MATCH
Communications in Mathematical and in Computer Chemistry

MATCH Commun. Math. Comput. Chem. **97** (2027) 963–1010
ISSN: 0340–6253
doi: 10.46793/match.97-3.12726

On Persistent Species and Organizations in Reaction–Diffusion–Advection Systems with Boundary Fluxes

Stephan Peter[a], **Bashar Ibrahim**[b,c,*]

[a] *Department of Basic Sciences, Ernst-Abbe University of Applied Sciences Jena, Carl-Zeiss-Promenade 2, Jena, 07745, Germany*
[b] *Department of Mathematics and Computer Science, Friedrich Schiller University Jena, Fürstengraben, Jena, 07743 Germany*
[c] *European Virus Bioinformatics Center, Leutragraben 1, Jena, 07743, Germany*

stephan.peter@eah-jena.de , bashar.ibrahim@uni-jena.de

(Received April 9, 2026)

Abstract

We establish a structural correspondence between persistent species sets and organizations of the augmented reaction network under suitable assumptions. Building upon the framework of Chemical Organization Theory, we introduce an augmented reaction network that incorporates advective transport, inflows, and outflows directly into the stoichiometric structure. This formulation allows the persistence analysis of open and spatially distributed systems to be expressed in purely algebraic terms. The main theorem proves that, for every bounded solution of a RDAS, the set of persistent species forms an organization of the augmented network, while the inverse theorem shows that every such organization can be realized as the persistent set of an appropriately constructed RDAS, independently of kinetic details. Together, these results yield a bidirectional correspondence between algebraic organization

*Corresponding author.

This work is licensed under a Creative Commons "Attribution 4.0 International" license.

and dynamical persistence, extending previous diffusion-only results to systems with advection and boundary-driven fluxes. The proposed framework unifies reaction–transport dynamics, boundary exchange, and organizational structure within a single analytical theory. Applications to biological and chemical transport processes, including viral infection dynamics with advective clearance, demonstrate how advection and boundary interactions generate novel distributed organizations and spatially localized persistence patterns. This work establishes the theoretical foundation for structural analysis and inverse design of open reactive media governed by reaction–diffusion–advection equations.

1 Introduction

Reaction networks provide a concise mathematical abstraction for the transformation and interaction of discrete species through specified reaction rules [1–4]. They offer a universal framework for modeling dynamical systems in chemistry, biology, and related areas, encompassing metabolic and ecological processes as well as engineered and distributed systems [5–10]. Within this framework, the concept of organizations captures subsets of species that are closed and self-maintaining under the given reaction rules and flux conditions. Originally introduced within the Chemical Organization Theory (COT) [8,9], organizations have since become a fundamental analytical tool for understanding the qualitative structure of reaction systems [10–12].

Earlier studies of organizations were primarily restricted to well-mixed systems governed by ordinary differential equations (ODEs). In this context, organizations identify invariant sets in which the reaction dynamics preserve the presence of certain species combinations. The main results of [10] demonstrated that the organizations of a reaction network form a complete lattice and that the persistent species of the corresponding dynamical system are always contained within at least one organization. These results established a structural foundation for analyzing complex reaction systems independently of particular kinetic assumptions.

However, many natural and technological systems exhibit spatially distributed dynamics that cannot be described by homogeneous ODE models. Diffusion, advection, and exchange processes across domain bound-

aries introduce qualitatively new effects that influence both persistence and self-maintenance [13]. Examples include advective–diffusive transport in biochemical or environmental media, reactive flows in porous materials, and energy or matter exchange through system boundaries [14–20]. While the analytical theory of reaction–diffusion and advection–diffusion systems is well established, the integration of these transport and boundary effects into the framework of organizational structures has remained an open problem.

The present work extends the concept of organizations from homogeneous reaction networks to spatially distributed reaction–diffusion–advection systems (RDAS) with general boundary conditions. To achieve this, the internal reaction network is augmented by exterior reactions representing inflows, outflows, or other boundary exchange processes. The resulting augmented reaction network captures both bulk and boundary dynamics within a unified formalism described by an extended stoichiometric matrix N_{aug}. This formulation allows for a consistent definition of organizations that remain closed and self-maintaining even in the presence of diffusion, advection, and boundary fluxes.

Building upon the theoretical foundations developed in [10,11,21], this paper proves that the extended organizations preserve the essential structural properties of the classical theory. In particular, they form a lattice under set inclusion and establish a direct link between the persistent subsets of species and the spatio-temporal dynamics of the RDAS. The main theorems show that any persistent configuration of the PDE system is contained within an organization of the augmented reaction network and, conversely, that each organization defines an invariant subset under the induced fluxes.

The framework presented here generalizes the algebraic and logical foundations of Chemical Organization Theory to systems with spatial extension and boundary coupling. It provides a mathematical foundation for the analysis of persistence, invariance, and self-maintenance in distributed reactive systems governed by transport and boundary interactions. Beyond the mathematical results, this approach also opens new perspectives for applications in physical chemistry, bioprocess modeling, and environ-

mental systems, where spatial fluxes and boundary sources are intrinsic features of the dynamics [16, 22–24].

Unlike previous formulations limited to purely diffusive transport, the present work provides an algebraic characterization of persistent species in reaction–advection–diffusion systems with inhomogeneous boundary conditions. It rigorously incorporates advective fluxes and arbitrary boundary inflows and outflows into the algebraic persistence framework, thereby extending the previous diffusion-only theory [10, 25, 26] to a fully open spatial setting. Together, the forward and inverse results establish a bidirectional correspondence between algebraic organization and dynamical persistence, revealing advection and boundary exchange as integral components of structural self-maintenance.

The paper is organized as follows. Section 2 recalls the basic definitions of reaction networks and introduces both their ODE and PDE formulations. Section 3 presents the main theoretical results, including the construction of augmented reaction networks, the definition of organizations under boundary fluxes, and the proofs establishing the correspondence between organizations and persistence. It also contains illustrative minimal examples as well as an application to virus infection dynamics. Section 4 discusses the main achievements of this study. Finally, Section 5 summarizes the main conclusions and outlines possible extensions toward multi-domain systems, temporal boundary dynamics, and reactive interfaces.

2 Preliminaries

We recall the formal representation of reaction networks and their associated dynamical systems, namely reaction–diffusion systems (RDS). This provides the foundation for the main definitions and theorems on reaction–diffusion–advection systems (RDAS) developed in this study, which are presented in Section 3. The definitions and results presented in this section are largely based on [10].

2.1 Reaction networks

We use the standard notation of chemical reaction network theory and write a reaction network as a triple

$$(\mathcal{S}, \mathcal{C}, \mathcal{R}),$$

where $\mathcal{S} = \{s_1, \ldots, s_n\}$ is a finite set of species, $\mathcal{C} \subset \mathbb{N}_0^n$ is the finite set of complexes, and $\mathcal{R} \subset \mathcal{C} \times \mathcal{C}$ is the finite set of reactions. A reaction $r_j \in \mathcal{R}$, $j = 1, \ldots, m$, is written as

$$\sum_{i=1}^{n} a_{ij} s_i \longrightarrow \sum_{i=1}^{n} b_{ij} s_i,$$

where the vectors $a_{\cdot j}, b_{\cdot j} \in \mathcal{C}$ denote the educt and product complexes, respectively. The stoichiometric matrix is defined as

$$N = B - A \in \mathbb{Z}^{n \times m}.$$

In several places below, we abbreviate the network by $(\mathcal{S}, \mathcal{R})$ when the complex set $\mathcal{C}$ is either clear from the reactions or not explicitly needed.

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.

2.2 Ordinary differential equations

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,

$$\phi : \mathbb{R}^n_{\geq 0} \to \mathcal{P}(\mathcal{S}),\ c \mapsto \phi(c), \tag{1}$$

abstraction, if

$$\phi(c) \equiv \{s_i \in \mathcal{S} : c_i > 0 \text{ for any } i \in \{1, \ldots, n\}\}. \tag{2}$$

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 $\phi(c)$. This abstraction ϕ provides a formal bridge between the continuous concentration space and the discrete structure of the reaction network, allowing algebraic properties such as closure and self-maintenance to be related directly to the dynamics of the system.

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

$$v_j \begin{cases} > 0, & \text{iff } \mathit{support}(r_j) \subseteq S, \\ = 0, & \text{otherwise.} \end{cases} \tag{3}$$

A function

$$v : \mathbb{R}^n_+ \to \mathbb{R}^m_+,\ c \mapsto v(c), \tag{4}$$

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 [5].

By defining the derivatives of the concentrations with respect to time

we obtain a dynamical system as a system of ODEs

$$\frac{\mathrm{d}}{\mathrm{d}t}c(t) = \dot{c}(t) \equiv N \cdot v(c(t)), \tag{5}$$

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.*

2.3 Reaction-diffusion-advection systems

If besides the time variable t, a space variable $x \in \Omega$ from a *Lipschitz domain* $\Omega \subset \mathbb{R}^p$, $p \in \mathbb{N}$, (i.e., Ω is bounded and open) 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. The Lipschitz regularity of the boundary guarantees the existence of an outward unit normal $\nu(x)$ defined almost everywhere on $\partial\Omega$ and ensures the validity of the divergence theorem (cf. [16, 27]). Hence, this regularity class is sufficient to make boundary integrals such as $\int_{\partial\Omega} J\nu \, dS$ and Neumann flux conditions $J\nu = g$ well-defined in the weak sense. Thus, we arrive at describing the dynamics of the concentrations $c_i = c_i(x,t)$, $i = 1, \ldots, n$, of the species at each location $x \in \Omega$ by a system of PDEs:

$$\frac{\partial}{\partial t}c_i = f_i = \underbrace{(N \cdot v(c))_i}_{\text{reactions}} + \underbrace{\nabla \cdot (d_i \cdot \nabla c_i)}_{\text{diffusion}} + \underbrace{\nabla \cdot (u_i \, c_i)}_{\text{advection}}, \quad i = 1, \ldots, n, \tag{6}$$

where ∇ is the gradient; $\nabla\cdot$ is the divergence; $d_i = d_i(x,t) \geq 0$ with $d_i \in C^{1,1}(\bar{\Omega} \times [0,T])$ are the bounded and Lipschitz continuous *diffusion rate functions*; $u_i = u_i(x,t) \geq 0$ with $u_i \in C^{1,1}(\bar{\Omega} \times [0,T])$ denote the bounded *advection rate functions* of the species; and $f_i = f_i(x,t)$ represents the combined effects acting on the species. We assume incompressible transport,

$$\nabla\cdot u(x,t) = 0, \quad x \in \Omega, \tag{7}$$

which ensures conservation of total mass in the absence of boundary fluxes. We prescribe nonnegative initial data

$$c_i(x,0) = c_i^0(x) \geq 0, \quad x \in \Omega,\ i = 1, \ldots, n, \tag{8}$$

with $c_i^0 \in C^2(\bar{\Omega})$ for all i. We impose *flux-type (Neumann) boundary conditions* that include advection,

$$J_i(x,t) \cdot \nu = g_i(x,t), \quad x \in \partial\Omega,\ i = 1, \ldots, n, \tag{9}$$

where $J_i(x,t) = -\,d_i(x,t)\,\nabla c_i(x,t) + u(x,t)\,c_i(x,t)$ denotes the total flux of species s_i; $g_i(x,t)$ with $g_i \in L^2(0,T;L^2(\partial\Omega))$ prescribes the net flow of species $s_i \in \mathcal{S}$ across the boundary; and ν is the outward unit normal on $\partial\Omega$ [28, 29].

