504e Using Flux Balance Analysis to Estimate Qualitative Changes in Gene Expression Profile Purusharth Prakash and Jeremy S. Edwards

FBA methodology has been used to study relationship between genotype and phenotype for prokaryotes and eukaryotes, and to make predictions about the metabolic state of the cell under various environmental conditions. FBA methodology can also be used to make reliable predictions of metabolic characteristics at a systemic level, which makes the Flux Balance Approach an attractive candidate for metabolic engineering applications.

Here we show that FBA approach can be used to estimate qualitative changes in the gene expression profile with change in environmental conditions. A comparative analysis of the flux distribution under two conditions provides us with potential candidates which can undergo change in expression. These candidate genes can be further narrowed down if information is available for the regulatory interactions of the metabolic network.

In the present analysis we show application of above approach for Saccharomyces cerevisiae for growth under two different substrates ethanol and glucose. The gene expression profile was measured for growth on each of the two substrates using DNA Microarrays. Using Flux Balance Framework and a model of metabolic network of yeast, a set of genes undergoing differential expression is estimated. The Flux Balance predictions were further refined using network topology and regulatory information for the metabolic network. These predictions are compared to the experimental expression profile. Finally, we show the feasibility of Flux Balance Models for qualitative predictions of gene expression profiles.