System-level analysis of metabolism of *Kordia algicida* and its interaction with *Phaeodactylum tricornutum*

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Project Goals: The LLNL Bioenergy SFA seeks to support sustainable and predictable bioenergy crop production through a community systems biology understanding of microbial consortia that are closely associated with bioenergy-relevant crops. We focus on host-microbial interactions in algal ponds and perennial grasses, with the goal of understanding and predicting the system-scale consequences of these interactions for biomass productivity and robustness, the balance of resources, and the functionality of surrounding microbial communities. Our approach integrates 'omics measurements with quantitative isotope tracing, characterization of metabolites and biophysical factors, genome-enabled metabolic modeling, and trait-based representations of complex multi-trophic biological communities, to characterize the microscale impacts of single cells on system scale processes.

Planktonic microalgae play an outsized role in regulating the dynamics of earth's ecosystem. Their activity affects the global oxygen supply, the food chain, global biogeochemical cycling, and climate. Due to their ecological importance, as well as the industrial interest in using algae for production of renewable biofuels, understanding the factors that control algal productivity are crucial for devising strategies for mitigating damaging effects of climate change. Interactions between algae and bacteria are a major factor in the fate of algal populations. This includes parasitic interactions, wherein "algicidal" bacteria can lyse algal cells in order to acquire nutrients. The controls on algicidal bacteria are not well defined, so while they are sometimes detectable at low levels in algal microbiomes, we currently cannot predict what conditions will lead to an algicidal-induced algal population crash. In order to gain a system-level understanding we conducted a number of computational analyses of an algicidal bacterium's interaction with a model algae.

Kordia algicida is a marine bacterium that has exhibited algicidal behavior when co-cultured with a variety of algae[1], including *Phaeodactylum tricornutum*, a long-studied model organism for analysis of phytoplankton ecology and physiology. *P. tricornutum* is also recognized for its potential for biofuel production[2]. In order to gain a better understanding of the predatory algal-bacterial interactions we have examined the metabolism of *K. algicida* and its interaction with *P. tricornutum in silico*.

We studied the metabolic needs of *K. algicida* by developing a human curated genome-scale model of *K. algicida* strain OT-1. We previously showed that combining annotations from multiple sources will provide us with a more complete annotation and subsequently metabolic network reconstruction[3]. We initiated the model development process by using a new app developed by members of our team for the DOE KBase platform that combines annotations of *K. algicida* OT-1 genome from a number of sources. We then used the KBase's "Build Metabolic Model" app to generate a draft genome-scale model. The model was then curated using data from the literature as well as new bioinformatic analyses. The curated model was used to examine the metabolic capabilities and needs of *K. algicida* for a variety of different conditions. The results point to a metabolism adapted to consuming microbial biomass components such as amino acids and nucleotides as well as a variety of sugars and small organic acids. The analyses also showed that *K. algicida* is auxotrophic for a number of amino acids.

Using the results from the system-level analyses of *K. algicida* and published experimental measurements[1,4], we developed a computational model of the dynamics of interaction between *K. algicida* and *P. tricornutum*. It has been shown that the *K. algicida* uses a regulated protease excretion mechanism for algal lysis[1]. The model is composed of a series of coupled ordinary differential equations that solve for the transient changes in concentration of microbes, critical metabolites, and the protease. We used the model to examine various interaction scenarios and discovered that because of *K. algicida*'s dependence on *P. tricornutum* as its primary source of some amino acids, unregulated lysis of the algae will eventually result in cessation of growth by the bacterium. Additionally, significant accumulation of the protease in the co-culture media will result in decreased growth for *K. algicida* and elimination of *P. tricornutum*. These findings have provided novel avenues of research to experimentally test with *in vitro* cultures and with increasing community complexity.

References

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