dynamical stability of this fixed point is determined by the remaining two eigenvalues

$$\lambda_{3,4} = \frac{-(c_1+c_2) w_1 w_2 \pm \sqrt{(c_1+c_2)^2 w_1^2 w_2^2 - 2 c_1 c_2 w_1 w_2 (c_1 w_2 + c_2 w_1)}}{2(c_1 w_2 + c_2 w_1)} .$$

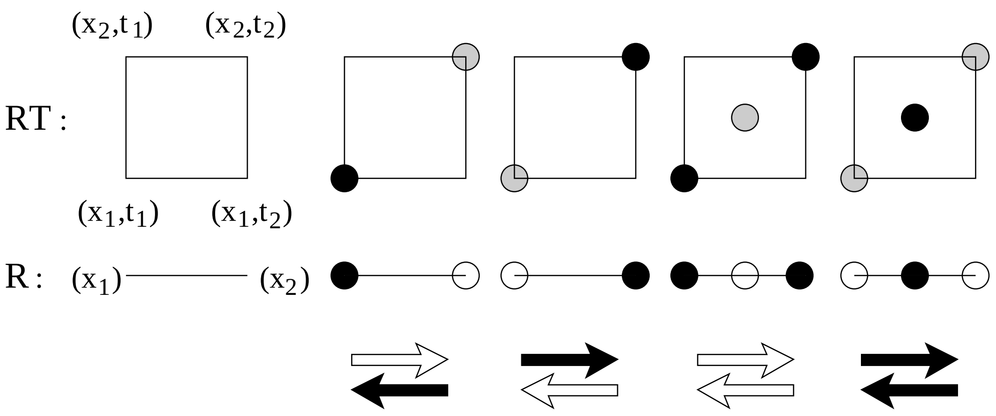

Figure 3: Comparison of the phase portraits of (RT) and ($\mathcal{R}$). Black circles indicate sinks, gray ones saddle-points, and white ones are sources. The corresponding graph $\vec{\Gamma}(RT)$ are shown below.

This is of the form $\alpha \pm \sqrt{\alpha^2 - \gamma}$, where α is always negative and $\text{sgn}\gamma = \text{sgn}c_1$, provided c_1 and c_2 have the same sign. Assume that $c_1, c_2 > 0$. Then the square root is either complex or if it is real then it is smaller than α. Consequently $\lambda_{3,4} < 0$ and the interior rest point is a sink. If $c_1, c_2 > 0$ then $\gamma < 0$ and the square root is real and larger than α, hence $\lambda_3 < 0$ and $\lambda_4 > 0$, and the interior equilibrium is a saddle point.

Finally, let us briefly consider the 1-species equilibria. Their stability is determined by the eigenvalues

$$\begin{array}{lll} (1,1;0,0) & : \lambda_1 = -\dfrac{a_{11} c_1}{c_1+c_2}\,, & \lambda_2 = -\dfrac{c_1 c_2}{c_1+c_2}\,, \\ (0,0;1,1) & : \lambda_1 = -\dfrac{a_{22} c_2}{c_1+c_2}\,, & \lambda_2 = -\dfrac{c_1 c_2}{c_1+c_2}\,. \end{array}$$

Summarizing our calculations we have

$c_1, c_2 < 0$	Both corners are sinks and the interior equilibrium is a saddle point. Its unstable manifold connects to both sinks.
$c_1 > 0, c_2 < 0$	Corner 1 is a sink and corner 2 a saddle point. The unstable manifold of corner 2 connects to the sink. There is no interior rest point.
$c_1 < 0, c_2 > 0$	Corner 2 is a sink and corner 1 a saddle point. The unstable manifold of corner 1 connects to the sink. There is no interior rest point.
$c_1, c_2 > 0$	Both corners are saddle points and the interior equilibrium is a sink. The unstable manifolds of both corner saddle points connect to the interior sink

The phase portraits corresponding to these four cases are shown in Fig. 3. They compare directly to the phase portraits of the second order replicator equation with interaction matrix A.

5. Barycentric Transformation

Before we proceed with the linear stability analysis of interior equilibria in larger systems, we briefly discuss a transformation that will turn out to be a crucial tool for most of our results. The following lemma is well known, see e.g. [31, sect. 12.4].

Lemma 2. *Let $D = \mathrm{diag}[d_1, \ldots, d_n]$ be a diagonal matrix with $d_i > 0$. Then there is a diffeomorphism $\mathcal{B} : S_n \to S_n$ mapping the phase portrait of the second order replicator equation with interaction matrix A to the phase portrait of the second order replicator equation with interaction matrix AD.*

This result can used to simplify the algebra for the stability analysis of an interior rest point. Suppose there is an interior rest point $\hat{x}$. Setting $d_i \stackrel{\text{def}}{=} 1/\hat{x}_i$ sends $\hat{x}$ results in $\mathcal{B}(\hat{x}) = \frac{1}{n}\mathbf{1}$, i.e., the interior rest point is mapped to the barycenter of the simplex. Therefore $\mathcal{B}$ is usually called *barycentric* transformation. The fact that the coordinates of the interior rest point are now of a very simple form simplifies the algebraic manipulations in many cases. Fortunately, a similar result holds for our replication-translations system (RT).

