

Structural Perturbations
of
Autocatalytic Reaction Networks

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... Für Heike

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Für Mutzi: ... schnurrrrrrrrr ...

ONE UNIVERSE, ON A ZEBRA CROSSING, IS CAUGHT
FOR AN INSTANT, BLINKING LIKE A RABBIT, IN THE
HEADLAMPS OF A MOTOR-VEHICLE IN WHICH AN EN-
TIRELY ALIEN AND CONTRADICTORY CONTINUUM IS
TO BE FOUND.

Salman Rushdi, *The Satanic Verses*

Abstract

Replicators are entities that are copied during interactions with other entities. Replicator equations, or Lotka-Volterra equations are commonly used to describe the population dynamics of replicators. In these models, replicators are usually assumed to be objects without internal structure, and the copying process is subsumed into a single reaction event. Because it is not at all clear that such a simplified mechanism can cover the qualitative behavior of the highly complicated interactions of replication, structural perturbations of the replicator equation are investigated.

Because of the rapidly increasing complexity of differential equations that result from more complicated mechanisms, singular perturbation theory is used to investigate the limits of fast intermediate steps. So two different models of replication with intermediates are used in order to avoid the highly improbable third order step which is needed to describe a catalyzed replication of a macromolecule. (i) A model that reduces to a replicator model with inhomogeneous response function, and a (ii) Michealis Menten mechanism that accounts for the stepwise incorporation of the monomers in the course of replication. Replication however, as it is known today, requires the aid of highly specialized proteins that not only account for the necessary speed, but particularly for the accuracy of the duplication. Thus a simple model of replication with translation is investigated.

The experimental setup that leads to constant organization is very trying, whereas the much simpler CSTR does not allow for a successful mathematical treatment. So the close relationship of the CSTR and Constant Organization is analyzed in the limit of small flux rates.

Since ODEs are deterministic by default, an attempt is made to introduce new species by assigning random interaction constants. Thus, a stochastic mutation model is set up and treated both analytically and numerically. It is demonstrated that permanence is a rare phenomena for newly introduced species, but arises from the long-time evolution of catalytic networks.

Zusammenfassung

Replikatoren werden im Verlauf von Wechselwirkungen mit anderen Einheiten kopiert. Zur Beschreibung dieser Vorgänge werden Replikatorgleichungen bzw. Lotka-Volterra Gleichungen benützt. In diesen Modellen werden die Replikatoren meist ohne interne Strukturen angenommen. Ob aber diese Annahmen tatsächlich den komplizierten Prozessen gerecht werden können, ist unklar. Aus diesem Grund werden strukturelle Störungen der Replikatorgleichung untersucht.

Da die aus detaillierteren Mechanismen abgeleiteten Differentialgleichungen sehr rasch an Komplexität zunehmen, wurde singuläre Störungstheorie zur Untersuchung dieser Modelle herangezogen.

Zwei verschiedene Modelle von Replikation mit Zwischenprodukten, die zur Auflösung der Reaktionen dritter Ordnung eingeführt worden sind, wurden analysiert. (i) Ein Beispiel, dessen singulärer Limit zu einer Replikatorgleichung mit inhomogener Responsefunktion führt, und (ii) ein Michaelis-Menten-artiges Modell. Dieses ist gut geeignet, um den schrittweisen Verbrauch an Monomeren zu beschreiben. Ebenso wurde ein vereinfachtes Modell von Replikation mit Translation untersucht.

Um eine Replikatorgleichung experimentell umzusetzen, muß ein enormer, fast unmöglicher Aufwand an Regel- und Meßeinrichtungen gemacht werden, während der experimentell sehr einfache Flußreaktor mathematisch schwierigere Gleichungen liefert. Daher wurde eine Untersuchung über den Zusammenhang von Evolutions- und Flußreaktor im Limit kleiner Flüsse durchgeführt.

Da es im Rahmen der Replikatorgleichung nicht möglich ist, neue Species einzuführen, wurde ein stochastisches Modell von Mutation und Immigration untersucht, wobei sich herausstellte, daß Permanenz für neueingeführte Spezies sehr unwahrscheinlich ist, während sie nach genügend langer Relaxationszeit sehr häufig wird.

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1. Introduction

Snce upon a time, when the earth was young, she was very, very hot. Afterwards, it became somewhat cooler, and it rained a lot. If someone had observed some wet, marshy patches among the hits of meteors, he would have been taken aback by the most fascinating process ever found:

The Origin of Life.

Only a short time later, Darwin [14] inspired innumerable scientists to publish about that topic.

1.1. The RNA world

1.1.1. Chicken or Egg ?

The most fundamental distinction in biology is between nucleic acids, with their role as carriers of information, and proteins, which generate the phenotype. In existing organisms, nucleic acids and proteins mutually presume each other. The former, owing to their template activity, store the heritable information: the latter, by the enzymatic activity, read and express this information. Which came first, nucleic acids or proteins? There are three possible answers:

- (i) *nucleic acids*
- (ii) *proteins*
- (iii) *neither*: they coevolved.

Nowadays, most scientists all over the world agree that in the early stages of life nucleic acids accounted both for the chicken and the egg.

1.1.2. RNA as an Enzyme

First one may consider why proteins can act as enzymes. An enzyme has a well-determined three-dimensional structure of chemical groups that, in most cases, arises automatically from the primary structure. Substrates of that enzyme are bound by chemical groups on the surface. This means that the reactants will be kept in close proximity, and hence experience a much higher local concentration of each other than in solution. This, by itself increases the rate of the reaction.

Enzymes speed up reactions in a second way as well. During a chemical reaction, an intermediate structure of high energy is formed, the so-called transition state complex. The higher this activation energy, the slower the reaction. As Linus Pauling suggested fifty years ago, enzymes decrease the activation energy by binding to and distorting the reactants. Further, enzymes are not rigid structures: By torsion and bending, they may guide the reaction. The effect of these various processes can be to increase the reaction rate by more than a millionfold. After the reaction is complete, the products leave the enzyme, and the latter, having completed its catalytic cycle, is ready to start the next one.

What of nucleic acids? RNA often forms well-defined, flexible, three dimensional structures, presenting various functional groups on its surface. In principle, therefore, one would expect some RNA molecules to act as enzymes.

1.2. Early RNA's

The general idea that, in the development of life on the earth, evolution based on RNA replication preceded the appearance of protein synthesis was first proposed more than twenty years ago [110, 13, 72].

It was suggested that catalysis made entirely of RNA are likely to have been important at this early stage in the origins of life, but the possibility that RNA catalysis might be present in contemporary organisms was overlooked. The unanticipated

discovery of ribozymes [64, 38] initiated extensive discussion of the role of RNA in the origins of life [73, 87, 65] and led to the coining of the phrase “*the RNA world*” [35].

Since it is not at all clear from the beginning what the term RNA world means, it seems convenient to attempt a rather restrictive definition. All RNA world hypotheses include three basic assumptions:

- (i) At some time in the evolution of life, genetic continuity was assured by the replication of RNA.
- (ii) Watson-Crick base-pairing was the key to replication;
- (iii) genetically encoded proteins were not involved as catalysts.

RNA world hypotheses differ in what they assume about life that may have preceded the RNA world, about the metabolic complexity of the RNA world, and about the role of low-molecular-weight cofactors, possibly including polypeptides, in the chemistry of the RNA world.

It should be emphasized that the existence of an RNA world as a precursor of our DNA/protein world is a hypothesis. Still, it is a very attractive hypothesis and there is support from the results of experiments that it has inspired. The demonstration that the peptide-bond-forming step of protein synthesis is catalyzed by largely protein-free ribosomal RNA is particularly striking [70].

1.3. Ribozymes

RNA is a particularly versatile molecule. Its many functions as messenger-RNA's, transfer-RNA's, ribosomal RNA's, \pm -strands as genome of viruses were enlarged by catalytic activity. Various types of ribozymes have been found [99]:

- Introns: There are group I and group II introns
- Hammerhead Ribozymes: very small ribozymes that were found in plant-viroids.

- Hepatitis Delta Virus (HDV).
- RNaseP: The RNA alone can do the catalytic part.
- Hairpin Ribozyme.

RNA can do quite a lot of different chemical reactions. Because of modern techniques, such as reverse transcriptase, PCR or 3SR, it has become possible to train RNA molecules for various purposes. see figure 1. These *selex*-experiments perform accelerated evolution, for they select the fitting molecules out of a pool, amplify them, and create a new pool by some means of diversification. After several cycles a properly “trained” target is likely to be found.

1.4. Template Chemistry

In order to find out whether self-sustaining chemical systems can have developed, and how, a variety of self-replicating chemical systems have been constructed and investigated experimentally in the past 25 years since Spiegelman’s [93] *in vitro* serial transfer experiments on Q β . The Q β system was subject to extensive studies in Manfred Eigen’s lab in Göttingen [8, 9, 10, 6]. Recently there has been quite some progress on artificial self-replicating molecules by Orgel [71], Rebek [91, 27, 75] and von Kiedrowski [106]. The notion of a *replicator* — originally introduced by Richard Dawkins [15] and now used in theoretical biology for “*an entity that passes on its structure largely intact in successive replications*” — is a useful characterization of these chemical systems.

In parallel to the advances in *template chemistry* a theory of molecular evolution has been developed, based on a series of pioneering papers by Manfred Eigen and Peter Schuster [18, 22, 23, 24]. Replication can be expressed formally as an auto-catalytic chemical reaction of the form



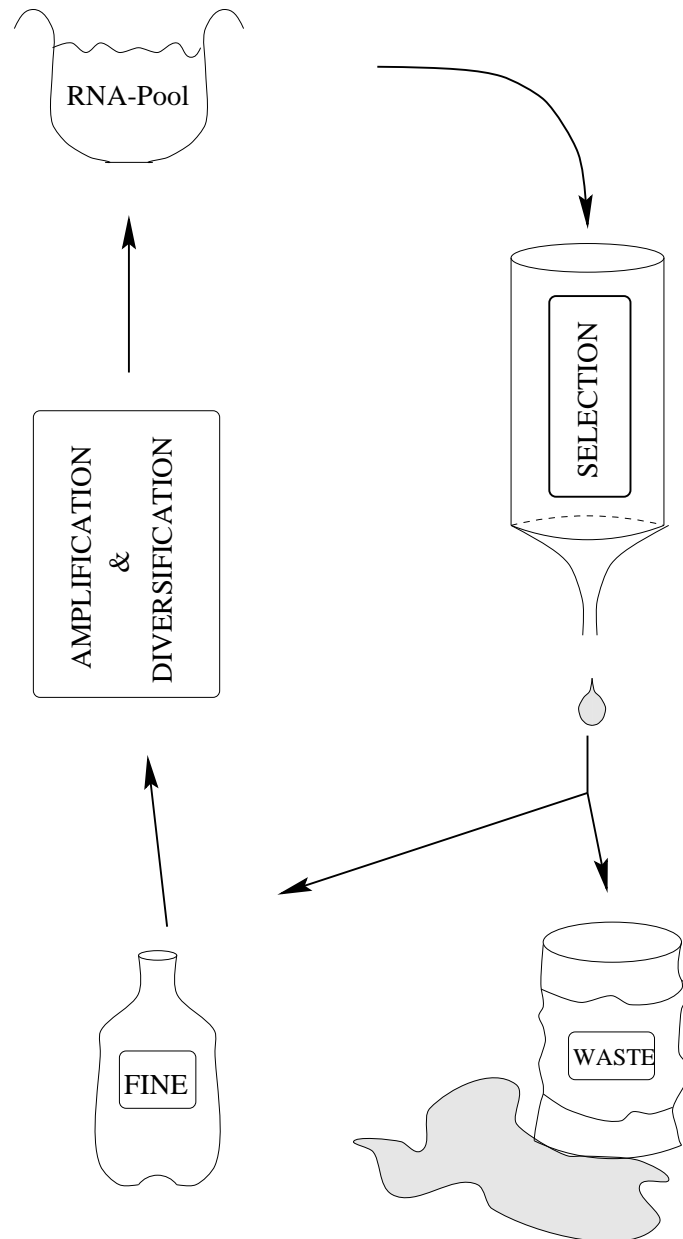
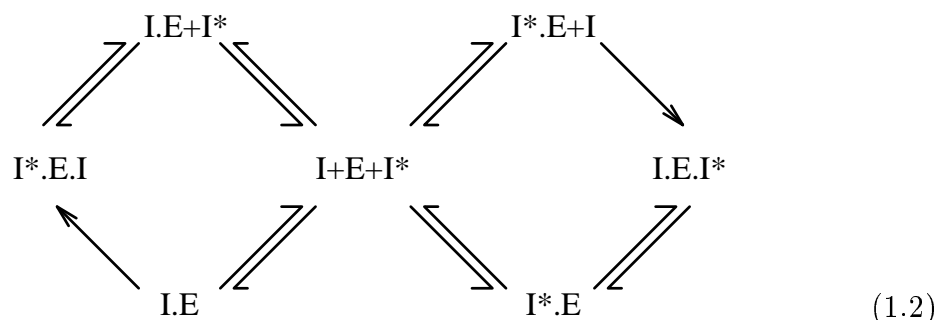


Figure 1: A schematic representation of a selex experiment. A (random) pool of RNA-molecules passes a affinity chromatographic column. The “fittest” of them are bound, while the rest passes and is thrown away. Afterwards the good ones are washed off the column and collected. After an amplification and diversification step (e.g. reverse transcriptase and PCR), the new pool undergoes the next round of selection, and so on . . . , until the required properties are found.

The collection of monomers necessary for building up the replicating species are subsumed under the symbol (A), and (W) stands for all waste produced by the

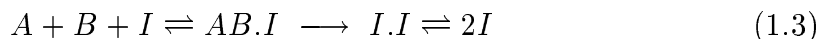
copy reaction.

Polynucleotide replication (both *in vivo* and *in vitro*) is an enormously complicated multi-step process. Commonly it involves two catalysts: the polynucleotide template and a replicase, which in present day biochemistry is a protein enzyme. In the context of an RNA world one may well speculate about a ribozyme replicase and hence neglect the problem of a translation apparatus. Extensive kinetic studies [93, 8, 9, 10] have shown that the following reaction scheme allows for a quantitative description of the replication dynamics:

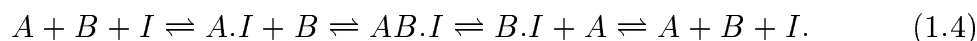


I^* denotes the complementary sequence to I . Binding and dissociation of the polynucleotides are reversible, while the polymerization process is an irreversible step. This model is still far removed from an elementary step mechanism, which would include, for instance, the kinetics of chain elongation by single nucleotides. On the other hand (1.2) is much more involved than the simple autocatalytic network (1.1). It is by no means clear therefore that the replicator equation is capable of capturing properties of the realistic reaction mechanism (1.2).

Other reaction mechanisms have been used to model the behavior of the artificial replicators of Rebek and von Kiedrowski [91, 105, 106]. All these models treat the building blocks explicitly, assuming



as the basic reaction scheme. More detailed descriptions resolve the first reversible step into successive bimolecular steps, e.g.,



It has been shown [106] that the mechanism (1.3) leads to approximately parabolic growth in wide range of conditions on rate constants and reactant concentrations. This is to say that the concentration x of the replicator fulfills $\dot{x} \propto \sqrt{x}$.

1.5. Replication as an Overall Reaction

Assume we are given a network of simple chemical reactions the dynamics of which is well known to us. Now we replace the elementary steps in this network by more realistic, that is more detailed, reaction mechanisms — thereby introducing additional intermediate species. What can we say about the dynamics of the extended reaction network?

We can view these additional reactions as perturbations of the *structure* of the reaction network; in general their effects on the dynamics can be huge. An important question is hence the following: *Under which conditions is a structural perturbation small?* A more precise formulation of this question might be: Under what conditions on the structural perturbation (in terms of both reaction mechanism and associated rate constants) does the time evolution of the original species remain essentially unchanged?

These questions have been asked recently by Fontana and Buss [29] at the level of their constructive dynamics, though no attempts have been made to deal with this problem in the context of kinetic equations. Within the limited scope of autocatalytic reaction networks this ansatz is not hopeless. The reason for this restriction is twofold:

- (1) There is a well developed body of theory for the structurally unperturbed systems: they are replicator equations [56].
- (2) Replicator equations have been used as the paradigm for catalytic networks in prebiotic chemistry [25], while the actual reaction mechanisms are known to be much more involved [7]. The applicability of replicator equations and the limits of their validity are therefore an important problem in its own right.

1.6. Structural Perturbations

The term *structural perturbation* can be defined in various different ways:

(i) By the term *structural stability*, which matches its formal definition.

Definition. [47] Let $f \in C^m(E)$, $m \in \mathbb{N}$ and $\epsilon > 0$. We say $g \in C^m(E)$ lies in an ϵ -neighborhood of f with respect to a compact set $K \subset E$, if for all $x \in K$ holds

$$\min\{\|f(x) - g(x)\|, \|\partial(f - g)(x)\|\} < \epsilon. \quad (1.5)$$

Definition. Two vector fields f and g are *topologically equivalent* if there exists a homeomorphism h which takes the orbits $\phi_t^f(x)$ of f to orbits $\phi_t^g(x)$ of g , preserving the senses but not necessarily parameterization by time.

Definition. A vectorfield f is called *structurally stable* if there is an $\epsilon > 0$ such that all C^1 functions g in an ϵ -neighborhood of f are topologically equivalent to f . For gradient systems there is an easy to verify sufficient condition for structural stability:

Theorem 1. *Gradient systems for which all fixed points are hyperbolic and all intersections of stable and unstable manifolds are transversal, are structurally stable.* It is an unsolved problem whether the union of all structurally stable flows is generic in arbitrary dimensions. For planar flows on compact manifolds the problem is solved by the following

Theorem 2. *(Peixoto) Let M be a compact two-dimensional manifold. (If M has a boundary then assume the flux transverse.) A C^r vector field on M is structurally stable iff*

- a) *the number of fixed points and periodic orbits is finite and they are all hyperbolic;*
- b) *there are no orbits connecting two saddle points;*
- c) *The set of nonwandering points consists of fixed points and periodic orbits;*

Moreover, if m is orientable, the set of structurally stable vector fields is generic, i.e. open dense in $C^r(M)$.

(ii) Beside this very restrictive definition often one is interested, whether large scale dynamical systems, consisting of many connected subsystems, remain stable if one or more connections are broken or new ones are generated [89]. So if for the beginning, no “outside world” effects are taken into account, it is convenient to consider the dynamical system

$$\dot{x} = Ax, \tag{1.6}$$

which may be represented by a directed graph, a *digraph*, see figure 2.

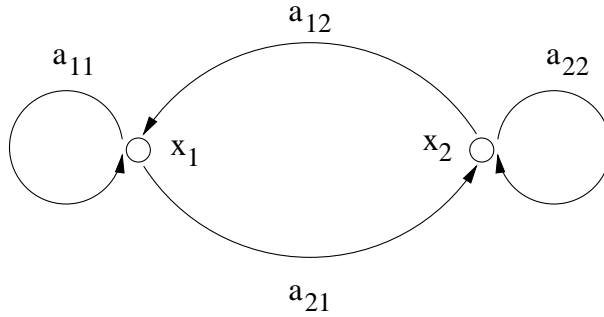


Figure 2: Full Digraph of a matrix A with two interacting subsystems.

To concentrate strictly on the *structure* of the system, we ignore the actual values of the elements of the matrix A , but replace them by the so called *interconnection* or *adjacency matrix* E , where

$$e_{ij} = \begin{cases} 1 & \text{if } x_j \text{ “acts” on } x_i \\ 0 & \text{otherwise.} \end{cases}$$

It is quite common in dynamic models of physical, social, and biological processes that agents are disconnected and again connected in various ways during the process. For example, a predator in a multispecies community stops preying on another species, causing a line removal in the corresponding digraph. This is a *structural perturbation* of the system and it is described by another adjacency

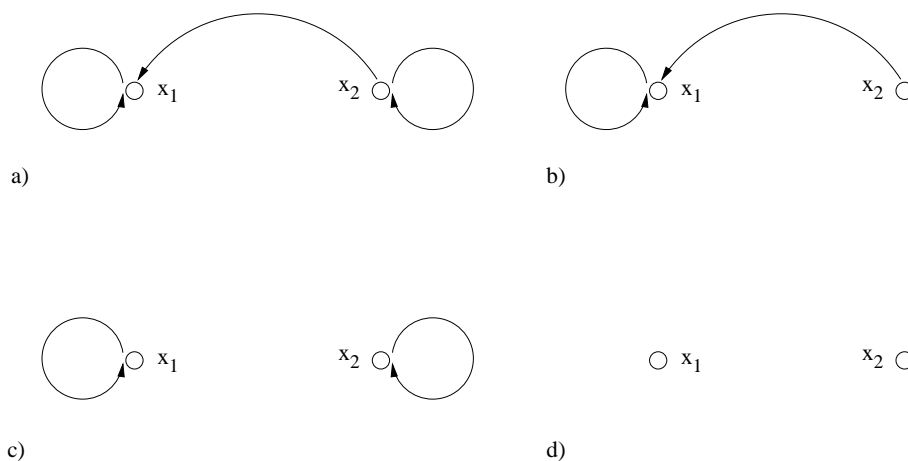


Figure 3: Structural perturbations of a simple 2 by 2 system by removal of interactions from the adjacency matrix.

The examples shown are **a)** $E_1 = \begin{pmatrix} 1 & 1 \\ 0 & 1 \end{pmatrix}$ **b)** $E_2 = \begin{pmatrix} 1 & 1 \\ 0 & 0 \end{pmatrix}$ **c)** $E_3 = \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix}$
d) $E_4 = \begin{pmatrix} 0 & 0 \\ 0 & 0 \end{pmatrix}$.

matrix where the corresponding unit element is changed to zero. (see, for example figure 3.)

(iii) Furthermore, structural perturbations can be defined in the sense of enriching (enlarging) equations of dynamical systems by replacing simpler mechanisms by more sophisticated ones, e.g., by considering the elementary steps of an overall mechanism. For such purposes, singular perturbation theory may be a means to deal with the almost certainly uncopable differential equations that arise from such refinement of mechanisms.

1.7. Differential Equations for Molecular Evolution

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, \dots, I_n . Very little is known on this topic in terms of the realistic replication

mechanisms described above. On the other hand there is a well developed theory for the most simple reaction scheme



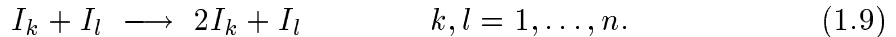
namely the theory of the *molecular quasispecies* [18, 66, 21]. Here the enzyme E is part of the environment provided by the experimentalist. Without going into details it can be remarked here that this framework has been very successful in describing the evolution of RNA viruses.

Self-replication on molecular level is the crucial “invention” at the origin of life. Nowadays, most experts agree that RNA or an RNA precursor was the first replicator in the history of life [20, 109], as pointed out in the earlier sections. In a model of prebiotic evolution we have to account for the production of the enzyme E that makes the replication possible. Assuming that E is a protein enzyme we have to add a translation mechanism with the over-all effect



to the model of the replication step. Of course one might envision a more sophisticated mechanism requiring additional catalysts (enzymes and/or polynucleotides) as precursor of present day ribosomes.

A translation step is not necessary if we assume a pure *RNA world* in which the task of the replicase E is performed by a ribozyme I' . In fact, recent discoveries of catalytically active RNAs [11, 12, 37, 108] make this assumption very appealing. In its most condensed form the logics of an RNA world is captured in the *autocatalytic reaction network*



A wealth of knowledge on this model has accumulated over the last two decades beginning with the theory of the hypercycle [22, 23, 25]. The dynamical system associated with (1.9) is now termed *replicator equation* [80]

$$\dot{x}_k = x_k \left(\sum_{j=1}^n a_{kj} x_j - \sum_{i,j} a_{ij} x_i x_j \right). \quad (1.10)$$

It is based on the chemical reaction scheme (1.9) and the assumption of *constant organization*, as described in chapter 3; the variables x_k refer to the relative concentrations of the species I_k . 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 [48]), economics, or laser physics. Their properties have been the subject of hundreds of research papers by many research groups, most prominently among them Schuster, Sigmund, Hofbauer and co-workers in Vienna. The results of the first decade of investigation are compiled in the book [56].

Replication schemes without specific catalyst, i.e., models of the form (1.3) could be used to model an even earlier stage of prebiotic evolution. In order to construct a self-sufficient system we have to assume a mechanism for producing the building blocks A , B used in the replication step. They could either be produced by external production pathways or they require catalytic assistance by the replicating polynucleotides for their formation. In the latter case (1.3) is augmented by reactions of the form



or more sophisticated versions thereof.

1.8. More Realistic Autocatalytic Networks

Very little is known on the dynamics of the more realistic replication mechanisms. The full RNA replication mechanism (1.2) has been studied in some detail for a single species [33]. A numerical study on competition in this system assuming constant enzyme concentration has been published recently by Biebricher and co-workers [7]. A number of systematic simplifications of this model have been mentioned in the literature, though non of them has been studied for more than a few simple special cases. In figure 4 their mutual relationships are shown.

Replacing the enzyme E by a ribozyme I' leads to the RNA world version of (1.2), which has not been considered at all so far. This model can be simplified further in two ways:

- (i) Neglecting the fact that nucleic acids exhibit complementary replication yields “model I” in [26]. It allows to study the effects of a Michaelis-Menten type kinetic for the formation of enzyme-template complexes. A few results on a hypercycle with this replication scheme are known [26].
- (ii) Ignoring the binding and dissociation steps and hence replacing each cycle in (1.2) by a single irreversible copy reaction of the form $I + I' \rightarrow I + I^* + I'$ extracts the effect of the complementary logic of the polynucleotide replication. This model has already been studied in some detail [96].

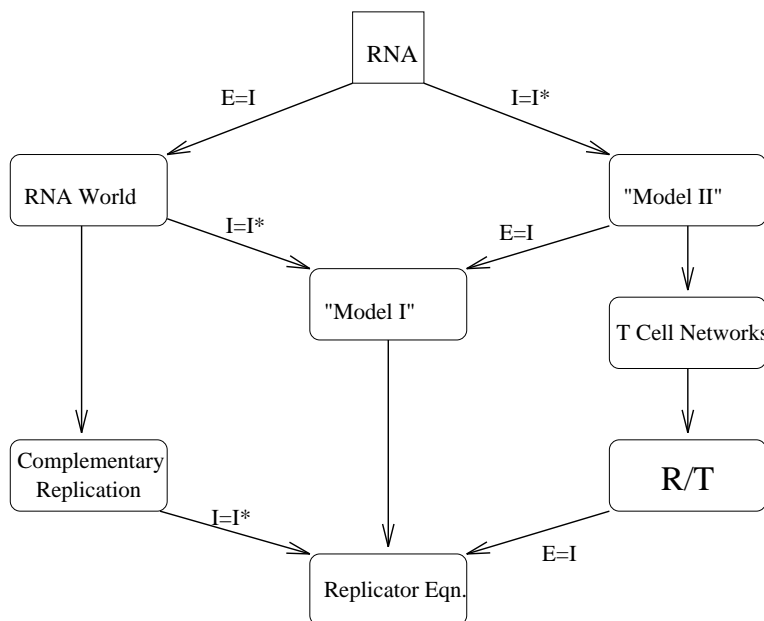
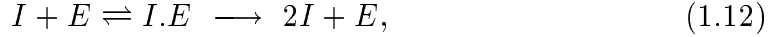


Figure 4: Models for polynucleotide replications.

Neglecting complementarity from the beginning leads to “model II” of reference [26]. It has been studied numerically for the special case of the hypercycle using a simple translation step. It reduces to “model I” if the enzyme E is replaced by

a ribozyme. A simplification of “model II” by neglecting one of the two enzyme-polynucleotide complexes, yielding



has received considerable interest in theoretical immunology as a model for T-cell growth under stimulation by anti-gen presenting cells [17, 67]. In this context it may be remarked that B-cell networks can as well be modeled by replicator equations [97] of the form

$$\dot{x}_k = x_k \left[f_k(x) - \sum_{j=1}^n x_j f_j(x) \right] \quad (1.13)$$

where f is non-linear response function instead of the linear interaction model (1.10).

Neglecting also the second complex formation step we arrive at the reaction scheme



which captures the basic separation of replicating material and enzymes. [41].

A closely related replication scheme has been found experimentally for the bacteriophage Q β infecting *E. coli*. This system constitutes the first example of a realistic hypercycle [19].

Even less is known about competition of replicators obeying scheme (1.3). An analogue of (1.10) for parabolically growing species has been investigated in some detail by Szatmary [100].

1.9. Summary

The *RNA-world*-assumption is a widely accepted model for the transition from chemical to biological evolution. It has been shown in a great variety of experiments that RNA-molecules are both capable of storing information and performing catalytic activities. But science is still very far away from a full understanding of the origins of life.

Replicator dynamics have been established as a model of interactions in prebiotic times and in order to demonstrate the increase of complexity.

