

Combinatorial aspects of the network reconstruction problem

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The reconstruction of biochemical, genetic, or signal transduction networks from experimental data by generating realistic models of structure and function with predictive power is an important challenge in biology and theoretical medicine.

The structure and function of a biological system can be probed by perturbing its elements and by measuring a set of parameters to see how this perturbation propagates through the network. The network reconstruction problem aims at reconstructing the network from such experimental data, that is, to determine in which way the measured parameters are linked to each other (and possibly to other, yet undetected factors that are causally involved) and to describe the dynamical behavior of the system.

In practice, this is typically done heuristically, based on subjective interpretations of the data which yields potentially incomplete information as neither network elements are considered that are causally involved but have not been measured nor a certificate can be given that no other model can explain the phenomena.

We present an exact approach to the network reconstruction problem that overcomes both difficulties as it provides a provenly complete list of feasible network alternatives that account for the time-dependent mass or signal flux in the system, using a minimal number of yet unconsidered network components.

Our approach addresses both aspects of biological systems, the network topology and the dynamical behavior, and involves such problems as representing the observed parameter changes as conic integer combinations of certain reaction vectors (to obtain the network topology), and constructing partial orders among the involved reactions by solving a stable set problem in a conflict graph (to reflect the dynamical behavior of the system).