Reference

415

Integration of proteomic data for predicting dynamic behaviour in an *E. coli* central carbon network after genetic perturbations

Costa, Rafael S.; Machado, Daniel; Rocha, Isabel; Ferreira, Eugénio Campos

IBB-Institute for Biotechnology and Bioengineering, Centre of Biological Engineering, University of Minho, Campus de Gualtar, 4710-057 Braga, Portugal

E-mail: ecferreira@deb.uminho.pt

Keywords: *E. coli* metabolism, linlog kinetics, constraint-based approach, prediction, dynamic modelling, data integration

Abstract

One of the great challenges in the post-genomic era is to understand the dynamic behaviour of a living cell. For that purpose, quantitative models describing metabolic network dynamics are a powerful tool as “dry lab” platforms to simulate experiments before they are performed *in vivo*. Kinetic models and stoichiometric genome scale models of the microbial metabolism are usually the two large-scale modelling approaches most used. So far, few large scale kinetic models have been successfully constructed. The main reasons for this are not only the associated mathematical complexity, but also the large number of unknown kinetic parameters required in the rate equations to define the system. In contrast to kinetic models, the genome scale modelling approach bypasses these difficulties by using basically only stoichiometric information with certain physicochemical constraints to limit the space of a network without large fitted parameters sets. Although these constraint-based models are highly relevant to predict a feasible set of steady-state fluxes under a diverse range of genetic conditions, the steady-state assumption may oversimplify cellular behaviour and cannot offer information about time dependent changes. To overcome these problems, combining these two approaches appears a reasonable alternative to modelling large-scale metabolic networks.

In this work, we used a large-scale central carbon metabolic network of *E. coli* [1] to investigate whether including high throughput enzyme concentrations data into a model allows an improved prediction of the response to different single-knockouts perturbations. For this purpose, a model based on the flux balance analysis (FBA) approach and linlog kinetics was constructed. As a first validation, we applied it to predict steady-state changes in fluxes and metabolite concentrations, as well as dynamic responses to perturbations in the central *E. coli* metabolism. Then, the approach was evaluated by comparison with various sets of published *in vivo* measurements [2]. Our results indicate that integration of the quantitative enzyme levels into the kinetic models, in general, can be used to predict dynamic behavior changes.

[1] Chassagnole,C.; Noisommit-Rizzi,N.; Schmid,J.W.; Mauch,K.; Reuss,M. Biotechnology and Bioengineering 2002, 79: 53-73.

[2] Ishii, N. et al. Science 2007, 316: 593-597