Michigan State University
Science at the Edge
Engineering Seminar

September 21, 2018
11:30 a.m., Room 1400 Biomedical and Physical Sciences Building
Refreshments served at 11:15 a.m.

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Using Subcellular Engineering and Optogenetics to Achieve Spatial and Dynamic Control of Engineered Metabolic Pathways for Isobutanol Production

Abstract

Subcellular localization and dynamic control of metabolic pathways have received much attention in metabolic engineering in recent years. Each subcellular compartment in yeast offers a unique physicochemical environment as well as distinct metabolite, enzyme, and cofactor compositions, which may benefit the activity of metabolic pathways. Furthermore, the spatial separation of organelles from cytosol offers unique opportunities to reduce the toxicity of intermediates, eliminate metabolic crosstalk, and enhance the efficiency of compartmentalized pathways. In the first part of my talk I will show how interesting and unexpected behaviors arise when organelles are involved in metabolic pathways, and present new data on how compartmentalizing the Ehrlich pathway in yeast mitochondria boosts isobutanol production.

In the second part of my talk I will show how optogenetics can be applied to metabolic engineering. Metabolic pathway optimization requires fine-tuning the timing and levels of expression of metabolic enzymes. Optogenetic controls are ideal for this, as light can be applied and removed instantly without complex media changes. I will present a new technological platform that utilizes a light-sensitive transcription factor to achieve unprecedented control over engineered metabolic pathways in yeast. Using this technology, we achieve robust and homogeneous transcriptional control at cell densities as high as 50 OD600 in 5L bioreactors. I will show how optogenetics enables a new mode of bioreactor operation, in which periodic light pulses are used to tune the levels and timing of enzyme expression during the fermentation to boost yields.

Combining mitochondrial engineering with dynamic regulation of metabolic pathways allows us to produce up to 8.49 ± 0.31 g/L of isobutanol and 2.38 ± 0.06 g/L of 2-methyl-1-butanol micro-aerobically from glucose in lab-scale bioreactors, which is more than a 10-fold improvement over strains lacking optogenetic controls. These results make a compelling case for the application of subcellular engineering and optogenetics to metabolic engineering to develop not only new strategies for metabolic pathway optimization, but also new capabilities for operating, optimizing, and automating bioreactors.

Bio

José Avalos is an Assistant Professor in the Department of Chemical and Biological Engineering, and the Andlinger Center for Energy and the Environment at Princeton University. He is also an associated faculty member in the Department of Molecular Biology. He received his PhD from Johns Hopkins University in Biochemistry and Biophysics, and completed postdoctoral research in the Department of Chemical Engineering at MIT, The Whitehead Institute, and The Rockefeller University. His fields of research include synthetic biology, metabolic engineering, protein engineering, systems biology and structural biology. He has been honored with the NSF CAREER award, The Alfred P. Sloan Foundation Fellowship Award, and The Pew Scholarship, among other awards.

For further information, please contact Prof. Alexandra Zevalkink, Department of Chemical Engineering and Materials Science at alexzev@egr.msu.edu.

Persons with disabilities have the right to request and receive reasonable accommodation. Please call the Department of Chemical Engineering and Materials Science at 355-5135 at least one day prior to the seminar; requests received after this date will be met when possible.