EDITORIAL

Design Principles of Microbial Communities: From Understanding to Engineering

Microorganisms in natural environments self-organize into communities through trophic interactions and/or signaling communication [1]. Microbes that evolve together over a period of time can even develop genetic dependencies through adaptive gene loss [2]. Complex, nonlinear microbial interactions lead the community to exhibit intriguing dynamics and behaviors as a whole, which cannot be observed from the analysis of single organisms alone. For the same reason, optimal growth conditions for the community can be very different when compared to those for individual species.

Engineering microbial communities for biotechnology and biomedical science is of keen interest to researchers and scientists. In contrast with isolated monoculture modification, the key to engineering multi-species systems lies in the design of their social behaviors (*i.e.*, interactions) [3]. The design of interactions is a new engineering paradigm that requires a mechanistic understanding of how microbes form species and gene interaction networks as a community and how these networks are reorganized in response to environmental variations and membership changes.

Interspecies interaction provides an organism with a means to survive nutrient-deficit environments that cannot fully support individual growth. Microbial economies in resource trade would be an important consideration in this regard [4]. Rational engineering strategies could be established based on such understanding. Simple intuition-based manipulation toward facilitated metabolic exchanges may not result in desired outputs unless the impact on the community-level behavior is appropriately evaluated or predicted. This challenge necessitates a systems-level approach that integrates advanced computational/modeling methods with unbiased multi-omics analyses [5, 6].

The goal of this thematic issue is to provide an overview of advances in fundamental and applied research on microbial communities - advances that promote our understanding of the design principles of microbial interactions. The three papers in this issue address this goal by providing focused reviews on the following key science topics: 1) the resistome, which is the collection of all genes and their precursors involved in antibiotic resistance; 2) community metabolic network modeling; and 3) synthesis of model consortia.

More detail on each science topic could be expressed this way:

- Antibiotic resistance genes are often found in human pathogens as the result of the therapeutic overuse of antibiotics for treating infections. Such genes are also found in nonclinical settings, *i.e.*, microorganisms growing in natural environments, because microbial secretion of antibiotics is a key survival strategy against competitors. Lim *et al.* provide a comprehensive discussion on the relationships among antibiotics, resistomes, and related bacterial species. They also outline advances in bioinformatics methods as essential tools [7]. This knowledge can be useful for understanding and predicting how antimicrobials could shape microbial community interaction networks and what their ultimate consequences could be in human health.
- Metabolic network modeling is an advanced simulation tool that could provide deep insights and mechanistic understanding of metabolic interactions among member species beyond gene-level interactions. The article by Ang *et al.* not only provides mathematical background on community metabolic network modeling, ranging from steady-state analyses to dynamic modeling approaches, but it also discusses practical applications and examples in various areas, including human microbiota, biogeochemical and bioremediation systems, wastewater treatment, and more [8]. This bottom-up modeling approach offers a molecular-level understanding of interactions, which could be synergistically combined with top-down network inference methods for improved predictions [5].
- Extending detailed analyses of microbial interactions to natural ecosystems is often challenging because of the overwhelming compositional/functional complexities. Model consortia synthesized to include only major players offer ideal settings for understanding microbial interactions since despite their reduced complexity, they still represent the key functionalities of original ecosystems [9]. In addition, model consortia are also often useful for producing industrially and medically valuable chemicals and molecules [8]. Haruta and Yamamoto discuss various utilities of model consortia. Their focus is on a mechanistic understanding of the interaction principles and emergent properties of microbial communities [10].

Altogether, the papers in this thematic issue provide complementary perspectives and knowledge regarding state-of-the-art microbial community research in both the experimental and computational/modeling areas.

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