An approach towards genome-scale kinetic modelling: application to the *Escherichia coli* metabolism

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Abstract

Understanding the dynamic behavior of living organisms is a great challenge in systems biology. To address this, computational dynamic modeling of metabolic networks is essential to guide experimentation and to explain properties of complex biological systems. Large-scale kinetic models at the reaction network level are usually constructed using mechanistic enzymatic rate equations and a large number of kinetic parameters. However, two of the biggest obstacles to construct accurate dynamic models are model complexity and limited *in vivo* kinetic information. In the present work, we test an alternative strategy with a relatively small number of kinetic parameters composed by the approximated lin-log kinetics, coupled with a constraint-based method and *a priori* model reduction based on time scale analysis and a *conjunctive fusion* approach (Machado et al., 2010).. This workflow was evaluated for the condensed version of a genome-scale kinetic model of *Escherichia coli* metabolism (Orth et al., 2010).

The presented approach seems to be a promising mechanism for detailed kinetic modeling even at the genome-scale of the metabolism of other organisms.

Keywords: dynamical modelling, approximate lin-log kinetics, constraint-based modelling, model reduction, model fitting, *E. coli* metabolic network

Machado, D., Costa, R. S., Rocha, M., Rocha, I., Tidor, B., and Ferreira, E. C. (2010) Model transformation of metabolic networks using a Petri net based framework. International Workshop on Biological Process & Petri Nets (BioPPN).

Orth JD, Fleming RMT, Palsson BO (2010) Reconstruction and use of microbial metabolic networks: the core Escherichia coli metabolic model as an Educational Guide. In: Escherichia coli and Salmonella: Cellular and Molecular Biology, ASM Press.