

Proposal for Tutorial at ICSB 2008

Title: Reaction network theory for systems biology

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Summary: One of the great challenges for Systems Biology is to deal with the size and complexity of biological networks and of the corresponding mathematical models. Moreover, in most applications the systems are barely characterized in terms of kinetic rate constants. It is thus important to develop methods and tools that elucidate the functionality (or at least some of it) of a reaction network based on network structure alone. Feinberg's Chemical Reaction Network Theory (CRNT; Craciun et al., 2006) has the potential to serve as such a tool: developed and established in Chemical Engineering since the 1980s, it connects the potential of a (bio)chemical reaction network to admit more than one steady state to the network structure alone. Moreover, for its application one does not need any numerical values of rate constants.

Application of CRNT in Systems Biology has occasionally been suggested in recent years, but it is, again, hampered by network size and (structural complexity). A combination of CRNT with Stoichiometric Network Analysis (SNA) can help to overcome these limitations, at least in some cases. The basic idea is based on a popular concept: modularization. Defining meaningful subnetworks that are easier to analyze is a promising approach in dealing with complexity. More specifically, SNA allows to identify subnetworks that have a structure such that, under some mild additional assumptions, it is guaranteed that one can decide about multistationarity and extend solutions to complex networks (Conradi et al., 2007). This offers a mathematical and algorithmic framework for the analysis of genetic, metabolic, signaling, and developmental networks.

Organization: The tutorial is organized in two parts, each of approximately 60 minutes. The two parts will cover (i) biochemical reaction network fundamentals, stoichiometric and dynamic models, basic terms and definitions of CRNT, main theorems of CRNT (deficiency zero and deficiency one theorems), applications to example networks; (ii) definition of subnetworks and their properties, obtaining (multiple) steady state solutions for the subnetwork, extension to the overall network, examples from signaling networks (MAPK cascade) and cellular regulation (cell cycle control).

References:

- C. Conradi, D. Flockerzi, J. Raisch & J. Stelling (2007). Subnetwork analysis reveals dynamic features of complex (bio)chemical networks. *PNAS* 104(49):19175-19180.
- G. Craciun, Y. Tang & M. Feinberg (2006). Understanding bistability in complex enzyme-driven reaction networks. *PNAS* 103(23):8697-8702.