Linking Network Structure and Dynamics to Describe the Set of Persistent Species in Reaction Diffusion Systems

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Abstract

In this work we characterize the set of persistent species in dynamical systems related to chemical reaction networks. Chemical reaction networks consist of a set of species and a set of reaction rules describing the interactions between the species. From a reaction network, by differentiation with respect to time and space, a reaction-diffusion system can be derived describing the dynamics of the concentrations of the species. We show how double integration with respect to time and space of the solutions of the RDS conversely leads back to the reaction network and reveals all the possibly persistent subsets of species. We show that organizations as defined in chemical organization theory (COT) are strongly related to the persistent subsets of species. Organizations are subsets of species that have two properties. Firstly, they are closed, that is, there is no reaction running on them that produces new species which are not contained in the organizations. Secondly, organizations are self-maintaining. By additionally allowing for the distribution of species we generalize organizations towards distributed organizations (DOs). After introducing our concept of persistence, as the first main result of this study, we prove that for a given reaction network the set of DOs is always a lattice. The second main result is that the set of persistent species of a solution of a RDS is always a DO. By linking these two results we achieve a connection between persistence concerning a single solution of a RDS and persistence with regard to all solutions of all RDS having one and the same underlying reaction network. We show how this strongly benefits reaction network analysis. By presenting simulation results performed with Matlab we illustrate the discussed phenomena.

Keywords: reaction-diffusion system, ordinary differential equation, partial differential equation, dynamical system, persistence, reaction network, chemical organization theory, distributed organizations, long-term behavior, attractor

List of Symbols

$\mathcal{S}$	finite set of species	chapter 1
$s_i \in \mathcal{S}$	Species	chapter 1
$n = \lvert\mathcal{S}\rvert$	Number of species	chapter 1
$\mathcal{R}$	finite set of reactions	chapter 1
$r_j \in \mathcal{R}$	Reaction	chapter 1
$m = \lvert\mathcal{R}\rvert$	Number of reactions	chapter 1
$(\mathcal{S}, \mathcal{R})$	Reaction network	chapter 1
$\phi(c)$	Abstraction of c	chapter 1
	= species of c with non-zero concentration	
$\mathbb{N}_0$	Set of natural numbers including 0	chapter 1
$a_{ij} \in \mathbb{N}_0$	Number of s_i in the LHS of the reaction r_j	chapter 1
$b_{ij} \in \mathbb{N}_0$	Number of s_i in the RHS of the reation r_j	chapter 1
$n_{ij} = b_{ij} - a_{ij} \in \mathbb{Z}$	Element of the stoichiometric matrix	chapter 1
$supp(r_j)$	Support of reaction r_j	chapter 1
$N \in \mathbb{Z}^{n \times m}$	Stoichiometric matrix	chapter 1
v	Feasible flux	chapter 1
$v()$	Flux vector function	chapter 1
$k_j > 0$	Reaction constants of r_j	chapter 1
$t \geq 0$	Time variable	chapter 1
$\Omega \subseteq \mathbb{R}^p$, $p \in \mathbb{N}$	Domain with $0 < \int_\Omega dx < \infty$	chapter 1
$x \in \Omega$	Space variable	chapter 1
$\mathbb{R}^n_+$	Set of vectors of non-negative reals, i.e.,	chapter 1
	$\mathbb{R}^n_+ \equiv \{(c_1, \ldots, c_n)^T \in \mathbb{R}^n : c_1, \ldots, c_n \geq 0\}$	
$d_i \geq 0$	Diffusion rate of the species s_i	chapter 1
ν	External normal vector to the boundary $\delta\Omega$	chapter 1
$c()$	Solution of a RDS	chapter 1
$(t_l)_{l=1}^\infty$	Sequence of points in time	chapter 1
$\hat{v} = \hat{v}(c, (t_l)_{l=1}^\infty)$	Total flux (with respect to c and $(t_l)_{l=1}^\infty$)	chapter 1
$clos_1(S) = clos_1^1(S)$	Union of S and the set of all species produced	definition 2.0.1
	reactions $r_j \in \mathcal{R}$ with $supp(r_j) \subseteq S$	
$clos_1^k(S)$	$= clos_1(clos_1^{k-1}(S))$, $k \geq 1$, $clos_1^0(S) \equiv S$	definition 2.0.1
$clos(S)$	Closure of a subset $S \subseteq \mathcal{S}$ of species	definition 2.0.1
	$= \cup_{k \in \mathbb{N}} clos_1^k(S)$	
$S^\epsilon \subseteq \mathbb{R}^n_+$	ϵ-neighborhood of S	definition 3.1.1
	= concentration vectors with $c_i > \epsilon \; \forall \, s_i \in S$	
$S^{\epsilon,\delta} \subseteq \mathbb{R}^n_+$	(ϵ, δ)-neighborhood of S	definition 3.1.1
	= concentration vectors with $c_i > \epsilon \; \forall \, s_i \in S$	
	and $c_i \leq \delta \; \forall \, s_i \notin S$	
$F(C) = F(C; c, (t_l)_{l=1}^\infty)$	Frequency of occurrence of the set $C \subseteq \mathbb{R}^n_+$ of	definition 3.1.2
	concentration vectors w.r.t. a solution c and $(t_l)_{l=1}^\infty$	
$P(c)$	Set of persistent subsets of species with respect to	definition 3.1.3
	solution c of a RDS	

$\Phi(c) = \cup_{S \in P(c)} S$	Set of persistent species w.r.t. c	definition 3.1.3
$D \in \mathbb{R}^{n \times n}$	Fickian diffusivity (diagonal) matrix	section 3.4

Chapter 1

Introduction

Reaction systems are widely used to describe and to study phenomena in various areas such as Biochemistry [54] or research on the origin of life [24, 56]. Those systems are often very complex. Reaction network theory provides various approaches to deal with that complexity like for example deficiency [12, 25], RAF theory [54], Chemical Organization Theory [7], subnetwork analysis [5], elementary modes [51], graph theory [16, 52] or Lyapunov functions [38]. Among others, these approaches allow for analyzing behavior of reaction systems including the question which species can persist in the long-run [47, 42].

In this work we broadly discuss this question: Which properties do those subsets of species have that persist in a dynamical reaction system, in which species interactions are described by reactions as known from chemistry?

First, we introduce (chemical) reaction networks and reaction-diffusion systems (RDS) and give an outline of this work. The symbols and abbreviations used in this paper are summarized in Table 1. Given a finite set $\mathcal{S} = \{s_1, \ldots, s_n\}$ of n *species* (or molecules) together with a finite set $\mathcal{R} = \{r_1, \ldots, r_m\}$ of m *reactions*, we call $(\mathcal{S}, \mathcal{R})$ a *(chemical) reaction network*. Each reaction $r_j \in \mathcal{R}$, $j = 1, \ldots, m$, can be depicted by a so-called *reaction equation* using a right arrow

$$\sum_{i=1}^{n} a_{ij} s_i \to \sum_{i=1}^{n} b_{ij} s_i \tag{1.1}$$

where $a_{ij}, b_{ij} \in \mathbb{N}_0 \equiv \mathbb{N} \cup \{0\}, i = 1, \ldots, n,\ j = 1, \ldots, m$. The difference of the matrices $A = (a_{ij}) \in \mathbb{N}^{n \times m}$ and $B = (b_{ij}) \in \mathbb{N}^{nxm}$ is called *stoichiometric matrix* $N = B - A \in \mathbb{Z}^{nxm}$. For a reaction $r_j \in \mathcal{R}$, $j \in \{1, \ldots, m\}$, we call the set of species s_i with $a_{ij} > 0$ the *support* of r_j, denominated by $support(r_j)$ or $supp(r_j)$. Note that if a species $s_i \in \mathcal{S}$ is reduced by a reaction $r_j \in \mathcal{R}$, that is $n_{ij} < 0$, then $s_i \in supp(r_j)$, that is, $a_{ij} > 0$. For a reaction $r_j \in \mathcal{R}$, $j \in \{1, \ldots, m\}$, the species s_i with $b_{ij} > 0$ are called *products* of r_j.

A dynamical system can be derived from a reaction network by assigning to each species $s_i \in \mathcal{S}$, $i = 1, \ldots, n$, and every time $t \in \mathbb{R}_+ \equiv \{u \in \mathbb{R} : u \geq 0\}$ a non-negative concentration value $c_i(t)$. We call a map ϕ mapping a concentration vector back to a subset of species from the power set $\mathcal{P}(\mathcal{S})$ of the set of species, that is,

$$\phi : \mathbb{R}^n_{\geq 0} \to \mathcal{P}(\mathcal{S}),\ c \mapsto \phi(c), \tag{1.2}$$

abstraction, if

$$\phi(c) \equiv \{s_i \in \mathcal{S} : c_i > 0 \text{ for any } i \in \{1, \ldots, n\}\}. \tag{1.3}$$

Thus $\phi(c)$ is the subset of species that contains exactly those species that have a strictly positive concentration value. Species with concentration equal zero do not belong to $\phi(c)$. The abstraction ϕ plays an important role in this work, since it allows

for linking the concentration vectors of a solution of a dynamical system with its underlying reaction network.

Now we come to the question of how the reactions rulethe concentration values of the species in a dynamical system. For a given subset $S \subseteq \mathcal{S}$ of species, we call a vector $v \in \mathbb{R}^n_+$ *feasible flux* with respect to S, if for all $r_j \in \mathcal{R}$, $j = 1, \ldots, m$, holds

$$v_j \begin{cases} > 0, & \text{iff } support(r_j) \subseteq S, \\ = 0, & \text{otherwise.} \end{cases} \tag{1.4}$$

A function

$$v : \mathbb{R}^n_+ \to \mathbb{R}^m_+, \; c \mapsto v(c), \tag{1.5}$$

that is Lipschitz continuous on every bounded subset of $\mathbb{R}^n_+$, is called *flux vector function*, if for every $c \in \mathbb{R}^n_+$ the vector $v(c)$ is a feasible flux with respect to $\phi(c)$. Thus the flux vector function maps any vector of concentrations to a vector of reaction rates. If for example mass-action kinetics is applied ($v_j(c) = k_j \cdot c_1^{a_{1j}} \cdot \ldots c_n^{a_{nj}}$ with real *reaction constants* $k_j > 0$, $j = 1, \ldots, m$,) to constructing v, then v is a flux vector function, because then it holds true that $v_j(c)$ is strictly positive, if and only if the concentrations of all the species from the support of $r_j \in \mathcal{R}$ are strictly positive. This represents the common assumption, that a reaction occurs, if and only if all of its reactants are present at the same time and place [12].

By defining the derivatives of the concentrations with respect to time we obtain a dynamical system as a system of ODEs

$$\frac{\mathrm{d}}{\mathrm{d}t} c(t) = \dot{c}(t) \equiv N \cdot v(c(t)), \tag{1.6}$$

which describes how the change of the concentrations of the species from $\mathcal{S}$ results from the concentrations via the set of reactions $\mathcal{R}$. In thiscase we say that the reaction network *underlies* the dynamical system. By adding initial conditions $c(0) = c^0 \in \mathbb{R}^n_+$ we get an *initial value problem.*

If besides the time variable t, a space variable $x \in \Omega$ from a connected *domain* $\Omega \subset \mathbb{R}^p$, $p \in \mathbb{N}$, with $0 < \int_\Omega dx < \infty$ and a C^2 smooth boundary $\partial\Omega$ is added, we can model effects like diffusion by differentiating twice with respect to x. Thus we arrive at describing the dynamics of the concentrations $c_i(x,t)$, $i = 1, \ldots, n$, of the species for each location $x \in \Omega$ by a system of PDEs

$$\frac{\partial}{\partial t} c_i(x,t) = \underbrace{N \cdot v(c(x,t))}_{reactions} + \underbrace{d_i \frac{\partial^2}{\partial x^2} c_i(x,t)}_{diffusion}, \; i = 1, \ldots, n, \tag{1.7}$$

where $d_i \geq 0$, $i = 1, \ldots, n$, are the *diffusion rates* of the species. By adding twice continuously differentiable nonnegative *initial conditions*

$$c_i(x,0) = c_i^0(x) \geq 0, \quad x \in \Omega, \; i = 1, \ldots, n, \tag{1.8}$$

and *homogeneous Neumann boundary conditions (BCs)*,

$$\frac{\partial}{\partial \nu} c_i(x,t) = 0, \quad x \in \partial\Omega, \; i = 1, \ldots, n, \tag{1.9}$$

where $\nu \in \mathbb{R}^n$ is the external normal vector to the boundary $\delta\Omega$, we get a boundary value problem, a so-called *reaction-diffusion system (RDS)* with a solution

$$c : \Omega \times \mathbb{R}_+ \to \mathbb{R}^n, \ (x,t) \mapsto c(x,t). \tag{1.10}$$

We assume that its derivatives $\frac{\partial c}{\partial t}$ and $\frac{\partial^2 c}{\partial x^2}$ are each continuous with respect to x and t (of course, for $t = 0$, continuity with respect to t holds from above only). Thus the solution c itself is continuous with respect to x and t too. We furthermore assume that it is bounded, that is, there exists a real $K \in \mathbb{R}$ such that $|c(x,t)| < K$ for all $x \in \Omega$, $t \geq 0$. Under certain conditions the existence and uniqueness of a solution to a RDS as defined above results from standard theorems [15].

After having introduced reaction networks and reaction-diffusion systems we now briefly outline the contributions of this paper. We call a monotonously increasing sequence $(t_j)_{j=1}^{\infty}$ of nonnegative real numbers tending towards infinity with

$$1 \leq t_{j+1} - t_j \leq Z,$$

$j \in \mathbb{N}$, for some $Z \in \mathbb{R}_+$ *sequence of points in time*. We call a vector

$$\hat{v} = \hat{v}(c, (t_l)_{l=1}^{\infty}) \equiv \lim_{j\to\infty} \frac{1}{t_{j+1} - t_j} \int_{t_j}^{t_{j+1}} \int_{x\in\Omega} v(c(x,t))\, dx\, dt \in \mathbb{R}_+^m \tag{1.11}$$

constructed from a single solution c of a RDS by using the sequence $(t_j)_{j=1}^{\infty}$ a *total flux* with respect to c and $(t_j)_{j=1}^{\infty}$ if

$$N\hat{v} = 0. \tag{1.12}$$

Thus double-integration of a solution of a RDS connects the dynamics to a property of the underlying reaction network, namely the stoichiometric matrix. Note that the total flux is not necessarily a feasible flux for any subset of species. In this work we focus on the question which of the components $\hat{v}_j$, $j = 1, \ldots, m$, of the vector $\hat{v}$ are strictly positive and which are equal zero. Each of the components, that is strictly positive, represents a reaction, that is active in the long-run of the solution c of the RDS. Thus, the components of $\hat{v}$ with $\hat{v}_j > 0$ determine, which species must persist in the long-run to support the respective reactions r_j.

In [7] it was shown, that if an ODE system approaches a fixed point, then the set of persistent species is an organization in the sense of Chemical Organization Theory (COT). An organization is a subset $S \subseteq \mathcal{S}$ of species that is

1. closed, that is, none of the reactions supported by this subset of species produces a species, that is not contained in this subset,

2. and self-maintaining, that is, there is a feasible flux $\hat{v} \in \mathbb{R}_+^m$ such that $N \cdot \hat{v} \geq 0$.

We will introduce COT in more detail in the Preliminaries. Since we regard bounded solutions only, all the results of this work concerning the dynamics of RDS hold for $N\hat{v} = 0$. Solely in section 2.0.1 and in section 3.2 the inequality $N\hat{v} \geq 0$ is used.

