Real-time Sensing and Adaptive Computing to Elucidate Microenvironment-Induced Cell Heterogeneities and Accelerate Scalable Bioprocesses

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The biological conversion of renewable and waste sources to fuels and chemicals is an integral component of a sustainable bioeconomy. While biomanufacturing has been successfully demonstrated at the laboratory scale for a wide range of products, only a few have been successfully been produced at industrial scales This transition between laboratory- and industrial-scale cultivations represents a 'valley of death' in biological processes, where uncertainties arise regarding the lack of predictability for microbial performance across scales.

Mixing becomes one of the significant challenges encountered in large-scale bioreactors. In contrast to the well-mixed cultivations at the laboratory scale, large-scale cultivations are not uniformly mixed which results in uneven distribution of nutrients, pH, gas composition, and temperature. These heterogeneities impact microbial performance in an unpredictable manner, decreasing bioconversion efficiency and ultimately increasing manufacturing costs. Unless the capability to predict microbial performance in largescale bioreactors can be realized, many biological conversion pathways will not come to fruition in the bioeconomy.

This multidisciplinary and multi-institutional project will develop and integrate experimental and computation tools and will acquire fundamental knowledge in microbial systems to address the uncertainty gap in scaling between laboratory- and industrial-scale cultivations. The team will establish a framework to predict and address the adequacy of a microbe at the beginning of the innovation cycle to mitigate risks during the development and scale-up of new bioprocesses. To achieve these goals, researchers seek to integrate two Key Technology Areas, 'Biology' (DOE-BER) and 'Computing and Data' (DOE-ASCR) within the DOE Office of Science. This team combines the strengths of the National Renewable Energy Laboratory in metabolic engineering, fermentation science, systems biology, computation and modeling with world leading capabilities in spectrometry at a DOE-BER's user facility (Environmental Molecular Sciences Laboratory facility in Pacific Northwest National Laboratory), an emerging research institution (University of Puerto Rico), and academic partners with expertise in genome-scale modeling and automated high throughput DNA sequencing and downstream analyses (University of California, San Diego), and development of genetic tools in non-model organisms (University of California, Davis). The knowledge gained through this work will serve as a foundation to address conversion issues at the microbial level and will extend to other biological disciplines that seek predictive understanding of multi-cellular system behavior, for example at an ecosystem level, which are relevant goals to DOE-BER. Overall, by advancing scale-up science, the team aims to shorten the time and reduce the cost required for scaling new fermentation technologies, thereby accelerating innovation in the bioeconomy.