Problems of Control and System Theory motivated by Biochemical Reaction Systems

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1 Extended abstract

Progress in the life sciences can benefit besides experimental and descriptive research also from the mathematical sciences for modeling, system identification, system theory, and control theory.

The motivation for the mathematics research of the life sciences comes (1) from biology for the understanding of the functioning of biological organisms; and (2) from biotechnology, the production of food and medicines. The aim of the research in control and system theory is to assist biologists and biotechnologists with the development of theory and algorithms.

The research program of the author for this topic includes the following research issues:

1. Algebraic properties of biochemical reaction systems.
2. Properties of rational (positive) systems.
3. Modeling of very large biochemical reaction systems preferably of the complete cell by methods of hierarchical system theory, modularity, and algebraic decomposition.
4. System identification of rational (positive) systems.
5. System reduction of biochemical reaction systems.
6. Control for biotechnology including rational drug design and production of chemical substances.

Examples of biological phenomena which may be mentioned during the lecture include: (1) Glycolysis in Baker's yeast (Saccharomyces cerevisiae) in connection with system reduction. (2) Protein network of the red blood cell during its first ten days of existence as an example of modeling a genetic network. (3) Nitrogen assimilation in Escherichia coli including a signalling and DNA reading activities.

Models of biochemical reaction networks will be treated using the approach developed by Martin Feinberg (1987). Biochemical reaction systems will be defined and their algebraic properties explored. Problems of modeling, system identification, and of analysis will be discussed.

Problems and preliminary solutions will be presented to several research issues. The problem of system reduction of metabolic networks is to find for a biochemical reaction system another system which approximates the input-output relation according to a certain criterion. This is very relevant for modeling of metabolic networks where the time scales of reactions can differ by several orders of magnitudes.

System identification of biochemical reaction systems requires addressing the following subproblems. The class of systems is that of rational positive systems. Formulation of theory and algorithms for checking controllability and observability of rational systems. Conditions for structural identifiability of rational systems. Approximation algorithm for rational systems like the subspace identification algorithm. Open problems are what to do in the case of multiple time scales in a biochemical reaction network.

Realization of rational systems. Rational systems are dynamic systems with inputs and outputs which have a dynamics specified by a rational system and a read-out function which is rational. The realization problem for rational systems is solved, see the references below. There are conditions for algebraic controllability, algebraic observability, and minimality of a realization all in terms of the observation field of rational functions or of the reachability check.

Control for biotechnology. Rational drug design. The problem is to identify in a biochemical reaction network that enzyme or those enzymes which when their function is blocked result in an effective malfunctioning of the network. This is a control problem for which various methods are suitable. A second problem is to optimize the production of particular chemicals by stimulation of the network by basic chemical species and by enzymes. This is a control theoretic problem for which control of nonlinear systems can be quite fruitful.

Concluding remarks

Control and system theoretic problems motivated by biochemical reaction networks have been discussed. There is much scope for further research. New problems are likely to appear, in particular problems which cannot be treated by existing control and system theory.

Researchers interested in this research area should start to work together with biologists who are interested in using mathematics for their biological research. The difference in knowledge between the life sciences and mathematics is large but building bridges over these differences is likely to be fruitful for both areas in the long run.

Further reading

A text book on biology is [2]. Books on biochemical reaction networks are [3, 6, 11, 14] and the recent book [15]. Papers on biochemical reaction systems by Martin Feinberg are [4, 5]. Publications by the CWI Research Group Control and System Theory on the topic include [1, 9, 10, 13, 12, 16] and papers on control of hybrid systems which are relevant for analysis of genetic networks are [7, 8].

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