In the field of computational modeling of biochemical networks, a key limiting factor in the past has been the attainment of various parameters required to provide an accurate description of a system and to suggest experimentally testable hypotheses. Constraint-based methods of modeling and analysis are based on the idea that ranges of feasible in silico phenotypes can be attained through the iterative addition of biologically relevant constraints to a model. Since ranges of feasible phenotypes are computed, as opposed to point solutions, large numbers of kinetic parameters are not necessary to obtain useful predictions. To provide feasible phenotypic ranges, constraints, such as stoichiometry, thermodynamics, regulation, size, etc., can be described mathematically, added to a mechanistic model, and used to provide important information on possible cellular phenotypes and suggest experimentally testable hypotheses.

Constraint-based Analysis

The metabolic reconstruction of the Arabidopsis thaliana chloroplast is in its early stages. All genes with a traditional mechanistic/bottom-up modeling approach strive for complete knowledge and precise predictions. In contrast, constraint-based methods, which dictate whether a gene is expressed/not expressed or whether an enzyme is activated or inhibited, can be added to a model.

Incorporating the Effects of Transcriptional Regulation

When a metabolic reconstruction is available, regulatory effects can be modeled. Boolean rules can be added that dictate whether a gene is expressed/not expressed or whether an enzyme is activated or inhibited [2]. These rules will shrink the solution space, allowing for improved predictions. These regulatory rules can be refined and novel regulatory interactions may be predicted by comparing experimental observations with computational predictions [3].

References and Acknowledgements


We would like to thank numerous colleagues & the NSF for IGERT funding during this project (# DGE-0504645).