504d An Optimization Framework for Elucidating Maximization Hypotheses in Metabolic Network Flux Distribution

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In this talk, we present an optimization based framework to test whether experimentally obtained flux data for a variety of metabolic networks are consistent with the maximization of a weighted combination of cellular resources. We model this hypothetical cellular resource composite as an artificial sink in the network that drains all plausible cellular resources such as metabolites, energy and redox potential in varying ratios. The relative ratios (i.e., stoichiometric coefficients) of resources in this drain flux are determined by solving a convex nonlinear optimization problem that identifies optimal values for the stoichiometric coefficients of the composite resource drain. The optimality of these stoichiometric values implies that the maximization of the composite resource flux leads to flux distributions in the network that are identical with experimental data obtained from isotopomer analysis. This analysis departs from earlier efforts by our group (Burgard and Maranas 2003) by ensuring that the composite resource drain is ultimately coupled with the network stoichiometry. The values obtained for these stoichiometric coefficients determine the relative importance that can be attributed to various hypothetical "cellular objectives" that are being examined. Notably by maximizing this "optimally designed" composite of cellular resources the experimental flux values are recovered in the network. The stoichiometric coefficient values of the derived composite drain flux are contrasted for different conditions and networks. Furthermore, by restricting the number of cellular resources that can participate in this composite drain flux we can identify the minimal set of cellular resources whose maximization explains the experimental data. Results of this study will be presented based on flux data for metabolic networks from prokaryotes, eukaryotes and plants species available in the open literature. The proposed procedure thus provides an unbiased framework to test the validity of different hypotheses leading to a better characterization of the driving forces for cellular metabolism.

References

Burgard, A. P. and Maranas, C. D. (2003). "Optimization-based framework for inferring and testing hypothesized metabolic objective functions." Biotechnol Bioeng 82(6): 670-7.