

Quantitative metabolic modeling at the Joint BioEnergy Institute

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Project Goals: The Quantitative Metabolic Modeling (QMM) group is devoted to developing predictive models of metabolism that can leverage high-throughput ‘omics data and direct metabolic engineering efforts.

The advent of synthetic biology as an effective tool to engineer biological cells has produced numerous beneficial applications, including the production of renewable biofuels[1]. However, effective design of biological systems is precluded by our inability to predict their behavior. New tools like CRISPR-enabled genetic editing, and DNA synthesis productivity that improves as fast as Moore’s law, allows us to engineer changes faster than ever but the end result on cell behavior is usually unpredictable. At the same time, there is an exponentially increasing amount of functional genomics data available to the experimenter in order to phenotype the resulting bioengineered organism. Furthermore, the miniaturization of these techniques and the progressive automation of laboratory work through microfluidics chips promises a future where data analysis will be the bottleneck in biological research. Unfortunately, the availability of all this data does not translate into better predictive capabilities for biological systems: converting these data into actionable insights to achieve a given goal (e.g. higher bioproduct yields) is far from trivial or routine.

Here we show the variety of methods created in the QMM group to leverage ‘omics data and guide metabolic engineering. We have used **machine learning** approaches to predict pathway dynamics directly from time-series data, without having to rely on Michaelis-Menten or other closed form of kinetics. We have also developed mechanistic models based on ¹³C **Metabolic Flux Analysis** to find mechanistic insights that have been shown to improve methyl ketone production by 110%. Finally we have also developed software tools to: guide **polyketide synthase (PKS) engineering** (clusterCAD [2]), **acquire and store data** systematically (EDD [3]), and perform ¹³C **MFA for genome-scale models** (jQMM library [4] [5,6]).

References

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