

“STRATIS V. SOTIRCHOS” 2007 Memorial Lectureship

Systems Engineering Challenges and Opportunities in Biological Networks

by

Professor Costas D. Maranas

Donald B. Broughton Professor of Chemical Engineering
The Pennsylvania State University, USA

Abstract

In this talk we will discuss how systems engineering and in particular optimization concepts can be used to elucidate, analyze and redesign metabolic pathways leading to targeted overproductions of desired chemical products. Using as a starting point stoichiometric models of metabolism, we will first explore how optimization can be used to pinpoint which new functionalities to add into a microbial production host to endow it with new capabilities extracted from a curated database of thousands of reactions. Conversely, we will describe how to identify minimal reactions sets that can still support growth with implications to the design of organisms with minimal genomes. We will next briefly highlight a bilevel optimization based tool (i.e., OptKnock) for identifying gene knock-outs in a microbial production host leading to coupling of growth with the production of the desired chemical product. Finally we will explore how optimization can be used to analyze the topological properties of metabolic networks, identify possible gaps and suggest ways of filling them. Moving beyond metabolic networks, a similar mathematical framework will also be described for elucidating the input-output structure of signaling networks and for pinpointing targeted disruptions leading to the silencing of undesirable outputs in therapeutic interventions. The developed computational tools will be highlighted using a number of case-studies and some of the predictions will be contrasted with experimental results.