Theorem 3. *Let a_{ij} be an arbitrary matrix, $(x,t) \in S_n \oplus S_n$ and let $(c,d) \in \operatorname{int}(S_n \oplus S_n)$. Then $\mathcal{B}: S_n \oplus S_n \to S_n \oplus S_n$, $(x,t) \mapsto (u,v)$ defined by*

$$u_i = \frac{c_i x_i}{\sum_j c_j x_j} \qquad \text{and} \qquad v_i = \frac{d_i t_i}{\sum_j d_j t_j}$$

is a diffeomorphism mapping the orbits of

$$\begin{aligned} \dot{x}_k &= x_k \left(\sum_i a_{ki} t_i - \sum_{i,j} x_i a_{ij} t_j \right) \\ \dot{t}_k &= w_k x_k - t_k \sum_i w_i x_i \end{aligned}$$

onto the orbits of

$$\begin{aligned} \dot{u}_k &= u_k \left(\sum_i b_{ki} v_i - \sum_i u_i \sum_j b_{ij} v_j \right) \\ \dot{v}_k &= \left(\gamma_k u_k - v_k \sum_j \gamma_j u_j \right) \phi(u,v), \end{aligned}$$

where the coefficients of the latter differential equations are $b_{ij} = a_{ij}/d_j$, $\gamma_i = d_i w_i / c_i$, and

$$\phi(u,v) = \left(\sum_l \frac{v_l}{d_l} \right)^2 \sum_l \frac{u_l}{c_l} \quad > 0.$$

Proof. The inverse map $\mathcal{B}^{-1}$ is given by

$$x_i = \frac{u_i}{c_i} \frac{1}{\sum_j c_j^{-1} u_j} \qquad \text{and} \qquad t_i = \frac{v_i}{d_i} \frac{1}{\sum_j d_j^{-1} v_j}.$$

Differentiating u_i and v_i yields

$$\begin{aligned} \dot{u}_i &= \frac{1}{\left(\sum_j c_j x_j\right)^2} \cdot \left[\dot{x}_i c_i \sum_j c_j x_j - c_i x_i \sum_j c_j \dot{x}_j \right] = \\ &= u_i \left(\sum_j a_{ij} t_j - \sum_j x_j \sum_l a_{jl} t_l \right) = \\ &= u_i \left(\sum_j \frac{a_{ij}}{d_j} v_j - \sum_j u_j \sum_l \frac{a_{jl}}{d_l} v_l \right) \frac{1}{\sum_j d_j^{-1} v_j} \\ \dot{v}_i &= \frac{d_i \dot{t}_i}{\sum_j d_j t_j} - v_i \sum_j \frac{d_j \dot{t}_j}{\sum_l d_l t_l} = \frac{d_i w_i x_i}{\sum_j d_j t_j} - v_i \sum_j \frac{d_j w_j x_j}{\sum_l d_l t_l} \\ &= \left(\frac{d_i w_i}{c_i} u_i - v_i \sum_j \frac{d_j w_j}{c_j} u_j \right) \frac{\sum_j d_j^{-1} v_j}{\sum_j c_j^{-1} u_j} \end{aligned}$$

By means of a change of velocity and setting $b_{ij} = a_{ij}/d_j$ and $\gamma_i = d_i w_i / c_i$ we obtain finally the proposition. ∎

Corollary 1. *Let $\hat{\xi} = (\hat{x}, \hat{t})$ be an equilibrium of* (CO) *and let*

$$u_i = \frac{x_i}{\hat{x}_i \sum_j \hat{x}_j^{-1} x_j} \quad \text{and} \quad v_i = \frac{t_i}{\hat{t}_i \sum_j \hat{t}_j^{-1} t_j} .$$

Then the fixed point of the dynamical system obtained from (CO) *by a barycentric transformation with parameters u_i, v_i is $\hat{\mathcal{B}}(\hat{\xi}) = \frac{1}{n}(\mathbf{1}, \mathbf{1})$.*

Proof. From theorem 3 one finds immediately
$$\hat{u}_i = \frac{\hat{x}_i}{\hat{x}_i \sum_j \hat{x}_j^{-1} \hat{x}_j} = \frac{1}{n} \qquad \text{and} \qquad \hat{v}_i = \frac{\hat{t}_i}{\hat{t}_i \sum_j \hat{t}_j^{-1} \hat{t}_j} = \frac{1}{n}. \blacksquare$$

6. Competitive Systems

Schlögl [37] investigated two model systems in which the substance X_i is formed from a substrate A via first order and second order autocatalysis, respectively: $A + X_i \to 2X_i$ (first order autocatalysis) and $A + 2X_i \to 3X_i$ (second order autocatalysis). In the (fully) competitive case the translation products catalyze only the replication of their own gene, i.e., the interaction matrix is diagonal $A = \text{diag}[k_1, k_2, \ldots, k_n]$. Therefore the differential equations for the competitive model simplify to

$$\dot{x}_k = x_k \left[k_k t_k - \sum_j k_j x_j t_j \right] \qquad \dot{t}_k = w_k x_k - t_k \sum_j w_j x_j$$

The phase portraits of this dynamical system as equivalent with the phase portraits of

$$\dot{u}_k = u_i \left[v_i - \sum_j u_j v_j \right] \qquad \dot{v}_k = (u_k - v_k)\, \phi(u, v)$$

as a consequence of the barycentric transformation.

The Jacobian matrix of this vector field is readily computed:

$$\begin{aligned}
\frac{\partial}{\partial u_j} \dot{u}_i &= -u_i v_j \\
\frac{\partial}{\partial v_j} \dot{u}_i &= -u_i u_j + u_i \delta_{ij} \\
\frac{\partial}{\partial u_j} \dot{v}_i &= (u_i - v_i) \frac{\partial \phi}{\partial u_j} + \delta_{ij} \phi(u, v) \\
\frac{\partial}{\partial v_j} \dot{v}_i &= (u_i - v_i) \frac{\partial \phi}{\partial v_j} - \delta_{ij} \phi(u, v)
\end{aligned}$$