In [42] we have generalized the fixed points result from [7] mentioned above. We have shown, that whenever the solution of an ODE system approaches an arbitrary attractor that exhibits only one single subset of persistent species, this subset is an organization [42]. Such attractors might include periodic or even chaotic behavior. But we have also cited solutions of reaction-diffusion systems with other types of

attractors, like for example heteroclinic orbits, that exhibit more than one subset of persistent species, which are 2distributed with respect to time [41]. We had proven that for such solutions the minimal subsets of persistent species are organizations 2but we could neither prove that statement for all subsets of persistent species nor for their union [42].

In this work we generalize the techniques developed for ODE systems in [42] to comprise reaction-diffusion systems with solutions exhibiting more than one subset of persistent species, especially systems with spatial extension and diffusion effects, that is, involving PDEs. We provide simulation results of RDS exhibiting solutions c with total fluxes $\hat{v}$ that are not feasible fluxes. Instead, reactions that would be active for a feasible flux, are inactive. This is due to a temporal or spatial separation of the persistent species amongst several subsets. We show that neither all of these subsets nor their union necessarily is an organization in the sense of classical COT. We therefore generalize the definition of organizations toward distributed organizations (DOs) to capture the newly identified phenomenon of the persistent species being distributed. Note, that like organizations, DOs solely depend on the reaction network underlying the dynamical system. We finally arrive at two main results. First, given a reaction network, the set of DOs forms a lattice which hierarchically relates the DOs to one another. Secondly, for every solution of a RDS the set of persistent species is always a DO of the underlying reaction network. Whereas the first result provides information about the overall structure of a reaction network the second one characterizes the inner structure of the set of persistent species with regard to a single solution of a RDS. We show how connecting these two perspectives supports reaction network analysis. The overall situation is illustrated in Fig. 1.1.

This paper is organized as follows. In the *Preliminaries*, we first give a short overview of Chemical Organization Theory (COT) including the most important definitions and then discuss the problem of persistence. In the *Results* we first state the concept of persistence this work relies on. Then we define distributed organizations (DOs) and prove that they always form a lattice as one of the two main results of this work. We discuss the role of closed subsets of species in the dynamics. Subsequently, as the second main result, we prove that the set of persistent species with respect to a solution of a RDS is always a DO of the underlying reaction network. Then we show how to apply the fore-mentioned results to analyze DO lattices and to draw conclusions about the long-term behavior of RDS. Then we state some remarks on how to compare several DO lattices and how to put them into hierarchies. Finally, we present three example simulation results and discuss them with respect to the theoretical results. In the *Conclusions* we discuss the results and mention some directions for future work. In the *Supplementary Materials*, by lemma 5.0.2, we rank our definition of persistence by comparing it to a weaker and a stronger definition often found in literature (see section 2.0.2).

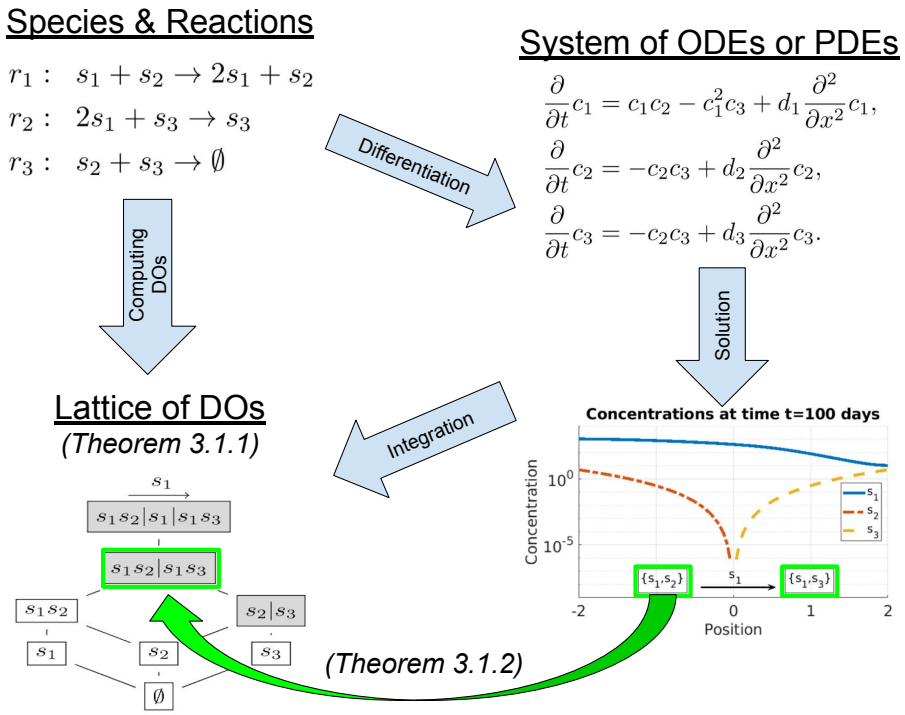


FIGURE 1.1: Illustration of the relation between a dynamical system (upper right), its solutions (lower right), its underlying reaction network (upper left), and the lattice of DOs (lower left) of the reaction network for Example 1 presented in section 3.6.1. Systems of ODEs or PDEs are built from reaction networks by fixing the derivatives of the species concentrations according to the reaction rules. Integrating all the solutions of a dynamical system leads back to the reaction network and reveals the lattice of DOs. Also notated in the figure, the main results of this paper: The set of persistent species of every bounded solution of a RDS is a DO (theorem 3.4.1) and the set of DOs of every reaction network forms a lattice (theorem 3.2.1). It is shown how the fact that every potentially persistent set of species is part of the lattice of DOs allows for studying the interplay of different subsets of species with regard to their persistence.

Chapter 2

Preliminaries

2.0.1 Organizations

Chemical Organization Theory (COT) is a branch of reaction network theory which deals with analyzing reaction networks to understand the behavior of dynamical systems. In the last decades a lot of properties of reaction networks were proven to be useful for this purpose. The first steps into that direction were taken by Feinberg, Horn, and Jackson [12, 25]. They defined terms like deficiency, balance, and reversibility to draw conclusions about the steady states, their stability, and the persistence of species in dynamical systems.

Inspired by Fontana and Buss [14], abstract models of autopoiesis [56], autocatalytc set evolution [10, 31, 49], and artificial chemistries [2, 29], Dittrich and Speroni d. F. [7] introduced Chemical Organization Theory in order to describe the time evolution of complex chemical systems undergoing qualitative transitions in their species compositions. Given a reaction network as a set of species and a set of reaction rules, COT identifies a hierarchy of closed and self-maintaining subsets of species, called organizations [7]. A chemical organization is derived from the rules of the reaction network [7] and thus is independent of kinetic details, such as rate constants. The COT approach allows for analyzing, understanding and engineering even complex, high-dimensional systems by decomposing it into a Hasse diagram of interrelated organizations. This allows for tracking the qualitative transitions as movements in the hierarchy of organizations [36, 39, 45]. Furthermore, there is a proven link to the long-term behavior, that is, all trajectories of the dynamical system converge to organizations [42, 33]. The approach can be applied in various domains where models can be formulated as reaction networks, like atmospheric and combustion chemistry [4], origin of life [24], systems biology [30], ecology [57], cognitive science [21], complex systems [22], computer science [40], and social sciences [8].

Now we state the basics of COT [13] by first introducing the closure of a subset of species and then defining organizations.

Definition 2.0.1 (Closure of a subset of species)**.** *Given a reaction network $(\mathcal{S}, \mathcal{R})$ and a subset $S \subseteq \mathcal{S}$ of species. We define the set operation*

$$clos_1(S) \equiv S \cup \{s_i \in \mathcal{S} : \exists r_j \in \mathcal{R} : supp(r_j) \subseteq S, b_{ij} > 0\}, \tag{2.1}$$

that is, the set of species from S together with all species, that are produced by the reactions, which are active on S. From this we define a monotonously increasing sequence of sets

$$\begin{aligned} clos_1^0(S) &= S, \\ clos_1^1(S) &= clos_1(S), \\ clos_1^2(S) &= clos_1(clos_1(S)), \\ clos_1^3(S) &= clos_1(clos_1(clos_1(S))), \\ &\dots \\ clos_1^{k_{min}+1}(S) &= clos_1(clos_1^{k_{min}}(S)), \end{aligned}$$

where $k_{min} = \min\{k \in \mathbb{N}_0 : clos_1^{k+1}(S) = clos_1^k(S)\}$. *Since the set of species and the set of reactions are finite,* k_{min} *is finite and thus the closure of S is unique and finite. We call the set*

$$clos(S) \equiv clos_1^{k_{min}}(S) \tag{2.2}$$

the closure of S.

For every subset S of species, the closure $clos(S)$ of S does not contain the support of any reaction, that produces a species, which is not already contained in S. We call this property, which the closure of any subset of species pertains, *closedness property*. Together with self-maintenance, these are the two properties of an organization. We assume that the set $\mathcal{S}$ of all species of a reaction network $(\mathcal{S}, \mathcal{R})$ is closed.

Definition 2.0.2 (Closedness, self-maintenance and organizations)**.** *Given a reaction network* $(\mathcal{S}, \mathcal{R})$ *and a subset* $S \subseteq \mathcal{S}$ *of species then we call S*

1. *self-maintaining if there is a feasible flux v with respect to S such that*

$$N \cdot v \geq 0, \tag{2.3}$$

   that is, all elements of $N \cdot v$ *are zero,*

2. *closed if*

$$clos(S) = S, \tag{2.4}$$

3. *organization if it is self-maintaining and closed.*

Spatial effects are crucial to systems of Partial Differential Equations (PDEs) particularly reaction-diffusion systems that are widely used in Biosciences, for example in virus dynamics [48, 35, 32, 50] as well as DNA segregation and cell division [9, 28, 34, 19, 28, 27, 26]. So far there is only one work combining COT and spatial effects [44]. In that work it is shown how different boundary conditions of RDS can be incorporated into COT analysis by adapting reaction networks appropriately. In this paper we bridge the remaining gap between COT and spatial systems.

2.0.2 Persistence

Persistence comprises various ideas from different fields, for example ecology, chemistry, and biology. It is applied to a huge multitude of different model types like for example, discrete and continuous models, ODE and PDE models, deterministic or stochastic models, models having a spatial dimension or not, and so on. As for all these types of models, for the reaction-diffusion systems discussed in this work ,

there are a lot of different terms related to persistence, such as permanence [23, 41, 6, 3], coexistence [20, 41], extinction [1, 20], strong persistence [1], uniform persistence [20] etc. For an overview of these concepts we refer the reader to [23, 1] e.g. There are many aspects of persistence regarding dynamical systems. For example, persistence can be analyzed with regard to a single species or a whole system of species. Also, persistence concerning a single solution and all possible solutions of a RDS arising from different initial conditions or reaction constants can be distinguished. Furthermore, there are different grades of persistence, named by terms like weak or strong persistence. In this work we concern the subsets of persistent species with regard to a single solution of a RDS and link it with the persistence regarding the whole of all solutions of any RDS with the same underlying reaction network.

Chapter 3

Results

3.1 Persistence

In this subsection we present the concept of persistence on which this study relies. For this purpose we first define two kinds of neighborhoods, which are special subsets of the state space of concentration vectors. We also define a frequency of occurrence for any subset of the state space and, based on that, we introduce persistent subsets of species. From the persistence of a subset of species we derive the persistence of a species, which we analyze further and compare to other grades of persistence based on the limits superior and the limits inferior of the concentration values of that species. In this subsection, we assume that the solution $c_i(x,t)$ of an RDS introduced in Section 1 is nonnegative for all $t > 0$, $x \in \Omega$, $s_i \in \mathcal{S}$. We will prove this in Section 3.3.

Definition 3.1.1 (Neighborhood of a subset of species in the space of concentrations)**.** *Given a subset $S \subseteq \mathcal{S}$ of species and real numbers $\varepsilon, \delta > 0$, we call the set*

$$S^{\varepsilon,\delta} \equiv \{c \in \mathbb{R}^n_+ : \ c_s \begin{cases} > \varepsilon & \text{iff } s \in S \\ \leq \delta & \text{iff } s \notin S \end{cases}\} \subseteq \mathbb{R}^n_{\geq 0} \tag{3.1}$$

of concentration vectors the (ε,δ)-neighborhood of S, and for $\delta = \infty$ we call the set

$$S^{\varepsilon} \equiv S^{\varepsilon,\infty} \equiv \{c \in \mathbb{R}^n_+ : \ c_s > \varepsilon \text{ iff } s \in S\} \subseteq \mathbb{R}^n_{\geq 0} \tag{3.2}$$

of concentration vectors the ε-neighborhood of S.

There are lower and upper boundaries for the flux vector function values $v(c)$ depending on whether or not c is in some special ε-neighborhoods. The following remark provides these boundaries, which we need to prove the results of this work.

Remark 3.1.1 (Boundaries of the fluxes)**.** *Given an RDS with underlying reaction network $(\mathcal{S},\mathcal{R})$, a reaction $r_j \in \mathcal{R}$ for a $j \in \{1,\ldots,m\}$, and a subset $S \subseteq \mathcal{S}$ of species, the following hold:*

- *If $supp(r_j) \subseteq S$ then for all $\varepsilon > 0$ there is a lower boundary $L(\varepsilon) > 0$ for the flux vectors $v_j(c)$ such that*

$$0 < L(\varepsilon) < v_j(c) \tag{3.3}$$

  for all $c \in S^{\varepsilon}$.

- *If $supp(r_j) \nsubseteq S$ then for all $\varepsilon > 0$ there is an upper boundary $U(\varepsilon) > 0$ for the flux vectors $v_j(c)$ such that*

$$0 \leq v_j(c) \leq U(\varepsilon) \ \Leftrightarrow \ c \notin support(r_j)^{\varepsilon} \tag{3.4}$$

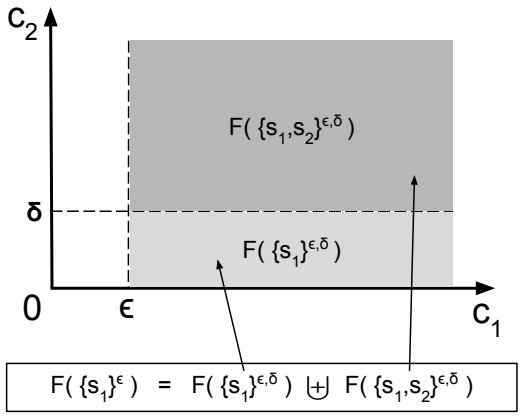


FIGURE 3.1: [46] Illustration of Remark 3.1.2 for an example with two species s_1 and s_2. The ε-environment of $\{s_1\}$ is a disjoint union of the (ε,δ)-environments of $\{s_1\}$ and $\{s_1,s_2\}$.

and $\lim_{\varepsilon\to 0} U(\varepsilon) = 0$.

Proof. The proof follows from the definition of the flux vector function $v()$ in the introduction, that is, its continuity and feasibility property, and from the definitions of neighborhoods in Definition 3.1.1. □

Remark 3.1.2 (Disjoint decomposition of ε-neighborhoods)**.** *Given a reaction network $(\mathcal{S},\mathcal{R})$, a subset $\tilde{S}\subseteq\mathcal{S}$ of species, and real numbers $\varepsilon,\delta>0$. Then the ε-environment $\tilde{S}^{\varepsilon}$ of $\tilde{S}$ is a disjoint union of (ε,δ)-environments $S^{\varepsilon,\delta}$ of all subsets $S\subseteq\mathcal{S}$ of species with $\tilde{S}\subseteq S$. That is,*

$$\tilde{S}^{\varepsilon} = \biguplus_{\tilde{S}\subseteq S} S^{\varepsilon,\delta}. \tag{3.5}$$

This holds true especially for $\varepsilon=\delta$.

This is illustrated in Figure 3.1. Definition 3.1.2 is a pre-stage to persistence and shows the strong relation to the construction of the vector $\hat{v}$ sketched in Equation 1.11.

