

# Computational metabolic engineering of *Arabidopsis thaliana* for increased biomass production

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**Abstract.** We have developed a computational method for determining the maximum theoretical production capability of a metabolic network and for identifying corresponding metabolic engineering strategies. The method relies on generating feasible chemical reactions and predicting the effect of their insertion into a host metabolic network. A chemical reaction which optimizes a given objective, such as growth or product yield, can further be decomposed into a set of enzyme-coding genes from a database of metabolic reactions. The resulting genes thus represent promising candidates for transformation into the host in order to optimize the specified objective. We have shown previously that the method correctly predicts enzymes required for the production of glucose from fatty acids in a model of the TCA cycle which does not include these enzymes.

Here, we extend and apply the method to identifying metabolic engineering strategies for optimizing growth in the model plant *Arabidopsis thaliana* using a recent compartmentalized genome-scale metabolic network reconstruction (Mintz-Oron et al. PNAS 2012). Our first aim is to recover metabolic engineering strategies which have been shown to increase biomass production, such as transformation of the glycolate catabolic pathway from *E. coli* or the glycolate catabolic cycle and catalase into chloroplasts. To this end, we extend the ability of the method to generating several alternative hypotheses for metabolic engineering. We then evaluate the identified reactions and enzyme-coding genes for their feasibility and potential for increasing biomass production in *A. thaliana*. The obtained results suggest valuable strategies for the metabolic engineering of crop plants aiming at improved yield.