

Probing the Stability of a Synthetic Symbiotic Microbial Consortium

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Project Goals:

To systematically quantify the robustness of an engineered mutualism between *Lactococcus lactis* and *Saccharomyces cerevisiae* under various perturbations, including initial population variations, chemical, physical and nutritional fluctuations and additional species invasion, and to identify key driving forces that shape ecosystem stability.

Abstract:

Microbial communities are constantly exposed to disturbances such as climate change and nutrition fluctuation in natural habitats, which shape their composition structure, population dynamics and ecological functioning. Understanding their resistance and resilience (i.e., stability) in disturbed environments is important for designing management strategies and creating artificial ecosystems. However, it remains difficult to quantitatively measure and predict due to the complexity of native ecologies. One alternative way to gain insights is to learn from well-defined, synthetic microbial consortia. Here we develop an engineered consortium of *Lactococcus lactis* and *Saccharomyces cerevisiae* that feed each other and use it to investigate the stability of symbiosis under a set of physical, chemical and biological perturbations. Our results show that the consortium is stable and converge to a single state for a wide range of initial population ratios. It also withstands upon two hours of modest pulse perturbations of pH, temperature, antibiotic and nutrition; however, under strong pulse or press perturbations, the ecosystem often transitions to an alternative stable state or even collapses depending on perturbation strength. Similarly, we observe the same characteristics of the consortium during invasion whereby the outcome is governed by specific types of perturbations introduced by foreign species. Learning from the findings, we show that modest supplement of cross-feeding metabolites confers long-term survival of community

populations during periodic dilution which crashes the ecosystem. We further extend the same cross-feeding mutualism to cases with different microbial species, demonstrating that the observed ecosystem stability arises primarily from underlying social interactions but not species. Together, our experiments provide a systematic understanding of the stability of a microbial symbiosis under pulse and press disturbances, providing insights into the organization of cooperative communities and applications of these ecosystems for biotechnological purposes.

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