Non-Confidential Description - PSU No. 4315
“Method for Designing Overall Stoichiometric Conversions and Intervening Metabolic Reactions”

Field of Invention/Keywords:
Metabolic network optimization, Computational framework, de novo
pathway design, Metabolic engineering

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Background
Microbial metabolism describes the full range of enzymatic conversions of carbon substrates to cellular biomass precursors, energy equivalents and biochemical molecules. Metabolic engineering harnesses this metabolic machinery for converting feedstock substrates to a growing range of products. Existing computational procedures for the de novo pathway design rely on either optimization techniques or graph-search approaches. Generally pathways are identified that maximize products yield given a single carbon substrate without considering co-substrates, co-products, or complex overall stoichiometry. These techniques, although powerful, has a major shortcoming that they aim to trace pathways connecting a single substrate to a single product. Metabolic conversions do not generally involve linear paths from substrate to product. The overall stoichiometries can interact in complex ways with the other metabolites forming highly non-intuitive networks constrained by thermodynamics. There is a need for a procedure that can take into account all the factors acting behind the complex metabolic reactions leading to formation of products.

Invention Description
The subject invention provides a computational framework for designing optimum overall stoichiometry, and intermediate metabolic reaction steps of achieving the conversion between a source and target metabolite with alternate co-reactants/co-products. The subject invention formulates a computational procedure for designing de novo networks that match an overall stoichiometry of chemical transformation. A stoichiometry and pathway design tool that optimizes the overall stoichiometry by exploring exhaustive co-reactant/co-product combinations, this invention can identify several non-intuitive solutions for driving forward thermodynamically unfavorable conversions. Apart from identifying intervening reactions, the software also allows ranking of the various identifies designs based on factors like overall carbon/energy yield, network size and free energy of change. Additionally, the invention can include economic considerations implied by the prices or reactant and product molecules in the optimization formulation for designing the overall stoichiometry.

Status of Invention
The project was supported by grants from the Department of Energy and National Science Foundation. A provisional patent application has been filed for this invention.