Replication is the most crucial process in biology, for it is the only way to pass genetic information from one generation to the next. The process of duplicating DNA today is a most complicated multi-step procedure, involving many highly specialized enzymes. Since it is absurd to think of such processes in prebiotic times, it is fruitful to investigate the limits of the one-step “overall” kinetics that are described by replicator equations.

Thus it is interesting to apply *structural perturbations* to the pure model and find out about their limits, i.e., see, whether the qualitative behavior of the replicator equation is still valid under different conditions.

There are different types of possible structural perturbations:

- (i) *Deterministic* perturbations that introduce new intermediate species by refining the underlying mechanisms.
- (ii) *Stochastic* perturbations by introducing new species that interact randomly with the existing ones.
- (iii) *Physical* perturbations in the sense of different physical boundary conditions.

See also figure 5.

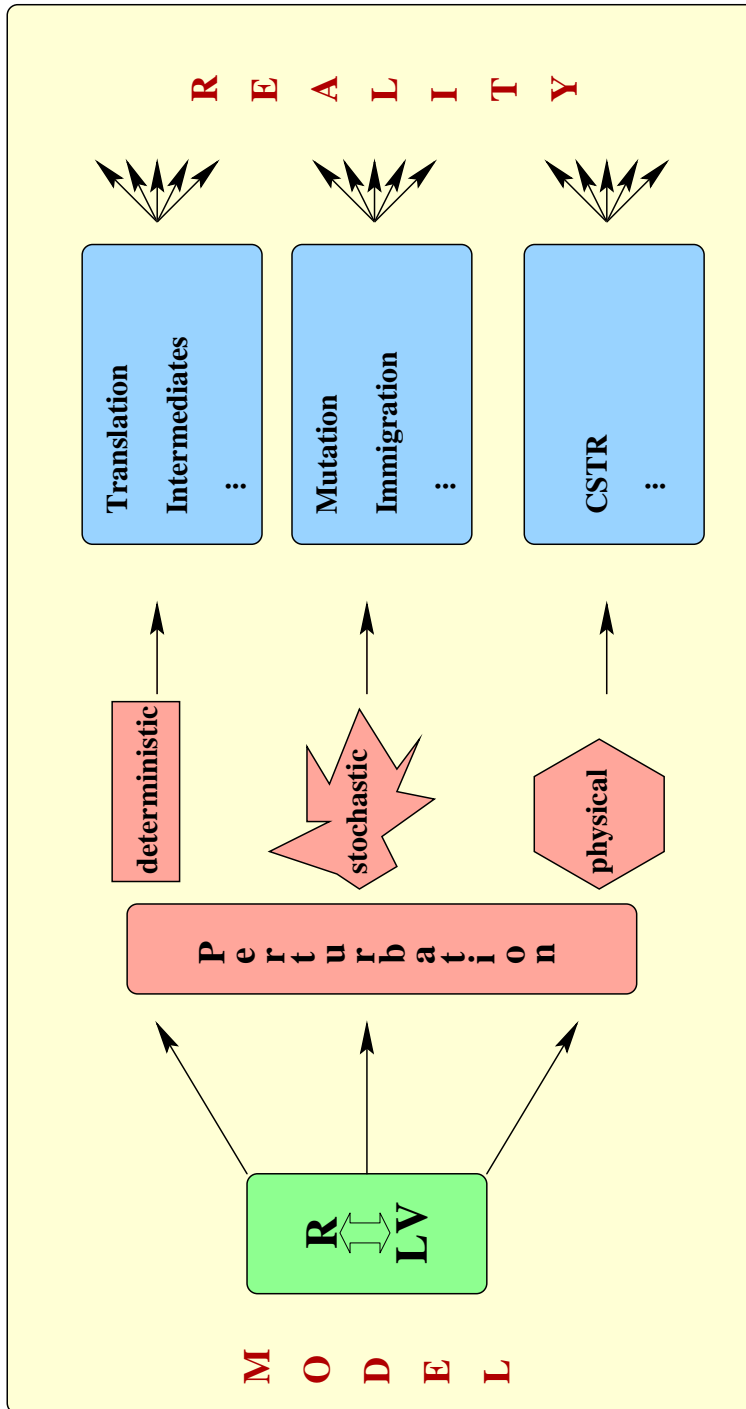


Figure 5: Different types of structural perturbations of the replicator equation. There is a wide field of possible perturbations and refinements that finally converges to models which are close to reality, but completely untreatable.

Part One:

Methods

IT WAS THE HISTORICAL MISSION OF ANALYSIS —
THIS WAS WHAT HE'D TOLD HIS OWN GUYS AT ONE
O'CLOCK IN THE MORNING — TO SCREW THINGS UP
AND THEREFORE MAKE OPERATIONS LOOK GOOD.

Peter Caray, *The Unusual Life of Tristan Smith*

2. Singular Perturbation Theory



Singular perturbation theory has become a powerful tool for dealing with a class of perturbation problems for which ordinary perturbation methods fail.

2.1. Introductory Definitions and Remarks

Definition:[74] A *regular perturbation problem* $P_\epsilon(y_\epsilon) = 0$ depends on its small parameter ϵ in such a way that its solution $y_\epsilon(x)$ converges as $\epsilon \rightarrow 0$ (uniformly with respect to the independent variable x in the relevant domain) to the solution $y_0(x)$ of the limiting problem $P_0(y_0) = 0$.

The parameter ϵ typically represents the influence of many nearly negligible physical influences. Usually, we will restrict attention to boundary value problems where P_ϵ is defined by differential operators and boundary forms, though one might also study integral or other operator equations or more global auxiliary conditions. Assuming sufficient smoothness (with respect to x , y , and ϵ), the solution of a regular perturbation problem can be approximated by a formal asymptotic power series expansion in ϵ having the leading term (i.e., asymptotic limit) y_0 . A good example for the application of regular perturbation theory is the treatment of mutation for replicator equations in [96].

A *singular perturbation* is said to occur whenever the regular perturbation limit $y_\epsilon(x) \rightarrow y_0(x)$ fails. Such a breakdown, typically, occurs in narrow intervals of space or short intervals of time (although secular problems with nonuniform behavior at infinity, such as the harmonic oscillator, are also common). Much of the special vocabulary of singular perturbations comes from physically natural terminology in high Reynolds number fluid flow past physical bodies [104]. In such a flow, a *no-slip* condition along the surface results in a thin *boundary layer* of

nonuniform convergence about the body where the velocity varies from zero to that of the uniform outside flow.

Singularly perturbed dynamical systems often occur when the underlying dynamics perform on different time scales, i.e., if the process of interest splits into subsystems, some of which are much faster than the overall dynamics. certainly the same is true if some processes are much slower, for in that case the time derivatives are almost zero and these variables can be held constant.

2.2. Singular Perturbations

A great deal of the mathematical theory of singular perturbation theory is compiled in the books [69, 74, 101]. The results outlined in the following few paragraphs are well known, see e.g., [28, 46, 63, 78].

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 $\epsilon \in I \subseteq \mathbb{R}$. Furthermore let $K \subseteq X \times Y$ be compact such that $\text{int } K$ 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 $\varphi : X \times A \rightarrow Y$ such that $g(x, \varphi(x, a), a, 0) = 0$.
- (ii) The Jacobian $J(x, a) = \frac{\partial g}{\partial y}[x, \varphi(x, a), a, 0]$ 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 3. *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 $X \times A'$:

$$\lim_{\epsilon \rightarrow 0} \psi(x, a, \epsilon) = \varphi(x, a) \quad \text{and} \quad \lim_{\epsilon \rightarrow 0} \frac{\partial \psi}{\partial x}[x, a, \epsilon] = \frac{\partial \varphi}{\partial x}[x, a].$$

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 of 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

$$\begin{aligned} F(x, a) &\stackrel{\text{def}}{=} f(x, \varphi(x, a), a, 0), \\ \Delta(x, a, \epsilon) &\stackrel{\text{def}}{=} f(x, \psi(x, a, \epsilon), a, \epsilon) - f(x, \varphi(x, a), a, 0). \end{aligned} \tag{2.2}$$

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 $\|\cdot\|_{\bullet}$ denotes the C^1 norm, see, e.g. [47, 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

$$\dot{x} = F(x, a) + \Delta(x, a, \epsilon) \tag{2.3}$$

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.

If (SPP) reduces to its degenerate system, then the following propositions are true:

- (i) If the degenerate system has a hyperbolic equilibrium \hat{x}_0 , then there is a hyperbolic equilibrium \hat{x}_ϵ of (SPP) nearby, at least for sufficiently small ϵ . In particular, \hat{x}_ϵ is asymptotically stable iff \hat{x}_0 is asymptotically stable [101].

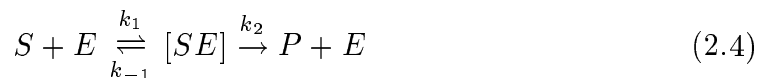
- (ii) If the degenerate system has a non-degenerate closed orbit $\hat{\pi}_0$ with primitive period T_0 , then (*) contains a nearby non-degenerate closed orbit $\hat{\pi}_\epsilon$ with primitive period T_ϵ close to T_0 for small enough $\epsilon > 0$ [3]
- (iii) The existence of a transversal homoclinic orbit in the degenerate system implies the existence of a nearby transversal homoclinic orbit in (SPP) for sufficiently small $\epsilon > 0$ [78, Thm. 3.1’].

Property (iii) also suggests that the existence of a strange attractor of the degenerate system implies the existence of chaotic orbits in the non-degenerate system [39]. In special cases, for instance Silnikov’s theorem [90] can be used to make this statement precise [78].

Remark: For a numerical example see, e.g. chapter 5, fig.11.

2.3. Example: Nonlinear Problem from Enzyme Kinetics

Following, a well-known example from biochemistry is given. The theory of Michaelis and Menten [68] and Briggs and Haldane [34] concerns a substrate S being converted irreversibly by a single enzyme E into a product P . There is an intermediate substrate–enzyme complex SE . Since the back reaction is negligible, we shall systematically write



Using the law of mass action, we shall take the rates of reactions to be proportional to the concentrations of the reactants. Introducing s , e , c and p to denote the respective concentrations of S , E , SE , and P , we thereby obtain the nonlinear autonomous differential system

$$\begin{aligned} \dot{s} &= -k_1 s e + k_{-1} c \\ \dot{e} &= -k_1 s e + (k_{-1} + k_2) c \\ \dot{c} &= k_1 s e - (k_{-1} + k_2) c \\ \dot{p} &= k_2 c \end{aligned} \quad (2.5)$$

subject to the initial conditions $s(0) = s_0 > 0$, $e(0) = e_0 > 0$, $c(0) = 0$ and $p(0) = 0$. Since $d(e + c)/dt = 0$ and $d(s + c + p)/dt = 0$,

$$\begin{aligned} e(t) &= e_0 - c(t) \\ p(t) &= s_0 - s(t) - c(t) \end{aligned} \tag{2.6}$$

and there remains a nonlinear initial value problem for the concentrations s and c .

$$\begin{aligned} \dot{s} &= -k_1 e_0 s + (k_1 s + k_{-1})c & s(0) &= s_0 \\ \dot{c} &= k_1 e_0 s - (k_1 s + k_{-1} + k_2)c & c(0) &= 0 \end{aligned} \tag{2.7}$$

We note that such redundancy in the original differential equation often occurs in chemical kinetics, circuit analysis, and other fields, due to constraints between variables which result from physical conservation or balance laws. Here, the resulting initial value problem for the two-dimensional system could be studied by describing all representative trajectories in the first quadrant of the $s - c$ plane.

Biochemists often explain the Michaelis Menten kinetics less mathematically by simply assuming a pseudo-steady state such as $\dot{c} \approx 0$. This approach set one derivative in this system equal to zero, but remains the other. It is used extensively though it is not always valid (as at $t = 0$, where $c(0) = 0$ while $s(0) > 0$).

For a better understanding of the true solution behavior the variables can be nondimensionalized by setting

$$\begin{aligned} \bar{t} &= k_1 e_0 t, & \lambda &= \frac{k_2}{k_1 s_0}, & \kappa &= \frac{k_{-1} + k_2}{k_1 s_0}, & \epsilon &= \frac{e_0}{s_0}, \\ x(\bar{t}) &= \frac{s(t)}{s_0}, & y(\bar{t}) &= \frac{c(t)}{e_0}. \end{aligned} \tag{2.8}$$

Typically, $\epsilon \approx 10^{-6}$. Omitting the bar on t we obtain the singularly perturbed initial value problem

$$\begin{aligned} \dot{x} &= -x + (x + \kappa - \lambda)y, & x(0) &= 1 \\ \epsilon \dot{y} &= x - (x + \kappa)y, & y(0) &= 0. \end{aligned} \tag{MM}$$

Because the fast variable is stable for $\epsilon \rightarrow 0$

$$\left. \frac{dy}{dy} \right|_{x(t)} = -\frac{x + \kappa}{\epsilon} < 0$$

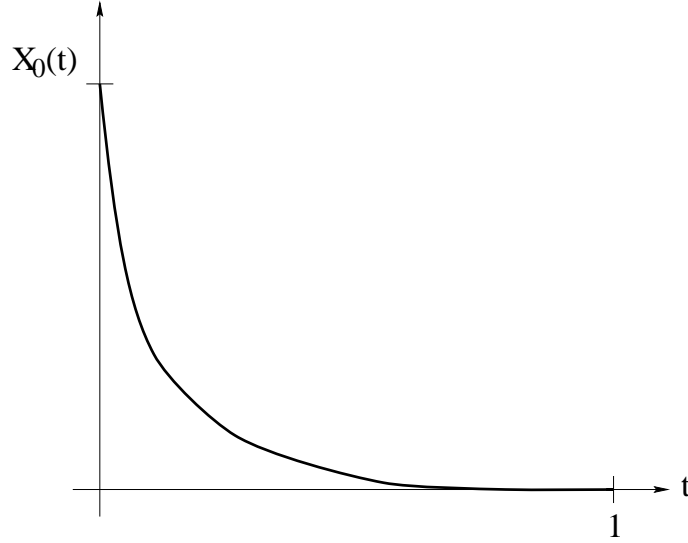


Figure 6: Outer Solution of Michaelis-Menten kinetics; corresponds to quasi-steady state assumption.

(assuming λ and κ positive and bounded), we get the corresponding reduced differential algebraic initial value problem

$$\begin{aligned} \frac{dX_0}{dt} &= -X_0 + (X_0 + \kappa - \lambda)Y_0, & X_0 &= 1 \\ 0 &= X_0 - (X_0 + \kappa)Y_0. \end{aligned} \quad (2.10)$$

That yields the outer solution $Y_0 = \frac{X_0}{X_0 + \kappa}$ and the reduced-order initial value problem

$$\frac{dX_0}{dt} = -\frac{\lambda X_0}{X_0 + \kappa}, \quad X_0 = 1. \quad (2.11)$$

They together correspond to the pseudo-steady state hypothesis of Michaelis-Menten, see figure 6. Because the limiting outer solution cannot describe the fast variable y near $t = 0$ there is need for an initial layer correction in y that suggests an asymptotic solution of the form

$$\begin{aligned} x(t, \epsilon) &= X(t, \epsilon) + \epsilon \xi(\tau, \epsilon) \\ y(t, \epsilon) &= Y(t, \epsilon) + \eta(\tau, \epsilon) \end{aligned} \quad (2.12)$$

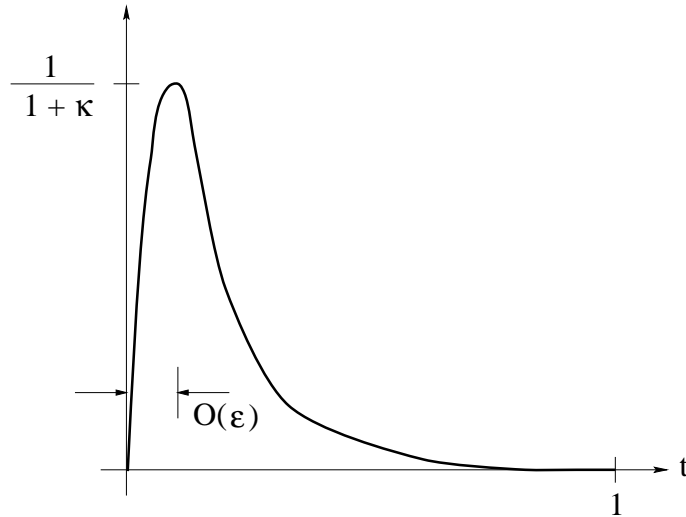


Figure 7: Concentration of enzyme-substrate complex; corresponds to fast variable of Michaelis-Menten system.

with an outer solution $\begin{pmatrix} X \\ Y \end{pmatrix}$ and an initial layer correction $\begin{pmatrix} \xi \\ \eta \end{pmatrix}$ which tends to zero as the stretched time

$$\tau = \frac{t}{\epsilon}$$

tends to infinity. See also figure 7. The asymptotic power series expansions

$$\begin{aligned} \begin{pmatrix} X(t, \epsilon) \\ Y(t, \epsilon) \end{pmatrix} &= \sum_{j=0}^{\infty} \begin{pmatrix} X(t) \\ Y(t) \end{pmatrix} \epsilon^j \\ \begin{pmatrix} \xi(\tau, \epsilon) \\ \eta(\tau, \epsilon) \end{pmatrix} &= \sum_{j=0}^{\infty} \begin{pmatrix} \xi(\tau) \\ \eta(\tau) \end{pmatrix} \epsilon^j \end{aligned} \tag{2.13}$$

will satisfy linearized variational differential-algebraic systems obtained from successively equating coefficients of higher powers of ϵ to zero.

3. Characterization of Permanence

Very few dynamical systems allow for analytical treatment. Besides, often one is not interested in all details of a dynamical system or in the structure of its ω -limit sets, less detailed knowledge may well be sufficient. In this context one could investigate the following question: *Can all species coexist in the system for arbitrarily long time? Or will some species die out in the long run?* Schuster *et al.* [84] introduced the notion of *permanence* (permanent coexistence) to formalize this question. A variety of different notions of cooperation, the first of which is now called *weak persistence* [31], have been proposed by various authors. For an overview see reference [30]. A recent review of permanence is [60].

Let S be a closed subset of \mathbb{R}^n and let $f : S \rightarrow \mathbb{R}^n$ be such that the solutions $x(t) \in S$ of the initial value problem

$$\dot{x} = f(x), \quad x(0) = x_0 \tag{3.1}$$

is unique and defined for all $t \geq 0$.

Definition. The dynamical system (3.1) is called *permanent*, if all orbits are uniformly bounded and there is a compact set C entirely contained in the interior of S , such that for all $x \in \text{int } S$ holds

$$\omega(x) \in C \tag{3.2}$$

An equivalent formulation for both bounded and unbounded state spaces is the following

Theorem 4. (Hofbauer and Sigmund [55]) *The dynamical system (3.1) is permanent iff there is a $\delta > 0$ and a $M > 0$ such that for all initial conditions $x \in \text{int } S$ holds*

$$\begin{aligned} \liminf_{t \rightarrow \infty} \text{dist}(x(t), \partial S) &> \delta \\ \limsup_{t \rightarrow \infty} |x(t)| &< M \end{aligned} \tag{3.3}$$

If the statespace S is compact, the second condition – uniform boundedness of the orbits – is always satisfied.

We remark that one obtains the definition of (*strong*) persistence for $\delta \rightarrow 0$ in equ.(3.3). [30]

Thus far there is only one necessary and sufficient condition for permanence.

Definition. Let $P : S \rightarrow \mathbb{R}$ be a nonnegative function, strictly positive in $\text{int } S$ and vanishing on ∂S . Furthermore, suppose that there is a lower semicontinuous function $\Psi : S \rightarrow \mathbb{R}$ such that the following conditions hold

(i) For all $x \in \text{int } S$ we have

$$\dot{P}(x) = P(x)\Psi(x) \tag{3.4}$$

(ii) For all $x \in \partial S$ we have for some $T > 1$

$$\frac{1}{T} \int_0^T \Psi(x(t)) dt > 0 \tag{3.5}$$

Then P is an *Average Ljapunov Function* for the differential equation (1).

Theorem 5. *Suppose all orbits are uniformly bounded. Then the dynamical system (3.1) is permanent iff it admits an Average Ljapunov Function. That existence of an Average Ljapunov Function implies permanence has been shown by Hofbauer [51], the converse is due to Hutson [59]. It has been shown [58] that it is sufficient to require condition (3.4) for all points in ω -limits on ∂S only.*

As a consequence of Brower's fixed point theorem it has been shown that if the dynamical system (3.1) is permanent then there is a rest point in the interior of S [61].

In the following, attention is restricted to only two types of ordinary differential equations:

(i) The *replicator equation*

$$\dot{x}_k = x_k \left[f_k(x) - \sum_{j=1}^n x_j f_j(x) \right] \quad (R)$$

is defined on the simplex

$$S_n = \{x \in \mathbb{R}_+^n \mid \sum_{j=1}^n x_j = 1\}$$

(ii) whereas the *ecological equation* (E) — also known as Kolmogorov system

$$\dot{y}_k = y_k \varphi_k(x) \quad (E)$$

is defined on the *positive orthant* \mathbb{R}_+^n .

Note that the simplex S_n is $n - 1$ -dimensional. The ecological and the replicator equation are closely related to each other. Let $\bar{F}_{\{n\}}$ be the face of S_n defined by $x_n = 0$. Let us now investigate the following transformation:

$$\begin{aligned} \mathcal{H} : S_n \setminus \bar{F}_{\{n\}} &\rightarrow \mathbb{R}_+^{n-1} : y_k = \frac{x_k}{x_n} \quad k < n \\ \mathcal{H}^{-1} : \mathbb{R}_+^n &\rightarrow S_{n+1} \setminus \bar{F}_{\{n+1\}} : x_k = \frac{y_k}{1 + \sum_{j=1}^n y_j}, \\ &x_{n+1} = \frac{1}{1 + \sum_{j=1}^n y_j} \end{aligned} \quad (3.8)$$

This diffeomorphism has originally been used by J. Hofbauer [49] to show flow equivalence between the second order replicator equation

$$\dot{x}_k = x_k [(Ax)_k - (xAx)], \quad k = 1, \dots, n \quad (SR)$$

and the Lotka-Volterra-Equation

$$\dot{y}_k = y_k [r_k + (By)_k], \quad k = 1, \dots, n - 1. \quad (LV)$$

The transformation allows us more generally to obtain an ODE of the form (E) from any ODE of the form (R) via

$$\varphi_k(y) := f_k\left(\frac{1}{1 + \sum_j y_j}(y, 1)\right) - f_n\left(\frac{1}{1 + \sum_j y_j}(y, 1)\right) \quad (3.11)$$

and *vice versa*.

We will use the notation F_K for the interior of the faces of S_n or \mathbb{R}_+^n defined by $x_k = 0$ for $x \in S_n$ (or $y_k = 0$ for $y \in \mathbb{R}_+^n$, resp.) if and only if $k \in K$.

Jansen [62] proved a sufficient condition for permanence of second order replicator equations (SR) and Lotka-Volterra Equations (LV) based on the Average Ljapunov Function

$$\mathcal{P}(x) = \prod_{j=1}^n x_j^{p_j} \quad \text{with } p = (p_1, \dots, p_n) \in \text{int } S_n \quad (3.12)$$

and the following theorem on time averages:

Theorem 6. *Let $x(t)$ be a trajectory in $\text{int } \mathbb{R}_+^n$ satisfying condition (3.3). Then there is a unique restpoint \hat{y} in $\text{int } \mathbb{R}_+^n$ satisfying*

$$\hat{y} = \lim_{T \rightarrow \infty} \frac{1}{T} \int_0^T y(t) dt \quad (3.13)$$

An analogous results holds for second order replicator equations [82].

Definition. [50] A rest point of (SR) $\hat{x}^K \in F_K$ is called *saturated* if for all transversal eigenvalues

$$\lambda_k(\hat{x}^K) = [A\hat{x}^K]_k - (\hat{x}^K A \hat{x}^K) \quad k \in K \quad (3.14)$$

holds $\lambda_k(\hat{x}^K) \leq 0$. Analogously we obtain for Lotka-Volterra systems

$$\lambda_k(\hat{y}^K) = r_k - [A\hat{y}^K] \quad (3.15)$$

for the transversal eigenvalues of a rest point $\hat{y}^K \in F_K$.

Theorem 7. (Jansen [62]) Let \hat{x}^K denote the isolated rest point of (SR) or (LV) in the interior of the boundary face F_K . In case of (LV) assume additionally that all orbits are uniformly bounded. Then (SR) or (LV) is permanent if there is a vector $p \in \text{int} S_n$ such that for all \hat{x}^K holds

$$\sum_{j \in K} p_j \cdot \lambda_j(\hat{x}^K) > 0. \quad (3.16)$$

Theorem 6 does not apply to the more general systems (R) or (E). Therefore, there seems to be no way to obtain a pure algebraic condition for permanence for more complicated systems than (SR) and (LV).

The following linear programming algorithm to solve the set of linear inequalities (3.16) is also due to Jansen [62]:

Theorem 8. Let \hat{x}^K as in theorem 7. The solution of the LP-problem

$$\begin{aligned} z &\rightarrow \min. \\ \sum_{j \in K}^n p_j \lambda_j(\hat{x}^K) + z &> 0 \quad \forall \hat{x}^K \\ \sum_{j=1}^n p_j &= 1 \end{aligned} \quad (3.17)$$

fulfills one of the following three alternatives

- (i) $z_{\min} < 0$ and all $p_j > 0$. Then (SR) is permanent.
- (ii) $z_{\min} < 0$ and some $p_i < 0$. Then (SR) is not permanent.
- (iii) $z_{\min} \geq 0$. Then the permanence-problem remains undecided.

A matrix A for which (SR) fulfills Jansen's permanence criterion (i) will be referred to as *type-j matrix*.

An analogous result holds for Lotka Volterra systems (LV) with uniformly bounded orbits.

Since the second order replicator equation (SR) is invariant under the transformation

$$a_{ij} \rightarrow a_{ij} + b_i \tag{3.18}$$

with arbitrary constants b_i we may assume the *normal form* $a_{ii} = 0$ without loss of generality.

Except for the existence of an interior equilibrium there are three additional necessary conditions for permanence in second order replicator equations

Theorem 9. (*Hofbauer and Sigmund [50, 55]*) *If the dynamical system (SR) is permanent and A is in normal form then the following conditions are fulfilled:*

- (i) *There is a unique interior equilibrium $\hat{x} \in \text{int}S_n$*
- (ii) $\Phi(\hat{x}) = \sum_{j=1}^n a_{ij}\hat{x}_i\hat{x}_j > 0$
- (iii) $(-1)^{n-1}\det A > 0$.
- (iv) *There is no regular saturated rest point in ∂S_n .*

We will say that a matrix A fulfilling (i) and (ii) is *type-a*, if (iii) also holds we call it *type-b* and if finally all four necessary conditions are fulfilled we call A a *type-c matrix*.

Remark. If A is a type-j matrix, it leads to permanence; thus it is also a type-c matrix. The converse is not true: neither type-j nor type-c is equivalent to permanence.

4. Boundary Conditions

Natural environments are always open systems. There is either in-/outflux of matter, or of energy, or of both. So one has to provide a both experimentally and mathematically suitable surrounding in order to keep the dynamical system away from equilibrium.

Given the choice of better experimental or better mathematical treatment, one has to select out of a couple of different models that allow for both necessities:

- (i) From the experimental point of view the most natural choice is the *continuously stirred tank reactor*, CSTR. It consists of a reaction vessel with constant volume V which is well stirred so that all concentrations are spatially homogeneous. An influx line introduces at a constant flux rate r which contains the building material (A) at a constant concentration. The volume is kept constant by an outflux of the reaction mixture at the same flux rate r . Considering replication only, the system of differential equations reads in this case

$$\begin{aligned} \dot{a} &= -a \sum_{j=1}^n y_j f_j(y) + r(a_0 - a) \\ \dot{y}_k &= y_k [a f_k(y) - r] \end{aligned} \quad (\text{CSTR})$$

- (ii) A simpler dynamical system can be obtained at the expense of a much more demanding experimental setting. The influx of the *evolution reactor* is regulated such that the concentration the building material (A) is constant in time, for instance by providing a large excess of (A) in the input flux. The outflux is regulated as well: two outflux channels, one for the reaction mixture and one equipped with a diaphragm that holds back all polymeric material are regulated such that both the volume of reaction mixture and the total concentration of the replicating species are kept constant. This setting has been termed *constant organization*. An approximate realization of an evolution reactor under constant organization is Husimi's *cellstat* [57]. The kinetic

differential equations for this system read

$$\dot{y}_k = y_k a_0 f_k(y) - y_k \frac{a_0}{\sum_j y_j} \sum_{j=1}^n y_j f_j(y). \quad (4.2)$$

In this case it is convenient to introduce relative concentrations $x_k \stackrel{\text{def}}{=} y_k / \sum_{j=1}^n y_j$ and to rescale the units such that $a_0 = 1$. The differential equations above then simplify to

$$\dot{x}_k = x_k \left[f_k(x) - \sum_{j=1}^n x_j f_j(x) \right] \quad (\text{R})$$

This dynamical system has been termed *replicator equation* [80]. 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 [48]), economics, or laser physics. Their properties have been the subject of hundreds of research papers by many research groups, see the book by Hofbauer and Sigmund [56] and the references therein. In this contribution we will be concerned with the relation between the dynamical systems (CSTR) and (R).

