439890 Reconciling Experimental Data With in Silico Predictions In Metabolic Engineering Applications

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The field of Metabolic Engineering (ME) has gained a major importance, since it allows the design of improved microorganisms for industrial applications, starting with wild-type strains that usually have low production capabilities in terms of the target compounds. The ultimate aim of ME is to identify genetic manipulations *in silico* leading to improved microbial strains, that can be implemented using novel molecular biology techniques. This task, however, is a complex one, requiring the existence of reliable metabolic models for strain simulation and robust optimization algorithms for target identification.

Strain simulation is usually performed by using Genome-scale stoichiometric models and Linear or Quadratic Programing methods that assume a steady state over the intracellular metabolites. However, a systematic evaluation of the predictive capacities of the available genome-scale models and simulation tools has not been performed, mainly regarding predictions other than reaction/gene essentiality. We have performed a thorough analysis of *in vivo* data of *S. cerevisiae* regarding flux distributions, auxotrophies and product excretion and have concluded that most of the available ME tools do not allow to make accurate predictions, ultimately leading to ineffective ME strategies. We also propose novel tools for the reconciliation of experimental data with model predictions.

Another important aspect associated with model predictions is the influence of the biomass equation added to the model. Since most simulation tools require directly or indirectly the computation of maximal biomass formation, this composition has a great impact in the predictive power of these models. Moreover, biomass composition is intrinsically related with essentiality predictions. In this talk, a detailed analysis of the impact of the biomass composition in essentiality and quantitative phenotype predictions will be presented for several dozens of organisms, also including the collection of experimental data on biomass composition under the same conditions for 8 different organisms. Based on these results,

unified frameworks and methods will be presented to minimize discrepancies associated with biomass equations.

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