Computational Design and Analysis of Modular Cells for Large Libraries of Exchangeable Product Synthesis Modules

U.S. DEPARTMENT OF ENERGY | Office of Science

Background

- Microbial metabolism can produce a large library of chemicals from biomass. It is laborious and expensive to create microbial biocatalysts for each new product.
- Modular cell (ModCell) design can facilitate rapid generation of production strains by assembling a modular (chassis) cell with exchangeable pathway modules. Existing ModCell design methods are limited to small libraries of products.

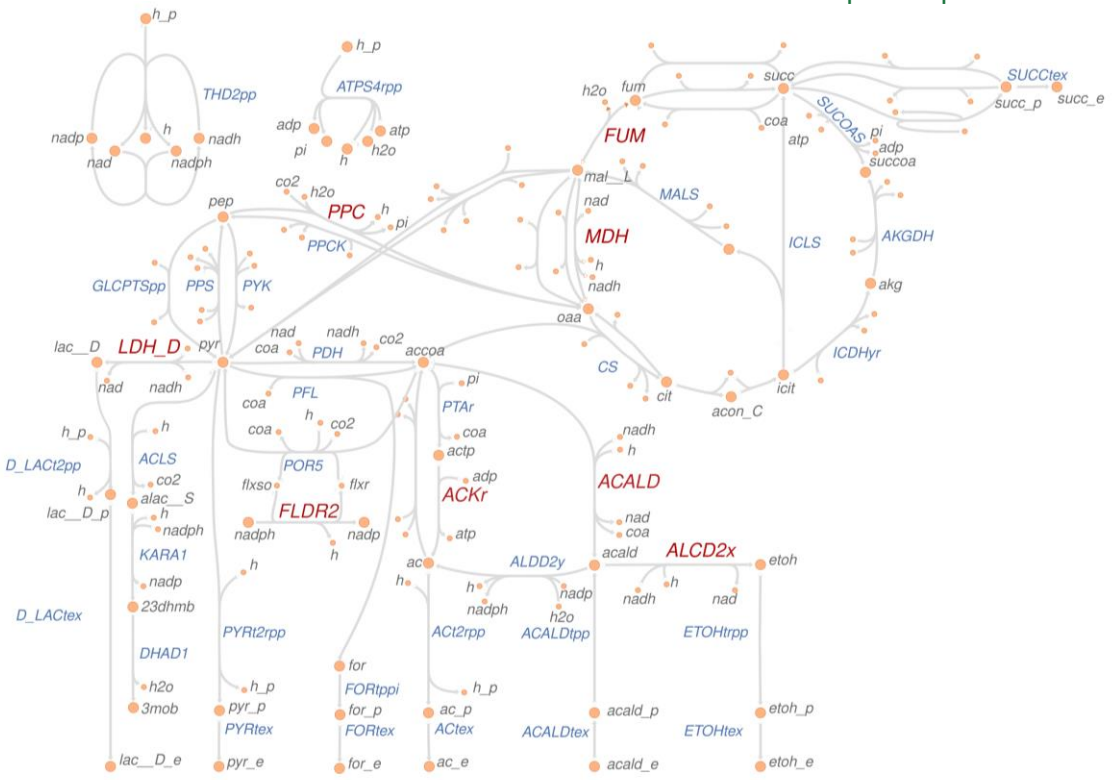
Approach

- Formulate a highly-parallel and multi-objective evolutionary algorithm, named ModCell-HPC, to enable modular cell designs for 100+ molecules and elucidate modular design properties.

Outcomes and Impacts

- Developed ModCell-HPC to design modular cells compatible with hundreds of product synthesis modules.

Three modular cells is the smallest set needed to cover all compatible products



- Designed three *E. coli* modular cells with few genetic manipulations that couple growth with product synthesis of a total of 85 molecules. (Panel B)
- Identified removal of major byproducts and modification of branch points in central metabolism as key interventions for the design of modular cells.
- Designed *E. coli* modular cells that consume various sugars for growth-coupled product synthesis.

Significance

- ModCell-HPC provides an innovative tool for understanding modularity of biological systems and guiding more efficient and generalizable design of modular cells that will help reduce research and development cost in biocatalysis.

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Garcia, S. and Trinh, C.T., *Metab Eng*, 2021 (accepted).