To ensure that the boundary fluxes do not violate nonnegativity of the concentrations, we impose the *standard compatibility condition*

$$g_i(x,t)\,c_i(x,t) \geq 0 \quad \text{for all } (x,t) \in \partial\Omega \times (0,T),\ i = 1, \ldots, n. \tag{10}$$

This condition guarantees that outflow ($g_i < 0$) can only occur if the concentration at the boundary is strictly positive, while inflow values ($g_i > 0$) remain nonnegative. Such compatibility conditions are classical in the theory of parabolic systems and ensure that the boundary terms do not violate the maximum principle (see, e.g., [15, Ch. 14]).

Thus, we get a boundary value problem, a so-called *reaction-diffusion-advection system (RDAS)* with a solution

$$c:\ \Omega \times \mathbb{R}_+ \to \mathbb{R}^n,\ (x,t) \mapsto c(x,t). \tag{11}$$

satisfying $c \in L^2(0,T;H^1(\Omega))^n \cap C([0,T];L^2(\Omega))^n$, with existence, uniqueness, and nonnegativity following from standard parabolic theory [16, 30]. We assume throughout that $c(x,t)$ is uniformly bounded in space and time, i.e., there exists a constant $K > 0$ such that

$$|c(x,t)| \leq K \quad \text{for all } (x,t) \in \Omega \times [0,\infty).$$

Such uniform boundedness and regularity of weak solutions under inhomogeneous Neumann boundary conditions follow from standard parabolic PDE theory [27].

2.4 Distributed organizations (DOs)

In this subsection, we first introduce the concept of DOs, which are composed of one or more subsets of species, each being closed, and which collectively satisfy a generalized form of self-maintenance. In this study, DOs serve as the foundation for the generalization formalized in Definition 6 in Section 3.

Definition 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 exists $k \in \mathbb{N}$ and subsets $S_1, \ldots, S_k \subseteq D$ such that

$$D = \bigcup_{i=1}^{k} S_i$$

and:

1. all $S_i,\ i = 1, \ldots, k$, are *closed*,
2. there exists a vector $\hat{v} \in \mathbb{R}^m_+$ such that

$$N\hat{v} \geq 0 \tag{12}$$

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

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

We refer to the subsets S_i as the distribution components of D, and say that D is distributed over $\{S_1, \ldots, S_k\}$.

When listing elements, we use the notation

$$D = S_1 \cup S_2 = \{s_1 s_2 \mid s_1 s_3\}.$$

Note that a species can be contained in several subsets S_i, $i = 1, \ldots, k$, of a distributed organization and that the empty set $\emptyset$ can formally satisfy the closure and self-maintenance conditions.

Condition 12 expresses the self-maintenance property of a distributed organization: the net production rates of all species are nonnegative under the flux $\hat{v}$, ensuring that every species in D can sustain itself without external supply.

The following theorem constitutes one of the principal results established in [10].

Theorem 1 (Lattice property of DOs)**.** *Given a reaction network* $(\mathcal{S}, \mathcal{R})$ *the set of its DOs forms a lattice.*

2.5 Main result for RDS

The following result, originally established for reaction–diffusion systems without advection and with homogeneous Neumann boundary conditions, provides the theoretical foundation for the generalization developed in the present work.

Theorem 2 (The set of persistent species is a DO)**.** *Given the solution* c *of a RDS as in 6 (without an advection term) with underlying reaction network and homogeneous Neumann BCs, then the set* $\Phi(c)$ *of persistent species is a DO.*

The result was first established for fixed points of ODEs in [8], and later extended to simple attractors in [21]. Its most general version for reaction–diffusion systems with homogeneous Neumann boundary conditions was presented in [10].

In this work, we extend it to RDAS, i.e., RDS with advection, which also include inhomogeneous Neumann boundary conditions. We also state an inverse theorem, which states that for every DO D of a given reaction network there is a RDAS with a solution for which the set of persistent species equals D.

A crucial basis for the proof of Theorem 2 is provided by the definition of a total flux in [10], which in this study is generalized towards RDAS in Definition 7.

2.6 Definition of persistence

The concept of persistence employed in this work is based on our earlier definition for reaction–diffusion systems (RDS) [10]. Classically, persistence refers to the long-term survival of species (or concentrations) in ecological and biochemical dynamical systems. In particular, the monographs by Smith and Thieme [31] established a comprehensive analytical foundation for persistence via invariant sets and semigroup methods, providing the main mathematical tools to guarantee long-term survival under advective transport. Several foundational works formalized this idea for ODE models in mathematical ecology, introducing terms such as permanence, coexistence, strong persistence, and uniform persistence [31–38]. These definitions focus on ensuring that all species concentrations eventually remain bounded away from zero for all admissible initial data. Furthermore, existing persistence analyses for spatially extended systems with advective transport and open boundaries remain confined to analytical conditions ensuring bounded survival, but do not provide a structural characterization of long-term behavior; see, e.g. [39]. Related propagation phenomena in heterogeneous environments have been studied in the ecological context, where transport modifies survival domains and long-term spatial occupancy patterns; see Xin [19].

The generalization of persistence from ODEs to spatial systems began with reaction–diffusion equations, where analytical techniques and maximum principles were used to guarantee nonnegativity and long-term survival of species distributions [37, 40, 41]. Boundary-driven persistence has also been investigated in non-autonomous and open diffusion systems, where coexistence is ensured despite inflow and outflow processes at the domain boundary; see Hetzer and Shen [36]. Mincheva and Siegel [42], employing so-called Volpert indices [43], extended these ideas to reaction–diffusion systems with mass-action kinetics, proving that reachable species remain positive on all finite time intervals. Reachability coincides with the closure concept from Chemical Organization Theory (COT), providing a bridge between kinetic reachability and algebraic network structure. Moreover, transport processes such as advection can actively promote survival by driving species towards favorable boundary regions or inflow

zones, a mechanism analytically captured in propagation-speed analyses for heterogeneous media; see Stevens [20].

The refinement introduced in [10] goes beyond identifying which species are reachable: it characterizes which species actually persist as time approaches infinity and which do not. These persistent subsets correspond to specific algebraic substructures of the augmented reaction network associated with a spatial system. This development links kinetic long-term behavior of a single solution trajectory with purely structural, network-level notions of sustainability. This structural viewpoint is consistent with algebraic conditions for persistence developed in the context of well-mixed reaction systems, which relate survival to the combinatorial organization of reaction networks [34, 35]. These results highlight that long-term viability can be determined independently of kinetic parameters, supporting the algebraic perspective pursued in this work.

If an explicit reaction network is not provided, the question whether a given polynomial kinetic differential equation admits a reaction-network realization is a classical inverse problem in chemical kinetics [44,45]. However, such reconstructions are generally not unique. It is well known that identical dynamical systems may admit several structurally different reaction-network realizations with different complexes, reaction sets, and stoichiometric representations [44, 45].

In the present work, however, the reaction network is not introduced as an arbitrary realization of a vector field. Instead, it is induced directly by the underlying modeling assumptions: reactions originate from the reaction terms appearing in the RDAS itself, while inflows and outflows are represented by augmenting the network with exterior reactions according to Definition 5. Hence, the augmented reaction network is determined constructively from the model formulation.

The proposed framework is therefore kinetics-free in the sense that it does not depend on numerical parameter values or specific rate constants. Rather, it characterizes persistence at the level of the chosen structural representation induced by the model itself. Questions regarding invariance of organization structures across equivalent reaction-network realizations constitute an interesting direction for future research.

In the present work, we use the framework of [10] to determine which subsets of species persist along a single RDAS solution trajectory and relate them to the structural persistence properties of the underlying augmented reaction network. This provides a unifying perspective on persistence across spatially extended dynamical systems with the same reaction topology.

In the following, we formally recall the persistence concept from [10] for the RDAS setting.

Definition 2 (Sequence of points in time)**.** 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.*

Definition 3 (Neighborhood of a subset of species in the space of concentrations)**.** Given a solution $c_i(x,t)$ of a RDAS as introduced in Section 2.3, which is nonnegative for all $t > 0$, $x \in \Omega$, $s_i \in \mathcal{S}$,a subset $S \subseteq \mathcal{S}$ of species and real numbers $\varepsilon, \delta > 0$, we call the set

$$S^{\varepsilon,\delta} \equiv \{c \in \mathbb{R}_+^n : \ c_s \begin{cases} > \varepsilon & \text{iff } s \in S \\ \leq \delta & \text{iff } s \notin S \end{cases} \} \subseteq \mathbb{R}_{\geq 0}^n \tag{13}$$

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

$$S^{\varepsilon} \equiv S^{\varepsilon,\infty} \equiv \{c \in \mathbb{R}_+^n : \ c_s > \varepsilon \text{ iff } s \in S\} \subseteq \mathbb{R}_{\geq 0}^n \tag{14}$$

of concentration vectors the ε-*neighborhood* of S.

Definition 4 (Persistent subsets of species and persistent species)**.** Given a solution c of a 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 $\varepsilon > 0$ 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,

$$F(S^{\varepsilon,\delta}) = \limsup_{j\to\infty} \frac{1}{t_{j+1}-t_j} \int_{t_j}^{t_{j+1}} \int_{\{x\in\Omega:\ c(x,t)\in S^{\varepsilon,\delta}\}} dx\,dt > 0. \tag{15}$$

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

$$P(c) \equiv \{S \subseteq \mathcal{S} :\ S \text{ is persistent with respect to } c\}. \tag{16}$$

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.,

$$s \in \cup\{S \subseteq \mathcal{S} :\ S \in P(c)\}. \tag{17}$$

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 denominate the set of persistent species $\Phi(c)$, i.e.,

$$\Phi(c) \equiv \{s \in \mathcal{S} :\ s \text{ is persistent with respect to } c\} = \cup\{S \subseteq \mathcal{S} :\ S \in P(c)\}. \tag{18}$$

It is important to note that Definition 18 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 not being elements of S.

Intuitively, a species is persistent if it reappears infinitely often with a concentration bounded away from zero, while species outside a persistent subset eventually vanish or remain arbitrarily small. This definition thus distinguishes long-term coexistence from transient presence and it forms the conceptual foundation for linking long-term dynamical behavior to the algebraic structure of organizations in the subsequent results.

2.7 Introductory example I: Illustration of persistence and distributed organizations

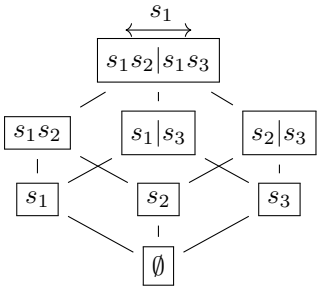
The following example, first analyzed in [10], illustrates how the lattice of distributed organizations (DOs) reflects the persistent subsets of species observed in a simulated reaction–diffusion system. Figure 1a shows the system of PDEs of a reaction–diffusion system. In Figure 1b the reactions of 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 that v is a flux vector function. In [25] an example of this procedure is described. Figure 1c shows the lattice of DOs of the reaction network of Example I. Figure 1d shows simulation results.

