

# Selecting among the multiple alternate optimal solutions of the Flux Balance Analysis of yeast metabolism: Use of the adaptational potential of the organism

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## Abstract

Organisms have to adapt physiologically to new conditions upon changes in their environment. Starting from a steady-state flux distribution the organism synthesises, degrades, activates or inhibits enzymes to bring about a new steady-state flux distribution corresponding to the adapted state on the new environmental conditions. For the *in silico* study of these biological processes, both kinetic and constraint-based modelling approaches have been applied. Even though the kinetic description of a metabolic network is almost always preferable, the size of genome-scale networks does not yet permit a detailed kinetic characterisation. At the same time, it can be useful to study the general capabilities of a metabolic network at a system-wide level. Flux Balance Analysis (FBA) is a powerful tool suitable to facilitate this kind of investigation. Nevertheless, one of the weaknesses of the FBA approach is that there is usually degeneracy in the model, leading to a large number of equivalent flux distributions that are predicted at each growing condition, which all satisfy the same optimality criterion.

Although all the solutions identified by a given FBA are plausible, only one of these flux distributions is actually reached by the cell in each of the growing conditions, if indeed any such optimality is reached in reality at all (it is not certain whether organisms are in fact optimising their activities against *any* known objective function, despite a widespread assumption that they have evolved to maximise biomass production). In this study, we try to predict the actual flux distribution by minimising the “adaptational work” the organism needs to perform. Adaptational work is defined as the number of enzymes the organism needs to synthesise newly when it shifts from one condition to another. If this number is minimal, then the organism can respond rapidly and (in an energetic sense) efficiently; in addition, it will require a less complex regulatory network. To find a flux state for each growth environment that requires minimal adaptational work upon an environmental change, we implement a two-step approach: (i) using FBA, we compute for each environment all the alternative flux distributions in yeast metabolism that maximise the growth rate in each of a set of different growing conditions, and (ii) we identify the set of flux distributions, one for each environment, that have the minimal difference in the identity of the enzymes that are being used. This set would minimise the adaptational work the organism needs to live in its changing environment.

## References

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