Development of an integrated metabolic and transcriptional regulatory model for *Saccharomyces cerevisiae*

Paul Drescher, Rafael Carreira, Paulo Vilaça, Isabel Rocha

Saccharomyces cerevisiae (*S. cerevisiae*) is commonly used as a cell factory for research and industrial applications. The development of optimization strategies for *S. cerevisiae* was extensively driven by the establishment of genome-scale metabolic models. Additionally, to aid metabolic modeling, multiple attempts to infer transcriptional regulatory networks from expression data have been made. However, these data-based regulatory networks may show limited applicability. Therefore, we propose a general, knowledge-based approach involving a pipeline to evaluate regulatory interactions of transcription factors (TFs) and target genes from the YEASTRACT database, and form a regulatory network from these filtered datasets. So far, we filtered regulatory interactions based on two criteria: the existence of direct binding evidence of the TFs and their target genes, and the consensus over the regulatory effects identified among multiple studies that investigated each interaction, respectively. From 230 TFs and over 6000 genes contained in YEASTRACT, we obtained a regulatory network of 69 TFs and 1187 target genes with 1813 regulatory interactions, including 346 metabolic genes with 622 regulatory interactions. These interactions cover the majority of genes in the central carbon metabolism. Next, these regulatory interactions will be evaluated by identifying the network's attractor states and simulating their effect on the metabolic system via steady-state regulatory flux balance analysis. Finally, this integrated metabolic and regulatory model may be used to identify efficient optimization strategies for *S. cerevisiae*.