Model-based Strategies for Improving Bioprocess Yield, Productivity and Robustness

Bioprocess development for biofuels and biochemicals typically requires several rounds of metabolic engineering to meet process targets including product yield, titer and productivity, all of which impact the process economics. Similar advances in computational modeling techniques have allowed the development of genome-scale models of metabolism in several organisms. In this talk, the use of such models for metabolic engineering will be presented. In the first part, a rational approach based on bi-level optimization to enhance bioprocess productivity by forcing co-utilization of substrates will be shown. Experimental results from the application of this approach to enforce substrate co-utilization in Escherichia coli will be discussed. In addition, we will present a synthetic biology approach for dynamic control of metabolism to improve productivity. In the next part of the talk, a novel nested nonlinear optimization method for metabolic engineering resulting in hundreds of different strain design strategies for biochemicals production will be presented. We will also examine the role of redundant production pathways from a design perspective and present computational results on how these pathways are valuable for robust design.