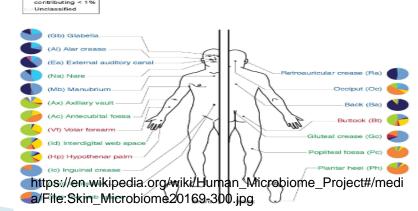
Competition and Stability- a New Perspective on the Microecology

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The Ecology of the Microbiome

- The human microbiome contains hundreds of species and trillions of cells that reside predominantly in the gastrointestinal tract.
- Any one individual tends to carry the same key set of species for long periods, major shifts in microbial community composition are often associated with ill health.

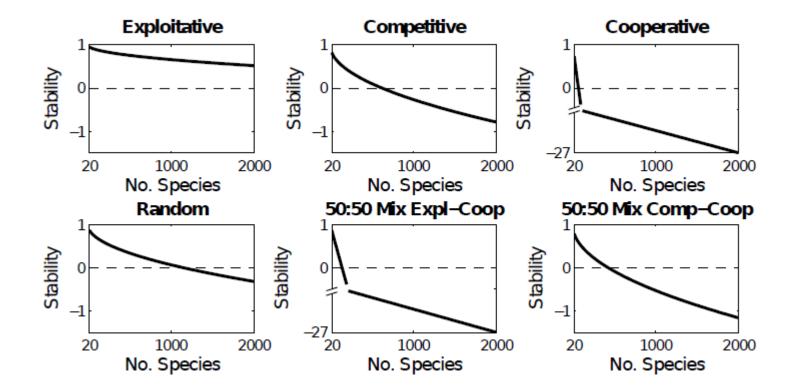


The Ecology of the Microbiome

- What promotes or disrupts the stability of microbiome communities ?
- Some progress has been made through the use of individual-based models and other analyses of twospecies communities.
- A long history of using network models that are specifically intended to deal with large and complex communities.

Diversity destabilizes communities

Diversity -problematic for community stability.



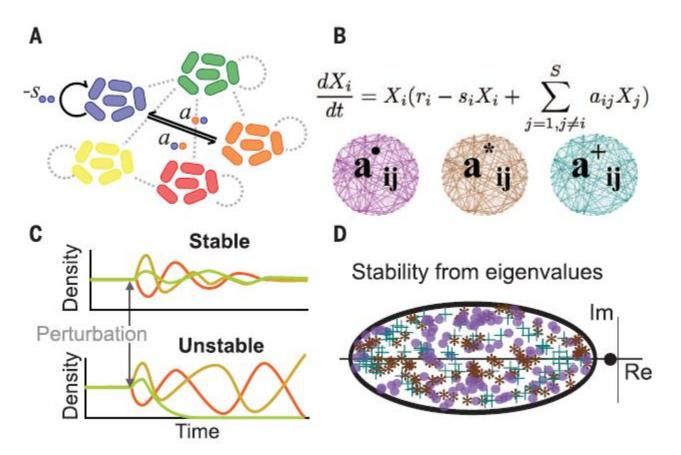
The Ecology of the Microbiome

The potential effects of cooperation or competition on the ecological stability of microbiome communities were neglected.

Three methods were established to understand ecological stability in the microbiome.

- Will a population return to this equilibrium following a perturbation?
- An approach that is well suited to the large population sizes of microbial species.
- Based upon calculating the eigenvalues of the Jacobian matrix of the dynamical system considered – a matrix that tells us how a change in the density of any of the species at equilibrium will affect the whole community.

- <u>Stability</u> is assessed from the network's eigenvalues, which give three measures of stability.
- (i) the probability that the community will return to its previous state after a small perturbation.
- (ii) the population dynamics during this return.
- (iii) how long the return will take, which is a form of resilience.

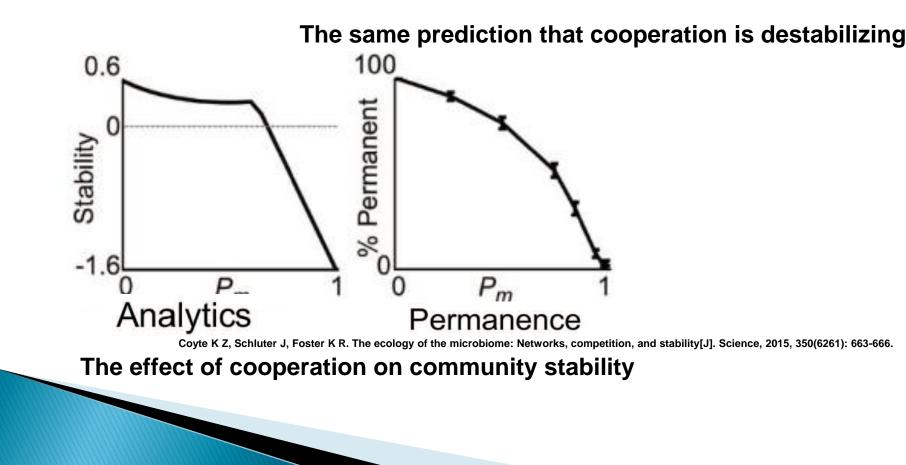


Coyte K Z, Schluter J, Foster K R. The ecology of the microbiome: Networks, competition, and stability[J]. Science, 2015, 350(6261): 663-666.

This approach is only able to analyze whether viable communities are stable when they are close to their equilibrium, it provides no information on how communities behave away from this equilibrium.

Method 2- Permanence Analysis

whether a community will retain all its members, independent of the scale of any perturbation ?

