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U–system approach for predicting metabolic behaviors and responses based on an alleged metabolic reaction network

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Abstract

Background

Progress in systems biology offers sophisticated approaches toward a comprehensive understanding of biological systems. Yet, computational analyses are held back due to difficulties in determining suitable model parameter values from experimental data which naturally are subject to biological fluctuations. The data may also be corrupted by experimental uncertainties and sometimes do not contain all information regarding variables that cannot be measured for technical reasons.

Results

We show here a streamlined approach for the construction of a coarse model that allows us to set up dynamic models with minimal input information. The approach uses a hybrid between a pure mass action system and a generalized mass action (GMA) system in the framework of biochemical systems theory (BST) with rate constants of 1, normal kinetic orders of 1, and –0.5 and 0.5 for inhibitory and activating effects, named Unity (U)–system. The U–system model does not necessarily fit all data well but is often sufficient for predicting metabolic behavior of metabolites which cannot be simultaneously measured, identifying inconsistencies between experimental data and the assumed underlying pathway structure, as well as predicting system responses to a modification of gene or enzyme. The U–system approach was validated with small, generic systems and implemented to model a large-scale metabolic reaction network of a higher plant, *Arabidopsis*. The dynamic behaviors obtained by predictive simulations agreed with actually available

metabolomic time-series data, identified probable errors in the experimental datasets, and estimated probable behavior of unmeasurable metabolites in a qualitative manner. The model could also predict metabolic responses of *Arabidopsis* with altered network structures due to genetic modification.

Conclusions

The U–system approach can effectively predict metabolic behaviors and responses based on structures of an alleged metabolic reaction network. Thus, it can be a useful first-line tool of data analysis, model diagnostics and aid the design of next-step experiments.