OptRAM: *In-silico* Strain Design via Integrative Regulatory-Metabolic Network Modeling

Background/objective

Computational strain optimization algorithms have been increasingly valuable for the design of strains capable of producing industrially useful compounds. However, most existing algorithms rely on metabolic networks alone, fail to incorporate transcriptional regulation, and rely on pre-existing regulatory networks. Here, researchers introduce a novel strain design algorithm, OptRAM (Optimization of Regulatory And Metabolic Networks), which addresses these key challenges.

Approach

❖ OptRAM was designed from the previous IDREAM framework, functioning such that bioproduct production is balanced with cell growth.

❖ OptRAM was tested for *in silico* strain design for succinate, 2,3-butanediol, and ethanol production in yeast. Predicted strain optimization strategies were compared with experimental data from the literature and, for ethanol, experimentally validated by the authors.

Results

❖ The OptRAM computational strain development algorithm can identify manipulations of both transcription factors and metabolic genes, including overexpression, knockdown, and knockout.

❖ Literature values and experimental data validated optimized strain designs for selected bioproducts.

Significance

❖ OptRAM improves on previous computational strain development algorithms by incorporating transcriptional regulation into metabolic network modeling.

❖ OptRAM will facilitate the design of engineered yeast strains for the next generation of valuable bioproducts.
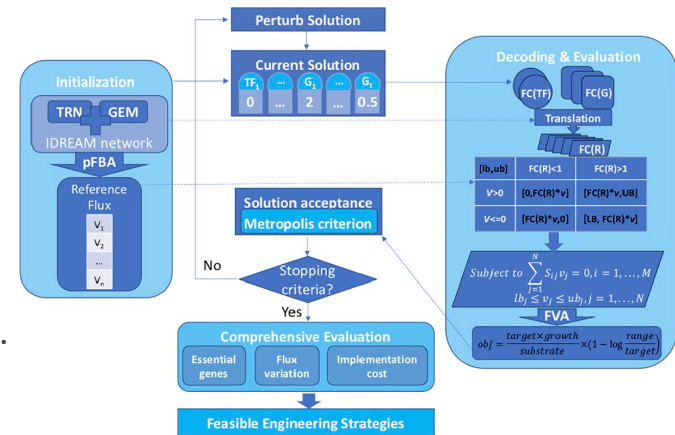
The overall framework of OptRAM: TRN = Transcriptional Regulatory Network; GEM = Genome-scale metabolic model; FC(TF), FC(G), and FC(R) = fold expression level of transcription factors, metabolic genes, and reactions, respectively, in the mutated strain vs. the wild type.

*Shen et al. 2019. "OptRAM: In-Silico Strain Design via Integrative Regulatory-Metabolic Network Modeling." **PLOS Computational Biology.** 15:e1006835. DOI:10.1371/journal.pcbi.1006835*