- (iii) Yet there is still another possible setting for boundary conditions. Sometimes it is convenient to assume that there is no flux of material at all, but only exchange of energy. The low molecular supply gets regenerated from degraded macromolecules by some more or less sophisticated mechanism which is driven by the energy flux, e.g., radiation. The kinetic differential equations for this system read

$$\dot{y}_k = y_k a_0 f_k(y) - y_k \frac{a_0}{\sum_j y_j} \sum_{j=1}^n y_j f_j(y). \quad (4.4)$$

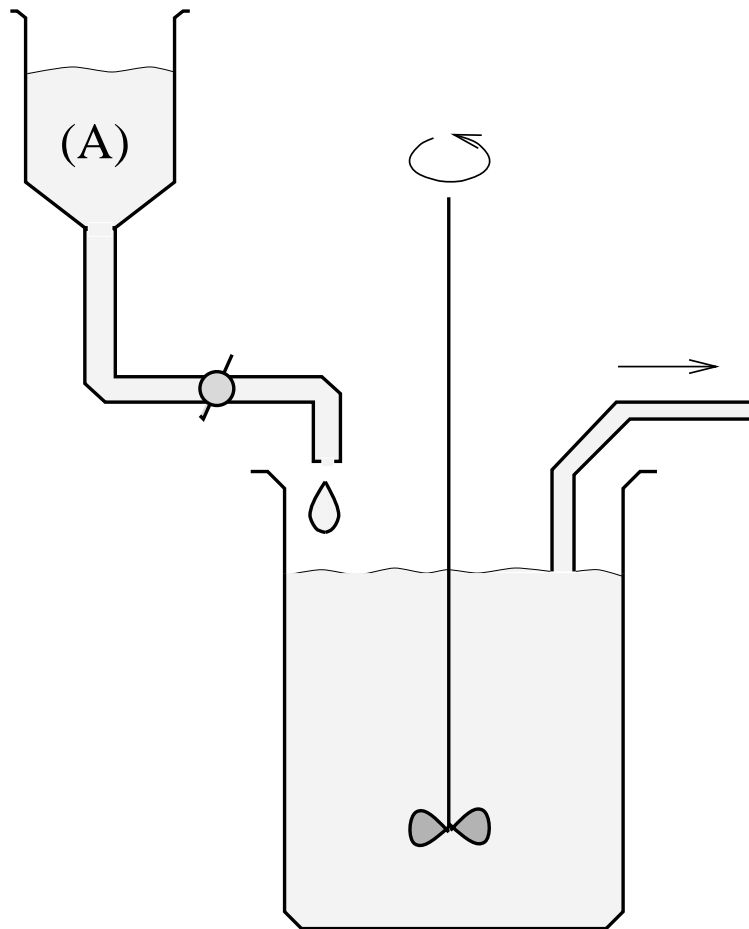


Figure 8: CSTR and Evolution Reactor under Constant Organization.

The continuously stirred flow reactor (CSTR) is known also as “chemostat” in microbiology. The reaction is maintained by the continuous influx of a solution containing the materials which are necessary for replication. In the simplified model systems to discussed here, we assume only one energy rich compound (A). The evolutionary constraint is provided by the continuous outflux of solution from the reactor. Replicating molecules are injected into the reactor at $t = t_0$. Then, their concentrations may increase and eventually reach a stationary value, or they may be diluted out of the reactor depending on the input solution and the flow rate r which is commonly measured in terms of the reciprocal residence time of the solution in the tank reactor [45].

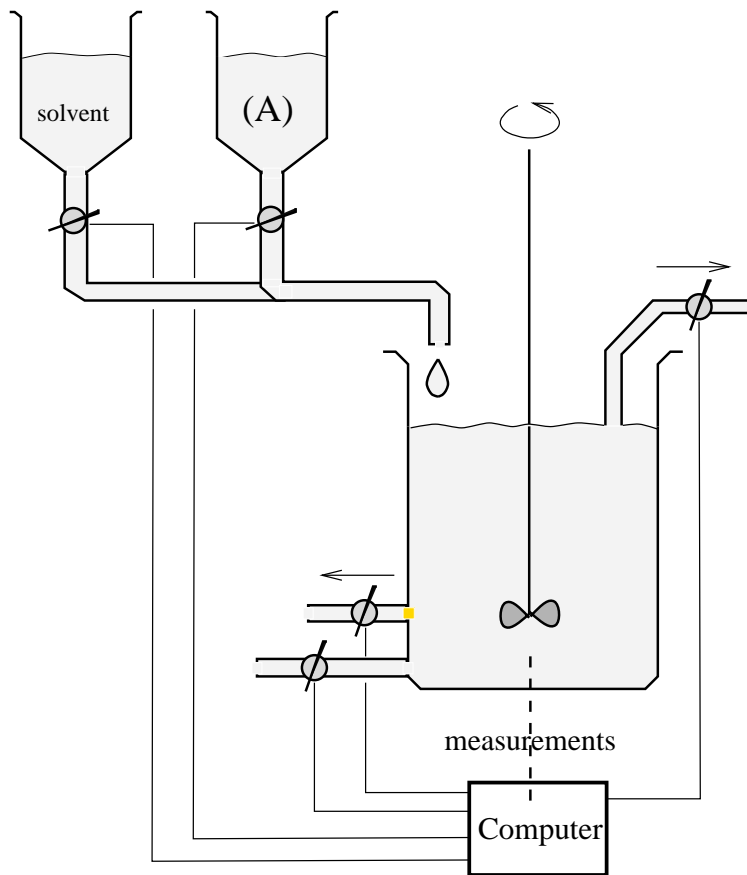


Figure 9: The evolution reactor is a more sophisticated version of a flow reactor. It consists of a reaction vessel which has walls which are impermeable to polymer material. Energy rich monomers are poured from the environment into the reactor. The degradation products are removed steadily. Material transport is adjusted in such a way that the concentrations of energy rich monomers are constant in the reactor. A dilution flux is installed in order to remove the excess of polymers produced by replication. Thus the sum of the polymer concentrations may be controlled by the dilution flux. Under “constant organization” it is adjusted such that the total polymer concentration is constant in time. This regulation requires internal control, which may be archived by analysis of the solution and data processing by a computer as indicated above.

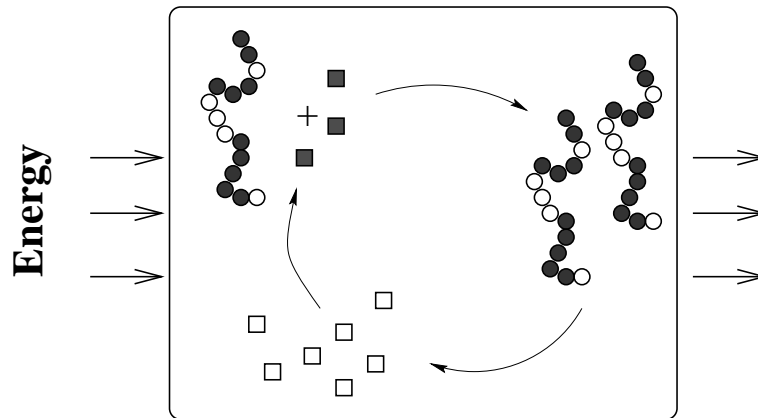


Figure 10: The regenerative dynamical setting is convenient for models with no flux of matter. The driving force is a flux of energy that supplies some mechanism of regeneration that provides the low molecular building material.

Part Two:

Results

SUDDENLY I FELT MY BRAIN SLIDING DOWN THE INSIDE OF MY LEFT NOSTRIL. [...] I KNEW I HAD TO GET IT BACK INSIDE, SO I GRABBED THE LUMP AND SWALLOWED IT QUICKLY. AFTER RECOVERING MY BRAIN I WENT BACK TO SLEEP AGAIN.

Nina Fitzpatrick, *Fables of the Irish Intelligentsia*

5. Reduction of the CSTR Equations to Constant Organization

As we have seen in the last chapter, there is a close resemblance of the CSTR and the constant organization setting. However, the mathematical treatment of the resulting differential equations from the CSTR is all but inviting. But the answer to the question, whether for some parameters the constant organization setting describes the behavior of the CSTR well enough, can be readily given [42].

Second order replication with arbitrary response-functions $f_k(y)$ yields the following system of differential equations.(see previous chapter.)

$$\begin{aligned} \dot{a} &= -a \sum_{j=1}^n y_j f_j(y) + r(a_0 - a) \\ \dot{y}_k &= y_k [a f_k(y) - r] \end{aligned} \tag{CSTR}$$

Let R denote the second order replicator equation with the same response functions f_k .

The limit of small flux rates r . In order to simplify the notation below let us introduce the total concentration of the replicators $z = \sum_{j=1}^n y_j$ and the activity of

the system $\Phi(y) = \sum_{j=1}^n y_j f_j(y)$. Throughout this contribution we will assume that the following to hypotheses hold:

- (H1) there is a continuous function $h : \mathbb{R}_{0+} \rightarrow \mathbb{R}_{0+}$ such that $h(z) \leq f_j(y)$ on any compact subset of \mathbb{R}_{+0}^n and $h(z) > 0$ for all $z > 0$.
- (H2) the initial conditions fulfills $z(t = 0) > 0$.

Hypothesis (H1) means that we limit ourselves to the species that are capable of replication in the absence of all other replicators. The self-catalyzed selfreplication can, however, be much less effective then replication catalyzed by other polymers

in the system. Hypothesis (H2) requires that some replicators are present in the initial condition.

It is well known that $a(t) + z(t)$ converges exponentially towards a_0 for $t \rightarrow \infty$ [81]. The following lemma shows that for small enough flow rates r the CSTR will eventually be filled almost entirely by replicators (as opposed to being filled by unprocessed building material) provided (H1) and (H2) are true.

Lemma 1. *For any initial value problem (CSTR) fulfilling (H1) and (H2) there exist two constants $m_1, m_2 > 0$ independent of the initial condition and a constant $r_0 = r_0(z(0)) > 0$ such that for all $r \leq r_0$ there exists a finite time $T = T(r, a(0), y(0)) < \infty$ with the property that the inequality $m_1 r < a(t) < m_2 r$ holds for all $t \geq T$.*

Proof. The first step is to show that there exists a constant $0 < \gamma < 1$, independent of r and the initial conditions such that $a(t) < \gamma a_0$. First we construct a differential equation for z :

$$\dot{z} = \sum_{j=1}^n \dot{y}_j = \Phi(y)a - rz \geq zh(z)a - rz. \quad (5.2)$$

Now suppose there is a $t^* > T$, which might depend on $r > r_0$, such that $a(t) > \gamma a_0$. Then

$$\dot{z}(t^*) \geq z(t^*) \underbrace{[\gamma a_0 h(z(t^*)) - r]}_{>0}$$

By continuity of h there is a continuous function $z_0(r) \geq 0$ such that $\gamma a_0 h(z) > 2r$ for all $z \geq z_0(r)$. Conversely, given $z(t^*)$, there exists a $r^* > 0$ such that the expression in the bracket is bounded from below by r^* . Then $z(t + t^*) \geq z(t^*) \exp(r^* t) \rightarrow \infty$, which contradicts the uniform upper bound $z(t) < 2a_0$, because of $z(t) + a(t) \rightarrow a_0$ for long times. Since γ is an arbitrary constant for which we have only required $0 < \gamma < 1$ we have in particular $z(t) > a_0/2$ and $a(t) < a_0/2$ for all $t > T$.

The second step is to use the differential equation $\dot{a} = -a\Phi(y) + r(a_0 - a)$ for obtaining tighter bounds on $a(t)$. For large enough t one finds

$$\frac{1}{2} \min \frac{ra_0}{\Phi(y) + r} < a(t) < 2 \max \frac{ra_0}{\Phi(y) + r}, \quad (5.3)$$

where the minimum and the maximum are taken over all $y(t)$ with $t > T$. The lower bound is easily obtained:

$$\frac{1}{2} \min \frac{ra_0}{\Phi(y) + r} > \frac{ra_0}{2} \cdot \frac{1}{\max \Phi(y) + r_0} > r \frac{a_0}{2} \cdot \frac{1}{2a_0M_1 + r_0} \stackrel{\text{def}}{=} m_1 r, \quad (5.4)$$

where we have used that $\max \Phi(y) \leq \max z \cdot \max f_j(y)$ and M_1 is a uniform upper bound for $f_j(y)$ on the box $[0, 2a_0]^n$ which exists by the continuity assumptions of f_j . Analogously we observe that

$$\min \Phi(y) \geq \min z \cdot \min h(z) > \frac{a_0}{2} \min_{z > a_0/2} \Phi(z) = \frac{a_0}{2} \eta$$

where the constant $\eta \stackrel{\text{def}}{=} \min_{z > a_0/2} \Phi(z) > 0$ as an immediate consequence of (H1). Collecting the inequalities for the upper bound we find

$$a(t) < \frac{a_0 r}{(\eta/2)a_0} \stackrel{\text{def}}{=} m_2 r.$$

Observing that m_2 is independent of r completes the proof. \blacksquare

Schuster and Sigmund [81] showed that the projections of the trajectories of (CSTR) to relative concentrations x_k follow a replicator equation (R) provided all functions f_k , $1 \leq k \leq n$ are homogeneous of degree p . They were not concerned with the survival or extinction of the replicators. As a consequence of Lemma 1 we can resolve this problem.

Theorem 10. *Consider the system (CSTR) together with the hypotheses (H1) and (H2) and let f_k be a homogeneous function of degree p for $1 \leq k \leq n$. Then there is a constant $r_0 > 0$ such that for all $r \leq r_0$ we have $z(t) > a_0/2$ for large enough times t and the relative concentrations x_k are given by the solutions of the replicator equation (R) up to a finite change in velocity.*

Proof. It has been shown in [81] that the x_k fulfill the differential equation

$$\dot{x}_k = ax_k \left[f_k(y) - \sum_{j=1}^n x_j f_j(y) \right] = a(t)z(t)^p \cdot x_k \left[f_k(x) - \sum_{j=1}^n x_j f_j(x) \right] \quad (5.5)$$

Lemma 1 now implies that $a(t)z(t) > m_1 r (a_0/2)^p > 0$ for large enough times, and thus we can invoke a change in velocity in order to drop the time-dependent factor $a(t)z(t)$ without changing the phase portraits. ■

Using $g \stackrel{\text{def}}{=} \ln(a/r)$ instead of a we can rewrite (CSTR) as

$$\begin{aligned} \dot{g} &= a_0 \exp(-g) - \Phi(y) - r \\ \dot{y}_k &= r y_k (f_k(y) \exp(g) - 1) \end{aligned} \tag{CSTR'}$$

Lemma 1 can be restated for this dynamical system in the following form:

Corollary 1. *Given $z_0 > 0$ there exists a constant $r_0 = r_0(z_0)$ such that the compact box $K \stackrel{\text{def}}{=} [\ln m_1, \ln m_2] \times [a_0/2, 2a_0]^n$ is strictly forward invariant under the flow of (CSTR') for all $r \leq r_0$, and K is reached in finite time from all initial condition fulfilling $z(0) \geq 0$.*

Lemma 2. *The phase portrait of (CSTR') and the phase portrait of the singular perturbation problem*

$$\begin{aligned} r\dot{g} &= \exp(-g) (a_0 \exp(-g) - \Phi(y) - r) \\ \dot{y}_k &= y_k (f_k(y) - \exp(-g)) \end{aligned} \tag{SPP}$$

are topologically equivalent on the compact box K provided $0 < r \leq r_0$.

Proof. The vector fields on the r.h.s of eqns. (CSTR') and (SPP) differ by simply by the factor $r \exp(g)$. Lemma 1 implies immediately that $r \exp(-g) = a(t)$ is bounded away from 0 on the box K . Thus (SPP) is obtained from (CSTR') by a change in velocity. ■

Now it is highly time to turn to the purpose of the whole game:

The Main Result. Let us now return to the limit $r \rightarrow 0$ our singular perturbation version of the CSTR equation. The main result of this contribution is that (SPP) reduces to a replicator equation in the above sense.

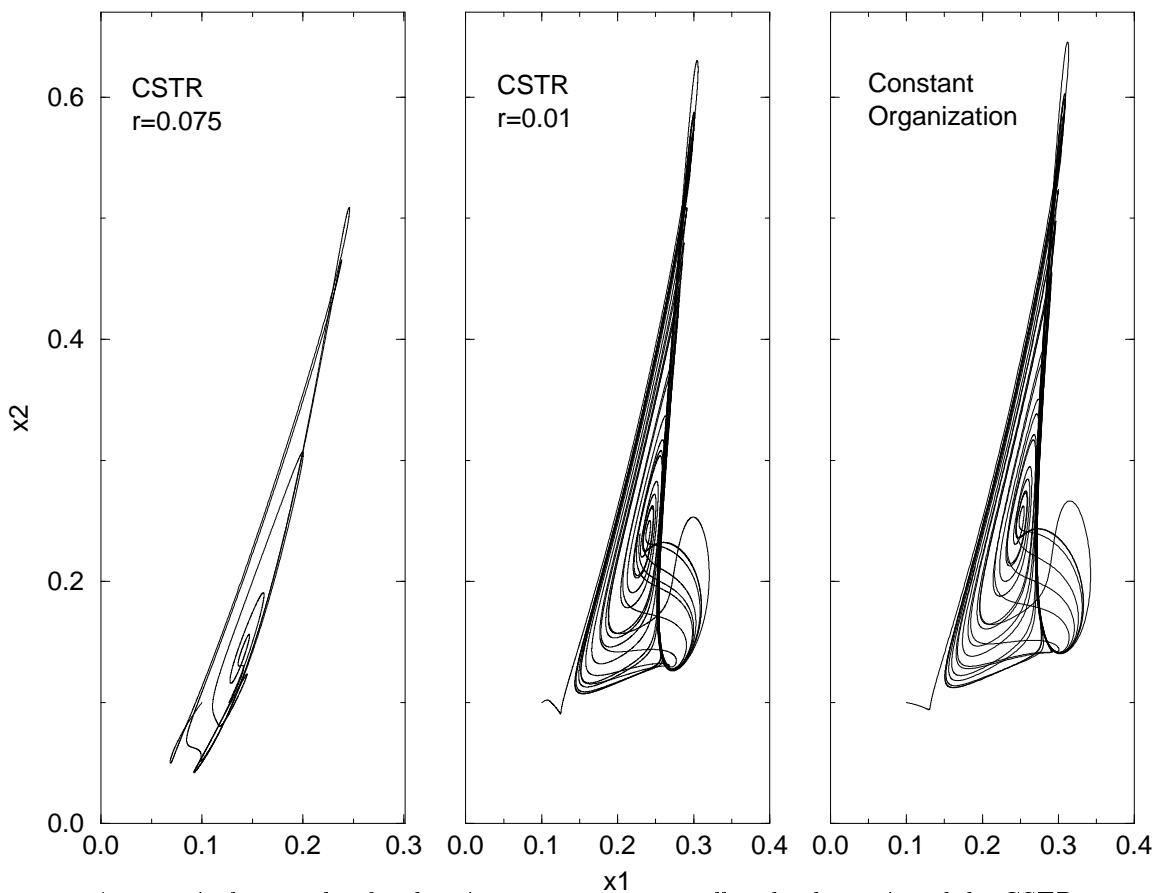


Figure 11: A numerical example of a chaotic attractor. For small r the dynamics of the CSTR and the corresponding replicator equation become virtually indistinguishable. We consider four replicating species with interaction functions $f_k(y) = \alpha_k + \sum_j a_{kj} y_j$, where $\alpha_k = 0.1$ and

$$a_{ij} = \begin{pmatrix} 0 & 0.5 & -0.1 & 0.1 \\ 1.1 & 0 & -0.6 & -0.001 \\ -0.5 & 1 & 0 & 0.655 \\ 1.7 & -1 & -0.2 & 0 \end{pmatrix}.$$

A was chosen according to [4, 5, 77]. Initial conditions were $y_{1,2,3} = 0.1, y_4 = 0.7, a = 0.1$ and $a_0 = 1$. From left to the right the flow rate r was reduced ($r_1 = 0.075, r_2 = 0.01, r_3 = 0.0$) The right-hand figure represents constant organization.

Theorem 11. (CSTR) *reduces to the second order replicator equation on K for small enough flow rates r .*

Proof. In our model the fast variable g is one-dimensional. Of course all our vector fields are smooth enough for the above arguments to be applicable to our models. For $r = 0$ the first equation reduces to $\Phi(\tilde{y}) = a_0 \exp(-\tilde{g})$, i.e., given y we obtain a unique solution for g on K . Its Jacobian at x is simply given by partial derivative

$$\frac{\partial \dot{g}}{\partial g} = \exp(-g) (a_0 \exp(-g) - \Phi(y) - r) - a_0 \exp(-2g) = -r\dot{g} - a_0 \exp(-2g). \quad (5.8)$$

For sufficiently small r we have $|r\dot{g}| < a_0 \exp(-2g)$ on K and hence the solution for g is stable on K . Consequently (CSTR') reduces to (R) for small enough r . ■

In particular there is a one-to-one correspondence of the fixed points of the replicator equation (R) and the equilibria of (SPP) for small non-zero flux rate r , *provided* the equilibria of the replicator equation are regular (i.e., if their Jacobian matrices are hyperbolic). Similarly, hyperbolic limit cycles carry over.

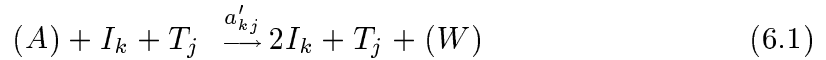
In general, if only the concentration of the low-molecular monomers is small enough then constant organization with its much less involved mathematics is sufficient to describe the dynamical behavior.

6. Autocatalytic Networks with Translation

Nodels of early stages of evolution cannot entirely ignore the fact that today (almost) all catalytic activity is carried out by proteins. Thus at some point the invention of translation is inevitable [41].

6.1. Model Equations

Let us consider a system of n species I_1, \dots, I_n of replicators or genotypes and their translation products T_1, \dots, 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 [79]. The replication processes involve translation products T_j of the genotype I_j as catalysts:



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:



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

$$\begin{aligned} \frac{d}{dt}[I_k] &= [I_k] \left\{ \sum_{j=1}^n a'_{kj} [(A)] [T_j] - \Phi \right\} \\ \frac{d}{dt}[T_k] &= w'_k [(B)] [I_k] - [T_k] \Phi^T \end{aligned} \quad (6.3)$$

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. The three types of boundary conditions, described earlier are used again in order to gain open dynamical systems. The structure of the differential equations is somewhat more involved than in the pure replicator case.

(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 constant in time.

It will be convenient to use the effective rate constants

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

A further simplification is achieved by switching to relative coordinates

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

As simple calculation then shows that

$$\Phi = \sum_{i,j} x_i a_{ij} t_j \quad \text{and} \quad \Phi^T = \sum_i w_i x_i. \quad (6.4)$$

In matrix notation we obtain thus

$$\dot{x}_k = x_k [(At)_k - \langle x, At \rangle] \quad \dot{t}_k = w_k x_k - t_k \langle w, x \rangle \quad (RT)$$

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, where $\langle \cdot \rangle$ denotes the scalar product.

- (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 $u_k = [T_k]$.

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

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 [107, 98, 43]. 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_k^T , respectively. Conservation of mass ensures that $[(A)] + \sum_k [I_k] = a_0$ and $[(B)] + \sum_k [T_k] = b_0$.

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

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. A complete derivation of the results is given 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 [40]. 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 a later chapter and also is compiled in [42]. For a partial result see [81].

6.2. 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 12. *Consider the reaction translation model under constant organization. Then there is a unique interior equilibrium $(\hat{x}, \hat{t}) \in \text{int}(S_n \oplus S_n)$ 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 (RT). An explicit computation shows

$$\hat{x}_k = \frac{(A^{-1}\mathbf{1})_k}{w_k \sum_{i=1}^n \frac{1}{w_i} (A^{-1}\mathbf{1})_i} \quad \text{and} \quad \hat{t}_k = \frac{(A^{-1}\mathbf{1})_k}{\langle \mathbf{1}, A^{-1}\mathbf{1} \rangle}. \quad (6.8)$$

Thus $\hat{t} \in \text{int } S_n$ 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

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

With this definition we may write

$$\hat{x} = \frac{1}{\langle \mathbf{1}, B^{-1}\mathbf{1} \rangle} B^{-1}\mathbf{1} \quad \text{and} \quad \hat{t} = \frac{1}{\langle \mathbf{1}, A^{-1}\mathbf{1} \rangle} A^{-1}\mathbf{1} \quad (6.9)$$

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 3. *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 $\hat{t}_k = -t_k \langle w, x \rangle$, 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 the 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* [56]. 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 $1 \leq i \leq m$. The entries of the Jacobian matrix in the first $2m$ rows and columns are readily computed:

$$\begin{aligned} \frac{\partial \dot{x}_k}{\partial x_\ell}(\xi) &= \delta_{kl}[(A\hat{t})_k - \langle \hat{x}, A\hat{t} \rangle] + 0 \stackrel{\text{def}}{=} L_k(\xi)\delta_{kl} \\ \frac{\partial \dot{x}_k}{\partial t_\ell}(\xi) &= 0 \\ \frac{\partial \dot{t}_k}{\partial x_\ell}(\xi) &= \delta_{kl}w_k \\ \frac{\partial \dot{t}_k}{\partial t_\ell}(\xi) &= -\langle w, \hat{x} \rangle \end{aligned} \tag{6.10}$$

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

$$\begin{pmatrix} \begin{pmatrix} L_1(\xi) & 0 \\ w_1 & \langle w, \hat{x} \rangle \end{pmatrix} & \mathbf{0} & \dots & \mathbf{0} & 0 & 0 & \dots & 0 \\ \mathbf{0} & \begin{pmatrix} L_2(\xi) & 0 \\ w_2 & \langle w, \hat{x} \rangle \end{pmatrix} & & \mathbf{0} & 0 & & & 0 \\ \vdots & & \ddots & & \vdots & & & \\ \mathbf{0} & \mathbf{0} & \dots & \begin{pmatrix} L_m(\xi) & 0 \\ w_m & \langle w, \hat{x} \rangle \end{pmatrix} & 0 & 0 & \dots & 0 \\ & \mathbf{X} & & & & \mathbf{Y} & & \end{pmatrix}$$

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

$$\lambda_k^{(1)} = L_k(\xi) \quad \text{and} \quad \lambda_k^{(2)} = -\langle w, \hat{x} \rangle \leq 0. \tag{6.11}$$

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

$$\lambda_k^{(1)} = \frac{1}{\langle w, \hat{x} \rangle} [(A \text{diag}[w] \hat{x})_k - \langle \hat{x}, A \text{diag}[w] \hat{x} \rangle] = \frac{1}{\langle w, \hat{x} \rangle} [(B\hat{x})_k - \langle \hat{x}, B\hat{x} \rangle]. \tag{6.12}$$

Following [50, 56] 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 13. 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 $B = \text{Adiag}[w]$, i.e., if and only if

$$\tilde{\lambda}_k(\xi) \stackrel{\text{def}}{=} (B\hat{x})_k - \langle \hat{x}, B\hat{x} \rangle \leq 0 \quad \text{for all } k \text{ with } \hat{x}_k = 0. \quad (6.13)$$

$b_{ij} > b_{jj}$	$b_{ij} = b_{jj}$	$b_{ij} < b_{jj}$	
$i \bullet \rightleftarrows \bullet j$ Mutualism Symbiosis	$i \bullet \longrightarrow \bullet j$ Commensalism	$i \bullet \rightleftarrows \bullet j$ Parasitism Predator-Prey	$b_{ji} > b_{ii}$
	$i \bullet \quad \bullet j$ Neutralism	$i \bullet \longleftarrow \bullet j$ Amensalism	$b_{ji} = b_{ii}$
		$i \bullet \rightleftarrows \bullet j$ Competition	$b_{ji} < b_{ii}$

Figure 12: The different types of interaction: full arrows indicate $b_{ij} - b_{ii} > 0$, empty arrows $b_{ij} - b_{jj} < 0$.

The matrix $B = \text{Adiag}[w]$ 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 [95] 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 $\vec{\Gamma}(RT)$ associated with the reaction-translation

model (RT) are the replicating species I_1, \dots, 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 12. 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 13.