At the fixed point $\mathcal{P} = \frac{1}{n}(\mathbf{1},\mathbf{1})$ we find that $\phi(\mathcal{P}) = w$. Since $u_i = v_i$ at this point, the values of $\partial\phi/\partial u_i$ and $\partial\phi/\partial v_i$ are irrelevant. The Jacobian is of the form

$$\partial f(\mathcal{P}) = \begin{pmatrix} A & B \\ C & D \end{pmatrix}$$

where each of the four quadratic matrices A, B, C, and D is circulant. We find explicitly:

$$A = -\frac{1}{n^2}J\,, \quad B = wI\,, \quad C = -\frac{1}{n^2}J + \frac{1}{n}I\,, \text{and } D = -wI\,,$$

where J is the matrix with all entries one and I is the identity matrix. Matrices of this type can be analyzed using the following interesting result:

Theorem 4. *Let M be a $mn \times mn$ matrix which has m^2 circulant blocks M_{ij} of size $n \times n$. The vectors $\omega^{(k)}$ with entries*

$$\omega_j^{(k)} = \exp(2\pi\imath\frac{j}{k})\,, \quad \textit{for } k = 0,\ldots,n-1 \textit{ and } j = 1\ldots n$$

are well known to be eigenvectors of any circulant $n \times n$ matrix. Set $M_{ij}\omega^{(k)} = \rho_{ij}^{(k)}\omega^{(k)}$, let $R^{(k)}$ be the $m \times m$ matrix with entries $\rho_{ij}^{(k)}$, and denote the eigenvalues of $R^{(k)}$ by $\Lambda_\ell^{(k)}$.
Then $\Lambda_\ell^{(k)}$ is an eigenvalue of M. In particular, if all matrices $R^{(k)}$ are diagonalizable, then we obtain all eigenvalues of M as eigenvalues of the matrices $R^{(k)}$.

Proof. We rely on the fact that the $\omega^{(k)}$ form a basis of eigenvectors for all circulant matrices. Let $z \in \mathbb{R}^m$ and suppose $\xi = z \times \omega^{(k)}$ is an eigenvector of M. Then

$$M\xi = \begin{pmatrix} M_{11}z_1\omega^{(k)} & M_{12}z_2\omega^{(k)} & \ldots & M_{1m}z_m\omega^{(k)} \\ M_{21}z_1\omega^{(k)} & M_{22}z_2\omega^{(k)} & \ldots & M_{2m}z_m\omega^{(k)} \\ \vdots & \vdots & & \vdots \\ M_{m1}z_1\omega^{(k)} & M_{m2}z_2\omega^{(k)} & \ldots & M_{mm}z_m\omega^{(k)} \end{pmatrix} = (R^{(k)}z) \times \omega^{(k)} = \Lambda^{(k)}\xi.$$

Since $\omega^{(k)}$ is non-zero, this equation is equivalent to the eigenvalue equation for the matrix $R^{(k)}$. Thus ξ is an eigenvector of M if z is an eigenvector of $R^{(k)}$, and all eigenvalues of $R^{(k)}$ are also eigenvalues of M.
Now suppose that all matrices $R^{(k)}$, $1 \leq k \leq m$ are diagonalizable. Denote by $z^{(k,\ell)}$, $\leq \ell \leq n$, an orthonormal eigensystem of $R^{(k)}$ and let $\xi^{(k,\ell)} \stackrel{\text{def}}{=} z^{(k,\ell)} \times \omega^{(k)}$ be the corresponding eigenvectors of M. We find that

$$\langle z^{(k,\ell)} \times \omega^{(k)}, z^{(k',\ell')} \times \omega^{(k')}\rangle = \langle z^{(k,\ell)}z^{(k',\ell')}\rangle\,\langle\omega^{(k)}\omega^{(k')}\rangle = \delta_{\ell,\ell'}\cdot\delta_{k\,k'}\,,$$

i.e., all eigenvectors corresponding to different k are orthogonal, even if the corresponding eigenvalues should coincide by chance. Thus the $\xi^{(k,\ell)}$ form a complete orthonormal basis of eigenvectors for M. ∎

In the terminology of theorem 4 we find

$$R^{(0)} = \begin{pmatrix} -\frac{1}{n} & 0 \\ w & -w \end{pmatrix} \qquad \text{and} \qquad R^{(j)} = \begin{pmatrix} 0 & \frac{1}{n} \\ w & -w \end{pmatrix}$$

for the competitive model. $R^{(0)}$ belongs to the external directions since $\omega^{(0)} = \mathbf{1}$. The corresponding eigenvalues are

$$\Lambda^{(0,1)} = -\frac{1}{n} \qquad \text{and} \qquad \Lambda^{(0,2)} = -w.$$

The remaining eigenvalues $\Lambda^{(j,\ell)}$ for $1 \leq j < n$ and $\ell = 1,2$ are now easily computed using theorem 4:

$$\Lambda^{(\pm)} = -\frac{w}{2} \pm \frac{1}{2}\sqrt{w^2 + 4w/n}$$

independent of j. Both $\Lambda^{(+)}$ and $\Lambda^{(-)}$ are $n-1$-fold degenerate, and it is easy to check that $\Lambda^{(-)} < 0 < \Lambda^{(+)}$ for all $n \geq 2$ and $w > 0$. Thus ξ is a saddle point with $n-1$ unstable eigenvalues.

The result immediately carries over to all equilibria on the boundary of the state space in the following form: Let ξ be a rest point on the boundary and suppose there are m non-vanishing species at ξ. Then ξ has $m-1$ positive and $m-1$ negative eigenvalues which all belong to the directions spanned by the non-vanishing species. In particular, if ξ is stable, then $m = 1$, i.e., only the single-species equilibria can be stable. That they are in fact stable is determined by the transversal eigenvalues $\lambda_k(\xi) = -w < 0$.

