Harnessing metabolism modules to design an optimal modular chassis cell for production of diverse chemicals

U.S. DEPARTMENT OF ENERGY | Office of Science

Background

- A large underexplored space of biofuels and biochemicals can be manufactured by microbial cell factories; however, R&D costs to create them remain high due to multiple laborious design-build-test-learn (DBTL) cycles of cell engineering.
- Modular design has been successfully applied across the engineering fields to enable rapid systematic production and development of more efficient systems.

Approach

- Developed the modular cell engineering strategy to minimize DBTL cycles for rapid strain generation by designing a modular (chassis) cell that can be readily coupled with exchangeable production modules to enable production phenotypes of interest with high efficiency.
- Employed laws of conservation of mass and thermodynamics, metabolic network modeling, and optimization theory to formulate the modular cell design framework, computational algorithms and implementation

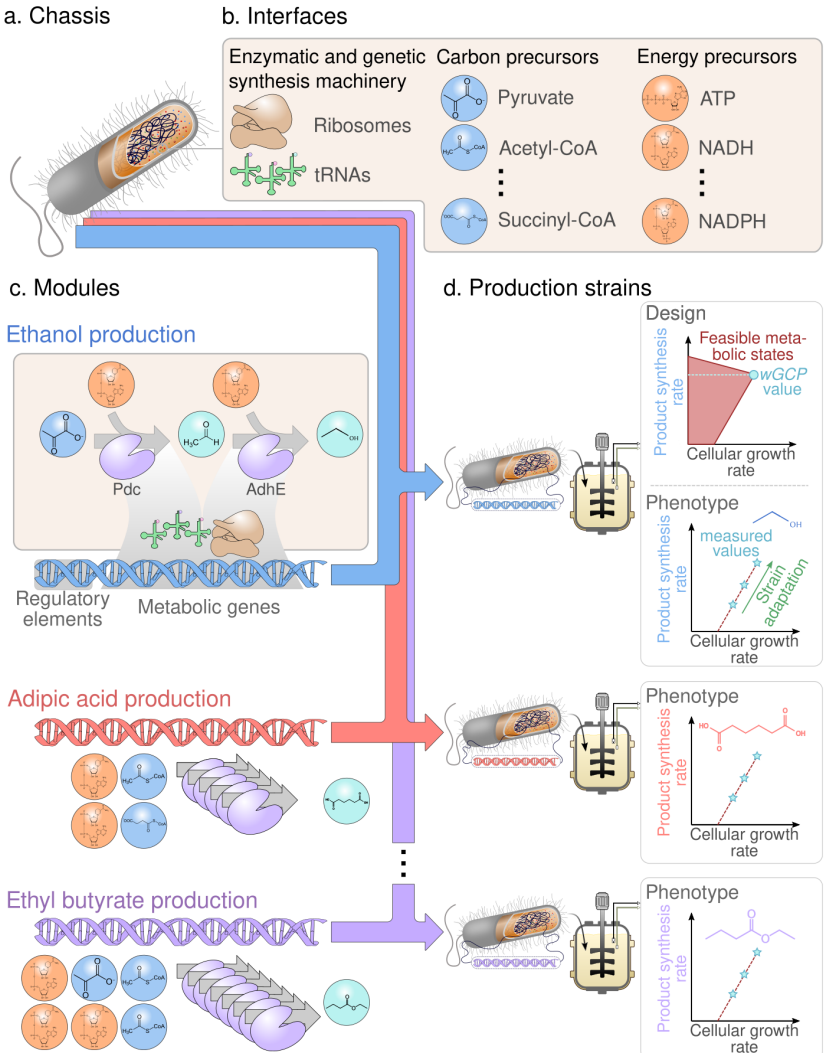
Outcomes and Impacts

- Developed a code (ModCell2-MILP) to solve the modular cell design problem by using blended and goal attainment mixed integer linear programming (MILP) formulations.
- Demonstrated a modular cell can be universally compatible with a diverse class of exchangeable production modules for efficient biosynthesis of various molecules.
- Elucidated the phenotype(s) of a universally compatible modular cell.
- Showed the feasibility of universal modular cell design by comparison of simulated and experimental fluxes.

Significance

- Develop a useful modular cell analysis tool for not only rapid strain engineering but also understanding metabolic modularity of natural biological systems.
- Application of modular design in microbial cell factories at systems level can address the current limitation of engineering cell factories.

Schematic of a thermophilic CBP microbial platform for production of esters from renewable resources.



Garcia and Trinh, "Harnessing natural modularity of metabolism with goal attainment optimization to design a modular chassis cell for production of diverse chemicals," *ACS Synth. Biol.* accepted (2020)

THE CENTER FOR BIOENERGY INNOVATION