6.3. 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 translation constants $(w_1, w_2) > 0$. It will be convenient to use the following abbreviations:

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

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

$$\lambda_1^{ext} = \frac{D}{2(c_1 + c_2)} \quad \text{and} \quad \lambda_2^{ext} = -\frac{w_1 w_2 (c_1 + c_2)}{c_1 w_2 + c_2 w_1} \quad (6.14)$$

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

$$\lambda_{3,4} = \frac{-(c_1 + c_2)w_1 w_2 \pm \sqrt{(c_1 + c_2)^2 w_1^2 w_2^2 - 2c_1 c_2 w_1 w_2 (c_1 w_2 + c_2 w_1)}}{2(c_1 w_2 + c_2 w_1)}. \quad (6.15)$$

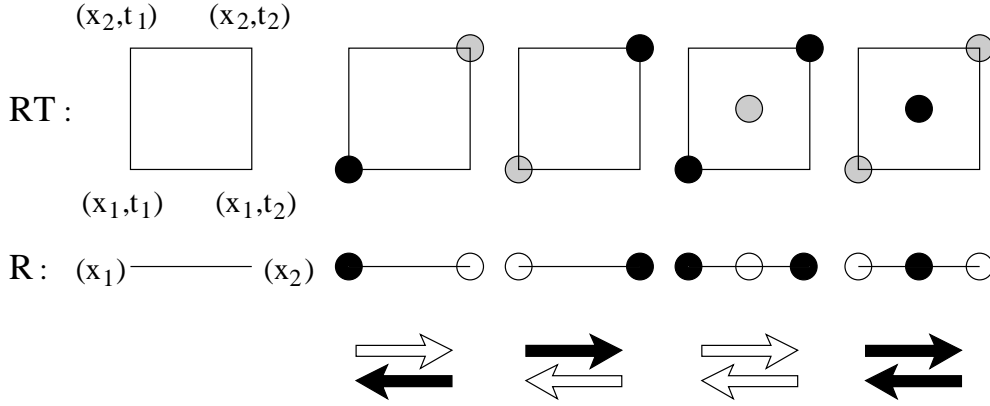


Figure 13: Comparison of the phase portraits of (RT) and (\mathcal{R}). Black circles indicate sinks, gray ones saddle-points, and white ones are sources. The corresponding graph $\vec{\Gamma}(RT)$ is shown below.

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

$$\begin{aligned}
 (1, 1; 0, 0) & : \lambda_1 = -\frac{a_{11}c_1}{c_1 + c_2}, & \lambda_2 = -\frac{c_1c_2}{c_1 + c_2}, \\
 (0, 0; 1, 1) & : \lambda_1 = -\frac{a_{22}c_2}{c_1 + c_2}, & \lambda_2 = -\frac{c_1c_2}{c_1 + c_2}.
 \end{aligned} \tag{6.16}$$

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. 13. They compare directly to the phase portraits of the second order replicator equation with interaction matrix A .

6.4. 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. [56, sect. 12.4].

Lemma 4. *Let $D = \text{diag}[d_1, \dots, d_n]$ be a diagonal matrix with $d_i > 0$. Then there is a diffeomorphism $\mathcal{B} : S_n \rightarrow S_n$ 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 be 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} to the barycenter of the simplex, $\mathcal{B}(\hat{x}) = \frac{1}{n}\mathbf{1}$, 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 14. *Let a_{ij} be an arbitrary matrix, $(x, t) \in S_n \oplus S_n$ and let $(c, d) \in \text{int}(S_n \oplus S_n)$. Then $\mathcal{B} : S_n \oplus S_n \rightarrow S_n \oplus S_n$, $(x, t) \mapsto (u, v)$ defined by*

$$u_i = \frac{c_i x_i}{\sum_j c_j x_j} \quad \text{and} \quad v_i = \frac{d_i t_i}{\sum_j d_j t_j} \quad (6.17)$$

is a diffeomorphism mapping the orbits of

$$\begin{aligned}\dot{x}_k &= x_k \left(\sum_i a_{ki} t_i - \sum_{i,j} x_i a_{ij} t_j \right) \\ \dot{t}_k &= w_k x_k - t_k \sum_i w_i x_i\end{aligned}\tag{6.18}$$

onto the orbits of

$$\begin{aligned}\dot{u}_k &= u_k \left(\sum_i b_{ki} v_i - \sum_i u_i \sum_j b_{ij} v_j \right) \\ \dot{v}_k &= \left(\gamma_k u_k - v_k \sum_j \gamma_j u_j \right) \phi(u, v),\end{aligned}\tag{6.19}$$

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

$$\phi(u, v) = \left(\sum_l \frac{v_l}{d_l} \right)^2 \sum_l \frac{u_l}{c_l} > 0.\tag{6.20}$$

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

$$x_i = \frac{u_i}{c_i} \frac{1}{\sum_j c_j^{-1} u_j} \quad \text{and} \quad t_i = \frac{v_i}{d_i} \frac{1}{\sum_j d_j^{-1} v_j}.\tag{6.21}$$

Differentiating u_i and v_i yields

$$\begin{aligned}\dot{u}_i &= \frac{1}{\left(\sum_j c_j x_j \right)^2} \cdot \left[\dot{x}_i c_i \sum_j c_j x_j - c_i x_i \sum_j c_j \dot{x}_j \right] = \\ &= u_i \left(\sum_j a_{ij} t_j - \sum_j x_j \sum_l a_{jl} t_l \right) = \\ &= u_i \left(\sum_j \frac{a_{ij}}{d_j} v_j - \sum_j u_j \sum_l \frac{a_{jl}}{d_l} v_l \right) \frac{1}{\sum_j d_j^{-1} v_j} \\ \dot{v}_i &= \frac{d_i \dot{t}_i}{\sum_j d_j t_j} - v_i \sum_j \frac{d_j \dot{t}_j}{\sum_l d_l t_l} = \frac{d_i w_i x_i}{\sum_j d_j t_j} - v_i \sum_j \frac{d_j w_j x_j}{\sum_l d_l t_l} \\ &= \left(\frac{d_i w_i}{c_i} u_i - v_i \sum_j \frac{d_j w_j}{c_j} u_j \right) \frac{\sum_j d_j^{-1} v_j}{\sum_j c_j^{-1} u_j}\end{aligned}\tag{6.22}$$

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

$$u_i = \frac{x_i}{\hat{x}_i \sum_j \hat{x}_j^{-1} x_j} \quad \text{and} \quad v_i = \frac{t_i}{\hat{t}_i \sum_j \hat{t}_j^{-1} t_j}. \quad (6.23)$$

Then the fixed point of the dynamical system obtained from (RT) 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 14 one finds immediately

$$\hat{u}_i = \frac{\hat{x}_i}{\hat{x}_i \sum_j \hat{x}_j^{-1} \hat{x}_j} = \frac{1}{n} \quad \text{and} \quad \hat{v}_i = \frac{\hat{t}_i}{\hat{t}_i \sum_j \hat{t}_j^{-1} \hat{t}_j} = \frac{1}{n}. \quad \blacksquare$$

6.5. Competitive Systems

Schlögl [76] investigated two model systems in which the substance X_i is formed from a substrate A via first order and second order autocatalysis, respectively: $A + X_i \rightarrow 2X_i$ (first order autocatalysis) and $A + 2X_i \rightarrow 3X_i$ (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 $A = \text{diag}[k_1, k_2, \dots, k_n]$. Therefore the differential equations for the competitive model simplify to

$$\dot{x}_k = x_k \left[k_k t_k - \sum_j k_j x_j t_j \right] \quad \dot{t}_k = w_k x_k - t_k \sum_j w_j x_j \quad (6.24)$$

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

$$\dot{u}_k = u_i \left[v_i - \sum_j u_j v_j \right] \quad \dot{v}_k = (u_k - v_k) \phi(u, v) \quad (6.25)$$

as a consequence of the barycentric transformation.

The Jacobian matrix of this vector field is readily computed:

$$\begin{aligned}
 \frac{\partial}{\partial u_j} \dot{u}_i &= -u_i v_j \\
 \frac{\partial}{\partial v_j} \dot{u}_i &= -u_i u_j + u_i \delta_{ij} \\
 \frac{\partial}{\partial u_j} \dot{v}_i &= (u_i - v_i) \frac{\partial \phi}{\partial u_j} + \delta_{ij} \phi(u, v) \\
 \frac{\partial}{\partial v_j} \dot{v}_i &= (u_i - v_i) \frac{\partial \phi}{\partial v_j} - \delta_{ij} \phi(u, v)
 \end{aligned} \tag{6.26}$$

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:

$$A = -\frac{1}{n^2}J, \quad B = wI, \quad C = -\frac{1}{n^2}J + \frac{1}{n}I, \quad \text{and} \quad D = -wI, \tag{6.27}$$

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 15. *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*

$$\omega_j^{(k)} = \exp(2\pi i \frac{jk}{n}), \quad \text{for } k = 0, \dots, n-1 \text{ and } j = 1 \dots n \tag{6.28}$$

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

$$M\xi = \begin{pmatrix} M_{11}z_1\omega^{(k)} & M_{12}z_2\omega^{(k)} & \dots & M_{1m}z_m\omega^{(k)} \\ M_{21}z_1\omega^{(k)} & M_{22}z_2\omega^{(k)} & \dots & M_{2m}z_m\omega^{(k)} \\ \vdots & \vdots & & \vdots \\ M_{m1}z_1\omega^{(k)} & M_{m2}z_2\omega^{(k)} & \dots & M_{mm}z_m\omega^{(k)} \end{pmatrix} = (R^{(k)}z) \times \omega^{(k)} = \Lambda^{(k)}\xi. \quad (6.29)$$

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

$$\langle z^{(k,\ell)} \times \omega^{(k)}, z^{(k',\ell')} \times \omega^{(k')} \rangle = \langle z^{(k,\ell)} z^{(k',\ell')} \rangle \langle \omega^{(k)} \omega^{(k')} \rangle = \delta_{\ell,\ell'} \cdot \delta_{k,k'}, \quad (6.30)$$

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 15 we find

$$R^{(0)} = \begin{pmatrix} -\frac{1}{n} & 0 \\ w & -w \end{pmatrix} \quad \text{and} \quad R^{(j)} = \begin{pmatrix} 0 & \frac{1}{n} \\ w & -w \end{pmatrix} \quad (6.31)$$

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

$$\Lambda^{(0,1)} = -\frac{1}{n} \quad \text{and} \quad \Lambda^{(0,2)} = -w. \quad (6.32)$$

The remaining eigenvalues $\Lambda^{(j,\ell)}$ for $1 \leq j < n$ and $\ell = 1, 2$ are now easily computed using theorem 15:

$$\Lambda^{(\pm)} = -\frac{w}{2} \pm \frac{1}{2} \sqrt{w^2 + 4w/n} \quad (6.33)$$

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 $\lambda_k(\xi) = -w < 0$.

6.6. Cooperation

The hypercycle [25] 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 14; consequently, the interaction matrix is circulant, and the corresponding system of differential equations reads:

$$\begin{aligned} \dot{x}_k &= x_k \left[k_k t_{k-1} - \sum_j k_j x_j t_{j-1} \right] \\ \dot{t}_k &= w_k x_k - t_k \sum_j w_j x_j. \end{aligned} \tag{6.34}$$

Again a barycentric transformation yields

$$\begin{aligned} \dot{u}_k &= u_i \left[v_i - \sum_j u_j v_{j-1} \right] \\ \dot{v}_k &= (u_k - v_k) \phi(u, v). \end{aligned} \tag{6.35}$$

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

$$\Lambda^{(0,1)} = -\frac{1}{n} \quad \text{and} \quad \Lambda^{(0,2)} = -w. \tag{6.36}$$

For the remaining eigenvalues we find

$$\Lambda_j^{(\pm)} = -\frac{w}{2} \pm \frac{1}{2} \sqrt{w^2 + \frac{4w}{n} e^{-2\pi j i/n}}, \quad (6.37)$$

and their real parts can be readily computed:

$$\Re(\Lambda_j) = -w + \sqrt{\frac{w}{2}} \sqrt{w + \frac{4}{n} \cos \varphi} + \sqrt{w^2 + \frac{8w}{n} \cos \varphi + \frac{16}{n^2}}. \quad (6.38)$$

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

$$\left(\frac{1}{w}\right)_{crit} = -\frac{1}{n} \frac{\sin^2\left(\frac{2\pi(n-1)j}{n}\right)}{\cos\left(\frac{2\pi(n-1)j}{n}\right)}. \quad (6.39)$$

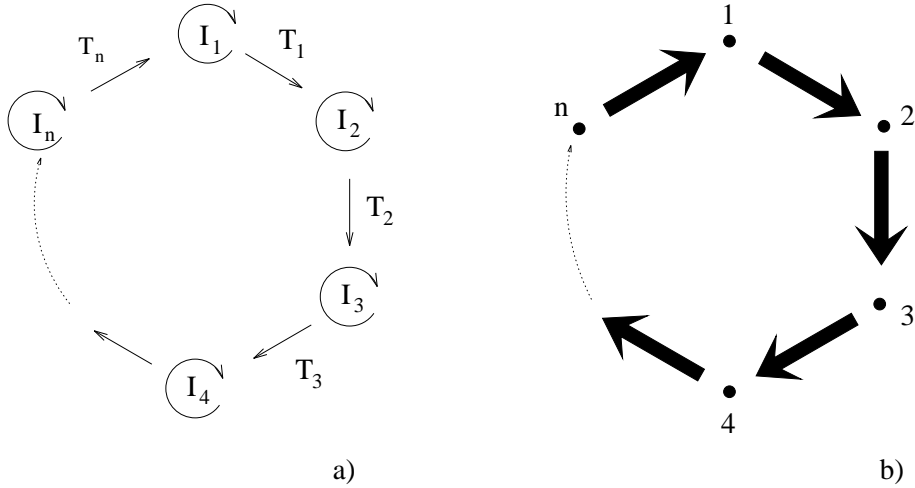


Figure 14: The hypercycle: a) chemical reaction scheme; b) graph representation.

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

For larger systems we find

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

$n = 4, j = \mathfrak{w}_{crit} = 0$. Since we consider only non-zero values of the translation rate, there is in fact no stable fixed point. The corresponding hypercycle equation, however, exhibits a marginally stable fixed point [25].

$n \geq 5$ 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 [52].

All equilibria on the boundary are non-saturated and degenerate, in complete analogy to the situation in the elementary hypercycle [83].

6.7. Reduction to Replicator Equations

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

Theorem 16. *The replication translation model (RT) reduces in the singular limit $w_i \rightarrow \infty$ to the second order replicator equation with interaction matrix $b_{ij} \stackrel{\text{def}}{=} a_{ij}\omega_j$.*

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

$$\begin{aligned} \dot{x}_k &= x_k \left(\sum_i a_{ki} t_i - \sum_i x_i \sum_j a_{ij} t_j \right) \\ \epsilon \dot{t}_k &= \omega_k x_k - t_k \sum_i \omega_i x_i \end{aligned} \tag{6.40}$$

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

$$\left. \frac{\partial \dot{t}_k}{\partial t_j} \right|_{t(x)} = -\frac{1}{\epsilon} \delta_{kj} \sum_i \omega_i x_i. \tag{6.41}$$

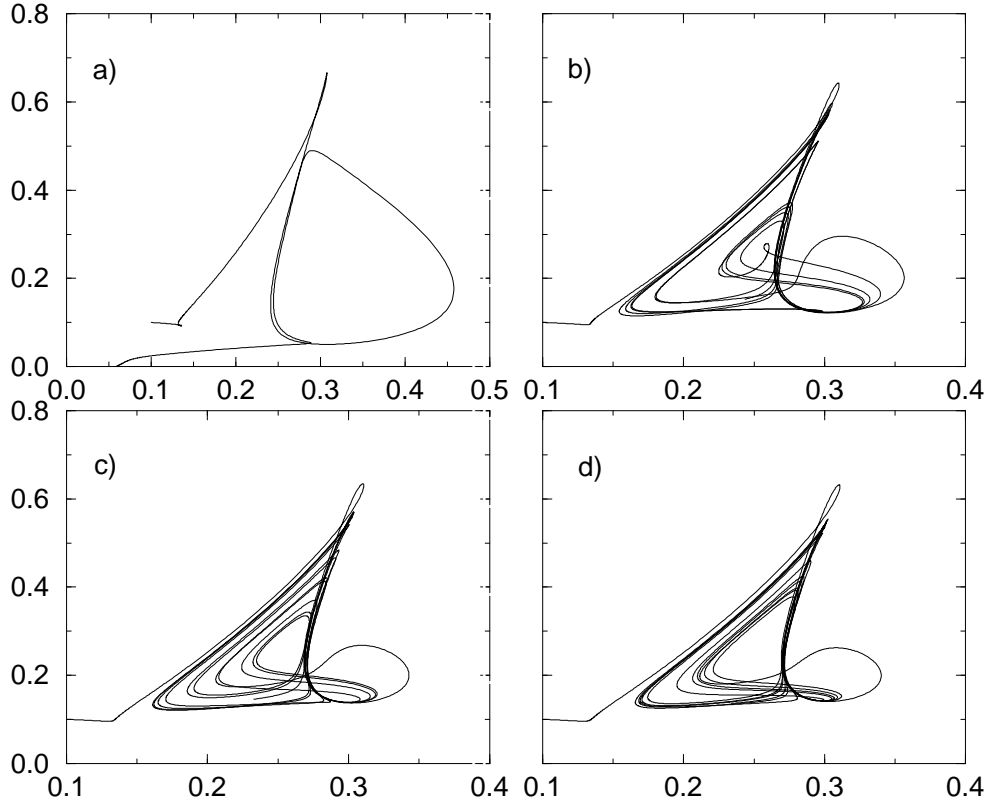


Figure 15: The close relations between (\mathcal{R}) and (RT) are perhaps best exemplified by strange attractors.

Chaotic attractors have been found in three-species Lotka-Volterra equations [36, 103, 5, 4, 102]. Using Hofbauer's transformation [48] 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 [77]. 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 replicator equation.

and hence the singular perturbation problem reduces to

$$\dot{x}_k = \frac{1}{\sum_j \omega_j x_j} x_k \left[\sum_i a_{ki} \omega_i x_i - \sum_{i,j} a_{ij} \omega_j x_j x_i \right]. \quad (6.42)$$

Using $b_{ij} = a_{ij} \omega_j$ 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 4 and 5 show that bifurcations leading away from “replicator like” behavior can occur for slow replication.

7. Replication with Intermediates: Part A

Whether the replicator equation can describe the overall reaction of more involved mechanisms sufficiently well, or not, will be treated on the example of a model with intermediates that are consumed in the course of the reaction. A detailed analysis of this model including stability analysis of analytically treatable cases can be found in [43, 44].

There are three different types of interacting species:

- (i) The replicating species X_i : These species are assumed to be capable of independent replication. In the act of replication the substrate A is used to form X_i , the kinetic constant of this reaction is k_i . Besides, there is an alternative way of formation of X_i , using the intermediates S_l instead of the substrate. The replicating species might represent DNA or RNA strings or simple monocellular organisms such as bacteria etc.
- (ii) The intermediates S_l : They are formed in a catalyzed reaction from the substrate A , using X_l as catalyst. The kinetic constant of this reaction is termed g_l . As mentioned above, the intermediates can be used by the replicating species replacing the substrate A ; the reaction constant of S_l in the reaction of producing X_i is b_{li} .
- (iii) The substrate A : This is the (energy-rich) material from which both the replicating species and the intermediates are built. If the replicating species are RNA molecules, one might think of a solution containing the nucleotide triphosphates.

All reactions are considered to be irreversible. This is, of course, a simplification if we consider chemical kinetics; however, since in many biochemical reactions the forward reaction is much faster than the backward reaction, the effects of neglecting the latter should be negligible.

The reaction scheme (\mathcal{R}) above implies a third order reaction with a rate proportional to $[A][I_k][I_l]$. Since third order reaction kinetics are a rare phenomenon, we replace this simple replication scheme by a two-step mechanism of the form



The intermediate product S_i can be interpreted as a specifically activated form of the substrate. In addition we shall incorporate the first order (uncatalyzed) replication mechanism



The emphasis of this chapter is not on a detailed description of the replication kinetics that was already done by Hecht in his Phd-thesis. We are interested here in the validity and the limits of these simple replicator dynamics. Certainly this model is still much simpler than models of RNA replication kinetics devised by Biebricher [7], but which is complicated enough to show significant deviations from the replicator picture. In fact, the model is simple enough even to allow for an analytical treatment of special limiting cases.

7.1. Model Equations

Assuming mass action kinetics it is straight forward to translate the reaction mechanism ($\mathcal{I}, \mathcal{I}'$) into the kinetic equations

$$\begin{aligned} \dot{x}_i &= x_i \left[ak_i + \sum_{j=1}^n c_{ij}s_j - \Psi \right] \\ \dot{s}_i &= g_i ax_i - s_i \sum_{j=1}^n x_j c_{ij} - s_i \Psi \end{aligned} \quad (7.3)$$

Explicit expressions for substrate concentration a and dilution flux Ψ specify the *dynamical boundary conditions*. In the case of *constant organization* we have $a \equiv 1$

(after a suitable renormalization of the time axis) and $\sum_i (x_i + s_i) = 1$ with a suitable normalization of the concentrations. As a consequence we obtain

$$\Psi_{\text{const.org.}} = a \sum_{j=1}^n (k_j + g_j) x_j = \sum_{j=1}^n \kappa_j x_j \stackrel{\text{def}}{=} \Phi. \quad (7.4)$$

The abbreviation $\kappa_i \stackrel{\text{def}}{=} k_i + g_i$ will be used throughout this manuscript. Note that the form of this flux function is quite different from the quadratic function in the second order replicator equation. Since the overall concentration is held constant, the phase space is the unit simplex

$$\mathbf{S}_{2n} = \left\{ (x_1, \dots, x_n, s_1, \dots, s_n) \mid x_i, s_i \geq 0 \wedge \sum (x_i + s_i) = 1 \right\}.$$

In the CSTR setting we have to take the influence of the substrate explicitly into account. We have $\Psi_{\text{CSTR}} = r$, a constant flux rate, while the building material a satisfies the differential equation

$$\dot{a} = a_0 r - a \left(\sum_{j=1}^n (k_j + g_j) x_j + r \right). \quad (7.5)$$

It is convenient to use the same variable names as in the constant organization setting since most of the results are of a very similar form. The total concentration $c_0 = a + \sum_i (x_i + s_i)$ converges to a_0 . Therefore all fixed points lie on the $2n + 1$ -dimensional simplex

$$\mathbf{S}_{2n+1}(a_0) = \left\{ (x_1, \dots, x_n, s_1, \dots, s_n, a) \mid x_i, s_i, a \geq 0 \wedge a + \sum (x_i + s_i) = a_0 \right\}.$$

From equ.(1-3) we see that if the replicating species X_i vanishes at a certain fixed point, then the corresponding intermediate S_i must also vanish and vice versa. We can therefore characterize a fixed point P_I by its *index set* I , i.e., by the set of the species with positive concentrations at the fixed point. The number of these species is denoted by $|I|$. It will be useful therefore to introduce the following

Definition. An index set I is *admissible* if the corresponding fixed point P_I exists in a non-empty range of total concentrations (or flux rates in the CSTR setting).

7.2. Simplified Examples

As in many other models, e.g., the replicator equation or the replication-translation model, there are two quite simple cases that allow for analytical treatment [43, 44].:

(i) **The Competitive Case**, that was first treated by Schlögl [76], where species are weakly coupled, meaning that no other interactions than competition for the common resources occur. There are close similarities between the CSTR and the constant organization model. Apart from details we observe the same behavior when c_0 is increased or r is decreased, respectively. This does not come as a surprise. For the replicator equation it was shown recently [42] that the CSTR can be viewed as a singularly perturbed constant organization model in the limit $r \rightarrow 0$. In this limit the full capacity of the CSTR is filled with polymeric materials, i.e., $c_0 = \sum_i (x_i + s_i)$ approaches a_0 . We can therefore interpret c_0 and $1/r$ as conceptually the same bifurcation parameter.

Secondly there is a cascade of transcritical bifurcations as c_0 or $1/r$ increases, in which fixed points with an increasing number of species are introduced into the physically meaningful part of the state space. This is due to the fact that c_0 or r affect the relative importance of the first order and the second order reactions. For very small c_0 the first order term dominates which leads to the selection of a single species, i.e., there is a single stable fixed point. In the CSTR only the trivial fixed point is stable if r becomes very large, of course.

For larger c_0 (or small r) the model behaves just like a replicator model: all 1-species equilibria are stable, all other fixed points are unstable. This matches exactly the phase portrait of the Schlögl model [76] in the replicator equation setting. We conclude hence, that the competitive model with intermediates in essence reproduces the behavior of the corresponding inhomogeneous replicator equation [94].

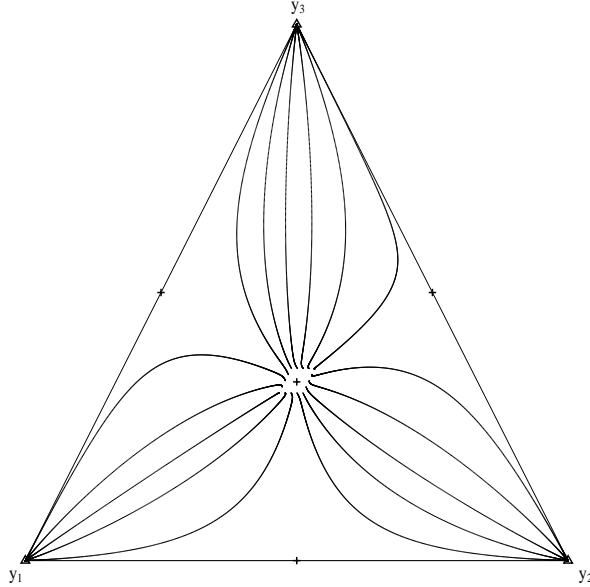


Figure 16: The competitive model with $n=3$ under constant organization, where all constants are equal. The sum $y_i = x_i + s_i$ is shown. The parameters used are: $k = 0.1$, $c_0 = 3$, $f = 1.5$ and $g = 2$.

As in the competitive model there is little difference in the qualitative behavior of CSTR and constant organization. A cascade of transcritical bifurcations introduces fixed points with an increasing number of species into the system as c_0 and $1/r$ increase. These are either stable or associated with stable limit cycles. This phenomenon has been observed in a variety of quite different dynamical systems that describe replication and selection: as the capacity c_0 of the environment increases the number of species that can be sustained increases as well, see e.g., [32, 49, 53, 92].

(ii) **The Mutualistic Model** [22, 23, 24], that admits cooperative behavior and a closed Hamiltonian graph.

Here we observe considerably different phase-portraits than in the “pure” replicator case (see figure 17).

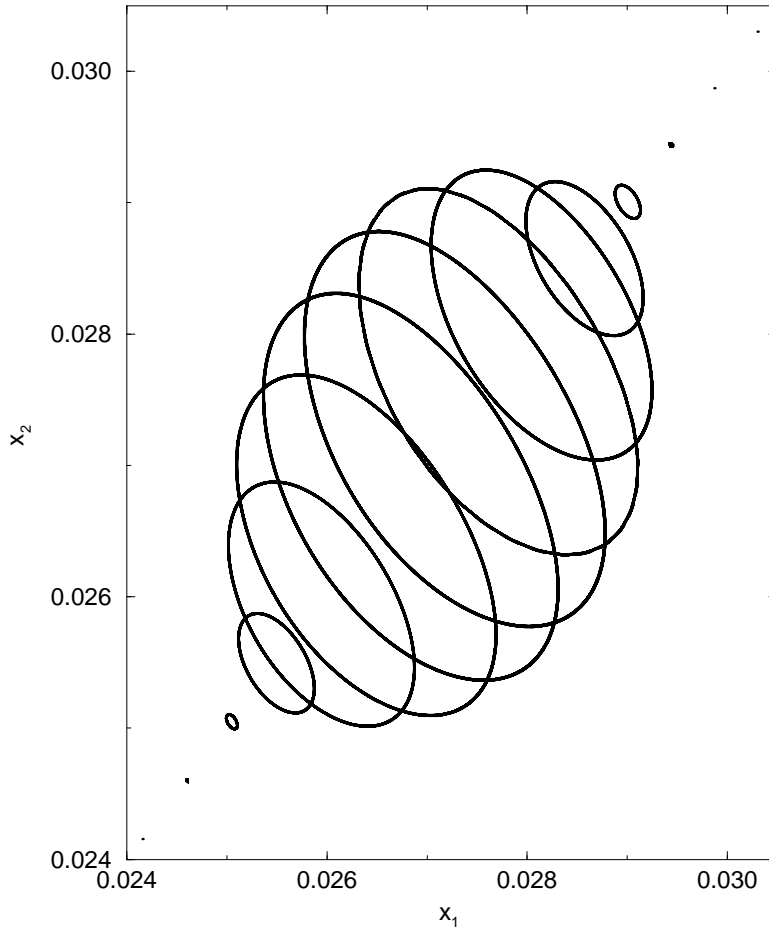


Figure 17: The cooperative model with $n=3$ under constant organization, where all constants are equal. $k = 0.1$, $f = 1.5$, $g = 6.4$ and c_0 ranges from 0.80-1.08 in 0.02 steps from left to right.