7. Cooperation

The hypercycle [15] may serve as the paradigm of a cooperative system. Each translation product catalyzes the replication of one other species in a circular arrangement, see figure 4; consequently, the interaction matrix is circulant, and the corresponding system of differential equations reads:

$$\begin{aligned}
\dot{x}_k &= x_k \left[k_k t_{k-1} - \sum_j k_j x_j t_{j-1} \right] \\
\dot{t}_k &= w_k x_k - t_k \sum_j w_j x_j \,.
\end{aligned}$$

Again a barycentric transformation yields

$$\dot{u}_k = u_i \left[v_i - \sum_j u_j v_{j-1} \right]$$
$$\dot{v}_k = (u_k - v_k)\, \phi(u, v)\,.$$

The external eigenvalues of the interior equilibrium $(\mathbf{1}, \mathbf{1})$ are

$$\Lambda^{(0,1)} = -\frac{1}{n} \qquad \text{and} \qquad \Lambda^{(0,2)} = -w\,.$$

For the remaining eigenvalues we find

$$\Lambda_j^{(\pm)} = -\frac{w}{2} \pm \frac{1}{2}\sqrt{w^2 + \frac{4w}{n} e^{-2\pi j \imath / n}}\,,$$

and their real parts can be readily computed:

$$\Re(\Lambda_j) = -w + \sqrt{\frac{w}{2}}\sqrt{w + \frac{4}{n}\cos\varphi + \sqrt{w^2 + \frac{8w}{n}\cos\varphi + \frac{16}{n^2}}}\,.$$

It is not complicated now to derive the critical value of w at which a Hopf-Bifurcations occurs:

$$\left(\frac{1}{w}\right)_{crit} = -\frac{1}{n}\,\frac{\sin^2\left(\dfrac{2\pi(n-1)j}{n}\right)}{\cos\left(\dfrac{2\pi(n-1)j}{n}\right)}\,.$$

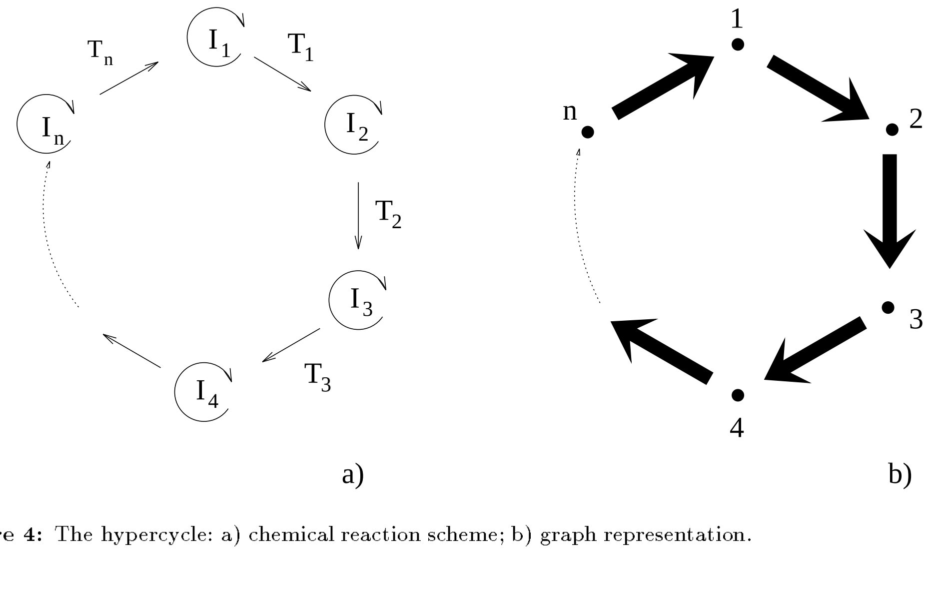

Figure 4: The hypercycle: a) chemical reaction scheme; b) graph representation.

Since $w > 0$, only values of j in the interval $n/4 < j < 3n/4$ can fulfil this condition. Consequently, there are no Hopf bifurcations in the two-species model. For larger systems we find

$n = 3, j = 1$ $w_{crit} = 1/2$.

$n = 4, j = 2$ $w_{crit} = 0$. Since we consider only non-zero values of the translation rate, there is in fact no stable fixed point. The corresponding hypercyle equation, however, exhibits a marginally stable fixed point [15].

$n \geq 5$ There are no stable interior fixed points. Computational studies indicate that there is a (globally) stable limit cycle, as in the case of the second order replicator equations [30].

All equilibria on the boundary are non-saturated and degenerate, in complete analogy to the situation in the elementary hypercycle [43].

8. Reduction to Replicator Equations

A good introduction to singular perturbation theory are the books [33, 35, 55]. The results outlined in the following few paragraphs are well known, see e.g., [18, 26, 32, 39]. We compile them here in order to make this contribution self-consistent. Consider the *singularly perturbed* problem

$$\begin{aligned} \dot{x} &= f(x, y, a, \epsilon) \\ \epsilon\dot{y} &= g(x, y, a, \epsilon) \end{aligned} \tag{SPP}$$

where $x \in X$ and $y \in Y$, $a \in A \subseteq \mathbb{R}^p$ is the admissible space of parameters, and $\epsilon \in I \subseteq R$. Furthermore let $K \subseteq X \times Y$ be compact such that int K is simply connected. We are interested in the dynamics in the compact set K.

Suppose g has the following properties:

(i) There is a unique function $\varphi : X \times A \to Y$ such that $g(x, \varphi(x, a), a, 0) = 0$.

(ii) The Jacobian $J(x, a) = \dfrac{\partial g}{\partial y}[x, \varphi(x, a), a, 0]$ is uniformly hyperbolic on $A \times X$, i.e., there is a positive constant $\vartheta > 0$ such that absolute value of all eigenvalues of $J(x, a)$ is bounded below by ϑ for all $x \in X$ and all $a \in A$.

(iii) For fixed $a \in A$ we have $\{(x, \varphi(x, a)) | x \in X\} \cap K \neq \emptyset$.

