PUBLIC ORAL EXAMINATION FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

PROGRAMMING SYNTHETIC MICROBIAL COMMUNITIES FOR COEXISTENCE, COORDINATION, AND INFORMATION PROCESSING

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- **Professor Xiaoxia Nina Lin, Chair**
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ABSTRACT

Synthetic microbial communities offer a variety of potential advantages over single-species approaches for many medical, industrial, and environmental applications. At the cellular level, metabolic pathways can be distributed amongst several community residents to lower the metabolic burden on individual cells and to enable optimization of reaction conditions for different parts of metabolic pathways. At the population level, diverse microbial communities in different natural contexts have been shown to be more productive, efficient, stable, and resistant to invasion by foreign agents. Along with these potential advantages, however, come a variety of new challenges as well. First, different species or cell types of interest must be able to coexist. Additionally, in many scenarios the relative abundance of each resident can impact the overall property of the community. Beyond coexistence and community composition, information processing and sharing is often essential to the types of complex, coordinated behavior that is required for many desired medical, industrial, and environmental applications.

My dissertation has centered around the design and implementation of two novel systems which address some of the challenges discussed above that must be overcome to realize the potential of synthetic microbial communities for use in technological applications. In the first system, I use temperature as a modality to enable coexistence of two microorganisms with different thermal niches and to further program the composition of this model synthetic bi-culture. Specifically, I developed two different approaches, referred to as a constant temperature regime and a cycling temperature regime. Employing a combination of wet-lab experiments and mathematical modeling, I showed that a variety of parameters such as temperature, cycle duration, etc. can be manipulated to achieve desired community compositions. Building on this work, I then used a mathematical framework developed by ecologists to explore design principles and specific mechanisms underlying the observed relationship between culture temperature and coexistence.

In the second system, I designed a novel synthetic microbial community with a distributed sensing and centralized reporting architecture that is enabled by what we have termed bacteriophage mediated information transfer. A modular genetic circuit was developed that connects the input of an environmental signal of interest to activation of a lysogenic lambda bacteriophage which is used to transfer information about the sensing event from the sensor cell population to a reporter cell population. A variety of different ways to encode and store information were explored.

While seemingly different, the lines of work described above are connected by a common thread of developing generalizable and modular approaches for engineering synthetic microbial communities to deliver the potential advantages they offer in a variety of medical, industrial, and environmental applications. Synthetic microbial communities are capable of performing complex and varied functions within these contexts and this dissertation is contributing to the rapidly growing body of research work for addressing the challenges that must be overcome to realize that potential.

PUBLICATIONS RELATED TO THESIS WORK

Krieger, A.G., Zhang, J., Lin, X.N. (2020) Temperature regulation as a tool to program synthetic microbial community composition. *Manuscript under revision at Biotechnology and Bioengineering. Available on Biorxiv*.

Krieger A.G., Hou, Z,. Zhang, Y,. Lin, X.N. (2020) Distributed sensing with centralized memory utilizing bacteriophage mediated information transfer in synthetic microbial communities. *Manuscript in preparation.*

Krieger, A.G., Lapp, Z,. Lin, X.N. (2020) The effect of temperature changes on Lotka-Volterra derived interspecies competition coefficients and coexistence in a synthetic microbial community. *Manuscript in preparation.*

ADDITIONAL PUBLICATIONS

Gray, M.J., Wholey, W.Y., Wagner, N.O., Cremers, C.M., Mueller-Schickert, A., Hock, N.T., **Krieger, A.G.**, Smith, E.M., Bender, R.A., Bardwell, J.C.A., and Jakob, U. (2014) Polyphosphate is a primordial chaperone. *Mol. Cell. 53*, start 689.

FUTURE PLANS

Adam will continue to work in the Lin lab while pursuing post-doctoral opportunities.