Replicator Networks with Intermediates

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Such nicht zu ergründen, was dir zu wunderbar ist
untersuche nicht, was dir verhüllt ist

Was dir zugewiesen ist, magst du erforschen,
doch das Verborgene hast du nicht nötig

Such nicht hartnäckig zu erfahren, was deine Kraft übersteigt
Es ist schon zuviel, was du sehen darfst.

Sir. 3, 21–23

Allen, die glauben, daß sie es verdient haben, sei an dieser Stelle summarisch gedankt.

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Zusammenfassung

Wir stellen eine Klasse von Reaktionsnetzwerken unter Einbeziehung von Reaktionszwischenstufen vor.

Ein allgemeines chemisches Modell wurde erstellt, und das Langzeitverhalten der daraus hervorgehenden kinetischen Differentialgleichungen werden mit analytischen und numerischen Methoden untersucht. Zwei Spezialfälle werden eingehender betrachtet: ein auf wechselseitiger Konkurrenz beruhendes, das eng mit einem von Schlögl vorgeschlagenen Modell verwandt ist, und ein mutualistisches, aus dem Hypercyclusmodell von Eigen und Schuster abgeleitetes, mit geschlossener zyklischer Katalyse.

Diese Modelle werden unter drei unterschiedlichen Randbedingungen behandelt; nämlich im gerührten Durchflußreaktor, in einem geschlossenen Reaktionsgefäß, wobei angenommen wird daß die Reaktionsprodukte unter Aufnahme von Energie von außerhalb des Systems wieder in die Edukte zerfallen, und schließlich im Evolutionsreaktor.

Für eine bestimmte Wahl der Reaktionskonstanten konnte die Stabilität aller Fixpunkte sowohl im Konkurrenz– als auch im mutualistischen Modell berechnet werden. Während im Konkurrenzmodell nur Tangentialbifurkationen auftreten können, wurden im mutualistischen Modell Serien von Hopf–Bifurkationen gefunden. Analytische Formeln zur Berechnung der kritischen Parameter, bei denen diese Bifurkationen stattfinden, werden abgeleitet.

Schließlich wird das Verhalten der Systeme bei der Einbeziehung von Diffusion untersucht. In beiden Modellen können Turing–Instabilitäten auftreten, wenn man die Anfangsbedingung in der Nähe eines stabilen Fixpunktes wählt. Im mutualistischen Modell tritt in der Nähe von stabilen Grenzzyklen ein interessantes Verhalten auf: es können sich, je nach Wahl der Reaktionskonstanten und Diffusionskoeffizienten, räumlich inhomogene, aber stationäre Muster oder oszillierende Bereiche ausbilden. Auf einer zweidimensionalen Domäne können sich darüberhinaus rotierende Spiralen bilden.

Abstract

The behaviour of a class of autocatalytic systems with intermediates has been studied.

A general chemical model has been derived, and the corresponding kinetic differential equations have been studied by both analytical and numerical methods. Two special cases were investigated in more detail: a competitive model, closely related to the second order Schlögl model, and a mutualistic model, derived from the hypercycle model due to Eigen and Schuster.

The reaction systems have been investigated under three different kinds of boundary conditions: the continuously stirred tank reactor, a closed system where reaction products decay to the substrate, consuming energy from outside the system, and the evolution reactor.

For a special choice of the rate constants, stabilities of all fixed points could be calculated both in the competitive and the mutualistic model. While the competitive model admits only saddle node bifurcations under these conditions, sequences of Hopf bifurcations can be found in the mutualistic model. Analytical formulae for the critical parameters where the bifurcations occur have been derived.

Finally, the behaviour of the systems under diffusion has been studied. In both models, Turing instabilities can be found under appropriate conditions when starting near a fixed point that is stable in the absence of diffusion. For stable limit cycles in the mutualistic model an interesting behaviour was found: they can form either stationary but spatially inhomogeneous patterns or oscillating patches. Limit cycles on a two dimensional domain can lead to the formation of spirals.

Contents

Chapter 1

Introduction

Não me enfileirem conquistas
Das ciências
(Das ciências, Deus meu, das ciências!)

Fernando Pessoa Nogueira: Lisbon revisited

1.1 Evolution

Very detailed knowledge of biological and biochemical processes governing the reproduction of cells has been accumulated in the last decades. With this knowledge, it became possible to ask questions concerning the physical nature of life itself in a very detailed and precise way. Among many others, this comprises questions about the uniqueness of the genetic code, about the optimality of enzymatic action as well as the origin of life itself.

It is a well established fact that conditions on Earth in the beginning (that is in the first hundreds of millions of years after its formation) would not have admitted the existence of complicated bio-polymers [50, 35]. This raises the question of emergence and evolution of these bio-polymers and the intricate systems of interactions between them.

The logic of evolution may be condensed into the following statements [9]:

- natural selection is a consequence of self-reproduction under conditions far from thermodynamic equilibrium.
- Variation is due to imprecise reproduction or other modifications involved in the reproduction process.
- Evolution is the result of variation and natural selection under conditions far from thermodynamic equilibrium.

Charles Darwin was the first to stress this interplay of selection and variation as the principle of evolution. To recognize the importance of advantages or disadvantage, however slight, of individuals over others as the fundamental driving force of selection seems to be one of the principal achievements of Darwin's work [6].

1.2 Self-Organization

"The self organization of matter associated with the origin of life must have started from random events in a sense of non-existing of fundamental organization." [8]. In his famous paper, which stimulated much research in this field, Manfred Eigen sets out the development of a theory about self organization. He addresses the question of self organizing matter into replicating 'individuals'.

In the last decades, a number of physical and chemical systems that show self organization has been observed. The selection of laser modes [20], the formation of coherent convection patterns [5], chemical oscillators, or the spontaneous formation of concentration patterns in autocatalytic chemical reaction systems may serve as examples.

Based on these findings, the self organization of life–like phenomena became — as thought experiment or as a computer simulations — rather the rule than a once witnessed exception. Trying to make definitions of life as an abstract quality so tight that they would still fit only to the phenomenon of life seems to become a way of reassuring ourselves of our uniqueness. Consequently, ploughing this field is left to philosophy and the theory of sciences. In recent years, the term 'artificial life' has become widely used (for developments in that field see [26]), generally without too much concern about precise definitions – 'Artificial organisms are logical automata which exhibit life-like processes' [25]; on the other hand, research in the field of the origin of life and of the mechanisms of evolution concentrated on the phenomena of living organisms.

1.3 Pattern and structure

The examples for physical systems exhibiting 'life-like behavior' given above lead to the question of the nature of the structures which these systems exhibit.

Commonly accepted precise definitions of the terms 'structure' and 'pattern', terms widely used in everyday language, describing 'obvious' phenomena, are lacking – a situation quite similar to the definition of the term 'complexity'. For the purposes of this work it will be sufficient to view patterns as structures with an appreciable degree of repetitivity (in space coordinates or in time), so that it is possible to concentrate on the term 'structure'.

From a thermodynamic point of view, a profound distinction was introduced by Glansdorff [18], namely between

- equilibrium structures and

- dissipative structures.

Equilibrium structures may be formed and maintained through reversible transformations implying no appreciable deviation from equilibrium. A crystal is a typical example of an equilibrium structure. Dissipative structures have a quite different status: they are formed and maintained through the effect of exchange of energy and possibly matter in nonequilibrium conditions.

In thermodynamics, ‘systems’ are regions with a well defined boundary, inside of which macroscopic properties are studied. For this, the following distinction regarding the exchange with the surroundings proved useful:

open systems	exchange of matter and energy
closed systems	exchange of energy
isolated systems	no exchange

In an isolated system, the entropy S tends to a maximum; the equilibrium state in an isolated system is characterized by $dS = 0$. For a closed system at a given temperature, a similar relation holds: The free energy F, defined by $F = E - TS$, with E the energy of the system and T the absolute temperature, at equilibrium reaches a minimum. For an open system, the generalized thermodynamic potential $\Theta = \Theta(T, V, \mu_i)$ (where μ_i is the chemical potential of substance i) attains a minimum.

For a closed or an open system, dS can be split into the contribution due to the irreversible processes inside the system and the contribution of the outside world,

$$dS = d_eS + d_iS$$

and still $d_iS \geq 0$. To maintain a steady nonequilibrium state, it is necessary to maintain a negative flow of entropy exactly compensating for the internal entropy production. Thus, dissipative structures can only be found in closed or open systems, but never in isolated ones.

A closed or open system can reach thermodynamic equilibrium only under special constraints (or boundary conditions); other boundary conditions might not admit equilibrium. For example a layer of liquid with a temperature T_0 maintained at the bottom and T_1 on top can only reach thermodynamic equilibrium if $T_0 = T_1$; else a gradient will be maintained, and the internal entropy production will be compensated by the flow of heat through the layer. For sufficiently small flows, the behavior of the system will be qualitatively equal to the equilibrium state. The range of the independent parameter governing the flow, for which this is valid, is called the 'thermodynamic branch'. Prigogine, in his thesis [37], showed that for isothermal closed or open systems in the thermodynamic branch, the total entropy production reaches a minimum. This principle of minimum entropy production is responsible for the fact that such systems are not able to develop ordered behavior; this statement is equivalent to the fact that no fluctuation around the thermodynamic branch can be amplified.

It is therefore that dissipative structures (which can be seen as the stabilization of an a priori extremely improbable fluctuation) only outside the thermodynamic branch (far from equilibrium).

1.4 Diffusion

Diffusion plays a key role in the formation of spatial patterns in reaction diffusion systems as well as in many biological systems.

There are two principal approaches to diffusion : the *macroscopic* and the *stochastic*; both will - under certain assumptions - lead to the same “law”.

In the case of the macroscopic (i.e. thermodynamic) approach, diffusion is the flux of a component that arises from a spatial concentration gradient of this component. The gradient represents the driving force of this process. Assume that the diffusion of component i takes place in a medium which is in excess; then

$$J_{i,diff}(x) = -L_{ii}\left(\nabla \frac{\mu_i}{T}\right)_{T,p}$$

where $J_{i,diff}$ is the flux of the component i due to diffusion at x, μ_i is its chemical potential and L_{ii} is the phenomenological coefficient. For an ideal solution this is equivalent to

$$J_{i,diff}(x) = -d_i \nabla c_i$$

with c_i the concentration of species i and d_i its diffusion coefficient; this is called *Fick's first law of diffusion.*

In a given volume element $\Delta\ V$ with interior Ω and surface $\partial\Omega$, the change of mass over dt in that volume element is

$$\frac{\partial c_i \Delta V}{\partial t} = -\oint_{\partial\Omega} \langle J_i d\mathbf{o} \rangle$$

with $\mathbf{o}$ the unit normal on the surface. The negative sign is caused by the fact that the flux is directed outward. With Green's theorem, this yields

$$\frac{\partial c_i \Delta V}{\partial t} = -\int_{\Omega} \nabla J_i dV.$$

Letting $\Delta V \longrightarrow 0$,

$$\frac{\partial c_i}{\partial t} = -\nabla J_i$$

If the diffusion coefficient is space independent, this yields *Fick's second law of diffusion.*

$$\frac{\partial c_i}{\partial t} = d_i \Delta c_i$$

The other approach to diffusion is to view it as a stochastic process involving individual particles. The microscopic process underlying diffusion in an isotropic medium is a random walk of the diffusing particles. The change of direction and momentum is due to collision with other particles. Under the assumption of several simplifications again the diffusion equation is obtained.

The space in which diffusion takes place is of central importance to the behavior of solutions of reaction diffusion systems. The natural domain for such models is a bounded subspace of $\mathbb{R}$, $\mathbb{R}^2$ or $\mathbb{R}^3$, with boundary conditions that can arise in a physical context. For a closed vessel, these would correspond to homogeneous *Neumann* or *no-flux boundary* conditions.

$$\langle \nabla \mathbf{u}, \mathbf{o} \rangle = 0 \qquad \text{on} \qquad \partial\Omega,$$

where again $\mathbf{o}$ denotes the unit outer normal. If the walls are permeable to some substances, mixed boundary conditions are appropriate; in the limit of infinite permeability, this yields *Dirichlet boundary conditions.*

$$\mathbf{u} = \mathbf{c} \qquad \text{on} \qquad \partial\Omega,$$

where $\mathbf{c}$ is a vector valued function of space, but usually is taken to be constant in subregions of the boundary $\partial\Omega$. *Mixed* boundary conditions are a linear combination of these two,

$$(1-\alpha)\langle \nabla \mathbf{u}, \mathbf{o} \rangle + \alpha(\mathbf{u} - \mathbf{c}) = 0.$$

Diffusion alone cannot produce any pattern-formation, since the pure diffusion equation $\dot{\mathbf{u}} = \mathbf{D}\Delta\mathbf{u}$ describes a process which tends to drive to equilibrium all local perturbations. But in the case of coupling with nonlinear reactions diffusion has a double role : 'on the one hand, it increases the stability of the steady state, but on the other hand, it increases the manifold of perturbations compatible with the macroscopic equations of change. ... if the second effect is dominant, we may expect symmetry breaking instabilities.'[38]

1.5 Experimental systems

In this section, we shall discuss some chemical reaction systems capable of oscillatory behaviour and pattern formation.

1.5.1 Halate oscillators

Among the first to describe chemical reactions exhibiting a non monotonous approach to thermodynamical equilibrium in closed systems are Morgan [28], who found a periodic release of carbon monoxide from a mixture of hydrogen peroxide, formic acid and sulfuric acid Babloyantz [1], and Bray [4], who observed a periodicity of iodine concentration in an acidic medium in which iodate catalyzed the decomposition of hydrogen peroxide to hydrogen and oxygen. The latter is the first example from the group of halate oscillators, which account for the largest number of known chemical oscillators of today. Epstein [13] gives a classification of the known halate driven oscillators, which can be divided into bromate, chlorate and iodate oscillators; among them, the bromate oscillators, which usually, but not always, contain metal ions as catalysts, form the largest group, whereas the group of the iodate oscillators has not experienced a substantial extension since Bray's discovery.

1.5.2 The Belousov–Žabotinskij reaction

In the course of studying the oxidation of citric acid by potassium bromate, catalyzed by the redox pair Ce^{3+}/Ce^{4+}, Belousov observed oscillations of concentrations manifested by the regular alternation of color of the solution between yellow and colorless. But it was not before the intensive study of the mechanism and the properties of that reaction by Žabotinskij in the early sixties that the phenomenon of oscillations in homogeneous solution was given attention ([2, 56]). Field, Körös and Noyes [14] have identified a set of reactions which since then has been taken as the basis of simplified models developed to simulate the behavior of the Belousov–Žabotinskij reaction. This set of reactions is referred to in the literature as the 'FKN-model'. After having analyzed this mechanism, Field and Noyes cast these reactions into the following model [15], called the 'Oregonator' to honor the university at which it was developed:

$$\begin{aligned} A+Y &\rightleftharpoons X \\ X+Y &\rightleftharpoons P \\ B+X &\rightleftharpoons 2X+Z \\ 2X &\rightleftharpoons Q \\ Z &\rightleftharpoons \mathrm{f}\,Y \end{aligned}$$

The model is related to the FKN-model by identifying X as $HBrO_2$, Y as Br^- and Z as Ce^{4+}, and, under certain constraints, A and B as BrO_3^-. f is a stoichiometric factor accounting for the diverse oxidations Ce^{4+} can perform.

Improvements on the original system were introduced in order to model the real chemical system better, which has since been studied by more and more refined methods. An early comprehensive work, describing the model and the chemical waves it exhibits, is by Tyson [49]. Innumerous articles on the model – ranging from experimental to purely mathematical – have been published since then, treating its behavior in the homogeneous case, also for other catalysts, and especially its capability to exhibit a very diverse spectrum of spatial patterns under diffusion. Among these, target patterns (circular symmetric wave trains in two spatial dimensions), one– and multi–armed spirals, three dimensional vortex dynamics, as well as chaotic behavior have to be mentioned; many phenomena exhibited by the reaction diffusion system have been observed only after mathematical analysis predicted them [29]. Among others, the group around Winfree has explored and classified two and three dimensional spirals in great detail, experimentally as well as theoretically (e.g. [52]).

The research group around Swinney in collaboration with that at the University of Bordeaux has designed different reactor types for the observation of spatial and spatiotemporal structures displayed by the Belousov–Žabotinskij reaction and its modifications. The so called Couette reactor, in which the reaction mixture fills the gap between two cylinders rotating against each other and is in contact with reservoirs at the two ends of the cylinders, proved useful to study reaction diffusion systems under Dirichlet boundary conditions; the rotation leads to equal effective diffusion coefficients three to five orders of magnitude larger than the conventional diffusion coefficients in the same medium, allowing the observation of appropriately larger spatial structures ([47, 36]). The Continuously Fed Unstirred Reactor (CFUR) can serve as a tool for systematic studies of spatial pattern formation in two dimensions; in the CFUR, the reaction diffusion process is observed in a gel that is sandwiched between a glass plate and a glass capillary array which is in contact with a well stirred reservoir [46]; an annular geometry instead of a gel sheet – nearly related to the cyclic arrangement discussed by Turing [48] – was realized by Noszticzius [32]. The principal advantage of these reactors over the conventional isolated systems is the possibility to remain away from thermodynamic equilibrium for arbitrary long times.

1.5.3 The peroxidase reaction

An interesting example of a chemical oscillator involving enzymes is the oxidation of NADH by O_2 catalyzed by horseradish peroxidase. In 1965, Yamazaki et al. [55, 54] found damped oscillations in oxygen concentration when they studied this reaction in an open system. Degn [7] proved that the system exhibits bistability under suitable experimental conditions due to the fact that the peroxidase is inhibited by oxygen at high concentrations, forming an inactive complex. Nakamura, Yokota and Yamazaki [30] then designed the first system of this kind that exhibits stable oscillations, using Lactoperoxidase, NADPH and methylene blue, which catalyzes the decomposition of the inactive complex (plus some additional stabilizing agents). In 1977, Olsen and Degn found chaotic oscillations in a similar system ([34, 33]). In a recent work by Geest ([17]), these oscillations were reproduced and a period doubling route to chaos was found.

1.5.4 Other examples

In the reaction described by Morgan [28] (see above), an interplay of chemical reactions and physical steps is responsible for the oscillations. In strong sulfuric acid, formic acid is dehydrated to form carbon monoxide which is only slightly soluble in aqueous solutions. The homogeneous nucleation of bubbles of carbon monoxide from a supersaturated solution and the practical irreversibility of its release as bubbles account for the oscillations.

Another example of a gas evolution oscillator is the formation of nitrogen from ammonium and nitrite in acidic solution in the presence of perchlorate (which presumably mainly has the effect of increasing the surface tension in the solution, an important factor in the kinetics of bubble formation) ([23]).

An example of a system exhibiting spatial structures, and in which physical processes play an important role besides chemical processes, is the class of the Liesegang reactions, the precipitation of a salt of very low solubility in a gel matrix. Usually, one ion is present in the gel matrix, whereas the other ion diffuses into that medium. At a certain level of supersaturation, precipitation sets in, depleting the surrounding region of ions and thus reducing the probability of precipitation in the neighborhood. Commonly, lead iodide or lead chromate are used. ([39, 27])

A chemically simple example of an excitable system admitting a traveling pulse was given by Kramer [24]: in a tube, the equilibrium between the fluorosulfate radical (SO_3F) and its dimer $S_2O_6F_2$ is disturbed by a laser beam the frequency of which is tuned as to only excite SO_3F. Again excitability is due to the fact that the rate of formation of the radical is a highly nonlinear process, leading to the phenomenon of hysteresis and multiple steady states.

1.6 Modelling ecosystems: Types of Interaction

After having presented experimental systems that show various kinds of self organization, this section is dedicated to purely mathematical models aimed to describe certain phenomena in ecological systems. The behavior of the solutions is in some cases quite similar to trajectories observed in chemical reaction diffusion system, including oscillations, pattern formation etc.

The analysis of the interaction between two species can be quite complicated, involving the effects of exterior and interior parameters. As a first approximation, however, one may distinguish (apart from the case of zero interaction) three basic situations.

- *Competition*: Two species are rivals in the exploitation of a common resource. The more there is of one species, the worse for the other one. Because of the importance of competition as a limiting factor in evolution, such situations have attracted considerable attention.
- *Symbiosis*: This is the reverse situation: both species benefit from each other. The more there is of one species, the better for the other one. Such *mutualistic* relationships have been treated by Eigen and Schuster [10, 11, 12] In particular, there are good reasons to think that also living cells of the type occurring in higher organisms are the outcome of a symbiosis between more primitive organisms.
- *Host-parasite relationship*: The situation, here, is asymmetrical. The parasites benefit from the host but they do it no good. Examples are e.g. viruses or interactions between predatory animals and their prey.

We now present one mathematical model for each of these interactions. They are all “classical” in the sense that have been created long ago and are well studied. The first two of them will play a particularly important role in this work.

1.6.1 Competition: The Schlögl model

Schlögl [40] investigated two model systems in which the substance X_i is formed from a substrate A via first order and second order autocatalysis, respectively:

$$A + X_i \xrightarrow{k_i} 2X_i \tag{1.1}$$

(first order autocatalysis) and

$$A + 2X_i \xrightarrow{f_i} 3X_i \tag{1.2}$$

(second order autocatalysis). Some additional reactions are required in order to guarantee boundedness of the solutions. Schlögl considered only one species X_i and thought of the reactants as ideal gases. Schuster and Sigmund [41] applied these models to selection and evolutionary optimization, extending the models to n species $X_1, \ldots, X_n$, which are thought of as RNA strands that compete for the common substrate A (the nucleoside triphosphates). They showed that in the continuously stirred tank reactor (CSTR) setting (see Chapter 3), an arbitrary number of species could coexist under suitable conditions in the case of first order autocatalysis, whereas for the second order autocatalysis all fixed points at which more than one species exists are unstable. The second order system is called *selective*, since all trajectories converge to fixed points at which only a single species exists. Which one of the species is selected depends not only on the rate constants f_i, but also on the initial conditions.

In both cases a generalized gradient could be found; hence, complicated dynamical behaviour like oscillations, quasiperiodicity and chaotic dynamics are impossible.

1.6.2 Symbiosis: The Hypercycle

Eigen [8] estimated that nucleic acids viewed as information carriers could not accumulate a stable information content of more than about 200 bits, corresponding to the formation of polymers not longer than approximately 100 base pairs. Since even the simplest bacteria have genomes that are several orders of magnitude large than this estimate, Eigen concluded that the competition of information carriers alone could not lead to any type of correlated function. This phenomenon was termed "information crisis".

In a collective of chemical species, where each species catalyzes the formation of another one, a closed loop of catalysis may be found. By this cyclic action, the individual members of the closed loop influence the probability of their reproduction as a collective. Then the collective of the members of the cycle is subject to selection and can, in contrast to single species, code an arbitrarily high amount of information, namely the sum of the information content over all individual information carriers which are members of the cycle, provided the replication network is stable against small perturbations caused, for instance, by stochastic fluctuations. By this, a way out of the information crisis can be found.

A model for this cyclically catalytic action was developed by Eigen and Schuster [8, 10, 11], in which n information carriers, that show the property of autocatalytic self-reproduction, are linked together by catalytic action into a "cyclic hierarchy", as each member also gives (possibly indirect) catalytic help to the reproduction of the next member:

$$\begin{aligned} A + X_i + X_{i-1} &\overset{f_{i-1}}{\rightarrow} 2X_i + X_{i-1} \qquad i = 2, \ldots, n \\ A + X_1 + X_n &\overset{f_n}{\rightarrow} 2X_1 + X_n \end{aligned} \tag{1.3}$$

This model has since gained fame as the "hypercycle". It is cooperative in the sense that either all species survive or all die out. Schuster and Sigmund [41] found that in the CSTR setting there are two fixed points at which all species coexist: one is always unstable, the other one is stable if $n \leq 4$ and unstable otherwise. In the latter case this fixed point is surrounded by a stable limit cycle. Much work has been done on the hypercycle, especially in the evolution reactor setting (see Chapter 3). Hofbauer and Sigmund [21] present an excellent survey.

1.6.3 Host-parasite relationship: The Lotka-Volterra model

In the years after the First world war, the amount of predatory fishes in the Adriatic was found to be considerably higher than in the years before. The hostilities between Austria and Italy had disrupted fishery to a great extent, but it was not clear why this was more favorable to the predators than to their prey. Volterra [51] created a mathematical model to describe the situation: He assumed that in absence of predators the rate of growth of the prey population x is given by some constant a, but it decreases linearly as a function of the population of the predators, y. The predators, on the other hand, would die out at rate c in the absence of prey, but their population grows linearly with x. This leads to the following system of differential equations:

$$\begin{aligned} \dot{x} &= a - by \\ \dot{y} &= -c + dx \end{aligned} \tag{1.4}$$

$(a, b, c, d > 0)$. This system has a fixed point where both predators and prey die out and one at which they coexist where $x = c/d,\ y = a/b$. The latter is surrounded by a set of periodic orbits. Volterra was able to show that the time average of the populations along the periodic orbits equals the populations at the fixed point which they surround.

Assuming that fishing reduces the growth rate of the prey to $a - k$ and augments the rate of decrease of the predators to $c+m$ and introducing these quantities instead of a and c into the equilibrium concentrations, we see that fishing leads to an increase in prey and a decrease in predator population. Stoppage of fishing, of course, has the converse effect.

1.7 Second order reaction networks

The equations (1.2) and (1.3) can be viewed as two special cases of a general reaction scheme with n species $X_1, \ldots, X_n$ that have certain catalytic activities and a substrate A of which they are formed:

$$A + X_i + X_j \xrightarrow{b_{ji}} 2X_i + X_j \tag{1.5}$$

Thus, X_i is formed from A with catalytic help of X_j. Again, we need some additional reactions to keep solutions bounded. The essential steps (1.5) require the collision of three reactants. Termolecular collisions are highly improbable and hence do not contribute to reactions kinetics. Superposition of catalytic reactions, nevertheless, may lead to an overall dynamics which can be modelled properly by second order catalytic reaction steps.

This work is mainly concerned with the effects of replacing the single step (1.5) by two successive first order catalytic reactions. This involves considering intermediates, which can be thought of as activated complexes if the X_i are chemical reactants. We shall present this model, along with the mathematical settings in which we investigate it, in detail in Chapter 3. In Chapter 2, we introduce the mathematical framework. Chapters 4 and 5 deal with two special cases, the competitive and the mutualistic model, which are equivalent two the Schlögl model and the hypercycle, respectively, in terms of second order reaction networks. In chapter 6 we shall present the effects of considering diffusion rather than reactions in well stirred mixtures as in chapter 4 and 5. Chapter 7 contains conclusions and outlook.

Chapter 2

Methods

2.1 Ordinary Differential Equations

2.1.1 Canonical Forms for Linear Operators

Let $T : E \to E$ be an operator. Its characteristic polynomial can be written as

$$p(t) = \prod_{k=1}^{r} (t - \lambda_k)^{n_k}$$

where λ_k are the r distinct eigenvalues and n_k are their multiplicities. Clearly $n_1 + n_2 + \ldots + n_r = \dim E$. The *generalized eigenspace of T belonging to λ_k* is defined as

$$E(T, \lambda_k) = \ker(T - \lambda_k)^{n_k} \subset E$$

Proposition 2.1 (Primary decomposition theorem) *Let T be an operator on a complex vector space E. Then E is the direct sum of the generalized eigenspaces of T. The dimension of the eigenspaces equals the multiplicity of the corresponding eigenvalue.*

We say an operator A is *semisimple* iff its complexification is diagonalizable. It is *nilpotent* if there is an $n \in N$ such that $A^n = 0$.

Proposition 2.2 *For any operator $T \in L(\mathbb{R}^n)$ there are unique operator S and N on $\mathbb{R}^n$ such that $T = S + N$, $SN = NS$, where S is semisimple and N is nilpotent.*

The semisimple part S itself may be decomposed into a part S_R corresponding to real eigenvalues and a part S_C corresponding to complex conjugate pairs of eigenvalues. By an appropriate change in coordinates S_R may be rewritten in diagonal form and S_C then consists of 2×2 blocks of the form

$$C_i = \begin{pmatrix} a & -b \\ b & a \end{pmatrix}$$

where a and b are real. This representation for S is called (real) canonical form. If we allow for complex entries S is diagonalizable as a whole; instead of the matrices A_i we have the pair of complex eigenvalues of A_i in the diagonal.

An *elementary nilpotent block* is a matrix of the form

$$N_1 = \begin{pmatrix} 0 & & & & & \\ 1 & . & & & & \\ & . & . & & & \\ & & . & . & & \\ & & & . & . & \\ & & & & 1 & 0 \end{pmatrix}$$

Proposition 2.3 *Let N be a nilpotent operator on a real vector space E. Then E has a basis such that N is represented by a matrix of the form $N =$ diag($N_1, \ldots, N_r$) in which N_k is an elementary nilpotent block and the size of N_k is a nonincreasing function of k. The number r of blocks is equal to* dim ker$A$. *Two nilpotent operators of the same vectorspace are similar iff they have the same canonical form N.*

Let us now consider an operator of the form $T = \lambda\ E + N$ where E is the unit operator and N is nilpotent. If we choose the basis such that the matrix

N is a nilpotent canonical form, we find the matrix representation of T to be $N + \lambda\ E$. This matrix has block diagonal form with identical blocks of the form

$$\begin{pmatrix} \lambda & & & & \\ 1 & \cdot & & & \\ & \cdot & \cdot & & \\ & & \cdot & \cdot & \\ & & & \cdot & \cdot \\ & & & 1 & \lambda \end{pmatrix}$$

which are called *elementary* JORDAN *blocks*. The number of such blocks is

$$r = \dim\ \ker\left(T - \lambda\right)$$

and their size is $\frac{m}{r}$, where m is the dimension of the vector space. If λ is complex the elementary blocks may be rewritten in real form for a *pair* of conjugate eigenvalues.

$$\begin{pmatrix} D & & & & \\ E_2 & \cdot & & & \\ & \cdot & \cdot & & \\ & & \cdot & \cdot & \\ & & & \cdot & \cdot \\ & & & E_2 & D \end{pmatrix}$$

$$D = \begin{pmatrix} a & -b \\ b & a \end{pmatrix} \quad \text{and} \quad E_2 = \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix}$$

Proposition 2.4 *The canonical form for an arbitrary operator T may now be written as the direct sum of matrices of the above form. It is therefore a block diagonal matrix consisting Jordan blocks corresponding to the eigenvalues λ_k of T. Each block has size n_k and is made up of dim* $\ker(T - \lambda_k)$ *elementary Jordan blocks.*

2.1.2 Linear ODEs with Constant Coefficients

Let $T : E \to E$ be a linear operator . Its *exponential* is defined as

$$\exp T = \sum_{k=1}^{\infty} \frac{T^k}{k!}.$$

This series converges for all $T \in L(E)$. If $Q = PTP^{-1}$ then the exponential of Q is given by

$$\exp Q = P \cdot \exp T \cdot P^{-1}$$

and if $\mathbf{x}$ is a real eigenvector of T belonging to λ, then $\mathbf{x}$ is also eigenvector to $\exp T$ belonging to e^{λ}.

Let us now consider the solutions of the homogeneous linear system

$$\dot{\mathbf{x}} = A \cdot \mathbf{x}$$

Proposition 2.5 *Let A be an operator on $I\!R^n$. Then the* initial value problem *$\dot{\mathbf{x}} = A \cdot \mathbf{x}$, $\mathbf{x}(0) = \mathbf{x}_0 \in I\!R^n$ has the unique solution.*

$$\mathbf{x}(t) = \exp(t \cdot A) \cdot \mathbf{x}_0$$

The exponential of an elementary n-dimensional Jordan block B may be readily calculated: with

$$\exp(t \cdot B) = e^{\lambda t} \cdot \begin{pmatrix} 1 & & & & & \\ t & 1 & & & & \\ p_2 & t & 1 & & & \\ . & . & . & . & & \\ . & . & . & . & . & \\ p_{n-1} & p_{n-2} & . & . & t & 1 \end{pmatrix}$$

In coordinates we may write down the solutions of the initial value problem as

$$x_j(t) = e^{\lambda t} \sum_{k=1}^{j-1} \frac{t^k}{k!} x_{j-k}^0;$$

where x_i^0 denotes the coordinates of $\mathbf{x}_0$.

If λ is complex we identify $\mathbb{C}^m$ and $\mathbb{R}^{2m}$ by the correspondence

$$(x_1 + \imath y_1, x_2 + \imath y_2, \ldots, x_m + \imath y_m) = (x_1, y_1, x_2, y_2, \ldots, x_m, y_m)$$

The solution is formally the same as above, but with the complex vector $\mathbf{z}$ instead of the real vector $\mathbf{x}$. With $z_i^0 = x_i^0 + \imath\, y_i^0$ we obtain the solution in real variables:

$$x_i(t) = e^{at} \sum_{k=0}^{j-1} \frac{t^k}{k!} \left[x_{j-k}^0 \cos bt - y_{j-k}^0 ybt \right]$$

$$y_i(t) = e^{at} \sum_{k=0}^{j-1} \frac{t^k}{k!} \left[y_{j-k}^0 \cos bt - x_{j-k}^0 ybt \right]$$

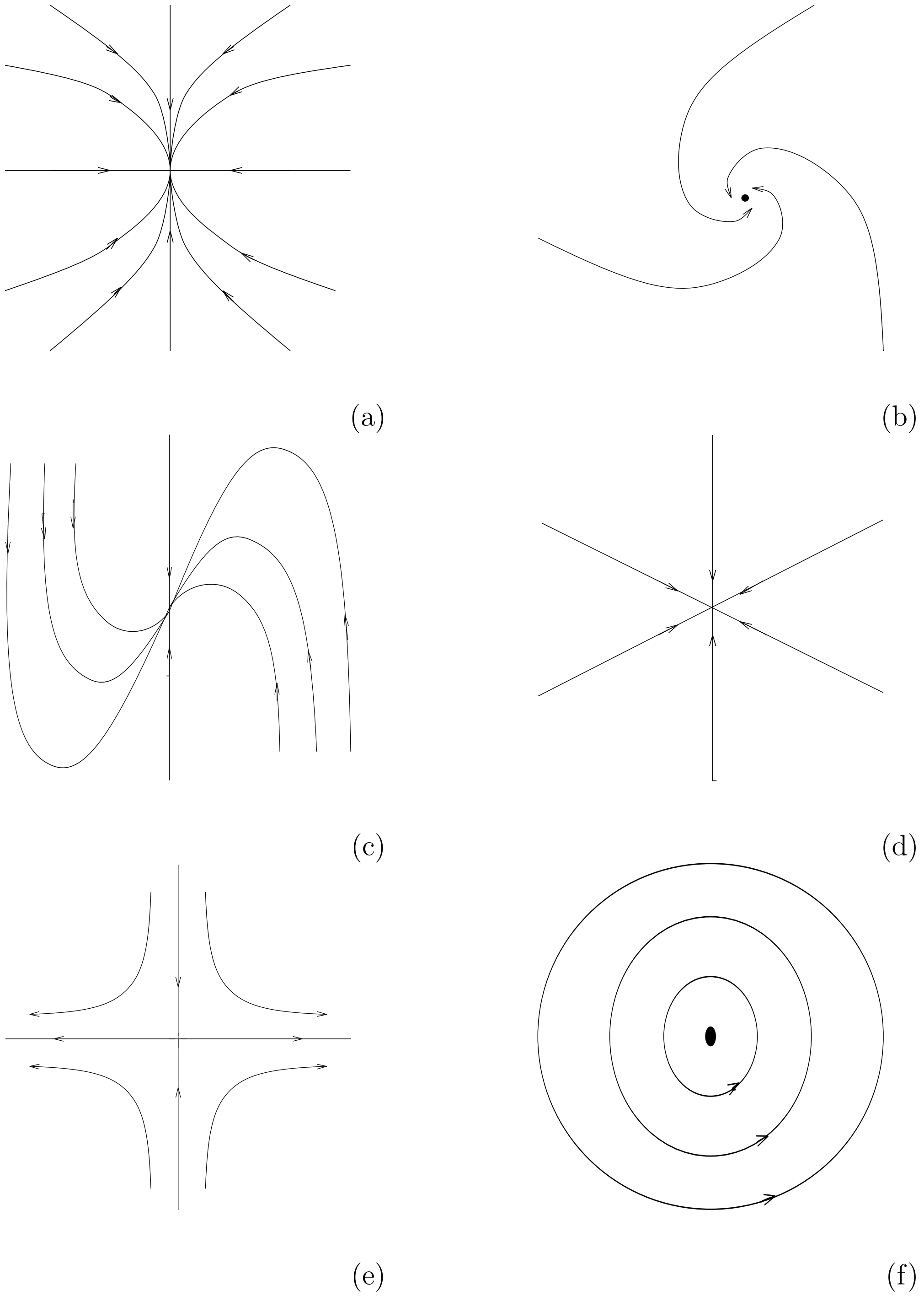
where $\lambda = a + \imath\, b$.

Proposition 2.6 *Every trajectory of $\dot{\mathbf{x}} = A\mathbf{x}$ tends to 0 for $t \longrightarrow \infty$, iff every eigenvalue of A has negative real part.*

Definition 2.1 *Let $(a, b) \subset \mathbb{R}$ be an open interval, $U \subseteq \mathbb{R}^n$ a region. A map $\Phi : U \times (a, b) \longrightarrow \mathbb{R}^n$ is called the* **flow**, *if $\Phi(\Phi(\mathbf{x}, t_1), t_2) = \Phi(\mathbf{x}, t_1 + t_2)$ holds.*

The linear *flow* exp (tA) induced by the linear operator A is a *contraction* iff the real parts of all eigenvalues of A are negative, i.e. if $|\exp(tA)\mathbf{x}|$ decays exponentially. If all eigenvalues have positive real parts this quantity grows exponentially and the flow is called an *expansion*. If all eigenvalues of A are nonzero the flow is called *regular*, and if the real parts of all eigenvalues are nonzero we have a *hyperbolic flow*. If the flow is hyperbolic it is just the direct sum of a contraction and an expansion.

We remember that when A is semisimple, the operator and thus also the differential equation breaks down into a number of uncoupled equations of



(a) (b) (c) (d) (e) (f)

Figure 2.1: Phase portraits a the two-dimensional ODE: Stable fixed points: (a)-(d); Structurally stable: (a),(b),(e);

dimensions one ore two. The classification of the one-dimensional flows is straight forward. A qualitative summary of the two-dimensional case is given in fig. 2.1 and a quantitative one in terms of trace and determinant of A in fig.2.2.

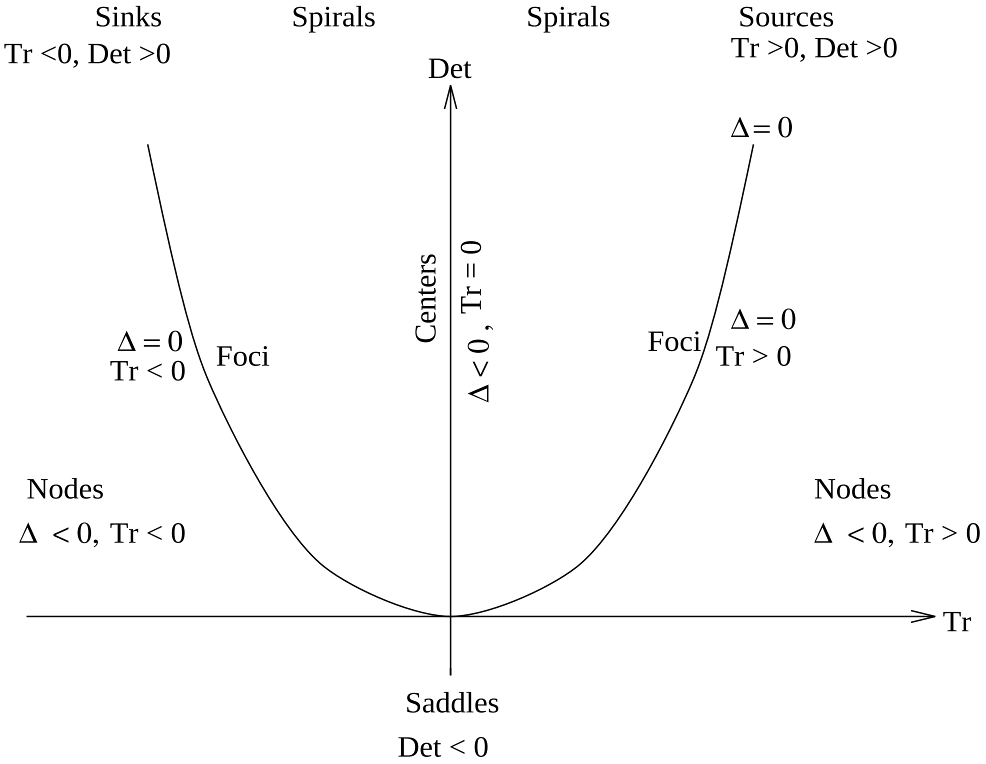


Figure 2.2: Classification of the two-dimensional linear ODE $\dot{\mathbf{x}} = A\mathbf{x}$ in terms of the invariant quantities $\Delta = \det A$ and Tr A.