Theorem 5. *Under the above hypotheses there are open sets $A' \subset A$, $I' \in I$ such that for all $(a,\epsilon) \in A' \times I'$ there is a unique integral manifold $\mathcal{M}_{a,\epsilon} = \{y = \psi(x,a,\epsilon) | x \in X\}$ with the following properties:*

(i) $\psi : X \times A' \times I' \mapsto Y$ *is continuously differentiable.*

(ii) ψ *satisfies uniformly on $X \times A'$:*

$$\lim_{\epsilon \to 0} \psi(x,a,\epsilon) = \varphi(x,a) \qquad \textit{and} \qquad \lim_{\epsilon \to 0} \frac{\partial \psi}{\partial x}[x,a,\epsilon] = \frac{\partial \varphi}{\partial x}[x,a] \,.$$

If $J(x,a)$ is stable on $X \times A$ then the long-time behavior of a trajectory passing through a point x_0 in a suitably small neighborhood ot the integral manifold $\mathcal{M}_{a,\epsilon}$ is determined by the dynamics on this manifold, i.e., by the differential equation $\dot{x} = f(x, \psi(x,a,\epsilon), a, \epsilon)$. Under these circumstances we introduce the notation

$$\begin{aligned} F(x,a) &\stackrel{\text{def}}{=} f(x, \varphi(x,a), a, 0)\,, \\ \Delta(x,a,\epsilon) &\stackrel{\text{def}}{=} f(x, \psi(x,a,\epsilon), a, \epsilon) - f(x, \varphi(x,a), a, 0)\,. \end{aligned}$$

The differential equation $\dot{x} = F(x,a)$ is known as the *degenerate system*. Property (ii) of ψ means that there is a continuous function $\theta(\epsilon)$ with $\theta(0) = 0$ such that $\|\psi(x,a,\epsilon) - \varphi(x,a)\|_\bullet < \theta(\epsilon)$. Here $\|\,.\,\|_\bullet$ denotes the C^1 norm, see, e.g. [27, p. 304]. If f is continuously differentiable with uniformly bounded derivatives on $X \times Y$ there is a continuous function $\theta_*(\epsilon)$ with $\theta_*(0) = 0$ such that $\|\Delta(x,a,\epsilon)\|_\bullet < \theta_*(\epsilon)$. In other words, the dynamics of trajectories near the integral manifold $\mathcal{M}_{a,\epsilon}$ is described by the differential equation

$$\dot{x} = F(x,a) + \Delta(x,a,\epsilon)$$

where $\Delta(x,a,\epsilon)$ is a regular perturbation of the degenerate system $\dot{x} = F(x,a)$. In such a case we will say the the singularly perturbed problem (SPP) *reduces to* the degenerate problem.

These facts from singular perturbation theory make precise in what sense our replicaton-translation system is related to replicator equations. We set $w_k = \omega_k/\epsilon$ and consider the limit $w_k \to \infty$, i.e, $\epsilon \to 0$ with constant ω_k and find the following very general correspondence:

Theorem 6. *The replication translation model* (CO) *reduces in the singular limit $w_i \to \infty$ to the second order replicator equation with interaction matrix $b_{ij} \stackrel{\text{def}}{=} a_{ij}\omega_j$.*

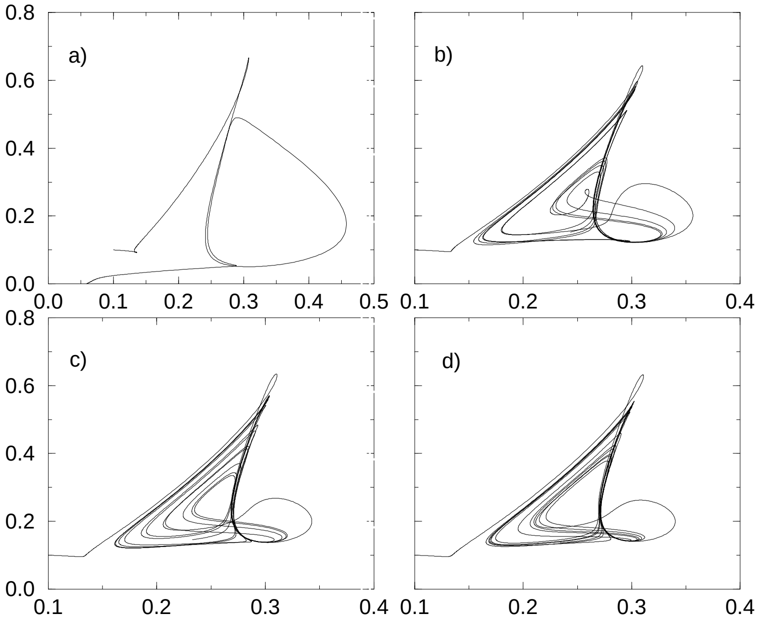

Figure 5: The close relations between ($\mathcal{R}$) and (RT) are perhaps best exemplified by strange attractors. Chaotic attractors have been found in three-species Lotka-Volterra equations [20, 57, 2, 1, 56]. Using Hofbauer's transformation [28] they can be translated to four-species second order replicator equations. A two-parameter family of strange attractors with interaction matrix

$$A(\mu,\nu)=\begin{pmatrix} 0 & 0.5-0.437\nu & -0.1+0.1\nu & 0.1+0.337\nu \\ 1.1-0.563\nu & 0 & -0.6+0.564\nu & -0.001\nu \\ -0.5-0.035\nu & 1-0.62\nu & 0 & 0.655\nu \\ 1.7+\mu-1.164\nu & -1-\mu+0.968\nu & -0.2+0.196\nu & 0 \end{pmatrix}$$

has been studied in detail [38]. The numerical examples shown here correspond to $\mu=-0.1$, $\nu=0$ and $w_k=w$ for all k.
The graphs show a two-dimensional projection of the x-coordinates. **a)** slow translation $w=0.5$, **b)** $w=2$, **c)** very fast translation $w=10$, and **d)** second order replicatior equation.

