MICROBIOME

# Ecology of stable gut communities

A recent analysis of microbial community dynamics shows that, contrary to current assumption, too much cooperation among species can destabilize their communities. This is a first step towards understanding what makes a stable microbiome and, thus, transforming microbiome research into a more predictive science.

## Luke McNally and Sam P. Brown

The human body is home to highly biodiverse communities of bacteria that are increasingly recognized to play an important role in human health. One of the most striking aspects of these complex communities is their long-term stability in healthy individuals — the composition of the microbiome shows remarkable permanence[1]. However, despite our rapidly increasing knowledge of the composition of the human microbiome, we know little about what determines the stability of these communities. Building on the tradition of mathematical approaches developed to study plant and animal communities[2,3], Foster and colleagues[4], writing in *Science*, provide a set of general principles for understanding microbiome stability.

When we think of the human microbiome, we often assume that mutualism (between the host and microorganisms) and cooperation (between microbial species) are critical to a productive microbiome[5]. However, Foster and colleagues report a mathematical analysis that shows that while cooperation among microorganisms may increase microbiome productivity, this can come at a cost to microbiome stability (Fig. 1). Cooperation is destabilizing because it introduces positive feedbacks, which can generate runaway effects. For example, when two species cooperate, an increase in the abundance of one species increases the abundance of the second, which in turn will increase the abundance of the first species and so on. If these increases are not sufficiently checked by other constraints, this can lead to runaway increases in cooperating groups of species that can cause the collapse of competing populations and the destabilization of the community. This means that adding species that primarily engage in competitive interactions to a microbial community may counterintuitively help to stabilize it by dampening positive feedbacks, stopping the community from cooperating its way to collapse.

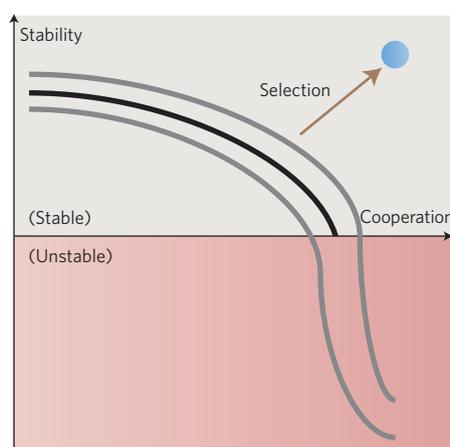Intriguingly, Foster and colleagues suggest that hosts may also suppress positive



**Figure 1 |** Microbiome community stability declines with the prevalence of cooperative interactions. The curve represents the principal result of Foster and colleagues[4], highlighting the risk that highly cooperative networks pose to community stability. The assumption of random networks allows important theoretical advances, but raises issues for future work. Firstly, not all random networks will be observed; for example, unstable networks (red) will be preferentially removed due to their instability. Secondly, of the remaining stable networks, adaptive processes and selection for stable productive communities (arrow) could bias observed networks towards maximal levels of stability (blue circle).

feedbacks between cooperating species in order to stabilize the microbiota. They propose three main mechanisms by which hosts could do this. First, the host immune response could be a stabilizing force. When certain species in the microbiome rapidly increase in abundance, this could provoke a targeted host immune response, thus stopping positive feedbacks between cooperating species in their tracks. Second, the host could attempt to block cooperative interactions among species by spatially segregating them — when species grow in separate locations, their interactions will be weakened preventing positive feedback. Finally, the host could feed microorganisms

to reduce cooperation among species by providing alternative carbon sources, so that these species no longer rely so strongly on their cooperative partners. Whether these stability-promoting mechanisms are host microbiome-engineering adaptations, or simply fortuitous by-products of existing host features and adaptations, remains an open question.

Foster and colleagues[4] analyse existing mouse gut microbiome data[6], and find that cooperative interactions are indeed rare in the gut microbiome (only ~10% of pairwise interactions are mutually beneficial), possibly because of their destabilizing effect. However, this result should not be taken as an indication that other microbiomes couldn't be both highly cooperative and stable. As we currently know little about the structure of microbiome interaction networks, Foster and colleagues assumed random interaction networks among species to allow greater analytical insight into broad patterns of stability. However, modelling work on plant and animal communities has shown that if community assembly is non-random, then highly cooperative communities can be stable, and work on plant-pollinator communities suggests that their non-random structuring maximizes the stability of a cooperative community[7]. Future work dissecting the interaction structures of microbial communities will be critical in evaluating the cooperative potential of the microbiome.

An additional unexplored factor that could drive microbiome stability is selection on both microbiomes and hosts (Fig. 1). The human microbiome is the product of long adaptive processes of constituent species, their interactions, and host factors governing their growth. Given the possibility of selection driving communities towards higher stability, it will be important for future work to ascertain not only how species interactions affect stability on average, as Foster and colleagues have done, but also what the characteristics of the most stable possible communities are, and whether they are achievable by evolution.

Work on animal and plant communities has shown that factors that decrease stability on average can also counterintuitively be over-represented in the most stable communities[8,9]. Applying a combination of these approaches will be critical in understanding both the evolutionary ecology of microbial communities, and in manipulating their compositions to promote healthy and stable microbiomes.

Foster and colleagues' results offer intriguing and provocative insights into how interspecies cooperation and host factors govern the stability of the microbiome. More broadly, the great value of this study is to awaken the microbiology community to a rich history of theory from macroorganism community ecology that can provide organizing principles for us to understand the microbiome. Importantly, microbiome research offers an unprecedented opportunity to study community stability from a grounded empirical perspective, and avoid repeating long-running debates from the community stability literature[8,10]. The proliferation of studies collecting time-series of microbiome composition, combined with new methods to parameterize models by estimating the interaction strengths among species[6], means that it is feasible for us to study questions such as how individual hosts vary in their microbiome stability and what factors underlie this variation in real microbiomes. By marrying two fields long destined to collide, Foster and colleagues offer the promise of transforming microbiome research into a more theory driven and predictive science. ❐

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### References
1. Faith, J. J. *et al. Science* **341,** 1237439 (2013).
2. May, R. M. *Nature* **238,** 413–414 (1972).
3. Allesina, S. & Tang, S. *Nature* **483,** 205–208 (2012).
4. Coyte, K. Z., Schluter, J. & Foster, K. R. *Science* **350,** 663–666 (2015).
5. Backhed, F., Ley, R. E., Sonnenburg, J. L., Peterson, D. A. & Gordon, J. I. *Science* **307,** 1915–1920 (2005).
6. Stein, R. R. *et al. PLoS Comput. Biol.* **9,** e1003388 (2013).
7. Rohr, R. P., Saavedra, S. & Bascompte, J. *Science* **345,** 1253497 (2014).
8. Haydon, D. *Am. Nat.* **144,** 14–29 (1994).
9. Haydon, D. *Ecology* **81,** 2631–2636 (2000).
10. McCann, K. S. *Nature* **405,** 228–233 (2000).