2.1.3 Nonlinear Dynamical Systems

A dynamical system is a way of describing the passage in time of all points in a given *state space* S. Mathematically this space S will be an Euclidean space or an open subset of an Euclidean space.

Definition 2.2 *A* dynamical system *is a C^1 map $S \times I\!R \longrightarrow S$. If we have $\phi_t(\mathbf{x}) = \phi(\mathbf{x}_j; t)$, the map $\phi_t : S \longrightarrow S$ satisfies*

- *$\phi_0 : S \longrightarrow$ is the identity;*
- *The composition $\phi_t \circ \phi_s = \phi_{s+t}$ for all s,t in $I\!R$.*

Definition 2.3 *Let E be an Euclidean vector space; $W \subseteq E$ and f: $W \longrightarrow E$ a continuous map. A solution of the (nonlinear) differential equation*

$$\dot{\mathbf{x}} = f(\mathbf{x})$$

is a differentiable function $u : J \longrightarrow W$ defined on some interval $J \subseteq I\!R$ such that for all $t \in J$ holds

$$\dot{u}(t) = f\left(u(t)\right).$$

So we repeat some fundamental theorems concerning existence, uniqueness and continuity of solutions for ODEs of the above form.

Proposition 2.7 (Existence and Uniqueness) *Let $f \in C^1(W)$ and $\mathbf{x}_0 \in W$. Then there is some open interval $J \subseteq R$ and a* unique solution

$$\mathbf{x} : J \longrightarrow E \qquad \textit{satisfying} \qquad \mathbf{x}(0) = \mathbf{x}_0.$$

Proposition 2.8 (Continuity of Solutions) *Let $f \in C^1(W)$ and $\mathbf{y}(t)$ be a solution of $\dot{\mathbf{x}} = f(\mathbf{x})$ defined on a closed interval [t_0,t_1] with $\mathbf{y}(t_0) = \mathbf{y}_0$. There is a neighborhood $U \subset E$ of $\mathbf{y}_0$ and a constant k such that if $\mathbf{z}_0 \in U$, then there is a unique solution $\mathbf{z}(t)$ also defined on [t_0,t_1] with $\mathbf{z}(t_0) = \mathbf{z}_0$; and $\mathbf{z}$ satisfies*

$$|\mathbf{y}(t) - \mathbf{z}(t)| \leq k|\mathbf{y}_0 - \mathbf{z}_0|e^{k(t-t_0)}$$

Proposition 2.9 *Every dynamical system on an Euclidean vector space gives rise to a differential equation:*

$$\dot{\mathbf{x}} = \frac{\partial}{\partial t}\phi_t\Big|_{t=0}(\mathbf{x})$$

and conversely every autonomous differential equation $\dot{\mathbf{x}} = f(\mathbf{x})$ *arising from a* C^1*-map defines a dynamical system:* $\phi(t, \mathbf{x}) = \mathbf{u}(t)$ *is the solution of the initial value problem with* $\mathbf{u}(0) = \mathbf{x}$ *and* $\dot{\mathbf{x}} = f(\mathbf{x})$*.*

2.2 Limit Sets

It is not possible in general to calculate the solution curves $u(t)$ explicitly. In fact we don't have to know the exact solutions for the investigation subjects to this thesis. But we ought to know where a trajectory comes from, where it goes to, i.e. the *asymptotic behavior* of a given trajectory.

Definition 2.4 *A invariant set* G *for a flow* ϕ_t *is a subset* $G \subseteq E$ *such that*

$$\phi_t(\mathbf{x}) \in G \quad \textit{for} \quad \mathbf{x} \in G \quad \forall \quad t \in \mathbb{R}.$$

The most simple examples are fixed points $\bar{\mathbf{x}}$, i.e. $(f(\bar{\mathbf{x}}) = 0)$.

Definition 2.5 $\bar{\mathbf{x}}$ *is called a* **fixed point** *(or rest point or equilibrium) of a system of differential equations* $\dot{\mathbf{x}} = F(\mathbf{x})$*, if* $F(\bar{\mathbf{x}}) = 0$*.*

We divide the subspaces spanned by the generalized eigenvectors $\xi_1, \ldots, \xi_r$ into three classes:

- $E_s = \mathrm{span}\{\xi_1^s, \ldots, \xi_r^s\}$ is called the **stable eigenspace**.It is spanned by the generalized eigenvectors with eigenvalues with negative real part.

- $E_u = \text{span}\{\xi_1^u, \ldots, \xi_r^u\}$ is called the **unstable eigenspace**.It is spanned by the generalized eigenvectors with eigenvalues with positive real part.
- $E_c = \text{span}\{\xi_1^c, \ldots, \xi_r^c\}$ is called the **center eigenspace**.It is spanned by the generalized eigenvectors belonging to eigenvalues with vanishing real part.

Definition 2.6 *A point* $\mathbf{p} \in W$ *is called* nonwandering for the flow ϕ_t *if, for any neighborhood* U *of* $\mathbf{p}$*, there exist arbitrarily large* T *such that* $\phi_t(U) \cap U \neq \emptyset$*.*

A nonwandering point lies on or near orbits which come back within a specified distance of themselves. Fixed points and periodic orbits are thus nonwandering. The set of all nonwandering points is closed. Note that all invariant sets consist of nonwandering points.

Definition 2.7 *The* ω*-limit of* $\mathbf{x}$*, denoted by* $\omega(\mathbf{x})$*, is the set of all points* p *which have the following property: there are points* $\phi_{t_1}(\mathbf{x})$*,* $\phi_{t_2}(\mathbf{x})$*, ... on the orbit of* $\mathbf{x}$ *and such that* $\phi_{t_i}(\mathbf{x}) \longrightarrow p$ *as* $t_i \longrightarrow \infty$*. Correspondingly the* α*-limit* $\alpha(\mathbf{x})$ *with all points* q *for which such a sequence exists for* $t_i \longrightarrow -\infty$*.*

Definition 2.8 *A closed invariant set* $A \subset E$ *is called an* attracting set *if there is some neighborhood of* A *such that* $\phi_t(\mathbf{x}) \in U$ *for all* $t \geq 0$ *and* $\phi_t(\mathbf{x}) \longrightarrow A$ *as* $t \longrightarrow \infty$ *for all* $\mathbf{x} \in U$*. The set* $\bigcup_{t \geq 0} \phi_t(U)$ *is the* domain of attraction *of* A*.*

There is an analogous definition for *repelling sets*.

Domains of attraction of disjoint attracting sets are necessarily nonintersecting and separated by the stable manifolds of non-attracting sets.

A fixed point $\bar{\mathbf{x}}$ is *stable* if for every neighborhood V of $\bar{\mathbf{x}}$ in U there is a neighborhood $V_1 \subset V$ such that every solution $\mathbf{x}(\mathbf{x}_0, t)$ with $\mathbf{x}_0 \in V_1$ is defined and lies in V for all $t > 0$. If, in addition, V_1 can be chosen such that $\mathbf{x}(\mathbf{x}_0, t) \longrightarrow \bar{\mathbf{x}}$ as $t \longrightarrow \infty$ then $\bar{\mathbf{x}}$ is said to be *asymptotically stable.* Asymptotically stable fixed points are called to be *sinks.* A fixed point is called a *source* if there is a neighborhood U of $\bar{\mathbf{x}}$ such that for every $\mathbf{y}_0 \in U| \bar{\mathbf{x}}$ there is a $T > 0$ such that $\mathbf{y}(\mathbf{y}_0, T) \notin U$.

We close this section with a working definition of an *attractor* as given by Guckenheimer and Holmes [19].

Definition 2.9 *The closed set* Λ *is* indecomposable *if for every pair of points* $\mathbf{x}$*,* $\mathbf{y}$ *in* Λ *and for all* $\epsilon > 0$ *there are points* $X = \mathbf{x}_0, \mathbf{x}_1, \ldots, \mathbf{x}_n = \mathbf{y}$ *and* $t_1, \ldots, t_n \geq 1$ *such that*

$$dist(\phi_{t_i}(\mathbf{x}_i - 1), \mathbf{x}_i) < \epsilon$$

Definition 2.10 *An* attractor *is an indecomposable closed invariant set* Λ *with the property that, given* $\epsilon > 0$*, there is a set* U *of positive Lebesgue measure in the* ϵ*-neighborhood of* Λ *such that* $\mathbf{x} \in U$ *implies that the* ω*-limit of* X *is contained in* Λ *and the forward orbit of* $\mathbf{x}$ *is contained in* U*.*

There are different types of attractors for dynamical systems: An equilibrium is by far the most simple case. Fixed points will often be treated by analytical methods in this work. Limit sets consisting of equilibria and orbits connecting them are important in the models discussed here, although the are not structurally stable. Limit cycles and continua of periodic orbits are in generally very difficult to treat analytically, whereas *strange attractors* do not allow for extensive analytical treatment.

2.3 Linearisation of Vector Fields

Suppose we know a fixed point $\bar{\mathbf{x}}$ of the differential equation $\dot{\mathbf{x}} = f(\mathbf{x})$ and we wish to know the behavior of the dynamical system in a neighborhood of this point. We answer this question by studying the linear system

$$\dot{\xi} = \mathbf{J} \cdot \xi,$$

where $\mathbf{J}_{ij} = [\partial f_i / \partial \mathbf{x}_j]$ at the position of the fixed point $\bar{\mathbf{x}}$. $\mathbf{J}$ is called the *Jacobian* (matrix) of the vector field f.

Proposition 2.10 (Hartman-Grobman) *If* $\mathbf{J}$ *is hyperbolic then there is a homeomorphism* h *defined on some neighborhood* U *of* $\bar{\mathbf{x}}$ *in* E *locally taking orbits of the nonlinear flow* ϕ_t *of* $\dot{\mathbf{x}} = f(\mathbf{x})$ *to those of the linear flow* $\exp \mathbf{J}t$*. The homeomorphism* h *preserves the sense of the orbits and can also be chosen to preserve parametrization by time.*

Definition 2.11 *The set* $W^s_{loc}(\bar{\mathbf{x}})$ *(*$W^u_{loc}(\bar{\mathbf{x}})$*) defined below is called the local stable (unstable) manifold of* $\bar{\mathbf{x}}$*.*

$$\begin{aligned} W^s_{loc}(\bar{\mathbf{x}}) &= \{\mathbf{x} \in U | \phi_t(\mathbf{x}) \to \bar{\mathbf{x}} \text{ as } t \to \infty, \text{and } \phi_t(\mathbf{x}) \in U \ \forall t \geq 0\} \\ W^u_{loc}(\bar{\mathbf{x}}) &= \{\mathbf{x} \in U | \phi_t(\mathbf{x}) \to \bar{\mathbf{x}} \text{ as } t \to -\infty, \text{and } \phi_t(\mathbf{x}) \in U \ \forall t \leq 0\} \end{aligned}$$

Proposition 2.11 *[Stable Manifold Theorem] Suppose that* $\dot{\mathbf{x}} = f(\mathbf{x})$ *has an equilibrium* $\bar{\mathbf{x}}$*. Then there exist local stable, unstable, and center manifolds* W^s_{loc}*,* W^u_{loc}*,* W^c_{loc} *of the same dimensions* n_s*,* n_u*, and* n_c *as the eigenspaces* E^s *and* E^u *of the linearized system and tangent to them at* $\bar{\mathbf{x}}$*. The local stable and unstable manifolds are as smooth as the vector field* f*. Whereas the stable and unstable manifold are unique, this is not true for the center manifold.*

Let $\bar{\mathbf{x}}$ be a hyperbolic equilibrium of $\dot{\mathbf{x}} = f(\mathbf{x})$. If $W^u_{loc} = \emptyset$ then $\bar{\mathbf{x}}$ is a sink. If $W^s_{loc} = \emptyset$ the fixed point is a source, otherwise it is a *saddle point.* (For nonhyperbolic flows we will define a saddle as homeomorph to a hyperbolic saddle.) There is method to determine whether a fixed point is stable which does not depend on the hyperbolicity of the flow:

Proposition 2.12 (Ljapunov) *Let* $\bar{\mathbf{x}}$ *be a fixed point for* $\dot{\mathbf{x}} = f(\mathbf{x})$ *and* $v : W \to I\!R$ *be a differentiable function defined on some neighborhood* $W \subseteq U$ *of* $\bar{\mathbf{x}}$ *such that:*

- $v(\bar{\mathbf{x}}) = 0$ *and* $v(\mathbf{x}) > 0$ *if* $\mathbf{x} \neq \bar{\mathbf{x}}$,
- $\dot{v}(\mathbf{x}) \leq 0$ *in* $W \setminus \{\bar{\mathbf{x}}\}$.
  Then $\bar{\mathbf{x}}$ *is stable. Moreover, if*
- $\dot{v}(\mathbf{x}) < 0$ *in* $W \setminus \{\bar{\mathbf{x}}\}$

then $\bar{\mathbf{x}}$ *is asymptotically stable.*

A stable fixed point is said to be globally stable if all trajectories tend towards it for $t \to \infty$.

A second class of limit sets – besides fixed points – consists of certain unions of equilibria and trajectories connecting them. If distinct fixed points are connected we have a *heteroclinic orbit*, if a fixed point is connected to itself we have a *homoclinic orbit*. Both are sets of nonwandering points.

2.4 Structural Stability

Definition 2.12 *Let* $f \in C^m(E)$, $m \in I\!N$ *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* $\mathbf{x} \in K$ *holds*

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

Definition 2.13 *Two vector fields* f *and* g *are* topologically equivalent *if there exists a homeomorphism* h *which takes the orbits* $\phi_t^f(\mathbf{x})$ *of* f *to orbits* $\phi_t^g(\mathbf{x})$ *of* g, *preserving the senses but not necessarily parametrization by time.*

Definition 2.14 *A vector field f is called* structurally stable *if there in an $\epsilon > 0$ such that all C^1 functions g in an ϵ-neighborhood of f are topologically equivalent to f.*

For gradients systems there is an easy to verify sufficient condition for structural stability:

Proposition 2.13 *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

Proposition 2.14 (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*

- *the number of fixed points and periodic orbits is finite and they are all hyperbolic;*
- *there are no orbits connecting two saddle points;*
- *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 $C^r(M)$.

It is a nice result that both hyperbolicity and semisimpicity are *generic* properties of linear operators, i.e. semisimple (hyperbolic) operators on E form an open dense subset of $L(E)$. This means that almost all operators have this property and that the slightest perturbation of a nongeneric operator leads to a generic one. That means if we do not know all entries of the matrix A exactly, we may assume any generic property we want to have; it would not make sense to insist on a single special form of A.

On the other hand there may be good reasons for not assuming a particular generic property. If there are natural symmetries in the ODE or if the flow must conserve some quantity, say the energy, then the assumption of a generic property may be a mistake.

2.5 Bifurcations

Consider a set of differential equations

$$\dot{\mathbf{x}} = f(\mathbf{x}, \mu), \qquad \mathbf{x} \in \mathbb{R}^n, \quad \mu \in \mathbb{R}^k \tag{2.1}$$

If μ is varied, the implicit function theorem states that the fixed points, i.e. the solutions of the equation $f(\mathbf{x}, \mu) = 0$, can be described by continuous functions $\mathbf{x}(\mu)$, if the Jacobian $\partial f(\mathbf{x}\mu)$ has no eigenvalue with zero real part. If $(\mathbf{x}_0,\ \mu_0)$ is a point where the Jacobian has at least one such eigenvalue, several functions $\mathbf{x}(\mu)$ can intersect in $(\mathbf{x}_0,\ \mu_0)$. We say there is a *bifurcation* at $(\mathbf{x}_0,\ \mu_0)$. At the bifurcation point the vector field is structurally unstable.

Theorem 2.1 *For* $\dot{\mathbf{x}} = f(\mathbf{x},\ \mu)$, $\mu \in \mathbb{R}$, *the types of bifurcation can be classified as follows:*

1. *saddle node bifurcations*
2. *pitchfork bifurcations*
3. *transcritical bifurcations*
4. *Hopf bifurcations*

The proof of this theorem is found in [19]. We just want to give a qualitative explanation of how the flow changes at the various bifurcations.

- Saddle node bifurcation: For μ “below” μ^0 there is no fixed point, for μ “above” this value there are two, namely a saddle and a node; hence the name.
- Pitchfork bifurcation: For μ “below” the critical value, there is one fixed point, “above” this value there are three. Of the newly created fixed points one is stable and the other one unstable. The stability of the fixed point that exists on both sides of the bifurcation also changes at μ^0. Pitchfork bifurcations are of special interest in reaction diffusion systems since Turing instabilities arise in such bifurcations.
- Transcritical bifurcation: Two fixed points exist on both sides of the bifurcation. At μ^0 they coincide and exchange stability.
- Hopf bifurcation: Two generic cases of Hopf bifurcations are possible: a stable fixed point surrounded by an unstable limit cycle “below” μ^0 and a stable fixed point “above” that value or a stable fixed point “below” the bifurcation and an unstable fixed point surrounded by a stable limit cycle “above” the bifurcation.

In the first three cases, a single real eigenvalue of the Jacobian changes sign at μ^0; in the Hopf bifurcation a pair of complex eigenvalues crosses the imaginary axis. The terms above and below are used with quotes, because they can be replaced by each other, according to the meaning of μ in the specific problem.

2.6 The effect of Diffusion

After we have introduced the concept of diffusion along with some basic considerations in chapter 1, we now want to make precise the setting we use to investigate reaction diffusion systems.

2.6.1 Reaction Diffusion Equations and Symmetry Breaking

In general, the reaction diffusion equation has the form:

$$\dot{\mathbf{u}} = \mathbf{D}\nabla^2\mathbf{u} + f(\mathbf{u})$$

where $f(\mathbf{u})$ is the reaction part and $\mathbf{D}\nabla^2\mathbf{u} = \mathbf{D}\Delta\mathbf{u}$ is the diffusion part.

If a uniform solution of a reaction diffusion system is unstable due to diffusion, a perturbation of that homogeneous state can be amplified by diffusion and ultimately lead to a new (steady or unsteady) state. But not all perturbation show this property. Especially, a uniform perturbation of a uniform state cannot induce the formation of a nonuniform state.

Conversely, if a uniform solution of the reaction diffusion system is stable against all sufficiently small perturbations, it is called *diffusion stable*.

Those perturbations that can lead to a nonuniform state were termed 'symmetry breaking' [18, 31], because a higher degree of symmetry can be ascribed to the uniform state.

Only in very limited number of cases, exact solutions for reaction diffusion equations are known. One example is the travelling wave solution for the FitzHugh-Nagumo-equation [16].

2.6.2 Approximation of Solutions of Reaction-Diffusion equations

Since most reaction diffusion equations cannot be solved analytically, it is necessary to use numerical methods. A variety of different approaches has been described. The simplest approach is to divide both space and time into small segments and to assume that solutions are constant within these segments. This is the approach we use here. Alternatively, one might replace the differential equations by appropriate maps. This is the so called coupled map lattice approach, described e.g. by Kaneko [22]. Going still one step further, one may discretize not only space and time, but also the state variables, obtaining cellular automata [53].

A partial differential equation $\dot{\mathbf{u}} = F(\mathbf{u}, \mathbf{u}_x, \mathbf{u}_{xx})$ an a domain Ω, subject to certain boundary conditions, can be approximated by dividing the domain into elements in which the solution is constant in space; the solutions in adjacent elements are coupled by discrete approximations of the space derivatives. For example the reaction diffusion equation $\dot{\mathbf{u}} = f(\mathbf{u}) + \mathbf{D}\mathbf{u}_{xx}$ in $\Omega = [0{,}1]$ under Neumann boundary conditions, after dividing Ω into N equal elements $e_i = [\frac{i}{N}, \frac{i+1}{N}]$ leads to the system of ordinary differential equations

$$\begin{aligned}
\dot{\mathbf{u}}_i &= f(\mathbf{u}_i) + m^2\mathbf{D}(\mathbf{u}_{i-1} + \mathbf{u}_{i+1} - 2\mathbf{u}_i) \quad \text{for } i = 2, \ldots, N-1 \\
\dot{\mathbf{u}}_1 &= f(\mathbf{u}_1) + m^2\mathbf{D}(\mathbf{u}_2 - \mathbf{u}_1) \\
\dot{\mathbf{u}}_N &= f(\mathbf{u}_N) + m^2\mathbf{D}(\mathbf{u}_{N-1} - \mathbf{u}_N).
\end{aligned}$$

Here we use

$$\lim_{\Delta x \to \infty} \frac{\Delta}{\delta x}\left(\frac{\Delta}{\delta x}\right) = \frac{\partial^2}{\partial x^2}$$

with $\Delta : \Delta f(x) = f(x + \frac{\Delta x}{2}) - f(x - \frac{\Delta x}{2})$. Setting $\Delta x = \frac{1}{N}$, the limit $N \to \infty$ thus yields the continuous formulation. It is obvious that the formulation for $\dot{\mathbf{u}}_1$ and $\dot{\mathbf{u}}_N$ corresponds to Neumann boundary conditions. In our numerical studies, we shall restrict ourselves to rectangular domains with Neumann boundary conditions.

For Dirichlet boundary conditions, the appropriate formulation is

$$\begin{aligned}
\dot{\mathbf{u}}_1 &= f(\mathbf{u}_1) + m^2\mathbf{D}(\mathbf{u}_2 + c_0 - 2\mathbf{u}_1) \\
\dot{\mathbf{u}}_N &= f(\mathbf{u}_N) + m^2\mathbf{D}(\mathbf{u}_{N-1} + c_1 - 2\mathbf{u}_N),
\end{aligned}$$

where c_0 and c_1 are the boundary values at $x = 0$ and $x = 1$ respectively. For cyclic boundary conditions,

$$\begin{aligned}\dot{\mathbf{u}}_1 &= f(\mathbf{u}_1) + N^2\mathbf{D}(\mathbf{u}_2 + \mathbf{u}_N - 2\mathbf{u}_1)\\ \dot{\mathbf{u}}_N &= f(\mathbf{u}_N) + N^2\mathbf{D}(\mathbf{u}_{N-1} + \mathbf{u}_1 - 2\mathbf{u}_N)\end{aligned}$$

are appropriate. Discretization of two– and threedimensional domains can be carried out analogously.

This approach approximates the reaction diffusion equation as an N-dimensional coupled system of sparsely coupled ordinary differential equations. If there are k components, the k dimensional system of partial differential equations is approximated as a $k \times N$ dimensional system of ordinary differential equations. If the discretization is made infinitely fine the original system is regained; for this reason, partial differential equations can be viewed as infinite dimensional systems of ordinary differential equations ([45]).

2.6.3 Diffusion Stability

When studying reaction diffusion systems, we are mainly interested in those fixed points that are stable in the reaction system but not diffusion stable, since only these can exhibit the diffusion breaking mentioned above. If we approximate the partial differential equations by a system of ordinary differential equations as described, a fixed point is diffusion stable if both the k–dimensional Jacobian of the reaction system $\mathbf{J}$ and the $N \times k$–dimensional Jacobian of the reaction diffusion system $\widehat{\mathbf{J}}$, evaluated at the fixed point, have only eigenvalues with negative real parts for all possible sets of diffusion coefficients. The following important theorem on that problem is found in Streissler [45]:

Theorem 2.2 *The matrix $\widehat{\mathbf{J}}$ (the Jacobian of the reaction diffusion system, evaluated with the concentration in all cells equal to that of a stable fixed* *point of the reaction system) has only eigenvalues with negative real parts if the matrix*

$$\mathbf{J} - \Lambda_{\mathbf{k}}\mathbf{D}$$

has only eigenvalues with negative real part for all possible choices of $\mathbf{k}$*, where* $\mathbf{D}$ *is the diagonal matrix of the diffusion coefficients,* $\mathbf{k} = (i_1, i_2, \ldots, i_n) \in [1, N_1] \times [1, N_2] \times \ldots \times [1, N_n]$*,* n *is the number of spatial coordinates,* N_i *is the number of cells for coordinate* i*,* $\Lambda_{\mathbf{k}} = (\lambda_{i_1} + \lambda_{i_2} + \ldots + \lambda_{i_n})$*, and* λ_j *is the* j*–th eigenvalue of the* $N_i \times N_i$ *matrix* $\mathbf{C}^1$ *that describes how the individual cells are coupled. If the matrix* $\mathbf{J} - \Lambda_{\mathbf{k}}\mathbf{D}$ *has eigenvalues with positive real part for a certaim choice of* $\mathbf{k}$*, a (suitable) perturbation of the uniform solution will lead to the formation of a nonuniform solution with* i_j *extrema in the spatial coordinate* j*.*

For Neumann boundary conditions, they are determined by

$$\lambda_j = 2\left(\cos\frac{2\pi\, j}{n} - 1\right), \qquad j = 1, \ldots, N_i - 1$$

Although the eigenvalues of $\mathbf{J} - \Lambda_{\mathbf{k}}\mathbf{D}$ are much easier to compute than those of $\widehat{\mathbf{J}}$, they can be used only to determine the stability of the fixed point for a given set of diffusion coefficients $\mathbf{D}$. The following theorem by Berman, Plemmons [3] and Streissler [45] can be used to find out if there is a matrix $\mathbf{D}$, which destabilizes the fixed point:

Theorem 2.3 *Let* $\mathbf{J}$ *be the Jacobian of a reaction system, evaluated at a fixed point with eigenvalues with negative real part except for one zero eigenvalue, let* $\mathbf{D} > 0$ *be a real diagonal* $n \times n$*-matrix with* $d_i \geq 0$ *and at least one* d_i *non-vanishing. Then all the principal minors of* $-\mathbf{J}$ *are nonnegative iff* $-\mathbf{J} + \mathbf{D}$ *is nonsingular for every* $\mathbf{D}$*. If the principal minor obtained by*

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[1] If the cells i and j couple (if there is exchange of matter between them), the entries c_{ij} and c_{ji} of $\mathbf{C}$ are 1, otherwise they are zero. If cell i couples with m other cells the diagonal entry c_{ii} is $-m$.

cancelling the rows and columns corresponding to $u_{i_1},\ u_{i_2}, \ldots,\ u_{i_k}$ *is negative, Turing instabilities can be induced by choosing the diffusion coefficients of these reactants larger than those of the others.*

The proof is found in Streissler [45], so that it will not be repeated here. Combining 2.2 with 2.3 we see that if all principal minors of $-\mathbf{J}$, evaluated at a certain fixed point, are nonnegative, then this fixed point is diffusion stable. Furthermore, if we can evaluate the eigenvalues of $\mathbf{J} - \Lambda_\mathbf{k}\mathbf{D}$ directly, we can conclude, that wherever one of these eigenvalues has a zero real part, there is a bifurcation in the spatial coordinates.

2.6.4 Implementation of the algorithm

All numerical results on reaction diffusion systems were obtained using the program package `STAR` by Christoph Streissler. This program uses a finite difference algorithm for the space and a variable time step Crank–Nicolson scheme for the time. In all one dimensional problems a lattice size of 100 cells was chosen. For two dimensional problems we used a square lattice of 25×25 cells. The program and the algorithms it uses is described in great detail in [45].

Chapter 3

General model

The reaction networks treated in this work are dealing with three different kinds of substances:

1. 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.
2. 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}.
3. 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.

We then have the following reaction network:

$$\begin{array}{rcl} A + X_i & \xrightarrow{k_i} & 2X_i \\ A + X_i & \xrightarrow{g_i} & X_i + S_i \\ X_i + S_l & \xrightarrow{b_{li}} & 2X_i \end{array} \tag{3.1}$$

with $i, l \in \{1, 2, \ldots, n\}$ and n is the total number of replicating species (and intermediates). From the definition of k_i, g_i, and b_{il} as reaction constants it is clear that they all are nonnegative. Moreover, since for $g_i = 0$ the intermediate S_i cannot exist (at least in the long term) and hence we loose the interesting part of the dynamics, namely the interaction of X_i with the other replicating species via the intermediate, we assume that all $g_i > 0$. The matrix $\mathbf{B} = (b_{il})$ is called coupling matrix or interaction matrix.

Occasionally, we shall compare the dynamics of system (3.1) with the simpler replicator–like systems:

$$\begin{array}{rcl} A + X_i & \xrightarrow{k'_i} & 2X_i \\ A + X_i + X_l & \xrightarrow{b'_{li}} & 2X_l \end{array} \tag{3.2}$$

The constants k'_i and b'_{il} will be zero wherever k_i and b_{il}, respectively, are zero and vice versa. The absolute values of the constants in the two systems need not coincide, however.

The difference between (3.1) and (3.2) is that the termolecular reaction step in the latter scheme is replaced by two consecutive bimolecular reactions in the former. Termolecular reactions, as mentioned in chapter 1, are physically very improbable, since the chance for termolecular collisions is normally some orders of magnitude less than that for bimolecular collisions. However, under certain circumstances, the differential equations based on the assumption of a termolecular reaction step can correctly predict the behaviour of the variables. We shall therefore occasionally compare the results for (3.1) with those for the "underlying replicator–like reaction scheme" (3.2).

Before we go on, I would like to point out that definitions in this chapter are valid throughout the text (unless explicitly redefined). Definitions in the remaining chapters are valid only in these chapters.

Since interesting dynamic behaviour occurs only for chemical systems far from thermodynamic equilibrium, we must consider an experimental setup with a constant flow of matter or energy (or both) through the system. In particular, three such setups, which are closely related to one another, are considered, namely

1. The continuously stirred tank reactor (CSTR)
2. The closed system with recycling reaction
3. The evolution reactor

We now consider them in turn.

3.1 The continuously stirred tank reactor (CSTR)

In experimental chemical kinetics, the CSTR is widely used to study fast chemical reactions shortly after the onset of the reaction. In the CSTR, the separate reactants flow into a reactor chamber continuously, where they mix, and the reaction products flow out with a rate exactly balancing the feed. Mixing should be achieved in a time negligible in comparison to the mean residence time τ of the reactants in the reactor. This is done by using specially designed nozzles and continuous stirring. The state that is reached in the reaction chamber after some time corresponds to the state of the reaction after the time τ. By varying the flow rate (designated by r in this work), different mean residence times are realized, yielding different data points for the time development of the composition of the reaction. A sketch of a CSTR is shown in figure 3.1

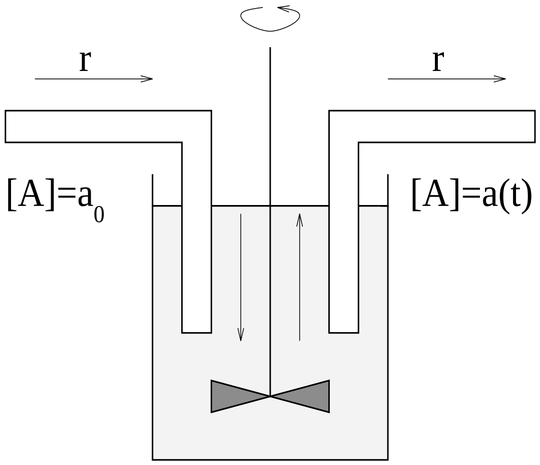


Figure 3.1: continuously stirred tank reactor

In modelling the reaction network (3.1) in the CSTR setting, we assume that the solution flowing into the reactor at rate r contains the substrate A at a concentration a_0 and that all X_i, S_i and the substrate are diluted out of the reactor at the same rate r. This keeps the solutions bounded. Writing x_i, s_i and a for the concentrations of X_i, S_i and A respectively, the kinetic differential equations for the above reaction network in the CSTR are:

$$\begin{aligned} \dot{x}_i &= x_i(k_i a + \textstyle\sum_{l=1}^n b_{li} s_l - r) \\ \dot{s}_l &= g_l x_l a - s_l(\textstyle\sum_{i=1}^n b_{li} x_i + r) \\ \dot{a} &= a_0 r - a\,(\textstyle\sum_{i=1}^n (k_i + g_i) x_i + r) \end{aligned} \tag{3.3}$$

It should be clear that the first two of the above equations stand for n analogous equations each. Adding together all the above equations we see that the total concentration $c_0 = a + \sum x_i + s_i$ tends to a_0. Therefore all fixed points (and all other ω–limits) must lie on the set $\mathbf{S}_{2n+1} = \{(u_1, \dots, u_{2n+1}) | \sum u_i = a_0,\ u_i \geq 0\}$, which is known as *concentration simplex.*

The kinetic constants $k_i,\ g_i$ and b_{il} are in general complicated functions of temperature, pressure etc. There is no obvious way to vary one of them, keeping the others fixed, in order to investigate the influence of a single parameter on the system. The flow rate r and the influx concentration of the substrate a_0, on the other hand, can be easily varied over a wide range in an experimental setting without changing any of the other parameters. We therefore describe how the behaviour of the system changes if for a given set of kinetic constants the flow rate is varied.

We shall assume the variables to be ordered in the following way: $(x_1, \dots, x_n, s_1, \dots, s_n, a)$. Moreover, unless explicitly stated otherwise, we shall assume that all k_i are different and that the labels are chosen such that $k_1 > k_i,\ i = 2, \dots, n$. (The importance of this assumption will become clear soon).

For any fixed point where the equilibrium concentration (which we shall denote by over bars) of the species X_i is zero, the concentration of S_i also vanishes and vice versa. This leads us to the following

Definition 3.1 *For every fixed point we define the* index set I *as the set of species that are present at the fixed point in positive concentrations:* $i \in I \iff \bar{x}_i, \bar{s}_i > 0$. *We label the corresponding fixed point* P_I*; if there is more than one fixed point for this index set, we shall distinguish them by superscripts. The number of entries in* I, n_I, *is called the dimension of the fixed point* P_I.

There may be index sets for which there is no fixed point, depending on the properties of the constants $b_{li},\ k_i$ and g_i.

There are three kinds of fixed points: the trivial fixed point, the interior fixed point and fixed points on the boundary of the simplex.

3.1.1 The trivial fixed point

The trivial fixed point is the one with $I = \emptyset$, that is, we have only the substrate A in the reactor. It then follows from what we have said above that $\bar{a} = a_0$. The trivial fixed point exists for all possible choices of the kinetic constants and the flow rate r. The Jacobian of the system, evaluated at the trivial fixed point is just a diagonal matrix with the entries (and hence eigenvalues) $k_i a_0 - r$ and $-r$ ($n+1$ times). Since we assumed k_1 to be the largest of the constants k_i, the trivial fixed point is stable for $r > a_0 k_1$.

3.1.2 The interior fixed point

At the interior fixed point, on the other hand, all species coexist: $I = \mathcal{N} = \{1, 2, \ldots, n\}$. It may be calculated as follows: calculate the values of $\bar{s}_i$ using the equations $\dot{x}_i = 0$ and treating $\bar{a}$ as parameter; insert these values into the set of equations $\bar{s}_i = 0$ and use them to calculate $\bar{x}_i$, treating $\bar{a}$ as above; finally, insert these values into the normalization condition

$$\bar{a} = \sum \bar{x}_i + \bar{s}_i = a_0 \tag{3.4}$$

To make the results readable, we adopt (column) vector notation for the equilibrium concentrations and kinetic constants: $\mathbf{x} = (x_1, \ldots, x_n)^t$, $\mathbf{s} = (s_1, \ldots, s_n)^t$, $\mathbf{k} = (k_1, \ldots, k_n)^t$, $\mathbf{g} = (g_1, \ldots g_n)^t$. Besides, we define the matrix $\mathbf{B} = (b_{li})$ and the vector $\mathbf{1}$ with n entries of unity. We then have the following equation system for $\mathbf{s}$:

$$\mathbf{B}\bar{\mathbf{s}} = r\mathbf{1} - \bar{a}\mathbf{k} \tag{3.5}$$

This equation system has a unique solution if the matrix $\mathbf{B}$ is invertible. The solution is then given by

$$\bar{\mathbf{s}} = \mathbf{B}^{-\mathbf{1}}(r\mathbf{1} - \bar{a}\mathbf{k}) \tag{3.6}$$

Thus, the $\bar{s}_i$ are linear in $\bar{a}$. They are not linear in r, however, for $k_i \neq 0$, since $\bar{a}$ is generally a nonlinear function of r.

To find the equilibrium concentrations of the replicating species, we define the matrix $\mathbf{C} = (c_{i,j})$ with $c_{i,j} = g_i \bar{a} \delta_{i,j} - b_{ji} \bar{s}_i$, where $\delta_{i,j}$ is Kronecker's symbol. If $\mathbf{B}$ is invertible, $\bar{a}$ can be chosen such that $\mathbf{C}$ is also invertible. We then have

$$\mathbf{C}\bar{\mathbf{x}} = r\bar{\mathbf{s}} \tag{3.7}$$

Then, if we define $\mathbf{C}^{(i)}$ as the matrix where the i–th column vector of $\mathbf{C}$ has been replaced by $r\bar{\mathbf{s}}$, we obtain

$$\bar{x}_i = \frac{|\mathbf{C}^{(i)}|}{|\mathbf{C}|} \tag{3.8}$$

Since all rows of $\mathbf{C}$ are linear in $\bar{a}$, the determinants $|\mathbf{C}|$ and $|\mathbf{C}^{(i)}|$ can be at most n–th order in $\bar{a}$. Inserting now the above results into (3.4), we see that it generally is an equation of $n+1$–th order in $\bar{a}$, that is, we have at most $n+1$ interior fixed points. However, some of the solutions of (3.4) might be negative or imaginary. Moreover, for the fixed point to lie in the interior of the simplex, we must have $0 < \bar{x}_i, \bar{s}_i < a_0 - \bar{a}$, which gives us $2n$ additional inequalities that must be fulfilled. The actual number of interior fixed points may thus be considerably lower than $n+1$.

The stability of the interior fixed point(s) can be computed only for very special cases. The only thing we know is that there is always one eigenvalue $-r$ (the so–called external eigenvalue, see below).

3.1.3 Fixed points on the boundary of the simplex

These are all remaining fixed points, that is, fixed points with $I \neq \emptyset$ and $I \neq \mathcal{N}$ (there may be no such fixed points at all). When we shall deal with fixed point on the boundary of the simplex in special cases, the following definition will be useful:

Definition 3.2 *We call an index set I* admissible *if a fixed point P_I exists at least for a certain range of flow rates.*

If n_I is the number of elements of I, the problem of finding the equilibrium concentrations $\bar{x}_i,\ \bar{s}_i,\ i \in I$ and $\bar{a}$ is equivalent to finding the interior fixed point of an n_I–species system with a matrix **B'**, where only rows and columns with indices that lie in I are retained.

The eigenvalues of the Jacobian, evaluated at a fixed point on the boundary of the simplex, can be split into three groups: *external, transversal* and *internal* eigenvalues.

There is always one eigenvalue $-r$, called the *external* eigenvalue. It exists in all CSTR systems, which follows from the fact that the sum of the entries of a column is always $-r$. Hence the vector with $2n+1$ entries of unity is a left eigenvector with the corresponding eigenvalue $-r$. Geometrically, this eigenvalue describes the stability of the fixed point against a perturbation in which all concentrations are raised (lowered) simultaneously, thus violating the normalization condition and leading off the simplex. Since we have seen that every solution converges to the simplex, it is clear that this eigenvalue must be negative. All the other eigenvectors can be chosen so that perturbing along them we do not leave the simplex (the sum of the components is zero).

The *transversal* eigenvalues provide information on stability against the introduction of new species. For every $l \notin I$, the l-th row of the Jacobian has only one nonzero entry, namely

$$\frac{\partial \dot{x}_l}{\partial x_l} = k_l \bar{a} + \sum_{i \in I} b_{il} \bar{s}_i - r = \lambda_l^{(tr,1)} \tag{3.9}$$

which is therefore an eigenvalue. The corresponding eigenvector has nonzero components both for x_l and s_l and thus describes a perturbation introducing x_l and s_l simultaneously. The eigenvalue can have either sign; if it is zero, there is a transcritical bifurcation with a fixed point that has the index set

$I \cup \{l\}$. In the $(l+n)$– th row there are two nonzero entries:

$$\frac{\partial \dot{s}_l}{\partial x_l} = g_l \bar{a} \qquad \text{and} \qquad \frac{\partial \dot{s}_l}{\partial s_l} = -\left(\sum_{i \in I} b_{li} \bar{x}_i + r \right) = \lambda_l^{(tr,2)} \tag{3.10}$$

The first of these terms cancels in the factorization of the secular determinant; the second is an eigenvalue of the Jacobian, which is, of course, always negative. The corresponding eigenvector has a nonzero component for s_l but not for x_l; thus, it describes the effect of introducing only s_l into the system. Since s_l cannot be produced in the absence of x_l, it is clear that any fixed point is stable against this perturbation. Since the sign of $\lambda^{(tr,2)}$ is always negative, we shall ignore it in stability considerations and speak of $\lambda^{(tr,1)}$ as "the" transversal eigenvalue.

The internal eigenvalues describe the stability within the sub-simplex in which the fixed point lies. As is seen easily from (3.9) and (3.10), their eigenvectors have zero entries for all x_l, s_l with $l \notin I$. Their computation is equivalent to calculating the eigenvalues of the corresponding n_I–species system.

