A globally convergent algorithm for computing non-equilibrium steady state concentrations in genome-scale biochemical networks Ronan M.T. Fleming*, Yuekai Sun, Ines Thiele, Michael A. Saunders

Abstract
At the core of computational systems biology lies a paradox. All of the currently available genome-scale modelling methods can only model chemical reaction rates, but not the concentration of the molecules involved in these reactions. At the same time, the vast majority of experimental omics data measure the abundance of metabolites, rather than reaction rates. The reason for this paradox is that modelling steady state reaction kinetics has been limited to small systems of chemical reactions as the inherently non-linear system of equations, at the core of such models, are difficult to solve. Even if one numerically integrates the corresponding kinetic equations, the absence of a long sought Lyapunov function prevents one from concluding the system will converge to a non-equilibrium steady state, for the most general class of biochemical reaction networks. Here we present the first globally convergent algorithm for simultaneously computing stable non-equilibrium steady state molecular concentrations and reaction rates for multi-scale biochemical reaction networks. Our result has implications for a wide variety of biochemical modeling scenarios, beyond reaction kinetics, wherever some non-negative flow is a strictly monotonically increasing function of an absolute potential.

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