The limitations of life: Modelling enzyme constraints in yeast metabolism

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Genome scale modelling (GEM) is a recurrent approach for modelling metabolic fluxes of *Saccharomyces cerevisiae* (budding yeast). However, by only modelling at the flux level there are various phenotypic responses that cannot be explained, in particular at conditions of high enzymatic demand. Examples of this are the Crabtree effect at high growth rates, stress-coping mechanisms and consumption of non-conventional carbon sources. Proteomics therefore stands as a promising omic that could give additional insight into cellular capabilities when integrated to GEMs[1]. Here we present the enhancement of a yeast GEM[2] to account for enzymatic constraints. This is done with the constraint-based approach[3] extended to include enzymes as part of the reactions[4]. With this formalism, reaction fluxes can be limited by the intracellular abundance and turnover number (k_{cat}) of each enzyme[5]. Using this approach with different levels of data, we show that we can predict metabolic strategies that regular constrained-based approaches cannot and significantly reduce variability of flux predictions. Most importantly, we can gain additional insight into enzyme usage and understand what limits yeast growth under different conditions. The approach is expected to be of great use in metabolic engineering applications, specifically for predicting enzymatic costs of highly-valued chemical compound production.

References:

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