Engineering model reduction of bio-chemical kinetic models

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Significance and Aim Bio-chemical kinetic models of enzyme kinetic processes, as well as of regulatory and signalling pathways in living cells are usually too complex for investigating their dynamics, estimating their parameters or designing rational drug injection schedule if they originate from a detailed reaction kinetic scheme. Therefore it is of great importance to develop bio-chemically meaningful and practically feasible ways to reduce these kinetic models, that is, to decrease the number of its state variables (concentrations of the chemical components) and/or parameters, or to simplify the form of the nonlinear relationships but leaving the dynamics of the target input-output relationships unchanged.

Model reduction steps There are two basic elementary steps of commonly used in engineering practice for reducing the number of state variables in a system justified by engineering judgement or operational experience on the dynamic behavior of the system [1]:

- removal of the variables being in (quasi-)steady-state,
- lumping similar variables together.

There are a few recent studies on effect of quasi-steady-state approximation on the dynamic modeling of signal transduction pathways [2] and enzyme kinetics [3], but no one has tried to apply the variable lumping to the reduction of bio-chemical kinetic models and investigate the effect of its application.

Results and Case Study The basis of our approach is the algebraic and graph-theoretical characterization of complex reaction kinetic networks based on the pioneering works of Gorban and Feinberg. The above model reduction steps are described in terms of their engineering (intuitive) meaning, their algebraic characterization and applicability conditions together with their induced graph transformation. The effect of these model reduction steps on the number of steady-states and on the local and global stability conditions is also derived.

The results are illustrated on different MAPK pathway configurations (following [4]) using the MAPK modular structure with different forward and backward regulatory control loops.

References

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