Proof. Let $w_k=\omega_k/\epsilon$ with $\omega_k,\epsilon>0$. With the notation we obtain the singular perturbation problem

$$\begin{aligned}\dot{x}_k &= x_k\left(\sum_i a_{ki}t_i-\sum_i x_i\sum_j a_{ij}t_j\right)\\ \epsilon\dot{t}_k &= \omega_k x_k - t_k\sum_i \omega_i x_i\end{aligned}$$

The fast time scale yields $t_k(x)=\dfrac{\omega_k x_k}{\sum_i \omega_i x_i}$ in the limit $\epsilon\to 0$. It is easy to see that this solution is stable for all x:

$$\frac{\partial \dot{t}_k}{\partial t_j}\Big|_{t(x)}=-\frac{1}{\epsilon}\delta_{kj}\sum_i \omega_i x_i.$$

and hence the singular perturbation problem reduces to

$$\dot{x}_k = \frac{1}{\sum_j \omega_j x_j} x_k \left[\sum_i a_{ki}\omega_i x_i - \sum_{i,j} a_{ij}\omega_j x_j x_i \right].$$

Using $b_{ij} = a_{ij} w_j$ and a change in velocity yields the second order replicator equation with interaction matrix B. ∎

Remark. A barycentric transformation shows that the replicator equation $(\mathcal{R})$ has qualitatively the same phase portraits since the constants ω_j are all positive.

Little can be said in general about the behavior for small translation rates. The extremal models discussed in sections 6 and 7 show that bifurcations leading away from "replicator like" behavior can occur for slow replication.

9. Replication, Translation, and Mutation

Mutation is an integral component of any evolving system. Since the effect of mutation is to introduce new, hitherto unknown species into the system it cannot be adequately modeled within the framework of differential equations if the number of *possible* species is very large. Nevertheless, it makes sense to consider the effect of mutations between the species in our reaction system. Mutation can be viewed as a perturbation that pushes the flow of the replicator equation away from the boundary into the interior of the state space [53]. Assuming both incorrect replication and incorrect translation we have to deal with the following reaction network

$$(A) + X_k + T_l \overset{Q_{km}a_{kl}}{\longrightarrow} I_k + I_m + T_l$$
$$(B) + I_k \overset{Q^T_{km}w_k}{\longrightarrow} I_k + T_m$$

The accuracy of the replication step is described by the probabilities Q_{mk} of forming a mutant I_m from a template I_k. Correspondingly, a translation product of type T_m is produced from a gene I_k with probability Q^T_{mk}. The kinetic equations read

$$\dot{x}_k = \sum_{j=1}^{n} Q_{kj} x_j \sum_{i=1}^{n} a_{ji} t_i - x_k \Phi$$
$$\dot{t}_k = \sum_{j=1}^{n} Q^T_{kj} w_j x_j - t_k \Phi^T$$

where the fluxes Φ and Φ^T are adjusted such that $\sum_j x_j = 1$ and $\sum_j t_j = 1$. The terms in the above equation can be rearranged in order to emphasize the perturbational nature of mutation in this model:

$$\begin{aligned} \dot{x}_k &= x_k \left[(At)_k - \langle x, At\rangle\right] + \sum_{j\neq k} \left[Q_{kj} x_j (At)_j - Q_{jk} x_k (At)_k\right] \\ \dot{t}_k &= w_k x_k - t_k \langle w, x\rangle + \sum_{j\neq k} \left[Q^T_{kj} w_j x_j - Q^T_{jk} w_k x_k\right] \end{aligned} \qquad (RTM)$$

For sake of definiteness we assume that the mutation matrix Q is of the form

$$Q = \begin{pmatrix} 1-(n-1)\epsilon & \epsilon & \dots & \epsilon \\ \epsilon & 1-(n-1)\epsilon & \dots & \epsilon \\ \vdots & \vdots & & \vdots \\ \epsilon & \epsilon & \dots & 1-(n-1)\epsilon \end{pmatrix}$$

An analogous representation is assumed for Q^T, with a translation error rate η replacing the mutation rate ϵ. Then (RTM) simplifies to

$$\begin{array}{rcccl} \dot{x}_k &=& x_k \left[(At)_k - \langle x, At\rangle\right] &+& \epsilon \sum_{j\neq k} \left[x_j (At)_j - x_k (At)_k\right] \\ \dot{t}_k &=& w_k x_k - t_k \langle w, x\rangle &+& \eta \sum_{j\neq k} \left[w_j x_j - w_k x_k\right] \end{array}$$

Let us use the notation $\xi = (x,t) \in S_n \oplus S_n \stackrel{\text{def}}{=} \mathcal{S}$. Then the replication-translation model with mutation takes the form

$$\dot{\xi} = \mathcal{RT}(\xi) + \mathcal{M}(\xi; \epsilon, \eta)$$

where $\mathcal{RT}$ is the error-free replication-translation part and $\mathcal{M}$ describes the effects of mutation. For the full model (RTM) even the computation of the equilibrium points can be done only numerically except for a few special cases discussed below. The perturbation methods described in [53] are applicable here.

First we need some notation for the subsimplices that constitute the boundary of the state space $\mathcal{S}$: Let $\bar{F}_K \subset S_n$ be the subsimplices on which $x_k = 0$ for all $k \in K$, where K is an index set which is neither $\{1, \dots, n\}$ nor empty. The relative interior of the sub-simplex $\bar{F}_K$ will be denoted by F_K.

