Project Goals: This project aims to expand existing carbon mapping models from core models to genome-scale models for flux elucidation using 13C-MFA using tools, algorithms and reaction information contained within the MetRxn database. The constructed mapping models will be deployed for genome-scale flux elucidation to obtain insights into the impact of model scale-up and loss of information, sensitivity of flux distributions to biomass composition, and novel carbon backbone scrambling patterns and pathway usage in cyanobacteria.
Overall, we find that both the topology and estimated values of the metabolic fluxes remain largely consistent between the core and GSMM models for *E. coli*. Stepping up to a genome-scale mapping model leads to wider flux inference ranges for 20 key reactions present in the core model. The glycolysis flux range doubles due to the possibility of active gluconeogenesis, the TCA flux range expanded by 80% due to the availability of a bypass through arginine consistent with labeling data, and the transhydrogenase reaction flux was essentially unresolved due to the presence of as many as five routes for the inter-conversion of NADPH to NADH afforded by the genome-scale model. By globally accounting for ATP demands in the GSMM model the unused ATP decreased drastically with the lower bound matching the maintenance ATP requirement. A non-zero flux for the arginine degradation pathway was identified to meet biomass precursor demands as detailed in the iAF1260 model. Inferred ranges for 81% of the reactions in the genome-scale metabolic (GSM) model varied less than one-tenth of the basis glucose uptake rate (95% confidence test). This is because as many as 411 reactions in the GSM are growth coupled meaning that the single measurement of biomass formation rate locks the reaction flux values. This implies that accurate biomass formation rate and composition are critical for resolving metabolic fluxes away from central metabolism and suggests the importance of biomass composition (re)assessment under different genetic and environmental backgrounds. In addition to better recapitulation of experimentally observed labeling distributions of all measured central metabolites, flux elucidation using the cyanobacterial mapping model predicts the existence of a serine biosynthesis route from 3PG and trace flux through the GABA shunt. The loss of information associated with mapping fluxes from MFA on a core model to a GSM model is quantified and its implications on inferences drawn on the metabolic capabilities of *E. coli* and cyanobacteria are discussed.

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