Identification of metabolic engineering targets through pathway analysis

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Given the complexity of metabolic networks, identification of optimal metabolic intervention strategies for redirecting fluxes towards desired products is a challenging task. Several algorithms based on linear programming and pathway analysis have been proposed. However, there is still a lack of an algorithmic framework that exploits the range of optimal and suboptimal routes and the structural/regulatory properties thereof. To this end, we are using a modified version of the concept “control effective flux (CEF)” [1] towards a novel algorithm for *in silico* metabolic engineering. CEFs represent the importance of each reaction for efficient and flexible operation of the entire metabolic network.

We propose four modifications on the CEFs. First, as the absolute values are not comparable across networks, we apply normalization. Second, we use “minimal generating sets” to facilitate the use of large-scale networks. Third, we take into account the reaction directionality within the modes. Fourth, we only take into account biologically relevant modes. We show that CEFs are good predictors of intra-cellular fluxes in *Escherichia coli* and *Sacharomyces cerevisiae*. Next, we introduce our metabolic engineering algorithm where the objective is to identify deletion targets that increase the CEF of the desired flux. Our formulation leads to solutions that couple growth with product formation while considering optimal as well as sub-optimal routes and their efficiency.

Reference

[1] Stelling et al. (2002), Nature 420: 190-193