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

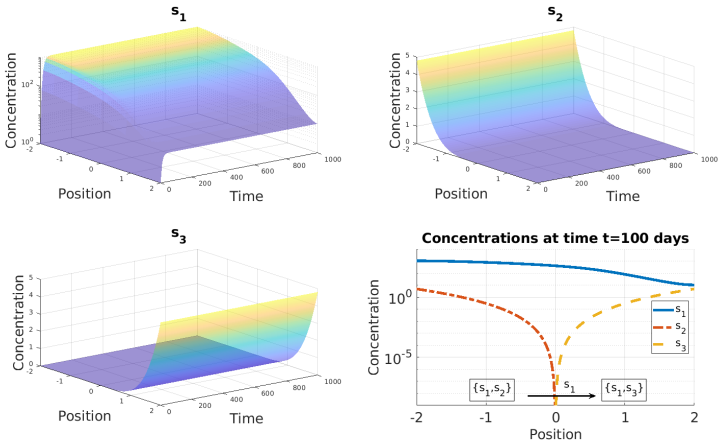
(a) PDEs

$$\begin{aligned}
r_1 &: \quad s_1 + s_2 \to 2s_1 + s_2 \\
r_2 &: \quad 2s_1 + s_3 \to s_3 \\
r_3 &: \quad s_2 + s_3 \to \emptyset
\end{aligned}$$

(b) Reactions



(c) Distributed organizations



(d) Simulation results

Figure 1. (a) PDEs, (b) set of reactions, (c) lattice of DOs and (d) simulation results of Example I. There are 3 DOs that are not organizations (compartments separated by vertical bars). For each DO, the corresponding minimal compartmental decomposition is shown, representing the smallest number of subsets required for self-maintenance. The upmost DO, containing all species, appears as the set of persistent species in the simulation shown in the lower right of Figure 1d. Simulations were performed using Matlab R2023b method 'pdepe'. Initial conditions: $c_1^0(x) = 1$ 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 $x < 0$. Diffusion rates: $d_1 = 5$, $d_2 = d_3 = 0$, that is, only species s_1 diffuses.

The simulation of the solution $c(x,t)$ shows that all three species are persistent, with the persistent subsets $\{s_1, s_2\}$ and $\{s_1, s_3\}$ distributed spatially across the domain. Hence, the set of persistent species $\Phi(c) = \{s_1, s_2, s_3\}$ constitutes a distributed organization, confirming the theoretical prediction of Theorem 2.

Remark (Dynamical realization of distributedness). The introductory simulation result shown in Figure 1 illustrates how distributed organizations can be realized or maintained through spatial separation. In [10], we demonstrated with a simulation example of a heteroclinic orbit that such a realization can also occur in time. Of course, distributedness may also result from a combination of both aforementioned types or from entirely

different causes, for instance functionally through a membrane separating different compartments.

The concepts introduced in this section establish the structural and analytical basis for the subsequent results, where we extend these notions to reaction–diffusion–advection systems with general boundary conditions.

3 Results

3.1 Extension of the reaction network

To incorporate inhomogeneous Neumann BCs into our framework, that is, to still capture the DOS representing persistent species, we augment the reaction network accordingly. More precisely, if there is a positive Neumann BC for a species s, we add an additional inflow reaction $\emptyset \to s$ for that species to the reaction network and if there is a negative Neumann BC, we add an outflow reaction $s \to \emptyset$.

Definition 5 (Extension of the reaction network to incorporate BCs)**.** Given a RDAS with underlying reaction network $(\mathcal{S}, \mathcal{R})$. To incorporate inhomogeneous Neumann BCs we add to $\mathcal{R}$, which we will call the set of **interior** reactions $\mathcal{R}_{int}$, the set

$$\mathcal{R}_{ext} \equiv \{r_{m+1}, \dots, r_{m+n}, r_{m+n+1}, \dots, r_{m+2n}\} \tag{19}$$

of so-called **exterior** reactions with

$$r_j : \begin{cases} \emptyset \to s_j, & \text{iff } s_j \text{ follows a } \textbf{positive} \text{ Neumann BC,} \\ \emptyset \to \emptyset, & \text{iff } s_j \text{ follows a homogeneous Neumann BC,} \end{cases} \tag{20}$$

for $j = m+1, \dots, m+n$, and

$$r_j : \begin{cases} s_j \to \emptyset, & \text{iff } s_j \text{ follows a } \textbf{negative} \text{ Neumann BC,} \\ \emptyset \to \emptyset, & \text{iff } s_j \text{ follows a homogeneous Neumann BC,} \end{cases} \tag{21}$$

for $j = 2m+n+1, \dots, m+2n$, to the reaction network.

We call

$$(\mathcal{S}, \mathcal{R}_{int} \cup \mathcal{R}_{ext}) = (\mathcal{S}, \mathcal{R}_{aug}). \tag{22}$$

the **augmented** reaction of the RDAS and the corresponding stoichiometric matrix $N_{aug} \in \mathbb{Z}^{nx(m+2n)}$ the augmented stoichiometric matrix of the RDAS. Note, that $N_{aug} = (N_{int}|N_{ext})$ is composed by the columns of the original stoichiometric matrix (without BCs etc.) $N_{int} \equiv N$ and the columns referring to the exterior reactions N_{ext}.

Thus, in the case of only homogeneous Neumann BCs and no advection the DOs are the same as defined in Definition 1.

Remark (Other types of BCs, Sources and Sinks).

1. The same extension of the reaction network as applied for positive Neumann boundary conditions should also be performed for more general RDAS whenever a species is not introduced into the system by reactions, but rather through other boundary conditions that justify an inflow, such as corresponding Dirichlet boundary conditions, or through a source.

2. The same applies conversely to sinks or any type of outflow.

3. If both inflows and outflows occur, for example at shared boundaries or under periodically alternating boundary conditions, then both an inflow and an outflow should be defined for the corresponding species in the extended reaction network. The same holds if, for instance, under Dirichlet boundary conditions either an inflow or an outflow may occur depending on the solution, since COT specifies all potentialities of an RDAS in the long-term behavior.

3.2 Adopted definition of organizations

We now present generalization of Definition 1 for DOs to account for inhomogeneous BCs, sinks, sources, etc. in RDASs. For simplicity, we again employ the term organization, although it represents a generalization of the original definition. The so-called distributed organizations (DOs) therefore constitute an intermediate stage between the original definition of

organizations and the new definition proposed in this work. In particular, the new definition of organizations not only incorporates inhomogeneous boundary conditions, sinks, and sources, but also accounts for the fact that an organization cannot, in general, be uniquely reduced to a set of species. Instead—at least in cases where ambiguities may occur—it must also involve an associated set of reactions [11]. Accordingly, the following definition builds upon the previous work on the computation of organizations, in which the inclusion of organizations themselves had already become necessary [11].

Definition 6 (Organizations of augmented reaction networks)**.** Let (S, R_{int}) be a reaction network with $|S| = n$ species and $|R_{\text{int}}| = m$ internal reactions, and let R_{ext} denote the set of exterior reactions that represent boundary inflows and outflows according to Definition 5. The augmented network is

$$(S, R_{\text{aug}}), \qquad R_{\text{aug}} := R_{\text{int}} \cup R_{\text{ext}},$$

with stoichiometric matrix $N_{\text{aug}} = [\, N_{\text{int}} \mid N_{\text{ext}} \,] \in \mathbb{Z}^{n \times (m + |R_{\text{ext}}|)}$.

A pair (O, R) with $O \subseteq S$ and $R \subseteq R_{\text{aug}}$ is called an organization of the augmented reaction network if and only if there exist $k \in \mathbb{N}$ triplets

$$(S_i, R_i, \hat{v}^{(i)}), \qquad i = 1, \ldots, k,$$

called compartments, such that the following conditions hold:

(1) Each $S_i \subseteq S$ is closed with respect to R_{int}, that is,

$$\forall r \in R_{\text{int}} : \ \text{supp}(r) \subseteq S_i \ \Rightarrow \ \text{prod}(r) \subseteq S_i.$$

(2) Covering: The overall set of species and reactions is obtained by

$$O = \bigcup_{i=1}^{k} S_i, \qquad R = \bigcup_{i=1}^{k} R_i.$$

(3) All exterior reactions are contained in at least one compartment,

$$R_{\text{ext}} \subseteq \bigcup_{i=1}^{k} R_i.$$

(4) Feasibility (for internal reactions): for every $r \in R_{\text{int}}$ and every $i \in \{1, \ldots, k\}$,

$$\text{supp}(r) \subseteq S_i \;\Rightarrow\; r \in R_i.$$

(5) Each compartment is associated with a nonnegative flux vector $\hat{v}^{(i)} \in \mathbb{R}_{\geq 0}^{m+|R_{\text{ext}}|}$ satisfying

$$\hat{v}_r^{(i)} > 0 \;\Leftrightarrow\; r \in R_i,$$

and the total flux fulfills the self-maintenance condition

$$N_{\text{aug}} \sum_{i=1}^{k} \hat{v}^{(i)} \;\geq\; 0. \tag{23}$$

If these conditions are met, we call (O, R) an organization of (S, R_{aug}) and write

$$O = \{\, S_1 \mid S_2 \mid \cdots \mid S_k \,\}$$

to denote the distribution of O into the closed compartments S_i.

Following Theorem 1 of [10], the set of all organizations of an augmented reaction network again forms a lattice. This follows because the generalized notion of organization preserves closure under unions and intersections of feasible compartment configurations. Hence the lattice structure carries over from the classical setting to the augmented case.

Computation of organization lattices. The lattice structure introduced above is not merely existential but can also be generated algorithmically. In previous work, algorithms were developed for computing all distributed organizations (DOs), sets of organizational reactions (SORs), maximal compartments (MCs), and their corresponding lattice structures

directly from reaction networks [11]. These methods require no knowledge of kinetic parameters or reaction-rate constants and therefore remain fully consistent with the kinetics-free philosophy of Chemical Organization Theory.

The computational procedure starts by constructing elementary reaction closures (ERCs), which represent minimal reaction structures that become activated together. Based on these ERCs, all admissible sets of organizational reactions are computed using mixed-integer linear programming (MILP) combined with integer cuts. Distributed organizations and their minimal compartmentalizations are then derived from these reaction sets.

Since the present framework extends classical reaction networks only by introducing augmented exterior reactions for inflows and outflows, the same computational strategy can be transferred directly to augmented reaction networks. In particular, exterior reactions simply enlarge the reaction set while preserving the closure and self-maintenance conditions underlying the algorithm.

As in related combinatorial approaches such as minimal siphon computation in Petri nets, the overall computational complexity may grow exponentially with network size. In fact, the underlying optimization problems are NP-hard in the worst case [11]. Consequently, organization lattices should primarily be regarded as exact structural objects rather than polynomial-time constructs in general.

3.3 Total flux of a RDAS

Definition 7 (Subsequential time-averaged internal and external fluxes)**.** Let $c : \Omega \times [0, \infty) \to \mathbb{R}^n_{\geq 0}$ be a bounded solution of the reaction–diffusion–advection system on a bounded domain $\Omega \subset \mathbb{R}^p$. Consider an increasing sequence of time points $(t_j)_{j\in\mathbb{N}}$ satisfying

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

for some constant $Z > 0$.