Definition 3.1.2 (Frequency of occurrence of concentration vectors)**.** *Given a solution c of an RDS, a subset $C\subseteq\mathbb{R}^n_+$ of the set of concentration vectors, and a sequence $(t_j)_{j=1}^{\infty}$ of points in time, we call the nonnegative number*

$$F(C;c,(t_j)_{j=1}^{\infty}) \equiv \limsup_{l\to\infty} \frac{1}{t_{j+1}-t_j}\int_{t_j}^{t_{j+1}}\int_{\{x\in\Omega:\, c(x,t)\in C\}} dx\,dt \tag{3.6}$$

the frequency of occurrence of C (with respect to c and $(t_j)_{j=1}^{\infty}$) and write for short $F(C)$ if it is clear to which solution c and which sequence $(t_j)_{j=1}^{\infty}$ it relates.

Now we state the main definition of persistence regarding a single solution c of an RDS.

Definition 3.1.3 (Persistent subsets of species and persistent species)**.** *Given a solution c of an RDS with an underlying reaction network $(\mathcal{S},\mathcal{R})$, we call a subset $S\subseteq\mathcal{S}$ of species persistent (with respect to c) if for all sequences $(t_j)_{j=1}^{\infty}$ of points in time there is an $\varepsilon>0$*

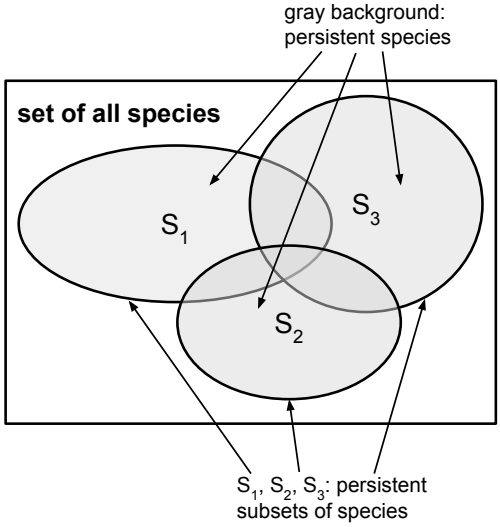


FIGURE 3.2: [46] Overview of the terms regarding persistence as defined and used in this work.

such that for all $\delta > 0$ *the frequency of occurrence* $F(S^{\varepsilon,\delta})$ *of* $S^{\varepsilon,\delta}$ *with respect to* c *and* $(t_j)_{j=1}^{\infty}$ *is strictly positive, that is,*

$$F(S^{\varepsilon,\delta}) = \limsup_{j\to\infty} \frac{1}{t_{j+1}-t_j} \int_{t_j}^{t_{j+1}} \int_{\{x\in\Omega:\, c(x,t)\in S^{\varepsilon,\delta}\}} dx\, dt > 0. \tag{3.7}$$

We denote the set of persistent subsets of species $P(c)$*, i.e.,*

$$P(c) \equiv \{S \subseteq \mathcal{S} :\ S \text{ is persistent with respect to } c\}. \tag{3.8}$$

We call a single species $s \in \mathcal{S}$ *persistent (with respect to* c*) if* s *is contained in at least one of the persistent subsets of species, i.e.,*

$$s \in \cup\{S \subseteq \mathcal{S} :\ S \in P(c)\}. \tag{3.9}$$

We say that a species $s \in \mathcal{S}$ *goes extinct (with respect to* c*) if it is not persistent with respect to* c*. We denote the set of persistent species* $\Phi(c)$*, i.e.,*

$$\Phi(c) \equiv \{s \in \mathcal{S} :\ s \text{ is persistent with respect to } c\} = \cup\{S \subseteq \mathcal{S} :\ S \in P(c)\}. \tag{3.10}$$

See Figure 3.2 for an illustration of the concept of persistence introduced above. It is important to note that Definition 3.1.3 draws a clear distinction between the species within a persistent set S and those outside of S. More precisely, a strictly positive frequency of occurrence of S not only demands the co-occurrence of the species from S but also the simultaneous disappearance of the species that are not elements of S. Our second simulation example in Section 3.6.2 illustrates this clearly, since there we have an RDS with solution c with a set $P(c) = \{\{s_1\}, \{s_2\}, \{s_3\}, \{s_1, s_2\}, \{s_1, s_3\}, \{s_2, s_3\}\}$ of persistent subsets of species. But the set $\mathcal{S} = \{s_1, s_2, s_3\}$ of all species is not persistent even though it contains persistent species.

Whereas in Definition 3.1.3 we derived the persistence of a single species from the persistence of subsets of species, in Lemma 3.1.1 we provide an immediate criterion for the persistence of a single species.

Lemma 3.1.1 (ε-neighborhood criterion for persistent species)**.** *Given a solution c of a RDS with an underlying reaction network $(\mathcal{S},\mathcal{R})$, a species $s_i \in \mathcal{S}$ is persistent with respect to c, that is,*

$$s_i \in \Phi(c) = \cup_{S\in P(c)} S \tag{3.11}$$

if and only if for all sufficiently small $\varepsilon > 0$ and every sequence $(t_j)_{j=1}^{\infty}$ of points in time the frequency $F(\{s_i\}^\varepsilon)$ of occurrence of $\{s_i\}^\varepsilon$ is strictly positive, that is,

$$F(\{s_i\}^\varepsilon) \equiv \limsup_{l\to\infty} \frac{1}{t_{l+1}-t_l} \int_{t_l}^{t_{l+1}} \int_{\{x\in\Omega:\, c_i(x,t)>\varepsilon\}} dx\,dt > 0. \tag{3.12}$$

Proof. 1. First we prove that Equation 3.12 follows from $s_i \in \Phi(c)$. Thus, we assume, that s_i is persistent, that is, there is a persistent subset $S \in P(c)$ with $s_i \in S$. Thenfor all sequences $(t_j)_{j=1}^{\infty}$ of points in time there is an $\varepsilon > 0$ such that for all $\delta > 0$,

$$F(S^{\varepsilon,\delta}) = \limsup_{j\to\infty} \frac{1}{t_{j+1}-t_j} \int_{t_j}^{t_{j+1}} \int_{\{x\in\Omega:\, c(x,t)\in S^{\varepsilon,\delta}\}} dx\,dt > 0, \tag{3.13}$$

and so

$$\begin{aligned}
0 \;<\; & F(S^{\varepsilon,\delta}) \\
= \; & \limsup_{j\to\infty} \frac{1}{t_{j+1}-t_j} \int_{t_j}^{t_{j+1}} \int_{\{x\in\Omega:\, c(x,t)\in S^{\varepsilon,\delta}\}} dx\,dt \\
\le \; & \limsup_{j\to\infty} \frac{1}{t_{j+1}-t_j} \int_{t_j}^{t_{j+1}} \int_{\{x\in\Omega:\, c(x,t)\in S^{\varepsilon}\}} dx\,dt \\
\le \; & \limsup_{j\to\infty} \frac{1}{t_{j+1}-t_j} \int_{t_j}^{t_{j+1}} \int_{\{x\in\Omega:\, c(x,t)\in \{s_i\}^{\varepsilon}\}} dx\,dt \\
= \; & \limsup_{j\to\infty} \frac{1}{t_{j+1}-t_j} \int_{t_j}^{t_{j+1}} \int_{\{x\in\Omega:\, c(x,t)>\varepsilon\}} dx\,dt.
\end{aligned} \tag{3.14}$$

From Definition 3.1.2 it follows that $F(\{s_i\}^\varepsilon) > 0$ for all sufficiently small $\varepsilon > 0$.

2. Now we prove the other direction, that is, we assume that there is an $\varepsilon > 0$ such that for every sequence $(t_j)_{j=1}^{\infty}$ of points in time, Equation 3.12 holds true. So for all $\delta > 0$,

$$\begin{aligned}
0 \quad & < \quad F(\{s_i\}^\varepsilon) \\
& \overset{\text{Remark 3.1.2}}{=} \quad F\Big(\biguplus_{s_i\in S} S^{\varepsilon,\delta}\Big) \\
& = \quad \sum_{s_i\in S} F(S^{\varepsilon,\delta}).
\end{aligned} \tag{3.15}$$

Since the sum is finite, there is a subset $S \subseteq \mathcal{S}$ of species with $F(S^{\varepsilon,\delta}) > 0$ and $s_i \in S$. Thus S is persistent, and the proof is completed.

□

In chapter 5 we provide Lemma 5.0.2 and Lemma 5.0.1. The latter is necessary to prove the former, and Lemma 3.1.1 is needed for the proofs of both. Both Lemma 5.0.2

and Lemma 5.0.1 are not necessary to prove the main results of this work. But Lemma 5.0.2 helps in assessing our concept of persistence of a species as defined in Definition 3.1.3 by comparing it to two other types of persistence which can be derived from the concentration values of a species as well. Briefly, Lemma 5.0.2 states that for a given solution c of an RDS with an underlying reaction network $(\mathcal{S}, \mathcal{R})$ and an arbitrary species $s_i \in \mathcal{S}$, the following two conclusions hold:

$$\liminf_{t\to\infty} \int_{x\in\Omega} c_i(x,t)\,dx > 0 \;\Rightarrow\; s_i \text{ is persistent w.r.t. } c \;\Rightarrow\; \limsup_{t\to\infty} \int_{x\in\Omega} c_i(x,t)\,dx > 0. \tag{3.16}$$

This shows that our concept of persistence can be regarded as a refinement of other definitions of persistence. Mincheva and Siegel [37], by using so-called Volpert indices, proved for an RDS with mass-action kinetics the nonnegativity of all concentrations of all species for all finite times. They also proved the positiveness of the concentration of all reachable species. The set of reachable species is what is called closure in COT. The Volpert indices correspond to the indices k in the notation of the sets $clos_1^k(S)$, $i \in \mathbb{N}$, that we used in Definition 2.0.1 of this work. In Section 3.3 of this study we prove for more general kinetics that the set of species existent at a location of the domain at an arbitrary time immediately produces its closure. Furthermore, we complement the results from [37] in Section 3.4 by identifying those subsets of species, that persist for time approaching infinity. We show that they are special substructures of the underlying reaction networks of the RDS which we call DOs and define in Section 3.2. Note, that if the reaction network is not given, one can derive it from the RDS or the ODE system. This is exemplified in [43], Fig. 1. More details about the relation between differential equations and their underlying reaction networks can be found in [53, 11].

3.2 Distributed Organizations

In this subsection we first define DOs as a generalization of organizations and then compare these two terms. After proving that computing DOs is NP-hard, we prove that the set of all DOs of a reaction network forms a lattice.

A DO consists of one or more subsets of species that are each closed and together obey a generalized kind of self-maintenance. We now present a precise definition.

Definition 3.2.1 (Distributed organizations (DOs))**.** *Given a reaction network $(\mathcal{S}, \mathcal{R})$, a subset $D \subseteq \mathcal{S}$ is a DO if and only if there are k, $k \in \mathbb{N}$, different subsets $S_1, \ldots, S_k \subseteq D$ with*

$$D = \cup_{i=1}^{k} S_i \tag{3.17}$$

such that

1. *all S_i, $i = 1, \ldots, k$, are closed;*
2. *there is a vector $\hat{v} \in \mathbb{R}_+^m$, $\hat{v} \geq 0$, such that*

$$N\hat{v} \geq 0; \tag{3.18}$$

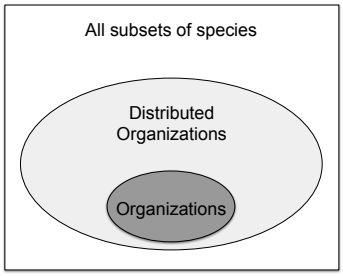


FIGURE 3.3: [46] Illustration of the relation between organizations and distributed organizations.

3. *and there is a feasible flux* $\hat{v}^i \in \mathbb{R}^m_+$, $\hat{v}^i \geq 0$, *with respect to each subset* S_i, $i = 1, \ldots, k$, *with*

$$\hat{v} = \sum_{i=1}^{k} \hat{v}^i. \tag{3.19}$$

Collectively, we call the second and third items of the list above the self-maintenance property of a DO. We say "D is distributed to the S_i*" or "the* S_i *are a distribution of D". When listing the elements of the subsets* S_i, $i = 1, \ldots, k$, *of species, we use a special notation, for example, if D is distributed to* $S_1 = \{s_1, s_2\}$ *and* $S_2 = \{s_1, s_3\}$, *we write*

$$D = S_1 \cup S_2 = \{s_1 s_2 | s_1 s_3\}. \tag{3.20}$$

Note that a species can be contained in several subsets S_i, $i = 1, \ldots, k$, of a DO, and a DO can be empty. The next lemma elucidates the relation between organizations and DOs. The situation is illustrated in Figure 3.3.

Lemma 3.2.1 (Relation of organizations and DOs)**.**

1. *Every organization of a reaction network* $(\mathcal{S}, \mathcal{R})$ *is a DO of that reaction network.*
2. *Every DO of a reaction network* $(\mathcal{S}, \mathcal{R})$ *that has a distribution to a single subset that is* $k = 1$ *in Definition 3.2.1 is an organization.*
3. *There exist reaction networks that exhibit DOs that are not organizations.*

Proof. 1. Let O be an organization of a reaction network $(\mathcal{S}, \mathcal{R})$. Then O is a DO that is distributed to a single subset $S_1 = O$, since O is closed and, furthermore, self-maintaining both, in the way organizations are self-maintaining and in the way DOs are self-maintaining.

2. This follows from the previous item.

3. Let $\mathcal{S} \equiv \{s_1, s_2\}$ and $\mathcal{R} \equiv \{r_1 : s_1 + s_2 \to \emptyset\}$ be the set of species (resp., reactions) of the reaction network $(\mathcal{S}, \mathcal{R})$. Then $D \equiv \{s_1 | s_2\}$ is a DO but not an organization. □

Remark 3.2.1 (DOs not being organizations)**.** *Assume a DO* $D = \{S_1 | S_2 | \ldots | S_k\}$ *with* $\hat{v} = \sum_{i=1}^{k} \hat{v}^i$ *such that* $N\hat{v} = 0$ *and* $\hat{v}^i$, $i = 1, \ldots, k$, *are feasible fluxes with respect to the subsets* S_i, $i = 1, \ldots, k$.

If $\cup_{i=1}^{k} S_i$ *is closed and self-maintaining, then D is an organization. This is especially the case if there is no reaction* $r_j \in \mathcal{R}$ *with* $supp(r_j) \subseteq \cup_{i=1}^{k} S_i$ *but* $supp(r_j) \nsubseteq S_i$ *for all*

$i = 1, \ldots, k$, since in this case $\hat{v}$ from above is a feasible flux with respect to $\cup_{i=1}^{k} S_i$ and $\cup_{i=1}^{k} S_i$ is closed because all the S_i, $i = 1, \ldots, k$, are closed.

On the other hand, if there is a reaction $r_j \in \mathcal{R}$ with $supp(r_j) \subseteq \cup_{i=1}^{k} S_i$ but $supp(r_j) \nsubseteq S_i$ for all $i = 1, \ldots, k$, then $\hat{v}$ is not a feasible flux with respect to $\cup_{i=1}^{k} S_i$ since $\hat{v}_j = 0$. Such a reaction can

1. *produce new species that are not contained in $\cup_{i=1}^{k} S_i$, and then $\cup_{i=1}^{k} S_i$ is not closed;*
2. *prevent $\cup_{i=1}^{k} S_i$ from being self-maintaining; or*
3. *do both.*

In any of the cases 1–3 $\cup_{i=1}^{k} S_i$ is not an organization.