The second order replicator equation corresponding to the limit of larger c_0 or small r , respectively, is the elementary hypercycle [25]. Our model exhibits a single, stable interior fixed point in this limit. The elementary hypercycle, on the other hand, shows stable limit cycles for $n > 4$ [52]. In our present model we find stable limit cycles as well. They occur only at intermediate values of the bifurcation parameters, however.

7.3. Singularly Perturbed Cases

Let us now return to the two-step replication mechanism:

Theorem 17. *The dynamical system with intermediates under constant organization*

$$\begin{aligned}\dot{x}_i &= x_i \left(k_i + \sum_j c_{ij} s_j - \sum_j (k_j + g_j) x_j \right) \\ \dot{s}_i &= g_i x_i - s_i \left(\sum_{j=1}^n (k_j + c_{ij} + g_j) x_j \right),\end{aligned}$$

reduces to the inhomogeneous replicator equation

$$\dot{y}_i = y_i \left[k_i + \sum_j c_{ij} y_j - \sum_l y_l \left(k_l + \sum_j c_{lj} y_j \right) \right].$$

in the limit of fast production of the intermediate.

Proof: Let $y_i = \frac{g_i x_i}{\sum_j g_j x_j}$. Then $x_i = \frac{g_i^{-1} y_i}{\sum_j g_j^{-1} y_j}$ and $\sum_j y_j = 1$. A short calculation yields

$$\begin{aligned}\dot{y}_i &= y_i \left\{ k_i + \sum_j c_{ij} s_j - \sum_l y_l \left(k_l + \sum_j c_{lj} s_j \right) \right\} \\ \dot{s}_i &= g_i x_i - s_i \sum_j (k_j + c_{ij} + g_j) x_j\end{aligned}\tag{7.6}$$

Now we set $g_i = \gamma_i/\epsilon$. The second equation becomes

$$\epsilon s_i = \frac{1}{\sum_l y_l / \gamma_l} \left\{ y_i - s_i - \epsilon \frac{s_i}{\gamma_i} (k_j + c_{ij}) \right\}.\tag{7.7}$$

In the limes $\epsilon \rightarrow 0$ this reduces to $s_i = y_i$. In order to verify that this solution is stable we compute the Jacobian

$$\frac{\partial \dot{s}_i}{\partial s_j} = -\delta_{ij} \frac{1}{\epsilon \sum_j \gamma_j^{-1} y_j} \left(\epsilon \sum_j c_{ij} \gamma_j^{-1} y_j + 1 + \epsilon \sum_j k_j \gamma_j^{-1} y_j \right) < 0,$$

which is stable for all y . Thus the above model is in fact a stable singular perturbation of the inhomogeneous replicator equation. ■

Interestingly, the CSTR version of this model does neither reduce to the analogous constant organization equation in the limit $g_i \rightarrow \infty$, nor in the limit $r \rightarrow 0$. Instead we have

Theorem 18. *The dynamical system under CSTR setting*

$$\begin{aligned}\dot{x}_i &= x_i \left(ak_i + \sum_j c_{ij} s_j - r \right) \\ \dot{s}_i &= g_i a x_i - s_i \left(\sum_{j=1}^n c_{ij} x_j + r \right) \\ \dot{a} &= -a \sum_j (k_j + g_j) x_j + r(a_0 - a)\end{aligned}$$

does not reduce to the equivalent replicator setting in the limit of fast production of the intermediates.

Proof: 1.) Let $g_j = \frac{w_j}{\epsilon}$, $G = \sum_j g_j = \frac{\Gamma}{\epsilon}$, and $b = \frac{\Gamma}{\epsilon} a$. Then $a = \frac{\epsilon}{\Gamma} a$. So we get

$$\begin{aligned}\dot{x}_i &= x_i \left(\frac{\epsilon b k_i}{\Gamma} + \sum_j c_{ij} s_j - r \right) \\ \dot{s}_i &= \frac{w_i b x_i}{\Gamma} - s_i \left(\sum_{j=1}^n c_{ij} x_j + r \right), \\ \epsilon \dot{b} &= \Gamma \left(-\frac{\epsilon b}{\Gamma} \sum_j \left(k_j + \frac{w_j}{\epsilon} \right) x_j + r \left(a_0 - \frac{\epsilon b}{\Gamma} \right) \right)\end{aligned}\tag{7.8}$$

In the limit of $\epsilon \rightarrow 0$ we get

$$\begin{aligned}\dot{x}_i &= x_i \left(\sum_j c_{ij} s_j - r \right) \\ \dot{s}_i &= \frac{w_i b x_i}{\Gamma} - s_i \left(\sum_{j=1}^n c_{ij} x_j + r \right). \\ b &= \frac{r a_0 \Gamma}{\sum_j w_j x_j}\end{aligned}\tag{7.9}$$

The Jacobian of the fast variable is stable

$$\frac{\partial \dot{b}}{\partial b} \Big|_x(t) = -\Gamma \left(\sum_j \left(k_j + \frac{w_j}{\epsilon} \right) x_j - \epsilon \right) < 0$$

is stable. The resulting model is

$$\begin{aligned} \dot{x}_i &= x_i \left(\sum_j c_{ij} s_j - r \right) \\ \dot{s}_i &= \frac{w_i r a_0 x_i}{\sum_j w_j x_j} - s_i \left(\sum_{j=1}^n c_{ij} x_j + r \right). \end{aligned} \tag{7.10}$$

■

A different result is obtained from the limit of $r \rightarrow 0$.

Theorem 19. *The dynamical system (1,3) reduces to the non-linear replicator equation*

$$\dot{y}_i = y_i \left[f_i(y) - \sum_j y_j f_j(y) \right] \tag{C}$$

with the response function

$$f_i(y) = k_i + \frac{\sum_j c_{ij} g_j y_j}{\sum_j c_{ij} y_j} \tag{D}$$

in the limit of small flux rates.

Proof: In order to verify that the reaction vessel is completely filled with replicating species and the intermediates we follow the discussion in [42]. We find that a/r remains finite in the limit $r \rightarrow 0$.

Hence we can use the transformation $b = a/r$. Furthermore we set $u_i = s_i/r$ and introduce $\Phi = \sum_j (k_j + g_j) x_j$. This yields

$$\begin{aligned} \dot{x}_i &= x_i \left(k_i + \frac{1}{b} \sum_j c_{ij} u_j - 1 \right) \\ r \dot{u}_i &= g_i x_i - \frac{u_i}{b} \left(\sum_{j=1}^n c_{ij} x_j + r \right), \\ r \dot{a} &= -\Phi + \frac{a_0}{b} - r \end{aligned} \tag{7.13}$$

In the limit $r \rightarrow 0$ we obtain the finite values

$$u_i = \frac{bg_i x_i a_0}{a_0 \sum_j c_{ij} x_j}. \quad (7.14)$$

and $b = a_0/\Phi$. This solution is stable since the Jacobian

$$\begin{aligned} \frac{\partial \dot{u}_i}{\partial u_j} &= -\frac{\delta_{ij}}{r} \left(\sum_j c_{ij} x_j + r \right) & \frac{\partial \dot{b}}{\partial u_j} &= 0 \\ \frac{\partial \dot{u}_i}{\partial b} &= \frac{1}{b^2} \left(\sum_j c_{ij} x_j + r \right) & \frac{\partial \dot{b}}{\partial b} &= -\frac{a_0}{b^2} \end{aligned} \quad (7.15)$$

has block-diagonal form and all eigenvalues are negative for all x . Thus the equation for x becomes

$$\dot{x}_i = x_i \left(k_i + \frac{\sum_j c_{ij} g_j x_j}{\sum_l c_{il} x_l} - \frac{\Phi}{a_0} \right) \quad (7.16)$$

in the singular limit. Introducing the new variables $y_i = x_i / \sum_j x_j$ finally yields a non-linear replicator equation with response function $f_i(y)$. ■

Note that for all $g_i = g$ we have a first order replicator equation with fitness values $k_i + g$.

Another interesting limit is obtained when the replication step is very fast, i.e., if $c_{ij} = d_{ij}/\epsilon$ and $\epsilon \rightarrow 0$. Interestingly, we obtain the same limit as above in this case:

Theorem 20. *The dynamical system (1) in both the constant organization and the CSTR setting reduces to the nonlinear replicator equation (C) with response function (D) in the limit large rate constants c_{ij} .*

Proof: The proof is the same for both the CSTR and the constant organization case. Set Let $c_{ij} = d_{ij}/\epsilon$ and $D_i = \sum_j d_{ij}$ and define $u_i = D_i s_i / \epsilon$. We obtain

$$\begin{aligned} \dot{x}_i &= x_i \left(ak_i + \sum_j \frac{d_{ij} u_j}{D_j} - \Psi \right) \\ \epsilon \dot{u}_i &= D_i \left(g_i a x_i - \frac{\epsilon u_i}{D_i} \left(\sum_{j=1}^n \frac{d_{ij}}{\epsilon} x_j + \Psi \right) \right) \\ \dot{a} &= -a \sum_j (k_j + g_j) x_j + r(a_0 - a) \end{aligned} \quad (7.17)$$

In the limit $\epsilon \rightarrow 0$ we find $\frac{u_i}{D_i} = \frac{g_i a x_i}{\sum_j d_{ij} x_j}$ because

$$\left. \frac{\partial \dot{u}_i}{\partial u_j} \right|_x = -\delta_{ij} u_i \left(\sum_j \frac{d_{ij}}{\epsilon} x_j + \Phi \right) < 0.$$

Thus we obtain for both constant organization and the CSTR

$$\dot{x}_i = x_i \left(a \left(k_i + \frac{\sum_j g_j d_{ij} x_j}{\sum_l d_{il} x_l} \right) - \Psi \right)$$

For the CSTR we have in addition:

$$\dot{a} = -a \sum_j (k_j + g_j) x_j + r(a_0 - a). \quad (7.18)$$


Introducing the rescaled variables by $y_i = x_i / \sum_j x_j$ we find the nonlinear replicator equation with response function

$$k_i + \frac{\sum_j d_{ij} g_j y_j}{\sum_j d_{ij} y_j} = k_i + \frac{\sum_j c_{ij} g_j y_j}{\sum_j c_{ij} y_j} = f_i(y) \quad (7.19)$$

as in the last theorem. ■

Summary: Here, a model with irreversible intermediate reactions is presented. Because it still includes the uncatalyzed reaction step, it is appropriate for very early stages of the RNA-world. The low-molecular support has a crucial role for the mechanism and thus the limits of fast reaction constants yield an intermediate model between first- and second order replicator equations.

8. Replication with Intermediates: Part B

 In this chapter, a different approach to replication is made. Here a Michaelis-Menten type mechanism is assumed. The replicating species reacts slowly and reversibly with the low-molecular substrate to give an activated intermediate that can either dissociate again to leave the react-ands unchanged or yield the replicated product.

As has been shown in the introduction, this kind of mechanism is found with some artificial replicators [91, 105, 106] as well as a model for T-cell growth [17, 67]. The dynamical setup in order to keep away from equilibrium was taken from the two most convenient choice: constant organization and CSTR.

8.1. Constant-Organization

8.1.1. First Order - 1 Intermediate

This is the simplest possible setting. A set of n replicating molecules associates with the low-molecular substrate and duplicates. This model corresponds to a first order replicator model.

Lemma 5. *The simple dynamical system with mass-action kinetics*



under the constraint of constant organization

$$\sum_{j=1}^n x_j + y_j = 1 \quad (8.2)$$

does not have isolated interior equilibria.

Proof: We get the following differential equations:

$$\begin{aligned}\dot{x}_i &= -x_i(\alpha_i + \Phi) + y_i(\beta_i + 2\gamma_i) \\ \dot{y}_i &= \alpha_i x_i - y_i(\beta_i + \gamma_i + \Phi).\end{aligned}\tag{MM1}$$

The flux is readily determined: $\Phi = \sum_j \gamma_j y_j$. The first order MM-type system does not have interior equilibria for non-degenerate reaction constants; At the interior fixed point (\hat{x}, \hat{y}) we find

$$\begin{aligned}\hat{y}_i &= \hat{x}_i \frac{\alpha_i + \hat{\Phi}}{\beta_i + 2\gamma_i} = \hat{x}_i \frac{\alpha_i}{\beta_i + \gamma_i + \hat{\Phi}} \Rightarrow \\ \hat{\Phi} &= -\frac{1}{2} \left(\alpha_i + \beta_i + \gamma_i \pm \sqrt{(\alpha_i + \beta_i)^2 + \gamma_i(6\alpha_i + 2\beta_i + \gamma_i)} \right).\end{aligned}\tag{8.4}$$

So if $\alpha_i = \alpha$, $\beta_i = \beta$ and $\gamma_i = \gamma$ then we have a fixed point line, while in all other cases only one replicator, say k and its intermediate can survive.

$$\begin{aligned}\hat{x}_k &= \frac{1}{2\gamma_k} \left(\alpha_k + \beta_k + 3\gamma_k \pm \sqrt{(\alpha_k + \beta_k)^2 + \gamma_k(6\alpha_k + 2\beta_k + \gamma_k)} \right) \\ \hat{y}_k &= \frac{1}{2\gamma_k} \left(-\alpha_k - \beta_k - \gamma_k \mp \sqrt{4\alpha_k\gamma_k + (\alpha_k + \beta_k + \gamma_k)^2} \right)\end{aligned}\tag{8.5}$$

Only the first of the two possible solutions is the physical meaningful one. ■

Next, let us investigate what happens if the irreversible reaction is fast.

Theorem 21. *The dynamical system (MM1) becomes a replicator system in the limit of $\gamma_i \rightarrow \infty$.*

Proof: After the transformation $z_i = \gamma_i y_i = \frac{w_i}{\epsilon} y_i$ the ODEs are:

$$\begin{aligned}\dot{x}_i &= -x_i \left(\alpha_i + \sum_j z_j \right) + \frac{\epsilon}{w_i} z_i \left(\beta_i + 2\frac{w_i}{\epsilon} \right) \\ \epsilon \dot{z}_i &= w_i \left(\alpha_i x_i - \frac{\epsilon}{w_i} z_i \left(\beta_i + \frac{w_i}{\epsilon} + \sum_j z_j \right) \right)\end{aligned}\tag{8.6}$$

In the limit of $\epsilon \rightarrow 0$ we get the resulting differential algebraic equation (DAE):

$$\begin{aligned}\dot{x}_i &= -x_i \left(\alpha_i + \sum_j z_j \right) + 2z_i \\ 0 &= \alpha_i x_i - z_i\end{aligned}\tag{8.7}$$

In order to find out if this solution is feasible, the Jacobian of the fast variables has to be stable.

$$J = \frac{\partial \dot{z}_i}{\partial z_j} \Big|_{z(x)} = -z_i - \delta_{ij} \left(\beta_i + \frac{w_i}{\epsilon} + \sum_j z_j \right)\tag{8.8}$$

For ϵ small enough the diagonal entries will be strictly diagonally dominant and hence the Jacobian will be stable. Thus we may replace $z_i = \alpha_i x_i$ and get the first order replicator equation

$$\dot{x}_i = x_i \left(\alpha_i - \sum_j \alpha_j x_j \right)$$

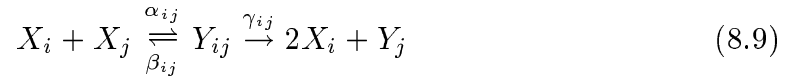
■

8.1.2. Second Order - 1 Intermediate

Because replication without any catalyst is not a very likely process, a second order approach is attempted. Here we assume a series of second order reactions:

- (i) the formation of the complex of replicator and substrate, and
- (ii) the addition of monomers (here taken to be a single step).

Theorem 22. *The dynamical system with mass-action kinetics*



under the constraint of constant organization

$$\sum_j^n x_j + \sum_k^n y_{jk} = 1\tag{8.10}$$

becomes a second order replicator system in the limit of $\gamma_{ij} \rightarrow \infty$.

Proof: The resulting differential equations are:

$$\begin{aligned}\dot{x}_i &= -x_i \left(\sum_j x_j (\alpha_{ij} + \alpha_{ji}) + \Phi(x, y) \right) + \sum_j y_{ij} (\beta_{ij} + 2\gamma_{ij}) + y_{ji} (\beta_{ji} + \gamma_{ji}) \\ \dot{y}_{ij} &= \alpha_{ij} x_i x_j - y_{ij} (\beta_{ij} + \gamma_{ij} + \Phi(x, y))\end{aligned}\tag{MM2}$$

After some unnerving calculations one gets the mean excess production

$$\Phi(x, y) = \sum_j \sum_l y_{jl} (\beta_{jl} + 2\gamma_{jl}) - \alpha_{jl} x_j x_l\tag{8.12}$$

After the transformation $z_{ij} = \gamma_{ij} y_{ij} = \frac{w_{ij}}{\epsilon} y_{ij}$ we get

$$\begin{aligned}\dot{x}_i &= -x_i \left(\sum_j x_j (\alpha_{ij} + \alpha_{ji}) + \phi(x, z) \right) \\ &\quad + \sum_j \frac{\epsilon}{w_{ij}} z_{ij} (\beta_{ij} + 2\frac{w_{ij}}{\epsilon}) + \frac{\epsilon}{w_{ji}} z_{ji} (\beta_{ji} + \frac{w_{ji}}{\epsilon}) \\ \epsilon \dot{z}_{ij} &= w_{ij} \left(\alpha_{ij} x_i x_j - \frac{\epsilon}{w_{ij}} z_{ij} (\beta_{ij} + \frac{w_{ij}}{\epsilon} + \phi(x, z)) \right) \\ \phi(x, z) &= \sum_j \sum_l \frac{\epsilon}{w_{jl}} z_{jl} (\beta_{jl} + 2\frac{w_{jl}}{\epsilon}) - \alpha_{jl} x_j x_l\end{aligned}\tag{8.13}$$

The limit $\epsilon \rightarrow 0$ yields again a differential algebraic equation

$$\begin{aligned}\dot{x}_i &= -x_i \left(\sum_j x_j (\alpha_{ij} + \alpha_{ji}) + \sum_j \sum_l (2z_{jl} - \alpha_{jl} x_j x_l) \right) \\ &\quad + \sum_j (2z_{ij} + z_{ji}) \\ 0 &= \alpha_{ij} x_i x_j - z_{ij}.\end{aligned}\tag{8.14}$$

The calculation of the $n^2 \times n^2$ Jacobian

$$J = \frac{\partial \dot{z}_{ij}}{\partial z_{kl}} \Big|_{z(x)} = -\frac{z_{ij}}{w_{kl}} (\epsilon \beta_{kl} + 2w_{kl}) - \delta_{(ij)(kl)} \left(\beta_{ij} + \frac{w_{ij}}{\epsilon} + \phi(x, z) \right)\tag{8.15}$$

shows that for ϵ small enough the diagonal elements will dominate all other terms and thus we get the second order replicator equation (using $A = \{\alpha_{ij}\}$)

$$\dot{x}_k = x_k ((Ax)_k - \langle x, Ax \rangle).$$

■

Conjecture: The dynamical system (MM2) has at most two inner equilibria.

Numerical experiments, using `Mathematica` suggest that.

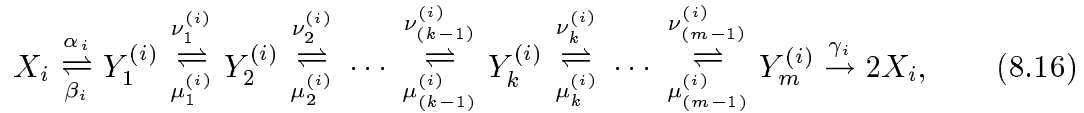
Corollary 3. *In the degenerated case of equal reaction constants $\alpha_{ij} = \alpha$, $\beta_{ij} = \beta$ and $\gamma_{ij} = \gamma$ (MM2) has at most two inner fixed points.*

Proof: Explicit calculations by `Mathematica`. The resulting expressions are *far* too ugly to be displayed here. ■

8.1.3. First Order - m Intermediates

Certainly the elongation of the new strand (even when neglecting complementarity) takes more than a single step. Thus one may ask, whether the model also holds for a more detailed mechanism. Multi-intermediate Michaelis–Menten systems were investigated by [85, 86], but they did neither treat replication, nor open dynamical systems.

So let us take the dynamical system



that describes a multi-intermediate Michaelis–Menten replication System.

Theorem 23. *System (8.16) becomes a first order replicator system in the singular perturbed limit $\gamma_i \rightarrow \infty$.*

Proof: Let us assume mass-action kinetics, as usual. The resulting system of differential equations is then

$$\begin{aligned}
 \dot{x}_i &= -x_i(\alpha_i + \Phi) + y_1^{(i)}\beta_i + 2y_m^{(i)}\gamma_i \\
 \dot{y}_1^{(i)} &= x_i\alpha_i - y_1^{(i)}(\beta_i + \nu_1^{(i)} + \Phi) + y_2^{(i)}\mu_1^{(i)} \\
 \dot{y}_k^{(i)} &= y_{(k-1)}^{(i)}\nu_{(k-1)}^{(i)} - y_k^{(i)}(\nu_k^{(i)} + \mu_{(k-1)}^{(i)} + \Phi) + y_{(k+1)}^{(i)}\mu_k^{(i)} \quad k = 2, \dots, m-1 \\
 \dot{y}_m^{(i)} &= y_{(m-1)}^{(i)}\nu_{(m-1)}^{(i)} - y_m^{(i)}(\gamma_i + \mu_{(m-1)}^{(i)} + \Phi).
 \end{aligned} \tag{MM3}$$

From the boundary condition of constant organization, the flux is derived

$$\sum_j^n \left(x_j + \sum_k^m y_k^{(j)} \right) = 1 \quad \Rightarrow \quad \Phi = \sum_j \gamma_j y_m^{(j)}. \tag{8.18}$$

In order to get a singularly perturbed system, we may apply the substitution

$$z_i^{(i)} = \frac{w_i}{\epsilon} y_i^{(i)}, \tag{8.19}$$

and get the new system of differential equations:

$$\begin{aligned}
 \dot{x}_i &= -x_i(\alpha_i + \sum_j z_m^{(i)}) + \frac{\epsilon z_1^{(i)}}{w_i} \beta_i + 2z_m^{(i)} \\
 \epsilon \dot{z}_1^{(i)} &= w_i \left(x_i \alpha_i - \frac{\epsilon z_1^{(i)}}{w_i} \left(\beta_i + \nu_1^{(i)} + \sum_j z_m^{(i)} \right) + \frac{\epsilon z_2^{(i)}}{w_i} \mu_1^{(i)} \right) \\
 \epsilon \dot{z}_k^{(i)} &= w_i \left(\frac{\epsilon z_{k-1}^{(i)}}{w_i} \nu_{k-1}^{(i)} - \frac{\epsilon z_k^{(i)}}{w_i} \left(\nu_k^{(i)} + \mu_{k-1}^{(i)} + \sum_j z_m^{(i)} \right) + \frac{\epsilon z_{k+1}^{(i)}}{w_i} \mu_k^{(i)} \right) \\
 \epsilon \dot{z}_m^{(i)} &= w_i \left(\frac{\epsilon z_{m-1}^{(i)}}{w_i} \nu_{m-1}^{(i)} - \frac{\epsilon z_m^{(i)}}{w_i} \left(\frac{w_i}{\epsilon} + \mu_{m-1}^{(i)} + \sum_j z_m^{(i)} \right) \right)
 \end{aligned} \tag{8.20}$$

The limit $\epsilon \rightarrow 0$ leaves a simple differential algebraic equation

$$\begin{aligned}
 \dot{x}_i &= -x_i(\alpha_i + \sum_j z_m^{(i)}) + 2z_m^{(i)} \\
 0 &= x_i \alpha_i - z_m^{(i)}.
 \end{aligned} \tag{8.21}$$

The Jacobian

$$\frac{\partial z_m^{(i)}}{\partial z_m^j} \Big|_x = -\frac{w_i}{\epsilon} \left(\frac{\epsilon z_m^{(i)}}{w_i} + \delta_{ij} \left(\frac{w_i}{\epsilon} + \mu_{m-1}^{(i)} + \sum_j z_m^{(i)} \right) \right)$$

is diagonally dominant for ϵ small enough and what we get is the first order replicator equation

$$\dot{x}_i = x_i \left(\alpha_i - \sum_j \alpha_j x_j \right).$$

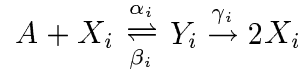
■

8.2. CSTR

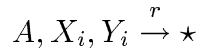
Just as under constant organization, the same phenomena are likely to happen in a CSTR.

8.2.1. First Order - 1 Intermediate

Theorem 24. *The dynamical system with mass-action kinetics*



in the continuously stirred tank reactor (CSTR)



becomes a CSTR-replicator system in the limit of $\gamma_i \rightarrow \infty$.

Proof: The sets of differential equations are now:

$$\begin{aligned} \dot{x}_i &= -x_i(a\alpha_i + r) + y_i(\beta_i + 2\gamma_i) \\ \dot{y}_i &= a\alpha_i x_i - y_i(\beta_i + \gamma_i + r) \\ \dot{a} &= -a \sum_j \alpha_j x_j + \sum_j \beta_j y_j + r(a_0 - a) \end{aligned} \tag{MC1}$$

The same procedure as under constant organization yields the desired results. By change of coordinates $z_i = \frac{w_i y_i}{\epsilon}$ we get in the limit of $\epsilon \rightarrow 0$

$$\begin{aligned}\dot{x}_i &= -x_i(a\alpha_i + r) + 2z_i \\ 0 &= a\alpha_i x_i - z_i\end{aligned}\tag{8.23}$$

Since

$$\left. \frac{\partial \dot{z}_i}{\partial z_j} \right|_x = -\delta_{ij}(\beta_i + \gamma_i + r)\tag{8.24}$$

is stable, we get

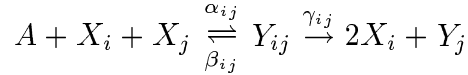
$$\begin{aligned}\dot{x}_i &= x_i(a\alpha_i - r) \\ \dot{a} &= -a \sum_j \alpha_j x_j + r(a_0 - a).\end{aligned}\tag{8.25}$$

These are the differential equations that correspond to a replicator setting in a CSTR. A second change of variables ($\xi_i = \frac{x_i}{\sum_j x_j}$) yields then the replicator-equation [81]: ■

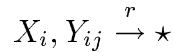
8.2.2. Second Order - 1 Intermediate

The second order case very much resembles constant organization.

Theorem 25. *The dynamical system with mass-action kinetics*



under the boundary conditions of a CSTR



becomes a replicator system in the limit of $\gamma_{ij} \rightarrow \infty$.

Proof: The differential equations are

$$\begin{aligned}\dot{x}_i &= -x_i \left(a \sum_j x_j (\alpha_{ij} + \alpha_{ji}) + r \right) + \sum_j y_{ij} (\beta_{ij} + 2\gamma_{ij}) + y_{ji} (\beta_{ji} + \gamma_{ji}) \\ \dot{y}_{ij} &= a\alpha_{ij} x_i x_j - y_{ij} (\beta_{ij} + \gamma_{ij} + r) \\ \dot{a} &= -a \sum_{i,j} \alpha_{ij} x_i x_j + \sum_{ij} \beta_{ij} y_{ij} + r(a_0 - a)\end{aligned}\tag{MC2}$$

Let $z_{ij} = \frac{w_{ij}y_{ij}}{\epsilon}$. In the limit of $\epsilon \rightarrow 0$ we get

$$\begin{aligned}\dot{x}_i &= -x_i \left(a \sum_j x_j (\alpha_{ij} + \alpha_{ji}) + r \right) + 2 \sum_j z_{ij} + \sum_j z_{ji} \\ 0 &= a \alpha_{ij} x_i x_j - z_{ij} \\ \dot{a} &= -a \sum_{i,j} \alpha_{ij} x_i x_j + r(a_0 - a)\end{aligned}\tag{8.27}$$

The fast variables are clearly stable and we finally get

$$\begin{aligned}\dot{x}_i &= x_i \left(a \sum_j \alpha_{ij} x_i x_j - r \right) \\ \dot{a} &= -a \sum_{i,j} \alpha_{ij} x_i x_j + r(a_0 - a)\end{aligned}\tag{8.28}$$

By change of coordinates follows the replicator equation. ■

Summary: Replication requires the successful incorporation of many nucleotides to produce a copy of the original source. Since Michaelis and Menten, their proposed mechanism of enzyme-action is a well-accepted paradigm of biochemical reactions. Therefore, this kind of mechanism was used to model replication processes that avoid the necessity of third order kinetics. Moreover, recent attempts to introduce artificial chemical replicators have yielded very similar mechanisms [91, 105, 106, 16].

For this kind of models, the replicator equation is a very good approximation in the case that the formation of the product is a very quick process, while the formation of the template–nucleotide complex is much slower.

9. The Probability of Permanence



he Jansen conditions [62] (see also chap. 3) provide an algorithm which does not characterize permanence, not even in the generic cases, but which allows to calculate bounds on the probability for an arbitrary second order replicator network to be permanent.

