The effects of parameter deviations on reactant concentrations in metabolic networks

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Recent advances in high-throughput techniques allow for simultaneously measuring a large number of metabolites, so called metabolic profiles. Handling the tremendous mass of data produced by these methods currently poses a major challenge in the field of theoretical biology. In particular, it is extremely difficult to interpret the data within a biological context and to derive molecular mechanisms which are responsible for the observed behavior. A straightforward approach is the construction of a metabolic network from correlation measurements between the metabolites. However, it is not a priori clear whether correlations reflect the underlying reactions.

We present a theoretical approach to reversely determine the covariances of the parameters of the system from covariance measurements of the concentrations of the reactants. Our theory relies on concentration control coefficients. Thus it is restricted by the existence of a mathematical model of the investigated metabolism and knowledge of the mean parameter values. To overcome the latter restriction, we developed a fitting tool using the concept of simulated annealing that yields parameter values for any common kinetics, e.g. Michaelis-Menten, from measured steady-state metabolite concentrations. These assumptions are necessary to calculate the concentration control coefficients which connect the standard deviations with the covariances.

Often there are competing models describing the same metabolism, for example for Glycolysis or the Calvin cycle several models exist. As a further application, we have used our theory to differential between two competing models based on experimental data. Therefore, while we cannot completely reconstruct a metabolic network based on the covariances of the parameters and the metabolic concentrations, we can state which network out of a set is most likely, given the data.