Corollary 3.2.1 (Complexity of the computation of DOs)**.** *The computation of DOs is NP-hard.*

Proof. In [4] it was proven that deciding whether a given reaction network contains a reactive organization is NP-complete and thus that computing organizations is NP-hard. This was done by constructing a reaction network containing an organization such that finding that organization is equivalent to the 3-SAT problem. Since we know from Lemma 3.2.1 that every organization is a DO, the proof from [4] works for DOs too. □

For more information about the complexity of relevant subsets of species in a reaction network the reader is referred to [58]. The next lemma is the first part of a sequence of statements culminating in a theorem about the lattice property of the set of DOs of a given reaction network.

Lemma 3.2.2 (Existence of a unique smallest organization)**.** *For every reaction network $(\mathcal{S}, \mathcal{R})$ there is a unique smallest DO O_{min}, which is an organization. That is, O_{min} is a subset of any other DO of that reaction network. For any DO $D = \{S_1 | \ldots | S_k\}$, O_{min} is even a subset of all S_i. Note, that O_{min} might be empty.*

Proof. We define

$$O_{min} \equiv clos(\emptyset); \tag{3.21}$$

then O_{min} is closed. Furthermore, since O_{min} is produced from the empty set $\emptyset$, it is a subset of all S_i, $i = 1, \ldots, k$, for any DO $D = \{S_1 | \ldots | S_k\}$. Thus, to prove that O_{min} is an organization, it remains to prove, that there is a feasible flux $\hat{v} \in \mathbb{R}_+^m$ with respect to O_{min} with $N\hat{v} \geq 0$. With $k_{min} \in \mathbb{N}_0$ from Definition 2.0.1, we define the vector $\hat{v}^{k_{min}} \in \mathbb{R}_+^m$ by

$$\hat{v}_j^{k_{min}} \begin{cases} = 1, & \text{iff } supp(r_j) \cap clos_1^{k_{min}}(\emptyset) \neq \emptyset, \\ = \lambda_{k_{min},j}, & \text{iff } supp(r_j) \subseteq clos_1^{k_{min}-1}(\emptyset) \text{ and} \\ & a_{ij} = 0,\ b_{ij} > 0 \text{ for a species } s_i \in clos_1^{k_{min}} \setminus clos_1^{k_{min}-1} \\ = 0, & \text{otherwise,} \end{cases} \tag{3.22}$$

for $j = 1, \ldots, m$, and by strictly positive real numbers $\lambda_{k_{min},j}$, such that

$$(N\hat{v}^{k_{min}})_i \geq 0 \; \forall \, s_i \in clos_1^{k_{min}}(\emptyset) \setminus clos_1^{k_{min}-1}(\emptyset). \tag{3.23}$$

Then for k from $k_{min}-1$ stepwise decreasing by 1 to $k=1$, we construct the vectors $\hat{v}^k \equiv \hat{v}^{k+1} + \Delta\hat{v}^k \in \mathbb{R}_+^m$ by adding to $\hat{v}^k$ the vector $\Delta\hat{v}^k$ defined by

$$\Delta\hat{v}_j^k = \begin{cases} 1, & \text{iff } supp(r_j) \subseteq clos_1^k(\emptyset) \text{ and} \\ & a_{ij} > 0 \text{ for all species } s_i \in clos_1^k \setminus clos_1^{k-1} \\ \lambda_{k,j}, & \text{iff } supp(r_j) \subseteq clos_1^{k-1}(\emptyset) \text{ and} \\ & a_{ij} = 0,\ b_{ij} > 0 \text{ for a species } s_i \in clos_1^k \setminus clos_1^{k-1} \\ 0, & \text{otherwise,} \end{cases} \tag{3.24}$$

for $j = 1, \ldots, m$, and by strictly positive real numbers $\lambda_{k,j}$, such that

$$(N\hat{v}^k)_i \geq 0 \,\forall\, s_i \in clos_1^k(\emptyset) \setminus clos_1^{k-1}(\emptyset) \tag{3.25}$$

and so

$$(N\hat{v}^k)_i \geq 0 \,\forall\, s_i \in clos_1^{k_{min}}(\emptyset) \setminus clos_1^{k-1}(\emptyset). \tag{3.26}$$

Finally, by defining $\hat{v} \equiv \hat{v}^1$ we obtain a feasible flux with respect to $clos(\emptyset)$ such that

$$(N\hat{v}^k)_i \geq 0 \,\forall\, s_i \in clos(\emptyset), \tag{3.27}$$

that is, O_{min} is self-maintaining and thus an organization. □

Note that this subsection and Section 2.0.1 are the only parts of this section where it is necessary to define self-maintenance of organizations and DOs by the inequality $N\hat{v} \geq 0$ instead of the equation $N\hat{v} = 0$. The rest of this section indeed still holds true if the inequality $N\hat{v} \geq 0$ in the definitions of organizations and DOs is replaced by the equation $N\hat{v} = 0$. Thus, all results of this section dealing with organizations or DOs with regard to the dynamics of RDSs are, strictly speaking, not formulated in their strongest possible forms.

Lemma 3.2.3 (Union of DOs)**.** *Given a reaction network $(\mathcal{S}, \mathcal{R})$ and two DOs $D_1, D_2 \in \mathcal{S}$, the union $D_1 \cup D_2$ is also a DO.*

Proof. Let $D_1 = \{S_1|\ldots|S_k\}$ and $D_2 = \{T_1|\ldots|T_l\}$ be DOs with closed subsets $S_i, T_j \subseteq D_1$, $i = 1, \ldots, k$, $j = 1, \ldots, l$, of species and let their feasible fluxes be $\hat{v}^i, \hat{\hat{v}}^j$, $i = 1, \ldots, k$, $j = 1, \ldots, l$, such that $N\sum_{i=1}^k \hat{v}^i = 0$ and $N\sum_{j=1}^l \hat{\hat{v}}^j = 0$.

Then $D \equiv D_1 \cup D_2$ with the distribution $D \equiv \{S_1|\ldots|S_k|T_1|\ldots|T_l\}$, $i = 1, \ldots, k$, $j = 1, \ldots, l$, is a DO, since $N(\sum_{i=1}^k \hat{v}^i + \sum_{j=1}^l \hat{\hat{v}}^j) = N\sum_{i=1}^k \hat{v}^i + N\sum_{j=1}^l \hat{\hat{v}}^j = 0$. □

Note that the union of two DOs as constructed in Lemma 3.2.3 is always a DO but not necessarily an organization. The next lemma complements Lemma 3.2.2.

Corollary 3.2.2 (Existence of a unique biggest DO)**.** *Given a reaction network $(\mathcal{S}, \mathcal{R})$ and a subset $S \subseteq \mathcal{S}$ of species with $O_{min} \subseteq S$ for O_{min} from Lemma 3.2.2, the union*

$$D_{max}(S) \equiv \cup\{D \subseteq S :\ D \text{ is a DO}\} \tag{3.28}$$

of all DOs contained in S is the unique biggest DO contained in S in the sense that all other DOs contained in S are subsets of $D_{max}(S)$.

Proof. Let $S \subseteq \mathcal{S}$ be an arbitrary closed subset of species. It follows from Lemma 3.2.3 that $D_{max}(S)$ is a DO.From lemma 3.2.2 it follows that the union is never empty, since it always contains the smallest organization $O_{min} \equiv clos(\emptyset)$ of the reaction network. □

Based on the previous results, the next theorem states the lattice property of the set of DOs of a reaction network.

Theorem 3.2.1 (Lattice property of DOs)**.** *Given a reaction network* $(\mathcal{S}, \mathcal{R})$ *the set of its DOs forms a lattice.*

Proof. According to the subarea of mathematics called order theory, a lattice is a partially ordered set in which every two elements have a unique supremum and a unique infimum Therefore, the set of DOs is a lattice if the following three conditions hold:

1. *Partial order of the set of DOs*: The subset relation for sets provides a partial order.

2. *Unique supremum*: Given two DOs $D_1, D_2 \subseteq \mathcal{S}$, following Lemma 3.2.3, a unique supremum is given by the set union

$$D_{sup} \equiv D_1 \cup D_2. \tag{3.29}$$

3. *Unique infimum*: Given two DOs $D_1, D_2 \subseteq \mathcal{S}$ of the reaction network we take the union of all DOs in $D_1 \cap D_2$ as the infimum, that is,

$$D_{inf} \equiv D_{max}(D_1 \cap D_2) = \cup\{D \subseteq D_1 \cap D_2 : \text{ D is a DO}\}. \tag{3.30}$$

   The existence of D_{inf} follows from Corollary 3.2.2.

□

Summarizing, we visualize the previous statements in Figure 3.4. Note that besides the lattice of DOs, also the set of all subsets of species forms a lattice by taking set union and set intersection as supremum and infimum, respectively. Thus the lattice of DOs can be embedded as a subset into the lattice of all subsets of species. In contrast, the set of organizations and the set of all closed subsets of species are not lattices in general.

We derive Corollary 3.2.3 from Theorem 3.2.1.

Corollary 3.2.3 (Lattice criterion for DOs)**.** *Given a reaction network* $(\mathcal{S}, \mathcal{R})$*, if the Hasse diagram of organizations is not a lattice, then there exists at least one DO that is not an organization.*

Proof. Since by Lemma 3.2.1 every organization is a DO, the set of organizations of the Hasse diagram must be a proper subset of the set of DOs if the Hasse diagram of organizations is not a lattice. □

We conclude this subsection by providing an example reaction network, which is visualized in Figure 3.5 together with its lattice of DOs. The lattice contains five DOs that are all organizations. Note that the biggest DO $\mathcal{S} = \{s_1, s_2, s_3\}$ exhibits different distributions, for example, one for which it is distributed to only one subset $\mathcal{S}$ of species and another for which it is distributed to two subsets $S_1 = \{s_1, s_2\}$ and $S_2 = \{s_2, s_3\}$ of species. But the two different distributions share the same total fluxes, since no reaction is deactivated by distributing the species.

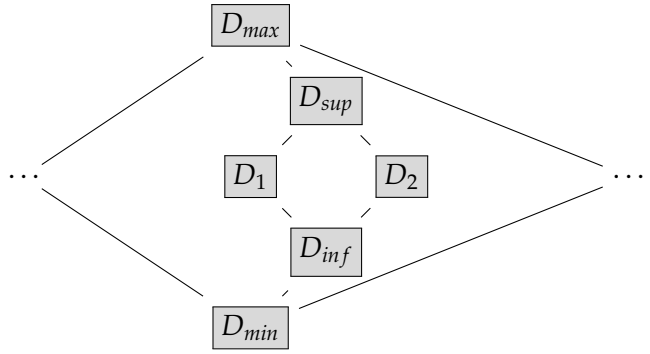
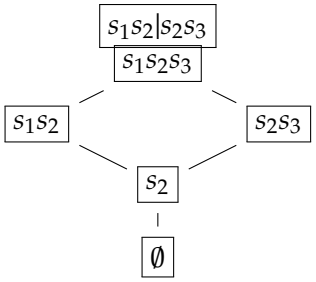


FIGURE 3.4: [46] Visualization of the lattice property of the set of DOs (that were proven in Theorem 3.2.1) of a given reaction network.

$r_1: \quad s_1 \to s_2$
$r_2: \quad s_1 + s_2 \to 2s_1$
$r_3: \quad s_2 + s_3 \to s_2 + 2s_3$
$r_4: \quad s_3 \to \emptyset$

(A) Reactions



(B) (Distributed) organizations

FIGURE 3.5: [46] An example reaction network pertaining to five different DOs. The vertical bar in the uppermost DO represents the fact that this DO can be distributed to two different subsets of species such that the species s_1 and s_3 are separated from each other.

3.3 The role closedness plays in the dynamics

In this subsection we first derive some statements about the effects of the diffusion term appearing in the RDS and prove the nonnegativity of any solution of a RDS. Then we show that for any time and any location the closure of the species existing there leads to the immediate production of the closure of these species. Finally we prove the first part of the main result of this work, that it, that a subset of species that is persistent with respect to a solution of an RDS is always closed.

Remark 3.3.1 (Nonnegative diffusion for concentration equal zero)**.** *Given the solution c of an RDS with the underlying reaction network $(\mathcal{S}, \mathcal{R})$, a species $s_i \in \mathcal{S}$, a time $t_0 \geq 0$, and a location $x_0 \in \Omega$, the following conclusion holds:*

$$c_i(x_0, t_0) = 0 \text{ and } c_i(x, t_0) \geq 0 \; \forall x \neq x_0 \Rightarrow \frac{\partial^2 c_i}{\partial x^2}(x_0, t_0) \geq 0. \tag{3.31}$$

Proof. For readability we assume $\Omega \subseteq \mathbb{R}$, since the proof for $\Omega \subseteq \mathbb{R}^p$ for $p > 1$ can be deduced easily. Furthermore, we assume that $x_0 \in \Omega$ is an element of the interior of Ω, since in the case $x_0 \in \delta\Omega$, the proof holds for the one-sided derivatives too.

From $c_i(x_0, t_0) = 0$ and $c_i(x, t_0) \geq 0$ for all $x \neq x_0$ it follows that

$$\begin{aligned} \frac{\partial^2 c_i}{\partial x^2}(x_0, t_0) &= \lim_{h \to 0} \frac{c_i(x_0 + h, t_0) - 2c_i(x_0, t_0) + c_i(x_0 - h, t_0)}{h^2} \\ &= \lim_{h \to 0} \frac{c_i(x_0 + h, t_0) + c_i(x_0 - h, t_0)}{h^2} \geq 0. \end{aligned} \tag{3.32}$$

□

Now we prove the nonnegativity of the solutions of an RDS.

Lemma 3.3.1 (Nonnegativity of the solution of a RDS)**.** *Given the solution c of an RDS with the underlying reaction network $(\mathcal{S}, \mathcal{R})$, c is nonnegative, that is,*

$$c_i(x, t) \geq 0 \quad \forall s_i \in \mathcal{S}, t \geq 0, x \in \Omega. \tag{3.33}$$

Proof. The proof is by contradiction. Therefore we assume that the supremum

$$\tilde{t} \equiv \sup\{t \geq 0 : \ c_i(x, t) \geq 0 \ \forall s_i \in \mathcal{S}, x \in \Omega\} \tag{3.34}$$

is finite, that is, $0 \leq \tilde{t} < \infty$. Since c is continuous, there is a location $\tilde{x} \in \Omega$ and an $i \in \{1, \ldots, n\}$ such that for the concentration of the species $s_i \in \mathcal{S}$ it holds that

$$c_i(\tilde{x}, t) \begin{cases} \geq 0 : & t \leq \tilde{t}, \\ = 0 : & t = \tilde{t}, \\ < 0 : & \text{for all sufficiently small } t > \tilde{t}. \end{cases} \tag{3.35}$$

and $c_i(x, \tilde{t}) \geq 0$ for all $x \in \Omega$. From Remark 3.3.1 it follows that $\frac{\partial^2 c_i}{\partial x^2}(\tilde{x}, \tilde{t}) \geq 0$, and thus

$$\begin{aligned} \frac{\partial c_i}{\partial t}(\tilde{x}, \tilde{t}) &= N \cdot v(c(\tilde{x}, \tilde{t})) + \frac{\partial^2 c_i}{\partial x^2}(\tilde{x}, \tilde{t}) \\ &\geq N \cdot v(c(\tilde{x}, \tilde{t})) \\ &\overset{c_i(\tilde{x}, \tilde{t}) = 0}{\geq} 0. \end{aligned} \tag{3.36}$$

The last inequality holds true, since when $c_i = 0$ there is no reaction that can consume the species s_i since $v()$ is defined to be a flux vector function. The resulting inequality $\frac{\partial c_i}{\partial t}(\tilde{x}, \tilde{t}) \geq 0$ contradicts $c_i(\tilde{x}, t) < 0$ for all sufficiently small $t > \tilde{t}$, that is, the third case of 3.35. Thus the assumption is false and the solution of an RDS is nonnegative for all $t \geq 0$ and $x \in \Omega$ and all species. □

From Lemma 3.3.1 and Remark 3.3.1 we easily derive the following corollary.