Table 1. Probability Density functions *.

	A	B^\dagger
Normal	$\frac{1}{\sqrt{\pi}} \exp -x^2/2$	$\frac{1}{\sqrt{2\pi}} \exp -x^2/4$
Uniform	$\frac{1}{2}$ for $x \in [-1, 1]$ 0 otherwise	$1 + x/2$ for $x \in [-2, 0]$ $1 - x/2$ for $x \in [0, 2]$ 0 otherwise
Cauchy	$\frac{1}{\pi} \frac{1}{1+x^2}$	$\frac{1}{\pi} \frac{2}{4+x^2}$
Laplace	$\frac{1}{2} \exp - x $	

* All calculations have been performed for the replicator model (SR) (column A). The results carry over to Lotka Volterra (LV) models with somewhat different distribution functions of the coefficients (column B).

† off-diagonal elements only. r and the diagonal elements of B have the same distribution as A .

We assume that the entries in interaction matrices A (in normal form) are random variables with a given probability distribution. The assumption of normal form only implies that there is nothing special with the replication of an entity X with itself as catalyst compared to its replication with the aid of other catalysts. Since the flow of the replicator equation does not change when the r.h.s. of equ.(SR) is multiplied by a positive constant we may assume that the measure for the width of the distribution is unity provided the mean is zero.

The following theorem is repeated from section 3 (Thm.9).

Theorem 26. (Hofbauer and Sigmund [50, 55]) *If the second order replicator equation (SR) is permanent and A is in normal form then the following conditions are fulfilled:*

- (i) *There is a unique interior equilibrium $\hat{x} \in \text{int} S_n$*
- (ii) $\Phi(\hat{x}) = \sum_{j=1}^n a_{ij} \hat{x}_i \hat{x}_j > 0$
- (iii) $(-1)^{n-1} \det A > 0$.
- (iv) *There is no regular saturated rest point in ∂S_n .*

As stated in section 3, a matrix A that fulfills (i) and (ii) is *type-a*, if (iii) also holds we call it *type-b* and if finally all four necessary conditions are fulfilled we call A a *type-c matrix*.

9.1. Numerical Survey

For our numerical survey we use

- (i) the Gaussian normal distribution $N(0; 1)$ with mean 0 and variance 1;
- (ii) the uniform distribution $U(-1; 1)$ on the interval $[-1, 1]$;
- (iii) the Cauchy distribution $C(0; 1)$ with zero mean and parameter 1.
- (iv) the Laplace distribution $L(0; 1)$ with zero mean and unit parameter.

For each of these distributions we expect the probability to find an interior equilibrium in $\text{int} S_n$ to be

$$\text{prob}\{\hat{x} \in \text{int} S_n\} = 1/2^{n-1} \tag{9.1}$$

since the replicator equation (SR) is topologically equivalent to a Lotka Volterra equation in $n - 1$ dimensions. To find the interior equilibrium of this differential equation we have to find a solution $By = r$ where the entries in B and r are independent random variables with zero mean. Thus the solution y lies in each orthant with equal probability, i.e. with probability $1/2^{n-1}$.

Table 2. Numerical survey for permanence using 1,000,000 random matrices with zero diagonal.*

(1) <i>n</i>	(2) <i>p</i>	(3) int. equil.	(4) <i>type a</i>	(5) <i>type b</i>	(6) <i>type c</i>	(8) undec.	(9) type j
2	<i>th.</i>	500,000	250,000	250,000	250,000	0	250,000
3	<i>N^a</i>	249,730	125,214	69,926	66,954	0	66,954
	<i>U^b</i>	249,860	124,190	66,520	64,330	0	64,330
	<i>C^b</i>	250,550	126,340	74,670	70,780	0	70,780
	<i>L^b</i>	250,370	123,710	71,220	67,630	0	67,630
4	<i>N^a</i>	124,316	62,408	31,274	16,864	5,334	11,530
	<i>U^a</i>	124,758	62,358	31,458	16,028	5,948	10,080
	<i>C^a</i>	124,984	62,296	31,846	19,022	4,330	14,692
	<i>L</i>	124,642	62,455	31,696	18,098	5,077	13,021
5	<i>N^c</i>	62,192	31,256	15,880	4,492	3,024	1,468
	<i>U^a</i>	62,112	31,222	15,652	4,134	3,030	1,104
	<i>C</i>	62,456	31,327	15,748	5,404	2,685	2,719
	<i>L</i>	62,426	31,381	15,676	4,704	2,921	1,783
6	<i>N</i>	31,159	15,451	7,707	1,075	965	110
	<i>U</i>	31,487	15,735	8,004	1,001	938	63
	<i>C</i>	31,307	15,649	7,819	1,412	1,022	390
	<i>L</i>	31,127	15,647	7,794	1,101	999	156
7	<i>N</i>	15,682	7,826	3,969	280	276	4
	<i>U</i>	15,522	7,731	3,917	234	232	2
	<i>C</i>	15,579	7,826	3,936	396	236	50
	<i>L</i>	15,403	7,721	3,839	290	275	15
8	<i>N</i>	7,832	3,884	1,927	48	48	0
	<i>U</i>	7,785	3,940	1,960	65	65	0
	<i>C</i>	7,770	3,962	2,075	116	109	7
	<i>L</i>	7,636	3,823	1,894	67	67	0
9	<i>N</i>	3,889	1,920	964	11	11	0
	<i>U</i>	4,034	2,046	1,026	8	8	0
	<i>C</i>	3,962	1,966	1,003	18	18	0
	<i>L</i>	3,883	1,931	955	4	4	0
10	<i>N</i>	1,989	993	506	6	6	0
	<i>U</i>	1,942	943	464	4	4	0
	<i>C</i>	1,945	975	487	9	9	0
	<i>L</i>	1,953	987	501	4	4	0

* Column (1) and (2) indicate dimension of the matrices and density function. Columns (3) through (7) contain the number of matrices fulfilling criterion (*n*) and all previous ones. Columns (8) and (9) give the number of undecidable cases and of permanent matrices, resp. (see also fig.1)

^{a-c} Calculated from smaller sample sizes and multiplied by a factor of (a) 2, (b) 10, (c) 4 in order to facilitate comparison.

Note that because of the flow equivalence pointed out in section 3 our estimates for the probability of permanence also apply to Lotka-Volterra (LV) equations with

one dimension less and

$$r_k = a_{kn}, \quad b_{ij} = a_{ij} - a_{nj}$$

However, the probability distributions are not the same for the elements of A in the replicator equation and for the off-diagonal elements of B in the Lotka-Volterra model. Table 1 lists the density functions used in this contribution.

The probability for the quadratic form xAx and $\det A$ to have a certain sign is clearly $1/2$. Note that these probabilities need not be independent of the existence of an interior equilibrium. In fact, if there is an interior rest point for $n = 2$, then $xAx > 0$ and $\det A < 0$ are equivalent. For larger n , however, these two conditions become more and more independent (*cf.* table 2 and figure 16). The conditions (i), (ii) and (iii) in Theorem (3.17) are readily checked within polynomial time.

All numerical calculations in this contribution have been performed on IBM 3090 mainframes in Vienna and Göttingen. As programming language FORTRAN has been used and various subroutines (random number generators, solving of linear equations, determinant of a matrix and the simplex algorithm) have been taken from the library package NAGLIB. Our numerical results (table 2) show that

$$\text{Prob}\{A \text{ is "type-b"}\} \approx 2^{-(n+1)} \tag{9.2}$$

for large n .

The probability that there is no saturated rest point on the boundary cannot be estimated easily since the events "rest point $x(K) \in S_n$ " and " $x(K)$ is saturated" are not independent. In fact there is always at least one saturated rest point for the replicator equation (R). Numerical results (tab.2) suggest

$$\text{Prob}\{A \text{ is "type-c"}\} \approx 4^{-n} \tag{9.3}$$

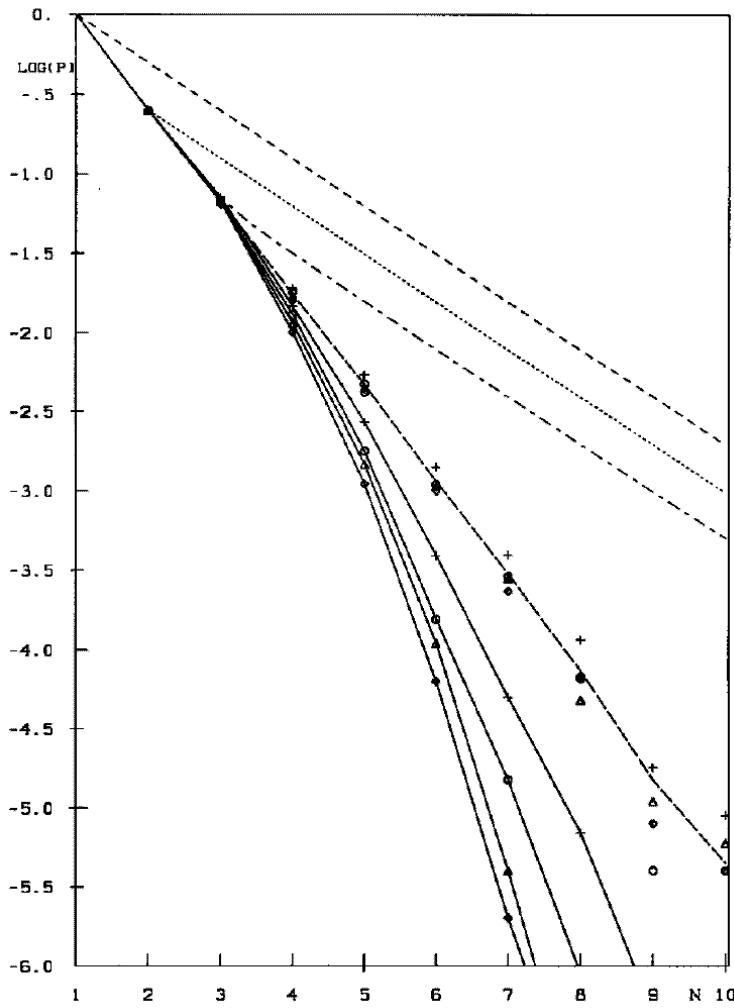


Figure 18: Probability for Permanence. The probabilities for an internal equilibrium (dashed line) and the appropriate signs of $\text{Tr}J$ (dotted line) and $\det A$ (dash-dotted line) are equal for all density functions. The dashed line with narrow spaces gives the average of the probabilities for type-c matrices and the solid line shows the probabilities for type-j matrices for different density functions: Gaussian (\triangle), uniform (\diamond), Cauchy ($+$) and Laplace (\circ).

9.2. Special Types of Interaction Matrices

In this section we investigate two special sign patterns of the interaction matrix. The first class consists of *catalytic networks* [1]-[56]: $a_{ij} \geq 0$ for $i \neq j$ and $a_{jj} = 0$. Table 3 lists results for them. We remark that the probability for an arbitrary

interaction matrix to be a catalytic network is $2^{-n(n-1)}$.

For small catalytic networks there is an algebraic characterization of permanence. Note that whenever there is an interior equilibrium \hat{x} of (SR) with $A \geq 0$ then $(\hat{x}A\hat{x})$ is strictly positive.

- n=2 The network is permanent iff the non-diagonal elements of A are strictly positive.
- n=3 The network is permanent iff there is an interior rest point.
- n=4 The network is permanent iff A is of “type c”.

Catalytic networks have been investigated for two distinct probability distributions, a uniform distribution on the unit interval and an exponential distribution with parameter 1. We find that permanence is a relatively probable property compared to permanence in a sample of random matrices.

The second class consists of *essentially hypercyclic networks*, i.e. matrices which, after a suitable permutation of indices, have the following sign pattern

$$A = \begin{pmatrix} 0 & - & - & \dots & - & + \\ + & 0 & - & \dots & - & - \\ - & + & 0 & \dots & - & - \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots \\ - & - & - & \dots & 0 & - \\ - & - & - & \dots & + & 0 \end{pmatrix} \tag{9.4}$$

For such matrices permanence can be characterized in terms of M-matrices.

Theorem 27. (Amann and Hofbauer [2]) *Let A be as in equ. 9.4. Then the following statements are equivalent:*

- (i) *The second order replicator equation with interaction matrix A is permanent.*
- (ii) *The matrix C obtained by moving the top row of A to the bottom is an M-matrix.*
- (iii) *The second order replicator equation has an interior equilibrium \hat{x} and $(\hat{x}A\hat{x}) > 0$.*

Table 3. Numerical survey for permanence in 1×10^5 random matrices with zero diagonal and positive non-diagonal entries (catalytic networks)*.

(1) n	(2) p	(3) int. equil.	(4) $\det A$	(5) sat.bd.	(6) undec.	(7) perm.
2	$th.$	100,000	100,000	100,000	0	100,000
3	U_+	62,615	62,615	62,615	0	62,615
	E	46,070	46,070	46,070	0	46,070
4	U_+	34,403	33,457	33,457	0	33,457
	E	20,785	20,785	18,238	0	18,238
5	U_+	17,577	16,080	16,014	0	16,014
	E	9,781	7,171	6,952	16	6,936
6	U_+	8,746	7,385	7,260	40	7,220
	E	4,612	2,861	2,502	110	2,392
7	U_+	4,391	3,318	3,134	73	3,061
	E	2,257	1,263	921	116	805
8	U_+	2,163	1,429	1,280	87	1,193
	E	1,112	599	332	102	230
9	U_+	1,080	667	499	90	419
	E^a	560 ₅	299 ₅	125	74	51
10	U_+	529	286	175	55	120
	E^a	285 ₅	142 ₅	39	29 ₅	9 ₅
11	U_+	279	165	91	40	51
	E^a	127	65 ₅	12 ₅	11 ₅	1
12	U_+^a	116 ₅	57	29	20	9
	E^a	61 ₅	31	4	4	0

* A uniform distribution on the unit-interval, U_+ , and an exponential distribution with parameter 1, E , was used. As for table 2, columns (3) through (7) display the numbers of matrices passing subsequent “filters” requiring interior equilibria (3), the correct sign of $\det A$ (4) and the absence (5) of saturated rest points on the boundary of S_n . Columns (6) and (7) show the numbers of permanent and undecidable *type-c* matrices.

^a calculated from 200,000 matrices

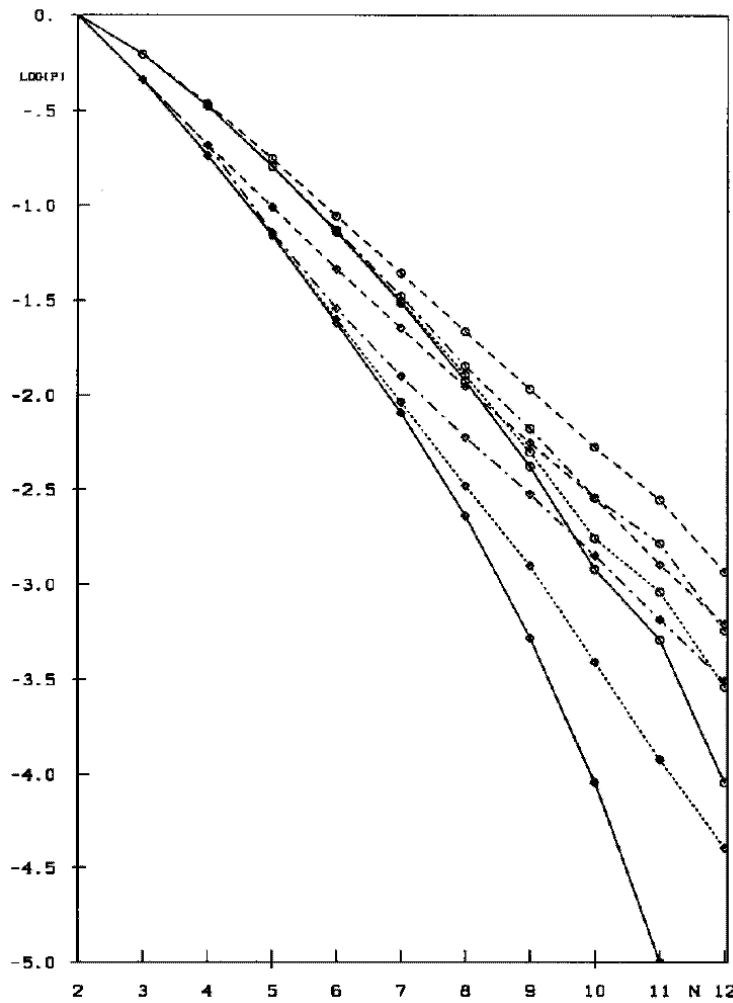


Figure 19: Permanence for Catalytic Networks. The dashed line refers to the probability for an interior rest point, the dash-dotted line accounts for the appropriate sign of $\det A$, the dotted line corresponds to the probability of type-c matrices and the solid line refers to the probability of type-j matrices. Data are shown for the uniform distribution \diamond and the exponential distribution \circ .

For $n = 2$ all essentially hypercyclic systems are permanent. For $n = 3$ there is always an interior equilibrium \hat{x} . It is stable iff $\det A$ is positive. With $p_i, n_i > 0$ and thus

$$A = \begin{pmatrix} 0 & -n_1 & p_3 \\ p_1 & 0 & -n_2 \\ -n_3 & p_2 & 0 \end{pmatrix} \quad (9.5)$$

we find $\det A = p_1 p_2 p_3 - n_1 n_2 n_3$. Therefore the replicator equation is permanent

Table 4. Numerical survey for permanence in 100,000 random *essentially hypercyclic* matrices for three different probability distributions of $|a_{ij}|$, $i \neq j$.

(1)	(2) (3)		(4) (5)		(6) (7)	
n	<i>uniform</i>		<i>Gaussian</i>		<i>exponential</i>	
	equil.	perm.	equil.	perm.	equil.	perm.
3	100,000	49,927	100,000	50,219	100,000	49,852
4	70,717	2,706	62,691	4,233	55,622	5,836
5^a	56,715	8_3	43,649	57_7	33,506	229_2
6^a	38,036	0	25,323	0_2	17,097	2_6
7^b	25,430	0	17,097	0	14,423	0

^a calculated from 10^6 matrices.
^b calculated from $3 \cdot 10^5$ matrices.

with probability $1/2$.

Numerical results are shown in table 4. Note that although these matrices are closely related to the paradigm of permanence – the hypercycle – it is extremely unlikely to find cooperative behavior for $n > 5$ for this type of interaction. The reason for this is the large number of negative entries in A likely to violate condition (ii) of theorem (3.17).

Note that if A is a *nonpositive* matrix the corresponding network may not be permanent since in this case the quadratic form (xAx) is nonpositive on S_n contradicting condition (ii) of theorem (3.17).

9.3. Permanence and Graphs

Definition. Let $A \in \mathbb{R}^{n \times n}$ with zero diagonal. By A^\ddagger we denote the positive part of A , i.e. $a_{ij}^\ddagger = a_{ij}$ if $a_{ij} \geq 0$ and $a_{ij}^\ddagger = 0$ if $a_{ij} < 0$. Let $G(A)$ be the directed graph associated with the nonnegative matrix A^\ddagger .

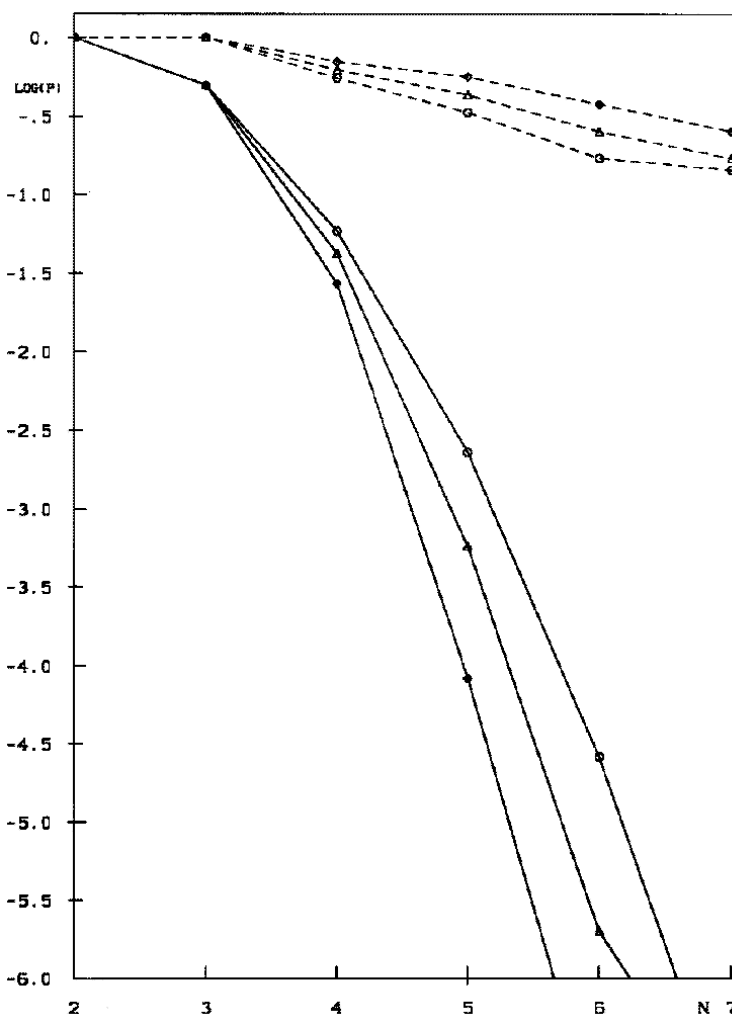


Figure 20: Permanence for essentially hypercyclic networks. The probability for an interior rest point (dashed line) and for permanence (solid line) shown for Gaussian distribution (\triangle), uniform distribution (\diamond) and exponential distribution (\circ).

Conjecture. (Jansen) If the second order replicator equation with interaction matrix A in normal form is permanent, then $G(A)$ is strongly connected, i.e. A^\ddagger is irreducible.

This conjecture has been proven for catalytic networks ($A = A^\ddagger$) by Sigmund and Schuster [88]. We tested all permanent and undecidable matrices produced by our simulations for irreducibility. The results are tabulated in tab.5. Indeed, there are no reducible matrices among all the thousands of permanent matrices

Table 5. Permanence and graphs.*

(1) n	(2) t	(3) Gaussian		(5) Uniform		(7) Cauchy		(9) Laplace	
		n.h.	red.	n.h.	red.	n.h.	red.	n.h.	red.
2	p	0	0	0	0	0	0	0	0
3	p	0	0	0	0	0	0	0	0
4	p	3.8	0	1.2	0	7.8	0	5.4	0
4	u	16	0	9	0	40	0	25	0
5	p	5	0	2	0	9	0	3	0
5	u	13	0	12	0	37	0	23	0
6	p	—	0	—	0	—	0	6	0
6	u	5	0	2	0	2	0	14	0

* Columns (3) through (10) give the probability for finding permanent p (or undecidable u) matrices which contain no Hamiltonian circle (n.h.) or which are reducible (red). Probabilities are given in promille.

we produced.

A directed graph is said to be *Hamiltonian* if it contains a closed circuit visiting every vertex exactly once. For $G(A)$ this means that the Hypercycle would be a subgraph.

Theorem 28. *If a catalytic network with $n \leq 5$ is permanent, then its graph is Hamiltonian.*

The above theorem due to Amann [56] motivated us to look for Hamiltonian circles in the graphs $G(A)$ of permanent and undecidable matrices although we did not expect that an analogue to theorem 28 holds for general networks, since for $n \geq 6$ counterexamples are known [1, 56].

We find that there are indeed permanent matrices with $n \geq 4$ for which $G(A)$ is not Hamiltonian corresponding to many different graphs even for small n . The overwhelming majority of permanent networks however is Hamiltonian. (*cf.* tab.5).

For $n = 3$ there are only non-robust permanent networks with non-hamiltonian

graph. This follows from the classification for $n = 3$ [95]. We thus expect probability 0 for finding such a network.

9.4. Permanence and Connectivity

Definition. Let $A \in \mathbb{R}^n$ with zero diagonal entries and m be the number of positive entries in A ; equivalently m is the number of edges in $G(A)$. We define the *connectivity* of A by

$$\mathcal{C}(A) = \frac{m}{n(n-1)} \tag{9.6}$$

The probability for finding a matrix A with connectivity $\mathcal{C}(A) = \frac{k}{n(n-1)}$ is clearly

$$\pi_k = \frac{1}{2^{n(n-1)}} \binom{n(n-1)}{k} \tag{9.7}$$

Let p_k be the probability that a matrix with connectivity $k/n(n-1)$ is permanent and let N_k be the number of permanent matrices with connectivity this among a sample of M random matrices. We may then estimate p_k by

$$p_k = \frac{N_k}{M\pi_k} \tag{9.8}$$

Since most matrices have a connectivity around $1/2$ we can expect sufficiently large values of N_k only in this region. Our simulations however provide data for catalytic networks and for essentially hypercyclic networks. It is clear that

$$p_{n(n-1)} = p_{\text{CN}}$$

the probability for finding a permanent catalytic network.

If we assume that Jansen's Conjecture is true at least in the generic cases we may estimate p_n from p_{EH} , the probability for finding a permanent essentially hypercyclic network. There are exactly $(n-1)!$ permutations for the signature

Table 6. Permanence and connectivity for $n = 3, 4$ and 5 *.

(1)	(2)	(3)	(4)	(5)	(6)
n	$c(A)$	Gaussian	Uniform	Cauchy	Laplace
3	0.50*	$5 \cdot 10^{-2}$	$5 \cdot 10^{-2}$	$5 \cdot 10^{-2}$	$5 \cdot 10^{-2}$
	0.66	$1.12 \cdot 10^{-1}$	$1.02 \cdot 10^{-1}$	$1.31 \cdot 10^{-1}$	$1.23 \cdot 10^{-1}$
	0.83	$1.76 \cdot 10^{-1}$	$1.62 \cdot 10^{-1}$	$1.89 \cdot 10^{-1}$	$1.78 \cdot 10^{-1}$
	1.00	$5.36 \cdot 10^{-1}$	$5.83 \cdot 10^{-1}$	$3.90 \cdot 10^{-1}$	$4.61 \cdot 10^{-1}$
4	0.33*	$4.23 \cdot 10^{-4}$	$3.28 \cdot 10^{-4}$	—	$7.1 \cdot 10^{-4}$
	0.42	$1.9 \cdot 10^{-3}$	$1.3 \cdot 10^{-3}$	$3.6 \cdot 10^{-3}$	$4.3 \cdot 10^{-3}$
	0.50	$5.3 \cdot 10^{-3}$	$3.7 \cdot 10^{-3}$	$8.7 \cdot 10^{-3}$	$1.26 \cdot 10^{-2}$
	0.58	$1.32 \cdot 10^{-2}$	$9.8 \cdot 10^{-3}$	$1.86 \cdot 10^{-2}$	$2.51 \cdot 10^{-2}$
	0.67	$2.1 \cdot 10^{-2}$	$2.41 \cdot 10^{-2}$	$3.34 \cdot 10^{-2}$	$4.03 \cdot 10^{-2}$
	0.75	$5.0 \cdot 10^{-2}$	$4.5 \cdot 10^{-2}$	$5.3 \cdot 10^{-2}$	$5.6 \cdot 10^{-2}$
	0.83	$7.2 \cdot 10^{-2}$	$7.8 \cdot 10^{-2}$	$7.2 \cdot 10^{-2}$	$7.6 \cdot 10^{-2}$
	0.92	$1.2 \cdot 10^{-2}$	$1.3 \cdot 10^{-1}$	$1.1 \cdot 10^{-1}$	$1.04 \cdot 10^{-1}$
1.00†	$2.6 \cdot 10^{-1}$	$3.36 \cdot 10^{-1}$	$1.5 \cdot 10^{-1}$	$1.82 \cdot 10^{-1}$	
5	0.25*	$9.0 \cdot 10^{-7}$	$1.3 \cdot 10^{-7}$	—	$3.55 \cdot 10^{-6}$
	0.30	—	—	$8 \cdot 10^{-5}$	—
	0.35	—	—	$2 \cdot 10^{-4}$	$5 \cdot 10^{-5}$
	0.40	—	—	$3.3 \cdot 10^{-4}$	$1.9 \cdot 10^{-4}$
	0.45	$1.5 \cdot 10^{-4}$	$5 \cdot 10^{-5}$	$9.0 \cdot 10^{-4}$	$3.5 \cdot 10^{-4}$
	0.50	$4 \cdot 10^{-4}$	$2.3 \cdot 10^{-4}$	$1.5 \cdot 10^{-3}$	$7.7 \cdot 10^{-4}$
	0.55	$9 \cdot 10^{-4}$	$6.6 \cdot 10^{-4}$	$2.8 \cdot 10^{-3}$	$1.9 \cdot 10^{-3}$
	0.60	$2.6 \cdot 10^{-3}$	$1.5 \cdot 10^{-3}$	$4.5 \cdot 10^{-3}$	$2.7 \cdot 10^{-3}$
	0.65	$4.0 \cdot 10^{-3}$	$3.1 \cdot 10^{-3}$	$6.8 \cdot 10^{-3}$	$4.7 \cdot 10^{-3}$
	0.70	$8 \cdot 10^{-3}$	$5.8 \cdot 10^{-3}$	$1.07 \cdot 10^{-2}$	$7.4 \cdot 10^{-3}$
	0.75	$1.4 \cdot 10^{-2}$	$6.6 \cdot 10^{-3}$	$1.6 \cdot 10^{-2}$	$1.4 \cdot 10^{-2}$
	0.80	$1.6 \cdot 10^{-2}$	$9 \cdot 10^{-3}$	$1.9 \cdot 10^{-2}$	$1.8 \cdot 10^{-2}$
	0.85	$2 \cdot 10^{-2}$	$1.9 \cdot 10^{-2}$	$2.5 \cdot 10^{-2}$	$1.8 \cdot 10^{-2}$
	0.90	—	—	$3 \cdot 10^{-2}$	$2 \cdot 10^{-2}$
	0.95	—	—	—	—
1.00†	—	$1.61 \cdot 10^{-1}$	—	$6.94 \cdot 10^{-2}$	

* calculated from essentially hypercyclic matrices for columns (3),(4) and (6).

