A model reduction method for biochemical reaction networks

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ABSTRACT

For many purposes one may wish to reduce the number of dynamical equations of a biochemical reaction network in such a way that the behaviour of a number of key metabolites is approximated in a satisfactory way. We propose a novel method for model reduction of biochemical reaction networks governed by enzyme kinetics. The method is based on reduction of the complex graph associated with the reaction network. The complexes of a chemical reaction network are the different left- and right-hand sides of the reactions in the network. The vertices of the complex graph associated with the network are the complexes and its edges correspond to the reactions in the network. The reduction procedure works by deleting complexes from the complex graph associated with the network. The reduced network thus has fewer complexes, reactions, variables and parameters as compared to the original network, and yet the behaviour of a number of significant metabolites in the reduced network is approximately the same as in the original network. The effect of the stepwise reduction is monitored by an error integral, which quantifies how much the behaviour of the reduced model deviates from its original. The model reduction accelerates computations and facilitates parameter fitting, especially when we deal with models of huge biochemical reaction networks. Moreover the method results in a reduced model that retains the kinetics and structure of the original model. This enables a direct biochemical interpretation and yields insight into which parts of the network have the highest influence on its behaviour. We have applied our model reduction technique on a yeast glycolysis [1] and a rat liver beta-oxidation model [2]. It is found that a 30 % reduction of the number of variables still leads to a good agreement between the transient behaviour of most metabolites concentrations in the full and the reduced network.

We then observe that the model reduction procedure explained above and published in [3] works effectively only in reducing the connected components of the complex graphs that have more than two complexes. Thus the method does not provide meaningful reductions in case, each connected component of the complex graph of the network has only two complexes, which is generally the case for biochemical reaction networks. We therefore provide a method for combining smaller linkage classes that have common species. This enables the method proposed in [3] to also reduce models of reaction networks whose complex graphs have small connected components.

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