Assume that the corresponding averaged internal and external fluxes

admit convergent subsequences. Then we define

$$\hat{v}^{\mathrm{int}} = \lim_{k\to\infty} \frac{1}{t_{j_k+1} - t_{j_k}} \int_{t_{j_k}}^{t_{j_k+1}} \int_{\Omega} v(c(x,t))\, dx\, dt$$

and

$$\hat{v}^{\mathrm{ext}} = \lim_{k\to\infty} \frac{1}{t_{j_k+1} - t_{j_k}} \int_{t_{j_k}}^{t_{j_k+1}} \int_{\partial\Omega} g(x,t)\, dS\, dt.$$

Remark. The use of bounded moving windows follows the philosophy of local persistence developed in the context of distributed organizations in reaction–diffusion systems [10]. In contrast to global Cesàro averages over $[0,T]$, bounded windows allow the detection of persistent local activity patterns that may recur intermittently over time.

3.4 Standing assumptions for the main results

In order to formulate the main structural results in a mathematically rigorous way, we impose the following assumptions throughout this section.

Consider the reaction–diffusion–advection system

$$\partial_t c_i(x,t) = D_i \Delta c_i(x,t) - \nabla\cdot(u_i(x,t)c_i(x,t)) + \sum_{r=1}^{m} N_{ir} v_r(c(x,t)), \qquad i = 1,\dots,n, \tag{24}$$

on a bounded domain $\Omega \subset \mathbb{R}^d$ with sufficiently smooth boundary $\partial\Omega$, supplemented with boundary flux conditions

$$D_i \nabla c_i(x,t)\cdot\nu(x) - u_i(x,t)c_i(x,t)\cdot\nu(x) = g_i(x,t), \qquad x \in \partial\Omega, \tag{25}$$

where ν denotes the outward unit normal vector.

Throughout the following, we assume:

(A1) **Bounded domain and regularity.** The domain Ω is bounded and has piecewise smooth boundary. The diffusion coefficients satisfy $D_i > 0$ for all $i \in \{1,\dots,n\}$.

(A2) **Existence of bounded weak solutions.** There exists a global weak solution

$$c : \Omega \times [0,\infty) \to \mathbb{R}^n_{\geq 0}$$

that remains nonnegative and uniformly bounded, i.e., there exists a constant $M > 0$ such that

$$0 \le c_i(x,t) \le M$$

for all $i \in \{1,\dots,n\}$, $x \in \Omega$, and $t \ge 0$.

(A3) **Regularity of advection and boundary fluxes.** The advection fields $u_i(x,t)$ and boundary fluxes $g_i(x,t)$ are measurable and bounded. Moreover, for each species s_i, the boundary flux is assumed to possess a well-defined long-term sign structure in the sense that there exist measurable subsets

$$\partial\Omega_i^+, \qquad \partial\Omega_i^-, \qquad \partial\Omega_i^0$$

with

$$\partial\Omega = \partial\Omega_i^+ \cup \partial\Omega_i^- \cup \partial\Omega_i^0$$

such that, asymptotically in time, positive time-averaged boundary fluxes prevail on $\partial\Omega_i^+$, negative time-averaged boundary fluxes prevail on $\partial\Omega_i^-$, and asymptotically vanishing boundary fluxes prevail on $\partial\Omega_i^0$.

(A4) **Existence of subsequential moving-window flux averages.** For every bounded solution $c(x,t)$, there exists an increasing sequence $(t_j)_{j\in\mathbb{N}}$ with $1 \le t_{j+1} - t_j \le Z$ such that the corresponding moving-window averages of the internal and external fluxes admit convergent subsequences.

(A5) **Persistence in the sense of positive recurrence.** A species set $S \subseteq \mathcal{M}$ is called persistent if there exists $\varepsilon > 0$ such that the set of times

$$\left\{ t \ge 0 : \inf_{x\in\Omega} c_i(x,t) \ge \varepsilon \text{ for all } s_i \in S \right\}$$

has positive upper density in time.

Assumptions of this type are standard in the study of asymptotic properties of dissipative reaction–diffusion systems, persistence theory, and

long-time averaging arguments; see, e.g., [15, 46, 47].

3.5 Generalized main theorem

Lemma 1 (Divergence theorem for diffusion and advection)**.** *Let* $c = (c_1, \ldots, c_n)$ *be a sufficiently smooth solution of the reaction–diffusion–advection system 6. Then, for every species index* i *and every time interval* $[t_j, t_{j+1}]$*, the following identities hold:*

$$\int_{t_j}^{t_{j+1}} \int_{\Omega} \nabla \cdot \big(d_i \nabla c_i\big)\, dx\, dt = \int_{t_j}^{t_{j+1}} \int_{\partial\Omega} (d_i \nabla c_i \cdot \nu)\, dS\, dt, \tag{26}$$

$$\int_{t_j}^{t_{j+1}} \int_{\Omega} \nabla \cdot \big(u\, c_i\big)\, dx\, dt = \int_{t_j}^{t_{j+1}} \int_{\partial\Omega} (u \cdot \nu)\, c_i\, dS\, dt. \tag{27}$$

Consequently, all boundary contributions originating from diffusion and advection are fully contained in the single boundary integral

$$\int_{t_j}^{t_{j+1}} \int_{\partial\Omega} J_i \cdot \nu\, dS\, dt = \int_{t_j}^{t_{j+1}} \int_{\partial\Omega} g_i\, dS\, dt. \tag{28}$$

Hence, no advective volume term remains in the integral balance; mass exchange due to transport processes occurs exclusively through $\partial\Omega$*.*

The proof is given in Appendix 6.

The divergence-free condition $\nabla \cdot u = 0$ ensures that advection acts purely as transport without internal sources. Hence advective effects enter the persistence balance only through the boundary integral. Persistence can therefore be sustained by convective inflow, even when internal reactions alone would not maintain positivity.

The sequence of results leading to the following theorem follows a clear progression: first for ODEs describing well-mixed systems, then for spatially extended reaction–diffusion systems, and finally for the general case considered here. In contrast to these earlier formulations, the present work extends the correspondence between persistence and organizations to reaction–diffusion–advection systems with general inhomogeneous boundary conditions and arbitrary advective transport.

Theorem 3 (The set of persistent species of a RDAS is a DO)**.** *Assume that the RDAS satisfies assumptions (A1)–(A5). Then the set* $\Phi(c)$ *of persistent species is a DO of the underlying augmented reaction network* $(\mathcal{S}, \mathcal{R}_{int} \cup \mathcal{R}_{ext})$.

The full proof is given in Appendix 7.

3.6 Inverse theorem

Theorem 4 (Inverse Theorem for RDAS organizations — kinetics-free formulation)**.** *Assume that the RDAS satisfies assumptions (A1)–(A5). Let* (S, R_{int}) *be a reaction network and* R_{ext} *the exterior reactions forming the augmented network* (S, R_{aug}) *with stoichiometric matrix* $N_{\text{aug}} = [\, N_{\text{int}} \mid N_{\text{ext}} \,]$. *Assume* (O, R) *is an organization of* (S, R_{aug}) *in the sense of Definition 6. Then there exists an RDAS* (6)–(10) *with diffusion coefficients* $d_i \equiv 0$ *and* $u \equiv 0$, *a (time-independent) boundary flux* g, *and locally Lipschitz reaction rates* $v : \mathbb{R}^n_{\geq 0} \to \mathbb{R}^{|R_{\text{int}}|}_{\geq 0}$ *such that the corresponding bounded solution* $c : \Omega \times \mathbb{R}_+ \to \mathbb{R}^n_{\geq 0}$ *satisfies*

$$\Phi(c) = O.$$

The proof is given in Appendix 8.

Remark on internal interfaces Since diffusion and advection are set to zero in the constructed RDAS ($d_i \equiv 0$, $u \equiv 0$), there are no fluxes across the internal interfaces $\partial\Omega_i \cap \partial\Omega_j$. Hence each subdomain Ω_i evolves independently, and the piecewise constant stationary state c^*, although discontinuous across these interfaces, satisfies the equations in the weak sense.

If one prefers strictly positive diffusion coefficients

$$d_i \equiv \varepsilon > 0,$$

standard elliptic regularization results (see, e.g., [18]) imply the existence of smooth stationary solutions c^ε that converge to c^* as $\varepsilon \to 0$. Thus, the inverse construction is robust under small diffusive perturbations.

The inequality $N\hat{v} \geq 0$ in Definition 6 ensures that, for the stationary solutions constructed in the proof of the Inverse Theorem 4, the external inflows and outflows of each species sum to a value that is greater than or equal to zero. This value can be interpreted as representing the state of an internal reservoir for each species, which requires no external supply, thereby allowing the entire system to be regarded as effectively closed.

3.7 Illustrating examples

To elucidate how the generalized definitions and theorems apply in practice, we present two variants of the introductory Example I from Subsection 2.7. Both examples demonstrate how boundary conditions and advection modify the organizational structure predicted by the theory.

3.7.1 Example II

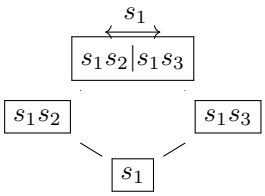
In this example, reaction $r_1 : \quad s_1 + s_2 \rightarrow 2s_1 + s_2$, which produces s_1, is eliminated and compensated for by a positive Dirichlet BC at the left boundary, which replaces the former homogeneous Neumann BC (see Figure 2a for the PDEs). The positive Dirichlet BC is represented by the new inflow reaction $r_{1,ext} : \emptyset \rightarrow s_1$ of the extended reaction network (see Figure 2b). This in turn is used to compute the corresponding lattice of organizations (see Figure 2c), which differs from the one of Example I but contains the same DO $\{s_1s_2|s_1s_3\}$. All other parameters were chosen as in Example I. The simulation results are shown in Figure 2d with the initial state on the left and the long-term behavior on the right, which is ruled by the organization $\{s_1s_2|s_1s_3\}$ as for Example I.

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

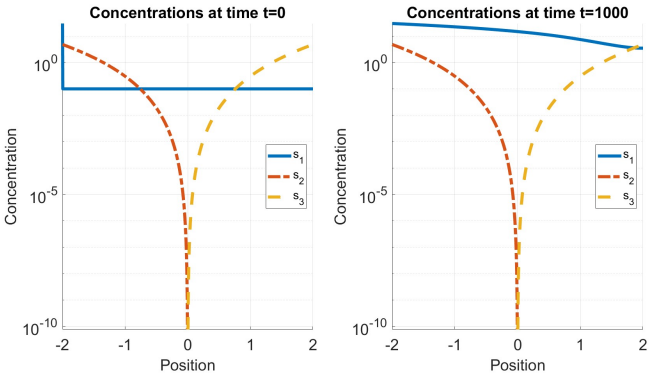
(a) PDEs

$$r_{1,ext}: \ \emptyset \to s_1$$
$$r_2: \ 2s_1 + s_3 \to s_3$$
$$r_3: \ s_2 + s_3 \to \emptyset$$

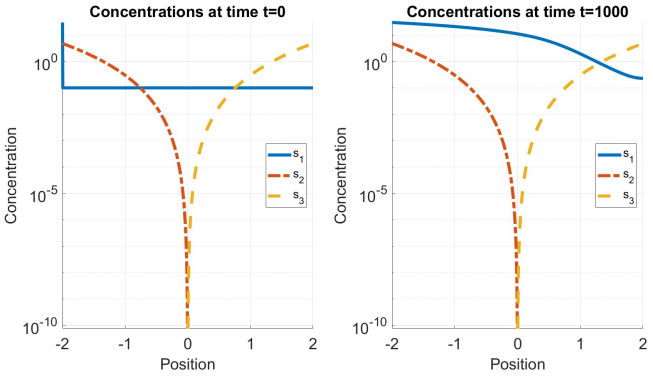
(b) Reactions



(c) Organizations



(d) Example II simulation: ICs (left) and steady state (right)



(e) Example III simulation: ICs (left) and steady state (right)

Figure 2. (a) PDEs, (b) set of reactions, (c) lattice of organizations and simulation results of Example II (d) and Example III (e) both with positive Dirichlet BC $\frac{\partial}{\partial n} c_1(-2, t) = 30$, $t \geq 0$, for s_1 at the left boundary of the domain. Furthermore, for Example III, the diffusion constant of s_1 was reduced by $\frac{1}{50}$ to $d_1 = 0.1$, which was compensated by a homogeneous rightward advection with constant $a_1 = 0.01$. Simulations were performed using Matlab R2023b method 'pdepe'. All other parameters as for Example I.