* Column (1) gives the dimension of the network and column (2) displays the connectivity. A graphical representation of these data is given in fig.4.

† calculated from catalytic networks for columns (4) and (6).

equ.9.4; on the other hand all other graphs with connectivity $\mathcal{C}(A) = \frac{n}{n(n-1)} = 1/(n-1)$ are reducible and the networks are therefore not permanent. Thus we

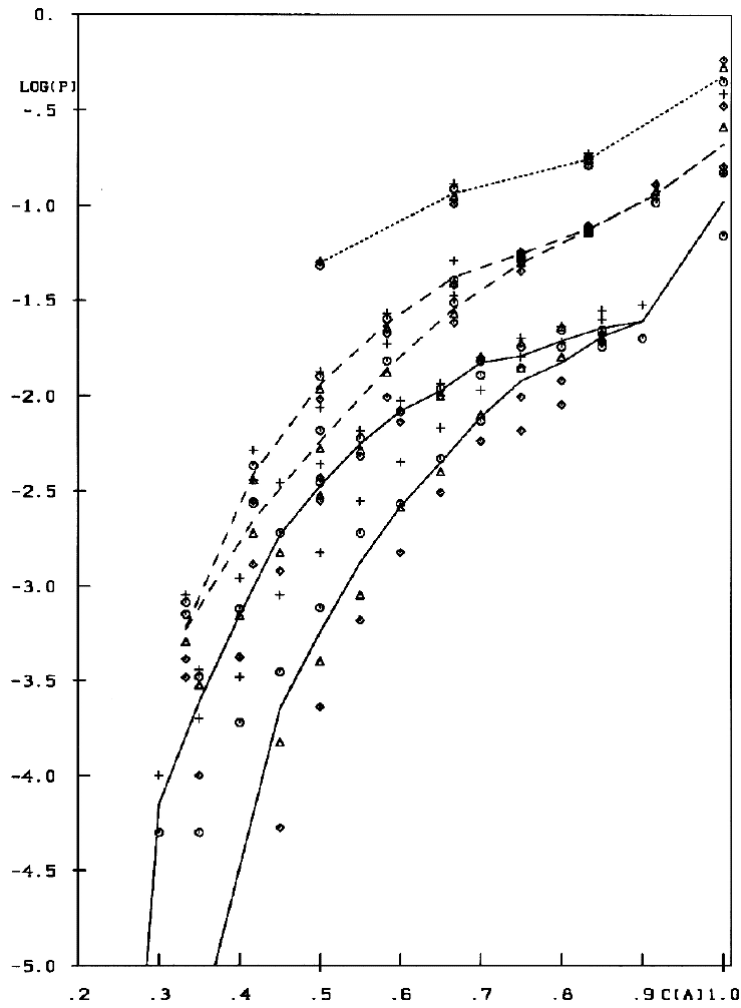


Figure 21: The probabilities for type-c (dashed line) and type-j (solid line) are shown for different density functions (symbols as in fig. 18) depending on the connectivity of the matrices for 3, 4 and 5 species networks. The lines refer to the averages for a given connectivity and dimension.

have

$$p_n = \frac{(n-1)!}{\binom{n(n-1)}{n}} \cdot p_{\text{EH}} \quad (9.9)$$

Note that for $\mathcal{C}(A) \leq 1/n$ the graph $G(A)$ is reducible and we do not expect permanent networks in this case. Table 6. lists the probability for permanence for $n = 3, 4$ and 5 depending on the connectivity $\mathcal{C}(A)$ for different density functions. These data are shown together with the data for undecidable matrices in

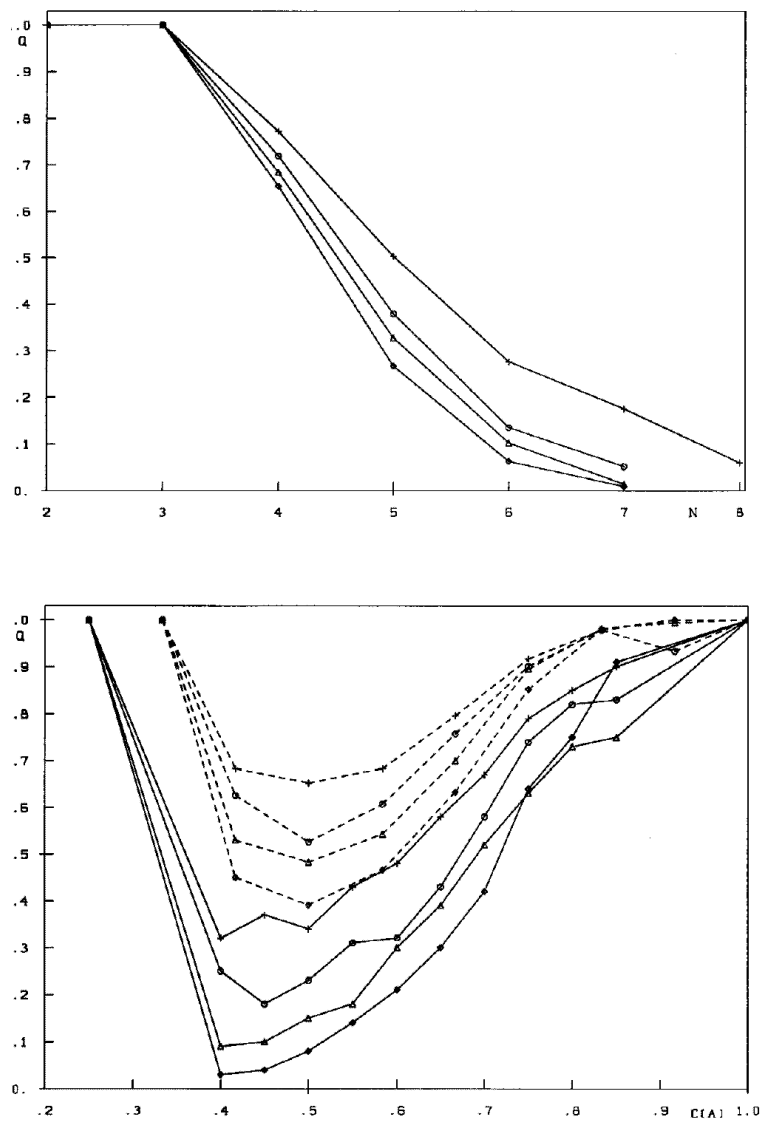


Figure 22: Ratio of type-j matrices and type-c matrices q depending on (above) the dimension n and (below) the connectivity of networks for $n=4$ (dashed line) and $n=5$ (solid line). Symbols as in fig. 18.

figure 4. The probability for finding permanent behavior depends strongly on the connectivity of the matrix A ; it decreases by several orders of magnitude with $\mathcal{C}(A)$.

The frequency $1 - q$ for a type-c matrix to be undecidable also depends on the connectivity $\mathcal{C}(A)$. Figure 5 shows how the probability q that a type-c matrix can be shown to be permanent by Jansen's criterion varies with n and $\mathcal{C}(A)$. For

$n = 3$ we find $q = 1$ independent of the connectivity. q then decreases by at least 2 orders of magnitude between $n = 4$ and $n = 7$. For larger networks q cannot be estimated with sufficient accuracy since the number of type-c matrices which can be produced with reasonable amount of computer time is too small.

A plot of q versus connectivity $\mathcal{C}(A)$ shows a minimum for $\mathcal{C}(A) \approx 0.5$ and reaches 1.0 for $\mathcal{C}(A) = \frac{1}{n-1}$, which corresponds to essentially hypercyclic systems for all $n \geq 4$. Unfortunately, thus, the only known sufficient condition for permanence — Jansen’s criterion — works worst for the most probable type of matrices.

9.5. Growth of Cooperative Networks

Cooperative behavior and especially permanence have been shown to be rather rare events in random networks. In this section we will investigate the fate of a cooperative network when an additional species enters, for example a mutant of one of its elements.

For second order replicator equations the minimum requirement for any type of cooperative behavior is the existence of an interior restpoint – otherwise all trajectories converge to the boundary of the simplex.

Suppose $A \in \mathbb{R}^{n \times n}$ leads to an interior equilibrium of (SR) in S_n . An additional species is introduced by extending A to $A' \in \mathbb{R}^{(n+1) \times (n+1)}$ by a random column and a random row. We define

$$\wp_{EE}(n+1) = \text{Prob}\{A' \text{ yields an interior equilibrium}\}. \quad (9.10)$$

In complete analogy we may ask for the probability of permanent network to incorporate an additional species such that the resulting network is again permanent. Since we have no unambiguous algebraic characterization of permanence we have to be content with an rather crude estimates, namely the probability \wp_{jj} that a

Table 7. Growth of Cooperative Networks.*

(1) n	(2) t	(3) $\wp_{EE}(n)$	(4) $\wp_{cc}(n)$	(5) \wp_{jc}	(6) $\wp_{cj}(n)$	(7) $\wp_{jj}(n)$
2	th	$5 \cdot 10^{-1}$	$2.5 \cdot 10^{-1}$	$2.5 \cdot 10^{-1}$	$2.5 \cdot 10^{-1}$	$2.5 \cdot 10^{-1}$
3	N	$2.84 \cdot 10^{-1}$	$1.14 \cdot 10^{-1}$	$1.14 \cdot 10^{-1}$	$1.14 \cdot 10^{-1}$	$1.14 \cdot 10^{-1}$
	L	$2.77 \cdot 10^{-1}$	$1.17 \cdot 10^{-1}$	$1.17 \cdot 10^{-1}$	$1.17 \cdot 10^{-1}$	$1.17 \cdot 10^{-1}$
4	N	$2.17 \cdot 10^{-1}$	$6.68 \cdot 10^{-2}$	$6.30 \cdot 10^{-2}$	$6.68 \cdot 10^{-2}$	$6.30 \cdot 10^{-2}$
	L	$2.12 \cdot 10^{-1}$	$7.01 \cdot 10^{-1}$	$6.66 \cdot 10^{-1}$	$7.01 \cdot 10^{-2}$	$6.66 \cdot 10^{-2}$
5	N	$1.73 \cdot 10^{-1}$	$4.39 \cdot 10^{-2}$	$3.33 \cdot 10^{-2}$	$4.55 \cdot 10^{-2}$	$3.70 \cdot 10^{-2}$
	L	$1.71 \cdot 10^{-1}$	$4.82 \cdot 10^{-2}$	$3.83 \cdot 10^{-2}$	$4.78 \cdot 10^{-2}$	$3.98 \cdot 10^{-2}$
6	N	$1.46 \cdot 10^{-1}$	$3.31 \cdot 10^{-2}$	$1.59 \cdot 10^{-2}$	$3.02 \cdot 10^{-2}$	$1.92 \cdot 10^{-2}$
	L	$1.43 \cdot 10^{-1}$	$3.56 \cdot 10^{-2}$	$1.86 \cdot 10^{-2}$	$3.51 \cdot 10^{-2}$	$2.29 \cdot 10^{-2}$
7	N	$1.27 \cdot 10^{-1}$	$2.50 \cdot 10^{-2}$	$4.71 \cdot 10^{-3}$	$2.30 \cdot 10^{-2}$	$1.03 \cdot 10^{-2}$
	L	$1.23 \cdot 10^{-1}$	$2.77 \cdot 10^{-2}$	$6.50 \cdot 10^{-3}$	$2.67 \cdot 10^{-2}$	$1.28 \cdot 10^{-2}$
8	N	$1.13 \cdot 10^{-1}$	$1.92 \cdot 10^{-2}$	$1.2 \cdot 10^{-3}$	$1.66 \cdot 10^{-2}$	$4.4 \cdot 10^{-3}$
	L	$1.11 \cdot 10^{-2}$	$2.04 \cdot 10^{-2}$	$1.5 \cdot 10^{-3}$	$1.92 \cdot 10^{-2}$	$5.8 \cdot 10^{-3}$
9	N	$1.01 \cdot 10^{-2}$	$1.48 \cdot 10^{-2}$	$2.1 \cdot 10^{-4}$	$1.1 \cdot 10^{-2}$	$2.1 \cdot 10^{-3}$
	L	$9.73 \cdot 10^{-2}$	$1.74 \cdot 10^{-2}$	$3.2 \cdot 10^{-4}$	$1.5 \cdot 10^{-2}$	$3.2 \cdot 10^{-3}$
10	N	$8.99 \cdot 10^{-2}$	$1.09 \cdot 10^{-2}$	$8 \cdot 10^{-5}$	$7 \cdot 10^{-3}$	$\approx 10^{-3}$
	L	$8.88 \cdot 10^{-2}$	$1.33 \cdot 10^{-2}$	$\leq 10^{-4}$	$8 \cdot 10^{-3}$	$\leq 10^{-3}$

* $\wp_{yx}(n)$ denotes the probability for a network of type-x (E refers to networks with interior equilibrium, c and j to type-c and type-j networks resp.) to form a type-y network by incorporation of an external species. Column (1) gives the dimension of initial network and column (2) specifies the density function: Gaussian (N) or Laplace (L).

matrix which fulfills Jansen's criterion is extended such that the resulting network again passes this test and the probability \wp_{cc} for type-c matrices to form type-c matrices again. Other possible estimate are \wp_{cj} , the probability for obtaining a type-c matrix from one which passed Jansen's test and \wp_{jc} that a type-c matrix is extended to matrix passing Jansen's test.

Computational results are compiled in table 7. As all four of these estimates seem to decrease (at least) exponentially we conjecture that the probability to extend a permanent system to a system which is permanent again will decrease exponentially with the number n of coexisting species.

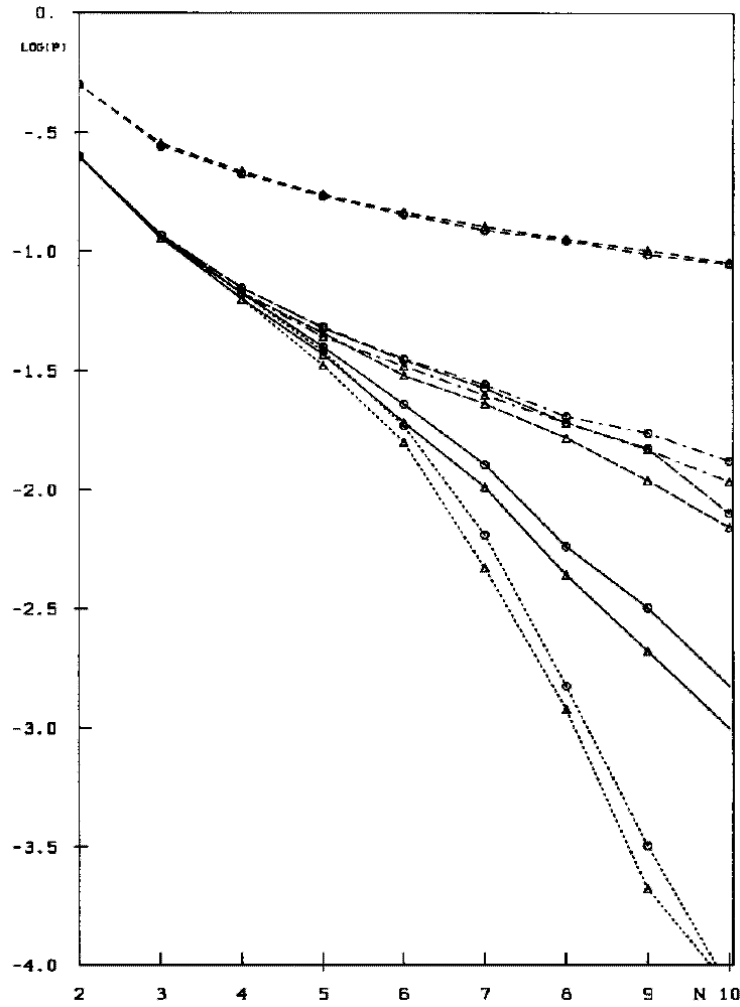


Figure 23: Probabilities for incorporation of external species into networks of dimension n . Dashed line φ_{EE} , dash-dotted line φ_{cc} , dotted line φ_{jc} , dashed line with narrow spaces φ_{cj} and solid line φ_{jj} . \triangle and \circ refer to Gaussian and Laplace distribution resp. See text for further explanation.

We may roughly estimate the chance to get a cooperative n -species network by successive incorporation of other species by

$$\hat{\varphi}(n) = \prod_{k=2}^n \varphi(k). \quad (9.11)$$

Fig. 23 compares these values with the probability for finding a cooperative $n \times n$ network by chance. The chance to get permanent networks stepwise by incorporation of random “invaders” is orders of magnitudes smaller than the chance to

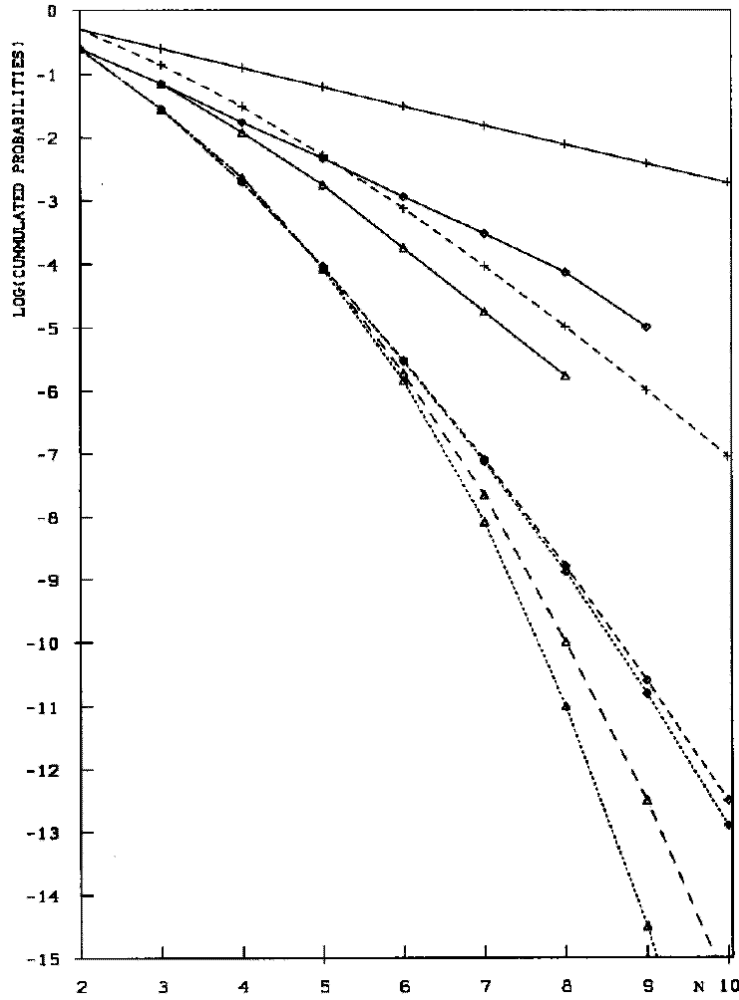


Figure 24: Cumulative probabilities for cooperative behavior by subsequent incorporation of external species into cooperative networks (equ.(31)). For simplicity only averages over the different density functions are plotted. $+$ refers to the existence of an interior equilibrium, \diamond refers to type-c networks and \triangle refers to type-j networks. Solid lines give the probabilities for accidentally finding a network of the above types, dashed lines give the probabilities for obtaining a network of given type from a network of the same type by subsequent incorporation of additional species ($\varphi_{EE}, \varphi_{cc}, \varphi_{jj}$). The dotted lines show φ_{jc} and φ_{cj} for comparison.

find a large permanent network at random.

What happens if an invading species is not incorporated thereby enlarging the permanent network? If the transversal eigenvalue in the direction of the invader is negative, than it cannot be successful and the previous network persists. We

estimate a probability of 0.5 for this process. If, on the other hand, the network is not stable against invasion, at least one of its members dies out in most cases because – as we have seen above – it is very improbable that the whole system is still cooperative. It may be replaced by the invading species, but we expect that in most cases more than one species disappears. The contact of a cooperative network and an external species might well be lethal for almost all species in the system. Unfortunately there are no algebraic tools known to calculate the outcome of such an event.

10. Replicators with Stochastic Perturbations

The “pure” replicator equation can only model selection of the interacting species, but does not permit the generation of new species. Although successful attempts have been made to include mutation, see for example [7, 96, 42], no *new* species are introduced. There is only change within the density of given species. Obviously there are two different ways to introduce a new species in a stochastic way:

- (i) *Mutation* takes a randomly chosen species and modifies it, such that the new species interacts in quite a similar way as the old ones.
- (ii) *Immigration* happens if a species from outside intrudes a given catalytic network. Because there can be no knowledge of the species inside, the interactions will be entirely of stochastic type.

So let us have a closer look on these different models.

10.1. Mutation

We start with the usual second order replicator equation.

$$\dot{x}_k = x_k ((Ax)_k - \langle x, Ax \rangle). \quad (10.1)$$

Because at the inner equilibrium \hat{x} no species vanishes, we have the fixed-point condition

$$(A\hat{x})_k = \langle \hat{x}, A\hat{x} \rangle. \quad (10.2)$$

So if a mutation occurs to the species x_i , the new species will be quite similar to the old one. Even if the relative change of parameters is large, it will nonetheless

depend on its former value. Thus the selection new matrix A' will be of the form:

$$A' = \begin{pmatrix} 0 & & \dots & a_{1k} & \dots & a_{1k} + \epsilon'_1 \\ & 0 & \dots & a_{2k} & \dots & a_{2k} + \epsilon'_2 \\ \vdots & \vdots & \ddots & \vdots & \dots & \vdots \\ a_{k1} & a_{k2} & \dots & 0 & \dots & \epsilon'_k \\ \vdots & \vdots & \dots & \vdots & \ddots & \vdots \\ a_{k1} + \epsilon_1 & a_{k2} + \epsilon_2 & \dots & 0 & \dots & 0 \end{pmatrix}, \quad (10.3)$$

with $|\vec{a}_{n+1} - \vec{a}_n| < \max|\epsilon_j|$.

Theorem 29. *Consider a second order replicator model. If a new species is introduced by mutation, the probability of intrusion will not depend on the existing species.*

Proof: From Hofbauer [56] we know that the transversal eigenvalues of Replicator equations are

$$\begin{aligned} \lambda_{n+1} &= (A\hat{x})_{n+1} - \langle \hat{x}, A\hat{x} \rangle \\ &= \sum_{j=1}^n \epsilon_j \hat{x}_j + \underbrace{\sum_{j=1}^n a_{kj} \hat{x}_j - \sum_{l,m=1}^n a_{lm} \hat{x}_l \hat{x}_m}_{=0} \\ &= \sum_{j=1}^n \epsilon_j \hat{x}_j. \end{aligned} \quad (10.4)$$

Because of the interior equilibrium, the second part of the equation is zero and the impact of the mutation depends only on the values of the new species. If a barycentric transformation is applied to the replicator equation, the transversal eigenvalue λ_{n+1} will simply be:

$$\lambda_{n+1} = \frac{1}{n} \sum_{j=1}^n \epsilon_j. \quad (10.5)$$

■

Remark: So if the differences of $A - A' = \epsilon_i$ is symmetrically distributed around zero, such that the expectation value $\langle \epsilon_j \rangle = 0$, we will have $\langle \lambda_{n+1} \rangle = 0$ and expect half the mutations to have no impact on the dynamical system at all. Bemuse more often positive values of ϵ_i will cause positive transversal eigenvalues, the mean fitness of the model at the interior fixed point $\hat{\Phi}$, on the average, will increase.

Mutations of single interactions:

Corollary 4. *A Replicator equation that is perturbed only by element $a_{n+1,n+1}$ can have no interior equilibrium.*

Proof: At the interior restpoint we have

$$A\hat{x} = \hat{\Phi}\mathbf{1}.$$

Therefore we have

$$\begin{aligned} k : \sum_{j=1}^n a_{kj} \hat{x}_j &= \hat{\Phi} \\ n+1 : \sum_{j=1}^n (a_{kj} - \epsilon) \hat{x}_j &= \hat{\Phi}, \quad \epsilon > 0 \end{aligned} \tag{10.6}$$

Thus follows that $\sum_j \hat{x}_j = 0$, which is a contradiction to $\sum_j x_j = 1$. ■

Corollary 5. *A Replicator equation that is perturbed only by element $a_{n+1,k}$ can have no interior equilibrium.*

Proof: At the interior restpoint we have

$$\begin{aligned} k : \sum_{j=1}^n a_{kj} \hat{x}_j &= \hat{\Phi} \\ n+1 : \sum_{j=1}^n a_{kj} \hat{x}_j + \epsilon \hat{x}_k &= \hat{\Phi}, \quad \epsilon > 0 \end{aligned} \tag{10.7}$$

From $\epsilon \hat{x}_k = 0$ follows a contradiction to the assumption of the existence of an inner equilibrium for n species. ■

10.2. Immigration

If the new species is independent of the old ones, we may expect different behavior. Let us call the immigrating species C and the interactions with the existing species

c_{ij} . The new selection matrix A' is

$$A' = \begin{pmatrix} 0 & & \dots & a_{1k} & \dots & c'_1 \\ & 0 & \dots & a_{2k} & \dots & c'_2 \\ \vdots & \vdots & \ddots & \vdots & \dots & \vdots \\ a_{k1} & a_{k2} & \dots & 0 & \dots & c'_k \\ \vdots & \vdots & \dots & \vdots & \ddots & \vdots \\ c_1 & c_2 & \dots & c_k & \dots & 0 \end{pmatrix}, \quad (10.8)$$

Theorem 30. *Consider a second order replicator model. If a new species is introduced by immigration, the probability of intrusion will depend on the existing species as well.*

Proof: The transversal eigenvalue again will be

$$\lambda_{n+1} = \sum_j^n c_j \hat{x}_j - \sum_{l,m}^n a_{lm} \hat{x}_l \hat{x}_m$$

Here the flux does not cancel and therefore the new species depends crucially on the old ones. ■

Proposition:[Flux] *The time-average of the flux $\langle \hat{x}, A\hat{x} \rangle$ is positive for every trajectory on an attractor that is in the interior of a subsimplex \mathcal{S}_n (with $n \geq 2$).*

Proof: We follow Hofbauer and Sigmund [56] (Chap.19). ■

Remark: The proposition does not hold for rare phenomena such as heteroclinic orbits.

Because immigration is a rare process, the relaxation time for each species is sufficient to equilibrate.

Corollary 6. *The expectation value $\langle \lambda_{n+1} \rangle$ of the transversal eigenvalue of a immigrating new species is less than $\langle c_j \rangle$.*

Proof: Let $\langle c_j \rangle$ be the expectation value for the transversal eigenvalue of an immigrating species. Then we have

$$\langle \lambda_{n+1} \rangle = \langle \sum_j^n c_{lm} \hat{x}_l \rangle - \underbrace{\langle \sum_{l,m}^n a_{lm} \hat{x}_l \hat{x}_m \rangle}_{>0} < \langle c_j \rangle. \quad (10.9)$$

Because of proposition (flux) the flux is expected to be positive. ■

Remark: If $\langle c_j \rangle = 0$ than less than half of the immigrating species are expected to invade. Moreover, let $\max(|c_j|) < \epsilon$. If ϵ becomes very small then

$$\lim_{\epsilon \rightarrow 0} \lambda_{n+1} = -\langle \hat{x}, A\hat{x} \rangle < 0.$$

If the interactions of the intruding species with the existing are small, we do not expect any effect at all. On the other hand, if these interactions become very large, the effect on the probability to invade will be dominated by the expectation value.

10.3. Numerical-Experiments

Because the analysis of stochastic perturbations of replicator equations is rather involved, it was supported by intensive numerical studies.

