Amgen Seminar Series in Chemical Engineering

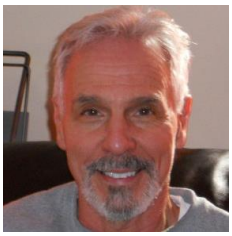
in

Cherry Auditorium, Kirk Hall, 1 PM

Presents on February 8, 2018

Are Metabolic Pathways Nash Equilibria?

By



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Flux balance analysis (FBA) has been the mainstay for understanding metabolic networks for many years. However, recently Lucia and DiMaggio have shown that metabolic pathways are more correctly modeled using game theory, specifically Nash Equilibrium, because it captures the natural competition among enzymes. The key ideas behind the Nash equilibrium approach to metabolic pathway analysis are that

1. Enzymes are treated as players in a multi-player game.
2. The objective or payoff function for each player is a constrained nonlinear programming (NLP) problem where each player (enzyme) minimizes the Gibbs free energy of the reaction it catalyzes subject to element mass balances.
3. The goal of the metabolic network is to find the best overall solution given the natural competition for nutrients among enzymes.

The Nash equilibrium approach has many advantages over FBA and its many variants, constraint-based modeling (CBM), and kinetic approaches to determining fluxes and other information associated with any metabolic network. One can

1. include co-factors in modeling sub-networks.
2. model electrolyte solution behavior and incorporate charge balancing.
3. include feedback, allosteric, and other forms of inhibition.
4. explicitly include enzyme-substrate reactions as part of the model.
5. up-scale genetic information and consider mutations and/or re-engineered enzymes.
6. model up/down regulation of enzymes.

In this talk, I will present the fundamentals of Nash Equilibrium as it applies to metabolic pathways and present a survey of results for a number of common pathway including glycolysis, the Krebs cycle, Acetone-Butanol-Ethanol (ABE) production, the mevalonate and methionine salvage pathways, and the ornithine cycle. I will also show that, in cases where experimental data is available, numerical predictions using the Nash Equilibrium approach show remarkably good agreement with experimental metabolite concentrations and other biological metrics such as turnover ratio.

This series at the University of Rhode Island is made possible through the generosity of Amgen, West Greenwich, R.I.

Refreshments provided by the Joseph Estrin Endowment.