One dimensional fixed points ($n_I = 1$)

The fixed points with $n_I = 1$, i.e. $I = \{i\}$ are of special importance, because they exist for every coupling matrix $\mathbf{B}$ at least for sufficiently low flow rates. If they are stable, any initial distribution of concentrations that contains enough of species i will eventually converge to a state where only species i survives: the system is selective. Moreover, we can obtain analytical expressions for the equilibrium concentrations and for the eigenvalues of the Jacobian. We distinguish two principal cases which differ very much in their behaviour: $b_{ii} = 0$ and $b_{ii} > 0$.

Case 1: $b_{ii} = 0$: If $b_{ii} = 0$, we have

$$\bar{x}_i = \frac{k_i a_0 - r}{\kappa_i}, \qquad \bar{s}_i = \frac{g_i(k_i a_0 - r)}{k_i \kappa_i}, \qquad \bar{a} = \frac{r}{k_i} \tag{3.11}$$

where $\kappa_i = k_i + g_i$. The internal eigenvalues (and the external eigenvalue) are obtained by finding the eigenvalues of the matrix

$$\begin{pmatrix} k_i\bar{a} - r & 0 & k_i\bar{x}_i \\ g_i\bar{a} & -r & g_i\bar{x}_i \\ -\kappa_i\bar{a} & 0 & -r - \kappa_i\bar{x}_i \end{pmatrix} \tag{3.12}$$

The characteristic polynomial – after division by $(\lambda - r)$ to get rid of the external eigenvalue – is easily found:

$$(\lambda - r)\left(-\lambda + k_i\bar{a} - r - \kappa_i\bar{x}_i\right) = 0 \tag{3.13}$$

and since $\bar{a} = r/k_i$, the second eigenvalue is $-\kappa_i\bar{x}_i = r - k_i a_0$. This eigenvalue is nonnegative if the fixed point lies on the simplex. Moreover, we see that for $r = k_i a_0$, there is a transcritical bifurcation with the trivial fixed point and for flow rates above this value the fixed point lies outside the simplex. The internal eigenvalues therefore are both negative.

The transversal eigenvalues are obtained by combining (3.11) with (3.9) and (3.10) as:

$$\lambda_l^{(tr,1)} = \frac{r}{k_i}\left(k_l - k_i - \frac{g_i b_{il}}{\kappa_i}\right) + \frac{g_i k_i a_0 b_{il}}{k_i \kappa_i}, \qquad \lambda_l^{(tr,2)} = -(b_{il}\bar{x}_i + r) \tag{3.14}$$

While the latter is always negative, the sign of the former depends on k_i, k_l, and b_{il}:

1. If $b_{il} = 0$, the eigenvalue is negative if and only if $k_l < k_i$.
2. If $b_{il} > 0$ and $k_l > k_i$, the eigenvalue is positive for all flow rates for which the fixed point exists. Conversely, if $k_l < k_i$, the eigenvalue is positive for flow rates less than

$$r^{i\times l} = \frac{g_i k_i a_0 b_{il}}{g_i b_{il} + (k_i - k_l)\kappa_i} < k_i a_0 \tag{3.15}$$

> At this flow rate, there is a transcritical bifurcation with the fixed point $P_{\{i,l\}}$, and the transversal eigenvalue of $P_{\{i\}}$ is negative for higher flow rates.

Since it is not clear in general that the fixed point $P_{\{i,l\}}$ exists and can pass through $P_{\{i\}}$, we now prove that this is indeed the case if $k_l > k_i$ and $b_{il} > 0$. At $P_{\{i,l\}}$, the equilibrium concentrations fulfill the following equations:

$$\begin{aligned} k_i\bar{a} + b_{il}\bar{s}_l - r &= 0 \\ k_l\bar{a} + b_{ll}\bar{s}_l + b_{li}\bar{s}_i &= 0 \\ g_i\bar{x}_i\bar{a} - \bar{s}_i(b_{li}\bar{x}_i + r) &= 0 \\ g_l\bar{x}_l\bar{a} - \bar{s}_l(b_{ll}\bar{x}_l + b_{li}\bar{x}_i + r) &= 0 \\ a_0 - \bar{x}_1 - \bar{x}_2 - \bar{s}_1 - \bar{s}_2 - \bar{a} &= 0 \end{aligned} \tag{3.16}$$

From the first equation it is clear that if $\bar{s}_l$ vanishes, $\bar{a}$ must equal r/k_i. Inserting this into the fourth equation, we see that then $\bar{x}_l = 0$. We can now calculate $\bar{x}_i$ and $\bar{s}_i$ from the second and third equation:

$$\bar{x}_i = \frac{r(k_i - k_l)}{b_{li}g_i}, \qquad \bar{s}_i = \frac{r(k_i - k_l)}{b_{li}k_i} \tag{3.17}$$

Since $k_i > k_l$, both concentrations are positive. If there is a flow rate for which these results fulfill the last equation, there is indeed a transcritical bifurcation between $P_{\{i,l\}}$ and $P_{\{i\}}$:

$$a_0 - r\left(\frac{k_i - k_l}{b_{il}k_i} + \frac{k_i - k_l}{b_{il}g_i} + \frac{1}{k_i}\right) = 0 \tag{3.18}$$

Solving this equation for r, we obtain again $r^{i\times l}$.

The results of this paragraph are summarized on the next page.

One dimensional fixed points in the CSTR, $b_{ii} = 0$

1. There is exactly one fixed point P_I with $I = \{i\}$ for flow rates below $a_0 k_i$
2. If all entries b_{il} are zero, the fixed point $P_{\{1\}}$ is stable for $0 < r < a_0 k_1$, that is, for all flow rates at which it exists, while all other one–dimensional fixed points are saddles.
3. If some of the b_{1l} are greater than zero, $P_{\{1\}}$ is stable at least for flow rates sufficiently close to $a_0 k_1$, but it becomes unstable for sufficiently small flow rates (due to a transcritical bifurcation with the fixed point $P_{\{1,l\}}$).
4. All the remaining one–dimensional fixed points are unstable.
5. The fixed point $P_{\{i\}}$ lies outside the simplex for flow rates above $a_0 k_i$. For flow rates above $a_0 k_1$, i. e. after all one dimensional fixed points have left the simplex, the trivial fixed point is stable.

Case 2: $b_{ii} > 0$**:** If $b_{ii} > 0$, the equilibrium concentrations are

$$\bar{x}_i = \frac{r(r - k_i \bar{a})}{b_{ii}(\kappa_i \bar{a} - r)}, \qquad \bar{s}_i = \frac{r - k_i \bar{a}}{b_{ii}} \tag{3.19}$$

with $\kappa_i = (k_i + g_i)$. (3.19) implies that for every solution that lies on the simplex $\bar{a}$ must fulfill the inequalities $\bar{a} k_i \leq r < \bar{a} \kappa_i$. $\bar{a}$ fulfills the equation

$$\bar{a}^2 \kappa_i (b_{ii} - k_i) - \bar{a}(b_{ii} a_0 \kappa_i + r(b_{ii} - \kappa_i)) + b_{ii} a_0 r = 0 \tag{3.20}$$

This equation has two positive solutions if $b_{ii} > k_i$ and one positive solution in the converse case. If there are two positive solutions, we have a saddle node bifurcation at

$$r^*_\pm = \frac{a_0 b_{ii} \kappa_i \left(b_{ii} + g_i - k_i \pm 2\sqrt{g_i(b_{ii} - k_i)}\right)}{(b_{ii} - \kappa_i)^2}, \qquad \bar{a}^*_\pm = a_0 \frac{b_{ii}\left(1 \pm \sqrt{\frac{g_i}{b_{ii} - k_i}}\right)}{b_{ii} - \kappa_i} \tag{3.21}$$

These critical parameters were calculated by setting the discriminant of (3.20) to zero. Since the value $\bar{a}^*_+$ with the plus sign before the square root is greater than a_0, we are only interested in the solutions with the minus sign. Setting $\Delta_i = b_{ii} - k_i$, we can rewrite the latter

$$r^*_- = \frac{a_0 b_{ii} \kappa_i}{(\sqrt{g_i} + \sqrt{\Delta_i})^2}, \qquad \bar{a}^*_- = \frac{a_0 b_{ii}}{\Delta_i + \sqrt{g_i \Delta_i}} \tag{3.22}$$

$\bar{a}^*_-$ is less than a_0 if $b_{ii} > b^c_{ii} = k_i \kappa_i / g_i$, which means that the saddle node bifurcation occurs on the simplex if the above inequality is fulfilled, and outside the simplex otherwise. If we have two solutions of (3.20) that lie on the simplex, we call the fixed point with the lower equilibrium concentration of $\bar{a}$ $P^{(1)}_{\{i\}}$ and the other one $P^{(2)}_{\{i\}}$.

As in the case $b_{ii} = 0$, there is a transcritical bifurcation at $r^{\{i\}\times\emptyset} = a_0 k_i$, which can be easily verified from (3.20) and (3.19). There is no other transcritical bifurcation with the trivial fixed point even if there are two (meaningful) solutions of (3.20).

For very small values of r we see from (3.20) that there is exactly one solution that fulfills the inequality $\bar{a} k_i < r < \bar{a}\kappa$. If $b_{ii} > b^c_{ii}$, a second solution enters the simplex if the flow rate is raised above $a_0 k_i$ and the two fixed points disappear in a saddle node bifurcation at r^*_-. In the converse case, the fixed point lies outside the simplex for $r > a_0 k_i$.

To find the internal eigenvalues (and the external eigenvalue) is equivalent to finding the eigenvalues of

$$\begin{pmatrix} 0 & b_{ii}\bar{x}_i & k_i \bar{x}_i \\ g_i \bar{a} - b_{ii}\bar{s}_i & -b_{ii}\bar{s}_i - r & g_i \bar{x}_i \\ -\kappa_i \bar{x}_i & 0 & -r - \kappa_i \bar{x}_i \end{pmatrix} \tag{3.23}$$

If $b_{ii} > k_i$ we can write the characteristic polynomial of (3.23), using (3.19), (3.20), and (3.22), after dividing by $(\lambda + r)$:

$$\lambda^2 b_{ii}(\bar{a}\kappa_i - r)^2 + \lambda r(\bar{a}\kappa_i - r)[\kappa_i(r - \bar{a}k_i) + \bar{a}g_i b_{ii}] + (\bar{a} - \bar{a}^*_-)K_i = 0 \quad (3.24)$$

with

$$K_i = \frac{2a_0 b_{ii}\kappa_i^2 r\sqrt{g_i\Delta_i}(r - \bar{a}k_i)\left(\sqrt{g_i} + \sqrt{\Delta_i})^2\right)}{(b_{ii} - \kappa_i)^2} > 0 \quad (3.25)$$

From the sign of the coefficients of λ in (3.24) we see that there are three negative eigenvalues for $\bar{a} < \bar{a}^*$ and two negative and one positive for $\bar{a} > \bar{a}^*$. Thus, if all transversal eigenvalues are negative, the fixed point with the lower concentration of the substrate is a sink, while the one with the higher concentration (if it lies on the simplex) is a saddle.

If $b_{ii} < k_i$, we have $\Delta_i < 0$. The characteristic polynomial of the Jacobian (after division by $(\lambda + r)$) then reads:

$$\begin{aligned} \lambda^2 b_{ii}(\bar{a}\kappa_i - r)^2 \quad & +\lambda r(\bar{a}\kappa_i - r)[\kappa_i(r - \bar{a}k_i) + \bar{a}g_i b_{ii}] + \\ & +r(r - \bar{a}k_1)[g_1 r^2 - \Delta_i(\bar{a}\kappa_i - r)^2] = 0 \end{aligned} \quad (3.26)$$

and since all coefficients of λ are positive, both internal eigenvalues are negative.

The computation of the transversal eigenvalues is a little more complicated than in the case $b_{ii} = 0$. Inserting (3.19) into (3.9), we obtain

$$\lambda = (k_l\bar{a} - r) - \frac{b_{il}}{b_{ii}}(k_i\bar{a} - r) \quad (3.27)$$

The following three cases can be distinguished:

1. $k_i > k_l b_{ii}/b_{il}$, $b_{ii} > b_{il}$: The transversal eigenvalue is negative for all flow rates.

2. $k_i > k_l b_{ii}/b_{il}$, $b_{ii} < b_{il}$ or $k_i < k_l b_{ii}/b_{il}$, $b_{ii} > b_{il}$: There is a transcritical bifurcation with a fixed point $P_{\{il\}}$ (the transversal eigenvalue changes sign).

3. $k_i < k_l b_{ii}/b_{il}$, $b_{ii} < b_{il}$: The transversal eigenvalue is positive for all flow rates.

The transcritical bifurcation of $P_{\{i\}}$ and $P_{\{i,l\}}$ (if there is any) takes place at

$$r^{i\times l} = \bar{a}^{i\times l} \frac{b_{ii}k_l - b_{il}k_i}{b_{ii} - b_{il}} \tag{3.28}$$

where $\bar{a}^{i\times l}$ is calculated by inserting (3.28) into (3.20) :

$$\bar{a}^{i\times l} = a_0 \frac{g_i(b_{ii} - b_{il}) - \Delta_{il} b_{ii}}{g_i(b_{ii} - b_{il}) - \Delta_{il}(b_{ii} - \kappa_i)} < a_0 \tag{3.29}$$

with $\Delta_{il} = k_l - k_i > 0$. However, for $\bar{a}^{i\times l}$ to lie between zero and a_0, Δ_{il} must be less than $g_i(b_{ii} - b_{il})/b_{ii}$.

If there are two solutions of (3.20), we want to know which one of them is undergoing the transcritical bifurcation. Comparing (3.22) with (3.29), we see that $P_{\{i,l\}}$ passes through $P^{(2)}_{\{i\}}$ if

$$\Delta_{il} > \Delta^c_{il} = \frac{(b_{ii} - b_{il}) \left(b_{ii} g_i + \kappa_i \sqrt{g_i \Delta}\right)}{b_{ii}(b_{ii} - \kappa_i)} \tag{3.30}$$

The proof that the fixed point $P_{\{i,l\}}$ really passes through $P_{\{i\}}$ is very similar to that for the case $b_{ii} = 0$ and is therefore omitted.

To find out how the transversal eigenvalue changes at the transcritical bifurcation, we examine the its derivative with respect to the flow rate:

$$\frac{\mathrm{d}\lambda}{\mathrm{d}r} = \left[\Delta_{il} + k_i \left(1 + \frac{b_{il}}{b_{ii}}\right)\right] \frac{\mathrm{d}\bar{a}}{\mathrm{d}r} - \left(1 + \frac{b_{il}}{b_{ii}}\right) \tag{3.31}$$

Evaluating this at $\left(\bar{a}^{i\times l},\ r^{i\times l}\right)$ and using (3.22), we obtain, after some algebra:

$$\left(\frac{\mathrm{d}\lambda}{\mathrm{d}r}\right)_{\bar{a}^{i\times l},\ r^{i\times l}} = \frac{a_0 b_{ii}(b_{ii} + b_{il}) g_i \bar{a}^{i\times l}}{(\bar{a}^* - \bar{a}^{i\times l}) N(\bar{a}^{i\times l})} \tag{3.32}$$

where

$$N(\bar{a}^{i\times l}) = \Delta_i \left[b_{ii}\left(a_0 - \bar{a}^{i\times l}\right) + \bar{a}^{i\times l}\kappa_i\right] + a_0\sqrt{g_i\Delta_i} > 0 \tag{3.33}$$

If $b_{ii} < k_i$, we cannot use (3.32) since $\bar{a}^*$ is complex in this case. However, using the fact that $\Delta_i < 0$ we can rewrite (3.32):

$$\left(\frac{\mathrm{d}\lambda}{\mathrm{d}r}\right)_{\bar{a}^{i\times l},\ r^{i\times l}} = \frac{a_0 b_{ii}(b_{ii} + b_{il})g_i\bar{a}^{i\times l}}{\left(\Delta_i(a_0 - \bar{a}^{i\times l}) + a_0 k_i\right)^2 - \Delta_i g_i \bar{a}^{i\times l}} > 0 \tag{3.34}$$

Hence, if we raise the flow rate above $r^{i\times l}$, the transversal eigenvalue of the fixed point $P^{(2)}_{\{i\}}$ becomes positive if $P_{\{i,l\}}$ passes through this point. Conversely, if $P_{\{i,l\}}$ passes through $P^{(1)}_{\{i\}}$, its transversal eigenvalues becomes negative for $r > r^{i\times l}$.

The results of this paragraph are summarized in the box on the next page.

One dimensional fixed points in the CSTR, $b_{ii} > 0$

1. For flow rates below $a_0 k_i$ there is exactly one fixed point $P_{\{i\}}$. Above this flow rate, there may be none or two; the latter is the case if $b_{ii} > b^c_{ii}$. In this case, there is a saddlenode bifurcation in which the two fixed point disappear at $r = r^*$.
2. If two fixed points are possible for a given index set, the fixed point with the higher concentration of the substrate is always a saddle.
3. The fixed point with the lower concentration of a (the only one for $b_{ii} < b^c_{ii}$) is a sink if for all l one of the following three conditions is fulfilled
   (a) $k_i > k_l b_{ii}/b_{il}$ and $b_{ii} > b_{il}$ or
   (b) $k_i > k_l b_{ii}/b_{il}$, $b_{ii} < b_{il}$ and
      i. $r < r^{i\times l}$ or
      ii. $\bar{a}^{i\times l} > \bar{a}^*$

   or

   (c) $k_i < k_l b_{ii}/b_{il}$ and $b_{ii} > b_{il}$ and
   $r > r^{i\times l}$ and $\bar{a}^{i\times l} < \bar{a}^*$.

3.2 The recycling reaction

In this model, we consider a closed system in which the amount of substrate is limited and the species and intermediates decay (irreversibly) back to the substrate. Fig. 3.2 shows a sketch of the setting. We then have the following

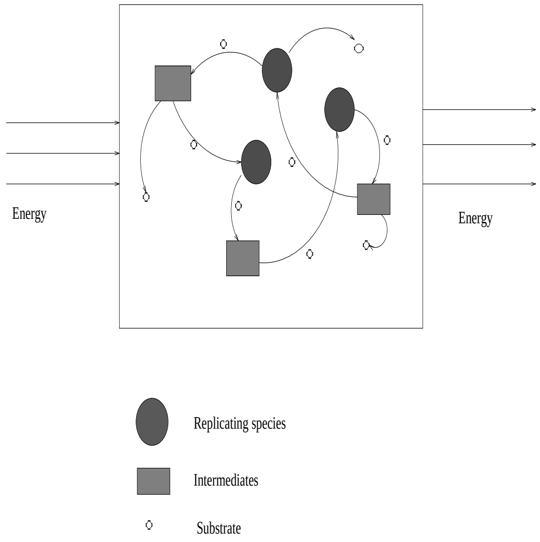


Figure 3.2: A model for a closed system with regenerating substrate

reaction scheme:

$$\begin{array}{rcl} A+X_i & \xrightarrow{k_i} & 2X_i \\ A+X_i & \xrightarrow{g_i} & X_i+S_i \\ X_i+S_l & \xrightarrow{b_{li}} & 2X_i \\ X_i & \xrightarrow{d_i} & A \\ S_i & \xrightarrow{e_i} & A \end{array} \tag{3.35}$$

which is identical to the analogous scheme in the last section, except for the last two entries. Taking the above reaction scheme as it stands violates the principle of detailed balancing and thus contradicts the laws of physical chemistry, but if some kind of energy is pumped into the reaction vessel, this objection does not hold anymore.

The closed system approach is particularly suited for treating diffusion, which is the main reason for introducing it.

We shall only deal with the case of equal decay constants, i.e. $d_i = e_i = r$. In this case the kinetic differential equations for $\dot{x}_i$ and $\dot{s}_i$ are identical to those for the CSTR (3.3). For the substrate we have

$$\dot{a} = -\sum_{i=1}^{n}(k_i + g_i)x_i + r\sum(x_i + s_i) \tag{3.36}$$

If the total concentration of all reactants is a_0, we can substitute $\sum_{i=1}^{n}(x_i + s_i) = a_0 - a$ into (3.36) and see that this equation is identical to the one for the CSTR case. Thus both systems have the same fixed points. This is not very surprising since we know that the CSTR system converges to a constant total concentration of a_0.

The eigenvalues of the Jacobian at a fixed point are identical to those of the CSTR system except for the external eigenvalue, which is zero (rather than $-r$), which is obvious from the fact that the kinetic equations are linearly dependent: $\dot{a} = -\sum(\dot{x}_i + \dot{s}_i)$. This follows from the fact that the Jacobian of the closed system can be obtained from the one of the CSTR just by adding r to all entries in the last line. Since for the CSTR the sum of the components of all eigenvectors besides the external one is zero, it is clear that all these eigenvectors of the CSTR system are also eigenvectors of the closed system with the same eigenvalues. The only difference between the two systems is that the CSTR system starts somewhere in the positive orthant and converges to the simplex $\mathbf{S}_{2n+1}$, whereas the closed system never leaves this simplex.

3.3 The evolution reactor

The evolution reactor, as shown in fig. 3.3, is a kind of dialysis reactor with walls impermeable to replicating species and intermediates. A flow is provided, which keeps the reaction mixture away from equilibrium. Transport of the substrate is adjusted such that the concentration of the substrate and the sum of the concentrations is held constant. Furthermore, we assume that the substrate is present in excess (buffered), so that we can ignore it in the

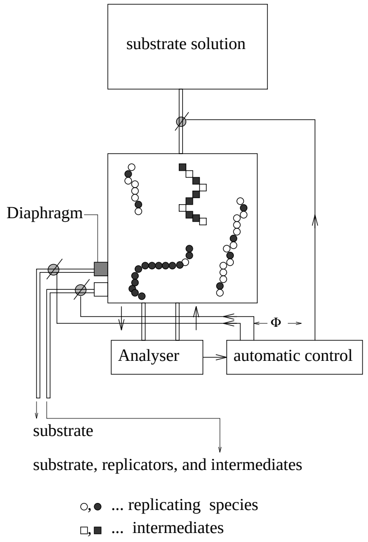


Figure 3.3: Evolution-reactor with external controlling device.

differential equations and absorb its influence in the reaction constants. An unspecific dilution flux is provided to keep the total concentration of replicating species and intermediates constant. Reactors of this kind are somewhat difficult to realize, but the resulting differential equations are much simpler than in the CSTR.

To simplify the kinetic equations, we consider relative concentrations: $x_i := [X_i]/c_0,\ s_i = [S_i]/c_0,\ c_0 = \sum([X_i] + [S_i])$. Thus we obtain

$$\begin{aligned} \dot{x}_i &= x_i(k_i + c_0 \textstyle\sum_{l=1}^{n} b_{li} s_i - \Phi) \\ \dot{s}_l &= g_l x_l - s_l(c_0 \textstyle\sum_{i=1}^{n} b_{li} x_i + \Phi) \end{aligned} \tag{3.37}$$

where Φ represents the flux term:

$$\Phi = \sum \kappa_i x_i \tag{3.38}$$

where $\kappa_i = k_i + g_i$.

Since of all parameters the total concentration is the one that is most easily varied in experimental settings, we choose it as the critical parameter and describe the behaviour for a fixed set of kinetic reaction constants in dependence of c_0. Thus the total concentration has in some sense the role that was played by the flow rate in the CSTR.

As in the CSTR setting, we shall assume the variables to be ordered as follows $(x_1, \ldots, x_n, s_1, \ldots, s_n)$. We shall also assume that all the constants k_i are different and that k_1 is the largest of them. Index sets, the vectors **k, g, f, x, s**, and the matrix **B** are defined as in the CSTR case.

In the evolution reactor, we have only the interior fixed point(s) and fixed points on the boundary of the simplex; the trivial fixed point does not exist since the concentrations of the replicating species and the intermediates must sum to c_0. Many of the results in the next two sections will look familiar to you if you have read the section on the CSTR, but I include them here for completeness.

3.3.1 The interior fixed point

The equilibrium concentrations of the intermediates at an interior fixed point are uniquely determined if the matrix **B** is invertible. In this case we have

$$\bar{\mathbf{s}} = \mathbf{B}^{-1}(\bar{\Phi}\mathbf{1} - \mathbf{k}) \tag{3.39}$$

where $\bar{\Phi}$ denotes the flux at the fixed point. Thus the $\bar{s}_i$ are linear in $\bar{\Phi}$. Defining a matrix $\mathbf{D} = (d_{il})$ with $d_{il} = g_i \delta_{i,l} + b_{li}\bar{s}_l$ and matrices $\mathbf{D}^{(i)}$, where the i–th column vector of **D** is replaced by $\bar{\Phi}\bar{\mathbf{s}}$, we obtain the equilibrium concentration of x_i:

$$\bar{x}_i = \frac{|\mathbf{D}^{(i)}|}{|\mathbf{D}|} \tag{3.40}$$

Since all rows of **D** are linear in $\bar{\Phi}$ (the $\bar{s}_l$ depend linearly on $\bar{\Phi}$), the determinants $|\mathbf{D}|$ and $|\mathbf{D}^{(i)}|$ can be at most of n–th order in Φ. Inserting now the above results into the equation $\sum(\bar{x}_i + \bar{s}_i) = 1$ to determine $\bar{\Phi}$, we get generally a $n + 1$–th order equation, i.e. there may be at most n fixed points in the interior of the simplex. However, some of the solutions may be negative or imaginary. Moreover, for the fixed point to lie on the simplex, we must have $0 < \bar{x}_i, \bar{s}_i < c_0$, which gives us $2n$ additional inequalities that must be fulfilled. The actual number of interior fixed points may thus be considerably lower than $n + 1$.

3.3.2 Fixed points on the boundary of the simplex

These are all fixed points except the interior one. Finding the fixed point(s) for the index set I is equivalent to finding the interior fixed point of the n_I–species system with the matrix **B'** which is obtained from **B** by cancelling rows and columns for all species $l \notin I$.

The eigenvalues of the Jacobian at a given fixed point can again be split in external, transversal and internal eigenvalues.

The external eigenvalue is $-\bar{\Phi}$, as is easily verified by checking that the vector with $2n$ entries of unity is a left eigenvector. All (right) eigenvectors but one (the one corresponding to the eigenvalue $-\bar{\Phi}$ can be chosen such that the sum of their entries is zero.

The transversal eigenvalues are

$$\lambda_l^{(tr,1)} = k_l - \bar{\Phi} + c_0 \sum_{i \in I} b_{il} \bar{s}_i, \qquad \lambda_l^{(tr,2)} = -\left(c_0 \sum_{i \in I} b_{li} \bar{x}_i + \bar{\Phi} \right) < 0 \quad (3.41)$$

The latter, which is always negative, describes the effect of introducing S_l into the system, while the former describes the introduction of both X_l and S_l and may have either sign. If it becomes zero, there is a transcritical bifurcation of $P_{\{i\}}$ with $P_{\{i,l\}}$ at this value of c_0.

The computation of the internal eigenvalues is equivalent to finding the eigenvalues of the Jacobian of the corresponding reduced system. As in the CSTR case, there is no general way to calculate them.

One dimensional fixed points ($n_I = 1$)

We now examine the one dimensional fixed points and their stability. The cases $b_{ii} = 0$ and $b_{ii} > 0$ are again quite different and are therefore treated separately. In the latter case we shall see how much the evolution reactor setting simplifies the calculations.

Case 1:$b_{ii} = 0$**:** The equilibrium concentration at the fixed point with the index set $I = \{i\}$ are

$$\bar{x}_i = \frac{k_i}{\kappa_i}, \qquad \bar{s}_i = \frac{g_i}{\kappa_i}, \qquad \bar{\Phi} = k_i \tag{3.42}$$

In contrast to the CSTR setting, the fixed point exists for all values of c_0.

The internal eigenvalue is found by solving the eigenvalue problem for (the other eigenvalue of this system is the external one)

$$\begin{pmatrix} -\kappa_i \bar{x}_i & 0 \\ g_i - \kappa_i \bar{x}_i \bar{s}_i & -\kappa_i \bar{x}_i \end{pmatrix} \tag{3.43}$$

Hence, the internal eigenvalue is $-\kappa_i \bar{x}_i = -\bar{\Phi} < 0$.

The transversal eigenvalue $\lambda_l^{(tr,1)}$ for coordinate l is

$$\lambda_l^{(tr,1)} = k_l + c_0 b_{il} \bar{s}_i - \bar{\Phi} = k_l + c_0 \frac{b_{il} g_i}{\kappa_i} - k_i \tag{3.44}$$

which is negative for

$$c_0 < c_0^{i \times l} = \frac{(k_i - k_l)\kappa_i}{b_{il} g_i} \tag{3.45}$$

if $k_i > k_l$ (otherwise it is always positive).

Thus, the fixed point $P_{\{1\}}$ is stable for $c_0 < \min c_0^{(1\times l)}$. If $b_{1l} = 0,\ l = 2, \ldots, n$, $P_{\{1\}}$ is stable for all values of c_0. All the other one–dimensional fixed points are saddles.

Case 2: $b_{ii} > 0$**:** The equilibrium concentrations at the fixed point $P_{\{i\}}$ are

$$\bar{x}_i = \frac{b_{ii} + k_i}{b_{ii} + \kappa_i}, \qquad \bar{s}_i = \frac{g_i}{b_{ii} + \kappa_i}, \qquad \bar{\Phi} = \frac{\kappa_i(b_{ii} + k_i)}{b_{ii} + \kappa_i} \tag{3.46}$$

The internal and the external eigenvalue are found by solving the eigenvalue problem for

$$\begin{pmatrix} -\kappa_i \bar{x}_i & b_{ii}\bar{x}_i \\ g_i - \bar{s}_i(b_{ii} + \kappa_i) & -\kappa_i - b_{ii}\bar{x}_i \end{pmatrix} \tag{3.47}$$

The internal eigenvalue is $-(\kappa_i + b_{ii})\bar{x}_i < 0$.

For the transversal eigenvalue $\lambda_l^{(tr,1)}$ we have

$$\lambda_l^{(tr,1)} = k_l + c_0 b_{il}\bar{s}_i - \bar{\Phi} = k_l + c_0 b_{il} - \frac{\kappa_i(c_0 b_{ii} + k_i)}{c_0 b_{ii} + \kappa_i} \tag{3.48}$$

Introducing $\Delta_{il} = k_i - k_l$, we see that the eigenvalue is negative if

$$c_0 < c_0^{i \times l} = \frac{\kappa_i \Delta_{il}}{g_i(b_{il} - bii) - b_{ii}\Delta_{il}} \tag{3.49}$$

Thus, if $\Delta_{il} > 0$ and $b_{ii} \geq b_{il}$, the eigenvalue is always negative, while for $\Delta_{il} < 0$, $b_{ii} \leq b_{il}$ it is always positive. In the remaining two cases there can be a change of the sign of the transversal eigenvalue (transcritical bifurcation with $P_{\{i,l\}}$) if

$$|\Delta_{il}| < \Delta_{il}^c = \left| \frac{g_i(b_{il} - bii)}{b_{ii}} \right| \tag{3.50}$$

which is almost the same formula as in the CSTR, with the difference that in the evolution reactor transcritical bifurcations can occur also for negative values of Δ_{il}.

Thus, in the evolution reactor setting, a one–dimensional fixed point is stable if for all indices $l \neq i$

1. $k_i > k_l$ and
   (a) $b_{ii} \geq b_{il}$ or

   (b) $\Delta_{il} > \Delta_{il}^{c}$ or
   (c) $\Delta_{il} < \Delta_{il}^{c}$ and $c_0 < c_0^{i \times l}$

2. or if $k_i < k_l$, $|\Delta_{il}| < \Delta_{il}^{c}$ and $c_0 > c_0^{i \times l}$

Chapter 4

The competitive model

In this model we consider a particularly simple form of the interaction matrix **B**, namely $b_{il} = f_i \delta_{il}$, where δ_{il} is Kronecker's symbol. In this model the species interact only via the substrate A (in the CSTR and in the recycling reaction system) or via the flux Φ (in the evolution reactor). The reaction scheme is

$$\begin{array}{rcl} A + X_i & \xrightarrow{k_i} & 2X_i \\ A + X_i & \xrightarrow{g_i} & X_i + S_i \\ X_i + S_i & \xrightarrow{f_i} & 2X_i \end{array} \tag{4.1}$$

Since the diagonal form of the coupling matrix **B** is not changed if we relabel the species, we are free to choose the labelling so that the constants k_i form a decreasing sequence.

The corresponding replicator–like system is known as "Schlögl model" [40]:

$$\begin{array}{rcl} A + X_i & \xrightarrow{k_i'} & 2X_i \\ A + 2X_i & \xrightarrow{f_i'} & 3X_i \end{array} \tag{4.2}$$

Models of this kind (special cases with $f_i' = 0$ or $k_i' = 0$) have been analyzed by Schuster and Sigmund [42] in the CSTR setting.

4.1 General results

4.1.1 CSTR

In the CSTR setting, the kinetic differential equations read

$$\begin{aligned} \dot{x}_i &= x_i(k_i a + f_{i-1}s_{i-1} - r) \\ \dot{s}_i &= g_i a x_i - s_i(f_i x_{i+1} + r) \\ \dot{a} &= a_0 r - a(r + \sum(k_i + g_i)x_i) \end{aligned} \tag{4.3}$$

where i runs from 1 to n, the total number of reacting species. The total concentration $c_0 = a + \sum(x_i + s_i)$ converges to a_0. Therefore all fixed points lie on the $2n+1-$ dimensional simplex S_{2n+1}.

Besides the trivial fixed point there may be numerous other fixed points if the flow rate is sufficiently small. From the form of the matrix $\mathbf{B}$ it is clear that the equilibrium concentrations of the interior fixed point of a n–species system are equal to a fixed point on the boundary of a m–species system ($m > n$, with the appropriate rate constants) with an index set that contains only the species of the lower dimensional system. Thus the formulae for equilibrium concentrations for the interior fixed points and the fixed points on the boundary are identical.

The equilibrium concentrations (marked by bars) for the fixed point P_I with the index set I are:

$$\bar{s}_i = \frac{r - k_i\bar{a}}{f_i}, \qquad \bar{x}_i = \frac{r(r - k_i\bar{a})}{f_i(\kappa_i\bar{a} - r)} \tag{4.4}$$

Definition 4.1 *Let m be the index so that $\kappa_m = \min_{i\in I}\kappa_i$*[1] *and $\mathcal{M}$ the index so that $k_{\mathcal{M}} = \max_{i\in I} k_i$.*

---

[1] m need not be uniquely defined. If more than one index fulfills the above definition, we may just pick any one of them.

Then a necessary condition for the fixed point to lie on the simplex is

$$\frac{r}{\kappa_m} \leq \bar{a} \leq \left(\frac{r}{k_{\mathcal{M}}}\right) \tag{4.5}$$

This motivates the following

Lemma 4.1 *An index set is* admissible *in the competitive model if and only if* $k_{\mathcal{M}} < \kappa_m$. *For each admissible index set* I *we define the set* $I' = I \setminus \{\mathcal{M}\}$, *which is also admissible.*

Proof: The "only if" part follows directly from (4.5). That the condition given in the lemma is sufficient, follows from the proof of Theorem 4.1.1, where we show that we need no additional condition for the fixed point to exist at sufficiently small flow rates.

$\square$

The equilibrium concentration of the substrate is implicitly given by the function

$$F(a, r) := a_0 - a - \sum_{i \in I} \frac{r - k_i a}{f_i} \left(1 + \frac{r}{\kappa_i a - r}\right) \tag{4.6}$$

At the equilibrium concentration this function vanishes: $F(\bar{a}(r), r) = 0$. If all κ_i are different, this is an equation of order $n_I + 1$ in a. In general, if there are s different values of κ in I, the equation is of order $s + 1$. We can give no analytic solution for arbitrary n_I, but we can derive the number of solutions that lie on the simplex.

Theorem 4.1 *For every admissible index set* I *there is exactly one fixed point* P_I *that lies on the simplex for sufficiently small flow rates. At some flow rate* $r^{I \times I'} > 0$ *there is a transcritical bifurcation of a fixed point* P_I *with a fixed point* $P_{I'}$. *For higher flow rates, there is either no fixed point* P_I *on the simplex or there are two. We call the former case scenario 1 and the latter scenario 2. In scenario 2 there is a saddle node bifurcation at some* *flow rate* $r^* > r^{I\times I'}$*, in which the both fixed points disappear. There is no fixed point* P_I *for any flow rate* $r > r^*$ *in scenario 2 and for any* $r > r^{I\times I'}$ *in scenario 1.*

Proof: We start with remarking that at $r = 0$ we have a $s-$fold solution $\bar{a} = 0$ and one solution $\bar{a} = a_0(1 - \sum(k_i/f_i))^{-1}$. The latter is positive if $\sum(k_i/f_i) < 1$, but in any case it does not lie on the simplex. Next we observe that $F(a, r)$ goes to infinity and changes sign for $a = r/\kappa_i$. Therefore, if j and k are two indices with $\kappa_j \neq \kappa_k$ and there is no index for which κ lies between those two, then there must be a solution of (4.6) between $a = r/\kappa_i$ and $a = r/\kappa_{i+1}$, i. e. there are $s - 1$ solutions that cannot lie on the simplex because of (4.5). Thus there can be at most two solutions on the simplex. If $\sum(k_i/f_i) > 1$, however, there can be only one solution on the simplex, since then there is one negative solution. Hence $\sum(k_i/f_i) < 1$ is a necessary but not sufficient condition for having two fixed points.

To find the exact number of solutions, we investigate the behaviour of $F(a, r)$ along the line $a = r/k_{\mathcal{M}}$. We obtain

$$F\left(\frac{r}{k_{\mathcal{M}}}, r\right) = a_0 - \frac{r}{k_{\mathcal{M}}}\left(1 + \Gamma_{I'}\right), \qquad \Gamma_{I'} = \sum_{i\in I'} \frac{\kappa_i(k_{\mathcal{M}} - k_i)}{f_i(\kappa_i - k_{\mathcal{M}})} \geq 0 \tag{4.7}$$

This is positive for

$$r < r^{I\times I'} = \frac{a_0 k_{\mathcal{M}}}{1 + \Gamma_{I'}} \tag{4.8}$$

Since $F(r, (r/\kappa_m) + \epsilon)$ is negative for ϵ sufficiently small, there is one solution for $r < r^{I\times I'}$, and two or none for $r > r^{I\times I'}$. At $r = r^{I\times I'}$ there is a transcritical bifurcation of P_I with $P_{I'}$. For one-dimensional fixed points, this means that $P_{\{i\}}$ passes through the trivial fixed point at $r^{\{i\}\times\emptyset} = a_0 k_i$.

There are two ways in which this bifurcation can happen: The interior fixed point may leave the simplex (scenario 1) or a second fixed point may enter it (scenario 2). In the latter case the fixed point that enters the simplex in a transcritical bifurcation has the higher value of $\bar{a}$; we call it $P_I^{(2)}$ and the corresponding equilibrium concentration of the substrate $\bar{a}^{(2)}$. Since the fixed point cannot leave the simplex again at a higher flow rate, it is clear that $P_I^{(1)}$ and $P_I^{(2)}$ must disappear in a saddle node bifurcation at some flow rate $r_I^* > r^{I\times I'}$.

□

Fig. 4.1 shows the how the function F looks typically in scenario 1 (4.1.a) and 2 (4.1.b). The dashed lines are the functions $a = r/k_{\mathcal{M}}$, the dotted $a = r/\kappa_m$ that confine the region where physically meaningful solutions can lie. Note that there is always one solution that lies entirely below the line $a = r/\kappa_m$.

In fig. 4.2 we show how the fixed points move as the flow rate is changed. Since we need at least two species to show anything interesting and the simplex $\mathbf{S}_5$ is hard to draw, we have show the sum of each species and the corresponding intermediate instead of showing all individual concentrations. The figures (a) and (b) correspond to (a) and (b) of fig. 4.1. One can see here that there are two fixed points of all types in (a) and one in (b). Also, one can see the transcritical and saddle node bifurcations. In fig. (c) we have the case $k_{\mathcal{M}} > \kappa_m$ and hence there are only the one dimensional and the trivial fixed points.