Most of the simulations were performed as random walks. At the very beginning, two species were created by randomly choosing a selection matrix in normal form. Initial conditions were randomized as well. Then, after a integration step all species, whose relative concentrations were below a fixed limit were thrown away. Then a new species as invented according to the mutation and immigration models. In order to speed up performance of the algorithm several checks were made before starting the integration process. All random numbers were taken uniformly distributed with mean zero.

The algorithm was implemented in C, but used several subroutines from the public-domain Fortran libraries ODEpack, LAPACK and LINPACK. Moreover, for the permanence-checking routine some subroutines from the NAG-package were taken.

As predicted, the average fitness of the mutation model increases in time. There is a linear increase in flux, due to the increasing entries of the selection matrix A , see

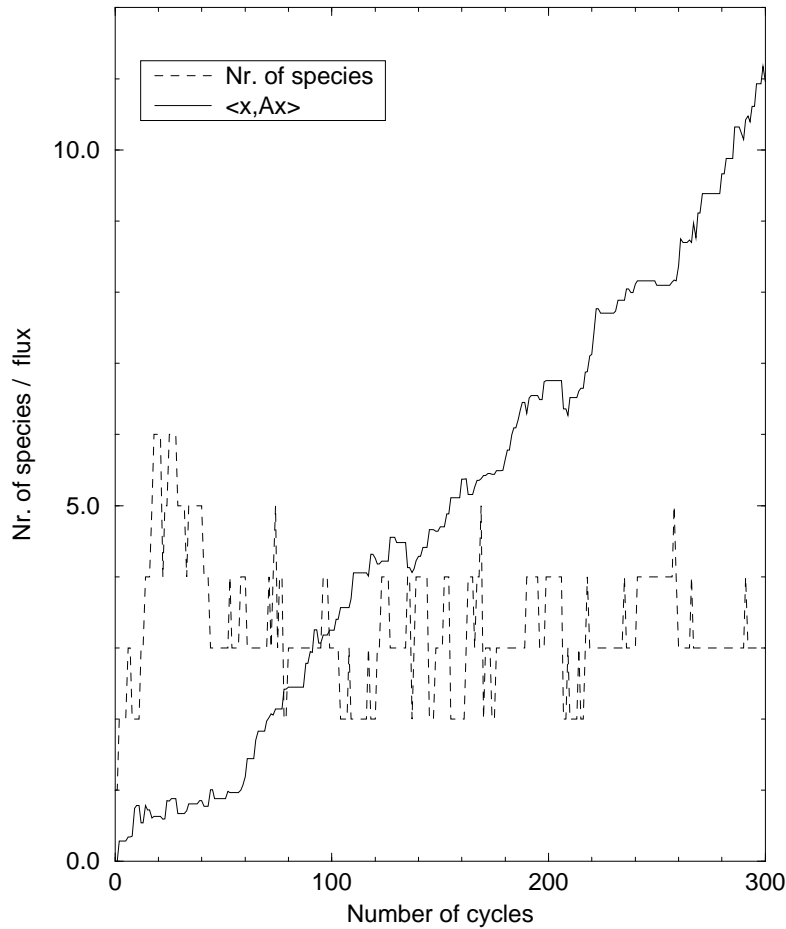


Figure 25: Example of a single run of the mutation-model. The average fitness is shown together with the changes of number of species. Although the increase is not monotonous, it clearly increases with time.

figure 25. Because for the immigration model the system is not stable, according to frequent breakdowns, where all but one species go extinct, there is no increase of the average fitness in time, see figure 26.

Since the immigration model cannot increase in size, it soon takes a stationary mean value of 2.72 living species per cycle. This means that on the average networks of less than three species occur. Let's have a look on the mutation model now: Does it increase? If it actually does, then very slowly. The data shown in

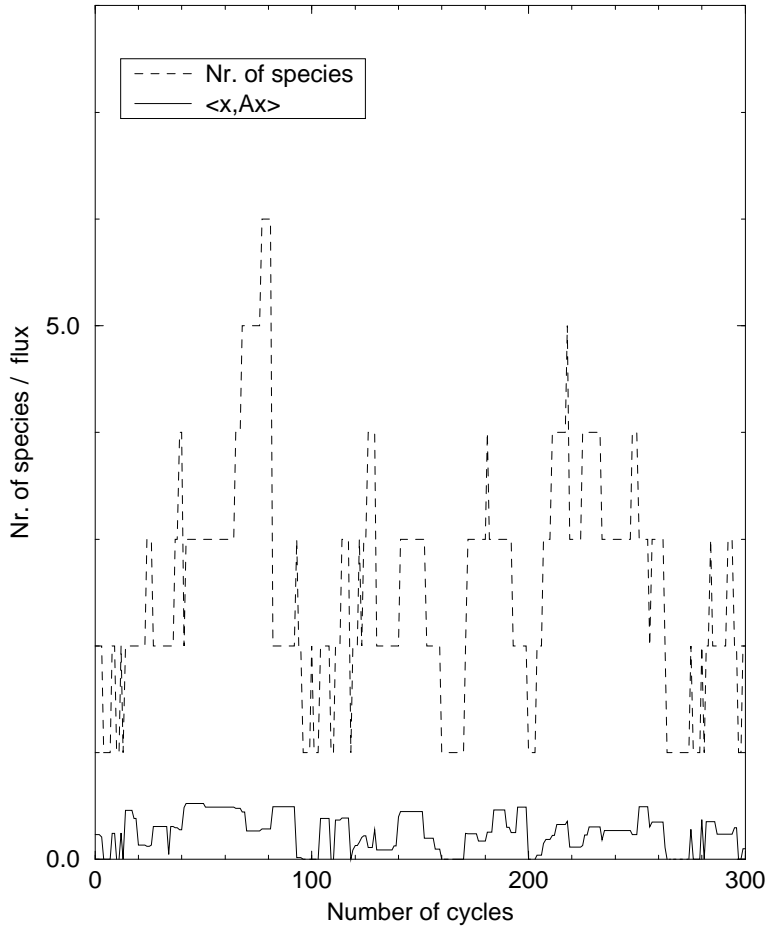


Figure 26: Example of a single run of the immigration-model. There are frequent breakdowns in the systems, where all but one species become extinct. Thus also the average fitness of the model does not increase.

figure 27 are the mean of ten independent runs of length $\geq 10^6$ cycles. A linear regression analysis yields a slope of 2.2×10^{-7} species/cycle for the growth of the system. The “stationary” number of living species has reached 5.25 at the end of the simulation.

A closer inspection of the data yields some interesting facts.

- (i) Mutation: neither the probability for a species to survive a certain number of cycles, nor the probability of living species per cycle depends on the dimension

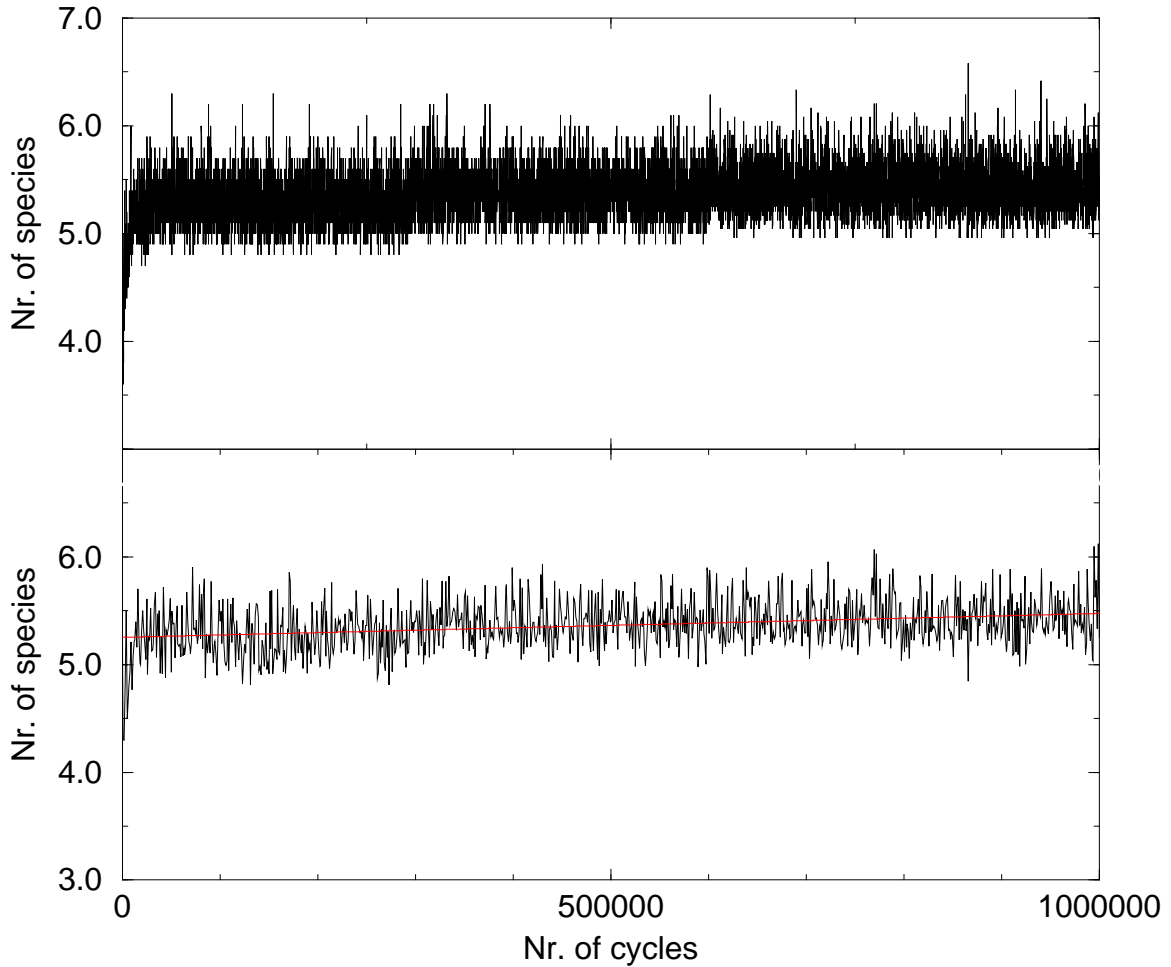


Figure 27: Time development of the mutation model. The data were sampled over 10^6 cycles. A spline over 1000 points is shown and a linear regression of the original data. (The first 10^5 point were cut off from the regression set.) The slope of the linear fit is 2.2×10^{-7} with intercept 5.25. For comparison, the immigration model has a mean number of living species of 2.72.

of the differences of the entries of the selection matrix A . A

- (ii) Immigration: here the relative size of the perturbation, compared to the entries of A have an influence of the development of the network. See also figures 30, 31 and 32.

Conjecture: *Replicator networks that have evolved over sufficiently large time are permanent.*

Evidence: *All networks that have been checked for permanence fulfill the Jansen*

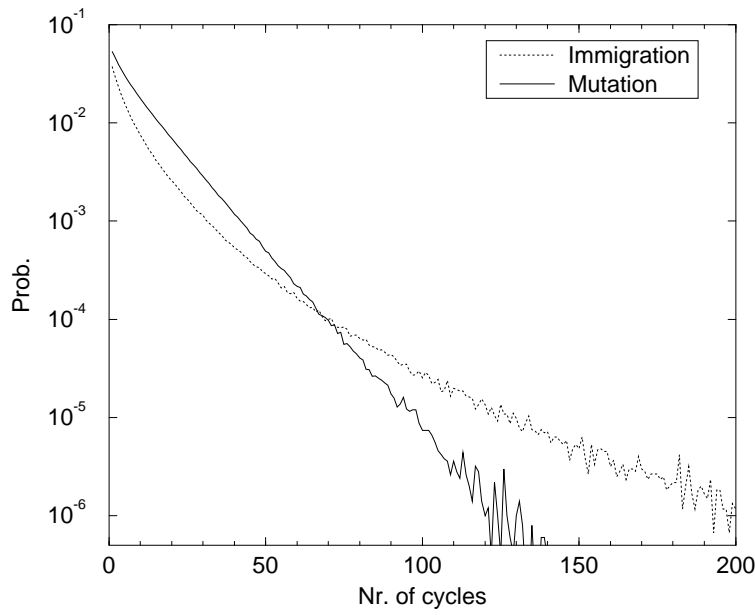


Figure 28: Probability of a species to survive a certain number of cycles. For the immigration model the value of $\epsilon=1$. is shown.

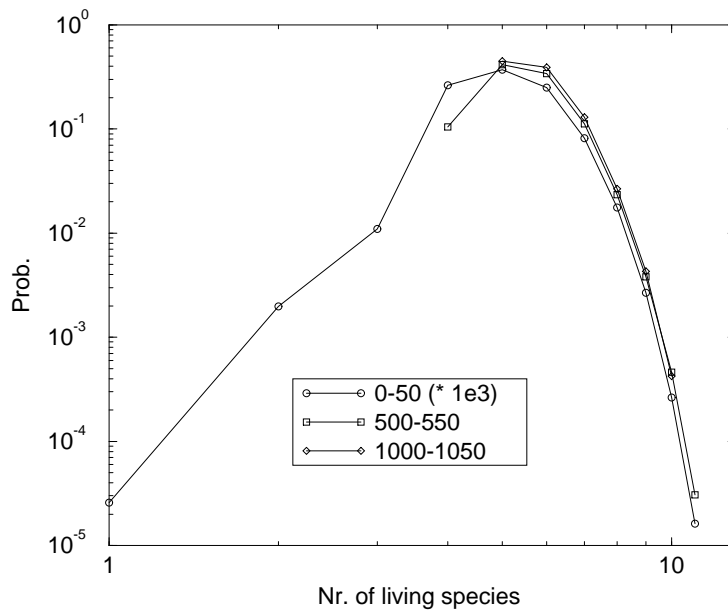


Figure 29: Mutation model: The average time development of the mean number of living species over 50000 cycles. Different times of the experiments are shown.

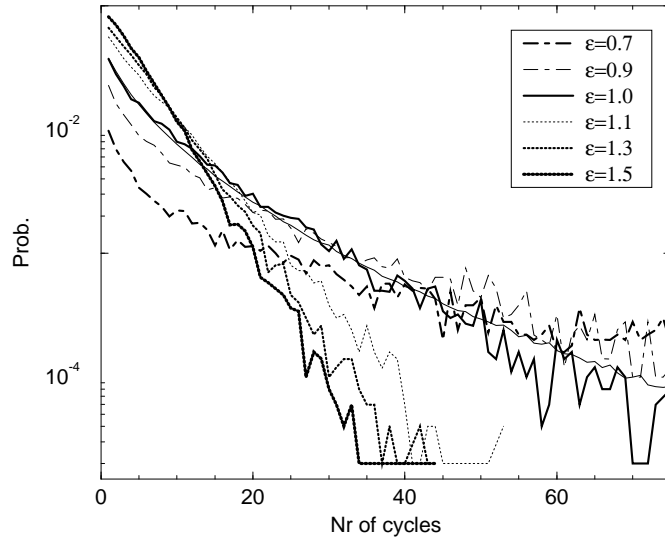


Figure 30: Immigration model: The probability for a species to survive a certain number of cycles depends on the relative size of interaction. Here a scaling of $\epsilon = 0.7-2.0$ demonstrates the effect. $\epsilon = 1$, means that the interaction with the existing species is expected to be equally strong as between the existing network.

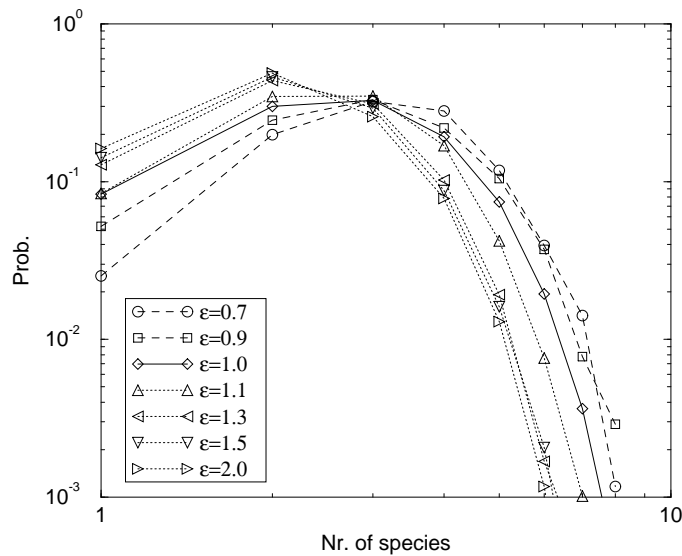


Figure 31: Immigration model: The Probability to find n living species at a randomly chosen cycle. Again, the range of ϵ was from 0.7 to 2.0.

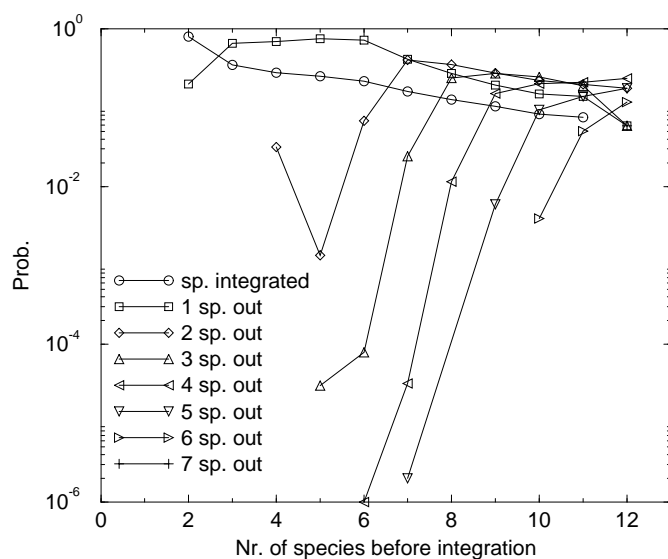


Figure 32: Mutation model: The probability that an invading species into a network of n species kills a number of old ones. (as shown in the legend) \circ denotes the fraction of species that enlarge the network by one.

criterion [62], i.e. they are in full permanent. 15 networks à 50000 cycles have been tested and 200 à 500 cycles.

10.4. Summary

The perturbation of catalytic networks is assumed to be a rare process. New species always appear in low concentrations, compared to the established ones. Thus enough time for relaxation was given between successive steps. The numerical experiments suggest that if the time between two deflections of the dynamical system is not long enough to reach equilibrium, then the number of species will rapidly grow, since the time for extinction is not sufficient before the next new species appears. One will get a situation of almost maximal increasing species until a fundamental collapse happens and only few, very likely only one species survive. Then the process repeats.

The perturbation of a given catalytic network can occur in two different ways:

- (i) A **Mutation** may happen. Although it is well known that even single point mutations can produce completely different phenotypes, we will assume that the appearance of the mutant is not too different from its wildtype. Thus the entries in the selection matrix depend on the former values of the mutant. Analytical calculations show that the probability of invading the existing catalytic network are independent of the “parent”. If the changes are symmetrically distributed around zero there will be fifty percent chance to find a positive transversal eigenvalue and thus the new species will be able to invade.

The most striking fact about mutation is that these networks are “persistent”, e.g. not all but one species can go extinct, but after some initial period at least three, and later on four species are the minimum that are alive together. There develops a network of similar species, whose mean fitness increases in time, while the single species come and vanish. A stationary state is reached after some time where the average number of species does not increase any more. (There is a very slight positive slope, but because of limited time resources it was not possible to continue the time evolution until equilibrium.)

In general, the probability for a species to survive a number of cycles decreases exponentially, i.e. there is no master sequence that produces a cloud of similar mutants, but the species are successively replaced by fitter ones.

- (ii) We see a different situation for the second model: **Immigration**. An immigrating species does not know about the network, it is invading. Therefore the interaction with the existing ones does not depend on the single entries of the selection matrix of the old network, but nonetheless it depends on the average fitness of the invaded species.

The relative size of the interaction with the existing network is crucial for the probability of a successful invasion of the new one. If, on the average, the size is much greater than those of the old ones, it will dominate the average fitness term and the chance to be successful will come close to fifty percent. On the other hand, if there is not much interaction (e.g. because the two systems inhabit different ecological niches) the probability of invasion becomes less and less, until it clearly vanishes in the limit of no interaction at all.

Invaded catalytic networks are unstable. They can survive over a few cycles, but it is very likely to find invading species that kill all the network, where only a single species can survive. So it collapses periodically and does not grow in size as much as the mutation model. Therefore the average expected number of species is just half a large as in the mutation model and the average fitness does not grow. But it seems that dominant species can be found much more easily, for the probability of surviving a large number of cycles is much higher, but depends on the relative size of the interactions, compared to the old network.

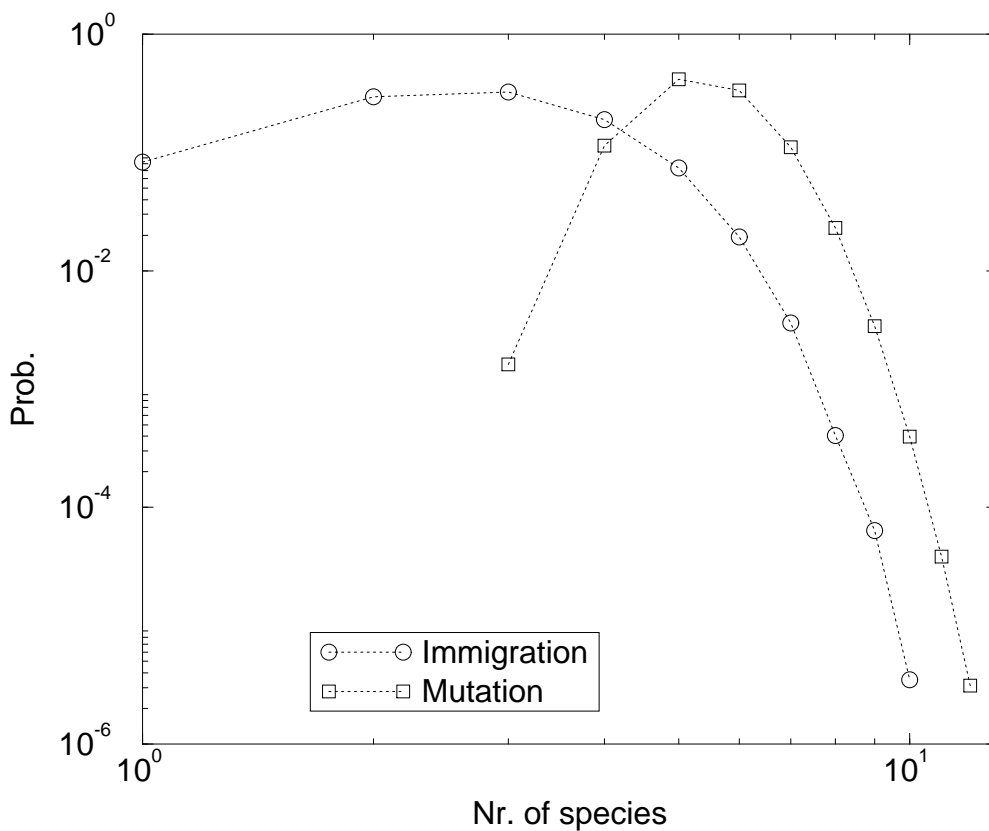


Figure 33: The Probability to find a number of living species at a randomly chosen cycle. Since the mutation model maybe increases in time very slowly, the according plot was taken from the average of late times, where no networks with less than three species occur; see also 30.

11. Conclusions and Outlook



Life is the most fascinating physical and chemical process that is known. At present, the complexity and variety of closely connected processes that in sum let a cell be alive is still far beyond reach, yet somehow all these steps must have evolved from some much simpler predecessor.

Nowadays, it is mostly agreed that at the very beginning of life some kind of *RNA-world* existed, where RNA-molecules both fulfilled the functions of *storing information* and having specific *catalytic activity*. A great deal of evidence for such a setting still can be found, and many groups around the world work on ribozymes.

Many important questions about how certain components of living cells can have developed are still unanswered, but what is common to all living creatures is **replication**. So, because replication is both the basis of conserving *and* changing information, it is the most crucial invention of life.

The most simple *model* of replication is to neglect all intermediates and regulation processes that are known today, but take replication as an *overall reaction*. The consequence of such a model is a simple one-step mechanism that describes the duplication of a molecule as a first order chemical reaction. Because this assumption is very unlikely even in the context of *very* basic mechanisms, a catalytic step is introduced. Then we have a second order reaction that consists of an autocatalytic part and interactions of the various species of the sample.

In order to create a model of replication, one has to take into account physical *boundary conditions* that keep away the system from equilibrium. There are different types of realizations of such boundary conditions, such as:

- (i) the *CSTR*, being the experimentally most easily realizable setting. It is kept constantly stirred in order to prevent spatial effects and provides the dynamical system with raw material at a constant rate. Also the volume is kept constant.

- (ii) the *Constant Organization* keeps the total sum of all species constant while the low-molecular building material is kept buffered, at the cost of enormous experimental effort. There is a flux through the system that represents the mean excess production. Mathematically, one gets *replicator equations*.
- (iii) finally one could set up a **regenerating** system that is closed to flux of matter, but only admits in-, and output of energy. Such a model is not of much practical value, but proves useful for creating spatial inhomogeneous dynamical systems.

Although it is clear that replicator equations are not sufficient to cover even the most simple features of a newly developing cell, they nonetheless do tell us a lot about the principal phenomena of chemically and physically interacting molecules. It seems straightforward to enrich the replicator equations with intermediate species or to include replication or some sort of regulation phenomena in order to enlarge the range of validity of our model, but unfortunately very soon the resulting equations are much too involved even to write them down.

Therefore, it is interesting find out to what extent such *structural perturbations* of the network are described correctly by the simpler model. It has turned out that *singular perturbation theory* is an efficient tool to check the validity of the overall reaction assumption.

Different ways have been attempted to deal with the task:

- (i) **Intermediates** have been introduced into the process of replication. First a model with intermediated that are consumed again in the course of the reaction was considered. Because a detailed analysis of this model already existed, the deviations to the plain replicator model could be worked out well. Then a second model with intermediates was set up. This time a Michaelis-Menten kinetics was assumed. Here a good agreement with the replicator model was observed.
- (ii) **Translation** was introduced by adding a simple one-step reaction that produces a protein translation product, which shows some replicase activity. Because there seems to be no reasons for a close coupling of the two subsystems,

each was taken to obey constant organization separately. A detailed analysis was performed and also effects of mutation were taken into account.

- (iii) It is clear that there exists a close relationship between the CSTR and the constant organization case. Thus the limit of low flux rates for the CSTR was investigated, in order to make mathematical treatment of dynamical systems more easy.

Moreover the effect of stochastic perturbations on the “pure” replicator equation was treated by numerical studies. Two types of perturbation could be worked out:

- (i) **Mutation** occurs when a new species is created by (slightly) altering an existing one.
- (ii) **Immigration** means the invasion of an existing network by a completely new species.

The immigration model frequently collapses to only one remaining species, while in the mutation model a stationary value is archived at an average size of approximately five species. Moreover, the mean fitness of such a model continually increases, while for immigration it keeps very low.

Since *Permanence* of biological systems is of great interest and Lotka-Volterra systems can be described by replicator-dynamics, the probability of permanence for these two models was studied. Extensive numerical work has been done on that topic. While permanence for immigration models is a very rare phenomena, it seems that selection is very good at creating permanence, for **all** systems were found to be permanent after sufficiently long time evolution.

Much time has been spent in order to find average Ljapunov-functions for the Michaelis-Menten type systems, but these efforts were in vain, just as an attempt to find projection-techniques for the determination of essential species of an reaction-network. A numerical investigation about the likelihood of chaotic behavior of the tree-species second order Michaelis-Menten type system was performed, but no chaotic behavior could be detected.

Outlook:

The validity of the replicator equation for certain models with more realistic settings have been checked, but this work is still far from completely finished. Some interesting information could be gained both by analytical and by numerical work in the future.

- The first replication model with intermediates seems to be neither of first, nor of second order, but somewhere in between. Especially the limits of small flux in the CSTR promise some nice new results about replicators with non-homogeneous response functions. Here, both analytical and numerical work may enlighten the situation.
- In this work, some rather simple attempts were made to include more realistic mechanisms into the family of replicator dynamics. Although even these were almost impossible to deal with, concerning “classical” stability analysis, it may be successful to find some models that are much closer to reality. Many phenomena, for example regulation processes are not at all accounted for.
- The stochastic model was just a beginning on that topic. Various combinations should be interesting, as well as spatial settings, where within the cells mutation happens, but always some species immigrate from the surrounding ones. This might prove a good way for modeling ecological niches in population dynamics.
- The actual rate-constants of interaction in a given chemical network depend on the structure of the RNA-molecules. Thus it seems possible to link both selection and mutation to the primary sequence of the interacting molecules and retrieve the rate-constants for selection from some folding-algorithm. If mutation is restricted to point mutations, the wandering of the species in sequence space could be traced.
- A generalization of the whole model in terms of λ -calculus is likely to provide work for years . . .

OH VANITY OF VANITIES !

Wyndham Lewis, *Apes of God*

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List of Publications

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