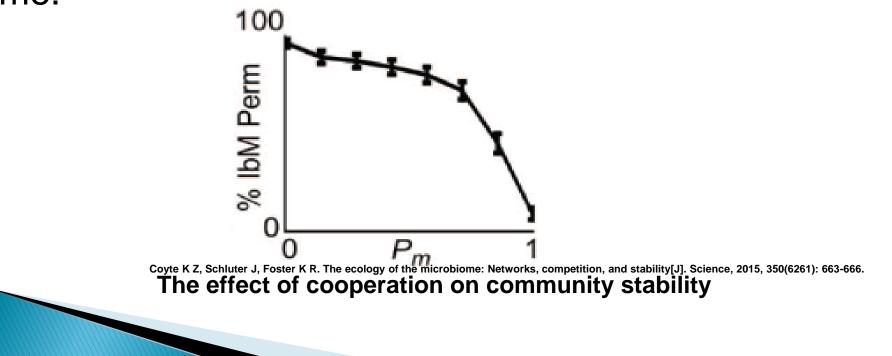


Method 2- Permanence analysis

Cons: positive feedbacks arising from cooperative interactions can still constrain this analysis, it may underestimate the number of permanent communities.

Method 3- Individual-based model

- Added information was given, such as how we expect a community to behave following perturbation.
- Allows us to track population sizes of all species over time.



A wide range of diversities of stabilizing effect

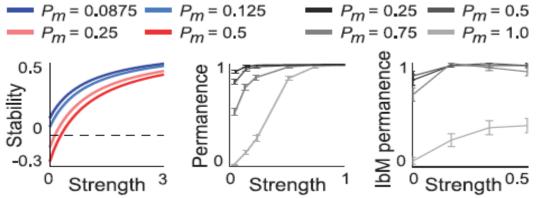
- Increasing species numbers is a destabilizing process, but the concurrent increase in competition introduces negative-feedback loops that have a stabilizing effect.
- A wide range of diversities was found for which this stabilizing effect dominates the destabilizing effect of increased species numbers.

 Stabilizing effect of competition reflects the more general principle that <u>dampening of positive-feedback</u> <u>loops promotes stability</u>.

- Immune system: During dysbiosis and infection, adaptive immunity is thought to help reestablish a healthy microbiome by suppressing species whose abundance is causing harm.
- We can add such density-dependent regulation to the model and find that it is indeed stabilizing.
- The reason is that immune regulation, like competition, will prevent run-away positive-feedback.

Redundancy can promote stability when a few strong cooperative interactions are replaced by several weaker ones.

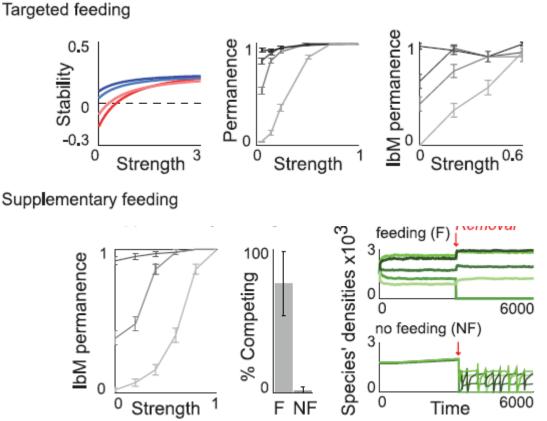
spatial structure



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Spatial structure promotes ecological stability

Host epithelial feeding



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Host strategies to promote ecological stability

Experimental Validation

- A stable community within the microbiome will contain only a small proportion of destabilizing cooperative interactions, amongst a larger number of competitive or exploitative links.
- A stable microbial community, the interactions between species should be predominantly weak relative to the self-regulation that each species experiences due to within-species competition.

Experimental Validation

we can validate our approach and test our key predictions with recently published data on interactions in the mouse gut microbiome Stein et al. used time-resolved metagenomics and machine learning to infer the interactions within communities. we



Experimental Validation

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PLOS BIOLOGY

The Evolution of Mutualism in Gut Microbiota Via Host Epithelial Selection

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Abstract

The human gut harbours a large and genetically diverse population of symbiotic microbes that both feed and protect the host. Evolutionary theory, however, predicts that such genetic diversity can destabilise mutualistic partnerships. How then can the mutualism of the human microbiota be explained? Here we develop an individual-based model of host-associated microbial communities. We first demonstrate the fundamental problem faced by a host. The presence of a genetically diverse microbiota leads to the dominance of the fastest growing microbes instead of the microbes that are most beneficial to the host. We next investigate the potential for host secretions to influence the microbiota. This reveals that the epithelium-microbiota interface acts as a selectivity amplifier. Modest amounts of moderately selective epithelial secretions cause a complete shift in the strains growing at the epithelial surface. This occurs because of the physical structure of the epithelium-microbiota interface: Epithelial secretions have effects that are soon to slough off. Finally, our model predicts that while antimicrobial secretion can promote host epithelial selection, epithelial nutrient secretion will often be key to host selection. Our findings are consistent with a growing number of empirical papers that indicate an influence of host factors upon microbiota, including growth-promoting glycoconjugates. We argue that host selection is likely to be a key mechanism in the stabilisation of the mutualism between a host and its microbiota.

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Abbreviations: IgA, Immunoglobulin A; ODE, ordinary differential equation

<u>Termit interview Data were used to parameterize our general model and show</u> that it correctly predicts stability within a real community.

Conclusion

- Hosts can act as ecosystem engineers that manipulate general, system-wide properties of their microbial communities to their benefit.
- To understand and manipulate the microbiome, we will need to dissect and engineer the interactions within these critical communities.

Synthetic Ecology.

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Thank you!