P27 *Selection Of Thermodynamically Feasible And Active Pathways*

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Although the network of metabolic reactions, together with constraints of (ir)reversibility of enzymes, determines the space of all potentially possible phenotypes, in actuality the cell does not invoke the large majority of those in given conditions. We propose two methods to restrict the space of potential phenotypes to obtain a more accurate description of cellular phenotypes through pathway analysis. The case study considers the central carbon metabolism of Escherichia coli. First, we applied thermodynamics analysis to check for thermodynamic inconsistencies in the dataset or model and we assigned reaction directionalities based on thermodynamic feasibilities in given environmental conditions. With this approach we eliminated up to 90% of the computed pathways. Second, we used a controlled random search algorithm to select an active subset of feasible pathways that describes a particular phenotype based on exchange rates. The algorithm is based on an iterative search procedure and was run several times to find the active pathways. In addition, we compared two methods of pathway analysis (elementary modes and generating vectors) with this perspective. Although several approaches, like elementary modes, extreme pathways, and generating vectors, have been successful, several authors concluded that elementary modes analysis is the preferred choice for finding possibly important routes Figure 1 shows that simulation of the reduced models using only 2 pathways (out of originally 6672 elementary modes or 295 generating vectors) gives an appropriate match with data from literature. We concluded that, in terms of modelling accuracy and computational intensity, generating vectors, the smallest subset of pathways, have preference over elementary modes, the largest set, to describe a particular phenotype. This work can be seen as a first step towards the use of metabolic models in real-time by presenting a two-step methodology to capture a large metabolic network by only a small number of pathways that are active and thermodynamically feasible under defined process conditions.
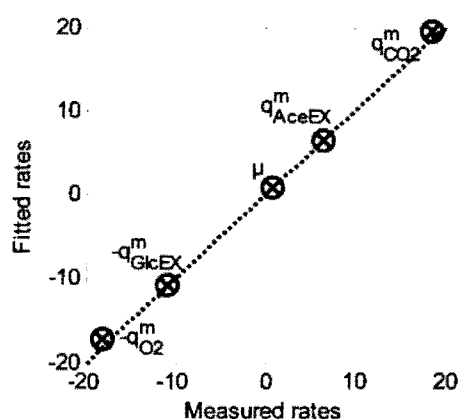

Figure 1. Measured versus fitted rates for the reduced models based on elementary modes (x) and based on generating vectors (O).