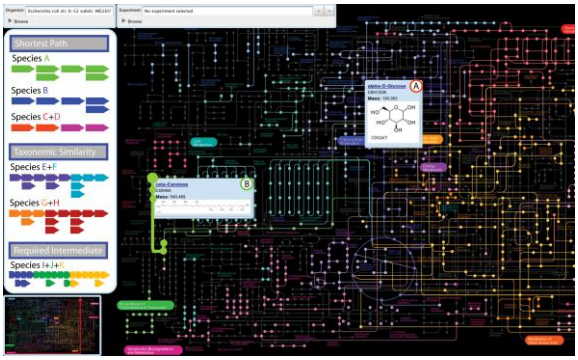
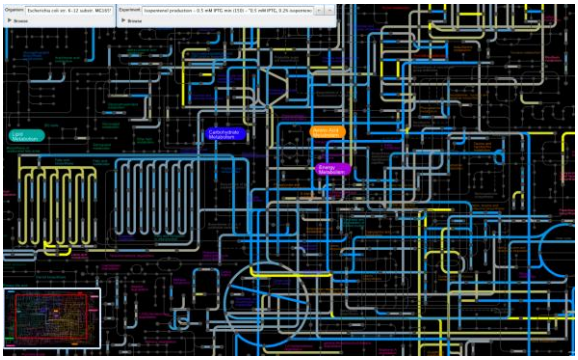
Pilot Project

Design Requirements and Prototypes of Workflows in the SBKB for Support of Engineering of Metabolic Pathways.

Dylan Chivian, John Bates, Paramvir Dehal, Marcin Joachimiak,
Morgan Price, Vinay Satish Kumar, and Adam Arkin.



GLAMM retrosynthesis interface



GLAMM functional data overlay

The use of microbial hosts for the production of chemicals has been one of the great success stories of biotechnology. We envision a key use of the systems biology knowledgebase for the engineering of new metabolic function in microbes for the production of fuels, high value chemicals, and environmental activities such as bioremediation. The fundamental workflow we envision has a user selecting a host organism based on qualities important for the industrial process envisioned or on the ability to make molecules related to those desired by the user. The user must then determine if the organism is able to utilize the feedstock molecules and transform them into internal metabolites from which production of the target chemicals becomes possible. Finally, the user needs to determine the optimal modification of the host microbe to efficiently create the target molecule without severe detriment to host health either by the unbalancing of metabolism through over-draw of essential metabolites, unbalancing of co-factors/energy molecules, or by producing intermediates toxic to the host organism.

Determining the range of chemical transformations accessible to a natural microorganism requires accurate, preferably evidence-based, assignment of function to genes for that organism. Metabolic reconstruction still suffers from a number of challenges surrounding accurate annotation of proteins. These same problems plague retrosynthesis where it is essential that the genes from diverse organisms have as accurate and specific functional assignments as possible so that the algorithms can efficiently find the needed chemistries. Lastly, we identified a need for and began addressing the development of interfaces for navigating metabolic networks and experimental functional *omics data using a “Google-Like” Application for Metabolic Maps (GLAMM).

Retrosynthesis pathways and genes will be linked back to MicrobesOnline to permit further examination with its powerful comparative systems biology tools, a prototype for the SBKB, including phylogenetic gene trees, genome context and operon predictions, functional residue alignments, protein-protein interaction data, and basic structural models to permit developing a mutually consistent set of genes for introducing the viable candidate retrosynthetic pathways into the host microorganism.