3.7.2 Example III

Example III builds upon Example II. The only difference is that for Example III diffusion of s_1 was reduced strongly to (a computationally affordable) $\frac{1}{50}$ compared to Example I and compensated by a rightward advection of s_1 with a coefficient of $a_1 = 0.01$. All other parameters were kept unchanged. PDEs, reactions and lattice of organizations were the same as for Example II (see Figures 2a to 2c). Figure 2e shows the simulation results for Example III.

3.8 Viral infection dynamics with interferon, antibodies, and advective clearance

Within-host infection of airway epithelia is classically described by target-cell models [48–50]. Spatial extensions incorporate viral diffusion and mucociliary advection in the respiratory tract, as well as boundary exposure and drainage [51–54]. To demonstrate a richer lattice of organizations in our framework, we consider the species: S (susceptible), E (eclipse), I_1 (productively infected), I_2 (late infected), V (free virus), F (type-I IFN), R (refractory), A (antibody), C (virus–Ab complex).

The setup follows a generic respiratory infection model inspired by influenza A dynamics in airway epithelia [51]. Unlike previous simulation-based studies, we here analyze the algebraic structure of persistence independent of kinetic parameters.

On a Lipschitz domain $\Omega \subset \mathbb{R}^p$ (upper airways) we pose the RDAS

$$\partial_t S = -\beta S V - \sigma F S + \rho R, \tag{29}$$

$$\partial_t E = \beta S V - \kappa E, \tag{30}$$

$$\partial_t I_1 = \kappa E - \gamma I_1, \tag{31}$$

$$\partial_t I_2 = \gamma I_1 - \delta I_2, \tag{32}$$

$$\partial_t V = p I_2 - c V - k A V + D_V \Delta V - u \cdot \nabla V, \tag{33}$$

$$\partial_t F = \pi I_1 - \mu F + D_F \Delta F, \tag{34}$$

$$\partial_t R = \sigma F S - \rho R, \tag{35}$$

$$\partial_t A = s_A - \eta A - k A V + D_A \Delta A, \tag{36}$$

$$\partial_t C = kAV - \xi C, \tag{37}$$

with nonnegative smooth initial data. Here u is a divergence-free advection field (mucociliary transport), $D_\bullet \geq 0$ are diffusion rates.

Boundary conditions and augmented reaction network At an exposure boundary $\Gamma_{\text{in}} \subset \partial\Omega$ we prescribe a viral inflow $J_V \cdot \nu = g_{\text{in}} > 0$; along drainage/clearance boundaries Γ_{out} we impose advective outflow $J_V \cdot \nu = -g_{\text{out}} V$. The inflow boundary Γ_{in} represents initial viral exposure in upper airways (e.g., inhaled inoculum), whereas Γ_{out} models mucociliary clearance through advective transport towards the pharynx. Elsewhere we use homogeneous flux or do-nothing conditions for transported fields. Antibody can be supplied from the periphery via a Robin/flux in A on vascular interfaces. Following Def. 5, the augmented network adds exterior reactions

$$\emptyset \to V, \quad V \to \emptyset, \quad \emptyset \to A,$$

to the interior set listed in Appendix 9. This augmentation transforms the open viral system into a closed algebraic framework to which Theorem 3 and Definition 6 directly apply. It yields an augmented stoichiometric matrix N_{aug} used to compute the organizations below according to Definition 6.

Table 1 summarizes the principal organizations of the augmented viral infection network, while Figure 3 visualizes their inclusion relations in schematic lattice form. This representation makes explicit which persistent regimes are organizationally admissible and which larger species sets fail because the self-maintenance condition is violated.

Possibly persistent subsets and their organizational relations are summarized in Table 1 and visualized schematically in Figure 3. The sets discussed below illustrate how antibody inflow, viral exposure, and interferon control give rise to distinct organizational regimes.

Due to the inflows of viruses and antibodies and the virus neutralization $V + A \to C \to \varnothing$, $O_1 = \{V|A\}$ represents the smallest possibly persistent set or organization, which merges into $O_2 = \{V, A, C\}$ once com-

Table 1. Selected organizations of the augmented viral infection network and their qualitative interpretation. Here, compartmentalization is indicated by vertical bars. Parentheses indicate optional occurrence of a species depending on the compartmental realization.

Org.	Species structure	Qualitative interpretation
O_1	$\{V \mid A\}$	Minimal compartmentalized antibody-control block sustained by viral and antibody inflow.
O_2	$\{V, A, C\}$	Non-compartmentalized antibody-neutralization block including the virus–antibody complex.
O_3	$\{S \mid V \mid A\}$	Susceptible cells spatially separated from the antibody-control block.
O_4	$\{S \mid V, A, C\}$	Susceptible cells coexisting with a non-compartmentalized antibody-neutralization block.
O_5	$\{F \mid S \mid V, A, (C)\}$	Compartmentalized realization of interferon control together with antibody-mediated persistence.
O_6	$\{F, S, R \mid V, A, (C)\}$	Interferon-control organization with refractory cells and antibody-mediated persistence.
–	$\{F, S, R, E, I_1, I_2, V\}$	Not an organization: the full infection chain is not self-maintaining because degradation dominates and $N_{\text{aug}}\hat{v} \not\geq 0$.

partmentalization is removed. These organizations represent the *antibody control* block, one of the two existing control mechanisms for the virus. Since the antibodies do not exhibit further interactions with other species, they can trivially be assigned to any compartment of the subsequently considered organizations that does not contain viruses, as long as their inflow is present. Thus, for example, the organizations $O_3 = \{S|V|A\}$ and $O_4 = \{S|V, A, C\}$ arise. If the antibodies are assigned to a compartment containing viruses, the balance for the virus concentration within this organization must be maintained either through their inflow or through virus release $I_2 \to I_2 + V$.

The mentioned virus release stands at the end of a chain of reactions that begins with the infection of susceptible cells: $S + V \to E + V$, $E \to I_1 \to I_2 \to I_2 + V$, and up to and including interferon produc-

tion $I_1 \to I_1 + F$, represents an *active infection* without control. Since this chain reproduces itself stepwise and (except for V) each of its elements is degraded, the set of elements involved in it must, from an organizational-theoretical perspective, always be considered as a whole. The aforementioned chain is closed by the two reactions $F + S \to F + R$ (IFN signalling towards refractory state) and $R \to S$ (recovery of refractory cells), which represent *IFN control*, the second control mechanism for the virus, and even include a positive feedback for S. However, this positive feedback is not sufficient to balance the two negative feedbacks ($S + V \to E + V$ and $F + S \to F + R$) and to turn the overall complex $\{F, S, R, E, I_1, I_2, A, V, C\}$ into an organization. Formally, this follows from violation of the non-negativity condition $N_{aug}\hat{v} \geq 0$ due to unbalanced degradation fluxes. Therefore, the species set $\{F, S, R, E, I_1, I_2, V\}$ cannot be part of any persistent set of any solution. Only organizations such as $O_5 = \{F|S|V, A, (C)\}$ and $O_6 = \{F, S, R|V, A, (C)\}$ can be persistent due to appropriate compartmentalization. The F (type-I IFN) makes them belonging to the IFN control block. Thus, the lattice partitions the viral dynamics into three algebraically distinct control regimes: antibody-mediated, interferon-mediated, and uncontrolled infection.

The predominance of compartmentalized organizations demonstrates the important role of spatial distributedness for the persistence of many organizations. This persistence becomes more difficult when V or A exhibit high diffusivity. Conversely, it can be supported by a suitably oriented strong advection of V with respect to the inflows and outflows of V and A. If the inflow of V vanishes, new infection-free organizations may naturally emerge.

Connection to published simulations (i) Spatial localization and transport: Quirouette et al. reproduce axial gradients and region-specific infection in the human respiratory tract; our organizations with advection ($u \neq 0$) and inflow/outflow capture transitions between persistence nodes when exposure (g_{in}) or clearance (g_{out}) shift [51]. Spatial pattern transitions induced by boundary inflow and advective transport have been demonstrated analytically and numerically in open reaction–diffusion

systems [18]. (ii) IFN ring/barrier effects: PDE simulations show that paracrine IFN creates expanding refractory "rings" that stall infection spread—consistent with transitions into O_6 resp. only $\{F, S, R\}$ in case the inflows from V and A are over [52]. (iii) Interferon fields in RD models: Reaction–diffusion models with IFN (and delay) generate fronts and reduced plaque growth, matching the same organizations, that is, those $\{F, S, R\}$ again [55]. (iv) Antibody layers: Hybrid continuum agents with antibodies support long-term coexistence of A and C aligning with the organization $\{S \mid V, A, C\}$ [56]. Although these simulations do not explicitly address persistence in the algebraic sense of Theorem 3, their long-term stationary patterns correspond to distinct persistent subsets predicted by the organizational framework. Collectively, these correspondences validate that the lattice structure captures all qualitatively distinct spatial outcomes observed in detailed PDE and hybrid models.

What the lattice predicts The lattice provides a structural phase map: increasing antibody supply (boundary inflow in A) moves $\Phi(c)$ from the set of all species to O_4 or further downward, while stronger IFN production (π) or signalling (σ) shifts towards O_6 and finally – when the inflows of V and A vanish – to its subset $\{F, S, R\}$, which is an organization in this case; reducing exposure g_{in} or increasing g_{out} induces a descent to $\{S\}$. These transitions reflect simulation results, yet they are themselves algebraic consequences of the augmented network and do not rely on fitted kinetics. Hence, the proposed algebraic approach provides a compact explanatory framework for complex spatio-temporal infection phenomena, revealing that persistence transitions follow from stoichiometric topology alone.

4 Discussion

This work generalizes the structural persistence framework from reaction–diffusion to reaction–advection–diffusion systems with open boundaries. The theoretical framework developed in this work establishes a unifying correspondence between algebraic structure and dynamical behav-

ior in reaction–diffusion–advection systems (RDAS). The Main Theorem demonstrates that the persistent species of any bounded RDAS solution form an organization of its augmented reaction network, while the Inverse Theorem proves the converse: every algebraically admissible organization can be dynamically realized as the persistent set of a suitable RDAS. Together, these results establish a two-way correspondence between structure and dynamics.

An important distinction concerns the role of reaction-network realizations. While equivalent dynamical systems may admit multiple reaction-network representations, the present framework operates on the model-induced augmented network obtained directly from the RDAS formulation. Thus, the structural correspondence established here is independent of kinetic parameter choices while remaining grounded in the mechanistic representation selected during model construction.

