Modeling Approaches for Understanding Metabolic Coupling in Microbial Communities

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Project Goals: The goal of the Metabolic and Spatial Interactions in Communities (MOSAIC) Foundational Scientific Focus Area is to understand the fundamental mechanisms by which microbial metabolic interactions and spatial organization impact carbon, nitrogen, and energy dynamics in microbial communities. Our studies focus on the coupling of carbon and nitrogen cycles in microbial communities, the role of environmental variables in governing the rates of these cycles, and the impact of environmental perturbations on microbial community dynamics. We employ tractable model consortia whose member genome sequences have been defined, advanced omics measurements, functional imaging, taxonomic profiling, and modeling to elucidate interaction mechanisms within complex microbial communities. Our research supports the DOE goals to achieve a predictive understanding of Earth's integrated biogeochemical processes.

Metabolic interactions within microbial communities exert a strong impact on nutrient cycling in the environment. Metabolic network models of microbial communities can be used to deepen our understanding of the drivers controlling interspecies metabolic coupling and how these interactions create emergent properties such as resilience and resistance, and to predict the interplay between microbial communities and their environment. In general, genome-scale metabolic network reconstruction is an iterative process in which community-level reconstructions are significantly more complex than single organism models, due to the need to account for interspecies interactions. Current modeling approaches focus on the reconstruction of high-quality individual networks followed by combining these individual networks to facilitate prediction of interspecies interactions and community behavior. However, this approach is challenging when exploring complex environmental communities containing members not characterized in isolation. To address this limitation, we tested a novel approach that leverages community (i.e., mixed culture) data as a critical input for network reconstruction. The community data includes phenotypic growth observations and multi-omics profiles, which provide key information on microbial interactions that are not necessarily obtainable from axenic cultures.

As a case study used to evaluate our method, we considered a photoautotroph-heterotroph binary consortium and reconstructed community metabolic networks based on alternative strategies of gapfilling: individual gapfilling (or pre-gapfilling) vs. community-level gapfilling (or post-gapfilling). We implemented all pipeline steps of network reconstruction and refinement using the DOE Systems Biology Knowledgebase (KBase) platform (www.kbase.us). Post-gapfilled metabolic networks provided predictions of organic carbon and nitrogen exchange that supported the growth of an obligate heterotrophic species, with these predictions being supported by transcriptomic data. The community network model provides a platform to perform flux

coupling analysis, identify metabolically coupled reactions across species, and evaluate associated metabolic costs (e.g., in terms of ATP consumption). Reproducible narratives of model building for both single species and community networks are publicly available in KBase (https://narrative.kbase.us/narrative/ws.13807.obj.1).

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