

Building a Computer Simulation of Threonine Synthesis in *Escherichia coli*

David A. Fell^{*}
School of Biological &
Molecular Sciences
Oxford Brookes University
Headington, Oxford
OX3 0BP, UK
dfell@brookes.ac.uk

Christophe Chassagnole[†]
INSERM EMI 9929
Université Victor Segalen
Bordeaux 2
146 rue Léo Saignat
33076 Bordeaux, France
chassagn@insatlse.insa-
tlse.fr

Jean-Pierre Mazat
INSERM EMI 9929
Université Victor Segalen
Bordeaux 2
146 rue Léo Saignat
33076 Bordeaux, France
Jean-Pierre.Mazat@u-
bordeaux2.fr

ABSTRACT

We have developed a computer simulation of the threonine synthesis pathway in *E. coli tir8* based on kinetic functions developed from measurements on the pathway enzymes under near-physiological conditions. An important lesson learnt, relevant to plans to build *in silico* models of bacterial metabolism, is that existing literature data may contain some relevant kinetic constants, but it generally lacks usable kinetic functions for this purpose. The model successfully simulates the main features of the time courses of threonine synthesis we observed in a cell-free extract, without alteration of the experimentally determined parameters. It was then used to predict the steady-state of the pathway under intracellular conditions. Flux control coefficients were calculated and show that the control of flux is shared between the first three enzymes: aspartate kinase, aspartate semialdehyde dehydrogenase and homoserine dehydrogenase, with no single activity dominating the control. When the model pathway was embedded in a larger model that simulated the variable demands for threonine at different growth rates, it reproduced accumulation of free threonine at low growth rates, as observed in this strain, and can deliver the threonine requirements required for high growth rates. We conclude that the *in vitro* kinetics appear compatible with the *in vivo* metabolism. At low growth rates, the control of threonine flux remains largely in the pathway enzymes, but switches to the demand for threonine at high growth rates.

^{*}Presenting author.

[†]Present address: INSA - dGBA Laboratoire de Biotechnologie-Bioprocédés 135 Av. de Ranguieu F-31077 Toulouse Cedex, France.