Understanding and Engineering Metabolic Heterogeneity for Enhanced Bioproduction

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Abstract

Biomanufacturing using engineered microbes offers the opportunity to produce renewable fuels, chemicals and materials. For this technology to be economically viable, engineered microbes must produce target compounds in high titers, yields, productivities, and robustness at large scales. Cell-to-cell variation in metabolic activity among isogenetic cell populations is ubiquitous and can substantially affect bioproduction of cell cultures. Although heterogeneity in gene expression has been well studied, little was known on metabolic heterogeneity. Using engineered metabolic pathways, we have quantified the size, fluctuation, and frequency of metabolic variation. I will discuss how metabolic heterogeneity affects bioproduction. Furthermore, we have developed synthetic biology tools that allowed us to continuously enrich non-genetic, high-producing variants within iso-genetic populations. Using these tools, we demonstrated significantly improved product titers, yields, productivities and genetic stability on multiple biosynthetic pathways. Design principles of these synthetic control tools are useful in other areas of biotechnology, enabling new avenues of research and applications.

Bio Sketch

Fuzhong Zhang is the Francis Ahmann Professor in the Department of Energy, Environmental & Chemical Engineering, Washington University in St. Louis. He received his bachelor degree at Peking University, master at McMaster University, Ph.D at University of Toronto, and postdoctoral training at UC Berkeley/Joint BioEnergy Institute. His research focuses on developing synthetic biology tools and systems for the sustainable production of structurally-defined chemicals and high-performance materials. Since he joined Washington University in 2012, he has received numerous awards, including DARPA Young Faculty Award (2013), ORAU Junior Faculty Enhancement Award (2013), NSF CAREER Award (2014), Young Investigator Program from AFOSR, ONR, and HFSP (2015), NASA Early Career Faculty Award (2015), Biotech & Bioeng Daniel Wang Award (2016), Dean’s Faculty Award for Innovation in Research (2016), the SIMB Young Investigator Award (2017), and NIH Maximizing Investigators' Research Award (2019).