Metabolic Flux Analysis for Engineers

by

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Abstract

The first step in a technical evaluation of a bio-reaction process using living cells is invariably concerned with the stoichiometry of the reaction. Cell reactions rarely have the same stoichiometry at all environmental conditions, and the “decoding” of an experimentally obtained black-box model into several key reactions will give valuable information for a reconstruction of the producing organism with the aim of obtaining a higher yield of the desired product.

A next step is to interpret a given metabolic network in terms of a set of independent pathways from substrate to so called key-products based on which the rate of production of all the metabolites from the network can be calculated. This analysis of the network by Substrate-to-Product net pathways will be shown to be an easy to learn, and easy to understand exercise that can later be expanded into a full Metabolic Flux Analysis up the scale of the full genome of the organism.

The lecture will define and exemplify the Substrate-to-Product (SP) network analysis method. It will be shown that the results obtained are exactly the same as will be obtained by the conventional internal-flux (IF) based MFA method which is currently used in textbooks on Metabolic Engineering. It is claimed that the SP method is much easier to implement than the IF method, and that fundamental insight into the working of the metabolic network is obtained with very little numerical work. Also, in cases where the experimental rates are corrupted by experimental errors, the calculated rates may have much smaller errors than when obtained by the IF method.

Several examples will be given to show how the SP-method for MFA can be applied on industrially relevant cultivations, e.g. in solvents production by Clostridium sp. and in the production of TCA-cycle metabolites by yeast.

Short Biosketch

Research and education career for Professor John Villadsen commenced from his MSc, PhD, postdoctoral, and D. Techn. studies at Danish Technical University (DTU) from 1959. He then took progressive positions at DTU Chemical and Biochemical Engineering Department until full professorship. John was also appointed as a professor at Chemical Engineering at University of Houston for 7 years, was elected as a “Super-Professor” by Danish Ministry of Education, the founding director of Centre for Process Biotechnology (CPB) at DTU, and the Novo-Nordisk Chair at DTU. John has worked with numerous international companies, notably DuPont (USA), Novo-Nordisk (Denmark), Dansk Bioprotein (Denmark), and Enviro-Chem (USA). Among many internationally renowned scientific papers and books, John has been a main author of the following book (for 1st, 2nd and 3rd editions): “Bioreaction Engineering Principles (3rd Edition), by J. Villadsen, J. Nielsen, G. Liden, Springer, 2011”. John has also been a chief editor for several main stream scientific journals in chemical engineering and biotechnology at large.

Date : 27 March 2015 (Friday)
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