Corollary 3.3.1 (Nonnegative diffusion for concentration equal zero)**.** *Given the solution c of an RDS with underlying reaction network $(\mathcal{S}, \mathcal{R})$, a species $s_i \in \mathcal{S}$, a time $t_0 \geq 0$, and a location $x_0 \in \Omega$, the following conclusion holds*

$$c_i(x_0, t_0) = 0 \Rightarrow \frac{\partial^2 c_i}{\partial x^2}(x_0, t_0) \geq 0. \tag{3.37}$$

Next we state another result about diffusion we use in this work.

Remark 3.3.2 (Integral over the divergence equals zero)**.** *Given the solution c of an RDS with the underlying reaction network $(\mathcal{S},\mathcal{R})$ and a time $t_0 \geq 0$, for every species $s_i \in \mathcal{S}$, $i = 1,\ldots,n$, it holds that*

$$\int_\Omega \frac{\partial^2 c_i}{\partial x^2}(x,t_0)\,dx = 0. \tag{3.38}$$

Proof. From the divergence theorem, also referred to as Gauss's theorem we know that

$$\int_\Omega \frac{\partial^2 c_i}{\partial x^2}(x,t_0)\,dx = \int_{\delta\Omega} \frac{\partial c_i}{\partial \nu}(x,t_0)\,dx \tag{3.39}$$

and the term on the right-hand side of this equation equals zero, since we apply homogeneous Neumann boundary conditions (see Section 1). □

From Remark 3.3.2 it follows that the diffusion does not change the total integral over the concentration values of the species, but, instead, the total concentration value of each species is determined solely by its interactions with the other species via the reactions. In [44] we have outlined, how the set of reactions is to be modified according to the boundary conditions applied, to return the right set of organizations and DOs of the reaction network. For homogeneous Neumann boundary conditions we had seen, that the set of reactions needs not to be changed and this result is confirmed by Remark 3.3.2.

Next we state a lemma necessary to prove the two main results of this subsection about closedness.

Lemma 3.3.2 (Production of the closure)**.** *Given a solution c of an RDS with underlying reaction network $(\mathcal{S},\mathcal{R})$, a subset $S \subseteq \mathcal{S}$, a location $x_0 \in \Omega$, a time $t_0 > 0$, and an $\varepsilon > 0$ such that for all species $s_i \in S$ it holds that*

$$c_i(x_0,t_0) > \varepsilon, \tag{3.40}$$

then

$$c_j(x_0,t_0) > 0 \tag{3.41}$$

for all $s_j \in clos(S)$.

Proof. By assumption there is an $\varepsilon > 0$ with $c_i(x_0,t_0) > \varepsilon$ for every $s_i \in S$. We prove this by contradiction. To this end we assume that there is a species $s_j \in clos(S)$ with $c_j(x_0,t_0) = 0$. For readability we assume $s_j \in clos_1(S)$, since from this case the proof can easily be transferred to the cases $s_j \in clos_1^k$, $k > 1$. From $s_j \in clos_1(S)$ it follows that there is a reaction $r_k \in \mathcal{R}$ with $supp(r_k) \subseteq S$, that produces s_j, that is, $a_{jk} = 0$ and $b_{jk} > 0$ and thus $n_{jk} > 0$. Due to the continuity of the involved functions, there is a $\delta > 0$ such that

- $f_+(c(x_0,t)) \equiv \sum_{k:\, n_{jk}>0} n_{jk} \cdot v_k(c(x_0,t)) > \varepsilon/2$,
- $f_-(c(x_0,t)) \equiv \sum_{k:\, n_{jk}<0} n_{jk} \cdot v_k(c(x_0,t)) < -\varepsilon/8$, and
- $d_j \dfrac{\partial^2 c_j}{\partial x^2}(x_0,t) > -\varepsilon/8$

for all $t \in (t_0 - \delta, t_0 + \delta)$. Thus, contrary to the assumption, we arrive at

$$c_j(x_0, t_0) = c_j(x_0, t_0 - \delta) + \int_{t_0-\delta}^{t_0} f_+(c(x_0, t)) + f_-(c(x_0, t)) + d_j \frac{\partial^2 c_j}{\partial x^2}(x_0, t)\, dt > \delta \frac{\varepsilon}{4} > 0, \tag{3.42}$$

which finishes the proof. □

Lemma 3.3.2 allows for proving our first main result about closedness with regard to the solutions c of an RDS. For ODEs, it was already proven in lemma 4 in [42].

Lemma 3.3.3 (Instant appearance of the closure)**.** *Given the solution c of an RDS with an underlying reaction network $(\mathcal{S}, \mathcal{R})$ and a location $x \in \Omega$ the following hold:*

1. *For all times $t > 0$, the set of species $\phi(c(x,t))$ with strictly positive concentration is closed.*
2. *For sufficiently small times $t > 0$, the set of species $\phi(c(x,t))$ with strictly positive concentration contains the closure of the set $\phi(c(x,0))$ of species with initial concentration strictly positive, that is,*

$$\phi(c(x,t)) \supseteq clos(\phi(c(x,0))). \tag{3.43}$$

Proof. 1. The closedness of $\phi(c(x,t))$ for any $t > 0$ follows directly from lemma 3.3.2.

2. Because of the continuity of c with respect to t, we know that for sufficiently small times $t > 0$,

$$\phi(c(x,t)) \supseteq \phi(c(x,0)), \tag{3.44}$$

and thus with lemma 3.3.2 it follows that

$$\phi(c(x,t)) \supseteq clos(\phi(c(x,0))). \tag{3.45}$$

□

We learn from lemma 3.3.3 that the immediate production of the closure of an initially present but not closed set of species is an intrinsic phenomenon of all solutions of any RDS. In the following we focus on the dynamics in the long-run. We prove that a persistent subset $S \in P(c)$ of species is always closed. In the next subsection, to complement this result, we prove that the set $\Phi(c)$ of persistent species with respect to c always fulfills the self-maintenance property of a DO.

Lemma 3.3.4 (Persistent subsets of species are closed)**.** *Given a solution c of an RDS with the underlying reaction network $(\mathcal{S}, \mathcal{R})$, every persistent subset $S \in P(c)$ of species is closed.*

Proof. We prove this by contradiction. Therefore we assume that there is a persistent subset $S \in P(c)$ of species that is not closed. From lemma 3.3.2 it follows that for every $\varepsilon > 0$ there is a $\delta_0 > 0$ such that for all concentration vectors $c \in \mathbb{R}^n_+$ and all $\delta \in (0, \delta_0)$, $x \in \Omega$, $t \geq 0$, it holds that

$$c(x,t) \in S^\varepsilon \Rightarrow c(x,t) \notin S^{\varepsilon,\delta}. \tag{3.46}$$

Thus the set $\{(x,t) \in \Omega \times (0,\infty) : c(x,t) \in S^{\varepsilon,\delta}\}$ is empty for all $\varepsilon > 0$ and all sufficiently small $\delta > 0$, so the frequency $F(S^{\varepsilon,\delta})$ is zero and S is not persistent in contradiction to the assumptions of this lemma. □

3.4 DOs and persistence

In this subsection we state the second main result of this work, that is, that the set $\Phi(c)$ of persistent species with respect to a solution c is always a DO. After having shown the closedness of each element of $P(c)$ in the previous subsection, it remains to prove self-maintenance. We do this in two steps:

- First, in Lemma 3.4.1 we construct from the solution c of the RDS a total flux $\hat{v} \in \mathbb{R}^m_{\geq 0}$ with respect to c with $N \cdot \hat{v} \geq 0$.
- Then, in Lemma 3.4.2 we show that there is a feasible flux with respect to each of the persistent subsets $S \in P(c)$ of species and that the sum of these feasible fluxes equals the total flux $\hat{v}$ constructed in Lemma 3.4.1.

Thereafter we transfer the result to initial value problems based on ODEs. Furthermore, given an organization, we present a way to construct an RDS with a (constant with respect to x) solution c such that the set $\Phi(c)$ of persistent species equals that organization.

Lemma 3.4.1 (Construction of a vector proving self-maintenance)**.** *Given a solution c of an RDS with underlying reaction network $(\mathcal{S},\mathcal{R})$, there is a sequence $(t_l)_{l=1}^{\infty}$ of points in time such that the total flux*

$$\hat{v} \equiv \lim_{l\to\infty} \frac{1}{t_{l+1}-t_l} \int_{t_l}^{t_{l+1}} \int_{x\in\Omega} v(c(x,t))\,dx\,dt \in \mathbb{R}^m_{\geq 0} \tag{3.47}$$

with respect to c and $(t_l)_{l=1}^{\infty}$ fulfills

$$N \cdot \hat{v} \geq 0. \tag{3.48}$$

Proof. Since

$$c^{\Omega}(t) \equiv \int_{x\in\Omega} c(x,t)\,dx \tag{3.49}$$

is bounded by assumption, it has at least one accumulation point $\tilde{c} \in \mathbb{R}^n_+$. Thus there is a sequence $(t_j)_{j=1}^{\infty}$ of points in time such that

$$\lim_{j\to\infty} c^{\Omega}(t_j) = \tilde{c} \tag{3.50}$$

and so

$$
\begin{aligned}
0 &\overset{(3.50)}{=} \lim_{j\to\infty}(c^{\Omega}(t_{j+1}) - c^{\Omega}(t_j)) \\
&\overset{(3.49)}{=} \lim_{j\to\infty}\Big(\int_{x\in\Omega} c(x,t_{j+1})\,dx - \int_{x\in\Omega} c(x,t_j)\,dx\Big) \\
&= \lim_{j\to\infty}\int_{x\in\Omega} c(x,t_{j+1}) - c(x,t_j)\,dx \\
&= \lim_{j\to\infty}\int_{x\in\Omega}\int_{t_j}^{t_{j+1}} \dot{c}(x,t)\,dt\,dx \\
&\geq \lim_{j\to\infty}\frac{1}{t_{j+1}-t_j}\int_{x\in\Omega}\int_{t_j}^{t_{j+1}} \dot{c}(x,t)\,dt\,dx \\
&\overset{(1.7)}{=} \lim_{j\to\infty}\frac{1}{t_{j+1}-t_j}\int_{x\in\Omega}\int_{t_j}^{t_{j+1}} Nv(c(x,t)) + \frac{\partial^2 c(x,t)}{\partial x^2}\cdot(d_1,\ldots,d_n)^T\,dt\,dx \\
&= \lim_{j\to\infty}\frac{1}{t_{j+1}-t_j}\Big[\int_{x\in\Omega}\int_{t_j}^{t_{j+1}} Nv(c(x,t))\,dt\,dx \\
&\qquad\qquad + \int_{x\in\Omega}\int_{t_j}^{t_{j+1}} D\frac{\partial^2 c(x,t)}{\partial x^2}\,dt\,dx\Big] \\
&= \lim_{j\to\infty}\frac{1}{t_{j+1}-t_j}\Big[\int_{t_j}^{t_{j+1}}\int_{x\in\Omega} Nv(c(x,t))\,dt\,dx \\
&\qquad\qquad + \int_{t_j}^{t_{j+1}} \underbrace{\int_{x\in\Omega}\frac{\partial^2 c(x,t)}{\partial x^2}\cdot(d_1,\ldots,d_n)^T\,dx}_{=0 \text{ (remark 3.3.2)}}\,dt\Big] \\
&= \lim_{j\to\infty}\frac{1}{t_{j+1}-t_j}\Big[\int_{t_j}^{t_{j+1}}\int_{x\in\Omega} Nv(c(x,t))\,dt\,dx\Big] \\
&= \lim_{j\to\infty} N\cdot\frac{1}{t_{j+1}-t_j}\Big[\int_{t_j}^{t_{j+1}}\int_{x\in\Omega} v(c(x,t))\,dt\,dx\Big] \\
&= \underbrace{N\cdot\lim_{l\to\infty}\frac{1}{t_{l+1}-t_l}\int_{t_j}^{t_{j+1}}\int_{x\in\Omega} v(c(x,t))\,dt\,dx}_{\equiv\hat{v},\,\hat{v}\geq 0},
\end{aligned}
$$

where $D \in \mathbb{R}^{n\times n}$ denotes the Fickian diffusivity matrix, which in this work is assumed to be a diagonal matrix containing the diffusion rates d_i, $i = 1,\ldots,n$, on its diagonal. Thus there is a subsequence $(t_l)_{l=1}^{\infty}$ of $(t_j)_{j=1}^{\infty}$ such that the total flux

$$
\hat{v} \equiv \lim_{l\to\infty}\frac{1}{t_{l+1}-t_l}\int_{t_l}^{t_{l+1}}\int_{x\in\Omega} v(c(x,t))\,dt\,dx \tag{3.51}
$$

with respect to c and $(t_l)_{l=1}^{\infty}$ exists, because the flux vector function $v()$ is by assumption Lipschitz continuous on every bounded subset of $\mathbb{R}^n_+$, and c is bounded by assumption too, and thus $v()$ is bounded for all $x \in \Omega$, $t \geq 0$. □

Next we prove that the vector $\hat{v}$ obtained in Lemma 3.4.1 can be written as a sum of feasible fluxes with respect to the persistent subsets of species.

Lemma 3.4.2 (Construction of a feasible flux (with respect to every persistent subset of species) summing up to $\hat{v}$)**.** *Given the solution c of an RDS with underlying reaction network $(\mathcal{S},\mathcal{R})$ and a vector $\hat{v} \in \mathbb{R}^m_+$ constructed as in Lemma 3.4.1, then there is a feasible flux $\hat{v}^i$ with respect to each $S_i \in P(c), i = 1,\dots,k$, such that*

$$\hat{v} = \lim_{l\to\infty} \frac{1}{t_{l+1}-t_l} \int_{t_l}^{t_{l+1}} \int_{x\in\Omega} v(c(x,t))\, dt\, dx = \sum_{i=1}^{k} \hat{v}^i. \tag{3.52}$$

Proof. Let $r_j \in \mathcal{R}$ be an arbitrarily chosen reaction, and let $n(r_j)$ be the number of persistent subsets $S \in P(c)$ of species with $support(r_j) \subseteq S$. We can distinguish the following two alternative cases:

- $n(r_j) > 0$, and
- $n(r_j) = 0$.

We will prove that

$$n(r_j) > 0 \Leftrightarrow \hat{v}_j > 0 \tag{3.53}$$

by proving the following two conclusions

1. $n(r_j) > 0 \Rightarrow \hat{v}_j > 0$, and
2. $n(r_j) = 0 \Rightarrow \hat{v}_j = 0$.

Then, for each persistent subset $S_i \in P(c),\ i = 1,\dots,k$, of species we construct the vector $\hat{v}^i$ by defining

$$\hat{v}^i_j \equiv \begin{cases} \hat{v}_j/n(r_j), & \text{if } n(r_j) > 0 \text{ and } supp(r_j) \subseteqq S_i \\ 0, & \text{otherwise} \end{cases} \tag{3.54}$$

for all reactions $r_j \in \mathcal{R}$. Then each vector $\hat{v}^i \in \mathbb{R}^m_{\geq 0}$ is a feasible flux with respect to the corresponding persistent subset $S_i \in P(c),\ i = 1,\dots,k$, of species and $\hat{v} = \sum_{i=1}^k \hat{v}^i$ as desired.

