

Metabolic Flux analysis for optimizing cell growth and recombinant protein production

A detailed metabolic network including carbohydrate and amino acid metabolism in both anabolic and catabolic reactions was developed for *Aspergillus niger*. The experimental observations suggested that the time course of fermentation could be divided into five phases each with unique physiological properties. Linear programming was used for the optimization of the specific growth rates in combination with the measured input and output fluxes of the key metabolites to evaluate corresponding intracellular flux distributions throughout the batch fermentations. Among the amino acids, proline and tyrosine had the highest logarithmic sensitivity. The solution of the flux network was very sensitive to sulphate and to a lesser degree to ammonia, proline, and ammonia uptake rates during the early stages of exponential phase when glucose was the primary carbon source. The proposed model is able to predict correctly the specific growth rate and oxygen uptake rate with good precision.