

Genome-Scale Metabolic Network Model of Arabidopsis

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Abstract

Metabolic network is often complex and highly interconnected. The fact that metabolic network encountered in plants is far more complex than in prokaryotes means that there is likely to be a greater opportunity for the use of computational models to investigate plant cellular function. In order to take a systematic investigation of metabolic properties and interrogation of available omics datasets for plants, a genome-scale metabolic network model for a photosynthetic plant cell has been reconstructed. The reconstruction was based on the Arabidopsis genome, on line database resources and biochemical information found in the literature. It represents the first attempt to collect and characterize a photosynthetic plant cell to perform fluxomics at the genome-scale. Carbon flux through the metabolic network is represented by 1320 unique reactions, 1438 metabolites and 130 transporters and is compartmentalized between the cytosol, mitochondria, vacuole, plastid, and peroxisome. The model has been validated using a number of classical plant physiological scenarios. The plant genome-scale model is being used to perform fluxomics for a better understanding of plant metabolic capabilities under different conditions. This is a potential platform to test hypothesis *in silico* and derive biological insights from the metabolism of plants. Fluxome profiles integrated to other omics datasets represent an important step towards genome-scale plant systems biology.

Keywords metabolic reconstruction; genome-scale model, Arabidopsis; systems biology.

1 Introduction

The procedure for the reconstruction of a metabolic network at genome-scale, and its use as predictive models, is established for metabolic engineering of microorganisms [2, 4]. The same approach has been also applied to mouse hybridomas [5] and more recently to the study of human metabolism [1]. In a bid to improve the success rate of plant metabolic engineering, a systems-based framework to study plant metabolism is needed [3, 6] Here, we establish a plant genome-scale model as a functional framework to investigate plant cell metabolism, using the *Arabidopsis* plant as a reference model. It represents the first genome-scale model of a compartmentalized photosynthetic plant cell. Most importantly, the framework represents a structured compilation of cell components and interactions, which enables systematic investigation of metabolic properties and interrogation of available omics datasets for plants. This is a potential platform to test hypothesis *in silico* and gain an insight into the metabolism of plants, and can be used as a tool for rational plant metabolic engineering purposes. The genome-scale model has been validated against a number of classical physiological scenarios typically encountered in a photosynthetic and a non-photosynthetic cell. Here we present the changes in the metabolic flux distribution of a plant cell shuffling ammonia between the sub-cellular compartments during photorespiration.

2 Method and Results

The genome-scale metabolic network of Arabidopsis was reconstructed using currently available genomic, biochemical, and physiological information. The metabolic reactions were compartmentalized between the cytosol, mitochondria, plastids, peroxisome, and vacuole. The Network Characteristics is shown in Table 1.

2.1 Tables

Table 1. Network Characteristics of the Reconstructed Metabolic Network of Arabidopsis thaliana. – Functional Annotation

Gene-reaction-association entries	4196
ORFs (unique)	1427
Metabolites	1438
Unique reactions	1320
Cytosolic reactions	997
Mitochondrial reactions	60
Plastidic reactions	159
Peroxisomal reactions	98
Transporters	135
Transporters not assigned to any particular ORF	41
Reactions not assigned to any particular ORF	67
Curation	
Number of gaps found in the network and completed	230
Number of modified reactions (corrected reversibility and/or stoichiometry)	33

2.2 Figures

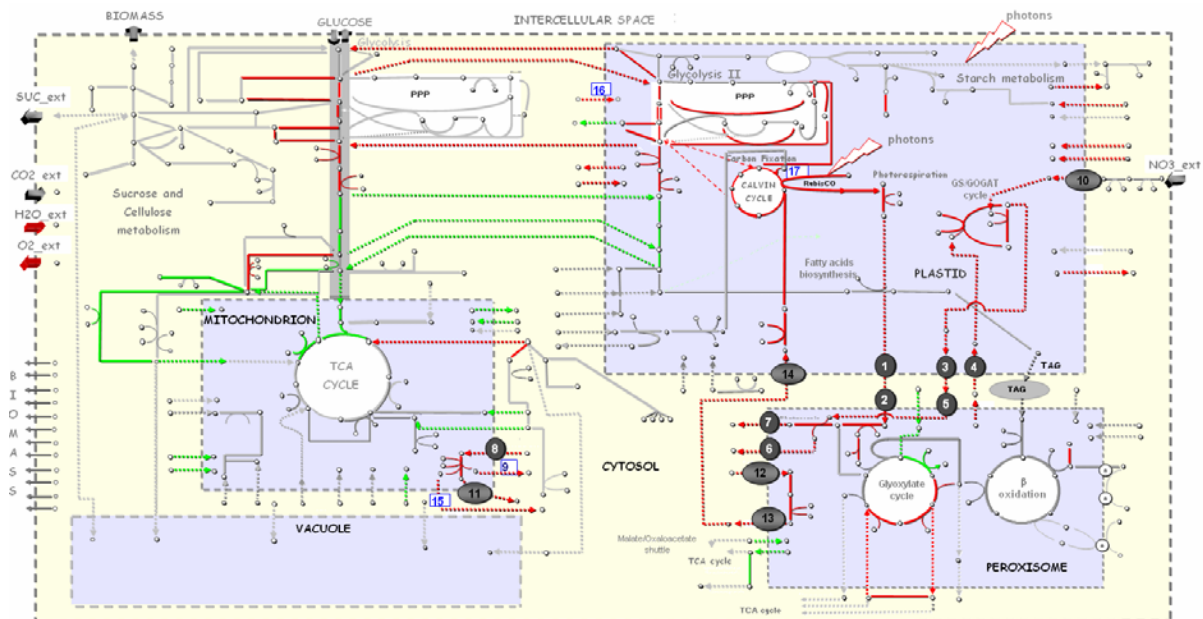


Figure 1. Simulation – Overall metabolic activity in the central metabolism for the classical photorespiratory cycle scenario (textbook). Red lines highlight fluxes that have increased during photorespiration. Green lines represent decreased fluxes during photorespiration when compared to photosynthesis. Gray lines represent flux values that have not changed significantly. Steps 1-17 represent the order of events during the photorespiration cycle.

3 Discussions

In this work we have introduced AraGEM; the first genome scale model to perform fluxomics *in silico* representing a functional compartmentalized photosynthetic and/or non-photosynthetic plant cell. We demonstrated that AraGEM was able to simulate metabolic cell function after an extensive curation. Even for the most studied plant model, more than 200 gaps were found in the genomic metabolic network (Table 1). The model has shown plasticity to represent different metabolic scenarios that are present in different plant tissues. This is a potential framework that can be used to test new hypotheses for analyzing plant metabolic systems, as it can provide a more complete overview of the metabolism. Flux distributions give us an idea about the complexity of plant metabolic network, its interconnectivity, and the overall metabolic activity under different physiological scenarios (Figure 1). AraGEM is being used to perform fluxomics for a better understanding of plant metabolic capabilities under different conditions and in the presence of additional drains for metabolic engineering purposes. The fact that the metabolic network encountered in plants is far more complex than in prokaryotes means that there is likely to be a greater opportunity for the use of computational models to understand the basis of plant cellular function. The refinement of AraGEM is on-going. We are working on a suitable platform for plant omics data integration. Fluxome profiles integrated into other omics dataset represents an important step towards genome-scale plant systems biology.

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