Now it only remains to prove the following two conclusions mentioned above:

1. $n(r_j) > 0 \Rightarrow \hat{v}_j > 0$.
   If for a reaction $r_j \in \mathcal{R}$ it holds that $n(r_j) > 0$, then there is a persistent subset $\tilde{S} \in P(c)$ of species with $support(r_j) \subseteq \tilde{S}$. Thus for all sufficiently small $\varepsilon > 0$ it holds that $F(\tilde{S}^\varepsilon) > 0$, and according to Remark 3.1.1 there is a lower boundary $L(\varepsilon) > 0$ for v_j such that

$$\begin{aligned}
\hat{v}_j \overset{(3.51)}{=}\ & \lim_{l\to\infty} \frac{1}{t_{l+1}-t_l} \int_{t_l}^{t_{l+1}} \int_{x\in\Omega} v_j(c(x,t))\, dt\, dx \\
\geq\ & \lim_{l\to\infty} \frac{1}{t_{l+1}-t_l} \int_{t_l}^{t_{l+1}} \int_{\{x\in\Omega:\, c(x,t)\in\tilde{S}^\epsilon\}} v_j(c(x,t))\, dt\, dx \\
\overset{\text{Remark 3.1.1}}{\geq}\ & \lim_{l\to\infty} \frac{1}{t_{l+1}-t_l} \int_{t_l}^{t_{l+1}} \int_{\{x\in\Omega:\, c(x,t)\in\tilde{S}^\epsilon\}} L(\epsilon)\, dt\, dx \\
\overset{\text{Remark 3.1.1}}{\geq}\ & L(\epsilon) \cdot \lim_{l\to\infty} \frac{1}{t_{l+1}-t_l} \int_{t_l}^{t_{l+1}} \int_{\{x\in\Omega:\, c(x,t)\in\tilde{S}^\epsilon\}} dt\, dx \\
=\ & L(\epsilon) \cdot F(\tilde{S}^\epsilon) \\
>\ & 0,
\end{aligned} \tag{3.55}$$

where $(t_l)_{l=1}^{\infty}$ is a sequence of points in time from Lemma 3.4.1.

2. $n(r_j) = 0 \Rightarrow \hat{v}_j = 0$.
We prove this by contradiction, that is, by showing that from $\hat{v}_j > 0$ it follows that $n(r_j) > 0$. Thus we assume $\hat{v}_j > 0$. For

$$K \equiv \sup\{v_j(c(x,t)) : \ t \geq 0, x \in \Omega\}, \tag{3.56}$$

$0 \leq K < \infty$ holds. Let $(t_l)_{l=1}^{\infty}$ be the sequence of points in time from Lemma 3.4.1. Then for all sufficiently small $\varepsilon > 0$, from Remark 3.1.1 it follows that there is an upper boundary $U(\varepsilon) > 0$ such that for every $\delta > 0$,

$$\begin{aligned}
0 \quad &< \quad \hat{v}_j \\
&\overset{(3.51)}{=} \quad \lim_{l\to\infty} \frac{1}{t_{l+1}-t_l} \int_{t_l}^{t_{l+1}} \int_{x\in\Omega} v_j(c(x,t))\, dx\, dt \\
&= \quad \lim_{l\to\infty} \frac{1}{t_{l+1}-t_l} \int_{t_l}^{t_{l+1}} \Bigg[\int_{\{x\in\Omega:\, c(x,t)\in support(r_j)^{\varepsilon}\}} v_j(c(x,t))\, dx \\
&\quad + \int_{\{x\in\Omega:\, c(x,t)\notin support(r_j)^{\varepsilon}\}} v_j(c(x,t))\, dx \Bigg] dt \\
&\overset{(3.56),\text{Remark } 3.1.1}{\leq} \quad \lim_{l\to\infty} \frac{1}{t_{l+1}-t_l} \Bigg[\int_{t_l}^{t_{l+1}} \int_{\{x\in\Omega:\, c(x,t)\in support(r_j)^{\varepsilon}\}} K\, dx\, dt \\
&\quad + \int_{t_l}^{t_{l+1}} \int_{\{x\in\Omega:\, c(x,t)\notin support(r_j)^{\varepsilon}\}} U(\varepsilon)\, dx\, dt \Bigg] \\
&= \quad K \cdot \lim_{l\to\infty} \frac{1}{t_{l+1}-t_l} \int_{t_l}^{t_{l+1}} \int_{\{x\in\Omega:\, c(x,t)\in support(r_j)^{\varepsilon}\}} dx\, dt \\
&\quad + U(\varepsilon) \cdot \lim_{l\to\infty} \frac{1}{t_{l+1}-t_l} \int_{t_l}^{t_{l+1}} \int_{\{x\in\Omega:\, c(x,t)\notin support(r_j)^{\varepsilon}\}} dx\, dt \\
&\overset{\text{Remark } 3.1.2}{=} \quad K \lim_{l\to\infty} \frac{1}{t_{l+1}-t_l} \int_{t_l}^{t_{l+1}} \sum_{S\supseteq support(r_j)} \int_{\{x\in\Omega:\, c(x,t)\in S^{\varepsilon,\delta}\}} dx\, dt \\
&\quad + U(\varepsilon) \lim_{l\to\infty} \frac{1}{t_{l+1}-t_l} \int_{t_l}^{t_{l+1}} \int_{\{x\in\Omega:\, c(x,t)\notin support(r_j)^{\varepsilon}\}} dx\, dt \\
&= \quad K \cdot \sum_{S\supseteq support(r_j)} \lim_{l\to\infty} \frac{1}{t_{l+1}-t_l} \int_{t_l}^{t_{l+1}} \int_{\{x\in\Omega:\, c(x,t)\in S^{\varepsilon,\delta}\}} dx\, dt \\
&\quad + U(\varepsilon) \cdot \lim_{l\to\infty} \frac{1}{t_{l+1}-t_l} \int_{t_l}^{t_{l+1}} \int_{\{x\in\Omega:\, c(x,t)\notin support(r_j)^{\epsilon}\}} dx\, dt \\
&= \quad K \cdot \sum_{S\supseteq support(r_j)} F(S^{\varepsilon,\delta}) \\
&\quad + U(\varepsilon) \cdot \lim_{l\to\infty} \frac{1}{t_{l+1}-t_l} \int_{t_l}^{t_{l+1}} \int_{\{x\in\Omega:\, c(x,t)\notin support(r_j)^{\varepsilon}\}} dx\, dt
\end{aligned} \tag{3.57}$$

By letting $\varepsilon \to 0$ we get

$$\begin{aligned} 0 \quad < \quad & \lim_{\varepsilon\to 0}\Bigg[K \cdot \sum_{S\supseteq support(r_j)} F(S^{\varepsilon,\delta}) \\ & + U(\epsilon) \cdot \lim_{l\to\infty} \frac{1}{t_{l+1}-t_l} \int_{t_l}^{t_{l+1}} \int_{\{x\in\Omega:\, c(x,t)\notin support(r_j)^{\varepsilon}\}} dx\, dt\Bigg] \\ \overset{\text{Remark 3.1.1}}{=} \quad & \lim_{\epsilon\to 0}\Bigg[K \cdot \sum_{S\supseteq support(r_j)} F(S^{\varepsilon,\delta})\Bigg] \\ = \quad & K \cdot \sum_{S\supseteq support(r_j)} \lim_{\epsilon\to 0} F(S^{\varepsilon,\delta}) \end{aligned} \tag{3.58}$$

for every $\delta > 0$. Thus from Definition 3.1.3 it follows that at least one subset S of species with $S \supseteq support(r_j)$ is persistent with respect to c, that is, $S \in P(c)$. This means $n(r_j) \geq 1 > 0$ in contradiction to the assumption.

This completes the proof of Lemma 3.4.2. □

Note that in Equation 3.54 we did not construct the vectors $\hat{v}^i$ such that they necessarily represent the frequency of their appearance in the solution c of the RDS. Rather we only considered whether or not their components are zero. Putting Lemma 3.3.4, Lemma 3.4.1, and Lemma 3.4.2 together, we are able to state the second main result of this paper.

Theorem 3.4.1 (The set of persistent species is a DO)**.** *Given the solution c of an RDS with an underlying reaction network, the set $\Phi(c)$ of persistent species is a DO.*

Remark 3.4.1 (Unbounded solutions)**.** *Note that this work does not examine unbounded solutions c to RDSs. A simple example might shed some light onto the consequences of this. Let $(\mathcal{S},\mathcal{R}) \equiv (\{s_1\},\{r_1 : \emptyset \to s_1\})$ be a reaction network. It exhibits only one DO, that is, the organization $O \equiv \{s_1\}$. For every solution c 0f any RDS with the same underlying reaction network $(\mathcal{S},\mathcal{R})$ it holds that $\lim_{t\to\infty} c_1(x,t) = \infty$ for all $x \in \Omega$. Even though this long-term behavior seems to be captured by the organization O, strictly speaking, the theory developed in this work does not apply to this case, and even the usage of the term "persistence" as defined here is not allowed in this case unless a thorough study for the case of unbounded solutions is made.*

The next corollary is some kind of counterpart to Theorem 3.4.1.

Corollary 3.4.1 (Equivalence of organizations and persistent subsets)**.** *Given a reaction network $(\mathcal{S},\mathcal{R})$ and a subset $S \subseteq \mathcal{S}$ of species, then the following two statements are equivalent:*

1. *There is an RDS with an underlying reaction network $(\mathcal{S},\mathcal{R})$ with a constant solution $c(x,t) = c \in \mathbb{R}^n_+$ for all $x \in \Omega$, $t \geq 0$, and $P(c) = \{S\}$.*
2. *S is an organization and there is a feasible flux $\hat{v}$ with respect to S such that $N\hat{v} = 0$.*

Proof. We prove the two directions of the equivalence separately.

- 1. ⇒ 2.
  From statement 1 it follows that by Theorem 3.4.1 that S is a DO. Since S is distributed to only one subset of species, that is, to S itself, from the second part of Lemma 3.2.1 it follows that S is an organization. Since statement 1 provides a fixed-point solution, for every sequence of points in time the total flux $\hat{v}$ constructed as in Equation 3.51 fulfills $N\hat{v} = 0$.

- 2. $\Rightarrow$ 1.
  Let S be an organization with $\hat{v} \in \mathbb{R}_+^m$ a feasible flux with respect to S fulfilling $N \cdot \hat{v} = 0$. We construct an RDS with the underlying reaction network $(\mathcal{S}, \mathcal{R})$ such that for its solution c it holds that $P(c) = \{S\}$, that is, S is the only persistent subset with respect to c. We set the diffusion rates of all species to zero and choose the domain $\Omega = [0,1] \subseteq \mathbb{R}$. We set the initial conditions

$$c_i^0(x) = \begin{cases} 1, & \text{iff } s_i \in S, \\ 0, & \text{otherwise.} \end{cases} \tag{3.59}$$

  for all species $s_i \in \mathcal{S}$, $i = 1, \ldots, n$, and all $x \in \Omega$. For the flux vector function $v()$ we choose mass-action kinetics. For all reactions $r_j \in \mathcal{R}$, $j = 1, \ldots, m$, we set the reaction constants

$$k_j \equiv \hat{v}_j. \tag{3.60}$$

  Then for all times $t \geq 0$ and all $x \in \Omega$,

$$v(c(x,t)) = \hat{v} \tag{3.61}$$

  holds, and thus

$$\dot{c}(x,t) = N\hat{v} = 0. \tag{3.62}$$

□

It might be possible (but it is more difficult) to prove that Corollary 3.4.1 holds also for DOs and not just for organizations. There are dynamical systems with a spatial domain for which the proof of Corollary 3.4.1 for DOs should be easier, for example, the patch models defined in [1], which are systems of ODEs with a discrete spatial domain. Given a DO distributed to subsets S_i, $i = 1, \ldots, k$, of species, such a system could be designed containing k patches such that in each patch exactly one of the S_i, $i = 1, \ldots, k$, is present as a fixed point, and the exchange of species between different patches is adjusted properly.

As a special case, Theorem 3.4.1 is applicable to ODE systems which do not have any space dimension and thus no diffusion.

Remark 3.4.2 (ODE systems as a special case)**.** *Given an initial value problem*

$$\dot{c}(t) = N \cdot v(c(t)), \quad c(0) = c^0 \tag{3.63}$$

with an underlying reaction network as outlined in the introduction, one can transfer the whole of this work to that problem by neglecting all aspects concerning the space variable x, for example, integration with respect to x.

3.5 Analysis of a DO lattices

In this subsection we bring together the two main results of this work, Theorem 3.2.1 (the set of DOs of a given reaction network forms a lattice) and Theorem 3.4.1 (the set of persistent species with respect to every bounded solution being a DO). That is, we show how to interpret a single DO lattice with regard to persistence. As for the Hasse diagram of organizations, analyzing a single lattice of DOs of a given reaction

network can reveal much information about the behavior of the solutions of RDSs with that underlying reaction network.

For example, the smallest DO of a lattice, which following Lemma 3.2.2 is a unique organization, tells us which species persist in every solution. Furthermore, if a subset of species does not appear in the lattice of DOs, following Theorem 3.4.1 it cannot appear as a set of persistent species with respect to any solution, since if it could, it would be a DO. So it is easy to check from the lattice of DOs whether, for example, the whole set of species $\mathcal{S}$ can persist in any solution, because if so, then it appears as a DO at the top of the lattice.

Given two DOs D_1 and D_2, it is interesting, for example for interpretation of ecological systems, to study the DOs that contain both these DOs. Doing so reveals, under which circumstances both DOs can coexist. The question of whether or not $D_1 \cup D_2$ is an organization tells us something about the possible modes of coexistence of D_1 and D_2. If $D_1 \cup D_2$ is an organization, all species can persist when mixed together. If not, they can only coexist when separated properly. Also it is interesting to analyze those DOs that contain more species than $D_1 \cup D_2$, because these species allow for the coexistence of D_1 and D_2 distributed either to different subsets of species or to the same.

Now, instead of subsets of species, let us consider a single species. If a species does not appear in any of the DOs of a lattice, it will not persist with respect to any solution of any RDS with the underlying reaction network, which the lattice of DOs was derived from. On the other hand, if a species appears in all DOs of a lattice, then it will persist with respect to every solution of every RDS with the respective reaction network.

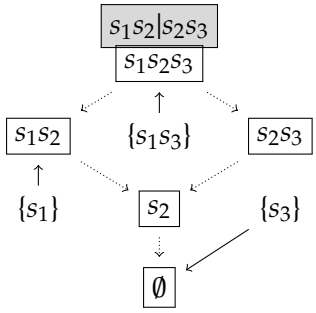
Using the lattice of DOs one can distinguish different degrees of persistence of a subset or a single species with regard to the reaction network (not with respect to a single solution of an RDS). In this sense, for example, a species is more persistent the further down it appears in the lattice and thus is an element of more DOs. Of all DOs that contain a given species, the one occupying the lowest position in the lattice determines which of the considered species definitely needs to persist. By discussing our third example model in Section 3.6.3 below we will learn more about such dependencies of species with regard to their persistence.

Contrary to dependency, if two species are elements of two different DOs that are not linked by a vertical chain of interlaced DOs in the lattice, then these species exhibit some sort of independence with regard to their persistence. Generally, the more vertical levels a lattice pertains to between its lowest and its highest DO, the more complex it is with regard to persistence.

For a solution c of an RDS, the dynamical changes of the set of species existent at any time t can be visualized within the lattice by arrows between different subsets of species indicating, which species are newly created (according to Lemma 3.3.3) or which go extinct due to missing self-maintenance. In Figure 3.6 we have exemplified this. Note that, as in Figure 3.6, it might be advantageous to augment the lattice of DOs by further sets of relevance, for example, important transient sets of species, which following Lemma 3.3.3 are initial sets of species and their closures. In Section **??** we provide an example simulation for an Influenza A virus infection dynamics model from [17] where we juxtaposed the diagram with the courses of the concentrations of the species from an ODE simulation (Figure **??**) and the respective movement in the Hasse diagram of organizations of the underlying reaction network (Figure **??**).

r_1 : $s_1 \to s_2$
r_2 : $s_1 + s_2 \to 2s_1$
r_3 : $s_2 + s_3 \to s_2 + 2s_3$
r_4 : $s_3 \to \emptyset$

(A) Reactions



(B) Distributed organizations

FIGURE 3.6: [46] An example reaction network (left) with the lattice of all subsets of species (right). Those subsets in the boxes are DOs. From each subset that is not a DO, a solid arrow points towards the DO that will be approached initially by any solution starting with that subset of species. More precisely, $\{s_3\}$ goes extinct since it is not self-maintaining, and both $\{s_1\}$ and $\{s_1, s_3\}$ will produce their closures $\{s_1, s_2\}$ (resp., $\{s_1, s_2, s_2\}$). Further possible movements from the DOs downward leading to one of their subsets are depicted by dotted arrows.

