55. How system biology can improve the production of L-carnitine using Escherichia coli?

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The aim of this work is the rational design of microbial biocatalysts using Systems Biology techniques. A stoichiometric model of the trimethylammonium compunds biotransformation into L-carnitine by the E. coli metabolism, including L-carnitine pathways, as well as dynamic version were developed. The limiting control-points of this process and a possible futile cycle were found.

System biology allows cellular complexity analysis and the optimization of cell metabolic pathways by using cell component enumeration, structured relationship between them, mathematical representation of the metabolic networks, knowledge of the metabolic properties and comparison with experimental outputs of the cell processes involved. Several clinical applications for L-carnitine have been identified and consequently the demand for L-carnitine has increased, with a corresponding increase in studies into chemical and biological processes to produce it. These systems, which are based on the resolution of racemic carnitine, produce D-carnitine as a waste product, which can be converted into L-carnitine by Escherichia coli. The principal aim of this work is the application of metabolic engineering principles to the rational design of microbial production processes like the production of L-carnitine. In this way two different strategies were applied. In the first one a stoichiometric model of the whole E. coli metabolism was developed and a MFA strategy was also applied. There was found a possible futile cycle in the transport of L-carnitine biotransformation. After that, a dynamic model of L-carnitine metabolism was developed to find the limiting points of this process. The results confirmed the previous ones: the transport system was a critical point. These findings show the importance of the analysis of metabolic networks in the understanding and improvement of bioprocess.