173. Mapping Inter-species Interactions and Metabolic Synergy for Next-generation Biofuel Production

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Project Goals: The goal of our research plan is to implement a high-throughput pipeline for the systematic, computationally-driven study and optimization of microbial interactions and their effect on lignocellulose degradation and biofuel production. We combine multiple approaches, including computer modeling of ecosystem-level microbial metabolism, mass spectrometry of metabolites, and experimental evolution.

The biologically mediated production of energy-dense fuels from the degradation of lignocellulosic material is a complex, multistep metabolic process. Harnessing microbial communities for biofuel production has the potential to enable efficient, robust, and adaptive approaches to consolidated bioprocessing. We are addressing this challenge through an integrated effort to engineer a consortium for biofuel production. In our strategy, we seek to take into account (i) the specific complex nature of the molecular substrates and intermediates consumed and produced by different organisms alone or in combinations; (ii) the natural tendency of microbes to operate at metabolic regimes that reflect their own evolutionary history and individual benefit rather than the laboratory environment and objectives, and finally, (iii) the great opportunity offered by recent developments in systems biology, in particular through predictive genome-scale models of metabolism. The set of organisms we have chosen for this project is driven by the criteria of immediate feasibility, as well as by the desire to develop a community that could serve as a prototype for follow-up practical developments. In particular, our approach is to use four different functional groups of microbes; a lignin degrader, a (hemi)cellulose degrader, a strain to remove and detoxify methoxy groups on lignin, and a biofuel producing yeast. Rather than the specific optimization of selected strains, our primary goal is a flexible, predictive strategy to maximize community output given the members present.

Towards the development of a prototype community, we have started characterizing in detail the metabolic inputs and outputs of the different members of our synthetic consortium using mass spectrometry (MS) to measure the use and production of plant hydrolysate and the microbial uptake and release of metabolites. These data will be used to test and improve genome scale metabolic network models of individual species. By extending these analyses to all pairs of organisms, we will comprehensively detect possible synergies and partner-induced changes in uptake/excretion. In parallel to these experimentally driven efforts, we are testing and refining stoichiometric models for the relevant organisms, starting from published reconstructions, and from gap-filled draft models obtained through the KBase pipeline. Simulations of the metabolic activities of these organisms can be performed through COMETS (Computation Of Microbial Ecosystems in Time and Space), our platform for dynamic flux balance modeling. Several ongoing COMETS improvements will help perform more accurate and comprehensive simulations, including a 3D convection-diffusion implementation of the growth process, and a streamlined pipeline for visualizing COMETS results through detailed multilayer networks that can highlight metabolic competition and cross-feeding interactions.

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