Dynamic metabolic constraints of *Phaeodactylum tricornutum* reveal bases on organelle-specific carbon and nitrogen partitioning during nitrogen depletion

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The goal of this project is to gain new insights into the photosynthetic eukaryote *Phaeodactylum tricornutum* using a systems biology approach. We will integrate various omics data into a metabolic modeling framework, to systematically identify and quantify the partitioning of carbon and nitrogen among cellular metabolism, cross-talk between organelles, and productive photosynthetic electron flow.

Diverse conditions, i.e. growth during day and night, and compartmental cellular organization require phototrophs to shift their proteome demands and therefore adjust their metabolism and biomass composition during the course of growth. The complex interplay between energy and carbon metabolism and its dynamics in phototrophs is still not fully understood. Constraint-based modeling is a systems biology tool that takes advantage of experimental data, such as uptake rates and biomass composition, for successful prediction of growth phenotypes. Currently, lack of time-course biomass composition data has restricted prediction accuracy, by forcing the models to assume that the biomass remains constant. Here, we used experimentally determined metabolomics data to determine biomass composition constrains for a genome-scale metabolic model of the diatom *P. tricornutum*. We found that time course constraints can be the sole driving force that causes the metabolic network to exhibit certain behaviors such as time-specific secretion rates, cross talk of organelles by the activation of the mitochondria, as well as activation of specific metabolic pathways. A growth rate sensitivity analysis of time-course flux distributions enabled identifying the main metabolite affecting growth. We also found that simulation results are sensitive to the accurate experimental quantification of some amino acids. Surprisingly growth sensitivity predictions are independent of biosynthetic cost and connectivity of metabolites.

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