MINISYMPOSIUM

REDUCTION AND STRUCTURE OF REACTION NETWORKS

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Minisymposium Keywords: Oscillation, Bistability, Toric steady states, Gröbner basis, Mass action

This minisymposium focusses on recent advances in understanding the behaviour and structure of systems of Ordinary Differential Equations (ODEs) built from reaction networks.

Dynamical systems built from networks of reactions are increasingly being used to study very complex cellular and bacterial systems. The idea is that theoretical understanding of such systems will assist in unravelling the important constituents and behaviour of empirical systems and provide means to predict future behaviour. However, the dynamical systems often have many variables (molecular species) and parameters, which makes them hard to analyse mathematically.

The set of reactions provides a structural, or graphical, description of the dynamical system, which is also visually appealing. In the minisymposium, questions about the relationship between the structure of the network, the ODE system and the behaviour of the ODE system are discussed. In particular, the minisymposium will focus on two aspects: inference on the structure, that is, the reactions, from an ODE system alone, and reductionist approaches to understanding the behaviour of the ODE system.

Reductionist approaches constitute a recent promising trend in network research. Two of the talks in the minisymposium deal specifically with relating the properties of subnetworks, so called network "motives", to properites of the ODE system. In the talk by Banaji, it is shown that the whole system might inherit an oscillatory behaviour from an oscillatory motif. By cataloging small oscillatory motifs it is therefore possible to infer the oscillatory behaviour of a vast amount of systems. The talk of Pantea continues in the same vein and sets out to relate the existence of multistationarity in large reaction networks from the existence of small multistationary motifs. Using these approaches, it becomes possible to identify oscillatory or multistationary ODE systems from just looking at the set of reactions and identifying small motifs.

In the talks by Sadeghimanesh and Wiuf, a different reductionist approach is taken in which a simplified reaction network is constructed, for example by eliminating intermediate species. Whereas the simplified reaction network might not be realistic, it might still carry important dynamical information about the whole network. Sadeghimanesh shows, using algebraic approaches, that properties of the reduced network can be lifted to the whole network. Wiuf shows that QSSA techniques might be used to relate the trajectories of the reduced and whole network to each other.

Finally, in the talk by Tóth, it is discussed whether the reactions underlying a dynamical system can be inferred from the ODE system itself. To what extend can we learn the chemical reactions from just observing the dynamical behaviour of the system? This is a highly relevant question in cellular biology where we might be able to observe (part of) trajectories of a system, but rarely have complete understanding of the stoichiometry involved.

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MODEL REDUCTION AND THE QSSA

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Keywords: Reaction Network, QSSA, Graphical reduction, Tichonov reduction, Network motifs.

The first part of the talk provides a short introduction to and overview of the minisymposium.

Reductionist approaches to analysis of models of reaction networks are becoming trendy. Simplifications of a reaction network might be carried out for various reasons. For example, a small subnetwork (motif) might carry information about the dynamical behaviour of the whole network (as illustrated in the second and third talk in the session). A simplification might also be carried out to reduce the number of variables (molecular species concentrations) or the number of parameters of the system. This might be done to simplify the mathematical analysis of the system (as in the fourth talk of the session) or because not all species are detectable in an experimental setting.

In this talk I will discuss a graphical procedure to simplify a reaction network, and its relationship to the QSSA procedure. In it simplest form it amounts to contract reaction paths, for example by eliminating intermediate species. In its general form it amounts to eliminate species that are conserved in loops of reactions in a particular graph. The method is akin to early work by King and Altman.

Furthermore, it will be shown that this graphical procedure might be interpreted in terms of the QSSA procedure by dividing the reactions in the original network into fast and slow reactions (in a particular way). Using results by Sebastian Walcher and co-workers, it will be shown that the trajectories of the reduced system approximates the trajectories of the full system.

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INHERITANCE OF OSCILLATION IN CHEMICAL REACTION NETWORKS

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Keywords: Oscillation, Chemical reaction network, Model reduction.

Oscillation is known to occur – and play a key role – in a great variety of biological contexts. At the heart of many biological systems are chemical reaction networks (CRNs), and the question of when these admit oscillation is of both theoretical and practical interest. Once a CRN admitting oscillation is identified, it is natural to wonder whether this network occurs as a "motif" in other larger networks and, if so, whether the larger networks must themselves admit oscillation. The goal of this work is to phrase this question precisely and provide some partial answers.

We describe four important ways in which a CRN can be enlarged while preserving its capacity for oscillation. The results hold under various kinetic assumptions, including mass action. Together they give us a partial order on the set of CRNs, and oscillation is inherited under this partial order. Armed with this partial order, the existence of a few small oscillatory CRNs immediately implies oscillation in a great number of CRNs, namely all those which are greater in this ordering than an oscillatory CRN.

The main results are for general CRNs, not necessarily fully open, but lead to an elegant corollary for fully open networks: if a fully open CRN $\mathcal{R}$ with mass action kinetics admits a nondegenerate (resp., linearly stable) periodic orbit, then so do all fully open CRNs which include $\mathcal{R}$ as an induced subnetwork. This result can be rephrased as "in fully open CRNs oscillation is inherited under the induced subnetwork partial ordering".

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BISTABILITY IN MASS ACTION: INHERITANCE FROM SMALL SUBNETWORKS

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Keywords: Multiple equilibria, Chemical reaction networks, Motifs.

Bistability, or existence of multiple stable positive equilibria, underlies important cellular processes, and is a recurring theme in recent work on reaction networks. Here we study cases when we can conclude that a network admits multiple stable positive equilibria based on analysis of its subnetworks, and we also present results on small two-species networks, viewed as building blocks, or "motifs" of bistable behavior.

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INTERMEDIATES, BINOMIALITY AND MULTISTATIONARITY

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Joint work with Elisenda Feliu (University of Copenhagen)

Keywords: Binomial equations, Reduction by intermediates, Mass action, Steady states.

In this work we consider reaction networks with intermediates (as described in [1]), with enzymes (as described in [4]) and networks with toric steady states (as considered in [3]). Specifically, given a core reaction network and an extension of it obtained by adding Gröbner bases of the steady state ideal of the core reaction network relate to the Gröbner bases of the steady state ideal of extended networks. We use this to (1) find Gröbner bases of large networks from Gröbner bases of simplified versions of them, thereby reducing substantially the computational cost; (2) infer when extensions of networks with toric steady states also have toric steady states; (3) pinpoint what/whether intermediates can be target as responsible for multistationarity.

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FURTHER INVERSE PROBLEMS

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Keywords: Inverse problem, Volpert index, Open problems.

Earlier [2] we have formulated and answered the question: Given a polynomial differential equation is there a reaction endowed with mass action type kinetics inducing it?

Reviewing results on related questions by Crăciun, Johnston, Pantea, Szederkényi and others we formulate similar problems and show the solution of some of them.

Given a polynomial differential how unique is the reaction inducing it? Can it happen that the induced kinetic differential equation has a zero right hand side? Can two reactions induce the same differential equation? Is it enough to take the exponents of the monomials of the polynomial right-hand side as reactant complexes to obtain an inducing reaction? Which are the minimal sets of initial species to produce all the species?

Finally, we formulate analogous questions for the stochastic model and also some open problems (collected in [5]).

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