The Summer Undergraduate Research Fellowship (SURF) Symposium
23 June 2017
Purdue University, West Lafayette, Indiana, USA

Improving Biomanufacturing Production with Tunable Transcriptional Regulation via Elastin-like Polypeptides

Rohit Chatterjee, Logan R. Readnour, and Kok Zhi Lee
Department of Agricultural & Biological Engineering, Purdue University
Kevin V. Solomon
Department of Agricultural & Biological Engineering, Purdue University

ABSTRACT

The metabolism of *E. coli* and other microbes can be engineered to create valuable chemicals such as biofuels, medicines, etc. However, process efficiency is limited by the toxicity of intermediates in the production pathway, which induces cellular stress and killing the production in cells. By fusing elastin-like polypeptides (ELPs) with sigma factors (SF), we propose a stress feedback system can be created to recognize cues of cellular health and autoregulate expression of bioproduction pathways for improved health and production. ELPs undergo a sharp, reversible, phase transition causing an aggregation above a certain temperature (Tt) based on conditions that align with intracellular health such as intracellular pH. This behavior, along with the ability to control Tt through sequence alterations, makes ELPs ideal sensors for controlling gene expression. Fused SF, which activated gene expression, are sequestered in ELP-SF aggregates above the transition temperature, reducing their free concentration. To evaluate the potential of ELP-SF to control gene expression, we expressed green fluorescent protein (GFP) from a promoter driven by the fused SF. *In vivo*, this system activated the expression of GFP at levels comparable to a SF control. However, at elevated temperatures, the system reduces gene expression by 20% relative to the control demonstrating the ability of the construct to control gene expression. The dynamic performance of the system was also modeled in MATLAB to reveal key parameters that affect system behavior. These results validate our main hypothesis and suggest a new strategy to optimize the sustainable production of valuable chemicals from microbes.

KEYWORDS

Biofuels, gene expression, elastin-like polypeptides, sigma factor