Definition 1. *A vector field $\mathcal{M}(\xi; \epsilon, \eta)$ on $\mathcal{S}$ is a* mutation field *if it has the following properties:*

(i) $\mathcal{M} = (\mathcal{M}^x, \mathcal{M}^t)$ *is continuously differentiable and $\|\mathcal{M}\|_\bullet$ is bounded on $\mathcal{S} \times I \times J$, where I and J are non-empty intervals $I, J \subset \mathbb{R}_0^+$.*

(ii) $\mathcal{M}(\xi; 0, 0) = 0$ *for all* $\xi \in \mathcal{S}$.

(iii) $\mathcal{M}^x_k(\xi; \epsilon, \eta) \geq 0$ *if* $x_k = 0$ *and* $\mathcal{M}^t_k(\xi; \epsilon, \eta) \geq 0$ *if* $t_k = 0$ *for all* $(\epsilon, \eta) \in (I \times J) \setminus \{(0,0)\}$.

We say that $\mathcal{M}$ is a strong mutation field *if the weak inequalities in condition (iii) are replaced by strong inequalities.*

Lemma 3. *(i) $\bar{F}_K \oplus \bar{F}_K$ is invariant under the flow of (RT). (ii) $\bar{F}_K \oplus S_n$ is invariant under the flow of (RTM) with $\epsilon = 0$ and arbitrary η.*

Proof. (i) Let $k \in K$. From $x_k = t_k = 0$ we infer immediately that $\dot{x}_k = \dot{t}_k = 0$ as well, thus $\bar{F}_{\{k\}} \times \bar{F}_{\{k\}}$ is invariant. Repeating this argument for all $k \in K$ implies the proposition.
(ii) If $\epsilon = 0$ and $\eta > 0$ we find $\dot{t}_k > 0$ if $t_k = 0$ and $x_k = 0 \implies \dot{x}_k = 0$. Thus $\bar{F}_K \times S_n$ is invariant.

∎

A direct analogue of the *rest-point migration theorem* which is proven in [53] for selection-mutation equations can be obtained for (RTM), and even more general versions of models of erroneous replication and translation. The proof of the following result parallels the selection-mutation version line by line, therefore we omit the details here.

Theorem 7. *Let $\hat{\xi} \in \bar{F}_K \times \bar{F}_K$ be a rest point of (RT), let $\mathcal{M}(\xi; \epsilon, \eta)$ be a strong mutation field. Then there is an $\epsilon_0 > 0$ such that for all $0 < \epsilon \leq \epsilon_0$ and all $0 \leq \eta \leq \epsilon_0$ the following statements are true:*

(i) If the rest point $\hat{\xi}$ is regular then $\xi(\epsilon) \in \operatorname{int} \mathcal{S}$ if and only if the transversal eigenspace $E_T(\hat{\xi})$ is stable, i.e., if $\hat{\xi}$ is saturated.

(ii) If the transversal eigenspace $E_T(\hat{\xi})$ has at least one positive eigenvalue, say $\lambda_l > 0$, then all fixed points $\xi_j(\epsilon)$ derived from $\hat{\xi}$ lie outside the state space $\mathcal{S}$.

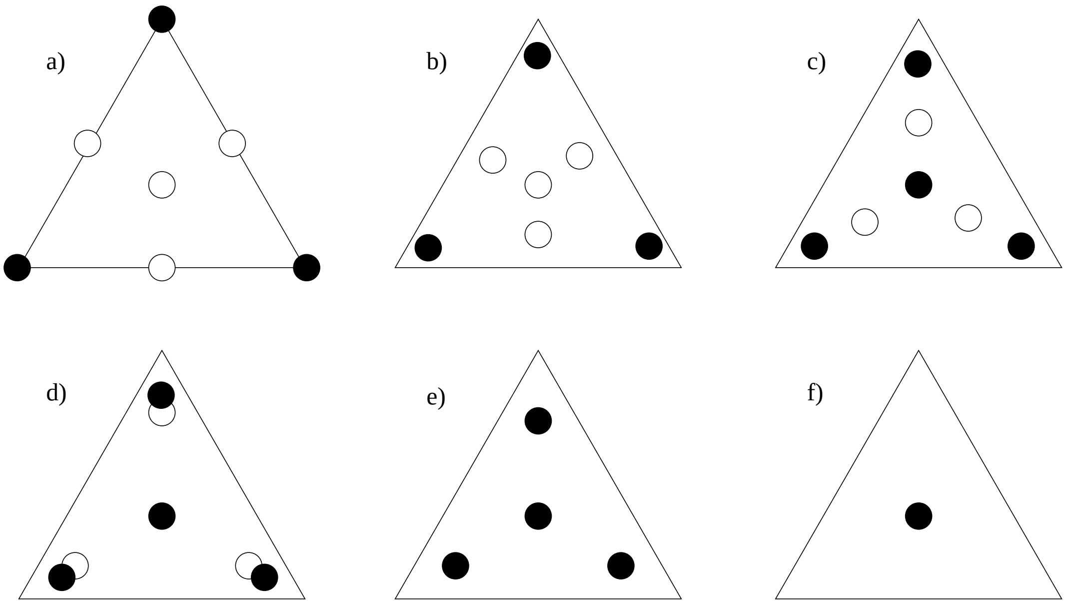

Figure 6: The development of the fixed points of the competitive model for various values of ϵ, where $\eta = 0$ for $n = 3$: a) no mutation; b) subcritical values for ϵ^x; c)–f) supercritical value for ϵ^x; $\bullet$:Sink; $\circ$: Saddle

The consequences of the rest point migration theorems are dramatic: Mutational perturbations drive all non-saturated rest points into the non-physical exterior of the state space. The dynamics of the systems are thus simplified due to the reduction in the number of the fixed points. This is the same behavior as has been observed for the selection mutation models in [53]. Figure 6 shows an exceptional case: all fixed points are saturated in this model and are therefore pushed into the interior of the state space. The hypercyclic model discussed in section 7, on the other hand, is left with a unique rest point for small $\epsilon > 0$.