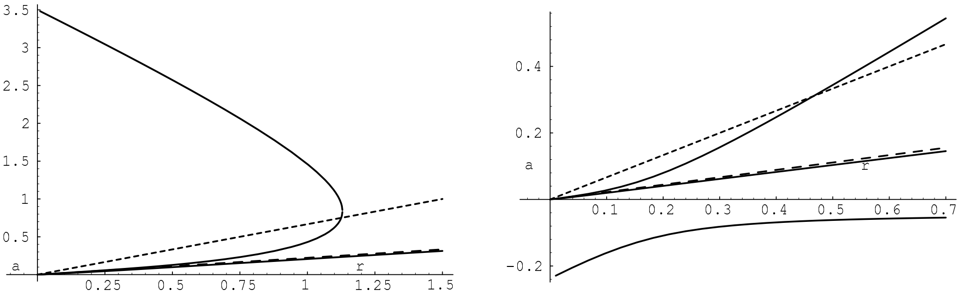
We now want to know how the equilibrium concentrations change with the flow rate. We can obtain the derivative of $\bar{a}$ by implicit differentiation:

$$\frac{d\bar{a}}{dr} = -\left(\frac{\partial F}{\partial r}\right)_{\bar{a}} \Big/ \left(\frac{\partial F}{\partial a}\right)_{\bar{a}} \tag{4.9}$$

where

$$\left(\frac{\partial F}{\partial r}\right)_{\bar{a}} = -\bar{a}^2 \sum_{i\in I} \frac{\kappa_i g_i}{f_i(\kappa_i \bar{a} - r)^2} < 0 \tag{4.10}$$

Therefore the signs of $d\bar{a}/dr$ and $(\partial F/\partial a)_{\bar{a}}$ coincide. Since $F(r, (r/\kappa_m) + \epsilon)$ is negative for ϵ sufficiently small, as remarked above, it is clear that the



(a) (b)

Figure 4.1: Competitive model; $n = 2,\ k_1 = 1.5,\ k_2 = 1,\ g_1 = 3,\ g_2 = 5,\ a_0 = 1$ and (a): $f_1 = 7,\ f_2 = 2$; (b) $f_1 = 0.8,\ f_2 = 0.3$

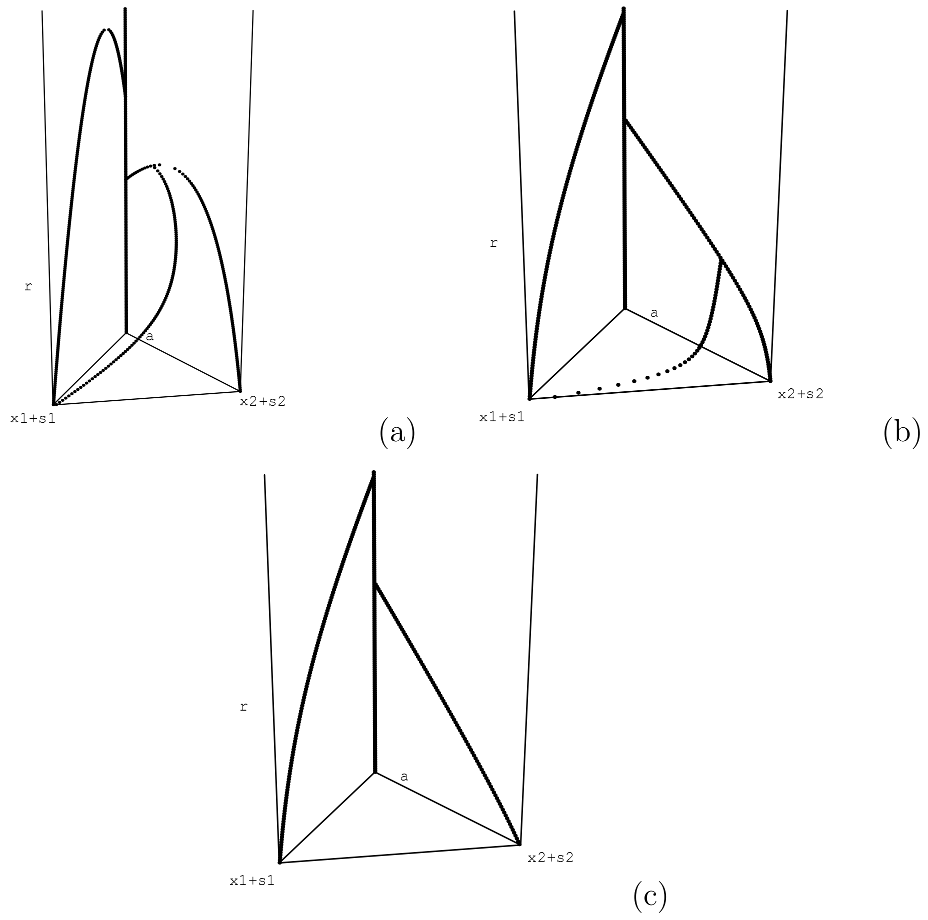


Figure 4.2: Competitive model; $n = 2,\ a_0 = 1$, constants for (a) and (b) see fig. 4.1; (c) $k_1 = 1.5,\ k_2 = 1,\ g_1 = 3,\ g_2 = 0.3,\ f_1 = 0.8,\ f_2 = 0.3$

partial derivative of F with respect to a is positive at $\bar{a}^{(1)}$: $(\partial F/\partial a)_{\bar{a}^{(1)}} > 0$. At $\bar{a}^{(2)}$ (if it exists), the sign of the partial derivative is therefore negative. Hence

$$\frac{d\bar{a}^{(1)}}{dr} > 0, \qquad \frac{d\bar{a}^{(2)}}{dr} < 0 \tag{4.11}$$

Stability properties

Transversal eigenvalues: We now investigate the stability properties of the fixed points. For each index $l \notin I$ (if P_I is not the interior fixed point), there are two transversal eigenvalues: $-r$ and $k_l\bar{a} - r$. The latter describes the stability of the fixed point against the introduction of replicating species l and the corresponding intermediate. We distinguish three cases:

1. $k_l < k_{\mathcal{M}}$: Since $r > k_{\mathcal{M}}\bar{a}$, the eigenvalue is always negative.
2. $k_{\mathcal{M}} < k_l < \kappa_m$: There is a transcritical bifurcation of P_I with P_{I^l}, where $I^l = I \cup \{l\}$. It takes place at $r = r^{I\times I^l} = k_l\bar{a}$. Evaluating the corresponding value of $\bar{a}$ from (4.6), we obtain

   $$\bar{a}^{I\times I^l} = \frac{a_0}{1+\Gamma_I}, \qquad r^{I\times I^l} = \frac{a_0 k_l}{1+\Gamma_I} \tag{4.12}$$

   where Γ_I is defined like $\Gamma_{I'}$ in (4.7), but extending the summation over all $i \in I$. It is not clear whether the eigenvalue is negative for flow rates above or below the critical flow rate. We therefore compute the derivative of the eigenvalue with respect to r

   $$\left(\frac{d\lambda}{dr}\right)_{r^{I\times I^l}} = -1 + k_l \left(\frac{d\bar{a}}{dr}\right)_{r^{I\times I^l},\bar{a}^{I\times I^l}} \tag{4.13}$$

   The partial derivatives of F at $\left(\bar{a}^{I\times I^l}, r^{I\times I^l}\right)$ are

   $$\left(\frac{\partial F}{\partial \bar{a}}\right)_{r^{I\times I^l},\bar{a}^{I\times I^l}} = -(1+\Gamma_I) + k_l\Theta_I, \qquad \left(\frac{\partial F}{\partial r}\right)_{r^{I\times I^l},\bar{a}^{I\times I^l}} = -\Theta_I \tag{4.14}$$

with

$$\Theta_I = \sum_{i \in I} \frac{\kappa_i g_i}{f_i(\kappa_i - k_l)^2} > 0 \tag{4.15}$$

If we now introduce these results into (4.9), (4.13) becomes

$$\left(\frac{d\lambda}{dr}\right)_{r^{I \times I^l}} = \frac{1 + \Gamma_I}{k_l \Theta_I - (1 + \Gamma_I)} \tag{4.16}$$

The sign of $d\lambda/dr$ is therefore the same as that of $(\partial F/\partial a)_{r^{I\times I^l}, \bar{a}^{I \times I^l}}$, i. e. it is positive if P_{I^l} passes through $P_I^{(1)}$ and negative if P_{I^l} passes through $P_I^{(2)}$. The last equation also allows us to distinguish between these two cases: P_{I^l} passes through $P_I^{(1)}$ if $k_l \Theta_{I^l} > 1 + \Gamma_I$.

If P_{I^l} passes through $P_I^{(1)}$, we have scenario 1 for I^l: This becomes clear by looking at the derivative $(d\bar{a}^{(I^l)}/dr)_{\bar{a}^{I\times I^l}, r^{I \times I^l}}$:

$$\left(\frac{\partial F}{\partial a}\right)_{\bar{a}^{I\times I^l}, r^{I\times I^l}} = -(1 + \Gamma_I) + k_l \Theta_{I^l}, \qquad \left(\frac{\partial F}{\partial r}\right)_{\bar{a}^{I\times I^l}, r^{I\times I^l}} = -\Theta_{I^l} \tag{4.17}$$

with $\Theta_{I^l} = \Theta_I + \kappa_l/f_l$ and therefore $\Theta_{I^l} > \Theta_I$. Hence

$$(d\bar{a}^{(I^l)}/dr)_{\bar{a}^{I\times I^l}, r^{I\times I^l}} > (d\bar{a}^{(I)}/dr)_{\bar{a}^{I\times I^l}, r^{I\times I^l}}$$

from which the above assertion follows.

The behaviour of the transversal eigenvalue can therefore be summarized as follows: At $r^{I \times I^l}$ there is a transcritical bifurcation of P_{I^l} with (one of the) fixed point(s) P_I. If P_{I^l} passes through $P_I^{(1)}$, its transversal eigenvalue is positive for flow rates above $r^{I\times I^l}$. Since $\bar{a}^{(2)} > \bar{a}^{(1)}$, it is clear that the transversal eigenvalue is also positive for $P_I^{(2)}$. Reverting this argument we see that if P_{I^l} passes through $P_I^{(2)}$, the transversal eigenvalue is negative for both fixed points P_I at flow rates above $r^{I\times I^l}$, while it is positive for $P_I^{(2)}$ for lower flow rates.

3. $k_l > \kappa_m$: In this case the index set I^l is not admissible. The transversal eigenvalue is positive for all flow rates since $\kappa_m \bar{a} - r > 0$.

Internal eigenvalues: The internal eigenvalues are much harder to calculate. In fact, except for the results on one dimensional fixed points, we can derive analytical results only for the case of equal reaction constants described in the next section. Still, we could obtain information on the sign of all eigenvalues using the fact that all fixed points undergo transcritical bifurcations with lower dimensional fixed points, if there were no Hopf bifurcations. There is a generalized potential for the corresponding second order replication network (at least for the one with $k_i = 0$), thus there can be no complex eigenvalues (and hence no Hopf bifurcations) for this system. I have spent several weeks in fruitless attempts to find a generalized potential or at least a Ljapunov function for (4.1); so I guess that either there is none or it should look quite disgusting.

The only thing I could do was to test the conjecture that there were no Hopf bifurcations by numerical experiments. Test series for $n = 3, 4$, and 5 were made, setting $k_1 = 1,\ a_0 = 1$ and choosing k_i from $(0, 1)$, r from $(0, r^{I \times I'})$, g_i from $(k_i, 5)$ (to ensure $k_{\mathcal{M}} < \kappa_m$) and f_i from $(0, 5)$. For each value of n 1000 samples were taken, checking if there were any complex eigenvalues of the Jacobian, evaluated at the interior fixed point and how many eigenvalues had positive sign. I never found complex eigenvalues and the number of positive eigenvalues was always $n - 1$. This is just what we would expect in absence of Hopf bifurcations, since from the fact that every n dimensional fixed point passes through an $n - 1$ dimensional fixed point and the changes of the sign of the transversal eigenvalue of the latter, it is clear that the former must have one positive eigenvalue more. Since the one dimensional fixed point has only negative interior eigenvalues, the above result on n dimensional fixed points follows. (remember that under the conditions chosen there is only one interior fixed point). A second series of experiments was carried out to study the stability of the second fixed point (where it exists). To that end I chose $k_i,\ g_i$ and a_0 as above, but r from $(r^{I \times I'}, r^{I \times I'} + 0.1)$ (since under the above conditions the saddle node bifurcation usually takes place at flow rates between these values) and f_i from $(5, 10)$ (since high values of f favor the occurrence of scenario 2). If the set of parameters chosen led to scenario 1 or the flow rate was above the critical flow rate for the saddle node bifurcation, it was discarded. Again 1000 samples were taken for each $n = 3,\ 4$ and 5. As expected, we found again that all eigenvalues were real and there were n and $n-1$ positive eigenvalues for the fixed point with the higher (lower) equilibrium concentration of the substrate, respectively.

4.1.2 The evolution reactor

In the evolution reactor it is convenient to describe the system in terms of relative concentrations $x_i = [\mathbf{X}_i]/c_0,\ s_i = [\mathbf{S_i}]/c_0$, where c_0 is the total concentration. The differential equations describing the system then are:

$$\begin{array}{rcl} \dot{x}_i &=& x_i(k_i + f_i c_0 s_i - \Phi) \\ \dot{s}_i &=& g_i x_i - s_i(f_i c_0 x_i + \Phi) \end{array} \tag{4.18}$$

the flow Φ being defined as

$$\Phi = \sum_{i \in I} \kappa_i x_i \tag{4.19}$$

Since the overall concentration is held constant, the phase space is the simplex S_{2n}.

The concentrations of the individual species are coupled only via Φ, so the computation of the equilibrium concentrations is the same for fixed points in the interior and on the boundary of the simplex, which are themselves simplices. (The stability properties, however, depend on *all* species.)

As in the CSTR setting, we define $\mathcal{M}$ and m with $k_{\mathcal{M}} = \max_{i \in I} k_i,\ \kappa_m = \min_{i \in I} \kappa_i$. Again, an index set admissible if $\kappa_m > k_{\mathcal{M}}$. For every admissible index set we define the set $I' = I \setminus \{\mathcal{M}\}$, which is also admissible.

The equilibrium concentrations at the fixed point P_I (denoted by bars) then are

$$\bar{s}_i = \frac{\bar{\Phi} - k_i}{f_i c_0} \qquad \bar{x}_i = \frac{\bar{\Phi}(\bar{\Phi} - k_i)}{f_i c_0(\kappa_i - \bar{\Phi})} \tag{4.20}$$

Therefore P_I can only lie on the simplex if

$$k_{\mathcal{M}} < \bar{\Phi} < \kappa_m \tag{4.21}$$

Therefore the fixed point P_I can exist only if the index set is admissible. The flow at the equilibrium $\bar{\Phi}$ can be determined by the condition that the sum of the relative concentrations must be 1:

$$F(\Phi, c_0) := 1 - \frac{1}{c_0} \sum_{i \in I} \frac{\Phi - k_i}{f_i} \left(1 + \frac{\Phi}{\kappa_i - \Phi}\right) = 0 \tag{4.22}$$

This is an equation of $n-$th order in Φ if all κ_i are different; in general, if there are only s different values of κ_i, $i \in I$, the equation is of order s.

Theorem 4.2 *For every admissible index set with $n_I > 1$, there is exactly one fixed point P_I for sufficiently large values of c_0. At a certain total concentration, a transcritical bifurcations with the fixed point $P_{I'}$ takes place. For c_0 below this value, P_I lies outside the simplex.*

Proof: At $\Phi = \kappa_i$, $F(c_0, \Phi)$ goes to infinity and changes sign, so there must be one solution of (4.22) between each pair of two adjoining lines $\Phi = \kappa_i$ and$\Phi = \kappa_j$. Thus there are $s - 1$ solutions that cannot lie on the simplex because of (4.21). In other words, there can be at most one solution on the simplex. To find out whether the last solution really lies on the simplex we determine the value of $F(\Phi, c_0)$ at $\Phi = k_{\mathcal{M}}$:

$$F(k_{\mathcal{M}}, c_0) = 1 - \frac{c_0^{I \times I'}}{c_0}, \qquad c_0^{I \times I'} = \sum_{i \in I} \frac{\kappa_i(k_{\mathcal{M}} - k_i)}{f_i(\kappa_i - k_{\mathcal{M}})} \tag{4.23}$$

This is negative for $c_0 < c_0^{I \times I'}$ and since $F(\kappa_m - \epsilon, c_0) < 0$ for ϵ sufficiently small, it follows that there is one fixed point on the simplex for $c_0 > c_0^{I \times I'}$

and none for $c_0 < c_0^{I\times I'}$. At $c_0^{I\times I'}$ P_I undergoes a transcritical bifurcation with the lower dimensional fixed point P_I'. $\square$

Fig. 4.3 shows the graph of F for the two typical situations in a two species system. In (a) we have $k_{\mathcal{M}} < \kappa_m$. One of solutions lies below the line $k_{\mathcal{M}}$ (the dotted line) for small total concentrations, then it crosses this line and remains between $k_{\mathcal{M}}$ and κ_m for all higher values of c_0. In (b), $k_{\mathcal{M}}$ is less than κ_m and thus there is no solution between $k_{\mathcal{M}}$ and κ_m for any total concentration. In both cases one of the two solutions lies above the line κ_m (the dashed line), as predicted by the theorem.

In fig. 4.4 we show how the fixed point moves through the system as c_0 is varied. Only the interior fixed point is shown. The rate constants are the same as in fig. 4.3.(a).

Note that, since the critical total concentration as defined by (4.23) is zero for $n_I = 1$, one–dimensional fixed points exist at all values of c_0 in accordance with the results on the general model.

Stability properties

Transversal eigenvalues: We now turn towards the investigation of the stability properties of the fixed points. For every $l \notin I$, the Jacobian at the fixed point P_I has one eigenvalue $-\bar{\Phi}$ and one $k_l - \bar{\Phi}$. While the former is always negative, for the latter we must distinguish the following cases:

1. $k_l < k_i$: The eigenvalue is negative for all values of c_0 because $k_{\mathcal{M}} < \bar{\Phi}$.
2. $k_{\mathcal{M}} < k_l < \kappa_m$: There is a transcritical bifurcation of the fixed point P_I with P_{I^l}, where $I^l := I \cup \{l\}$. It takes place at $c_0 = c_0^{I\times I^l}$, which is computed like $c_0^{I\times I'}$, replacing $k_{\mathcal{M}}$ by k_l and extending the summation over all $i \in I^l$. The fixed point P_{I^l} lies on the simplex for $c_0 > c_0^{I\times I^l}$, which can be shown by the same argument as above for P_I. The derivative of

the transversal eigenvalue is

$$\left(\frac{d\lambda}{dc_0}\right)_{c_0^{I\times I^l}} = \left(\frac{d\bar{\Phi}}{dc_0}\right)_{c_0^{I\times I^l}} > 0 \tag{4.24}$$

which follows from the fact that P_{I^l} *enters* the simplex if we raise the total concentration above $c_0^{I\times I^l}$ (it can also be shown directly by implicit differentiation of the function F). Therefore the transversal eigenvalue is positive for total concentration below and negative above $c_0^{I\times I^l}$. The Jacobian of P_{I^l} must therefore have one positive eigenvalue more than that of P_I at least for total concentrations not too much above $c_0^{I\times I^l}$.

3. $k_l > \kappa_m$: The eigenvalue is positive for all values of c_0. The fixed point P_{I^l} does not exist, since the index set I^l is not admissible.

The phase portrait of the system, depending on the total concentration, is therefore as follows: at $c_0 = 0$ only the one–dimensional fixed points exist. As c_0 is raised, all fixed points $P_{\{i\}}$ for which the conditions $k_i < \kappa_j$ and $k_j < \kappa_i$ are fulfilled, undergo transcritical bifurcations as two–dimensional fixed points $P_{\{i,j\}}$ enter the simplex. At higher concentrations, three–dimensional fixed points may pass through the two–dimensional ones etc. This means that if a fixed point P_I with $I = \{i_1, i_2, \ldots, i_n\}$ (the indices being ascending) exist at a certain total concentration, then the fixed point with $I' = \{i_2, i_3, \ldots, i_n\}$, $I'' = \{i_3, i_4, \ldots, i_n\}$ etc. also exist. Furthermore fixed points with $1 \in I$ cannot undergo transcritical bifurcations as c_0 is raised. Finally, condition (4.21) ensures that for no pair of indices i, j with $k_i > \kappa_j$ there is a fixed point containing x_i and x_j simultaneously.

Internal eigenvalues: As in the CSTR setting, we are not able to compute all internal eigenvalues. We can, however, prove that all even dimensional fixed points are unstable:

Theorem 4.3 *At all fixed points with even n_I, the Jacobian has at least one positive real (internal) eigenvalue.*

Proof: The (internal part of the) Jacobian $\mathbf{J} = (j_{ij})$ at the fixed point has the following form:

$$\begin{array}{ll} \frac{\partial \dot{x}_i}{\partial x_j} = -\kappa_j \bar{x}_i & \frac{\partial \dot{x}_i}{\partial s_j} = c_0 f_i \bar{x}_i \delta_{i,j} \\ \frac{\partial \dot{s}_i}{\partial x_j} = -\kappa_j \bar{s}_i + (g_i - \bar{s}_i c_0 f_i)\delta_{i,j} & \frac{\partial \dot{s}_i}{\partial s_j} = -(c_0 f_i \bar{x}_i + \bar{\Phi})\delta_{i,j} \end{array} \tag{4.25}$$

Since $g_i - \bar{s}_i c_0 f_i = \kappa_i - \bar{\Phi}$, we can write $\partial \dot{s}_i / \partial x_i = -\kappa_i \bar{s}_i + \kappa_i - \bar{\Phi}$. We now multiply the i–th row of J by $(c_0 f_i \bar{x}_i - \bar{\Phi})/c_0 f_i \bar{x}_i$ and add it to the $n+i$–th line. We then can expand the determinant with respect to the last n columns. Thus we obtain

$$\det \mathbf{J} = (-1)^n \prod_{i=1}^{n} c_0 f_i \bar{x}_i \, \det \widetilde{\mathbf{J}} \tag{4.26}$$

where $\widetilde{\mathbf{J}} = (\widetilde{\jmath}_{ij})$ is a $n \times n$ matrix with the entries

$$\widetilde{\jmath}j_{ij} = -\kappa_i \left(\bar{x}_j + \bar{s}_j + \frac{\bar{\Phi}}{c_0 f_j} \right) + (\kappa_i - \bar{\Phi})\delta_{i,j}$$

The determinant of $\widetilde{\mathbf{J}}$ is

$$\det \widetilde{\mathbf{J}} = 1 - \sum_{i=1}^{n} \frac{\kappa_i}{\kappa_i - \bar{\Phi}} \left(\bar{x}_i + \bar{s}_i + \frac{\bar{\Phi}}{c_0 f_i} \right)$$

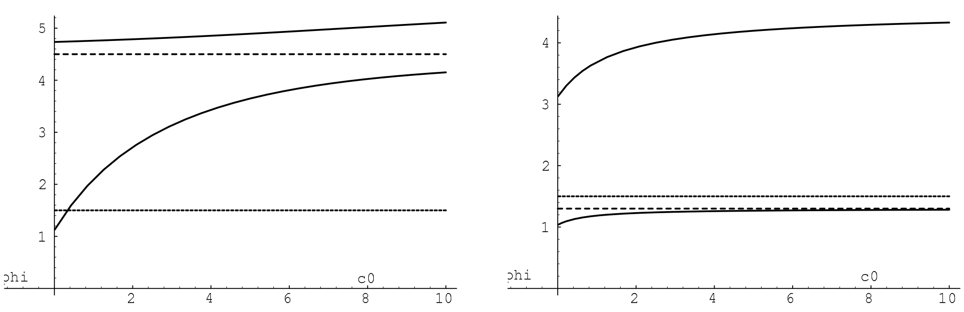
and since

$$\sum_{i=1}^{n} \frac{\kappa_i}{\kappa_i - \bar{\Phi}} (\bar{x}_i + \bar{s}_i + \frac{\bar{\Phi}}{c_0 f_i}) > \sum_{i=1}^{n} \bar{x}_i + \bar{s}_i + \frac{\bar{\Phi}}{c_0 f_i} = 1 + \bar{\Phi} \sum_{i=1}^{n} \frac{1}{c_0 f_i}$$

it follows that $\det \widetilde{\mathbf{J}}$ is negative. From (4.26) we now see that $\det \mathbf{J}$ is negative for even n_I. Since the determinant is the product of the eigenvalues, there must be at least one positive factor and hence the assertion of the theorem follows.

□

Numerical evidence leads us to the same conjecture as in the CSTR setting, namely that all eigenvalues are real and that an n_I dimensional fixed point



(a) (b)

Figure 4.3: Competitive model; $n = 2,\ k_1 = 1.5,\ k_2 = 1,\ g_1 = 3,\ f_1 = 7,\ f_2 = 2$ and (a): $g_2 = 5$; (b) $g_2 = 0.3$

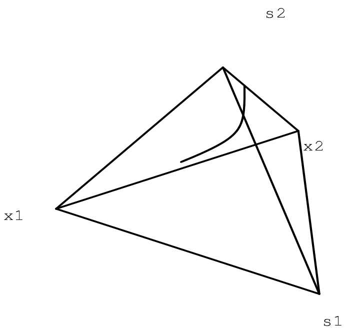


Figure 4.4: Competitive model; $n = 2,\ k_1 = 1.5,\ k_2 = 1,\ g_1 = 3,\ g_2 = 5,\ f_1 = 7,\ f_2 = 2$, $0.335 < c_0 < 10$

has $n_I - 1$ positive (internal) eigenvalues (which follows from the sequence of transcritical bifurcations through which the fixed point enters the simplex, if there are no Hopf bifurcations). This conjecture was tested for 1000 parameter sets for each $n = 3,\ 4$ and 5. k_1 and c_0 were set to unity, the other k_i were chosen from $(0, 1)$, g_i from $(1 - k_i, 5)$ (to ensure that the index set is admissible), and f_i from $(0, 10)$. If the interior fixed point did not exist for the parameter set, it was discarded. For each accepted parameter set, the eigenvalues of the Jacobian at the interior fixed point were calculated. The above conjecture held in all cases.

4.2 Equal reaction constants

The equations are very much simplified if we assume the rate constants to be equal for all species, i.e. $k_i = k,\ g_i = g,\ f_i = f,\ i = 1, \ldots, n$. The symmetry in the rate constants induces symmetry in the equilibrium concentrations: $\bar{x}_i = \bar{x},\ \bar{s}_i = \bar{s}\ \forall i \in I$. Under these condition (interior part of) the Jacobian has a special form: it consists of 4 circulant $n_I \times n_I$ blocks (plus one additional row and column for the substrate in the CSTR case). This enables us to derive analytical expressions for the (interior) eigenvalues of the Jacobian and thus determine the stability of the fixed points.

4.2.1 The CSTR

The differential equations are:

$$\begin{aligned}
\dot{x}_i &= x_i(ka + fs_i - r) \\
\dot{s}_i &= gx_ia - s_i(fx_i + r) \\
\dot{a} &= a_0r - a\left(r + \kappa \sum x_i\right)
\end{aligned} \tag{4.27}$$

where $\kappa = k + g$. Since $\kappa > k$, all possible index sets are admissible. Therefore, there are 2^n admissible index sets. The equilibrium concentrations at a fixed point P_I are:

$$\bar{x} = \frac{r(r - k\bar{a})}{f(\kappa\bar{a} - r)}, \qquad \bar{s} = \frac{r - k\bar{a}}{f} \tag{4.28}$$

The determining equation for $\bar{a}$ is

$$\bar{a}^2\kappa(f - n_I k) - \bar{a}(f a_0 \kappa + f r - n_I \kappa r) + f a_0 r = 0 \tag{4.29}$$

If $f < n_I k$, there is one positive and one negative solution, if $f > n_I k$ there are two positive solutions at least for sufficiently small r. In the latter case there is a saddle node bifurcation at

$$\bar{r}^* \quad = \frac{a_0 f \kappa \left(f - n_I(k - g)2 \pm \sqrt{n_I g(f - n_I k)}\right)}{(f - n_i\kappa)^2} \tag{4.30}$$

$$\bar{a}^* \qquad = \frac{a_0 f \left(f - n_I k \pm \sqrt{n_I g(f - n_I k)}\right)}{(f - n_I\kappa)(f - n_I k)} \tag{4.31}$$

Since the solution with the plus sign before the square root yields values of $\bar{a}^*$ that are either negative or greater than a_0, we are only interested in the formulae with the minus sign. Putting $\Delta = f - n_I k$, we can rewrite the latter as

$$r^* = \frac{a_0 \kappa f}{(\sqrt{\Delta} + \sqrt{n_I g})^2}, \qquad a^* = \frac{a_0 f}{\Delta + \sqrt{\Delta n_I g}} \tag{4.32}$$

For all index sets there is a transcritical bifurcation with the trivial fixed point at $r = k a_0$, as may be easily verified from (4.29). Again, there are the familiar scenarii 1 and 2 described in the last section; the latter occurs if

$$f > f^c = \frac{n_I k \kappa}{g} > n_I k \tag{4.33}$$

For different index sets, different scenarii may occur, depending on n_I.

Stability properties

The (internal part of the) Jacobian has the following form:

$$\begin{array}{lll} \frac{\partial \dot{x}_i}{\partial x_j}{=}0 & \frac{\partial \dot{x}_i}{\partial s_j}{=}f\bar{x}\delta_{i,j} & \frac{\partial \dot{x}_i}{\partial a}{=}k\bar{x} \\ \frac{\partial \dot{s}_i}{\partial x_j}{=}(g\bar{a}-f\bar{s})\delta_{i,j} & \frac{\partial \dot{s}_i}{\partial s_j}{=}-(f\bar{x}+r)\delta_{i,j} & \frac{\partial \dot{s}_i}{\partial a}{=}g\bar{x} \\ \frac{\partial \dot{a}}{\partial x_i}{=}-\kappa x & \frac{\partial \dot{a}}{\partial s_i}{=}0 & \frac{\partial \dot{a}}{\partial a}{=}-r-n_I\kappa\bar{x} \end{array} \tag{4.34}$$

Inserting the value of $\bar{s}$, we can write $\partial\dot{s}_i/\partial x_i = g\bar{a} - f\bar{s} = \kappa a - r > 0$.

The Jacobian consists of 4 circulant $n_I \times n_I$ blocks (plus one row and one column for the substrate). Since all circulant matrices have the same eigenvectors, namely

$$\nu_j = (1, z^j, z^{2j}, \dots, z^{(n-1)j}), \qquad z = e^{\frac{2\pi i}{n}} \tag{4.35}$$

with $0 \le j \le n-1$ and $i = \sqrt{-1}$, we make the following ansatz for the eigenvectors ξ_j of the Jacobian:

$$\xi_j = (1, z^j, \dots, z^{(n-1)j}, \beta_j, \beta_j z^j, \dots, \beta_j z^{(n-1)j}, \omega_j) \tag{4.36}$$

where we have to determine β_j and ω_j so that the equation

$$J\xi_j = \lambda_j \xi_j \tag{4.37}$$

is fulfilled. The corresponding eigenvalue is simply the first entry of $J\xi_j$, since the first entry of ξ_j is unity, and hence

$$\lambda_j = \beta_j f\bar{x} + \omega_j k\bar{x} \tag{4.38}$$

We now calculate β_j and ω_j:

$$J\xi_j = \Big(\underbrace{\bar{x}(\beta_j f + \omega_j k), \dots,}_{n_I \text{ terms}} \underbrace{\kappa\bar{a} - r - \beta_j(f\bar{x}+r) + \omega_j g\bar{x}, \dots,}_{n_I \text{ terms}} \\ -\kappa\bar{x}\textstyle\sum_{k=0}^{n-1} z^{jk} - \omega_j(r + n\kappa\bar{x})\Big) \tag{4.39}$$

Since $\sum_{k=0}^{n-1} z^{jk} = 0$ if $j \neq 0$, we can choose $\omega_j = 0$ in this case. Substituting (4.39) into (4.37), we get

$$\beta_j^2 f\bar{x} + \beta_j(f\bar{x} + r) - \kappa\bar{a} + r = 0, \qquad j = 1, 2, \ldots, n-1 \tag{4.40}$$

Since the quadratic and the absolute term have opposite signs, there is one positive and one negative solution for β_j (and also for λ_j). The eigenvalues are

$$\lambda_j^{(1)/(2)} = \frac{1}{2}\left(-f\bar{x} - r \pm \sqrt{(f\bar{x} + r)^2 + 4f\bar{x}(\kappa\bar{a} - r)}\right) \tag{4.41}$$

For $j = 0$, the following equations result:

$$\begin{aligned} \omega_0^2 k\bar{x} + \omega_0(\beta_0 f\bar{x} + r + n_I\kappa\bar{x}) + n_I\kappa\bar{a} &= 0 && (4.42)\\ \omega_0(\beta_0 k\bar{x} - g\bar{x}) + \beta_0^2 f\bar{x} + \beta_0(f\bar{x} + r) - \kappa\bar{a} + r &= 0 && (4.43) \end{aligned}$$

Solving the latter for ω_0

$$\omega_0 = \frac{\beta_0^2 f\bar{x} + \beta_0(f\bar{x} - r) - \kappa\bar{a} + r}{\beta_0\bar{x}(g - k)} \tag{4.44}$$

and inserting the solution into the former, we get

$$\begin{gathered} (\beta_0 f\bar{x} + r - k\bar{a})\times \\ \times\left(\beta_0^2\bar{x}(f - n_I k) + \beta_0\Big[r + \bar{x}\Big(f - n_I(k - g)\Big)\Big] + r - \kappa\bar{a} + n_I g\bar{x}\right) = 0 \end{gathered} \tag{4.45}$$

Thus, there is one solution

$$\beta_0^{(1)} = -\frac{r - k\bar{a}}{f}, \qquad \omega_0^{(1)} = -\frac{\bar{a}}{\bar{x}}, \qquad \lambda_0^{(1)} = -r \tag{4.46}$$

which is the external eigenvalue.

To find the remaining two solutions of (4.45), we eliminate $\bar{x}$ by introducing (4.28) and r by solving (4.29) for r and introducing this into (4.45):

$$\beta_0^2\Delta\gamma\alpha - \beta_0\gamma\left(\Delta\alpha + n_I(a_0 g + \bar{a}k)\right) - f\alpha^2 - n_I\bar{a}(\bar{a}g + 2\bar{a}k - a_0 k) = 0 \tag{4.47}$$

with $\gamma = f(a_0 - \bar{a}) + n_I k\bar{a} > 0$ and $\alpha = a_0 - \bar{a} > 0$. Introducing (4.44) into (4.38), we get

$$\lambda_0 = \frac{\kappa\,(\gamma^2\beta_0 - n_I^2 gk\bar{a}^2)}{\alpha(g - k\beta_0)(\gamma + n_I g\bar{a})} \tag{4.48}$$

The eigenvalue therefore becomes zero at

$$\beta_0 = \beta_0^* = \frac{n_I^2 gk\bar{a}^2}{\gamma^2} \tag{4.49}$$

We now introduce $\beta_0' = \beta_0 - \beta_0^*$. Since $k\beta_0 < g$ for $\bar{a} < a_0$, β_0' and λ_0 have the same sign. Equations (4.47) now becomes

$$\beta_0'^2\alpha\gamma^4 + \beta_0'\gamma^2 L + n_I\alpha^2 fg(\gamma + n_I k\bar{a})A = 0 \tag{4.50}$$

where the factor L in the linear coefficient is

$$L = \Delta^3\alpha^3 + \Delta^2\alpha^2(a_0 g + 2a_0 k + \bar{a}k) +$$

$$+\Delta\alpha n_I^2 k(2g\bar{a}^2 + 2ga_0^2 + 2ka_0\bar{a} + ka_0^2) + n_I^3 a_0^2 k^2(ga_0 + k\bar{a}) > 0$$

For $f < n_I k$ ($\Delta < 0$), the factor A in the absolute term can be written

$$A = (\Delta\alpha + n_I k a_0)^2 - n_I g\Delta\bar{a}^2 > 0 \tag{4.51}$$

The quadratic and the absolute term in (4.50) therefore are both positive; since the linear term is also positive, there are two negative solutions of (4.50) and hence two negative eigenvalues for $j = 0$.

For $\Delta > 0$, we can write the factor A using (4.32):

$$A = (\bar{a}^* - \bar{a})(\Delta + \sqrt{n_I g\Delta})(\alpha\Delta + \bar{a}\sqrt{n_I g\Delta} + n_I k a_0) \tag{4.52}$$

All terms but the first are positive; the sign of A is therefore positive if $\bar{a} < \bar{a}^*$, that is, for the fixed point with the lower equilibrium concentration of the substrate. Hence there are two negative eigenvalues for this fixed point, while for the other (if it exists), there is one positive and one negative eigenvalue.

There are 2 eigenvalues for each value of $j \neq 0$ and three for $j = 0$ and therefore totally $2n + 1$ eigenvalues, i.e. the ansatz we used allows us to compute all eigenvalues of the Jacobian. While the eigenvalues for $j \neq 0$ depend on the specific interaction matrix we used in this model, those for $j = 0$ depend only on the fact that there is exactly one entry per row and column and that they all have the same value. We shall use this fact later when we treat the mutualistic model.

The transversal eigenvalues (if any exist) are $k\bar{a} - r$ and $-r$, each of them with multiplicity $n - n_I$. They are all negative. Therefore, any fixed point is transversally stable, i.e. stable against the introduction of new species.

The overall behaviour is therefore as follows: For small values of r there is exactly one fixed point per index set. The one dimensional fixed points are sinks equilibrium concentration of the substrate), the other ones are saddles with $n_I - 1$–dimensional unstable manifolds. The trivial fixed point is also a saddle. At $r = a_0 k$, there is a transcritical bifurcation with the trivial fixed point for every index set. At this flow rate, either the fixed point P_I leaves the simplex or a second fixed point with the same index set enters it. The latter is more probable for small n_I. The fixed point with the higher equilibrium concentration of the substrate has one more positive eigenvalue than that with the lower concentration. If there are two fixed points with the index set I for $r > a_0 k$, they disappear in a saddle node bifurcation at a somewhat higher flow rate. The trivial fixed point is stable for $r > a_0 k$.

4.2.2 The evolution reactor

We now leave the domain of five–line–formulae and turn to the much simpler world of the evolution reactor.

The differential equations are

$$\begin{aligned} \dot{x}_i &= x_i(k + c_0 f s_i - \Phi) \\ \dot{s}_i &= g x_i - s_i(c_0 f x_i + \Phi \end{aligned} \tag{4.53}$$

where the flow is $\Phi = \kappa \sum x_i$. The equilibrium concentrations at the fixed point P_I then are

$$\bar{x} = \frac{\bar{\Phi}(\bar{\Phi} - k)}{fc_0(\kappa - \bar{\Phi})}, \qquad \bar{s} = \frac{\bar{\Phi} - k}{c_0 f} \tag{4.54}$$

As in the CSTR setting, all possible index sets are admissible. Thus there are $2^n - 1$ admissible index sets.

The flow at the fixed point is

$$\bar{\Phi} = \frac{\kappa(n_I k + c_0 f)}{n_I \kappa + c_0 f} \tag{4.55}$$

Inserting this into (4.54), we obtain

$$\bar{x} = \frac{n_I k + c_0 f}{n_I(n_I \kappa + c_0 f)}, \qquad \bar{s} = \frac{g}{n_I \kappa + c_0 f} \tag{4.56}$$

The fixed points exist for all values of c_0: in contrast to the general model, where only one dimensional fixed points exist for all total concentrations, there are no transcritical bifurcations of higher dimensional fixed points in the case of equal reaction constants.

Stability properties

The (internal part of the) Jacobian at the fixed point P_I has the following form:

$$\begin{array}{ll} \frac{\partial x_i}{\partial x_j} = -\kappa \bar{x} & \frac{\partial x_i}{\partial s_j} = c_0 f \bar{x} \delta_{i,j} \\ \frac{\partial s_i}{\partial x_j} = -\kappa \bar{s} + (g - \bar{s} c_0 f)\delta_{i,j} & \frac{\partial s_i}{\partial s_j} = -(c_0 f \bar{x} + \bar{\Phi})\delta_{i,j} \end{array} \tag{4.57}$$

Calculating the eigenvalues, we shall make use of the identity $g - \bar{s}c_0 f = \kappa - \bar{\Phi} > 0$. The Jacobian again consists of four $n_I \times n_I$ circulant matrices, so that our ansatz for the eigenvector is very similar to the one for the CSTR model:

$$\xi_j = (1, z^j, \ldots, z^{(n-1)j}, \beta_j, \beta_j z^j, \ldots, \beta_j z^{(n-1)j}) \tag{4.58}$$

where z is defined as above and j ranges from zero to $n_I - 1$. We must choose β so that the equation

$$J\xi_j = \lambda_j \xi_j \tag{4.59}$$

is fulfilled. With

$$J\xi_j = \underbrace{(\beta_j c_0 f\bar{x} - \kappa\bar{x}\sum_{k=0}^{n-1} z^{jk}, \ldots,}_{n_I \text{ terms}} \underbrace{\beta_j(c_0 f\bar{x} - \bar{\Phi}) + \kappa - \bar{\Phi} - \kappa\bar{s}\sum_{k=0}^{n-1} z^{jk}, \ldots)}_{n_I \text{ terms}} \tag{4.60}$$

we see that

$$\lambda_j = \beta_j c_0 f\bar{x} - n\kappa\bar{x}\sum_{k=0}^{n-1} z^{jk} \tag{4.61}$$

Since $\sum z^{jk} = n_I \delta_{0,j}$, we get different equations for the case $j = 0$ and $j \neq 0$. In the latter case β_j must fulfill the equation

$$\beta_j^2 c_0 f\bar{x} - \beta_j(c_0 f\bar{x} + \bar{\Phi}) - \kappa + \bar{\Phi} = 0 \tag{4.62}$$

and the corresponding eigenvalue is

$$\lambda_j = \beta_j c_0 f\bar{x} = \frac{1}{2}\left(-c_0 f\bar{x} - \bar{\Phi} \pm \sqrt{(c_0 f\bar{x} + \bar{\Phi})^2 + 4 f c_0 \bar{x}(\kappa - \bar{\Phi})}\right) \tag{4.63}$$

Since $\kappa - \bar{\Phi} > 0$, there is one positive and one negative eigenvalue for each $j \neq 0$. If $j = 0$, the β_0 must fulfill the equation

$$\beta_0^2 c_0 f\bar{x} + \beta_0(c_0 f\bar{x} + \bar{\Phi} - n_I\kappa\bar{x}) - \kappa + \bar{\Phi} + n_I\kappa\bar{s} = 0 \tag{4.64}$$

Since $\bar{\Phi} = n_I\kappa\bar{x}$ and $n_I\bar{s} + n_I\bar{x} = 1$ the linear and absolute coefficients reduce to $c_0 f\bar{x}$ and zero, respectively. The solutions of the above equation are therefore $\beta_0^{(1)} = 0$ and $\beta_0^{(2)} = -1$ with the associated eigenvalues $\lambda_0^{(1)} = -n_I\kappa\bar{x} = -\bar{\Phi}$ (the external eigenvalue) and $\lambda_0^{(2)} = -(n_I\kappa + c_0 f)\bar{x}$.