Conceptual significance. This bidirectional relation elevates the theory from a one-directional criterion,

$$\text{dynamical persistence} \;\Rightarrow\; \text{algebraic organization},$$

to a true correspondence

$$\text{structure} \;\Longleftrightarrow\; \text{dynamics}.$$

Hence, the lattice of organizations provides an algebraic description of a broad class of long-term behaviors of open reactive media satisfying assumptions (A1)–(A5). Persistence and extinction appear as topological phenomena governed by flux balance and boundary geometry rather than by kinetic parameter choices alone. This observation aligns with analytical results showing that advective transport and boundary exchange can fundamentally alter survival outcomes in spatially distributed systems. In particular, transport-induced localization and isolation of reactive regions have been demonstrated in open reaction–diffusion systems [18], while advection-driven propagation has been shown to facilitate persistence in heterogeneous media [20]. Together, these results underscore that bound-

ary geometry and transport fields are not merely quantitative modifiers but may qualitatively influence long-term viability.

From a theoretical standpoint, this result is analogous to completeness or realization theorems in other mathematical disciplines: it shows that the notion of organization is not only necessary but also sufficient for persistence. No algebraically admissible organization remains unrealizable; conversely, no dynamically persistent structure lies outside the algebraic framework. This shows that the organization formalism is sufficiently expressive to represent a wide range of persistent behaviors.

Relation to prior work. Classical Chemical Organization Theory (COT) [9] already established that persistent steady states of closed reaction networks correspond to self-maintaining, closed sets of reactions and species. Subsequent generalizations to spatially distributed systems [10, 11, 25] extended this correspondence to diffusion-driven persistence. The present contribution advances this line of reasoning to fully open systems with advection and inhomogeneous boundary fluxes, integrating continuous transport and discrete network topology within a single algebraic–topological framework. By introducing the concept of an augmented reaction network, the theory unifies PDE-based flux balance with combinatorial closure conditions and provides a mathematically rigorous bridge between network theory and partial differential equation analysis [16].

Relation to Petri-net approaches and siphons. Persistence in reaction networks has also been studied extensively using Petri-net approaches, particularly through the concept of siphons [57, 58]. A siphon is a subset of species with the property that every reaction producing a species of the subset also consumes at least one species from the same subset. Consequently, once all species of a siphon disappear simultaneously, the reaction structure alone cannot regenerate them.

Both siphons and organizations address persistence by studying structural properties independently of specific kinetic parameters. However, they focus on different aspects of network structure. Petri-net approaches

identify constraints associated with possible species disappearance, whereas organizations and distributed organizations characterize subsets of species that can maintain themselves through feasible reaction fluxes and compartmental organization.

The notions are therefore complementary rather than equivalent. While siphons describe structural restrictions on recovery after extinction events, distributed organizations describe structurally maintainable configurations of species and reactions. In particular, DOs additionally incorporate closure, self-maintenance, and compartmentalization properties, which become particularly relevant in spatially distributed systems such as RDAS.

From a computational perspective, both approaches lead to combinatorial problems. The computation of minimal siphons is known to exhibit exponential worst-case behavior [57], while the computation of distributed organizations likewise involves NP-hard optimization problems [11]. A detailed mathematical correspondence between siphons and DOs remains an interesting direction for future work.

An additional advantage of the presented framework is its direct extensibility to other types of boundary and coupling conditions. The augmentation principle used to incorporate inhomogeneous Neumann boundary conditions and advective fluxes applies likewise to Dirichlet, Robin, or mixed boundary conditions, as well as to time-dependent inflows, sinks, or cross-domain coupling terms. In each case, the boundary or external process can be represented by a corresponding inflow or outflow reaction in the augmented reaction network. This makes the approach broadly applicable to many open or boundary-driven reaction–transport systems.

Implications and perspectives. Because every organization satisfying the assumptions of Theorem 4 can be realized by an appropriate RDAS. Desired persistence patterns can, in principle, be engineered through targeted modifications of boundary fluxes, advection fields, or external inflows and sinks. This construction links algebraic feasibility with physical realizability and suggests new applications in synthetic biology, metabolic and ecosystem engineering, and the control of spatially extended reaction

networks [22, 59].

Beyond its immediate mathematical implications, the framework extends the reach of persistence theory to a broad class of spatially distributed systems. It invites future analytical work on: (i) bifurcations and connectivity within the lattice of organizations, (ii) stochastic and time-periodic boundary conditions, and (iii) data-driven inference of effective fluxes in complex media. In combination with numerical simulation, such analyses may contribute to a comprehensive theory of structural persistence—a principle unifying algebraic organization and dynamical viability in open reactive systems.

The proposed framework allows organizational structures and persistence constraints to be inferred directly from reaction topology and transport structure without simulation or parameter estimation. This may facilitate inverse design and structural screening of large distributed systems.

5 Conclusions

This work extends the mathematical foundations of persistence in open reaction systems by introducing an augmented network formalism for reaction–diffusion–advection systems (RDAS) with general, possibly inhomogeneous, boundary conditions. Within this framework we established two central results. The Main Theorem proves that the set of persistent species of any bounded RDAS solution corresponds exactly to an organization of its augmented reaction network. The Inverse Theorem complements this by showing that every such organization can be realized dynamically by a suitable RDAS, thus closing the logical loop between structure and dynamics.

Conceptually, these results generalize previous persistence theorems for reaction–diffusion systems to include transport processes, external sources, and sinks. They provide a unifying algebraic description of long-term behavior in open systems: persistence and extinction emerge as structural properties of the lattice of organizations, determined by flux balance and boundary topology rather than by kinetic details. The proposed framework therefore transforms the question of stability from a parameter-dependent

dynamical problem into a combinatorial and topological one.

An application from virology has demonstrated how the theoretical construct translates to realistic contexts [60, 61]. In each case, the augmented network correctly predicts which species persist under specified inflows, outflows, and advective transport, confirming the predictive power of the theory.

Beyond explaining existing systems, the Inverse Theorem provides a blueprint for inverse design: the intentional construction of RDAS that realize a desired persistent organization by suitable boundary and transport conditions. This perspective opens new opportunities for systematic control and design in fields such as biology [62], engineering [63], microbial communities [64], systems neurology [65, 66], cell cycle modeling [67], sustainable ecosystem modeling [26, 68, 69], and large-language modeling [70].

Future work may focus on rigorous characterization of bifurcations within the lattice of organizations, extensions to stochastic and time-periodic boundary conditions, and coupling with data-driven identification of effective fluxes. Together, these directions aim toward a comprehensive theory of structural persistence and design in spatially distributed reactive systems.

Data Availability

This study does not use any experimental or observational datasets. All results are based on theoretical analysis and mathematical derivations presented within the article.

***Acknowledgment*:** The authors acknowledge the financial support provided by Carl-Zeiss-Stiftung (062060-20), German Research Foundation (DFG) priority programs SPP 2191 (062098-18), and DFG Collaborative Research Center 1127 ChemBioSys (SFB 1127, Project C07).

References

[1] J. L. Andersen, C. Flamm, D. Merkle, P. F. Stadler, Chemical transformation motifs—modelling pathways as integer hyperflows, *IEEE/ACM Trans. Comput. Biol. Bioinform.* **16** (2017) 510–523.

[2] B. S. Hernandez, R. J. L. De la Cruz, Independent decompositions of chemical reaction networks, *Bull. Math. Biol.* **83** (2021) #76.

[3] W. Hordijk, M. Steel, P. Dittrich, Autocatalytic sets and chemical organizations: Modeling self-sustaining reaction networks at the origin of life, *New J. Phys.* **20** (2018) #015011.

[4] S. Peter, B. Ibrahim, Chemical organization theory: A structural framework for analyzing reaction networks, *MATCH Commun. Math. Comput. Chem.* **96** (2026) 781–817.

[5] M. Feinberg, Lectures on chemical reaction networks, *Notes of lectures given at the Mathematics Research Center, University of Wisconsin*, 1979.

[6] F. Horn, R. Jackson, General mass action kinetics, *Arch. Ration. Mech. Anal.* **47** (1972) 81–116.

[7] J. Gunawardena, Chemical reaction network theory for in-silico biologists, Lecture notes, Harvard University, Virtual Cell Program, 2003, `http://vcp.med.harvard.edu/papers/crnt.pdf`.

[8] P. Dittrich, J. Ziegler, W. Banzhaf, Artificial chemistries—a review and analysis, *Artif. Life* **7** (2001) 225–275.

[9] P. Dittrich, M. Ziegler, W. Banzhaf, Chemical organisation theory, *Bull. Math. Biol.* **69** (2007) 1199–1231.

[10] S. Peter, B. Ibrahim, P. Dittrich, Linking network structure and dynamics to describe the set of persistent species in reaction diffusion systems, *SIAM J. Appl. Dyn. Syst.* **20** (2021) 2037–2076.

[11] S. Peter, L. Woitke, P. Dittrich, B. Ibrahim, Computing all persistent subspaces of a reaction-diffusion system, *Sci. Rep.* **13** (2023) #17169.

[12] E. Busseniers, T. Veloz, F. Heylighen, Goal directedness, chemical organizations, and cybernetic mechanisms, *Entropy* **23** (2021) #1039.

[13] J. C. Baez, B. S. Pollard, A compositional framework for reaction networks, *Rev. Math. Phys.* **29** (2017) #1750028.

[14] H. Logemann, E. P. Ryan, *Ordinary Differential Equations: Analysis, Qualitative Theory and Control*, Springer, London, 2014.

[15] J. Smoller, *Shock Waves and Reaction–Diffusion Equations*, Springer–Verlag, Berlin, 1994.

[16] L. C. Evans, *Partial Differential Equations*, AMS, Providence, 2010.

[17] A. L. Krause, H. Ji, B. Sandstede, Emergent structures in reaction–advection–diffusion systems on the sphere, *Phys. Rev. E* **97** (2018) #042215.

[18] A. L. Krause, V. Klika, P. K. Maini, D. Headon, E. A. Gaffney, Isolating patterns in open reaction–diffusion systems, *Bull. Math. Biol.* **83** (2021) 1–35.

[19] J. Xin, Front propagation in heterogeneous media, *SIAM Rev.* **42** (2000) 161–230.

[20] A. Stevens, Variational principles for propagation speeds in inhomogeneous media, *SIAM J. Appl. Math.* **61** (2001) 113–132.

[21] S. Peter, P. Dittrich, On the relation between organizations and limit sets in chemical reaction systems, *Adv. Complex Syst.* **14** (2011) 77–96.

[22] J. D. Murray, *Mathematical Biology I: An Introduction*, Springer, New York, 2002.

[23] J. J. Tyson, B. Novak, Functional motifs in biochemical reaction networks, *Ann. Rev. Phys. Chem.* **54** (2003) 263–290.

[24] P. Deuflhard, M. Weiser, *Scientific Computing with Ordinary Differential Equations*, Springer, New York, 2012.

[25] B. Ibrahim, S. Peter, Persistent subspaces of reaction-based dynamical systems, *MATCH Commun. Math. Comput. Chem.* **90** (2023) 471–494.

[26] S. Peter, F. Ghanim, P. Dittrich, B. Ibrahim, Organizations in reaction-diffusion systems: Effects of diffusion and boundary conditions, *Ecol. Complexity* **43** (2020) #100855.

