

## Advanced Metabolic Modeling of Diurnal Growth in *Chlamydomonas reinhardtii*

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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 <sup>13</sup>C-MFA of cells grown in the lab as well as in large outdoor ponds.**

Photosynthetic microorganisms have the potential to become economical and sustainable sources of fuels, as the energy required for the cell to grow can be sourced from natural sunlight alone; 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, these models are less applicable to photosynthetic systems due to the transient nature of diurnal (day/night) growth. 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. Our work is focused on constructing an approach to diurnal modeling that allows for extension of current metabolic models into a transient space, using organism specific circadian information. We have used circadian gene expression data from *Chlamydomonas reinhardtii* to cluster gene expression and convert discrete data into continuous functions. We then implemented these functions as additional constraints on our metabolic model and are currently integrating this constrained model into an agent-based framework. We will present the result of this work and demonstrate how these modeling techniques are able to further improve the model and better predict growth in diurnal light. Ultimately, 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.

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