

90. Globally Convergent Algorithms to Solve Systems of Non-linear Biochemical Reaction Equations

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Project Goals: In experimental systems biology, the majority of high throughput experimental data is of molecular abundance and the minority is of reaction rates. We seek a modeling framework flexible enough to integrate experimental data on both rates and abundance. With explicit representation of molecular abundance it becomes possible to mechanistically model regulation, e.g., genetic regulation, where the abundance of an active transcription factor modulates the rate of transcription by binding to a sequence motif in competition with other genomic structural proteins. Phenomenological kinetic models (e.g., Michaelis-Menten kinetics) are potentially more biochemically realistic than flux balance models as they simultaneously represent concentration and flux, but their solution for a steady state concentration quickly becomes intractable for networks with over ~ 100 reactions. Our goal is to develop the first algorithms for tractable modeling of steady state flux and concentration at genome-scale.

Solving systems of non-linear biochemical reaction equations is an essential part of genome-scale kinetic modeling. We introduce a new class of function, called duplomonotone, which is strictly broader than the class of monotone function. We study some of the main properties of duplomonotone functions and provide an example of a nonlinear duplomonotone function used to model a system of biochemical reactions. We present three variations of a derivative-free line search algorithm for finding zeros of systems of duplomonotone equations, and we prove their linear convergence to a zero of the function [1]. This classification of the key function appearing in deterministic models of systems of biochemical reactions appears to hold more generally, opening up the realistic prospect of globally convergent algorithms for genome-scale kinetic modeling for the first time.

References

1. Aragon Artacho, F. J., and Fleming, R. M. T. Globally convergent algorithms for finding zeros of duplomonotone mappings. *Optimization Letters*, Sept. 2014.

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