There are 2 eigenvalues per value of j; since j can take n different values, we get all eigenvalues of the Jacobian using the above ansatz. As in the CSTR model, the eigenvalues for $j \neq 0$ depend on the coupling matrix B while those for $j = 0$ do not, which we shall use when treating the mutualistic model.

The properties of the competitive model in the evolution reactor with equal reaction constants is therefore as follows: There is exactly one fixed point for each index set; it exists for all values of c_0. There are no bifurcations of any kind. The one dimensional fixed points are all stable, higher dimensional fixed points are saddles with $n_I - 1$ dimensional unstable manifolds.

4.2.3 Comparison with the Schlögl model

Comparing the results of the competitive model with equal reaction constants with the corresponding second order reaction network, we see that they both in the CSTR and in the evolution reactor the number of fixed points and the stabilities coincide in both models if the constants are appropriately chosen.

Chapter 5

The mutualistic model

In the mutualistic model the entries of the interaction matrix $\mathbf{B}$ are $b_{li} = f_i \delta_{l+1,i}$, with the indices taken modulo n (which we shall imply wherever we treat the mutualistic model). Thus each X_i produces S_i, which in turn produces X_{i+1} ($i = 1, \ldots, n-1$), and S_n produces X_1: the species form a catalytic cycle. This is, of course, true only if all species are present in the system; otherwise we may get a (number of) catalytic chain(s). In contrast to the competitive model, where the fixed points in the interior of the simplex and those on the boundary were quite similar, we shall see that in the mutualistic model they really form two classes with very different physical behaviour.

The reaction scheme of the mutualistic model is:

$$\begin{array}{rcl} (A) + X_i & \xrightarrow{k_i} & 2X_i \\ (A) + X_i & \xrightarrow{g_i} & X_i + S_i \\ X_i + S_{i-1} & \xrightarrow{f_{i-1}} & 2X_i \\ X_i & \xrightarrow{r} & * \\ S_i & \xrightarrow{r} & * \end{array} \tag{5.1}$$

The corresponding second order reaction network is the famous hypercycle, invented by Eigen and Schuster [10, 11, 12] in an attempt to understand important questions in the evolution of live:

$$\begin{array}{rcl} (A) + X_i & \stackrel{k'_i}{\rightarrow} & 2X_i \\ (A) + X_i + X_{i-1} & \stackrel{f'_i}{\rightarrow} & 2X_i + X_{i-1} \end{array} \tag{5.2}$$

This system has been thoroughly investigated ([42]), particularly in the evolution reactor setting ([43, 44]). In this setting, (5.2) has only one interior fixed point. For the the case $k'_i = 0\ \forall i$ (called the homogeneous hypercycle), i.e. omission of the uncatalyzed formation, a barycentric transformation can be found, i.e., a coordinate transformation that shifts the interior fixed point to the barycentre of the simplex (regardless of the kinetic constants). In these coordinates, the Jacobian of the system at the interior fixed point becomes circulant, so that the eigenvalues can easily be evaluated. In this special case, stability depends only on n. Thus it can be shown that the interior fixed point is stable for $n < 4$ and unstable for $n > 4$. For $n = 4$ the stability of the fixed point can be shown using Ljapunov functions. For $n > 4$, the (unstable) interior fixed point is surrounded by a stable limit cycle.

In the next sections we first examine the mutualistic model in general in the CSTR. Then we examine the special case $k_i = 0$ for all i (we call this the homogeneous case in accordance with the corresponding hypercycle model) in the CSTR. We do this mainly because the general mutualistic model in the CSTR leads to confusing formulae and the proof of the essential theorem of section 1, although it must be modified a little, becomes much clearer in the homogeneous case. In the third section we treat the mutualistic model in the evolution reactor. Finally we investigate the case of equal reaction constants both in the CSTR and the evolution reactor. As in the mutualistic model, this simplifies all calculations a lot and enables us to derive analytic formulae for the fixed points and eigenvalues of the Jacobian.

5.1 The general mutualistic model in the CSTR

In the CSTR setting, system (5.1) produces the following kinetic differential equations:

$$\begin{array}{rcl} \dot{x}_i & = & x_i(k_i a + f_{i-1}s_{i-1} - r) \\ \dot{s}_i & = & g_i x_i a - s_i(f_i x_{i+1} + r) \\ \dot{a} & = & a_0 r - a(r + \sum_{i=1}^{n}(k_i + g_i)x_i) \end{array} \tag{5.3}$$

We shall assume that all k_i are different. Then we may assume (without loosing generality) $k_1 = \max k_i$.

Besides the trivial fixed point, the system (5.3) admits fixed points on the boundary and in the interior of the simplex. We now consider them in turn.

5.1.1 Nontrivial fixed points on the boundary of the simplex

We are first going to investigate for which index sets I the corresponding fixed point P_I can exist. As in the competitive model, we shall call them *admissible*. Since at very high flow rates only the trivial fixed point exists, "can exist" means here that the fixed point exists for suitably chosen flow rates (the exact meaning of this somewhat vague formulation will become clear later). The conditions on the index set will turn out to be quite restrictive.

We start with the following

Lemma 5.1 *In every admissible index set I, there is only one index j for which $j-1 \notin I,\ j \in I$.*

Proof: If I contains two indices j and $j',\ j' \neq j$ with $j-1 \notin I,\ j'-1 \notin I$, then inserting $\bar{s}_{j-1} = \bar{s}_{j'-1} = 0$ into the corresponding equations in (5.3) would yield

$$\begin{array}{rl} \bar{x}_j(k_j\bar{a} - r) & = 0 \\ \bar{x}_{j'}(k_{j'}\bar{a} - r) & = 0 \end{array}$$

or $\bar{a} = r/k_j = r/k_{j'}$, since $\bar{x}_j \neq 0,\ \bar{x}_{j'} \neq 0$. This is a contradiction, however, since we assumed that all k_i are different.

□

Thus, every admissible index set is of the form $I = \{j, j+1, \ldots, k-1, k\}$ (the species form a single catalytic chain). Throughout this chapter, we shall use the indices j and k to label the first (last) member of the catalytic chain formed at a fixed point on the boundary of the simplex.

Lemma 5.2 *If I is admissible then $k_j = \max_{i \in I} k_i$. If an admissible set contains both 1 and n, then $I = \mathcal{N}$.*

Proof: From the proof of (5.1) we see that $\bar{a} = r/k_j$ at the fixed point P_I. Hence the equilibrium concentrations of S_i are

$$\bar{s}_i = \frac{r(k_j - k_{i+1})}{f_i k_j} \qquad i \in I \setminus \{k\} \tag{5.4}$$

Since $\bar{s}_i$ must be positive, k_j must be greater than k_i. Specifically, if $1 \in I$, the fixed point can exist only if $j = 1$. Then, if $n \in I$, it is clear that $I = \mathcal{N}$.

□

Combining these lemmas, we get the following

Lemma 5.3 *For an index set to be* admissible *in the general mutualistic model, it must be of the form $I = \{j, j+1, \ldots, k-1, k\},\ 1 \leq j \leq k \leq n$ and if $k_j = \max_{i \in I} k_i$. For every admissible set I we define the set $I' = I \backslash \{k\}$, which is also admissible. For the set $\mathcal{N} = \{1, 2, \ldots, n\}$, we define the (admissible) set $\mathcal{N}' = \mathcal{N} \setminus \{n\}$.*

Remark: When we compute the equilibrium concentrations, we shall see that we need conditions on the index set besides those stated in the lemma.

The conditions given in the above lemma are therefore not only necessary but also sufficient.

There are at most two admissible index sets with $n-1$ species present ($I = \{1,2,\ldots,n-1\}$ and $I = \{2,\ldots,n\}$; the latter exists if $k_2 = \max_{i\in I} k_i$), at most three with $n-2$ species and so on. The maximal number of admissible index sets, namely $1+n(n+1)/2$ (including the trivial and the interior fixed point), is obtained if $k_2,\ k_3,\ldots,\ k_n$ form a decreasing sequence. On the other hand, if they form an increasing sequence, there are only $2n$ admissible index sets (this is the minimal number). In the general case, the number of admissible index sets will be between these two extremes.

The equilibrium values for $x_i,\ i\in I = \{j,\ldots,k\}$ can be calculated easily, if we don't insist on eliminating $\bar{s}_k$, leaving it as a parameter:

$$\begin{aligned} \bar{x}_i &= \sum_{m=i}^{k} \frac{\bar{s}_m k_j}{g_i} \prod_{l=i}^{m-1} \frac{\bar{s}_l f_l k_j}{g_l r} = \\ &= \frac{\bar{s}_k k_j}{g_k} \prod_{l=i}^{k-1} \frac{k_j - k_{l+1}}{g_l} + \sum_{m=i}^{k-1} \frac{r}{f_m} \prod_{l=i}^{m} \frac{k_j - k_{l+1}}{g_l} = \\ &= \bar{s}_k \frac{k_j f_{k-1}}{g_k} \mu_{k-1}^{(i,j)} + r \sum_{m=i}^{k-1} \mu_m^{(i,j)} \end{aligned} \tag{5.5}$$

where we have put

$$\mu_m^{(i,j)} = \frac{1}{f_m} \prod_{l=i}^{m} \frac{k_j - k_{l+1}}{g_l} \tag{5.6}$$

Now we can determine $\bar{s}_k$ from $\bar{a} - a_0 + \sum_{i\in I} \bar{x}_i + \bar{s}_i = 0$, using (5.4) and (5.5):

$$\bar{s}_k \left(1 + \frac{k_j f_{k-1}}{g_k} \sum_{i=j}^{k} \mu_{k-1}^{(i,j)}\right) + \frac{r}{k_j} \left(1 + k_j \psi^{(j,k)} - K^{(i,j)} + k_j \sum_{i=j}^{k-1} \sum_{m=i}^{k-1} \mu_m^{(i,j)}\right) - a_0 = 0 \tag{5.7}$$

with

$$\psi^{(j,k)} = \sum_{i=1}^{k-1} \frac{1}{f_i}, \qquad K^{(i,j)} = \sum_{i=1}^{k-1} \frac{k_{i+1}}{f_i} \tag{5.8}$$

$$\bar{s}_k = \frac{a_0 k_j - r\left(1 + k_j \psi^{j,k} - K^{(i,j)} + k_j \sum_{i=j}^{k-1} \sum_{m=i}^{k-1} \mu_m^{(i,j)}\right)}{k_j \left(1 + \dfrac{k_j f_{k-1}}{g_k} \displaystyle\sum_{i=j}^{k} \mu_{k-1}^{(i,j)}\right)} \tag{5.9}$$

Now we might substitute (5.9) into (5.5) to get the equilibrium concentrations $\bar{x}_i$ as a function of the kinetic parameters and I alone, but I guess everyone who kept reading up to this line will be glad if I don't do it.

For fixed points on the boundary on the simplex, the following theorem holds:

Theorem 5.1 *For each admissible index set I except $\mathcal{N}$ and $\emptyset$, there is exactly one fixed point P_I for sufficiently small flow rates. At $r = r^{I \times I'} > 0$, there is a transcritical bifurcation with $P_{I'}$ (P_I leaves the simplex through $P_{I'}$). For all $r > r^{I \times I'}$ the fixed point lies outside the simplex.*

Proof: Since $\bar{s}_k$ is uniquely determined by (5.9), there is only one fixed point P_I for each admissible index set $I \neq \mathcal{N}$. The equilibrium concentrations at P_I depend only on I and the flow rate. We see, however, from (5.9) that the fixed point does not exist for all flow rates: it leaves the simplex (that is, $\bar{x}_k$ and $\bar{s}_k$ become negative), if

$$r > r^{(I \times I')} = \frac{a_0 k_j}{\left(1 + k_j \psi^{(j,k)} - K^{(j,k)} + k_j \displaystyle\sum_{i=j}^{k-1} \sum_{m=1}^{k-1} \mu_m^{(i,j)}\right)} \tag{5.10}$$

Since $\bar{s}_k$ is linear in r, it is clear that the fixed point can not lie on the simplex for $r > r^{I \times I'}$.

To show that P_I passes through $P_{I'}$ at $r = r^{(I \times I')}$, it suffices to prove that $\bar{s}^{I}_{k-1} = \bar{s}^{I'}_{k-1}$ at the critical flow rate (the superscripts are used to distinguish the fixed points). From (5.7) we have

$$\bar{s}^{I'}_{k-1}\left(1 + \frac{k_j f_{k-2}}{g_k} \sum_{i=j}^{k-1} \mu_{k-2}^{(i,j)}\right) + \frac{r^{(I \times I')}}{k_j}\left(1 + k_j \psi^{(j,k-1)} - K^{(j,k-1)} + k_j \sum_{i=j}^{k-2} \sum_{m=i}^{k-2} \mu_m^{(i,j)}\right) - a_0 = 0 \tag{5.11}$$

Using (5.10) we obtain

$$\frac{r^{(I\times I')}}{k_j}\left(1+k_j\psi^{(j,k-1)}-K^{(j,k-1)}+k_j\sum_{i=j}^{k-2}\sum_{m=i}^{k-2}\mu_m^{(i,j)}\right)-a_0=-\frac{r^{(I\times I')}}{k_j}\left(\frac{k_j-k_k}{f_{k-1}}+k_j\sum_{i=j}^{k-1}\mu_{k-1}^{(i,j)}\right)>0 \tag{5.12}$$

Since $k_j = \max_{i\in I} k_i$, it follows that $k_j\psi^{(j,k)} > K^{(j,k)}$ and hence $r^{(I\times I')}$ is positive. If we take into account that

$$\mu_{k-2}^{(i,j)} = \frac{f_{k-1}g_{k-1}}{f_{k-2}(k_j-k_k)}\mu_{k-1}^{(i,j)} \tag{5.13}$$

we can rewrite (5.11) as

$$\left(\bar{s}_{k-1}^{I'}-\frac{r^{(I\times I')}(k_j-k_k)}{k_jf_{k-1}}\right)+\left(\frac{\bar{s}_{k-1}^{I'}f_{k-1}k_j}{k_j-k_k}-r^{(I\times I')}\right)\sum_{i=j}^{k-1}\mu_{k-1}^{(i,j)}=0 \tag{5.14}$$

and hence

$$\bar{s}_{k-1}^{I'}=\frac{r^{(I\times I')}(k_j-k_k)}{k_jf_{k-1}}=\bar{s}_{k-1}^{I} \tag{5.15}$$

□

5.1.2 Interior fixed point

Following the procedure outlined in chapter 3, we find the following expressions for the equilibrium concentration of the replicating species and the intermediates:

$$\bar{x}_i=\frac{\displaystyle\sum_{l=0}^{n-1}\frac{r}{f_{i+l}}\prod_{m=0}^{l}\frac{\bar{s}_{i+m}f_{i+m}}{g_{i+m}\bar{a}}}{\displaystyle 1-\prod_{m=1}^{n}\frac{f_m\bar{s}_m}{g_m}} \tag{5.16}$$

$$\bar{s}_i=\frac{r-k_{i+1}\bar{a}}{f_i} \tag{5.17}$$

For $\bar{a}\neq 0$, we may rewrite (5.16), using (5.17) and multiplying by $\bar{a}^n$:

$$\bar{x}_i=\frac{r\sum_{l=1}^{n}\gamma_{i,l}\bar{a}^{n-l}\phi_{i,l}}{a^n-\Gamma\phi_{1,n}} \tag{5.18}$$

with

$$\gamma_{i,l} = \frac{1}{f_{i+l-1}} \prod_{m=0}^{l-1} \frac{1}{g_{i+m}}, \qquad \Gamma = \prod_{m=1}^{n} \frac{1}{g_m}, \qquad \phi_{i,l} = \prod_{m=1}^{l} (r - k_{i+m}\bar{a}) \tag{5.19}$$

The equilibrium concentration of the substrate $\bar{a}$ is then implicitly determined by the function

$$\mathcal{F}(a,r) = a - a_0 + \sum_{i=1}^{n} x_i + s_i \tag{5.20}$$

Inserting (5.18) and (5.17) this function becomes:

$$\mathcal{F}(a,r) = a(1 - K^{(1,n)}) - a_0 + r\psi^{(1,n)} + \frac{r \sum_{i=1}^{n} \sum_{l=1}^{n} a^{n-l} \gamma_{i,l} \phi_{i,l}}{a^n - \Gamma \phi_{1,n}} = 0 \tag{5.21}$$

with

$$K^{(1,n)} = \sum_{i=1}^{n} \frac{k_{i+1}}{f_i}, \qquad \psi^{(1,n)} = \sum_{i=1}^{n} \frac{1}{f_i} \tag{5.22}$$

At the equilibrium concentration this function vanishes:$\mathcal{F}(\bar{a}(r), r) = 0$.

(5.21) has the general form

$$\mathcal{F}(a,r) = v(a,r) + \frac{w(a,r)}{z(a,r)} \tag{5.23}$$

with

$$\begin{aligned} v &= a(1 - K^{(1,n)}) - a_0 + r\psi^{(1,n)} && (5.24) \\ w &= r \sum_{i=1}^{n} \sum_{l=1}^{n} a^{n-l} \gamma_{i,l} \phi_{i,l} && (5.25) \\ z &= a^n - \Gamma \phi_{1,n} && (5.26) \end{aligned}$$

Since (5.21) is a $n+1$–order equation in a, there might be as much as $n+1$ interior fixed point. We shall see, however, that most of them lie outside the simplex:

Theorem 5.2 *For sufficiently small flow rates, there is exactly one interior fixed point. At* $r = r^{\mathcal{N}\times\mathcal{N}'}$*, there is a bifurcation of an interior fixed point with the unique fixed point* $P_{\mathcal{N}'}$*. There are two ways in which this bifurcation can happen: the fixed point that lay inside the simplex may pass through* $P_{\mathcal{N}'}$ *and leave the simplex (which we call scenario 1), or a second fixed point may enter the simplex (scenario 2). In the latter case, we call the fixed point that enters the simplex (the one with the higher equilibrium concentration of the substrate)* $P^{(2)}_{\mathcal{N}}$ *and the other one* $P^{(1)}_{\mathcal{N}}$*. They disappear in a saddle node bifurcation at* $r = r^* > r^{\mathcal{N}\times\mathcal{N}'}$*. In scenario 1, no interior fixed point exists for any flow rate greater than* $r^{\mathcal{N}\times\mathcal{N}'}$*. In scenario 2, no fixed point exists for any* $r > r^*$*.*

Proof: In this proof, the partial derivatives of $\mathcal{F}$ with respect to a and r play an important role. For simplicity, we shall denote partial derivative with respect to a by primes and those with respect to r by subscript r.

Now let us first define the part of the a, r–plane where we can expect physically acceptable solutions: since the total concentration at the fixed point is a_0, we must have $a \leq a_0$. Since $\bar{s}_i$ becomes negative if $a > r/k_i$ (5.17) and $k_1 = \max k_i$, the following condition must hold:

$$a \leq \min\{\frac{r}{k_1}, a_0\} \tag{5.27}$$

On the other hand, $z(a, r)$ must be positive; otherwise all $\bar{x}_i$ would be negative. We must therefore find the values $a_P(r) : z(a_P(r), r) = 0$ and choose $a > \max a_P(r)$. Since

$$z' = na^{n-1} - \Gamma\phi'_{1,n} \tag{5.28}$$

is nonnegative for $0 \leq a \leq r/k_1$ ($\phi'_{1,n}$ is negative if a is in this range), w is increasing in a (for r fixed) in this range. Thus there is at most one solution a_P between zero and $\min\{r/k_1, a_0\}$. With $w(0, r) = -r^n \leq 0,\ w(r/k_1, r) = r^n/k_1^n \geq 0$ we see that there is exactly one solution at least for $r \leq a_0 k_1$. We can even say that $\bar{a}_P(r)$ is strictly increasing, because $z_r = -(\phi_{1,n})_r < 0,\ 0 \leq a \leq r/k_1$ and hence $da_P/dr = -z_r/z' > 0$.

We define $\mathcal{S}$ as the part of the a, r–plane that is confined by the lines $a = r/k_1$, $a = a_0$, and the curve $a = a_P(r)$. Only solution of $\mathcal{F}(\bar{a}, r) = 0$ that lie in $\mathcal{S}$ give rise to fixed point on the simplex.

We first prove that there is exactly one solution of (5.21) with $\bar{a} = r/k_1$ and call the corresponding value $r^{\mathcal{N}\times\mathcal{N}'}$. Inserting $a = r/k_1$ into (5.21) we get

$$\mathcal{F}\left(\frac{r}{k_1}, r\right) = \frac{r}{k_1}\left(1 - K^{(1,n)} + k_1\psi^{(1,n)}\right) + \frac{r\sum_{i=1}^{n}\sum_{l=1}^{n}\gamma_{i,l}\phi_{i,l}}{\left(\frac{r}{k_1}\right)^l} \tag{5.29}$$

With

$$\begin{aligned} \gamma_{(i,l)}\phi_{i,l} =& \frac{1}{f_{i+l-1}}\prod_{m=1}^{l}\frac{(r - k_{i+m}\bar{a})}{g_{i+m-1}} \\ =& \frac{r^l}{k_1^l f_{i+l-1}}\prod_{m=1}^{l}\frac{(k_1 - k_{i+m})}{g_{i+m-1}}\begin{cases} = & \left(\frac{r}{k_1}\right)^l \mu_{i+l-1}^{(i,1)} \quad \text{if } i + l \leq n \\ = & 0 \quad \text{if } i + l > n \end{cases} \end{aligned}$$

this becomes

$$\mathcal{F}\left(\frac{r}{k_1}, r\right) = \frac{r^{\mathcal{N}\times\mathcal{N}'}}{k_1}\left(1 - K^{(1,n)} + k_1\psi^{(1,n)} + k_1\sum_{i=1}^{n-1}\sum_{l=i}^{n-1}\mu_l^{(i,1)}\right) \tag{5.30}$$

If there is a solution of (5.21) with $\bar{a} = r/k_1$, the right–hand–side of (5.30) must be zero, and hence we have for $r^{\mathcal{N}\times\mathcal{N}'}$ the unique value

$$r^{\mathcal{N}\times\mathcal{N}'} = \frac{a_0 k_1}{1 - K^{(1,n)} + k_1\psi^{(1,n)} + k_1\sum_{i=1}^{n-1}\sum_{l=i}^{n-1}\mu_l^{(i,1)}} \tag{5.31}$$

Since $k_1\psi^{(1,n)} - K$ is positive, the denominator in this equation is greater than one and $0 < r^{\mathcal{N}\times\mathcal{N}'} < a_0 k_1$.

We now prove that at this critical flow rate there is a transcritical bifurcation of an interior fixed point with the fixed point $P_{\mathcal{N}'}$. It is easy to see from (5.16) and (5.17) that $\bar{x}_n = \bar{s}_n = 0$ if $\bar{a} = r/k_1$. Besides, since $k_1\psi^{(1,n)} - K$ is just $\sum_{i=1}^{n-1}(k_1 - k_{i+1})/f_i$, (5.31) is equal to (5.10) with $j = 1$, $k = n$ and hence we don't need to repeat the proof that $\bar{s}_{n-1}^{\mathcal{N}'} = \bar{s}_{n-1}^{\mathcal{N}} = r(k_1 - k_n)/k_1 f_{n-1}$ at

$r = r^{\mathcal{N}\times\mathcal{N}'}$. For the remaining $\bar{s}_i$ $(i \neq n-1)$ we obtain with (5.17) and $\bar{a} = r/k_1$

$$\bar{s}_i^{\mathcal{N}} = \frac{r(k_1 - k_{i+1})}{k_1 f_i} = \bar{s}_i^{\mathcal{N}'}$$

Finally, for $\bar{x}_i,\ (i \neq n)$ we obtain

$$\bar{x}_i^{\mathcal{N}} = \frac{r\sum_{l=1}^{n-i} \bar{a}^{n-l}\bar{a}^{l}\mu_{i+l-1}^{(i,1)}}{\bar{a}^n} = r\sum_{l=i}^{n-1}\mu_l^{(i,1)} = x_i^{\mathcal{N}'} \tag{5.32}$$

if we insert the equilibrium value of $\bar{s}_{n-1}$ into (5.5). Hence $P_{\mathcal{N}}$ and $P_{\mathcal{N}'}$ coincide at $r^{\mathcal{N}\times\mathcal{N}'}$ and there is a transcritical bifurcation.

We see from (5.30) that for $r < r^{\mathcal{N}\times\mathcal{N}'}$, $\mathcal{F}(r/k_1, r)$ is negative, whereas $\mathcal{F}(\bar{a}_P + \epsilon, r)$ is positive for all r and $\epsilon > 0$ and sufficiently small. Thus there must be an odd number of interior fixed points for these flow rates (at least one). On the other hand, for $r > r^{\mathcal{N}\times\mathcal{N}'}$, $\mathcal{F}(r/k_1, r)$ is positive and we have an even number of interior fixed points.

$\mathcal{F}$ is monotonously increasing in r on $\mathcal{S}$, because the partial derivative with respect to r is everywhere positive:

$$\mathcal{F}_r = \psi^{(1,n)} + \frac{z\left(\frac{w}{r}\sum_{i=1} n\sum_{l=1}^{n} a^{n-l}\gamma_{i,l}(\phi_{i,l})_r\right) + w\Gamma(\phi_{1,n})_r}{z^2} > 0 \tag{5.33}$$

(this follows from $(\phi_{i,l})_r > 0$ for all i, l on $\mathcal{S}$.)

We now complete the proof by showing that the second partial derivative of $\mathcal{F}$ with respect to a does not change sign on the area bounded by (5.27). Hence there can be at most two solutions of the equation $\mathcal{F}(a, r) = 0$ for any fixed value of r that complies with (5.27). I have tried my best to keep the notation as lucid as possible; nevertheless I would not be too surprised if the next two pages just looked like a great confused heap of ϕ's and $\sum$'s to you.

The first partial derivative of $\mathcal{F}$ with respect to a is:

$$\mathcal{F}' = v' + \frac{w'z - wz'}{z^2} \tag{5.34}$$

With

$$\begin{array}{rcl} v' & = & 1 - K^{(1,n)} \\ w' & = & r \sum_{i=1} n \sum_{l=1}^{n} \gamma_{(i,l)} [a^{n-l} \phi'_{i,l} + (n-l) a^{n-l-1} \phi_{i,l}] \\ z' & = & n a^{n-1} - \Gamma \phi'_{1,n} \end{array} \qquad (5.35)$$

we have

$$\begin{array}{rcl} w'z - wz' & = & r \sum_{i=1}^{n} \sum_{l=1}^{n} \gamma_{(i,l)} a^{n-l-1} [\bar{a}^{n+1} \phi'_{i,l} - \\ & - & l a^n \phi_{i,l} + a\Gamma(\phi'_{1,n}\phi_{i,l} - \phi_{1,n}\phi'_{i,l}) - (n-l)\Gamma\phi_{1,n}\phi_{i,l}] \end{array} \qquad (5.36)$$

This is negative, because $\phi'_{i,l} < 0 \ \forall i, l$ and

$$\phi'_{1,n}\phi_{i,l} - \phi_{1,n}\phi'_{i,l} = - \sum_{p=l+1} k_{i+p} \prod_{\substack{m=1 \\ m \neq p}}^{n} (r - k_{i+m} a) \prod_{m=1}^{l} (r - k_{i+m} a) < 0 \qquad (5.37)$$

if (5.27) is fulfilled. Hence there can be no extrema on $\mathcal{S}$ unless $K^{(1,n)} < 1$ (in the converse case $\mathcal{F} < 0$ everywhere on $\mathcal{S}$). To calculate the number of extrema of $\mathcal{F}$ as a function of a for fixed r, we consider the second partial derivative of $\mathcal{F}$ with respect to a:

$$\mathcal{F}'' = \frac{z(w''z - wz'') - z'(w'z - wz')}{z^3} \qquad (5.38)$$

since $v'' = 0$. Inserting

$$\begin{array}{rcl} w'' & = & r \sum_{i=1}^{n} \sum_{l=1}^{n} \gamma_{(i,l)} a^{n-l-2} [\bar{a}^2 \phi''_{i,l} + 2(n-l) a \phi'_{i,l} + (n-l)(n-l-1)\phi_{i,l} \\ z'' & = & n(n-1) a^{n-2} - \Gamma \phi''_{1,n} \end{array} \qquad (5.39)$$

we see that that the quantity $w''z - wz''$ is always positive:

$$\begin{array}{rcl} w''z - wz'' & = & r \sum_{i=1}^{n} \sum_{l=1}^{n} \gamma_{(i,l)} a^{n-l-2} [a^{n+2} \phi''_{i,l} + 2(n-l) a^{n+1} \phi'_{i,l} - \\ & - & l(2n-l-1) a^n \phi_{i,l} + \Gamma a^2 (\phi''_{1,n}\phi_{i,l} - \phi_{1,n}\phi''_{i,l}) - \\ & - & 2(n-l) a \Gamma \phi_{1,n} - (n-l)(n-l-1)\Gamma\phi_{1,n}\phi_{i,l}] \end{array} \qquad (5.40)$$

since

$$\phi''_{1,n}\phi_{i,l} - \phi_{1,n}\phi''_{i,l} = \sum_{p=1}^{n} \sum_{\substack{q=l+1 \\ q\neq p}}^{n} k_{i+p}k_{i+q} \prod_{\substack{m=1 \\ m\neq p,q}}^{n} (r - k_{i+m}a) \prod_{m=1}^{l} (r - k_{i+m}a) > 0 \tag{5.41}$$

Putting together (5.38), (5.36) and (5.40) we finally get

$$\begin{array}{rcl} z(w''z & - & wz'') - 2z'(w'z - wz') = r\sum_{i=1}^{n}\sum_{l=1}^{n}\gamma_{(i,l)}a^{n-l-2}\Big\{a^{2n+2}\phi''_{i,l} - \\ & - & 2la^{2n+1}\phi'_{i,l} + l(l+1)a^{2n}\phi_{i,l} + \bar{a}^{n+2}\Gamma(\phi''_{1,n}\phi_{i,l} - 2\phi_{1,n}\phi''_{i,l} + 2\phi'_{1,n}\phi'_{i,l}) - \\ & - & 2a^{n+1}\Gamma\Big[2(n-l)\phi_{1,n}\phi'_{i,l} + l\phi'_{1,n}\phi_{i,l} + n(\phi'_{1,n}\phi_{i,l} - \phi_{1,n}\phi'_{i,l})\Big] + \\ & + & (n^2 - 2nl + n - 2l - 2l^2)a^n\Gamma\phi_{1,n}\phi_{i,l} + \\ & + & a^2\Gamma^2\Big[2\phi'_{1,n}(\phi'_{1,n}\phi_{i,l} - \phi_{1,n}\phi'_{i,l}) - \phi_{1,n}(\phi''_{1,n}\phi_{i,l} - \phi_{1,n}\phi''_{i,l})\Big] + \\ & + & 2(n-l)a\Gamma\phi_{1,n}(\phi_{1,n}\phi'_{i,l} - \phi'_{1,n}\phi_{i,l}) + (n-l)(n-l-1)\Gamma^2\phi^2_{1,n}\phi_{i,l}\Big\} \end{array} \tag{5.42}$$

All coefficients of this polynomial are nonnegative. For most of the coefficients this follows directly from the fact that $\phi_{i,l} > 0$, $\phi'_{i,l} \leq 0$, $\phi''_{i,l} \geq 0$ wherever (5.27) is fulfilled, and from (5.37) and (5.41). The coefficient of a^n, $(n^2 - 2nl + n - 2l - 2l^2)$, is positive since we can rewrite it as $(n-l)^2 + 4l(n-l) + (l-1)^2 + n - 1$ and $n \geq 1$, $n \geq l$, $l \geq 1$. All that remains to prove is that $(\phi''_{1,n}\phi_{i,l} - 2\phi_{1,n}\phi''_{i,l} + 2\phi'_{1,n}\phi'_{i,l})$, the coefficient of a^{n+2}, is nonnegative. Actually, we only need to consider $(\phi'_{1,n}\phi'_{i,l} - \phi_{1,n}\phi''_{i,l})$:

$$\begin{array}{rcl} \phi'_{1,n}\phi'_{i,l} & = & \sum_{p=1}^{n}\sum_{q=1}^{n} k_{i+p}k_{i+q} \prod_{\substack{m=1 \\ m\neq p}}^{n} (r - k_{i+m}a) \prod_{\substack{m=1 \\ m\neq q}}^{l} (r - k_{i+m}a) \\ \phi_{1,n}\phi''_{i,l} & = & \sum_{p=1}^{l}\sum_{q=1}^{l} k_{i+p}k_{i+q} \prod_{m=1}^{n} (r - k_{i+m}a) \prod_{\substack{m=1 \\ m\neq p,q}}^{l} (r - k_{i+m}a) \end{array}$$

Every term in the lower line is also present in the upper one, but not vice versa ($n \times l$ vs. $l^2 - l$ terms). Thus, since all terms are positive, $\phi'_{1,n}\phi'_{i,l} > \phi_{1,n}\phi''_{i,l}$ and the coefficient of a^{n+1} is positive.

We now have proved that $\mathcal{F}''$ does not change sign on $\mathcal{S}$, and thus there can be at most one extremum and two fixed points on the simplex.

□

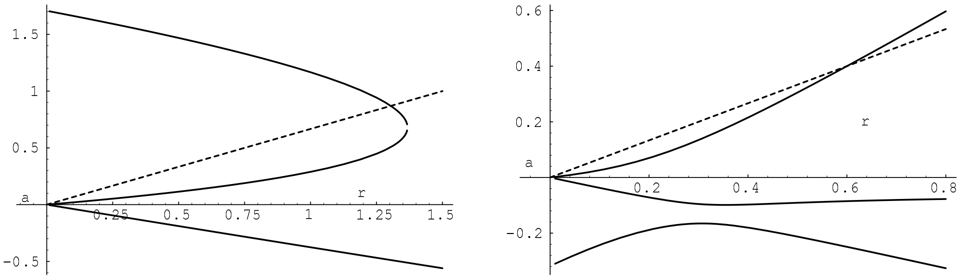
Fig. 5.1 shows the solutions of the equation $\mathcal{F} = 0$ in scenario 1 (a) and scenario 2 (b) in a two species system. The dashed line is the function $\bar{a} = r/k_1$; meaningful solutions must lie below this line. Fig. 5.2 shows how the positions of the fixed points change with the flow rate; the rate constants are the same as in 5.1.

5.1.3 Stability

Transversal eigenvalues

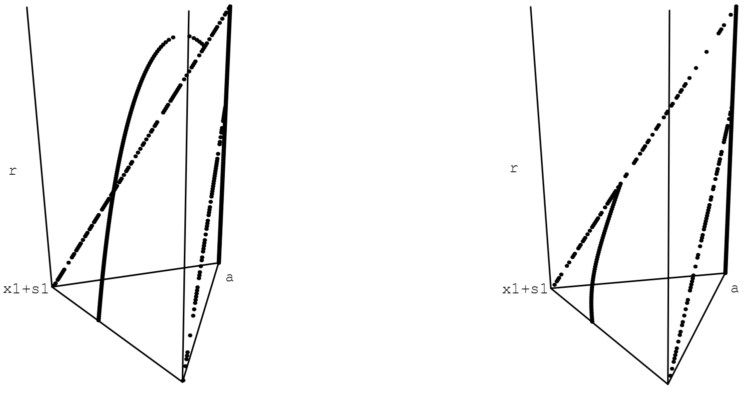
For an n_I dimensional $(n_I < n)$ fixed point there are each $n - n_I - 1$ (transversal) eigenvalues $-r$ and $k_s\bar{a} - r = r(k_s - k_j)/k_j,\ s \notin I,\ s \neq k+1$. The latter are negative if $k_s < k_j$ and positive in the converse case, but their sign does not change with the flow rate. There is one eigenvalue $-f_{k+1}\bar{x}_k - r < 0$. Finally, there is one eigenvalue $k_{k+1}\bar{a} - r + f_k\bar{s}_k$. It is positive if $k_{k+1} > k_j$, but in the converse case it may have either sign, depending on r. If define the set $\hat{I} = I \cup \{k+1\}$, the eigenvalue changes sign at $r = r^{\hat{I}\times I}$, as may be easily proved by inserting (5.9) into the condition $(k_{k+1} - k_j)r/k_j + f_k\bar{s}_k = 0$. Hence, if $\hat{I}$ is an admissible index set, it is clear that P_I is unstable for flow rates below $r^{\hat{I}\times I}$. On the other hand, if $\hat{I} \neq \mathcal{N}$, $P_{\hat{I}}$ has one more negative eigenvalue than P_I at least for r not too much below the critical flow rate. Specifically, if P_I was stable for flow rates a little higher than $r^{\hat{I}\times I}$, $P_{\hat{I}}$ is stable for flow rates a little lower than $r^{\hat{I}\times I}$.

The general phase portrait of the mutualistic system is therefore as follows: For very high flow rates, only the trivial fixed point exist, which is stable. At $r = a_0k_1$, the fixed point $P_{\{1\}}$, which is a sink, enters the simplex, and



(a) (b)

Figure 5.1: Mutualistic model; $n = 2,\ k_1 = 1.5,\ k_2 = 1,\ g_1 = 3,\ g_2 = 5,\ a_0 = 1$ and (a): $f_1 = 5,\ f_2 = 7$; (b) $f_1 = 0.5,\ f_2 = 0.7$



(a) (b)

Figure 5.2: Mutualistic model; $n = 2,\ k_1 = 1.5,\ k_2 = 1,\ g_1 = 3,\ g_2 = 5,\ a_0 = 1$ and (a): $f_1 = 5,\ f_2 = 7$; (b) $f_1 = 0.5,\ f_2 = 0.7$

the trivial fixed point becomes unstable. As r is lowered further, fixed points with $I_2 = \{1, 2\}$, $I_3 = \{1, 2, 3\}$ etc. enter the simplex, each one through the one that came in last. Each of them is stable at least transversally as long as the next one does not exist. Finally, the interior fixed point enters the simplex through $P_{\mathcal{N}'}$ (scenario 1), or two fixed points are born in the simplex in a saddle node bifurcation and one of them leaves the simplex through $P_{\mathcal{N}'}$ (scenario 2). Since Hopf bifurcations are likely to occur, as we shall see in the section on equal reaction constants and there is no general way to determine the internal eigenvalues, we can only determine the stability in transversal directions. The stability of the interior fixed point thus remains in the dark.

5.2 Homogeneous System

In the homogeneous mutualistic system we assume $k_i = 0$, $\forall i \in \mathcal{N}$, i.e. we omit the uncatalyzed formation of the replicating species. In the CSTR this yields the following equations:

$$\begin{aligned} \dot{x}_i &= x_i(f_{i-1}s_{i-1} - r) \\ \dot{s}_i &= g_i x_i a - s_i(f_i x_{i+1} + r) \\ \dot{a} &= a_0 r - a(r + \textstyle\sum_{i=1}^n (k_i + g_i)x_i) \end{aligned} \tag{5.43}$$

In contrast to the general mutualistic system, the homogeneous one has no fixed points on the boundary: if $\bar{x}_m = 0$ for some m, $\bar{s}_m$ is also zero. But then we have $\bar{x}_{m+1}(f_m\bar{s}_m - r) = -\bar{x}_{m+1}r = 0$ and hence $\bar{x}_{m+1} = 0$. Therefore $\bar{x}_i = \bar{s}_i = 0$ for all i, that is, we are at the trivial fixed point. (If we start with $\bar{s}_m = 0$ for some m, we get the same result.) Thus we have only the trivial and the interior fixed point. The former is stable at all flow rates (all eigenvalues of the Jacobian are $-r$).

