438871 Integrating Kinetic and Constraint-Based Models of Metabolism

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Modeling cellular metabolism has become a fundamental part of biotechnological research. Metabolic models are currently used in a wide range of applications from the study of disease mechanisms to the rational design of microbial cell factories. One current limitation in the field is the co-existence of two main mathematical frameworks to model metabolism. Kinetic models can simulate the transient profile of intracellular metabolism accounting for the mechanistic details of enzyme-metabolite interactions, including regulatory effects, but their construction is limited in scalability. Constraint-based models on the other hand, can be constructed at genome scale, but can only simulate intracellular reaction rates at steady-state without accounting for mechanistic details.

In previous work, we explored the gap between these two frameworks and proved that, for the same metabolic network, under unlimited variation of kinetic parameters, the space of steady-state solutions described by both models is the same [1]. In this work we analyze the kinetically feasible solution space generated by the variation of enzyme concentration levels in central carbon metabolism. Furthermore, we map this solution space onto the global solution space obtained with a genome-scale constraint-based model and compare optimality-based solutions predicted by e. g. Flux Balance Analysis obtained using both spaces. The integration of kinetic and constraint-based models is a suitable approach for refining genome-scale phenotype predictions with mechanistic constraints.

[1] Exploring the gap between dynamic and constraint-based models of metabolism. D Machado, RS Costa, EC Ferreira, I Rocha, B Tidor. Metabolic engineering, 14(2):112-119 2012

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