[27] D. Gilbarg, N. S. Trudinger, *Elliptic Partial Differential Equations of Second Order*, Springer, Berlin, 2001.

[28] M. J. Rodrigo, Analytical approach to solving linear diffusion–advection–reaction equations with general nonhomogeneous linear boundary conditions, *Math. Meth. Appl. Sci.* **47** (2024) 6551–6573.

[29] L. F. C. Almeida, C. B. Rodrigues, J. A. Ferreira, H. Oliveira, Steady-state solutions for a reaction–diffusion equation with robin boundary conditions: application to the control of dengue vectors, *Eur. J. Appl. Math.* **35** (2024) 382–408.

[30] H. Amann, Dynamic theory of quasilinear parabolic systems. III. Global existence, *Math. Z.* **202** (1989) 219–250.

[31] H. L. Smith, H. R. Thieme, *Dynamical Systems and Population Persistence*, AMS, Providence, 2011.

[32] J. Hofbauer, K. Sigmund, *Evolutionary Games and Population Dynamics*, Cambridge Univ. Press, Cambridge, 1998.

[33] G. Neumann, S. Schuster, Continuous model for the rock–scissors–paper game between bacteriocin producing bacteria, *J. Math. Biol.* **54** (2007) 815–846.

[34] G. Craciun, F. Nazarov, C. Pantea, Persistence and permanence of mass-action and power-law dynamical systems, *SIAM J. Appl. Math.* **73** (2013) 305–329.

[35] J. D. Brunner, G. Craciun, Robust persistence and permanence of polynomial and power law dynamical systems, *SIAM J. Appl. Math.* **78** (2018) 801–825.

[36] G. Hetzer, W. Shen, Uniform persistence, coexistence, and extinction in almost periodic nonautonomous competition diffusion systems, *SIAM J. Math. Anal.* **34** (2002) 204–227.

[37] L. J. Allen, *Applications of differential inequalities to persistence and extinction problems for reaction-diffusion systems*, Ph.D. thesis, Univ. Tennessee, Knoxville, 1981.

[38] V. Hutson, K. Schmitt, Permanence and the dynamics of biological systems, *Math. Biosci.* **111** (1992) 1–71.

[39] R. S. Cantrell, C. Cosner, *Spatial Ecology via Reaction–Diffusion–Advection Equations*, Cambridge Univ. Press, Cambridge, 2003.

[40] L. J. Allen, Persistence and extinction in Lotka-Volterra reaction-diffusion equations, *Math. Biosci.* **65** (1983) 1–12.

[41] L. J. Allen, Persistence, extinction, and critical patch number for island populations, *J. Math. Biol.* **24** (1987) 617–625.

[42] M. Mincheva, D. Siegel, Nonnegativity and positiveness of solutions to mass action reaction–diffusion systems, *J. Math. Chem.* **42** (2007) 1135–1145.

[43] A. Vol'pert, S. Hudjaev, *Analysis in Classes of Discontinuous Functions and Equations of Mathematical Physics*, Martinus Nijhoff, 1967.

[44] P. Érdi, J. Tóth, *Mathematical models of chemical reactions: theory and applications of deterministic and stochastic models*, Manchester Univ. Press, Manchester, 1989.

[45] G. Craciun, M. D. Johnston, G. Szederkényi, E. Tonello, J. Tóth, P. Y. Yu, Realizations of kinetic differential equations, *arXiv* (2019) **doi:** `https://doi.org/10.48550/arXiv.1907.07266`.

[46] D. Henry, *Geometric Theory of Semilinear Parabolic Equations*, Springer, Berlin, 1981.

[47] H. R. Thieme, *Mathematics in Population Biology*, Princeton Univ. Press, Princeton, 2003.

[48] J. Ewald, P. Sieber, R. Garde, S. N. Lang, S. Schuster, B. Ibrahim, Trends in mathematical modeling of host–pathogen interactions, *Cell. Mol. Life Sci.* **77** (2020) 467–480.

[49] W. Hwang, W. Lei, N. M. Katritsis, M. MacMahon, K. Chapman, N. Han, Current and prospective computational approaches and challenges for developing covid-19 vaccines, *Adv. Drug Deliv. Rev.* **172** (2021) 249–274.

[50] S. Marzban, R. Han, N. Juhász, G. Röst, A hybrid pde–abm model for viral dynamics with application to SARS-COV-2 and influenza, *R. Soc. Open Sci.* **8** (2021) #210787.

[51] C. Quirouette, N. P. Younis, M. B. Reddy, C. A. A. Beauchemin, A mathematical model describing the localization and spread of influenza A virus infection within the human respiratory tract, *PLoS Comput. Biol.* **16** (2020) #e1007705.

[52] G. M. Lavigne, H. Russell, B. Sherry, R. Ke, Autocrine and paracrine interferon signalling as 'ring vaccination' and 'contact tracing' strategies to suppress virus infection in a host, *J. Roy. Soc. Interf.* **18** (2021) #20200828.

[53] L. Xu, Hiu Yung Wong, Matteo Iannaccone, Qi Zhang, D .Vlachos, D. Kreft, M. Rubinstein, D. Dukhin, S. Bates, I. Sokolov, Mathematical modeling of mucociliary clearance: A mini-review, *Front. Physiol.* **10** (2019) 1–10.

[54] J. J. A. Weaver, Y. Lin, P. R. Krause, S. G. Krantz, D. Kirschner, M. M. Meerschaert, M. L. Huber, Quantitatively mapping immune control during influenza, *J. Immun. Res.* **38** (2024) #1234567.

[55] L. Aït Mahiout, N. Bessonov, B. Kazmierczak, G. Sadaka, V. Volpert, Infection spreading in cell culture as a reaction–diffusion system with delay: virus, cells and interferon, *ESAIM: M2AN* **56** (2022) 901–934.

[56] A. C. Aristotelous, A. Chen, M. G. Forest, A hybrid discrete–continuum model of immune responses to respiratory viral infection with interferon and antibodies, *J. Theor. Biol.* **547** (2022) #111178.

[57] D. Angeli, P. De Leenheer, E. D. Sontag, A petri net approach to the study of persistence in chemical reaction networks, *Math. Biosci.* **210** (2007) 598–618.

[58] D. Angeli, P. De Leenheer, E. D. Sontag, Persistence results for chemical reaction networks with time-dependent kinetics and no global conservation laws, *SIAM J. Appl. Math.* **71** (2011) 128–146.

[59] M. Feinberg, *Foundations of Chemical Reaction Network Theory*, Springer, Cham, 2019.

[60] S. Peter, P. Dittrich, B. Ibrahim, Structure and hierarchy of sars-cov-2 infection dynamics models revealed by reaction network analysis, *Viruses* **13** (2021) #14.

[61] S. Peter, M. Hölzer, K. Lamkiewic, P. S. di Fenizio, H. Al Hwaeer, M. Marz, S. Schuster, P. Dittrich, B. Ibrahim, Structure and hierarchy of influenza virus models revealed by reaction network analysis, *Viruses* **11** (2019) #449.

[62] L. Zhu, X. Tao, S. Shen, Pattern dynamics in a reaction–diffusion predator–prey model with allee effect based on network and non-network environments, *Eng. Appl. Artif. Intell.* **128** (2024) #107491.

[63] P. Mougkogiannis, A. Nikolaidou, A. Adamatzky, Kombucha–proteinoid crystal bioelectric circuits, *ACS Omega* **9** (2024) 45386–45401.

[64] B. Ruth, S. Peter, B. Ibrahim, P. Dittrich, Revealing the hierarchical structure of microbial communities, *Sci. Rep.* **14** (2024) #11202.

[65] S. Peter, B. Ibrahim, Intuitive innovation: Unconventional modeling and systems neurology, *Mathematics* **12** (2024) #3308.

[66] M. H. Khalil, Environmental affordance for physical activity, neurosustainability, and brain health: quantifying the built environment's ability to sustain bdnf release by reaching metabolic equivalents (mets), *Brain Sci.* **14** (2024) #1133.

[67] S. Peter, A. Josephraj, B. Ibrahim, Cell cycle complexity: Exploring the structure of persistent subsystems in 414 models, *Biomedicines* **12** (2024) #2334.

[68] S. Peter, M. Schirmer, P. Lathan, G. Stimpfl, B. Ibrahim, Performance analysis of a solar-powered multi-purpose supply container, *Sustainability* **14** (2022) #5525.

[69] S. Peter, M. B. Sunke, B. Ibrahim, Solar-driven atmospheric water yields under climate stress: A 23-year global data analysis, *Environ. Earth Sci.* **85** (2026) #72.

[70] A. J. Arokiaraj, S. Ibrahim, A. Then, B. Ibrahim, S. Peter, Adagram in python: An ai framework for multi-sense embedding in text and scientific formulas, *Mathematics* **13** (2025) #2241.

6 Appendix A

Proof of Lemma 1. Fix $i \in \{1, \dots, n\}$. For each fixed $t \in [t_j, t_{j+1}]$, the spatial divergence theorem applied to the vector fields $d_i \nabla c_i(\cdot, t)$ and $u(\cdot, t)\, c_i(\cdot, t)$ yields

$$\int_\Omega \nabla \cdot \big(d_i \nabla c_i\big)(x,t)\, dx = \int_{\partial\Omega} d_i \nabla c_i(x,t) \cdot \nu(x)\, dS(x),$$

$$\int_\Omega \nabla \cdot \big(u\, c_i\big)(x,t)\, dx = \int_{\partial\Omega} (u \cdot \nu)(x,t)\, c_i(x,t)\, dS(x).$$

Integrating these identities over $t \in [t_j, t_{j+1}]$ and using Fubini–Tonelli to interchange time and space integrals gives (26)–(27). Summing the boundary contributions associated with diffusion and advection, we obtain

$$\int_{t_j}^{t_{j+1}} \int_{\partial\Omega} \big(- d_i \nabla c_i + u\, c_i \big) \cdot \nu \, dS \, dt = \int_{t_j}^{t_{j+1}} \int_{\partial\Omega} J_i \cdot \nu \, dS \, dt,$$

which equals the right-hand side of (28) by the boundary condition in (9). ∎

7 Appendix B

Proof of Theorem 3. **Step 1: Time-averaged flux field.** By Lemma 1 and the boundary condition, the total (species-wise) balance over $[t_j, t_{j+1}]$ yields

$$\frac{1}{t_{j+1} - t_j} \int_{t_j}^{t_{j+1}} \int_\Omega \partial_t c(\cdot, t)\, dx\, dt = N_{\text{int}} \widehat{v}_{\text{int}} + N_{\text{ext}} \widehat{v}_{\text{ext}} \;=\; N_{\text{aug}}\, \widehat{v},$$

and passing to the limit uses boundedness of $c_\Omega(t) := \int_\Omega c(x,t)\, dx$, hence the left-hand side tends to 0. Therefore

$$N_{\text{aug}}\, \widehat{v} \;\geq\; 0. \tag{38}$$

(Nonnegativity follows componentwise from the compatibility condition 10)

Step 2: Decomposition by persistent subsets. For a persistent subset $S^\star \in P(c)$ and small $\varepsilon > 0$ consider the region

$$\Omega_{S^\star,\varepsilon}(t) \;:=\; \{\, x \in \Omega :\; \phi(c(x,t)) = S^\star, \text{ and } c_s(x,t) > \varepsilon \;\forall s \in S^\star \,\},$$

which has strictly positive time–space frequency by persistence. On $\Omega_{S^\star,\varepsilon}$,

$v(c)$ is a feasible flux for $S^\star$; integrating v over $\Omega_{S^\star,\varepsilon}\times[t_j,t_{j+1}]$, normalizing in time, and letting $j\to\infty$, $\varepsilon\downarrow 0$, defines a nonnegative vector $\widehat{v}^{(S^\star)}$ supported exactly on reactions whose support is contained in $S^\star$. Doing the same for the boundary integrals produces an external part. We set

$$\widehat{v}^{(S^\star)} := \big(\widehat{v}^{(S^\star)}_{\mathrm{int}}, \widehat{v}^{(S^\star)}_{\mathrm{ext}}\big) \in \mathbb{R}^{|R_{\mathrm{aug}}|}_{\geq 0}.$$

By construction, with

$$\widehat{v} \;=\; \sum_{S^\star\in P(c)} \widehat{v}^{(S^\star)}$$

we get

$$N_{\mathrm{aug}} \sum_{S^\star} \widehat{v}^{(S^\star)} \;=\; N_{\mathrm{aug}}\,\widehat{v} \;\geq 0,$$

and for each $S^\star$ feasibility is fulfilled for internal reactions.