3.6 Comparisons and hierarchies of several models using their signature

Above we have shown that computing the lattice of DOs allows for some sort of overall steady-state analysis of the whole set of possible solutions on the level of species. In [45] we used the lattices of organizations of different in-host Influenza A virus infection dynamics models based on ODEs to compare these models and to put them into a hierarchy revealing different degrees of complexity and different types of overall dynamic behavior.

In [43] we compute the lattices of DOs of different SARS-CoV-2 infection dynamics models including not only in-host but also host-to-host models and one mixed model. Furthermore we did not restrict that work to ODE models but included PDE models as well proving the universality of our approach that is due to the fact that it relies solely on the underlying reaction network of the models. We found DOs that were not organizations proving the purpose of this work from another perspective. Besides some similarities, the DO lattices showed significant differences which resulted in contradictory conclusions about their long-term behavior. Even though those models are mostly intended to capture only the quantitative aspect of a special subset of solutions, such conflicts regarding their overall qualitative dynamics can be interpreted as showing a weak point in such modeling. Finally, in [43], by using the lattice of DOs we also put the Influenza A and SARS-CoV-2 infection dynamics models into one common hierarchy, revealing not only some of their similarities but also their differences, for example, the lower complexity of the SARS-CoV-2 infection dynamics models.

3.6.1 Example I

Figure 3.7a exhibits the PDEs of an RDS that pertains to a solution for which a simulation result is shown in Figure 3.8. In Figure 3.7b the reactions of the underlying reaction network are shown. Note that these reactions can be derived easily from the

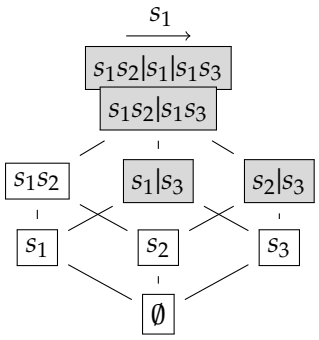
PDEs by writing the part related to the reactions in the form $N \cdot v(c)$ and obeying the fact that v is a flux vector function. In section 2 in [43] an example of this procedure is described. Figure 3.7c shows the lattice of DOs of the reaction network of Example I. Now, we want to retrace the simulation results illustrated in Figure 3.8. Since the

$$\frac{\partial c_1}{\partial t} = c_1 c_2 - c_1^2 c_3 + d_1 \frac{\partial^2 c_1}{\partial x^2}$$
$$\frac{\partial c_2}{\partial t} = -c_2 c_3$$
$$\frac{\partial c_3}{\partial t} = -c_2 c_3$$

(A) PDEs

$$r_1 : \quad s_1 + s_2 \to 2s_1 + s_2$$
$$r_2 : \quad 2s_1 + s_3 \to s_3$$
$$r_3 : \quad s_2 + s_3 \to \emptyset$$

(B) Reactions



(C) Distributed organizations

FIGURE 3.7: [46] PDEs, reactions and lattice of DOs of Example I. Unshaded boxes indicate organizations. Shaded boxes indicate DOs that are not organizations. Note that the Hasse diagram of organizations in this case is not a lattice. From Corollary 3.2.3 we know that there must be at least one DO (which is not an organization) containing the union of $\{s_1, s_2\}$, $\{s_2\}$ and $\{s_3\}$. For this example we have three DOs that are not organizations, one of which contains all species. For that DO we depicted two different distributions one upon the other. The lower one represents to the two subsets $\{s_1, s_2\}$ and $\{s_1, s_3\}$ which appear as persistent subsets of species in the simulation shown in Figure 3.8. There are feasible fluxes $\hat{v}^1 = (2, 0, 0)^T$ for $\{s_1, s_2\}$ and $\hat{v}^2 = (0, 1, 0)^T$ for $\{s_1, s_3\}$ for example proving the self-maintenance for the DO $\mathcal{S}$. It is also possible to calculate a total flux from the simulation numerically. The horizontal arrow symbolizes the necessary flow of the species s_1 from the subset $\{s_1, s_2\}$, where it is overproduced, to the subset $\{s_1, s_3\}$, where it is reduced. That flow is enabled by diffusion which does not have any preferred direction.

species s_2 and s_3 do not diffuse we can take a fixed location $x \in \Omega$ and analyze for it the ODE system

$$\frac{\partial c_2(t)}{\partial t} = -c_2(t)c_3(t) \tag{3.64}$$
$$\frac{\partial c_3(t)}{\partial t} = -c_2(t)c_3(t) \tag{3.65}$$

governing the concentrations $c_2(t) = c_2(x, t)$ (resp., $c_3(t) = c_3(x, t)$) of s_2 and s_3 at this location x. Then one of the following three cases occurs.

1. *Case I*: If $c_2(0) < c_3(0)$, then c_2 will tend towards zero and $c_3(t)$ towards the strictly positive value $c_3(0) - c_2(0)$ in the long-run, with both converging from above.

2. *Case II*: If, conversely, $c_2(0) > c_3(0)$, then $c_3(t)$ tends towards zero and $c_2(t)$ towards the strictly positive value $c_2(0) - c_3(0)$.

3. *Case III*: If $c_2^0 = c_3^0$, then c_2 and c_3 equally tend towards zero in the long-run.

The previously analyzed dynamics of the concentrations of s_2 and s_3 is independent of that of the concentration of c_1. With the initial conditions used in this example (see the caption of Figure 3.8) the system finally reaches a steady state with

- species s_2 only existing in the interval $[-2;0) \subseteq \Omega$,
- species s_3 only existing in the interval $(0;2] \subseteq \Omega$, and
- species s_1 existing in the whole domain, keeping the balance between its overproduction catalyzed by s_2 and its consumption catalyzed by s_3.

Thus the observed coexistence of all three species, which is impossible at any single location, is reached by the spatial separation of the two persistent subsets $\{s_1, s_2\}$ and $\{s_1, s_3\}$, which keep the overall concentration of s_1 in balance by their complementary action on it. Note that even though the subset $\{s_1\}$ exists in the long-run at the singular location $x = 0$, it is not persistent with regard to Definition 3.1.3 since the frequency of occurrence of its respective (ε, δ)-neighborhoods tends towards zero as $\delta \to 0$. In the next subsection we present a simulation where the persistent subsets are not separated spatially but with respect to time, that is, they disappear and reappear forever.

3.6.2 Example II

Our second example is adapted from an initial value problem based on a ODE system from Neumann and Schuster [41] which we extended towards an RDS by adding a spatial dimension x and using constant concentration values with regard to x for each species. It resembles many situations from game theory (for example, the rock-paper-scissors game or the prisoner's dilemma with three participants) and biology (for example, the coexistence of different strains of bacteria, such as E. coli, competing for nutrition, intoxicating, invading, and resisting one another). The underlying reaction network of Example II has three species s_1, s_2, and s_3 and 12 reactions:

$$\begin{array}{lll} r_1 : s_1 \to 2s_1, & r_5 : s_2 \to 2s_2, & r_9 : s_3 \to 2s_3, \\ r_2 : 2s_1 \to s_1, & r_6 : 2s_2 \to s_2, & r_{10} : 2s_3 \to s_3, \\ r_3 : s_1 + s_2 \to s_2, & r_7 : s_2 + s_1 \to s_1, & r_{11} : s_3 + s_1 \to s_1, \\ r_4 : s_1 + s_3 \to s_3, & r_8 : s_2 + s_3 \to s_3, & r_{12} : s_3 + s_2 \to s_2. \end{array} \tag{3.66}$$

Each species self-replicates (r_1, r_5, r_9). So every subset of species is an organization. Every species decays spontaneously (r_2, r_6, r_{10}). Furthermore each species can reduce any other (r_3, r_4, r_7, r_8, r_{11}, r_{12}). The dynamics of the species' concentration values in the domain $\Omega = [0;2]$ is described by the PDEs

$$\begin{aligned} \dot{c_1} &= \alpha c_1 - \kappa_1 c_1^2 - \mu c_1 c_2 - \mu c_1 c_3 + d_1 \frac{\partial^2 c_1}{\partial x^2}, \\ \dot{c_2} &= \beta c_2 - \kappa_2 c_2^2 - (\mu + \gamma) c_2 c_1 - \mu c_2 c_3 + d_2 \frac{\partial^2 c_2}{\partial x^2}, \\ \dot{c_3} &= \varepsilon c_3 - \kappa_3 c_3^2 - \mu c_3 c_1 - \mu c_3 c_2 + d_3 \frac{\partial^2 c_3}{\partial x^2}. \end{aligned} \tag{3.67}$$

Figure 3.9 shows the results of a simulation for the reaction constants $\alpha = 1.156, \beta = 2$, $\epsilon = 1$, $\kappa_1 = 2$, $\kappa_2 = 1.75$, $\kappa_3 = 0.844$, and $\mu = 1$, $\gamma = 4.6$, with the diffusion rates $d_1 = d_3 = 0.1$ and $d_2 = 0.2$ and the initial conditions $c_1(0, x) = 0.1$, $c_2(0, x) = 0.64$, $c_3(0, x) = 0.31$, $x \in \Omega$. Figure 3.10 shows the lattice of all subsets of species of

the reaction network. All of them are organizations. From [41] we know that the instances of the subsets of species with exactly one species are fixed points and thus their retention time gets longer and longer towards infinity with every passage of the trajectory. Thus they are persistent of course. The retention times of the subsets of species containing exactly two species converge towards strictly positive but finite values and so are persistent too. Nevertheless, the set $\mathcal{S}$ containing all species is not persistent. Thus for this example all species are persistent and the limit superior of them is strictly positive, but the limit inferior equals zero. This is consistent with lemma 5.0.2 in the supplementary material, which states that a strictly positive limit inferior of the concentration values of a species is sufficient for its persistence and this, in turn, is sufficient for a strictly positive limit superior of the concentration values.

3.6.3 Example III

Here we augment Example II by adding three further species s_4, s_5 and s_6. Each of these species is involved in two reactions, an outflow reaction reducing the species and a reaction producing the species out of a subset of the set $\{s_1, s_2, s_3\}$,

$$
\begin{aligned}
r_{13} &: \mathbf{s_4} \xrightarrow{k_{13}} \emptyset, \\
r_{14} &: s_1 \xrightarrow{k_{14}} s_1 + \mathbf{s_4} \\
r_{15} &: \mathbf{s_5} \xrightarrow{k_{15}} \emptyset, \\
r_{16} &: s_1 + s_2 \xrightarrow{k_{16}} s_1 + s_2 + \mathbf{s_5}, \\
r_{17} &: \mathbf{s_6} \xrightarrow{k_{17}} \emptyset, \\
r_{18} &: s_1 + s_2 + s_3 \xrightarrow{k_{18}} s_1 + s_2 + s_3 + \mathbf{s_6}.
\end{aligned}
$$

None of these reactions affects the concentrations of any of the species s_1, s_2, and s_3. Also there is no mutual influence among s_4, s_5 and s_6. Contrary to Example II, the lattice of DOs does not contain all subsets of species since some of them are not closed, for example, the subset $\{s_1\}$. Other subsets are no longer organizations but are still DOs, for example, $\{s_1, s_2\}$.

The dynamics of the concentration values of s_4 to s_6 is determined by the PDEs

$$
\begin{aligned}
\dot{c}_4 &= k_{14}c_1 - k_{13}c_4 + d_4\frac{\partial^2 c_4}{\partial x^2}, \\
\dot{c}_5 &= k_{16}c_1c_2 - k_{15}c_5 + d_5\frac{\partial^2 c_5}{\partial x^2}. \\
\dot{c}_6 &= k_{18}c_1c_2c_3 - k_{17}c_6 + d_5\frac{\partial^2 c_6}{\partial x^2}.
\end{aligned} \tag{3.68}
$$

In this example we choose for s_1 to s_3 the same PDEs, reaction constants and initial conditions as in Example II. So we get the same simulation results (see Figure 3.9), that is, a periodic alternate appearing, disappearing, and reappearing of the species $s_1 - s_3$, where each is persistent even though together they do not form a persistent subset.

With the reaction constants $k_{13} = \ldots = k_{18} = 0.05$, the homogeneous initial conditions $c_4(x, 0) = c_5(x, 0) = c_6(x, 0) = 0.1$, $x \in \Omega$, and some arbitrary diffusion constant,s we arrive at the simulation result for $c_4 - c_6$ shown in Figure 3.11. The

courses of the concentrations c_1 – c_3 are the same as in Example II. All species s_4 – s_6 are reduced by outflow reactions (r_{13}, r_{15}, r_{17}). For s_4 and s_5 this reduction is compensated by the reactions r_{14} (resp., r_{16}) in the sense that s_4 and s_5 are persistent. For s_6 the reduction by its outflow reaction r_{17} cannot be compensated by reaction r_{18}, that is, s_6 is not persistent but goes extinct in the long-run. The reason for this is that, contrary to r_{14} and r_{16}, the support of r_{18} is not a subset of any persistent subset of species. Figure 3.12 shows for Example II and Example III the sequences of persistent subsets of species traversed repeatedly in the long-run.

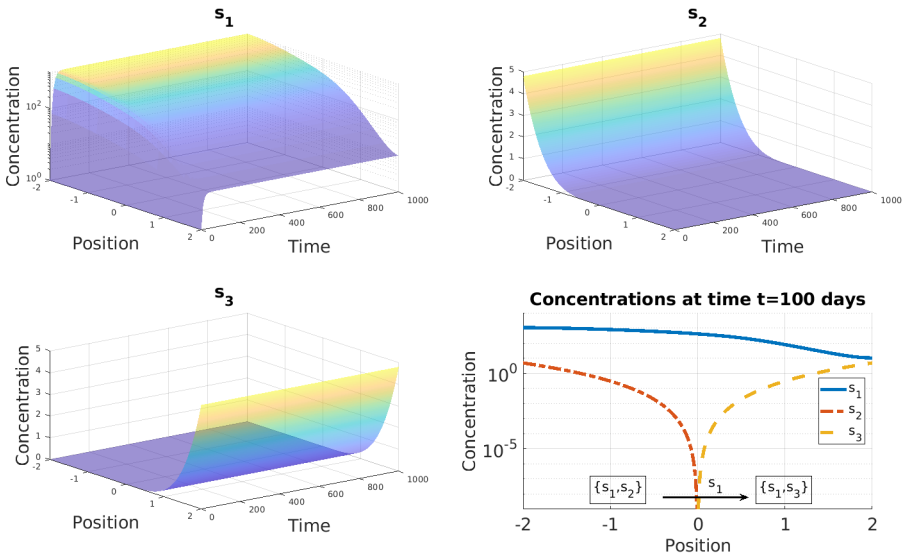


FIGURE 3.8: [46] Simulation result of Example I (see PDEs in Figure 3.7a) performed with MATLAB R2019a function **pdepe**. Note that we applied a logarithmic scale for the diagrams the upper left and in the lower right. The initial conditions are as follows: $c_1^0(x) = 1$ for $x \in \Omega$; $c_2^0(x) = 0.3x^4$ for $x < 0$ and $c_2^0(x) = 0$ for $x \geq 0$; and $c_3^0(x) = 0.3x^4$ for $x \geq 0$ and $c_3^0(x) = 0$ for $x < 0$. The diffusion rates are $d_1 = 5$, $d_2 = d_3 = 0$, that is, only species s_1 diffuses. By the initial conditions, the domain $\Omega = [-2;2]$ is divided into left and right regions which initially overlap, but the overlap is deleted by the reaction between the two competing species s_2 and s_3 in distinct parts of the domain. Thus, as time approaches infinity, only the species s_1 mediates between the left and right parts of the domain, where each of the two persistent subsets of species persists. In the left part $[-2;0)$ the species s_1 is overproduced whereas in the right part $(0;2]$ it is consumed. Altogether diffusion is responsible for the shift of s_1 from the left to the right part of the domain thus maintains the balance of the total concentration of s_1. Only species s_1 as an intermediary exists in both parts of the domain. The simulation of the solution c of this RDS shows that all three species are persistent and there are two persistent subsets $\{s_1, s_2\}$ and $\{s_1, s_3\}$. From the results of this paper it follows that the set $\Phi(c) = \{s_1, s_2, s_3\}$ of persistent species is a DO an,d we find from the simulation that it is distributed spatially to the two subsets $\{s_1, s_2\}$ and $\{s_1, s_3\}$.

