Enabling Predictive Metabolic Modeling of Diurnal Growth Using a Multi-Scale Multi-Paradigm Approach

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Project Goals: The main goal of this project is to develop more predictive metabolic models of diurnal growth for algal systems. We are using a multi-paradigm multi-scale approach which enables us to include phenomenon not previously integrated into metabolic models, such as diel light, diffusion of metabolites/nutrients, cell-cell interactions, as well as temporal and spatial tracking of cells. This model will further be enhanced with experimental data collected over 24 hour diel growth for transcript abundance and changes in biomass composition. Validation and improvement of the model will be performed by comparing predictions to 13C-MFA of cells grown in the lab as well as in large outdoor ponds.

Photosynthetic microorganisms have the potential to become sustainable sources of fuels; however, we have yet to harness their full power due to a general lack of tools for engineering their metabolism. Metabolic models have been shown to drastically reduce the development time for commercial production strains of heterotrophic bacteria; however, they are less applicable to photosynthetic systems due to the transient nature of diurnal (day/night) growth, which is the most economical option for large-scale production because energy provided to the cells can come strictly from sunlight alone. Current metabolic models are not capable of accurately predicting growth rates in day/night growth cycles, let alone genetic changes which would lead to increased yields. Therefore, it is imperative that the unique physiology of photosynthetic organisms be integrated into the next generation of metabolic models so that they can be used to design, build, and test photocatalytic biofuel production strains. The availability of such models will introduce a new frontier in the ability to use *in silico* tools to investigate the metabolism, growth and phenotype of photosynthetic microorganisms. It will enable us to gain insight into why photosynthetic organisms have drastically different productivities when grown in continuous light compared to diurnal cycles and how to circumvent this. We will present our work to date on the development of an advanced multi-paradigm multi-scale metabolic model of the green alga, *Chromochloris zofingiensis*, using an agent-based modeling framework that both incorporates, and is validated, by experimental data.

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