The equilibrium concentrations at the interior fixed point are:

$$\bar{x}_i = \frac{\sum_{l=1}^n \bar{a}^{n-l} r^{l+1} \gamma_{i,l}}{\bar{a}^n - r^n \Gamma}, \qquad \bar{s}_i = \frac{r}{f_i} \tag{5.44}$$

with

$$\gamma_{i,l} = \frac{1}{f_{i+l-1}} \prod_{m=0}^{l-1} \frac{1}{g_{i+m}}, \qquad \Gamma = \prod_{i=1}^{n} \frac{1}{g_i} \tag{5.45}$$

The equilibrium concentration of the substrate is given implicitly by the function

$$\begin{aligned} \mathcal{F}(a,r) &= a - a_0 + rK + \frac{\sum_{i=1}^{n}\sum_{l=1}^{n} a^{n-l} r^{l+1} \gamma_{i,l}}{a^n - r^n \Gamma} \\ &= v(a,r) + \frac{w(a,r)}{z(a,r)} \end{aligned} \tag{5.46}$$

with

$$K = \sum_{i=1}^{n} \frac{1}{f_i} \tag{5.47}$$

$$v(a,r) = a - a_0 + rK \tag{5.48}$$

$$w(a,r) = \sum_{i=1}^{n}\sum_{l=1}^{n} a^{n-l} r^{l+1} \gamma_{i,l} \tag{5.49}$$

$$z(a,r) = a^n - r^n \Gamma \tag{5.50}$$

At the equilibrium, the function vanishes: $\mathcal{F}(\bar{a}(r), r) = 0$.

The physically reasonable part of the $a, r-$plane (which we call again $\mathcal{S}$) is confined by the lines $r = 0$, $a = a_0$ and $a = r\Gamma^{1/n}$, since the total concentration at the fixed point is a_0 and all $\bar{x}_i$ become negative for $a < r\Gamma^{1/n}$. Hence, there is no solution for $r > a_0\Gamma^{-1/n}$. In all future considerations we shall therefore assume that r is below this value. Obviously, $w, z \geq 0$ everywhere on $\mathcal{S}$. Furthermore, since $w/z = \sum x_i \geq 0$, v must be non positive at the fixed point(s).

Since (5.46) is of order $n + 1$ in a, there may be $n + 1$ solutions. As in the general system, we can show that the actual number never exceeds two. More exactly, it is two or zero, since there are no transcritical bifurcation in the homogeneous system. The proof is very similar to that for the general system, but it must be slightly modified, since that proof depends heavily on the fact that $r < k_1 a$, which we cannot use in the homogeneous case.

We start with observing that $\mathcal{F}(a_0, r) > 0,\ \mathcal{F}(r\Gamma^{1/n} + \epsilon, r) > 0$ for ϵ sufficiently small and all r. Therefore the number of solutions of (5.46) must be even. For very small flow rates and $\bar{a} \approx a_0$ we may approximate (5.46) by

$$\mathcal{F} \approx \bar{a} - a_0 + rK = 0 \tag{5.51}$$

neglecting quadratic and higher order terms in r. (5.51) has one solution on $\mathcal{S}$, namely $\bar{a}^{(1)} = a_0 - rK$ and hence there are at least two solutions on $\mathcal{S}$ for r sufficiently small.

Next, we show that $\mathcal{F}(a, r)$ is monotonous in r on $\mathcal{S}$ and that the function has at most one extremum in a between $r\Gamma^{1/n}$ and a_0 for any fixed value of r. We consider the partial derivatives of $\mathcal{F}$ with respect to r (denoted by subscript r):

$$\mathcal{F}_r = K + \frac{z \sum_{i=1}^{n} \sum_{l=1}^{n} (l+1) a^{n-l} r^l + nwr^{n-1}\Gamma}{z^2} > 0 \tag{5.52}$$

The derivatives with respect to a (denoted by primes) are:

$$\mathcal{F}' = 1 + \frac{w'z - wz'}{z^2} \tag{5.53}$$

$$\mathcal{F}'' = \frac{z(w''z - wz'') - 2z'(w'z - wz')}{z^3} \tag{5.54}$$

since $v' = 1,\ v'' = 0$. With

$$w' = \sum_{i=1}^{n} \sum_{l=1}^{n} (n-l) a^{n-l-1} r^{l+1} \gamma_{i,l} \tag{5.55}$$

$$w'' = \sum_{i=1}^{n} \sum_{l=1}^{n} (n-l)(n-l-1) a^{n-l-2} r^{l+1} \gamma_{i,l} \tag{5.56}$$

$$z' = na^{n-1}, \qquad z'' = n(n-1)a^{n-2} \tag{5.57}$$

we obtain

$$w'z - wz' = -\sum_{i=1}^{n} \sum_{l=1}^{n} a^{n-l-1} f^{l+1} \gamma_{i,l} [la^n + (n-l) r^n \Gamma] < 0 \tag{5.58}$$

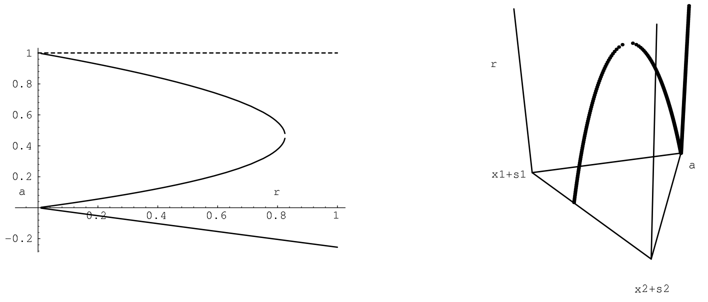
$$w''z-wz''=-\sum_{i=1}^{n}\sum_{l=1}^{n}a^{n-l-2}r^{l+1}\gamma_{i,l}[l(2n-l-1)a^n+(n-l)(n-l-1)r^n\Gamma]<0 \tag{5.59}$$

and therefore

$$\begin{aligned}\mathcal{F}'' &= \frac{1}{z^3}\sum_{i=1}^{n}\sum_{l=1}^{n}a^{n-l-2}r^{l+1}\gamma_{i,l}[l(l+1)a^{2n}+ \\ &+ (n^2-2nl+n-2l-2l^2)a^nr^n\Gamma+(n-l)(n-l-1)r^{2n}\Gamma^2]\end{aligned} \tag{5.60}$$

Since $n^2-2nl+n-2l-2l^2 \geq 0$ (see last chapter) the coefficient of the second and the third term in brackets are nonnegative and thus the whole expression is positive. Therefore $\mathcal{F}'$ can change sign only once on $\mathcal{S}$ for fixed r and (5.46) has at most two solutions on $\mathcal{S}$. We know already that for small flow rates there are at least two solutions on $\mathcal{S}$, so there must be exactly two.

Fig. 5.3 shows the solutions of $\mathcal{F}=0$ and the position of the fixed points for a two species homogeneous mutualistic model. At $r=0$ the unstable interior fixed point coincides with the trivial fixed point.



(a) (b)

Figure 5.3: Homogeneous mutualistic model; $n=2,\ g_1=3,\ g_2=5,\ f_1=5,\ f_2=7,\ a_0=1$. (a) Solutions of $\mathcal{F}=0$ (b) Position of fixed points

5.3 The evolution reactor

We now examine the mutualistic model in the evolution reactor. Using relative concentrations $x_i = [X_i]/c_0,\ s_i = [S_i]/c_0$, we obtain the following differential equations

$$\begin{aligned} \dot{x}_i &= x_i(k_i + f_{i-1}c_0 s_{i-1} - \Phi) \\ \dot{s}_i &= g_i x_i - s_i(f_i c_0 x_{i+1} + \Phi) \end{aligned} \tag{5.61}$$

Φ is the already familiar dilution flux:

$$\Phi = \sum_{j=1}^{n} \kappa_i x_i \tag{5.62}$$

with $\kappa_i = k_i + g_i$.

As in the CSTR setting, we assume that all k_i are different and that k_1 is the greatest of the rate constants k_i.

We now turn to the description of fixed points on the boundary of the simplex and then to the interior fixed point(s).

5.3.1 Fixed points on the boundary of the simplex

Some of the basic considerations on fixed points on the boundary of the simplex obtained for the CSTR apply also under constant organization and the arguments are so similar that we don't want to repeat them here, namely

1. An index set I is *admissible* if it is of the form $I = \{j, j+1, \ldots, k\},\ 1 \leq j \leq k \leq n$ and if $k_j = \max_{i \in I} k_i$. For every admissible index set I we define the set $I' = I \setminus \{k\}$. For the interior fixed point we define the set $\mathcal{N} = \{1, 2, \ldots, n\}$ and the set $\mathcal{N}' = \mathcal{N} \setminus \{n\}$ (which are also admissible). For all admissible index sets with more than one element, the set I' is also admissible.

2. The maximal possible number of fixed points (including the interior one) is $n(n+1)/2$. It is obtained if $k_2,\ k_3, \dots,\ k_n$ form a decreasing sequence. The minimal number is $2n-1$; it is obtained if they form an increasing sequence. In the general case, the number of possible fixed points will lie between these two numbers. We must stress the word *possible*, since these fixed points will generally not exist for all values of c_0.

In analogy with the results on the mutualistic model in the CSTR, we now shall prove the following

Theorem 5.3 *For every admissible index set with $n_I > 1$, there is exactly one fixed point on the boundary of the simplex if $c_0 > c_0^{I\times I'}$ and none for total concentrations below that value. At $c^{I\times I'}$, P_I and $P_{I'}$ undergo an transcritical bifurcation. For index sets with $n_I = 1$, there is exactly one fixed point which exists for all values of c_0.*

Proof: From $\dot{x}_j = \bar{x}_j(k_j - \bar{\Phi}) = 0$ we get $\bar{\Phi} = k_j$ and hence the equilibrium concentration of the intermediates is

$$\bar{s}_i = \frac{k_i - k_j}{f_i c_0} \tag{5.63}$$

for all $i \in I'$. The corresponding equilibrium concentrations for the replicators are

$$\bar{x}_i = k_j \left(\sum_{l=i}^{k} \frac{\bar{s}_l}{g_l} \prod_{m=i}^{l-1} \frac{\bar{s}_m f_m c_0}{g_m} \right) \tag{5.64}$$

This formula is valid also for $i = k$. Inserting the values $\bar{s}_i$ and defining

$$\mu_m^{(i,j)} = \frac{1}{f_m} \prod_{l=i}^{j} \frac{k_j - k_{l+1}}{g_l} \tag{5.65}$$

this becomes

$$\bar{x}_i = k_i \left(\frac{\bar{s}_k f_{k-1}}{g_k} \mu_{k-1}^{(i,j)} + \frac{1}{c_0} \sum_{m=i}^{k-1} \mu_m^{(i,j)} \right) \tag{5.66}$$

Now we can calculate $\bar{s}_k$ using the condition $\bar{\Phi} = k_j = \sum_{i\in I} \kappa_i \bar{x}_i$:

$$k_i = k_i \sum_{i\in I} \kappa_i \left(\frac{\bar{s}_k f_{k-1}}{g_k} \mu_{k-1}^{(i,j)} + \frac{1}{c_0} \sum_{m=i}^{k-1} \mu_m^{(i,j)} \right) \tag{5.67}$$

$$\bar{s}_k = \frac{g_k}{f_{k-1} \sum\limits_{i\in I} \kappa_i \mu_{k-1}^{(i,j)}} \left(1 - \frac{1}{c_0} \sum_{i\in I} \kappa_i \sum_{l=i}^{k-1} \mu_l^{(i,j)} \right) \tag{5.68}$$

Since the equilibrium concentrations are uniquely determined by the reaction constants and the total concentration, there is only on fixed point for every admissible index set.

From (5.68) we see that the fixed points do not exist for all values of c_0: if c_0 is lowered below the critical value $c_0^{I\times I'}$,

$$c_0^{I\times I'} = \sum_{i=j}^{k} \kappa_i \sum_{l=i}^{k-1} \mu_l^{(i,j)} \tag{5.69}$$

$\bar{s}_k^I$ becomes negative and hence P^I leaves the simplex, passing through $P^{I'}$. However, this is valid only if I has at least two elements, since otherwise we have $I' = \emptyset$. The fixed points at which only one species is present with $I = \{i\}$ and

$$\bar{x}_i = k_i/\kappa_i, \qquad \bar{s}_i = g_i/\kappa_i \tag{5.70}$$

do not depend on the total concentration and are therefore present at all values of c_0.

□

Comparing these formulae with the corresponding ones in the CSTR system, we see that they are quite similar (except for (5.68)). The role of the control parameter played by the flow rate r in the previous chapter is here taken by $1/c_0$.

5.3.2 Interior fixed point

If the system has an interior fixed point, the equilibrium values of s_i are determined by

$$\bar{s}_i = \frac{\bar{\Phi} - k_{i+1}}{f_i c_0} \tag{5.71}$$

The equilibrium values of x_i are obtained by solving the equations $\dot{s}_i = 0$ for x_i:

$$\begin{aligned}
\bar{x}_i &= \frac{\bar{\Phi} \sum\limits_{l=0}^{n-1} \frac{1}{f_{i+l} c_0} \prod\limits_{m=0}^{l} \frac{\bar{s}_{i+l} f_{i+l} c_0}{g_{i+l}}}{1 - \prod\limits_{l=1}^{n} \frac{\bar{s}_l f_l c_0}{g_l}} \\
&= \frac{\sum\limits_{l=0}^{n-1} \Phi \frac{1}{g_{i+l} f_{i+l} c_0} \prod\limits_{m=0}^{l} \frac{\bar{\Phi} - k_{i+m+1}}{g_{i+m}}}{1 - \prod\limits_{l=1}^{n} \frac{\bar{\Phi} - k_{l+1}}{g_l}}
\end{aligned}$$

With the abbreviations

$$\gamma_{i,l} = \frac{1}{f_{i+l-1}} \prod_{m=0}^{l-1} \frac{1}{g_{i+m}}, \qquad \Gamma = \prod_{l=1}^{n} \frac{1}{g_l}, \qquad \phi_{i,l} = \prod_{m=1}^{l} \bar{\Phi} - k_{i+m} \tag{5.72}$$

we obtain

$$\bar{x}_j = \frac{\bar{\Phi} \sum_{l=1}^{n} \gamma_{i,l} \phi_{i,l}}{c_0 \left(1 - \Gamma \phi_{1,n}\right)} \tag{5.73}$$

From (5.73) and (5.71) we conclude that an interior fixed point can only exist for $\bar{\Phi} \geq k_1$, otherwise $\bar{s}_1$ would be negative.

Inserting (5.73) and (5.71) into the normalization condition $\sum(x_j + s_j) - 1 = 0$ yields

$$\bar{\Phi} \left(\psi^{(1,n)} + \frac{\sum\limits_{i=1}^{n} \sum\limits_{l=1}^{n} \gamma_{i,l} \phi_{i,l}}{1 - \Gamma \phi_{1,n}} \right) + K^{(1,n)} - c_0 = 0 \tag{5.74}$$

where

$$K^{(1,n)} = \sum_{l=1}^{n} \frac{k_{l+1}}{f_l}, \qquad \psi^{(1,n)} = \sum_{l=1}^{n} \frac{1}{f_l} \tag{5.75}$$

as determining equation for $\bar{\Phi}$. This equation is only n–th order in $\bar{\Phi}$, since the term in $\bar{\Phi}^{n+1}$ cancel, and hence there can be at most n interior fixed points.

The next two theorems shed light on the behaviour of fixed points in the interior of the simplex:

Theorem 5.4 *There are no saddle node or transcritical bifurcations in the interior of the simplex*

Proof: Consider the entries of the Jacobian for a fixed point in the interior of the simplex:

$$\begin{array}{lll} \frac{\partial \dot{x}_i}{\partial x_l} & = -\kappa_l \bar{x}_i & \forall l \\ \frac{\partial \dot{x}_i}{\partial s_l} & = f_{i-1} c_0 \bar{x}_i \delta_{i,l+1} & \\ \frac{\partial \dot{s}_i}{\partial x_l} & = \begin{cases} g_i - \bar{s}_i \kappa_i & l = i \\ -\bar{s}_i (f_i c_0 + \kappa_{i+1}) & l = i+1 \\ -\kappa_l \bar{s}_i & \text{otherwise} \end{cases} & \\ \frac{\partial \dot{s}_i}{\partial s_l} & = -(f_i c_0 \bar{x}_{i+1} + \bar{\Phi}) \delta_{i,l} & \end{array}$$

If there were saddle node or transcritical bifurcations, this would mean that the determinant of the Jacobian would become zero. In this case the Jacobian must be linearly dependent, so that there must be a set of numbers α_i and β_i so that

$$\begin{array}{ll} \sum_{i=1}^{n} \alpha_i \frac{\partial \dot{x}_l}{\partial x_i} + \beta_i \frac{\partial \dot{x}_l}{\partial s_i} & = 0 \\ \sum_{i=1}^{n} \alpha_i \frac{\partial \dot{s}_l}{\partial x_i} + \beta_i \frac{\partial \dot{s}_l}{\partial s_i} & = 0 \end{array}$$

for all l. Inserting the elements of the Jacobian yields:

$$\sum_{i=1}^{n} \alpha_i \kappa_i \bar{x}_l = \beta_i \bar{x}_l f_{l-1} c_0$$

$$-\left(\sum_{i=1}^{n}\alpha_i\kappa_i\bar{s}_l\right)+\alpha_l g_l-\alpha_{l+1}\bar{s}_l f_l c_0-\beta_l(f_l c_0\bar{x}_{l+1}+\bar{\Phi})=0$$

The first of these equations can be used to obtain β_l:

$$\beta_l=\frac{1}{f_l c_0}\sum_{i=1}^{n}\alpha_i\kappa_i$$

Inserting this into the second equation, we have

$$-\left(\sum_{i=1}^{n}\alpha_i\kappa_i\right)\left(\bar{s}_l+\bar{x}_{l+1}+\frac{\bar{\Phi}}{f_l c_0}\right)+\alpha_l g_l-\alpha_{l+1}\bar{s}_l f_l c_0=0$$

Now we sum the last equation over all l

$$-\left(\sum_{i=1}^{n}\alpha_i\kappa_i\right)\left(\sum_{l=1}^{n}\bar{s}_l+\bar{x}_{l+1}+\frac{\bar{\Phi}}{f_l c_0}\right)+\sum_{l=1}^{n}\alpha_l g_l-\sum_{l=1}^{n}\alpha_{l+1}\bar{s}_l f_l c_0=0$$

Since $\sum_{l=1}^{n}\bar{s}_l+\bar{x}_l=1$ and $\bar{s}_l f_l c_0=\bar{\Phi}-k_{l+1}$ we may rewrite this as

$$-\left(\sum_{i=1}^{n}\alpha_i\kappa_i\right)\left(1+\bar{\Phi}\sum_{l=1}^{n}\frac{1}{f_l c_0}\right)+\sum_{l=1}^{n}\alpha_l\kappa_l-\bar{\Phi}\sum_{l=1}^{n}\alpha_l=0$$

$$-\bar{\Phi}\left(\sum_{i=1}^{n}\alpha_i\kappa_i\right)\sum_{l=1}^{n}\frac{1}{f_l c_0}-\Phi\sum_{l=1}^{n}\alpha_l=0$$

$$\sum_{l=1}^{n}\frac{1}{f_l c_0}\sum_{i=1}^{n}\alpha_i\kappa_i=-\sum_{l=1}^{n}\alpha_i$$

Since $\sum_{l=1}^{n}\frac{1}{f_l c_0}>0$, it follows that $\sum_{i=1}^{n}\alpha_i\kappa_i$ and $\sum_{l=1}^{n}\alpha_i$ must have opposite sign. Therefore at least one of the α_i's must be positive and at least one negative.

Now assume $\sum_{i+1}^{n}\alpha_i(k_i+g_i)>0$. Then $\sum_{i+1}^{n}\alpha_i<0$. Then at least one α_i must be positive, which we call α_{l+1}. Then we have

$$\left(\sum_{i+1}^{n}\alpha_i\kappa_i\right)\left(s_l+x_{l+1}+\frac{\Phi}{f_l c_0}\right)+\alpha_{l+1}s_l f_l c_0=\alpha_l g_l$$

Since all terms on the left hand side are positive, α_l must be positive too. Applying this argument recursively, we see that all α_i must be positive, which is a contradiction to what we have stated before. The same argument holds if $\sum_{i+1}^{n} \alpha_i \kappa_i < 0$.

$\square$

Theorem 5.5 *At low total concentrations, system (5.61) has no interior fixed point. At* $c_0 = c_0^{\mathcal{N}\times\mathcal{N}'}$ *a fixed point enters the simplex, passing through* $P_{\mathcal{N}'}$*. It lies in the interior of the simplex for all* $c_0 > c_0^{\mathcal{N}\times\mathcal{N}'}$*.*

Proof: For c_0 small enough there are no interior fixed points, since the kinetic equations for x_i may then be written (neglecting the term $f_{i-1}s_{i-1}c_0$) as

$$\dot{x}_i = x_i(k_i - \Phi)$$

and therefore $\Phi = k_i$ at the fixed point, which cannot be fulfilled for all i simultaneously, as we assumed the k_i to be different.

Since there are no saddle node bifurcations, fixed points can come into the interior of the simplex only through the lower dimensional simplices that form the boundary of $\mathbf{S_{2n}}$, passing through a fixed point on this boundary in a transcritical bifurcation. It is clear from (5.71) that $P_{\mathcal{N}}$ can only pass through $P_{\mathcal{N}'}$ and that it does so if $\bar{\Phi} = k_1$. Inserting this condition into (5.74), we find the corresponding value of the total concentration at which the bifurcation takes place (we call it $c_0^{\mathcal{N}\times\mathcal{N}'}$):

$$k_1 \left(\psi^{(1,n)} + \sum_{i=1}^{n-1} \sum_{l=1}^{n-i-1} \gamma_{i,l} \prod_{m=1}^{l} (k_1 - k_{i+l}) \right) + K^{(1,n)} - c_0^{\mathcal{N}\times\mathcal{N}'} = 0 \qquad (5.76)$$

where we have changed the summation indices so that summands that are zero do not appear. Taking into account that

$$\gamma_{i,l} \prod_{m=1}^{l} (k_1 - k_{i+l}) = \mu_{i+l-1}^{i,1} \qquad (5.77)$$

we have

$$c_0^{\mathcal{N}\times\mathcal{N}'} = k_1\left(\psi^{(1,n)} + \sum_{i=1}^{n-1}\sum_{l=i}^{n-1}\mu_l^{i,1}\right) + K^{(1,n)} \tag{5.78}$$

Inserting this and the condition $\bar{\Phi} = k_1$ into (5.71) and (5.73) and comparing with (5.66), (5.63), and (5.68) we see that $P_{\mathcal{N}}$ and $P_{\mathcal{N}'}$ coincide indeed at $c_0^{\mathcal{N}\times\mathcal{N}'}$. Since there is only solution of (5.78), there can be no other transcritical bifurcations at the interior fixed point. Moreover, we can verify by implicit differentiation of (5.74) that $\partial\bar{\Phi}/\partial c_0$ is positive at $c_0 = c_0^{\mathcal{N}\times\mathcal{N}'}$ and hence $\bar{\Phi} > k_1$ if the total concentration is raised above the critical value. Thus there is no interior fixed point for $c_0 < c_0^{\mathcal{N}\times\mathcal{N}'}$ and exactly one for $c_0 > c_0^{\mathcal{N}\times\mathcal{N}'}$.

5.3.3 Stability of the fixed points

As in the CSTR setting, we can give no general analytical formulae for the internal eigenvalues. We therefore focus on the transversal eigenvalues.

Transversal eigenvalues

If I has n_I elements, there are $n_I - 1$ transversal eigenvalues $-k_j$, one eigenvalue $-(k_j + f_{k-1}c_0\bar{x}_k)$ (these are always negative), $n_I - 1$ eigenvalues $k_s - k_j$ $s \notin I,\ s \neq k+1$, (these are negative if $k_j > k_s$ and positive in the converse case), and one eigenvalue $k_{k+1} - k_i + f_k c_0 \bar{s}_k$. If $k_i > k_{k+1}$, the last eigenvalue is negative for small c_0 and becomes positive at $c_0^{\hat{I}\times I}$, (where $\hat{I} = I \cup \{k+1\}$), that is, at the concentration at which $P_{\hat{I}}$ enters the simplex in a transcritical bifurcation. Thus for the fixed point P_I to be stable in all transversal directions, k_j must be greater than any other k_s (which means $i = 1$) and the fixed point $P_{\hat{I}}$ must not exist.

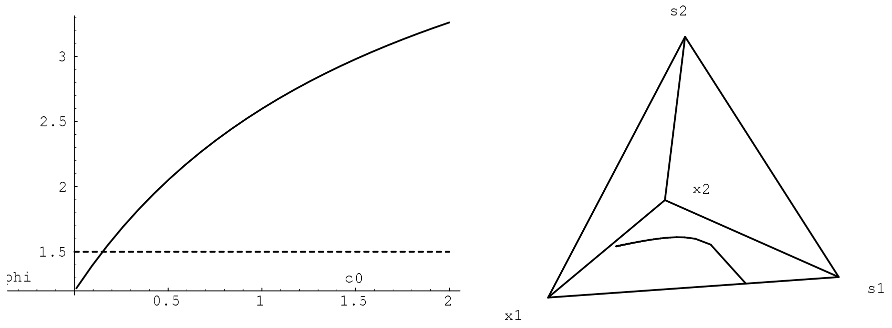
For low overall concentrations we have therefore the following picture: there are n fixed points, at each of which only one species is present. The fixed point P_{I_1} with $I_1 = \{1\}$ is stable, and since all other fixed points have at least one positive transversal eigenvalue, it is globally stable. As c_0 is raised, the fixed point P_{I_2}, $I_2 = \{1, 2\}$ passes through P_{I_1}. P_{I_2} must be globally stable at least for overall concentrations not too much above $c_0^{I_1 \times I_2}$. If c_0 is raised further, however, a Hopf bifurcation might occur and make P^{I_2} unstable in the non traversal directions. The transversal eigenvalues stay negative, so that any trajectory starting in the interior of the simplex must end up eventually in the boundary subsimplex that contains P_{I_3}. As c_0 is raised further, a series of transcritical bifurcations leads to the state where $P_{\mathcal{N}}$ lies in the interior of the simplex and all fixed points on the boundary of the simplex are transversally unstable. There may be also transcritical bifurcations on the other faces of the simplex, but the fixed points that enter the boundary in these bifurcations do not greatly affect the dynamics in the interior of the simplex, since they have at least one positive transversal eigenvalue (they are unstable against introduction of X_1 and S_1).

□

Fig. 5.4 is likely to produce the so called "déjà vu" effect. It shows the solutions of $\mathcal{F} = 0$ (a) and the position of the interior fixed point at various total concentrations for a two species mutualistic model in the evolution reactor. The dashed line in (a) is $\bar{a} = k_1$, which confines the region where meaningful solutions can lie.

5.4 Equal reaction constants

If we assume the rate constants to be the same for all species, i.e. $k_i = k,\ g_i = g,\ f_i = f,\ \forall i$, we get again symmetry in equilibrium concentrations. In fact, the equilibrium concentrations are identical to those observed in the competitive model for equal reaction constants; so we need not discuss them



(a) (b)

Figure 5.4: Homogeneous mutualistic model; $n = 2,\ k_1 = 1.5,\ k_2 = 1,\ g_1 = 3,\ g_2 = 5,\ f_1 = 5,\ f_2 = 7,\ a_0 = 1$. (a) Solutions of $\mathcal{F} = 0$ (b) Position of fixed points

again. The Jacobian at the interior fixed point consists again of four circulant blocks (plus one row and one column for the substrate in the CSTR setting), but most eigenvalues are complex and thus there can be Hopf bifurcations. We can even derive analytical formulae for the flow rates at which these bifurcations take place. This is an important difference to the hypercycle with equal reaction constants, for which there are no Hopf bifurcations.

5.4.1 Continuously stirred tank reactor

The kinetic differential equations for the mutualistic model with equal reaction constants in the CSTR setting are:

$$\begin{aligned}\dot{x}_i &= x_i(ka + fs_{i-1} - r)\\ \dot{s}_i &= gx_ia - s_i(fx + r)\\ \dot{a} &= a_0r - a(r + \kappa \textstyle\sum x_i)\end{aligned} \tag{5.79}$$

with $\kappa = k + g$.

Fixed points on the boundary of the simplex

There are some fixed points on the boundary of the simplex. The admissible index sets are, however, quite different from those of the general model, where we assumed all k_i to be different.

Lemma 5.4 *An index set is admissible for the mutualistic model with equal reaction constants if* $I = \mathcal{N}$ *or for all* $i \in I$ $i-1,\ i+1 \notin I$*. If* $I \neq \mathcal{N}$*, there is exactly one fixed point* P_I *if and only if the* I *is admissible. It exists for* $r < a_0 k$*. This fixed point is unstable.*

Proof: Assume $I \neq \mathcal{N}$ and the fixed point exists. Then there is at least one index j such that $j \in I$, $j-1 \notin I$. Therefore $\bar{a} = r/k$. If $j+1 \in I$, this would imply $k\bar{a} + f\bar{s}_j - r = 0$. But since $\bar{s}_j \neq 0$, we must conclude $j+1 \notin I$. Using the same argument, we can show that for all $i \in I$, $i+1 \notin I$ and reverting it we see that for $i \in I$, $i-1 \notin I$.

If I is admissible, the equilibrium concentrations are

$$\bar{x} = \frac{a_0 k - r}{nk\kappa}, \qquad \bar{s} = \frac{g(a_0 k - r)}{n\kappa}, \qquad \bar{a} = \frac{r}{k} \qquad \forall i \in I \tag{5.80}$$

It is clear that these fixed points can exist only if $r < a_0 k$.

For all $i \in I$, one (transversal) eigenvalue of the Jacobian at P_I is $k\bar{a} + f\bar{s}_i - r = f\bar{s} > 0$ and hence the fixed point is unstable.

□

Interior fixed point

We repeat briefly the results on equilibrium concentrations and existence of fixed points.

The equilibrium concentrations of replicating species and intermediates are:

$$\bar{x}_i = \frac{r(r-k\bar{a})}{f(\bar{a}\kappa - r)} \qquad \bar{s}_i = \frac{r-k\bar{a}}{f} \tag{5.81}$$

where $\bar{a}$ is a solution of the equation

$$\bar{a}^2\kappa(nk-f) + \bar{a}[\kappa(fa_0 - nr) + fr] - fa_0 r = 0 \tag{5.82}$$

For a solution of (5.82) to lie inside the simplex, it must fulfill the following inequalities:

$$\bar{a} < a_0 \tag{5.83}$$

$$\frac{r}{\kappa} < \bar{a} < \frac{r}{k} \tag{5.84}$$

At $r = a_0 k$ there is a transcritical bifurcation with the trivial fixed point; for higher flow rates there are two fixed points if

$$f > f^c = \frac{nk\kappa}{g} \tag{5.85}$$

(scenario 2) and none in the converse case (scenario 1). In scenario 2 there is a saddle node bifurcation at

$$r^* = \frac{a_0\kappa f}{(\sqrt{\Delta} + \sqrt{ng})^2}, \qquad \bar{a}^* = \frac{a_0 f}{\Delta + \sqrt{\Delta n g}} \tag{5.86}$$

If there are two interior fixed point, the one with the higher concentration of A is called $P_{\mathcal{N}}^{(2)}$ and the other one $P_{\mathcal{N}}^{(1)}$.

Stability properties

The Jacobian $\mathbf{J}$ of (5.79) at the interior fixed point is of the form

$$\left(\begin{array}{ccccc|cccc|c}
0 & 0 & 0 & \cdots & 0 & 0 & 0 & \cdots\ 0 & f\bar{x} & k\bar{x} \\
0 & 0 & 0 & \cdots & 0 & f\bar{x} & 0 & \cdots\ 0 & 0 & k\bar{x} \\
\vdots & \vdots & \vdots & \cdots & \vdots & \vdots & \vdots & \cdots & \vdots & \vdots \\
0 & 0 & 0 & \cdots & 0 & 0 & 0 & \cdots\ f\bar{x} & 0 & k\bar{x} \\
\hline
g\bar{a} & k\bar{a}-r & 0 & \cdots & 0 & -f\bar{x}-r & 0 & \cdots\ 0 & 0 & g\bar{x} \\
0 & g\bar{a} & k\bar{a}-r & \cdots & 0 & 0 & -f\bar{x}-r & \cdots\ 0 & 0 & g\bar{x} \\
\vdots & \vdots & \vdots & \cdots & \vdots & \vdots & \vdots & \cdots & \vdots & \vdots \\
k\bar{a}-r & 0 & 0 & \cdots & g\bar{a} & 0 & 0 & \cdots\ 0 & -f\bar{x}-r & g\bar{x} \\
\hline
-\kappa\bar{a} & -\kappa\bar{a} & -\kappa\bar{a} & \cdots & -\kappa\bar{a} & 0 & 0 & \cdots\ 0 & 0 & -r-n\kappa\bar{x}
\end{array}\right)$$

The lines have been introduced to make the block structure visible. Again, we have 4 $n \times n$ circulant sub-matrices (plus one extra line and column), so we try an approach similar to the one we used for the competitive model to find the eigenvalues λ_j and the eigenvectors ξ_j:

$$\xi_j = (z^0, z^j, \ldots, z^{(n-1)j}, \beta_j z^0, \beta_j z^j, \ldots, \beta_j z^{(n-1)j}, \omega_j) \tag{5.87}$$

where $z = e^{\frac{2\pi i}{n}}$ and i is the imaginary unit.

For $j = 0$ we get the same results an in the competitive model: the external eigenvalue $-r$, two negative real internal eigenvalues for $P_{\mathcal{N}}^{(1)}$ and one positive and one negative real internal eigenvalue for $P_{\mathcal{N}}^{(2)}$ (if the latter exists).

For $j \neq 0$, we can assume $\omega_j = 0$. Evaluating the equation

$$\mathbf{J}\xi_j = \lambda_j \xi_j \tag{5.88}$$

we obtain the following equation for β_j:

$$\beta_j^2 f\bar{x}z^{-j} = g\bar{a} + (\bar{a}k - r)z^j - \beta_j(f\bar{x} + r) \tag{5.89}$$

with the solutions

$$\beta_j^{+/-} = \frac{-(f\bar{x} + r) \pm \sqrt{(f\bar{x} + r)^2 + 4f\bar{x}(\bar{a}k - r + g\bar{a}z^{-j})}}{2f\bar{x}z^{-j}} \tag{5.90}$$

Since the first component of ξ_j is unity, the eigenvalues are

$$\lambda_j = \beta_j f\bar{x}z^{-j} \tag{5.91}$$

and hence

$$\lambda_j^{+/-} = \frac{1}{2}\left(-(f\bar{x}+r) \pm \sqrt{(f\bar{x}+r)^2 + 4f\bar{x}(\bar{a}k - r + g\bar{a}z^{-j})}\right) \tag{5.92}$$

For $j = n/2$ (5.92) becomes

$$\lambda_{n/2} = \frac{1}{2}\left(-(f\bar{x}+r) \pm \sqrt{(f\bar{x}+r)^2 + 4f\bar{x}(ak - r - ag)}\right) \tag{5.93}$$

Since the second term under the root is always negative because of (5.84), both eigenvalues are negative or have negative real parts. Thus there can be no Hopf bifurcation for $j = n/2$ (if n is even). Hence for $n = 2$ the fixed point $P_{\mathcal{N}}^{(1)}$ is always stable.

For $j \neq 0,\ j \neq n/2$, we rewrite equation (5.92) as

$$\lambda_j^{+/-} = \frac{1}{2}\left(-u \pm \sqrt{u^2 - 4v + w(\cos\phi + iy\phi)}\right) \tag{5.94}$$

with

$$\begin{aligned} u &= f\bar{x} + r \\ v &= f\bar{x}(r - k\bar{a}) \\ w &= fg\bar{x}\bar{a} \\ \phi &= \tfrac{-2\pi j}{n} \end{aligned} \tag{5.95}$$

A Hopf bifurcation occurs if the real part of the square root becomes equal to u. It is clear, however, that Hopf bifurcations are possible only for λ_j^+, since the real part of the root is always positive.

Since the real parts of the eigenvalues are the same for j and $n-j$ and we are interested only in the real parts, we can restrict attention to $1 \leq j \leq n/2$. Thus all statements that are made e.g. for $j = n/4$ are valid also for $j = 3n/4$ etc.

From the relation

$$\Re\left(\sqrt{a+ib}\right)=\sqrt{\frac{1}{2}\left(a+\sqrt{a^2+b^2}\right)} \qquad a,b,\in\mathbf{R} \tag{5.96}$$

we obtain the following condition for the real part of λ_j^+ to become zero:

$$u=\Re\left(\sqrt{u^2-4v+4w(\cos\phi+iy\phi)}\right) \tag{5.97}$$

$$u=\sqrt{\frac{1}{2}\left(u^2-4v+4w\cos\phi+\sqrt{(u^2-4v)^2+2(u^2-4v)w\cos\phi+w^2}\right)} \tag{5.98}$$

$$u^2+4v-4w\cos\phi=\sqrt{(u^2-4v)^2+2(u^2-4c)w\cos\phi+w^2} \tag{5.99}$$

$$u^2(v-w\cos\phi)-w^2y^2\phi=0 \tag{5.100}$$

For $1\le j\le n/2$, the real part λ_j^+ is decreasing in j. Since we are only interested in Hopf bifurcations that lead from sinks to saddles, we need consider (5.100) only for $j=1$; if (5.100) is fulfilled for $j>1$, λ_1^+ is already positive and the Hopf bifurcation leads only from one saddle to another, which is not very exciting.

Inserting (5.95) into (5.100) and dividing by $f\bar{x}$, we obtain

$$(f\bar{x}+r)^2(r-k\bar{a}-g\bar{a}\cos\phi)-(r-\bar{a}k)(\bar{a}k+\bar{a}g-r)y^2\phi=0 \tag{5.101}$$

Inserting (5.81) and dividing by $\frac{\bar{a}^2g^2r}{(\kappa\bar{a}-r)^2}$ yields

$$r(r-\bar{a}k-\bar{a}g\cos\phi)-(r-\bar{a}k)(\kappa\bar{a}-r)y^2\phi=0 \tag{5.102}$$

Finally, inserting the solutions of (5.82) we obtain, after squaring to get rid of the roots and division by r^2, a very clumsy equation of second order in r, which is not shown here. However, the fact that the equation is quadratic means that there are at most two Hopf bifurcation for any $j\neq 0$. For $n=3$ and $n=4$ however, the formulae are quite simple. For $n=3$ we have

$$r_H=\frac{a_0f}{14}\frac{2fg+20fk+33gk-48k^2\pm(2f-9k)\sqrt{g^2-64gk+k^2}}{2f^2+fg-8fk+6gk+6k^2} \tag{5.103}$$

For $n = 4$ we have

$$r_H^{(1)} = \frac{a_0 f(g+k)}{2(f+4(g-k)} \qquad r_H^{(2)} = a_0 k \tag{5.104}$$

Solving (5.82) for r instead of $\bar{a}$ and inserting the solution into (5.102), we can calculate the values of $\bar{a}$ at which the Hopf bifurcation takes place (which we shall call $\bar{a}_H$):

$$\bar{a}^2[f(f-nk)(1-\cos\phi)+n\cos\phi(fg-nk\kappa)+nf(gy^2\phi+k\cos\phi)]+$$
$$+\bar{a}a_0 f[\cos\phi(2(f-nk)-ng)-(2f-n(k-g))+ng\cos^2\phi]+a_0^2f^2(1-\cos\phi)=0 \tag{5.105}$$

Substituting $\alpha = \bar{a} - a_0$ gives

$$\alpha^2[f(f-nk)(1-\cos\phi)+n\cos\phi(fg-nk\kappa)+nf(g(1-\cos^2\phi)+k\cos\phi)]+$$
$$\alpha a_0 n[fg(1+\cos\phi-\cos^2\phi)-fk(1-2\cos\phi)-2nk\kappa\cos\phi]-a_0^2n^2k\kappa\cos\phi=0 \tag{5.106}$$

Inserting $n = 3$ into the first equation and solving for $\bar{a}$ yields

$$\bar{a}_H = \frac{a_0 f(4f + \left(g - 8k \pm \sqrt{g^2 - 64gk + 16k^2}\right)}{2(2f^2 + f(g-8k) + 6k\kappa)}$$

Thus, for $\bar{a}_H$ to be real and between zero and a_0 we must choose g greater than roughly $64k$.

For $j = n/4$ the solution of (5.105) reads

$$\bar{a}_H = \frac{a_0 f}{f + n(g-k)}$$

which lies on the simplex if and only if $g > k$.