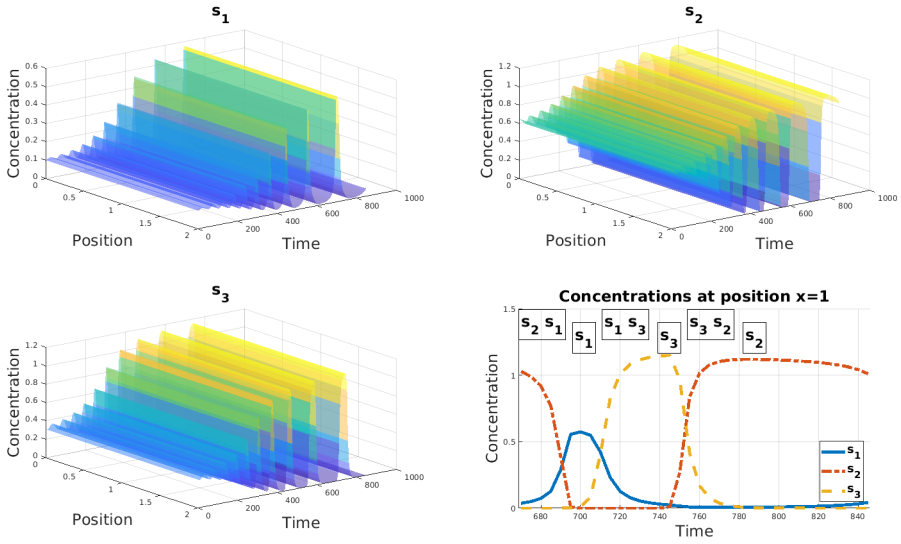


FIGURE 3.9: [46] Simulation result of Example II (see PDEs (3.67)) performed with MATLAB R2019a function **pdepe**. The periodicity (with increasing period) of the dynamic behavior is visible. From the lower right diagram it can be seen how the concentration values periodically approach different subsets of species depicted at the top. Those are the persistent subsets of species, that is, $\{s_1\}$, $\{s_1, s_3\}$, $\{s_3\}$, $\{s_3, s_2\}$, $\{s_2\}$, and $\{s_2, s_1\}$. The periodic behavior continues infinitely beyond the time span captured in the diagrams.

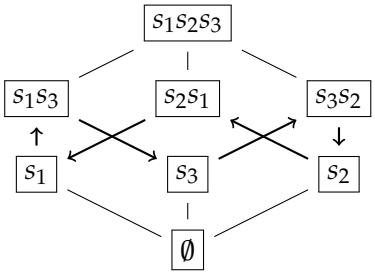


FIGURE 3.10: [46] All subsets of species of the reaction network of Example II are organizations. The arrows indicate the movement that is approached by the trajectory in the long-run.

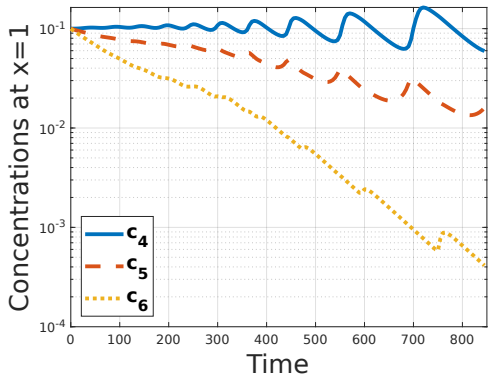


FIGURE 3.11: [46] Simulation result for species s_4, s_5, and s_6 of Example III (see PDEs (3.68)) performed with MATLAB R2019a function **pdepe**. s_4 and s_5 are persistent, whereas s_6 does not persist. The reaction constant values are $k_{13} = \ldots = k_{18} = 0.05$, and the homogeneous initial conditions are $c_4(x,0) = c_5(x,0) = c_6(x,0) = 0.1$, $x \in \Omega$.

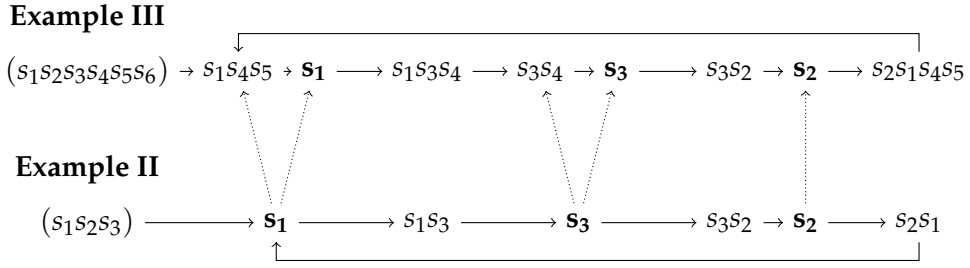


FIGURE 3.12: [46] The sequences of persistent subsets of species in the order they are periodically approached in the long-run. Shown in brackets are subsets of species referring to the initial conditions. Printed in bold are subsets of species with retention times approaching infinity as $t \to \infty$. The retention times of the other subsets converge towards finite values. Dotted lines indicate how the infinitely growing time periods of Example II each split into two time periods in Example III. Note that for Example III the transition from $\{s_1, s_4, s_5\}$ to $\{s_1\}$ might pass either the subset $\{s_1, s_4\}$ or $\{s_1, s_5\}$ depending on which of the species s_4 and s_5 vanishes more rapidly. Note that, consistent with the results of this paper, for both examples either of the persistent subsets of species of the illustrated sequences is closed and, together as DOs, they are self-maintaining.

Chapter 4

Conclusions

In this work we analyzed and discussed the persistence of species in dynamical systems relying on chemical reaction networks. In particular, we characterized the set of persistent species of bounded solutions of reaction-diffusion systems. We revealed the important fact that this set can consist of different closed subsets which are separated from each other temporally or spatially and nonetheless complement one another to achieve self-maintenance as a whole. We named sets of species with the properties mentioned above distributed organizations (DOs), noting that a DO can be identified solely from the reaction network, without requiring details about the kinetics.

By proving that the set of DOs of a reaction network forms a lattice we revealed a hierarchy relating all the potentially persistent sets of species of a dynamical system to one another. Finally, we exemplified how such information can be used to understand the behavior of complex dynamical systems with regard to appearance, extinction and persistence of their species. Taken together, the novel approach presented here will contribute to understanding and coping with complex systems particularly where spatial properties play an important role and different subsystems, though separated, cooperate to ensure their survival as a whole. Examples can be found in biology, like cell differentiation, ecology, like cooperative behavior, and chemistry, like combustion.

This study opens up several problems for future work: If nonnegativity of the solutions of the RDS (see lemma 3.3.1) can be proven for non-diagonal Fickian diffusivity matrices D, then our results hold true also in the case of cross-diffusion as described by [55]. Other types of dynamical systems derived from reaction networks can be considered, like the patch systems [1], which are connected ODE systems existing on a discrete domain, or stochastic reaction systems [39, 18]. Our approach can also be extended to RDS with other boundary conditions than the homogeneous Neumann BCs considered here, for example, by modifying the reaction network [44]. Furthermore, this work did not consider unbounded solutions. The problem with unbounded solutions is that the concept of feasibility of flux vectors breaks down since, for example, a reaction can be active even though one of its reactants has a concentration value approaching zero. An algorithm to compute all DOs of a given reaction network and an implementation as an online tool is in preparation.

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Chapter 5

Comparison of different concepts of persistence

Here we present two lemmas mentioned in Section 2.0.2. Lemma 5.0.2, already sketched in Equation 3.16, provides a comparison of our concept of persistence to a stronger and a weaker one. Lemma 5.0.1 is used to prove Lemma 5.0.2.

Lemma 5.0.1 (Equivalence criterion for the persistence of a species)**.** *Given a solution c of a RDS with an underlying reaction network $(\mathcal{S},\mathcal{R})$. A species $s_i \in \mathcal{S}$ with respect to c is persistent if and only if for all sequences $(t_j)_{j=1}^{\infty}$ of points in time*

$$\limsup_{j\to\infty} \frac{1}{t_{j+1}-t_j} \int_{t_j}^{t_{j+1}} \int_{x\in\Omega} c_i(x,t)\,dx\,dt > 0. \tag{5.1}$$

Proof. 1. First we assume that s_i is persistent with respect to c. From Lemma 3.1.1 follows that there is an $\varepsilon > 0$ such that $F(\{s_i\}^{\varepsilon}) > 0$ with respect to c and to all sequences $(t_j)_{j=1}^{\infty}$ of points in time. Thus,

$$\begin{aligned} & \limsup_{j\to\infty} \frac{1}{t_{j+1}-t_j} \int_{t_j}^{t_{j+1}} \int_{x\in\Omega} c_i(x,t)\,dx\,dt \\ \geq\ & \limsup_{j\to\infty} \frac{1}{t_{j+1}-t_j} \int_{t_j}^{t_{j+1}} \int_{x\in\Omega:\, c_i(x,t)>\varepsilon} \varepsilon\,dx\,dt \\ =\ & \varepsilon \cdot F(\{s_i\}^{\varepsilon}) \\ >\ & 0. \end{aligned}$$

2. Now we prove the other direction by contradiction. We assume, that Equation 5.1 holds true for all sequences $(t_j)_{j=1}^{\infty}$ of points in time and that s_i is not persistent with respect to c, that is (following Lema 3.1.1), $F(\{s_i\}^{\varepsilon}) = 0$ for all sufficiently small $\varepsilon > 0$ and all sequences $(t_j)_{j=1}^{\infty}$ of points in time. Thus, for all

sufficiently small $\varepsilon > 0$ holds

$$\begin{aligned}
0 \quad &< \quad \limsup_{j\to\infty} \frac{1}{t_{j+1}-t_j} \int_{t_j}^{t_{j+1}} \int_{x\in\Omega} c_i(x,t)\,dx\,dt \\
&= \quad \limsup_{j\to\infty} \frac{1}{t_{j+1}-t_j} \int_{t_j}^{t_{j+1}} \Bigg[\int_{x\in\Omega:\, c_i(x,t)\le\varepsilon} c_i(x,t)\,dx \\
&\quad + \int_{x\in\Omega:\, c_i(x,t)>\varepsilon} c_i(x,t)\,dx \Bigg] dt \\
&\le \quad \limsup_{j\to\infty} \frac{1}{t_{j+1}-t_j} \int_{t_j}^{t_{j+1}} \Bigg[\varepsilon\cdot|\Omega| + K \int_{x\in\Omega:\, c_i(x,t)>\varepsilon} dx \Bigg] dt \\
&= \quad \varepsilon\cdot|\Omega| + K\cdot F(\{s_i\}^\varepsilon) \\
&= \quad \varepsilon\cdot|\Omega| \\
&\xrightarrow{\varepsilon\to 0} 0,
\end{aligned}$$

where $K \in \mathbb{R}_+$ is an upper boundary for $c_i(x,t)$, $x \in \Omega$, $t \ge 0$. This is a contradiction and thus the proof is completed.

□

Next we state the promised lemma ranking different grades of persistence of a species including the definition used in this work (see Definition 3.1.3).

Lemma 5.0.2 (Comparison of different grades of persistence)**.** *Given a solution c of a RDS with an underlying reaction network $(\mathcal{S},\mathcal{R})$ and an arbitrary species $s_i \in S$. Then the following two conclusions hold true:*

1. $\liminf_{t\to\infty} \int_{x\in\Omega} c_i(x,t)\,dx > 0 \quad \Rightarrow \quad$ *s_i is persistent with respect to c.*
2. *s_i is persistent with respect to c,* $\quad\Rightarrow\quad \limsup_{t\to\infty} \int_{x\in\Omega} c_i(x,t)\,dx > 0.$

Proof. 1. We assume

$$\liminf_{t\to\infty} \int_{x\in\Omega} c_i(x,t)\,dx > 0. \tag{5.2}$$

So there is a time $T > 0$ such that

$$\int_{x\in\Omega} c_i(x,t)\,dx > \varepsilon. \tag{5.3}$$

for all $t > T$ and all sufficiently small $\varepsilon > 0$. Thus, for every sequence $(t_j)_{j=1}^\infty$ of points in time there is a natural number j_0 such that for all $j > j_0$ and all sufficiently small $\varepsilon > 0$

$$\frac{1}{t_{j+1}-t_j} \int_{t_j}^{t_{j+1}} \int_{x\in\Omega} c_i(x,t)\,dx\,dt > \frac{t_{j+1}-t_j}{t_{j+1}-t_j}\varepsilon = \varepsilon > 0. \tag{5.4}$$

With Lemma 3.1.1 we deduce that s_i is persistent.

2. We prove the equivalent statement that from

$$\limsup_{t\to\infty} \int_{x\in\Omega} c_i(x,t)\,dx = 0. \tag{5.5}$$

follows that s_i is not persistent. Thus we assume that Equation 5.5 holds true. Then for all $\delta_1 > 0$ there is a $T(\delta_1) > 0$ such that

$$\int_{x\in\Omega} c_s(x,t)\,dx < \delta_1 \tag{5.6}$$

for all $t > T(\delta_1)$. Then for all $\varepsilon > 0$

$$\int_{\{x\in\Omega:\, c_i(x,t)>\varepsilon\}} dx \overset{t\to\infty}{\to} 0. \tag{5.7}$$

We deduce that for all $\delta_2, \varepsilon > 0$ there is a $T(\delta_2, \varepsilon) > 0$ such that

$$\int_{\{x\in\Omega:\, c_i(x,t)>\varepsilon\}} dx < \delta_2 \tag{5.8}$$

for all $t > T(\delta_2, \varepsilon)$. Thus for all sequences $(t_j)_{j=1}^{\infty}$ of points in time and all $\delta_2, \varepsilon > 0$ there is a natural number $j(\delta_2, \varepsilon)$ such that

$$\int_{t_j}^{t_{j+1}} \int_{\{x\in\Omega:\, c_i(x,t)>\varepsilon\}} dx\,dt < (t_{j+1} - t_j)\delta_2 \tag{5.9}$$

for all $j > j(\delta_2, \varepsilon)$. Thus for all sequences $(t_j)_{j=1}^{\infty}$ of points in time

$$\limsup_{j\to\infty} \frac{1}{t_{j+1}-t_j} \int_{t_j}^{t_{j+1}} \int_{\{x\in\Omega:\, c_i(x,t)>\varepsilon\}} dx\,dt < \frac{t_{j+1}-t_j}{t_{j+1}-t_j}\delta_2 \tag{5.10}$$

for all $\delta_2, \varepsilon > 0$. By letting $\delta_2 \to 0$ we conclude

$$F(\{s_i\}^{\varepsilon}) = 0 \tag{5.11}$$

for all $\varepsilon > 0$, that is, s_i is not persistent.

□