Non-perturbative results can be obtained only for very simple interaction matrices. This matches the situation for selection-mutation equations discussed in [51]. A few results can be obtained for circulant interaction matrices A and equal translation rates $w_k = w$ for all k.

Lemma 4. *Suppose $A \neq 0$ is circulant and all translation rates are equal to $w > 0$. Then $\hat{\xi} = (\hat{x}, \hat{t}) = \frac{1}{n}(\mathbf{1}, \mathbf{1})$ is the unique interior equilibrium of (RTM).*

Proof. Since A is circulant, $(A, \hat{t})_j = \alpha \; \forall j$. Thus $\langle \hat{x}, A\hat{t} \rangle = \alpha \langle \hat{x}, \mathbf{1} \rangle = \alpha$ and $\langle w, \hat{x} \rangle = w$. Substituting this into (RTM) immediately yields the lemma. ∎

Let us now consider two special cases in more detail. The symmetric competitive model has interaction matrix $A = kI$. The differential equation (RTM) reduces to

$$\begin{aligned}
\dot{x}_k &= k \cdot x_k \left[t_k - \langle x, t \rangle \right] + \epsilon\, k \left[-(n-1) x_k t_k + \sum_{j \neq k} x_j t_j \right] \\
\dot{t}_k &= w(x_k - t_k) + \eta \left[-(n-1) + w x_k \right]
\end{aligned}$$

The eigenvalues at the interior equilibrium $\frac{1}{n}(\mathbf{1}, \mathbf{1})$ are readily computed. For the two external eigenvalues we find $\Lambda_{0:x} = -k/n$ and $\Lambda_{0:t} = -w$. For the remaining eigenvalues one finds

$$\Lambda_{j\pm} = \frac{-k\epsilon - w}{2} \pm \frac{1}{2} \sqrt{(n - k\epsilon)^2 + 4 \frac{kw}{n} (1 - n\epsilon)(1 - n\eta)}$$

The critical values of ϵ and η for which the interior fixed point becomes stable are readily obtained from the above expression.

$$\epsilon_{\text{crit}} = \frac{n\eta - 1}{n(n\eta - 2)} \qquad \text{and} \qquad \eta_{\text{crit}} = \frac{2n\epsilon - 1}{n(n\epsilon - 1)}.$$

The stability of the unique interior rest point $\frac{1}{n}(\mathbf{1}, \mathbf{1})$ can be determined also for the symmetric cooperation model with interaction matrix $a_{kj} = \delta_{i,j-1}$. The Jacobian has the same external eigenvalues as in the case of the symmetric competition model discussed above. For the physically relevant eigenvalue we find

$$\Lambda_{j\pm} = -\frac{k\epsilon + w}{2} \pm \frac{1}{2}\sqrt{(w - k\epsilon)^2 + 4\frac{kw}{n}(1 - n\epsilon)(1 - n\eta)\exp(-2\pi\imath\frac{j}{n})}$$

The critical values of the mutation rate can be computed from the above equation as solutions of a cubic equation. In the case $n = 3$ the analytical solution is tractable but too messy to be printed here. With the help of `Mathematica` we could show that if $\frac{1}{n}(\mathbf{1}, \mathbf{1})$ is a stable equilibrium for $\epsilon = 0$, then it remains stable for arbitrary values of ϵ. For higher dimensions numerical studies show that the interior rest point becomes stable for large enough mutation rates.

The behavior of (RTM) is in general very similar to the behavior of a second order replicator network under the influence of mutation: Increasing mutation rates force the flow towards the "middle" of the state space, and very high mutation rates lead yield a globally stable interior equilibrium [50, 51].

10. Discussion

In this contribution we have compared the dynamics of the most simple replication-translation model (RT) and the dynamics of second order replicator equations ($\mathcal{R}$). The version of (RT) considered here is the simplest extension of the replicator equation model that separates the replicating entities (genomes) from the catalysts mediating the replication process. We find that the behavior of such a system is very closely related to the dynamics of an autocatalyic replication process which does not involve translation. More precisely:

- The replication-translation model with rate constants a_{ij} for the replication of a genome of type i using the catalytic activity of translation product j and with a translation rate w_j for the translation of a genome of type j corresponds to a second order replicator equation ($\mathcal{R}$) with interaction coefficients $b_{ij} = a_{ij}w_j$. We have shown that the replicator equation with these interaction coefficients is in fact the singular perturbation limit of (RT) for fast translation.
- The dynamics of ($\mathcal{R}$) and (RT) are also closely related for small translation rates. In particular, the there is an interior rest point of (RT) if and only if the corresponding replicator

equation has an interior equilibrium. Furthermore, a rest point of (RT) is saturated if and only if the corresponding equilibrium of ($\mathcal{R}$) is saturated.

- The dynamics of a two-species system is the same in both models.
- Mutations affect both models in qualitatively the same way.

Not surprisingly, non-generic features of second-order replicator equations are not shared by the replication-translation model. For instance, we find super-critical Hopf-bifurcation in three-species models which do not occur in second order replicator equations. It is interesting to note in this context that a monotonic distortion of the linear-response functions $(Ax)_k$ in a the second order replicator equation can have the same effect [47].

Of course, our model of translation is unrealistically simple: it does not consider the formation of a complicated translational apparatus such as a ribosome, nor does it contain any regulatory mechanism. But then, we have never claimed to model a "realistic early translation mechanism". The purpose of this contribution is to show that networks that are based on replication can be (roughly) described by replicator equations even if the replicating entities, in our case the genotypes together with their translation products, have non-trivial internal structure. A similar question was raised in [48, 49] for quite different variations of the replicator theme.

This investigation is thus only a first step towards a much more ambitious goal. Given a chemical reaction network can we devise a coarse grained description in which the players are collections of chemical species, such that the dynamics of the original reaction network is well simulated by a dynamics on the coarse grained level?

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