Estimating the solution space of Metabolic Networks

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Motivation

Cellular metabolism is one of the most investigated system of biological interactions. While the topological nature of individual reactions and pathways in the network is quite well understood there is still a lack of comprehension regarding the global functional behavior of the system. In the last few years flux-balance analysis (FBA) has been the most successful and widely used technique for studying metabolism at system level. This method strongly relies on the hypothesis that the organism maximizes an objective function. However only under very specific biological conditions the cell seems to obey such optimization law. A more refined analysis not assuming extremization remains an elusive task for large metabolic systems due to algorithmic limitations.

Methods

In this work we propose a novel algorithmic strategy that provides an efficient characterization of the whole set of stable fluxes compatible with the metabolic constraints. Using a message passing technique derived from the fields of statistical physics and information theory we designed a stochastic algorithm to estimate the size of the affine space containing all possible steady-state flux distributions of metabolic networks. The algorithm, based on the well-known Bethe approximation, can be used to approximately compute the volume of a non full-dimensional convex polytope in high dimensions.

Results

We compare the accuracy of the predictions with an exact algorithm on small random metabolic networks. We also verify that the predictions of the algorithm match closely those of Monte Carlo based methods in the case of the Red Blood Cell metabolic network. Then we test the effect of gene knock-outs on the size of the solution space in the case of E-Coli central metabolism. Finally we analyze the statistical properties of the average fluxes of the reactions in the it on the complete E-Coli metabolic network.

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