In scenario 2 there is still another problem to be solved: we do not know *which one* of the two fixed points is undergoing the Hopf bifurcation. Obviously, if $\bar{a}_H < \bar{a}^*$ it is $P_{\mathcal{N}}^{(1)}$, in the converse case it is $P_{\mathcal{N}}^{(2)}$. The limiting case is $\bar{a}_H = \bar{a}^*$, that is the saddle node bifurcation and the Hopf bifurcation coincide. Thus we may calculate a critical value of f, using (5.105) and (5.86) and substituting $\hat{f} = f - nk\kappa/g = f - f^c$:

$$\begin{aligned} &\widehat{f}^2 g(\cos\phi - 1)^2 + \\ &+\widehat{f} ng[k^2(1 - 4\cos\phi + 2\cos^2\phi) - 2gk\cos\phi(1 + y^2\phi) - g^2(\cos\phi + y^2\phi)] - \\ &-\cos\phi k^2\kappa n^2[k(2 - \cos\phi) + g(\cos\phi + 2y^2\phi)] = 0 \end{aligned} \tag{5.107}$$

At the solutions of this equation, which we call f_{cr}, the saddle node bifurcation and the Hopf bifurcation coincide. Since the quadratic coefficient is positive and the absolute coefficient negative for $n > 4,\ j = 1$, there is exactly one positive $\widehat{f}_{cr}$. The other solution is irrelevant, because $\widehat{f} < 0$ means that we are in scenario 1. Besides, since at $\widehat{f} = 0$ we have $\bar{a}^* = a_0 > \bar{a}_H$, it is clear that the Hopf bifurcation occurs for $P_{\mathcal{N}}^{(1)}$ if $\widehat{f} < \widehat{f}_{cr}$ and for $P_{\mathcal{N}}^{(2)}$ otherwise. In the latter case the fixed point $P_{\mathcal{N}}^{(1)}$ is stable for all flow rates $r < r^*$.

For $n = 4,\ j = 1$ the equation (5.107) reduces to $\widehat{f}_{cr} = 4(g^2 - k^2)$, since the absolute coefficient then vanishes. Since Hopf bifurcations for $n = 4$ require $g > k$, $\widehat{f}_{cr}$ is positive. Thus if $g > k$, we obtain the same picture as for $n > 4$.

For $n = 3,\ j = 1$ both the quadratic and the absolute coefficient are positive, while the linear coefficient is negative, as can be easily verified by inserting $\phi = \pi/3$ into (5.107) and taking into account that g must be greater than $64k$. Therefore there are two positive solutions of (5.107), one of which is close to zero. Thus for very small positive values of $\widehat{f}$ both Hopf bifurcations occur at $P_{\mathcal{N}}^{(1)}$, for values between the two solutions of (5.107),there is one Hopf bifurcation at each fixed point, while for large $\widehat{f}$ there are two Hopf bifurcations at $P_{\mathcal{N}}^{(2)}$.

At $r = 0,\ \bar{a} = 0$ and at $r = a_0 k, \bar{a} = a_0$, all $\lambda_j^+,\ j \neq 0$ are zero. The sign of the eigenvalue near these flow rates is therefore determined by the sign of the derivative with respect to r:

$$\frac{d\lambda_j^+}{dr} = \frac{\partial\lambda_j^+}{\partial r} + \frac{\partial\lambda_j^+}{\partial\bar{a}}\frac{d\bar{a}}{dr} + \frac{\partial\lambda_j^+}{\partial\bar{x}}\left(\frac{\partial\bar{x}}{\partial r} + \frac{\partial\bar{x}}{\partial\bar{a}}\frac{d\bar{a}}{dr}\right) \tag{5.108}$$

The derivative of $\bar{a}$ with respect to r (found by implicit differentiation of (5.82)) is:

$$\frac{d\bar{a}}{dr} = \frac{\bar{a}(f - n\kappa) + fa_0}{2\bar{a}\kappa(nk - f) + \kappa(fa_0 - nr) + fr} \tag{5.109}$$

The partial derivatives in (5.108) are:

$$\begin{array}{ll}
\frac{\partial\lambda_j^+}{\partial r}=-\frac{1}{2} + \frac{r-f\bar{x}}{2\sqrt{(f\bar{x})^2+4f\bar{x}(\bar{a}-r+\bar{a}gz^{-j})}} & \frac{\partial\lambda_j^+}{\partial\bar{a}}=\frac{f\bar{x}(k+gz^{-j})}{\sqrt{(f\bar{x})^2+4f\bar{x}(\bar{a}-r+\bar{a}gz^{-j})}} \\
\frac{\partial\lambda_j^+}{\partial\bar{x}}=-\frac{f}{2} + \frac{f(f\bar{x}+r+2\bar{a}k-2r+2\bar{a}gz^{-j})}{\sqrt{(f\bar{x})^2+4f\bar{x}(\bar{a}-r+\bar{a}gz^{-j})}} & \frac{\partial\bar{x}}{\partial r}=\frac{r-k\bar{a}}{f} \\
\frac{\partial\bar{x}}{\partial\bar{a}}=-\frac{rk}{f\kappa} &
\end{array} \tag{5.110}$$

At $r = 0,\ \bar{a} = 0$, this evaluates to

$$\begin{array}{ll}
\left(\frac{d\bar{a}}{dr}\right)_{r=0,\bar{a}=0}=\frac{1}{\kappa} & \left(\frac{\partial\lambda_j^+}{\partial r}\right)_{r=0,\bar{a}=0}=-1 \\
\left(\frac{\partial\lambda_j^+}{\partial\bar{a}}\right)_{r=0,\bar{a}=0}=k + gz^{-j} & \left(\frac{\partial\lambda_j^+}{\partial\bar{x}}\right)_{r=0,\bar{a}=0}=0 \\
\left(\frac{\partial\bar{x}}{\partial r}\right)_{r=0,\bar{a}=0}=0 & \\
\left(\frac{\partial\bar{x}}{\partial\bar{a}}\right)_{r=0,\bar{a}=0}=0 &
\end{array} \tag{5.111}$$

and hence

$$\left(\frac{d\lambda_j^+}{dr}\right)_{r=0,\ \bar{a}=0} = \frac{g}{\kappa}(z^{-j} - 1) \tag{5.112}$$

Since this formula is valid for $j \neq 0$ only, we see that all $\lambda_j^+,\ j \neq 0$ have negative real parts for sufficiently small flow rates, regardless of the rate constants.

At $r = a_0k,\ \bar{a} = a_0,\ \bar{x} = 0$, the partial derivatives are

$$\begin{array}{ll}
\left(\frac{d\bar{a}}{dr}\right)_{r=a_0k,\ \bar{a}=a_0}=\frac{n\kappa}{-fg+nk\kappa} & \left(\frac{\partial\lambda_j^+}{\partial r}\right)_{r=a_0k,\ \bar{a}=a_0}=0 \\
\left(\frac{\partial\lambda_j^+}{\partial\bar{a}}\right)_{r=a_0k,\ \bar{a}=a_0}=0 & \left(\frac{\partial\lambda_j^+}{\partial\bar{x}}\right)_{r=a_0k,\ \bar{a}=a_0}=\frac{fg}{k}z^{-j} \\
\left(\frac{\partial\bar{x}}{\partial\bar{r}}\right)_{r=a_0k,\ \bar{a}=a_0}=\frac{k}{fg} & \left(\frac{\partial\bar{x}}{\partial\bar{a}}\right)_{r=a_0k,\ \bar{a}=a_0}=-\frac{k^2}{fg}
\end{array} \tag{5.113}$$

Therefore we have

$$\left(\frac{d\lambda_j^+}{dr}\right)_{r=a_0k,\bar{a}=a_0} = \frac{fg}{fg - nk\kappa} z^{-j} \tag{5.114}$$

The denominator is positive if $f > f^c$, that is, if we are in scenario 2. In this case the sign of the real parts of the eigenvalues equals the sign of $\cos 2\pi j/n$ for flow rates that are not too much greater than a_0k. Otherwise, we have scenario 1 and the denominator is negative. This means that the sign of the real part of the eigenvalue coincides with the sign of $\cos 2\pi j/n$ for flow rates not too much *below* a_0k. Thus the sign of the eigenvalues is the sign of $\cos\phi$ if the interior fixed point is sufficiently close to $P^{\emptyset}$, regardless of the scenario. These results could also have been obtained by examination of the quadratic and absolute coefficients of (5.105) and (5.106).

Thus, for the eigenvalues with $j < n/4$ we have two Hopf bifurcations or none inside the simplex and for $j > n/4$ we have exactly one. For$j = n/4$ there is at most one Hopf bifurcation inside the simplex.

We now summarize the results for the CSTR:

- At low flow rates there is one globally stable fixed point $P_{\mathcal{N}}^{(1)}$ in the interior of the simplex and the unstable trivial fixed point.
- At $r = a_0k$ the trivial fixed point becomes stable and either $P_{\mathcal{N}}^{(1)}$ leaves the simplex (scenario 1) or a second fixed point enters it (scenario 2), in which case both fixed points disappear in a saddle node bifurcation at some higher flow rate.
- At all flow rates there are at least $n+2$ eigenvalues with negative real part for $P_{\mathcal{N}}^{(1)}$ and $n+1$ for $P_{\mathcal{N}}^{(2)}$. (if n is even the number of negative eigenvalues is one higher).
- For $n = 4$ there is one Hopf bifurcation on the simplex if $g > k$. For $n = 3$ there can be none or two, $g > k$ being a necessary condition for

the latter case. For $n > 4$, finally, there is exactly one. In scenario 2 it depends on the value of f, at which of the two fixed points the Hopf bifurcation(s) take(s) place. Generally speaking, the Hopf bifurcations occur at the unstable fixed point $P_{\mathcal{N}}^{(2)}$ for large f and at the stable fixed point $P_{\mathcal{N}}^{(1)}$ for low f.

Special case: $f = nk$

The equations for the CSTR become considerably simpler if we choose $f = nk$, since in this case the quadratic coefficient of (5.82) vanishes. Therefore, there is only one fixed point with the coordinates:

$$\bar{a} = \frac{a_0 k r}{a_0 k \kappa - r g} \qquad \bar{x} = \frac{a_0 k - r}{f} \qquad \bar{s} = \frac{r g (a_0 k - r)}{f(a_0 k \kappa - r g)} \tag{5.115}$$

The eigenvectors for $j = 0$ are:

$$\xi = (1, 1, \ldots, -\frac{g r}{a_0 k \kappa - r g}, \ldots, \frac{a_0 k^2 n r}{(a_0 k - r)((a_0 k \kappa - r g)}) \qquad \lambda = -r \tag{5.116}$$

$$\xi = (1, \ldots, -\frac{g((a_0 k - r)^2 \kappa + k r (a_0 k - 2r))}{((a_0 k \kappa - r g)((a_0 k - r) + k r)}, \ldots, \frac{a_0 k^2 n r \kappa}{((a_0 k \kappa - r g)((a_0 k - r) + k r)})$$

$$\lambda = -a_0 k + r \tag{5.117}$$

$$\xi = (0, 0, \ldots, \frac{1}{n}, \frac{1}{n}, \ldots, -1) \qquad \lambda = -\frac{a_0 k \kappa - r g}{k} \tag{5.118}$$

It is quite obvious that all these eigenvalues are negative. For the remaining eigenvalues there are Hopf bifurcations where r fulfills the equation

$$r^2 g(2 - \cos^2\phi) - r a_0 k(g(3 - \cos\phi - \cos^2\phi) + k) - a_0^2 k^2 \kappa(\cos\phi - 1) = 0 \tag{5.119}$$

The value of $\bar{a}$ at the bifurcation can be found by solving the equation

$$\bar{a}^2 g y^2 \phi + \bar{a} a_0(-g(y^2\phi + \cos\phi) - k) + a_0^2 k(1 - \cos\phi) = 0 \tag{5.120}$$

5.4.2 The evolution reactor

In the evolution reactor, we obtain the following kinetic equations for the relative concentrations x_i and s_i:

$$\begin{aligned} \dot{x}_i &= x_i(k + c_0\, f\, s_{i-1} - \Phi) \\ \dot{s}_i &= g x_i - s_i(c_0\, f\, x_{i+1} + \Phi) \end{aligned} \tag{5.121}$$

with $\Phi = \kappa \sum x_i$ and $\kappa = k + g$. There are fixed points on the boundary of the simplex for the same index sets as in the CSTR, but they are also unstable and the proofs are so similar that I don't want to repeat them.

The equilibrium concentration at the interior fixed point are

$$\bar{x} = \frac{\bar{\Phi}(\bar{\Phi} - k)}{c_0 f(\kappa - \bar{\Phi})}, \qquad \bar{s} = \frac{\bar{\Phi} - k}{c_0 f} \tag{5.122}$$

If we insert

$$\bar{\Phi} = \frac{\kappa(nk + c_0 f)}{n\kappa + c_0 f} \tag{5.123}$$

into the above formulae, we get

$$\bar{x} = \frac{nk + c_0 f}{n(n\kappa + c_0 f)}, \qquad \bar{s} = \frac{g}{n\kappa + c_0 f} \tag{5.124}$$

Stability properties

The Jacobian of (5.121) at the interior fixed point has the following form:

$$\left(\begin{array}{cccc|cccc}
-\kappa\bar{x} & -\kappa\bar{x} & \dots & -\kappa\bar{x} & 0 & 0 & \dots & -c_0 f\bar{x} \\
-\kappa\bar{x} & -\kappa\bar{x} & \dots & -\kappa\bar{x} & -c_0 f\bar{x} & 0 & \dots & 0 \\
\vdots & \vdots & \ddots & \vdots & \vdots & \vdots & \ddots & \vdots \\
-\kappa\bar{x} & -\kappa\bar{x} & \dots & -\kappa\bar{x} & 0 & 0 & \dots & 0 \\
\hline
g - \kappa\bar{s} & -c_0 f\bar{s} - \kappa\bar{s} & \dots & -\kappa\bar{s} & -c_0 f\bar{x} - \bar{\Phi} & 0 & \dots & 0 \\
-\kappa\bar{s} & g - \kappa\bar{s} & \dots & -\kappa\bar{s} & 0 & -c_0 f\bar{x} - \bar{\Phi} & \dots & 0 \\
\vdots & \vdots & \ddots & \vdots & \vdots & \vdots & \ddots & \vdots \\
-c_0 f\bar{s} - \kappa\bar{s} & -\kappa\bar{s} & \dots & g - \kappa\bar{s} & 0 & 0 & \dots & -c_0 f\bar{x} - \bar{\Phi}
\end{array}\right)$$

where we have used lines to make the block structure visible.

We make the following ansatz for the eigenvectors:

$$\xi_j = (1, z^j, z^{2j}, \ldots, z^{(n-1)j}, \beta_j \beta_j z^j, \ldots, \beta_j z^{(n-1)j}) \tag{5.125}$$

with $z = e^{\frac{2\pi i}{n}}$. The constants β_j are found by evaluating the equation

$$\mathbf{J}\xi_j = \lambda_j \xi_j \tag{5.126}$$

The eigenvectors and eigenvalues for $j = 0$ are identical to those found in the competitive model: one eigenvalue is the external eigenvalue $-\bar{\Phi}$, the other one is $-(n\kappa + c_0 f)\bar{x}$. For $j \neq 0$ we get

$$\lambda_j = c_0 f \bar{x} \beta_j z^{-j} \tag{5.127}$$

$$\beta_j^2 c_0 f \bar{x} z^{-j} = g - c_0 f \bar{s} z^j - \beta_j (c_0 f \bar{x} + \bar{\Phi}) \tag{5.128}$$

Solving the latter equation for β_j and inserting it into the former, we obtain

$$\beta_j = \frac{-c_0 f \bar{x} - \bar{\Phi} \pm \sqrt{(c_0 f \bar{x} - \bar{\Phi})^2 - 4 c_0 f \bar{x}(\bar{\Phi} - k - g z^j)}}{2 c_0 f \bar{x}} \tag{5.129}$$

$$\lambda_j^{+/-} = \frac{1}{2}\left(-c_0 f \bar{x} - \bar{\Phi} \pm \sqrt{(c_0 f \bar{x} - \bar{\Phi})^2 - 4 c_0 f \bar{x}(\bar{\Phi} - k - g z^j)}\right) \tag{5.130}$$

or, inserting the equilibrium values for $\bar{x}$ and $\bar{\Phi}$

$$\lambda_j^{+/-} = \frac{1}{2}\left(-\frac{nk + c_0 f}{n} \pm \sqrt{\left(\frac{nk + c_0 f}{n}\right)^2 + 4\frac{c_0 f g(nk + c_0 f)}{n(n\kappa + c_0 f)}\left(z^{-j} - \frac{c_0 f}{n\kappa + c_0 f}\right)}\right) \tag{5.131}$$

We rewrite the latter as

$$\frac{1}{2}\left(-u \pm \sqrt{u^2 - 4v + 4w(\cos\phi + iy\phi)}\right) \tag{5.132}$$

with

$$\begin{aligned} u &= \tfrac{nk+c_0 f}{n} \\ v &= \tfrac{f^2 g(nk+c_0 f)}{n(n\kappa+c_0 f)^2} \\ w &= \tfrac{f g(nk+c_0 f)}{n(n\kappa+c_0 f)} \\ \phi &= \tfrac{-2\pi i j}{n} \end{aligned} \tag{5.133}$$

Since (5.132) has the same form as (5.94), the condition for finding a Hopf bifurcation is again (5.100). Inserting (5.133) into this yields the following condition for Hopf bifurcations in the evolution reactor:

$$(c_0 f - (n\kappa + c_0 f)\cos\phi)\,(nk + c_0 f) - nc_0 fgy^2\phi = 0 \tag{5.134}$$

Since c_0 is the parameter which is most easily varied we order (5.134) in powers of c_0:

$$\begin{aligned} c_0^2 f^2(1-\cos\phi) + c_0 fn\left(k(1-2\cos\phi) - g(y^2\phi + \cos\phi)\right) - \\ - kn^2\cos\phi\kappa = 0 \end{aligned} \tag{5.135}$$

As in the CSTR setting, we can restrict the discussion to the case $j = 1$, since we are mainly interested in Hopf bifurcation that lead from stable fixed points to saddles.

The quadratic coefficient of (5.135) is always positive; the absolute coefficient is positive if $n > 4$. Therefore, if $n > 4$, there is exactly one positive value of c_0 where a Hopf bifurcation takes place, whereas for $n < 4$ there are either two or none. For $n = 4$ one solution of (5.135) is $c_0 = 0$, which is then doubly degenerate, and the other one is $c_0 = 4(g-k)/f$, which is positive if $g > k$.

To determine whether the fixed point becomes stable or unstable if we raise c_0 above the critical value (i.e. the solutions of (5.135)), we expand the eigenvalue in powers of c_0 at $c_0 = 0$. Since $\lambda_j^+ = 0$ if $c_0 = 0$, the sign of the eigenvalue is determined by the derivative with respect to c_0 for small total concentrations:

$$\left(\frac{d\lambda_j^+}{dc_0}\right)_{c_0=0} = \frac{fgz^j}{n\kappa} \tag{5.136}$$

Obviously, the real part of λ_1^+ is negative for $n < 4$ and positive for $n > 4$, if c_0 is sufficiently small. For $n = 4$, the first order expansion term is zero. We therefore consider the second derivative of the real part of λ_1^+ with respect to c_0 at $c_0 = 0$:

$$\Re\left(\frac{d^2\lambda_1^+}{df^2}\right)_{c_0=0} = \frac{f^2 g(g-k)}{8k\kappa^2}$$

For $n = 4$ the eigenvalue λ_1^+ is therefore positive in the range $0 < f < 4(g-k)$ if $g > k$ and negative for all $f > 0$ if $g < k$ (calculation of the corresponding third derivative shows that in fact the eigenvalue is also negative for all $f > 0$ if $g = k$).

For the important special cases of $n = 3$ and $n = 4$ we have:

$n = 3$: The critical values are

$$c_0 = \frac{g - 8k \pm \sqrt{g^2 - 64gk + 16k^2}}{4f}$$

Bifurcations can therefore only take place if g exceeds a value of roughly $64k$. Numerical studies indicate the existence of a limit cycle between the two bifurcations. If g is less than the stated value, the fixed point is a sink for all c_0.

$n = 4$: The fixed point is a saddle for $0 < c_0 < 4(g-k)/f$ if $g < k$ and a sink otherwise. In the region where the fixed point is unstable there seems to be a limit cycle as for $n = 3$.

The behaviour of the eigenvalues when c_0 is gradually raised from zero is therefore as follows:

- There is one interior fixed point which determines the dynamics on the simplex and several transversally instable fixed points on the boundary of the simplex.
- For $n = 2$ the (interior) fixed point is always stable.
- For $n = 3$ the (interior) fixed point is stable for small c_0. If bifurcations occur (which is possible only if $g \gg k$), the first one leads to instability and the second one to stability.

- For $n = 4$ two eigenvalues of the Jacobian at the interior fixed point have positive real parts and become negative at $c_0 = 4(g-k)/f$ if $g > k$. Otherwise they are negative for all $c_0 > 0$.
- For $n > 4$ the eigenvalues are positive for small c_0, but become negative at the positive solution of (5.135) and then remain negative.
- For any choice of the remaining parameters we can find a c_0^{crit} such that the real parts of all eigenvalues are negative if $c_0 > c_0^{crit}$.
- The behaviour of the system in the CSTR at low flow rates resembles the behaviour in the evolution reactor for high c_0. This can be understood from the equations, since in both cases the terms with fs_i are predominant.

5.4.3 Comparison with the inhomogeneous hypercycle

It is instructive to compare the system (5.1) with the inhomogeneous hypercycle with equal reaction constants. The latter is given by the equations

$$\begin{array}{rcl} A + X_j & \overset{\widehat{k}_j}{\rightarrow} & 2X_j \\ A + X_j + X_{j-1} & \overset{\widehat{f}_{j-1}}{\rightarrow} & 2X_j + X_{j-1} \\ A & \overset{r}{\rightarrow} & * \\ X_j & \overset{r}{\rightarrow} & * \end{array} \tag{5.137}$$

In the CSTR, putting $\widehat{k}_i = k,\ \widehat{f}_i = f$, we have the following kinetic equations

$$\begin{array}{l} \dot{x}_i = x_i[a(k + fx_{i-1}) - r] \\ \dot{a} = a_0 r - a[r + \sum x_i(k + fx_{i-1})] \end{array} \tag{5.138}$$

The interior fixed point has the coordinates

$$\bar{x} = \frac{r - \bar{a}k}{\bar{a}f} \qquad \bar{a} = \frac{nk + a_0 f \pm \sqrt{(nk + a_0 f)^2 - 4nfr}}{2f} \tag{5.139}$$

At $r = a_0 k$ we have one solution $\bar{a} = a_0$ (transcritical bifurcation with the trivial fixed point). The second solution is $\bar{a} = nk/f$. Thus the second fixed point lies inside the simplex at $r = a_0 k$ if $nk < a_0 f$, in which case we have scenario 2. Otherwise we have scenario 1.

The saddle node bifurcation takes place at

$$r^* = \frac{(nk + a_0 f)^2}{4nf} \qquad \bar{a}^* = \frac{nk + a_0 f}{2f}$$

The Jacobian at the interior fixed point has the form

$$\mathbf{J} = \begin{pmatrix} 0 & 0 & \dots & 0 & r - \bar{a}k & \frac{r(r-\bar{a}k)}{\bar{a}^2 f} \\ r - \bar{a}k & 0 & \dots & 0 & 0 & \frac{r(r-\bar{a}k)}{\bar{a}^2 f} \\ \vdots & \ddots & \dots & & & \vdots \\ 0 & 0 & \dots\, r - \bar{a}k & & 0 & \frac{r(r-\bar{a}k)}{\bar{a}^2 f} \\ \bar{a}k - 2r & \bar{a}k - 2r \dots & \bar{a}k - 2r & & \bar{a}k - 2r & -r\left(1 + \frac{n(r-\bar{a}k)}{a^2 f}\right) \end{pmatrix} \tag{5.140}$$

Following the procedure outlined above, we find $n - 1$ eigenvectors of the form

$$\xi_j = (z^0, z^j, z^{2j}, \dots, z^{(n-1)j}, 0) \qquad j = 1, \dots, n-1$$

with corresponding eigenvalues

$$\lambda_j = (r - \bar{a}k) z^{(n-1)j} = (r - \bar{a}k) z^{-j}$$

Since $r - \bar{a}k > 0$, these eigenvalues have the sign of the corresponding unit roots.

Additionally, we have two eigenvectors of the form

$$\xi_0 = (1, 1, \dots, 1, \omega)$$

where ω fulfills the equation

$$\omega[(r - \bar{a}k)(1 + \frac{\omega r}{\bar{a}^2 f})] + n(2r - \bar{a}k) + \omega r(1 + \frac{n(r - \bar{a}k)}{\bar{a}^2 f}) = 0$$

with the solutions

$$\omega^{(1)} = -n, \qquad \lambda_0^{(1)} = (r - \bar{a}k)(1 - \frac{nr}{\bar{a}^2 f})$$

$$\omega^{(2)} = \frac{\bar{a}^2 f(\bar{a}k - 2r)}{r(r - \bar{a}k)}, \qquad \lambda_0^{(2)} = -r$$

To find the sign of $\lambda_0^{(1)}$, we compute r as function of $\bar{a}$

$$r(\bar{a}) = \frac{\bar{a}(f(a_0 - a) + nk)}{n}$$

Thus we obtain

$$\lambda_0^{(1)} = \frac{(\bar{a} - a_0)(f(a_0 - 2\bar{a}) + nk)}{n} = \frac{2f(\bar{a} - a_0)(\bar{a}^* - \bar{a})}{n}$$

Therefore, we have $\lambda_0^{(1)} < 0$ for $0 < \bar{a}^*$ and $\lambda_0^{(1)} > 0$ for $\bar{a}^* < \bar{a} < a_0$. In other words, this eigenvalue is always negative for the fixed point with the lower equilibrium concentration of a and positive for the other one.

Under the constraint of constant organization, considering relative concentrations and setting $\widehat{k}_i = k, \quad \widehat{f}_i = f$ as above, we obtain the equations

$$\dot{x}_i = x_i(k + c_0 f x_{i-1} - \Phi) \tag{5.141}$$

The dilution flux Φ is defined by

$$\Phi = k + c_0 f \sum x_i x_{i-1} \tag{5.142}$$

Hence, the terms k in the kinetic equations cancel and we are left with the homogeneous hypercycle. The interior fixed point has the coordinates

$$\bar{x} = \frac{1}{n} \qquad \bar{\Phi} = \frac{c_0 f + nk}{n} \tag{5.143}$$

The Jacobian at the interior fixed point is circulant and has the form

$$\mathbf{J} = \begin{pmatrix} -2c_0 f\bar{x}^2 & -2c_0 f\bar{x}^2 \ldots & -2c_0 f\bar{x}^2 & -2c_0 f\bar{x}^2 + c_0 f\bar{x} \\ -2c_0 f\bar{x}^2 + c_0 f\bar{x} & -2c_0 f\bar{x}^2 \ldots & -2c_0 f\bar{x}^2 & -2c_0 f\bar{x}^2 \\ \vdots & \ddots \quad \ldots & & \vdots \\ -2c_0 f\bar{x}^2 & -2c_0 f\bar{x}^2 \ldots & -2c_0 f\bar{x}^2 + c_0 f\bar{x} & -2c_0 f\bar{x}^2 \end{pmatrix} \tag{5.144}$$

Therefore the eigenvalues are

$$\begin{aligned}\lambda_0 &= c_0 f\bar{x}(-2n\bar{x}+1) = -\frac{c_0 f}{n}\\ \lambda_j &= \ c_0 f\bar{x}e^{\frac{2\pi i(n-1)j}{n}} \ = \frac{c_0 f}{n}e^{-\frac{2\pi i j}{n}}\end{aligned}$$

If we now compare the results for (5.121) and (5.79) with those for (5.141) and (5.138) resp., we see that for a suitable choice of parameters the inhomogeneous hypercycle reproduces many of the features of the more complex system, such as number of fixed points, transcritical bifurcations etc. The most important difference between the two systems is that the sign of the complex eigenvalues of the hypercycle depends only on n and that therefore, in contrast to the other system *there can be no Hopf bifurcation in the hypercycle*.

Chapter 6

Spatial resolution

In this chapter we shall investigate the properties of our models under diffusion. To that end we use the discretization formalism presented in section 2.7. and the recycling reaction setting, since neither the CSTR nor the evolution reactor are compatible with diffusion. We recall that the fixed points in the recycling reaction system are the same as in the CSTR and that the Jacobian at a fixed point in the recycling reaction system can be obtained from that in the CSTR by adding r to all entries in the last row.

We shall present both analytical and numerical results in this chapter. In all numerical studies we started with a fixed point of the reaction system and added a 1% perturbation.

The trivial fixed point is diffusion stable in both models and thus not very interesting.

For the competitive model we investigate diffusion stability only for stable one dimensional fixed points.

For the mutualistic model we can show that one dimensional fixed points are diffusion stable, but the higher dimensional ones are not. We know that higher dimensional fixed points can be stable in the absence of diffusion, and therefore Turing instabilities can be found. Particularly, for the case of equal reaction constants, with the additional assumption that all replicating species and all intermediates have the same diffusion coefficient, we can explicitly calculate at which diffusion coefficients the bifurcation takes place. The behaviour of the stable limit cycles that were found for the reaction system is investigated numerically.

We now show the diffusion stability of the trivial fixed point, using theorem 2.3, which said the fixed point was diffusion stable iff all principal minors of **-J** were nonnegative. The entries of **-J** are:

$$-j_{i,l} = \begin{cases} (r - a_0 k_i)\delta_{il} & i \leq n, \\ r\delta_{il} & n < i \leq 2n \\ -r + r\delta_{il} & i = 2n+1 \end{cases}$$

Therefore, all principal minors can be written as products of factors $(r - a_0 k_i)$ and r and since the trivial fixed point is stable if $r > a_0 k_1$ (assuming that $k_1 = \max k_i$), the trivial fixed point is diffusion stable iff it is stable.

6.1 The competitive model

We first show that stable one dimensional fixed points are not diffusion stable by finding a negative principal minor of **-J**. If $I = \{j\}$, the principal minor where only the rows and columns corresponding to x_j and s_j are retained is

$$\det \begin{pmatrix} 0 & -f_j \bar{x}_j \\ -g_j \bar{a} + f_j \bar{s}_j & f_j \bar{x}_j + r \end{pmatrix} = f_j \bar{x}_j (r - \kappa_j \bar{a}) < 0$$

Therefore, Turing instabilities can be induced by choosing the diffusion coefficient of the substrate d_A larger than that of the replicating species and the intermediates. We can even calculate the critical value d_A^* at which this bifurcation takes place by setting

$$\det \begin{pmatrix} -\Lambda d_{X_j} & f_j \bar{x}_j & k\bar{x} \\ \kappa_j \bar{a} - r & -f_j \bar{x}_j - r - \Lambda d_{S_j} & g\bar{x} \\ -\kappa_j \bar{a} & r & -\kappa_j \bar{x}_j = \Lambda d_A \end{pmatrix} = 0 \qquad (6.1)$$

where Λ is defined as in section 2.7.4 and d_{X_j} and d_{S_j} are the diffusion coefficients of X_j and S_j, respectively. Thus we obtain

$$d_A^* = \frac{\bar{x}(d_{S_j} k_j (r - \kappa_j \bar{a}) - d_{S_j} d_{X_j} \Lambda \kappa_j - d_{X_j} k_j r - d_{X_j} f_j \kappa_j \bar{x}_j)}{f_j \bar{x}(r - \kappa_j \bar{a}) + d_{X_j} \Lambda (f_j \bar{x}_j + r + d_{S_j} \Lambda)} \qquad (6.2)$$

In fig. 6.1 we show an example for pattern formation by Turing instabilities. The diffusion coefficient of the substrate was chosen twice the critical value. We start near the fixed point. The plot shows how small fluctuations around the fixed point are amplified and a stable pattern is formed after short time.

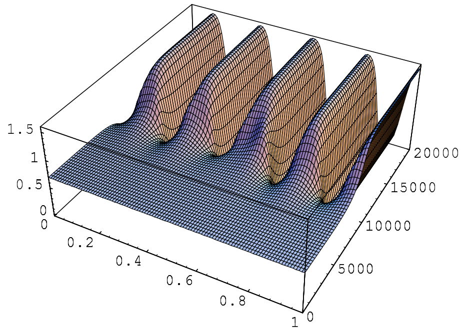


Figure 6.1: Turing instabilties in one species competitve model: $k = 1,\ g = 5,\ f = 2,\ a_0 = 1,\ r = 0.5,\ d_X = d_S = 2 \times 10^{-5},\ d_A = 1.3 \times 10^{-3}$. The plot shows the concentration of X vs. space and time.

Since we conjecture that all the other fixed points are unstable in the absence of diffusion and that there are no limit cycles, we do not expect any interesting results for starting at one of these fixed points.

6.2 The mutualistic model

6.2.1 General results

We first prove the following

Lemma 6.1 *In the mutualistic model, one dimensional fixed points are diffusion stable if they are stable.*

Proof: All principal minors of $-\mathbf{J}$ at the fixed point $P_{\{j\}}$ can be written as product of

1. $-\lambda_s^{(tr,1)} = r - k_s\bar{a} > 0$
2. $-\lambda_s^{(tr,2)} = f_{j-1}\bar{x}_j\delta_{s,j-1} + r > 0$
3. Principal minors of

$$\begin{pmatrix} 0 & 0 & -k_j\bar{x}_j \\ -g_j\bar{a} & r & -g_j\bar{x}_j \\ \kappa_j\bar{a} - r & -r & \kappa_j\bar{x}_j \end{pmatrix} \tag{6.3}$$

with $s \neq j$. Since the factors of the first two types are just the negative of the transversal eigenvalues, they are trivially positive if the fixed point is stable. Thus we only have to show that all principal minors of (6.3) are nonnegative. For the principal minors of rank 1 (the diagonal elements) this is obviously the case. The principal minors of rank 2 are

$$\begin{gathered} 0 \\ k_j\bar{x}_j(\kappa_j\bar{a} - r) > 0 \\ r(k_j\bar{x}_j) \geq 0 \end{gathered}$$

The principal minor of rank 3 (the determinant) is also positive, since it is just the product of the internal eigenvalues and the external eigenvalue, multiplied by -1.

$\square$

Lemma 6.2 *All stable fixed points at which at least two species coexist are not diffusion stable*

Proof: For the fixed point P_I with $I = \{j, j+1, \dots, k\}$, consider the principal minor of $-\mathbf{J}$ that is obtained by cancelling all rows and columns corresponding to x_s and s_s for all $s \notin I$ (if any) and those for the substrate a. It has the following form:

$$\det \left(\begin{array}{cccc|cccc}
0 & 0 & \dots & 0 & 0 & \dots & 0 & -f_{j-1}\bar{x}_j \\
0 & 0 & \dots & 0 & -f_j\bar{x}_{j+1} & \dots & 0 & 0 \\
\vdots & \vdots & \ddots & \vdots & \vdots & \vdots & \ddots & \vdots \\
0 & 0 & \dots & 0 & 0 & \dots & -f_{k-1}\bar{x}_k & 0 \\
\hline
-g_j\bar{a} & f_j\bar{s}_j & \dots & 0 & f_j\bar{x}_{j+1} + r & \dots & 0 & 0 \\
0 & -g_{j+1}\bar{a} & \dots & 0 & 0 & \dots & 0 & 0 \\
\vdots & \vdots & \ddots & \vdots & \vdots & \vdots & \ddots & \vdots \\
\Xi & 0 & \dots & -g_k\bar{a} & 0 & \dots & 0 & \Psi
\end{array} \right) \tag{6.4}$$

where $\Psi = f_n\bar{x}_n + r,\ \Xi = f_n\bar{s}_n$ if $I = \mathcal{N}$ and $\Psi = r,\ \Xi = 0$ otherwise. If $I = \mathcal{N}$, this determinant equals

$$-\prod_{i=1}^{n} f_i\bar{x}_i \left(\prod_{i=1}^{n} (r - k_i\bar{a}) - \bar{a}^n \prod_{i+1}^{n} g_i \right)$$

The factor in the brackets is positive, since it is just the denominator of $\bar{x}_i$ in (5.18). If $I \neq \mathcal{N}$, the principal minor equals

$$-\bar{a}^{n_I} \prod_{i=j}^{k} g_i f_{i-1}\bar{x}_i < 0$$

□

Thus we see that also in the mutualistic model, Turing instabilities can be induced by choosing d_A larger than the diffusion coefficients of the reacting species and intermediates. Since the picture would look exactly the same as for the competitive model, we do not show it here.

6.2.2 Equal reaction constants

In the case of equal reaction constants, we can calculate the critical diffusion coefficient d_A^* at which the bifurcation occurs, if we assume that $d_{X_i} = d_X$, $d_{S_i} = d_S$ for all $i = 1, \ldots, n$. This additional assumption is not too artificial, since equal reaction constants imply that the reactants are very similar and it should not be surprising if they diffuse with the same speed. In this case the matrix $\mathbf{J} - \Lambda\mathbf{D}$ (where $\mathbf{D}$ is the matrix of diffusion coefficients) consists again of four circulant blocks plus one additional row and column, and we can apply the now already familiar methods of section 5.4. From this section it is clear that only the eigenvalues λ_0 can vanish; all the others have at least nonzero imaginary parts. Thus, since we are interested mainly in pitchfork bifurcations, we consider only eigenvectors of the form

$$\xi_0 = (1, 1, \ldots, 1, \beta_0, \ldots, \beta_0, \omega) \tag{6.5}$$

β_0 and ω can be determined from the equations

$$\begin{aligned} \beta_0(-\Lambda d_X + \beta_0 f\bar{x} + \omega k\bar{x}) &= \kappa\bar{a} - r - \beta_0(f\bar{x} + r + \Lambda d_S) + \omega g\bar{x} && (6.6) \\ \omega(-\Lambda d_X + \beta_0 f\bar{x} + \omega k\bar{x}) &= n(r - \kappa\bar{a}) + n\beta_0 r - \omega(n\kappa\bar{x} + \Lambda d_A) && (6.7) \end{aligned}$$

The corresponding eigenvalue is

$$\lambda_0 = -\Lambda d_X + \beta_0 f\bar{x} + \omega k\bar{x} \tag{6.8}$$

If λ_0 vanishes, we can calculate β_0 from (6.8):

$$\beta_0 = \frac{\Lambda d_X - \omega k \bar{x}}{f \bar{x}} \tag{6.9}$$

Inserting this into the above equations, we obtain the critical value d_A^*:

$$d_A^* = \frac{n\bar{x}(\Lambda d_S d_X \kappa d_S k \kappa \bar{a} + (d_X - d_S)kr + d_X f \kappa)}{\Lambda^2 d_X d_S - \Lambda d_X (f\bar{x} + r) + f\bar{x}(\kappa a - r)} \tag{6.10}$$

If $d_S = d_X$, this simplifies to

$$d_A^* = \frac{n d_X \kappa \bar{x}(\Lambda d_X + k\bar{a} + f\bar{x})}{\Lambda^2 d_X^2 - \Lambda d_X (f\bar{x} + r) + f\bar{x}(\kappa a - r)} \tag{6.11}$$

Equations (6.10) and (6.11) are, strictly speaking, valid only for stable fixed points. Numerical studies showed, however, that symmetry breaking occurs also for unstable fixed points surrounded by stable limit cycles at roughly the same values of the diffusion coefficient of the substrate as predicted by these equations. Streissler [45] found that hypercycles with 5 or more members (for which there is a stable limit cycle) formed patches within which oscillations were going, when diffusion coefficients were chosen appropriately. The periods were somewhat different than without diffusion.

In the mutualistic model[1], two basic ways of symmetry breaking behavior were found: formation of oscillating patches, as described for the hypercycle, and formation of inhomogeneous but stationary patterns.

In some cases it was difficult to distinguish between oscillatory and stationary behaviour, since oscillatory transients can sustain quite a long time before the system evolves to a stationary state. On the other hand, in some cases it took a long time before oscillations started and the system looked at the beginning as if it were stationary. We therefore used the following methods to distinguish these two kinds of behaviour:

---

[1] We investigated only the case of equal reaction constant, because this is the only case where we could derive formulae for the critical diffusion coefficients

- For symmetry reasons, the system cannot start to oscillate if the concentration of all species and of all intermediates is equal in every single cell. Thus it is easy to check if the system has reached the stationary state.

- Checking if the system will stay oscillatory is much harder. We adopted the following scheme: the system is integrated over some time to get rid of initial conditions. Then, the state of the system at some time t_0 is chosen as reference state. For each time step t_i, the configuration of the system at step t_{i-1} and t_{i-2} is saved. At each integration step, the $(2n+1) \times N$ dimensional vector of the concentrations of all reactants in all N cells is subtracted from that of the reference state. If the norm of the difference vector goes through a minimum at time t_m, integration is started again from t_{m-1} with a smaller time step. This procedure is repeated until the norm of the difference vector changes less than 10%. Then the time since the last minimum was found is measured. Also, we monitored the maxima of the difference vector (the “amplitude” of the oscillation). When both period and amplitude of the oscillations remained almost constant and deviations were distributed randomly, the oscillation was the final state. When periods changed always in one direction and amplitudes became always smaller, it was a transient.

  The greatest setback of this method is that it works only if there is only *one* oscillatory patch. If there are two or more, the oscillations do not have the same period (probably due to boundary effects), and hence, in general, the system approaches its initial state only after very long time.

