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Constraint-based approach for *in silico Escherichia coli* combined regulatory/metabolic modelling

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The annotation of the *Escherichia coli* genome sequence allowed the development of *in silico* models based on the reconstruction of metabolic networks, able to predict phenotypic behaviour under different environmental and genetic conditions[1]. The constrained-based approach has been used to analyze the capabilities of a reconstructed metabolic network, described by a solution space that contains all possible steady-state metabolic flux distributions in the network[2]. Narrowing down the range of the solution space by including regulatory constraints can simplify the search for the best flux distribution. Studies have shown that metabolic enzymes are differentially expressed under different nutrient conditions and certain metabolites influence the activities of transcription factors. This explicitly establishes the links between specific metabolites and transcription factors. The regulatory network consists of a large number of regulatory elements of interacting genes and proteins organized in a hierarchical organization. The present study leads to the reconstruction of an existing genome-scale model of *E. coli*[3], incorporating transcriptional regulation described by Boolean logic equations, and subsequently analysed by flux balance analysis. The addition of regulatory constraints improved the predictive capacity of flux balance models, which contributes to accurately identify the phenotypic behaviours under different environmental conditions.

1. Covert, M. and Palsson, B. (2003) *Journal of Theoretical Biology* **221**:309-325.
2. Edwards, J. *et al.* (2001) *Nature Biotechnology* **19**:125-130.
3. Reed, J. *et al.* (2003) *Genome Biology* **4**.