“Spatial and Dynamical Control in Metabolic Engineering Using Organelle Engineering and Optogenetics”

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Wu and Chen Auditorium
Levine Hall

José L. Avalos
Assistant Professor
Chemical and Biological Engineering
Princeton University

Abstract

Metabolic engineering aims to rewire cellular metabolism, typically of microorganisms, to produce fuels, chemicals, pharmaceuticals, and other valuable products from renewable resources. However, it is often challenging to achieve the titers, yields, and productivities required for commercial viability. Spatial and dynamical control of engineered metabolic pathways can greatly improve their efficiency to address this obstacle. We have developed strategies to enhance the flux and specificity of metabolic pathways by spatially compartmentalizing them in yeast mitochondria and synthetic organelles. This helps increase the local concentrations of enzymes and intermediate metabolites, prevent metabolic bottlenecks, and reduce metabolite loss to competing pathways. In addition, I will present a new strategy to dynamically control metabolic pathways using optogenetics. There are many advantages of using light to control metabolic pathways, including its orthogonality, tunability, and the ease with which it can be applied or removed instantly in any schedule to continuously manipulate metabolism throughout fermentations. I will present several optogenetic circuits we have built to control microbial growth and production with light, the impact they have on chemical production, and the strategies we have developed to overcome the limited light penetration of fermentations operating at high cell density in lab scale bioreactors. Finally, I will provide a perspective on how these technologies may come together to prescribe a new paradigm for spatial and dynamical control in metabolic engineering to improve microbial chemical production.

Bio

José L. Avalos earned a B.E. in Chemical Engineering from Universidad Iberoamericana in Mexico City and an MSc in Biochemical Research from Imperial College in London. He then received a Ph.D. in Biochemistry and Biophysics from Johns Hopkins University. He conducted postdoctoral research at The Rockefeller University on ion channels and membrane biophysics, and then at MIT, in the Department of Chemical Engineering, and the Whitehead Institute for Biomedical Research in metabolic engineering and synthetic biology. He has been a faculty member at Princeton University since 2015, where he leads a research group focused on the use of biotechnology to address challenges in renewable energy, sustainable manufacturing, the environment, and human health. He has received several awards, including the Damon Runyon Cancer Research Fellowship, the Ruth L. Kirschstein National Research Service Award, the Alfred P. Sloan Foundation Research Fellowship Award, the Pew scholarship, the NSF CAREER Award, the Camille Dreyfus Teacher-Scholar Award, and the HHMI Gilliam Award.