In fig. 6.2 we show the three basic situations for a five species mutualistic model on a one dimensional domain. The concentration of X_1 is plotted vs. the space coordinate x and time. In (a), the diffusion coefficient of the substrate was equal to that of the replicating species and intermediates.

After a short initial period, the whole domain oscillates at the same phase. In (b), the diffusion coefficient of the substrate was chosen twice the critical value as computed in (6.11). After an initial period, oscillating patches form. In (c), d_A was chosen five times larger than in (b). The oscillations are now strongly damped and the system convergens rapidly to the stationary (spatially inhomogeneous) state.

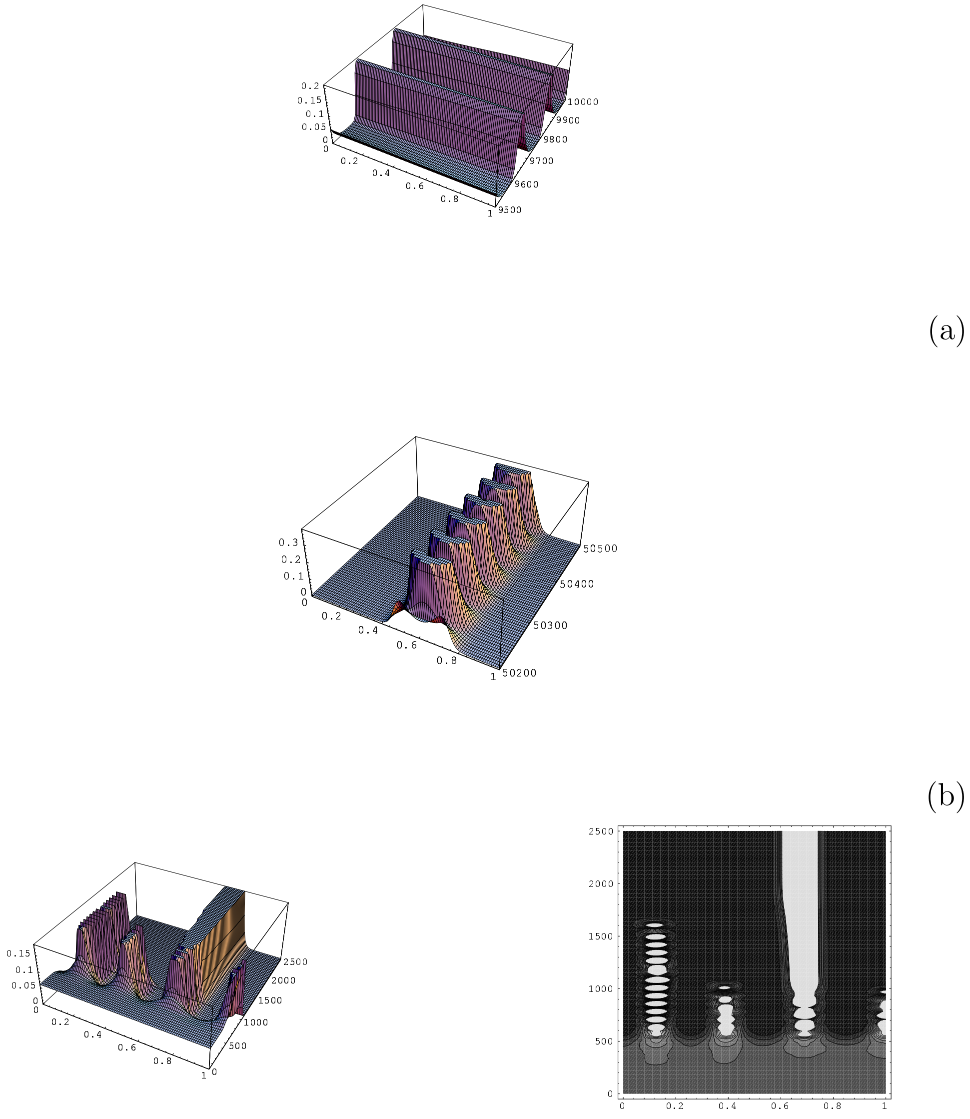
The stationary state is favored by the following factors:

1. Large diffusion coefficients of the substrate. Indeed it was in all investigated cases possible to suppress the oscillations by choosing d_A large enough.
2. Low value of k. For the case $k = 0$ (homogeneous model) we could not observe oscillations.
3. Large value of f. It is not possible to choose f bigger than one or two orders of magnitude bigger than k, since then the Hopf bifurcation occurs at the unstable fixed point $P_{\mathcal{N}}^{(2)}$ and $P_{\mathcal{N}}^{(1)}$ remains stable for all values of r.

In fig. 6.3 we try to show how the interplay of k, g, and f influences the behaviour of the system.

On two dimensional domains, spirals can form if we start close to a stable limit cycle and the diffusion coefficient of the substrate is not too high. Spirals are thus, in a way, the two dimensional counterpart to the synchronized oscillation of the whole domain in the one dimensional system. Fig. 6.4 show how the spirals develop in time. Although the time intervals between the individual pictures is somewhat large, one can still see how they rotate. In fig. 6.5 and 6.6, the concentration of all species at the end of the simulation is shown.

The other two possible cases we found on two dimensional domains are completely equivalent to what we have seen in one dimension: oscillating patches



(a)

(b)

(c) (d)

Figure 6.2: Mutualistic five species model: $k = 1$, $g = 1$, $f = 1$, $a_0 = 1$, $d_X = d_S = 2 \times 10^{-5}$. Concentration of X_1 is shown as function of space and time coordinates. (a) $d_A = 2 \times 10^{-5}$. The whole domain oscillates in phase. (b) $d_A = 5 \times 10^{-4}$ A single oscillating patch forms (there might also be several patches if we scaled all diffusion coefficients down). (c) $d_A = 2.5 \times 10^{-3}$ After some oscillations, a stable stationary state forms. (d) Contour plot of (c)

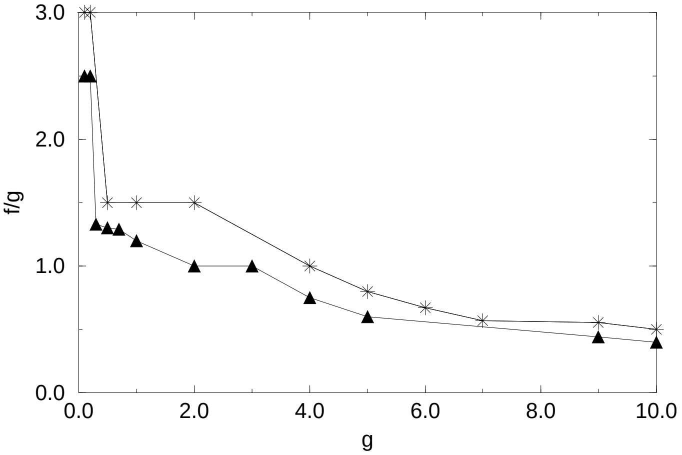
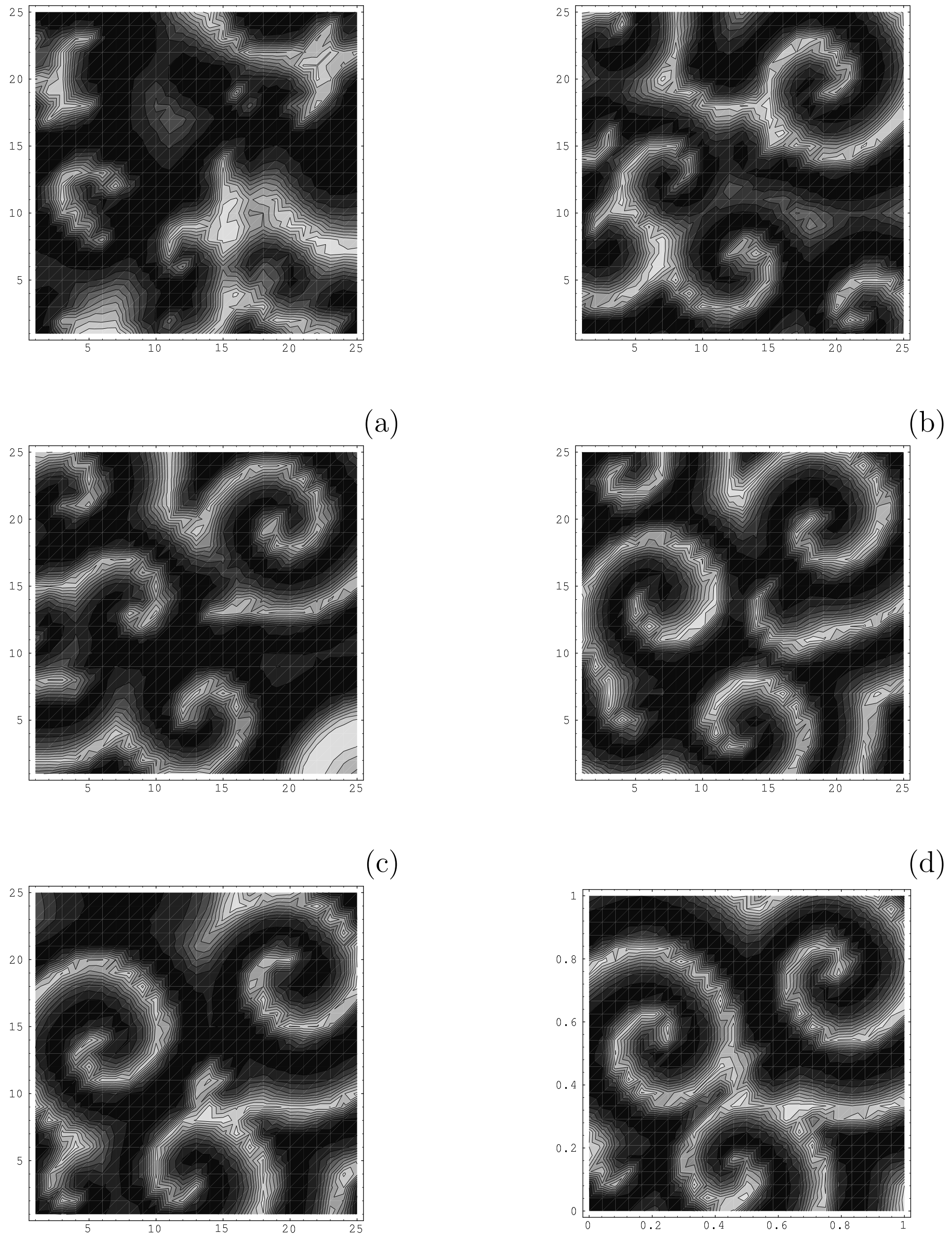


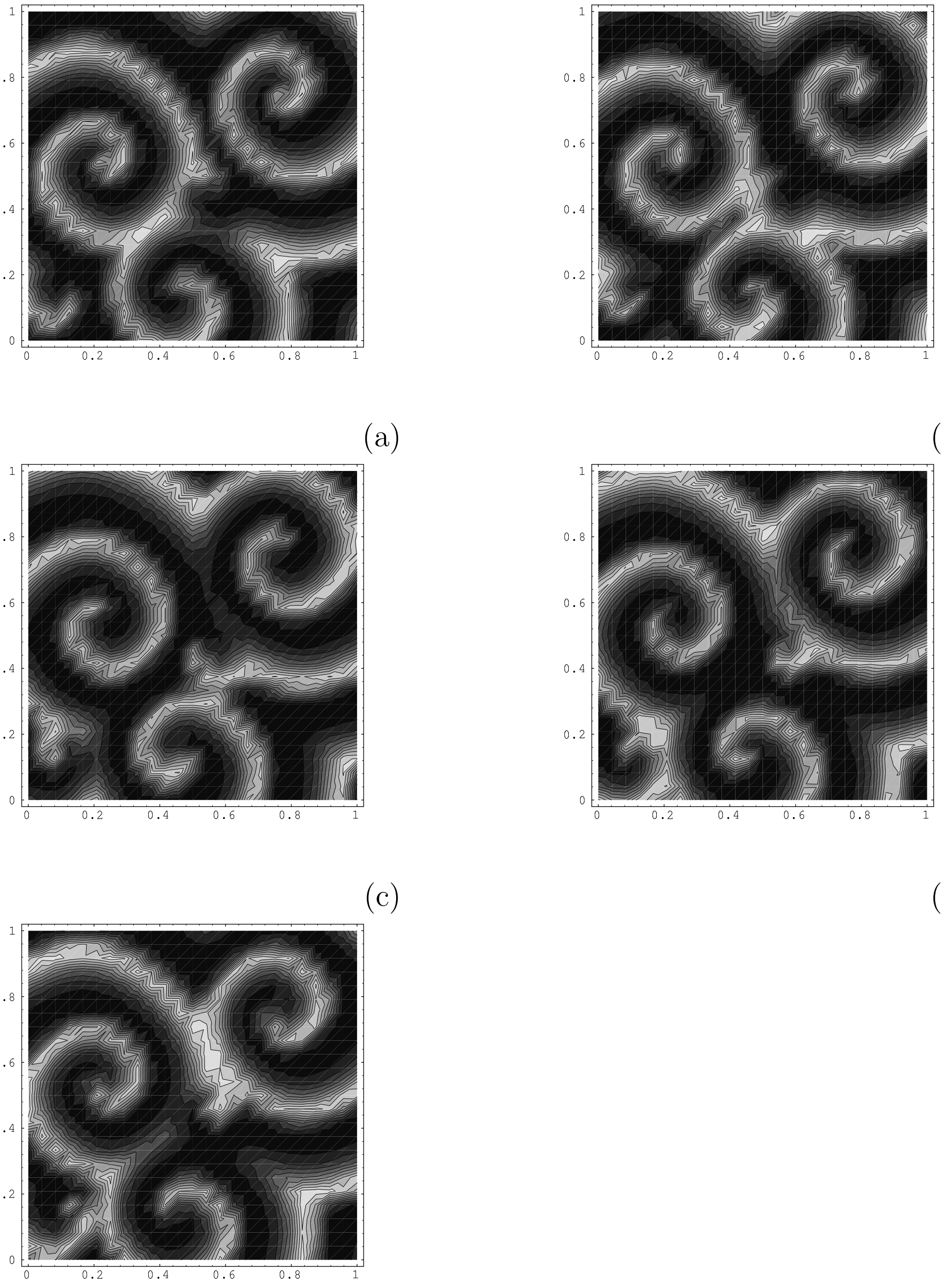
Figure 6.3: Dependence of stationary and oscillatory behaviour on rate constants: $k = 1$, the diffusion coefficient of the substrate was twice the critical value in all calculations. The stars represent the stationary states, the triangles the oscillatory states.

(shown in fig. 6.7) and stationary patterns (fig. 6.8). In the latter case we show only the concentration of X_1, S_1, and A, since the concentrations of the other species and intermediates are distributed in exactly the same way. As in one dimension, high diffusion coefficients of the substrate favor stationary solutions. We did not check, however, the influence of the kinetic constants, since this would have been too time consuming.



(a) (b) (c) (d) (e) (f)

Figure 6.4: Mutualistic five species model: $k = 1,\ g = 2,\ f = 5,\ a_0 = 1,\ d_X = d_S = d_A = 2 \times 10^{-6}$. Contour plots showing distribution of X_2 over the lattice, ranging from black=0 *mM* to white=0.2 *mM*. Time: (a) 5 000 s, (b) 10 000 s, (c) 15 000 s, (d) 20 000 s (e) 25 000 s and (f) 30 000 s



(a)

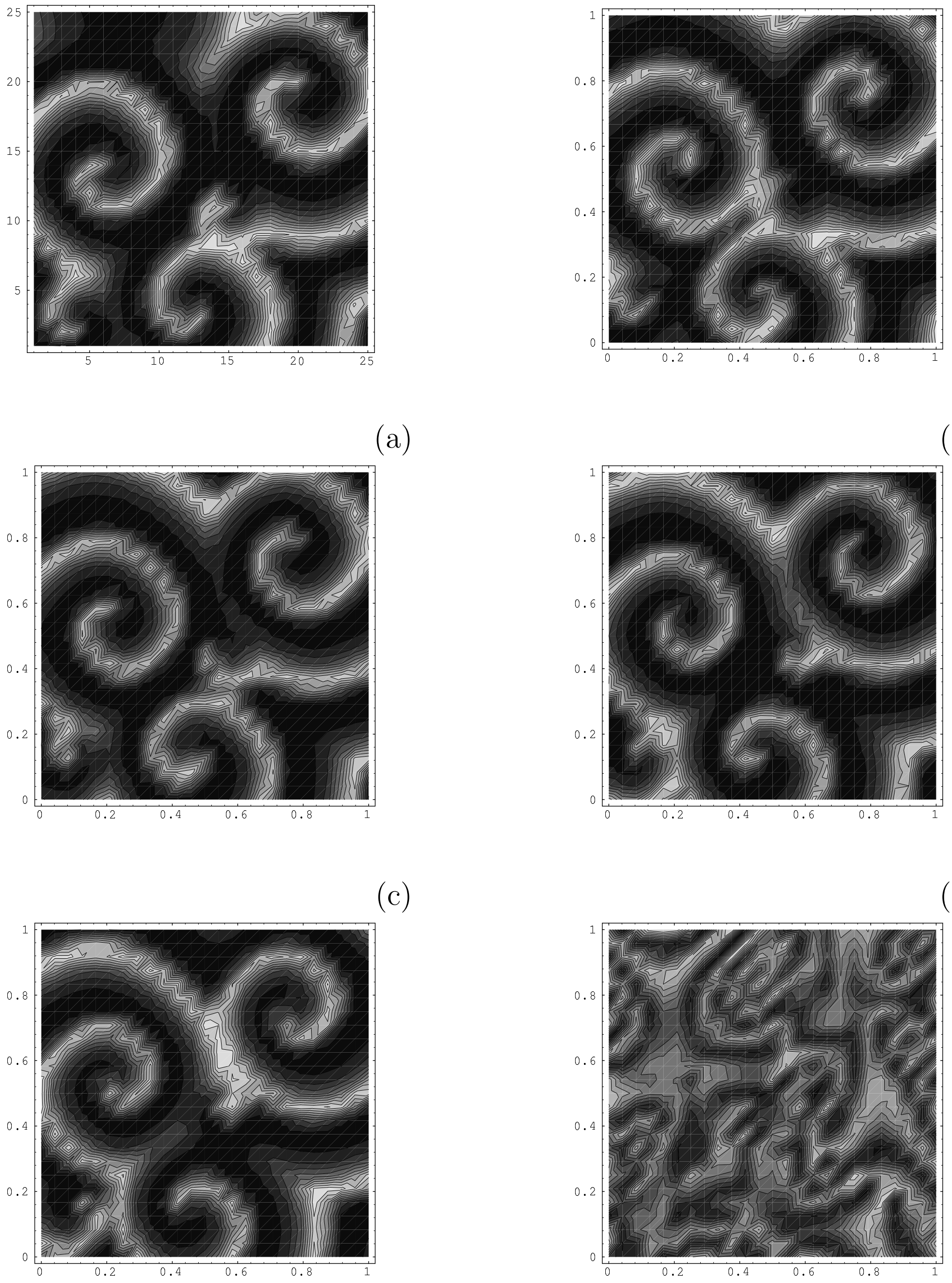
(b)

(c)

(d)

(e)

Figure 6.5: Mutualistic five species model: $k = 1$, $g = 2$, $f = 5$, $a_0 = 1$, $d_X = d_S = d_A = 2 \times 10^{-6}$. Contour plots showing distribution of X_1 (a) to X_5 (e) over the lattice, ranging from black=0mM to white=0.15 mM at $t = 30000s$.

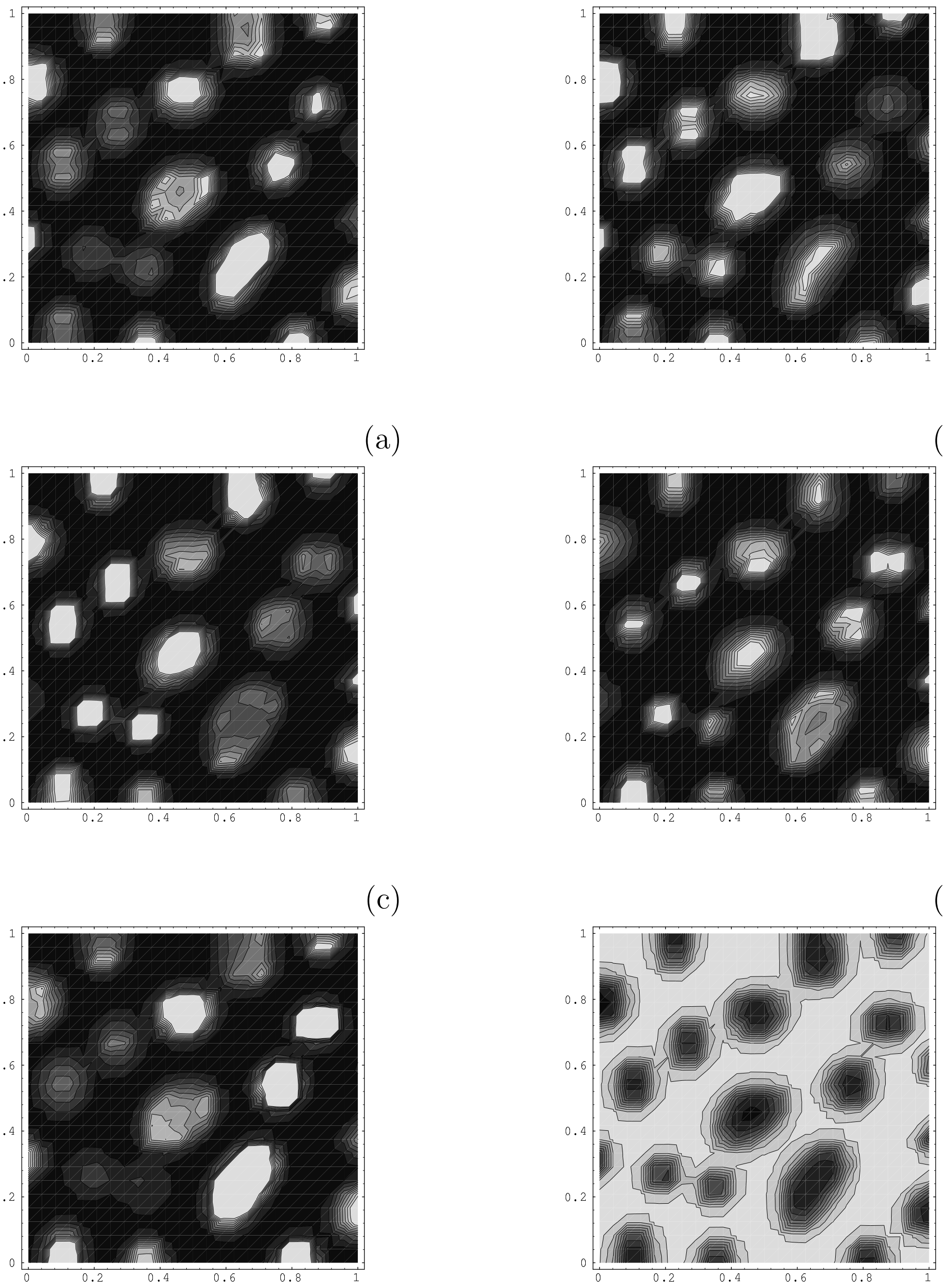


(a) (b)

(c) (d)

(e) (f)

Figure 6.6: Mutualistic five species model, constants as above. Contour plots showing distribution of S_1 (a) to S_5 (e) over the lattice, ranging from black=$0mM$ to white=0.15 mM, and distribution of A (f), ranging from 0.44 to 0.46 mM at $t = 30000s$.

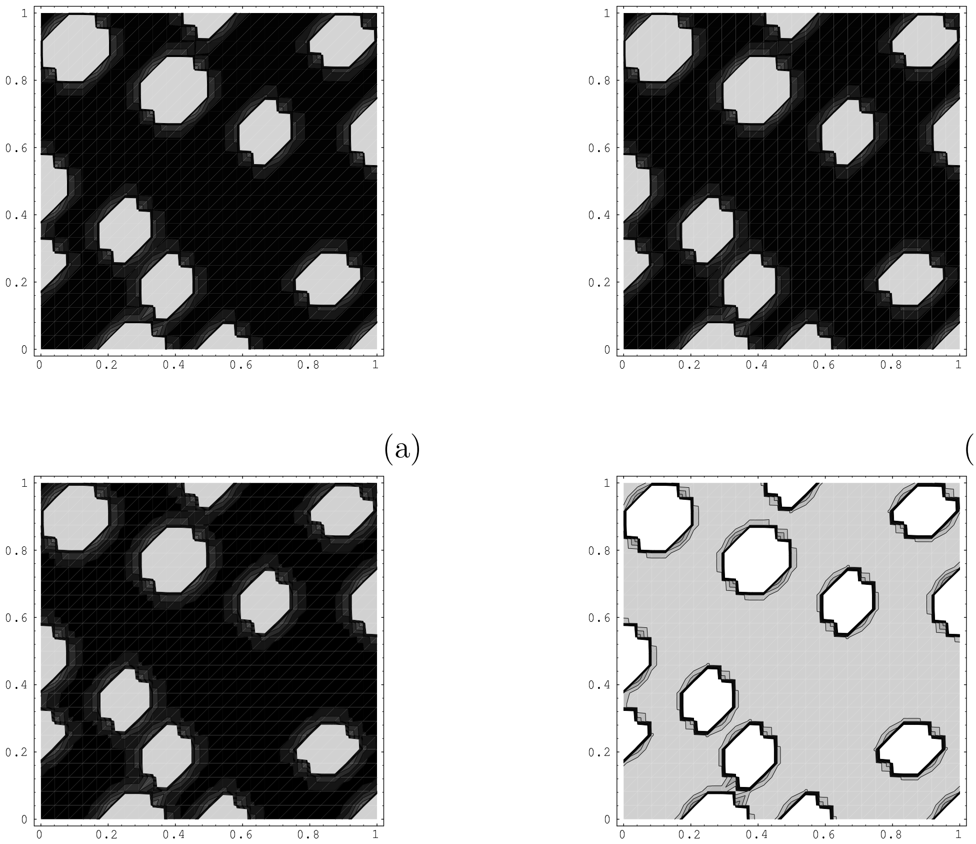


(a) (b)

(c) (d)

(e) (f)

Figure 6.7: Mutualistic five species model: $k = 1$, $g = 2$, $f = 5$, $a_0 = 1$, $d_X = d_S = 10^{-5}$, $d_A = 2.5 \times 10^{-4}$. Contour plots showing distribution of X_1 (a) to X_5 (e) over the lattice, ranging from black=$0mM$ to white=0.6 mM, and of A, ranging from 0.35 (black) to 0.46 mM (white), at $t = 6000s$.



(a) (b)

(c) (d)

Figure 6.8: Mutualistic five species model: $k = 1$, $g = 2$, $f = 5$, $a_0 = 1$, $d_X = d_S = 10^{-5}$, $d_A = 2.5 \times 10^{-3}$. Contour plots showing distribution of X_1 at (a) 50 000 s and (b) 100 000 s, ranging from 0 (black)to 2.5 mM (white); distribution of S_1 (c) and A (d) at 100 000 s, ranging from 0 to 0.25 and from 0.28 to 0.33 mM respectively

Chapter 7

Conclusions

Não me venham com conclusões!
A única conclusão é morrer.

Fernando Pessoa Nogueira: Lisbon revisited

In this work we have investigated the effect of substituting the trimolecular autocatalytic reaction step of second order replicator systems by two subsequent bimolecular reaction steps. The resulting reaction networks have been investigated in three different settings:

- The Continuously Stirred Tank Reactor (CSTR)
- The closed system with recycling reaction
- The evolution reactor

The results for the closed system coincide almost completely with those obtained for the CSTR, if we assume all degradation rates to be equal. In fact, the closed system approach has been introduced mainly because it facilitates the study of the reaction diffusion system. On the other hand, the results for the evolution reactor can differ considerably from those for the CSTR, because the former causes generally simpler equations and admits less fixed points. In what follows we state results for the CSTR (results for the evolution reactor are given in parentheses).

Reaction without diffusion: Fixed points at which only one species is present have been studied for general interaction matrices. The results depend largely upon the diagonal elements of the interaction matrix: if the diagonal terms are zero, these fixed points tend to become unstable for high flow rates (low total concentrations), while with positive diagonal term they can be stable for all flow rates (total concentrations) at which they exist. Furthermore, in the CSTR there can be two fixed point at which only species i exists if the corresponding diagonal element of the interaction matrix is positive, but only one if it vanishes.

Two special types of interaction have been investigated in more detail: the competitive model, which corresponds to a Schlögl model where the species interact only via the substrate (via the dilution flux) and the mutualistic model, which corresponds to the hypercycle where each species catalyzes the formation of the next and the reaction form a cycle.

In the competitive model there can be at most two (one) fixed points for each index set that admits a fixed point. For fixed points with only one species present we can prove that if there are two, the one with the higher equilibrium concentration of the substrate is unstable. The ones with the lower equilibrium concentration of the substrate can be stable. We conjecture that all fixed points at which several species coexist are unstable. Numerical evidence supports this conjecture, but we are not able to give an analytical proof in the general case. If the rate constants are equal for all species, we can show that all fixed points with one species present are stable and the other ones are unstable and that there are no changes in stablility induced by Hopf bifurcations. The behavior of the competitive model resembles that of a Schlögl model.

In the mutualistic model, there can be at most one fixed point for every index set on the boundary of the simplex, but two (one) interior fixed points. A fixed point P_I on the boundary of the simplex can be stable only if there exists no fixed point $P_{I'}$ such that I' is a superset of I. For the case of equal reaction constants, we can compute the stability of the interior fixed point: if there are two, the one with the higher equilibrium concentration of the substrate is unstable. The other one is stable in the two species system. For more than two species it can be destabilized by a Hopf bifurcation. For more than five species, it is generally unstable for sufficiently high flow rates (low total concentrations). Independent of the number of species, this fixed point is always stable at sufficiently low flow rates (high total concentrations). If the interior fixed point is unstable, a stable limit cycle surrounds it. The existence of Hopf bifurcations is an interesting feature absent in the elementary hypercycle.

The influence of diffusion: In the competitive model we can show that the spatially uniform solution for the fixed points at which only one species is present (the only ones we know to be stable) can be destabilized by choosing the diffusion coefficient of the substrate greater than that of the replicating species and the intermediate (formation of Turing patterns). We can calculate the critical diffusion coefficient at which this bifurcation occurs.

In the mutualistic model the fixed points at which only one species exists are stable against diffusion. For all remaining (stable) fixed points the uniform solution can be destabilized by choosing the diffusion coefficient of the substrate greater than that of the replicating species and intermediates. For the case of equal reaction constants and equal diffusion coefficients for all species and all intermediates we can calculate the critical diffusion coefficient at which the interior fixed point is destabilized. If the interior fixed point is unstable and surrounded by a stable limit cycle, symmetry breaking occurs at diffusion coefficients near the calculated critical value. Two different kinds of behaviour can be distinguished in this case: Oscillation in patches and stationary patterns. The second case has not been reported so far for limit cycles in the hypercycle.

In two dimensons, the formation of spirals could be observed if we started from an unstable fixed point surrounded by a limit cycle and chose the diffusion coefficient of the substrate equal to that of the replicating species and intermediates. For higher diffusuion coefficients of the substrate, we could observe qualitatively the same behaviour like in one dimension, namely oscillation in patches or formation of stationary patterns.

Outlook: Although my own experiences in this field have been quite frustrating, there may be some way to prove analytically the conjecture that all fixed points at which several species coexist are unstable in the competitive model. In the mutualistic model it might be possible to find analytical formulae for the eigenvalues of fixed points on the boundary of the simplex, since the equilibrium concentrations at these fixed points are linear functions of the flow rate (the total concentration). For the interior fixed point(s) this task seems to be hopeless.

More general interaction matrices could be examined, at least for two or three species.

It would also be worth wile to check if it is possible for some limiting case (e.g. high rates f_i) to deduce results on our model from known results on second order replication networks, using perturbation theory.

In the mutualistic model with diffusion, it is not at all clear what causes the transition between oscillatory and stationary solutions. Some qualitative model that explains why stationary solutions are favoured e.g. by high diffusion coefficients of the substrate should be found. The behaviour of the system on a two dimensional domain should be investigated in more detail.

Bibliography

[1] A. Babloyantz. *Molecules, Dynamics, and Life.* Wiley (New York), 1986.

[2] B. P. Belousov. *Sborn. referat. radiat. med.*, chapter An oscillating Reaction and its Mechanism, page 145. Medgiz (Moscow), 1959.

[3] A. Berman and R. J. Plemmons. *Nonnegative Matrices in the Mathematical Sciences.* Academic Press, New york, London, San Francisco, 1979.

[4] W. Bray. A periodic reaction in homogeneous solution and its relation to catalysis. *J. Am. Chem. Soc.*, 43:1262–1267, 1921.

[5] S. Chandrasekar. *Hydrodynamic and Hydromagnetic Stability.* Clarendon Press (Oxford), 1961.

[6] C. Darwin. *The Origin of Species.* reprinted in Penguin Classics, 1859.

[7] H. Degn. Bistability caused by substrate inhibition of peroxidase in an open reaction system. *Nature*, 217:1047, 1968.

[8] M. Eigen. Selforganization of matter and the evolution of biological macromolecules. *Die Naturwissenschaften*, 10:465–523, 1971.

[9] M. Eigen, J. McCaskill, and P. Schuster. The molecular Quasispecies. volume 75, pages 149 – 263. J. Wiley & Sons, 1989.

[10] M. Eigen and P. Schuster. The hypercycle A: A principle of natural self-organization : Emergence of the hypercycle. *Naturwissenschaften*, 64:541–565, 1977.

[11] M. Eigen and P. Schuster. The Hpercycle B: The abstract hypercycle. *Naturwissenschaften*, 65:7–41, 1978.

[12] M. Eigen and P. Schuster. The hypercycle C: The realistic hypercycle. *Naturwissenschaften*, 65:341–369, 1978.

[13] I. R. Epstein. Oscillating chemical reactions. *Sci. Am.*, 248(3):96–108, 1983.

[14] R. J. Field, E. Körös, and R. M. Noyes. Oscillations in chemical systes II: Thorough analysis of temporal oscillations in the bromate–cerium–malonic acid system. *J. Am. Chem. Soc.*, 94:8649–8664, 1972.

[15] R. J. Field and R. M. Noyes. Oscillations in chemical systems IV: Limit cycle behavior in a model of a real chemical reaction. *J. Chem. Phys.*, 60:1844–1877, 1974.

[16] P. C. Fife. *Mathematical Aspects of Reacting and Diffusing Systems.* Number 28 in Lecture notes in Biomathematics. Springer, Berlin,Heidelberg,New York, 1979.

[17] T. Geest, C. Steinmetz, R. Larter, and L. F. Olsen. Period- Doubling Bifurcations and Chaos in an Enzyme Reaction. *J. Phys. Chem*, 96:5678, 1992.

[18] P. Glansdorff and I. Prigogine. *Thermodynamic Theory of Structure, Stability and Fluctuations.* John Wiley, New York, 1971.

[19] J. Guckenheimer and P. Holmes. *Nonlinear Oscillations, Dynamical Systems, and Bifurcations of Vector Fields.* Springer (New York), 1983.

[20] H. Haken. Cooperative phenomena in systems far form equilibrium. *Rev. Mod. Phys.*, 47:67–121, 1975.

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

[22] K. Kaneko. Pattern dynamics in spatiotemporal chaos. *Physica*, 34 D:1–41, 1989.

[23] S. M. Kaushkin, Z. Yuan, and R. M. Noyes. A simple demonstration of a gas evolution oscillator. *J. Chem. Educ.*, 63(1):76–80, 1986.

[24] J. Kramer, J. Reiter, and J. Ross. Propagation of a chemical pulse in an illuminated thermochemical bistable system. *J. Chem. Phys.*, 84:1492–1499, 1986.

[25] R. Laing. *Artificial Life*, chapter Artificial Organisms: History, Problems, Directions, pages 49–61. Santa Fe Institute Studies in the Sciences of Complexity, Proc. Vol. VI. Addison Wesley (Redwood City), 1989.

[26] C. E. Langton. *Artificial Life.* Santa Fe Institute Studies in the Sciences of Complexity, Proc. Vol. VI. Addison Wesley (Redwood City), 1989.

[27] M. E. Le Van and J. Ross. Measurement and a hypothesis on periodic precitipitation processes. *J. Phys. Chem.*, 91:6300–6308, 1987.

[28] J. S. Morgan. *J. Chem. Soc. Trans.*, 109:274–283, 1916.

[29] J. D. Murray. *Mathematical Biology.* Springer (Berlin, Heidelberg, New York), 1989.

[30] S. Nakamura, K. Yokota, and I. Yamazaki. Sustained oscillations in a lactoperoxidase, NADPH and O_2 system. *Nature*, 222:794, 1969.

[31] G. Nicolis and I. Prigogine. *Self-organisation in non-equilibrium systems.* John Wiley, New York, 1977.

[32] Z. Noszticzius, W. Horsthemke, W. D. McCormick, H. L. Swinney, and W. Y. Tam. Sustained chemical waves in an annular gel reactor: a chemical pinwheel. *Nature*, 329:619–620, 1987.

[33] L. F. Olsen. The oscillatory peroxidase – oxidase reaction in an open system. *Biochim. Biophys. Acta*, 527:212, 1978.

[34] L. F. Olsen and H. Degn. Chaos in an enzyme reaction. *Nature*, 267:177, 1977.

[35] A. I. Oparin. *The Origin of Life on the Earth.* Oliver & Boyd, Edinbourgh, 1957.

[36] Q. Ouyang, V. Castets, J. Boissonade, J. C. Roux, P. De Kepper, and H. L. Swinney. Sustained patterns in chlorite–iodide reactions in a one–dimensional reactor. *Chem. Phys.*, 95:351–360, 1991.

[37] I. Prigogine. *Bull. Acad. Roy. Belg. Cl. Sci.*, 31:600, 1945.

[38] I. Prigogine and R. Lefever. Symmetry breaking instabilities in dissipative systems ii. *J. Chem. Phys.*, 48:1665–1700, 1968.

[39] J. Ross. Non–linearities in chemical reactions. temporal and spatial structures; efficiency. *Ber. Bunsenges. Phys. Chem.*, 89:605–619, 1985.

[40] F. Schlögel. Chemical Reaction Models for Non-Equilibrium Phase Transitions. *Z. Physik*, 253:147 – 161, 1972.

[41] P. Schuster and K. Sigmund. Dynamics of evolutionary optimization. *Berichte der Bunsen-Gesellschaft für physikalische Chemie*, 89:668–682, 1985.

[42] P. Schuster and K. Sigmund. Dynamics of evolutionary optimization. *Ber. Bunsenges. Phys. Chem.*, 89:668–682, 1985.

[43] P. Schuster, K. Sigmund, and R. Wolff. Dynamical systems under constant organisation I.topologigal analysis of a family of non-linear differential equations - a model for catalytic hypercycles. *Bull. Math. Biophys.*, 40:743–769, 1978.

[44] P. Schuster, K. Sigmund, and R. Wolff. Dynamical systems under constant organisation III.cooperative ond competitive behaviour of hypercycles. *J. Diff. Equ.*, 32:357–368, 1979.

[45] C. Streissler. *Autocatalytic Networks under Diffusion.* PhD thesis, Universität Wien, 1992.

[46] W. Y. Tam, W. Horsthemke, Z. Noszticzius, and H. L. Swinney. Sustained spiral waves in a continously fed unstirred chemical reactor. *J. Chem. Phys.*, 88:3395–3396, 1988.

[47] W. Y. Tam and H. L. Swinney. Spatiotemporal patterns in a one–dimensional reaction–diffusion system. *Physica*, 46D:10–22, 90.

[48] A. M. Turing. The chemical basis of morphogenesis. *Phil. Trans. Roy. Soc. - B*, 237:37–72, 1952.

[49] J. J. Tyson. *The Belousov-Zhabotinskii Reaction*, volume 10 of *Lecture Notes in Biomathematics.* Springer (Berlin, Heidelberg, New York), 1976.

[50] H. C. Urey. The plants, their origin and development. New Haven, 1952.

[51] V. Volterra. *Leçons sur la théorie mathematique de la lutte pour la vie.* Gauthier-Villars (Paris), 1931.

[52] A. T. Winfree. Varieties of spiral wave behavior: an experimentalist's approach to the theory of excitable media. *Chaos*, 1:303–334, 1991.

[53] S. E. Wolfram. *Theory and Applications of Cellular Automata.* World Scientific (Singapore), 1986.

[54] I. Yamazaki and K. Yokota. *Biochim. Biophys. Acta*, 132:310, 1967.

[55] I. Yamazaki, K. Yokota, and R. Nakajama. Analysis of the conditions causing the oscillatory oxidations of recduced nicotinamide adenine dinucleotide by horseradish peroxidase. *Biochem. Biophys. Res. Commun.*, 21:582, 1965.

[56] A. M. Žabotinskij. Periodic course of oxidation of malonic acid in solution. *Biophysics*, 9:329–335, 1964.