Step 3: Structure of the organisation. Define compartments $(S_i, R_i, \widehat{v}^{(i)})$ by enumerating the nonempty persistent subsets $S_i \in P(c)$and taking $\widehat{v}^{(i)} := \widehat{v}^{(S_i)}$ and

$$R_i \;:=\; \{\, r\in R_{\mathrm{aug}} :\; \widehat{v}^{(i)}_r > 0 \,\}.$$

Then:

(i) Closedness: Each S_i is closed w.r.t. R_{int} since reactions with $\mathrm{supp}(r)\subseteq S_i$ contribute nonnegatively and cannot create products outside S_i on a set of positive measure (else S_i would not recur with positive frequency).

(ii) Covering: Set $O := \bigcup_i S_i = \Phi(c)$ and $R := \bigcup_i R_i$.

(iii) Exterior reactions: Active boundary inflow/outflow reactions appear in at least one R_i by the construction of $\widehat{v}^{(i)}_{\mathrm{ext}}$ from the boundary integrals.

(iv) Feasibility: If $r\in R_{\mathrm{int}}$ and $\mathrm{supp}(r)\subseteq S_i$, then $r\in R_i$ by the definition of R_i; conversely, $\widehat{v}^{(i)}_r > 0$ implies $r\in R_i$.

(v) Self-maintenance: From (38) we obtain

$$N_{\mathrm{aug}} \sum_i \widehat{v}^{(i)} \geq 0,$$

which establishes the self-maintenance condition.

Thus $(O,R) = \{S_1|\ldots|S_k\}$ satisfies Definition 6 and $O=\Phi(c)$, which proves the claim. ∎

8 Appendix C

Proof of Theorem 4. **Step 1: Geometric setting and target state.** Let $\Omega \subset \mathbb{R}^n$ be a bounded Lipschitz domain. For a finite index set $\mathcal{I} = \{1, \dots, k\}$, let $\{\Omega_i\}_{i\in\mathcal{I}}$ be a measurable partition of Ω into pairwise disjoint Lipschitz subdomains of positive measure,

$$\Omega = \cup_{i\in\mathcal{I}}\Omega_i, \qquad |\Omega_i| > 0, \quad |\Omega_i \cap \Omega_j| = 0 \text{ for } i \neq j.$$

These subdomains correspond to the compartments in Definition 6. The interfaces $\partial\Omega_i \cap \partial\Omega_j$ are assumed impermeable ($J\cdot\nu = 0$), so that each Ω_i evolves independently. No further geometric or topological assumptions on the shape or adjacency of the subdomains are required.

For each compartment pick a vector $c^{*(i)} \in \mathbb{R}^n_{\geq 0}$ with $c_s^{*(i)} > 0$ for $s \in S_i$ and $c_s^{*(i)} = 0$ for $s \notin S_i$. Define the piecewise constant target state $c^*(x) = c^{*(i)}$ for $x \in \Omega_i$.

Step 2: Construction of admissible kinetics. We require a locally Lipschitz rate function

$$v : \mathbb{R}^n_{\geq 0} \longrightarrow \mathbb{R}^{|R_{\text{int}}|}_{\geq 0}$$

such that, for each compartment Ω_i, the prescribed flux $\widehat{v}_{\text{int}}^{(i)}$ (see Definition 6) is attained at the target state $c^{*(i)}$:

$$v(c^{*(i)}) = \widehat{v}_{\text{int}}^{(i)}.$$

To this end, define smooth, compactly supported weight functions $\psi_i : \mathbb{R}^n \to [0,1]$ with $\psi_i(c^{*(i)}) = 1$ and $\psi_i(c^{*(j)}) = 0$ for $j \neq i$. Then set

$$v(c) \;:=\; \sum_{i=1}^{k} \psi_i(c)\, \widehat{v}_{\text{int}}^{(i)}.$$

This v is globally Lipschitz and nonnegative. Moreover, to respect the chemical support of each reaction $r \in R_i$, one may multiply the corresponding component $v_r(c)$ by $\prod_{s\in\text{reactants}(r)} \frac{c_s}{c_s+1}$, which ensures $v_r(c) = 0$ whenever a required reactant concentration $c_s = 0$. Hence $v(c)$ satisfies $v(c^*) = v^*$ while remaining admissible for all $c \geq 0$.

Step 3: Exterior reactions via boundary flux. Let $\widehat{v}_{\text{ext}}^{(i)}$ be the exterior part from Definition 6. Choose a (time-independent) boundary flux density g so that on each Ω_i

$$\frac{1}{|\Omega_i|}\int_{\Omega_i} N_{\text{int}}\, v^*\, dx \;+\; \frac{1}{|\Omega_i|}\int_{\partial\Omega_i} g\cdot\nu\, dS \;=\; 0.$$

This is possible because the organization's self-maintenance condition ensures that the net surplus induced by internal fluxes can be balanced by admissible exterior (outflow) reactions; we distribute the signs of g along inflow/outflow portions and enforce the nonnegativity compatibility $g_s\,\gamma_s \geq 0$ with traces γ_s of c on the boundary (cf. compatibility condition (10)). Since Ω is Lipschitz, the existence of a continuous linear trace operator $\gamma : H^1(\Omega) \to L^2(\partial\Omega)$ is guaranteed by the standard trace theorem (cf. Thm. 5.36 [16]). Hence for every weak solution $c \in H^1(\Omega)^n$ the boundary values $\gamma(c_s)$ are well-defined in $L^2(\partial\Omega)$. The nonnegativity compatibility condition $g_s\,\gamma(c_s) \geq 0$ thus holds almost everywhere on $\partial\Omega$, ensuring that the boundary flux does not drive concentrations negative.

Step 3: Stationary solution. Consider the RDAS with diffusion $d_i \equiv \varepsilon > 0$, $u \equiv 0$, reaction term $N_{\text{int}}v(c)$, and boundary condition $J{\cdot}\nu = g$. By construction, c^* is a stationary solution: $\partial_t c^* = 0$ in Ω and $J(c^*){\cdot}\nu = g$ on $\partial\Omega$. Pick the initial condition $c_0 = c^*$. Then the (classical) solution satisfies $c(\cdot, t) \equiv c^*$ for all $t \geq 0$, and is hence bounded and nonnegative.

Step 4: Persistence set. On each Ω_i and for each $s \in S_i$ we have $c_s^* > 0$, while for $s \notin O = \bigcup_i S_i$ we have $c_s^* \equiv 0$. By the definition of persistence (Definition 4) it follows that $\Phi(c) = O$.

This completes the proof. ■

9 Appendix D

Set of reactions of the virus infection dynamics model of subsection 3.8 (before colon: corresponding term in the PDEs):

$\beta SV : S + V \to E + V,$	infection of susceptible cells,
$\kappa E : E \to I_1,$	transition to productive infection,
$\gamma I_1 : I_1 \to I_2,$	progression to late infection,
$pI_2 : I_2 \to I_2 + V,$	virus release,
$cV : V \to \emptyset,$	viral clearance,
$kAV : V + A \to C,$	antibody neutralization,
$\xi C : C \to \emptyset,$	complex degradation,
$\pi I_1 : I_1 \to I_1 + F,$	IFN production,
$\mu F : F \to \emptyset,$	IFN degradation,
$\sigma FS : F + S \to F + R,$	IFN signalling $\to$ refractory state,
$\rho R : R \to S,$	recovery of refractory cells,
$sA : \emptyset \to A,$	antibody synthesis,
$\eta A : A \to \emptyset,$	antibody decay.

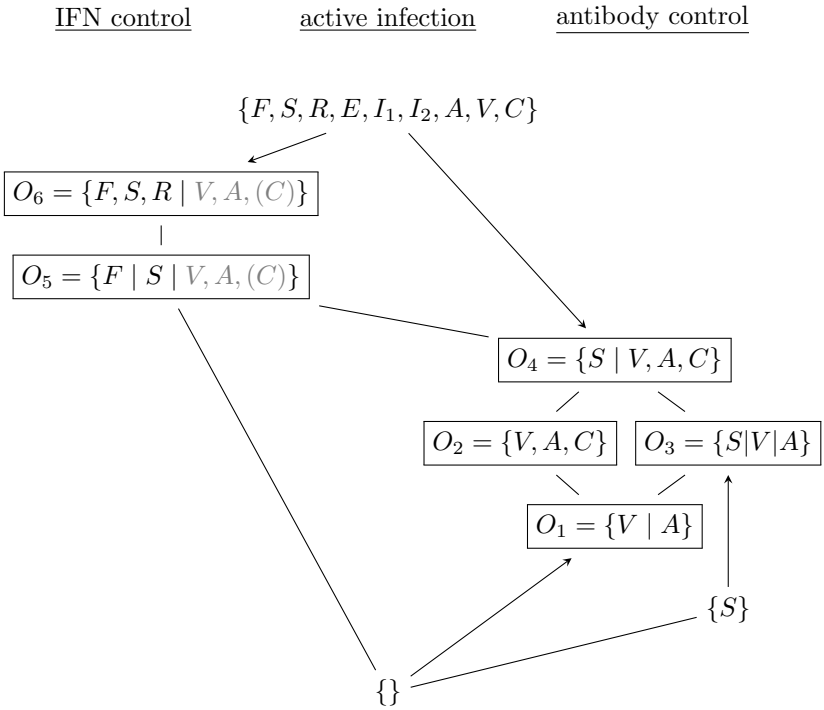


Figure 3. Meaningful species subsets of the virus infection dynamics application: organizations are framed, others unframed. Lines resp. arrows stand for subset relations. Due to the BCs, the antibody control block, that is, A, V, and optionally – depending on the compartmentalization – also C are present in every organization as long as the inflows of V and A are active. If these inflows are inactive, new species subsets such as $\{F, S, R\}$, $\{F \mid S\}$ or $\{S\}$ can persist as organizations. Furthermore, the empty set as well as $\{S\}$ are not closed and transit directly upward, which is marked by the upward arrow. Conversely for the full set of species, which is not self-maintaining, downward arrows show that it must decay in the long-run. The subsets of species can be subdivided into three kinds: active infection, IFN control, and antibody control.