



## Research Highlights

## Distinct dynamic phases observed in bacterial microcosms

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## ABSTRACT

Predicting biodiversity and dynamics of complex communities is a fundamental challenge in ecology. Leveraging bacterial microcosms with well-controlled laboratory conditions, Hu et al. recently performed a direct test of theory predicting that two community-level parameters (i.e., species pool size and inter-species interaction strength) dictate transitions between three dynamical phases: stable full coexistence, stable partial coexistence, and persistent fluctuations. Generally, communities experience species extinctions before they lose stability as either of the two parameters increases.

As we witness the deterioration of the planet's environment and the decay in the services that natural ecosystems provide, the central problem in ecology of understanding species coexistence and the rules that regulate it has gained increasing importance. In particular, the study of species coexistence in microbial communities is more relevant than ever due to technological advances that allow us to quantify their abundances and interactions and unveil their importance. From waste management [1-3], to food production [4,5] and health regulation [6,7] microbial communities have been found to play crucial roles in human daily activities.

In a recent paper published in Science [8], Dr. Jiliang Hu and collaborators successfully manipulated the species pool size and the characteristic inter-species interaction strength of bacterial microcosms (using a library of 48 bacterial isolates from terrestrial environments). For the first time, they experimentally observed three distinct dynamical phases: (1) stable full coexistence; (2) stable partial coexistence; and (3) persistent fluctuation (Fig. 1). In particular, Hu et al. observed that communities with weak interactions and/or that have few species tend to have a feasible and stable equilibrium and, as either parameter is increased (more species are added or interactions are strengthened), communities first lose species and then lose stability, giving way to persistent fluctuations. These observations conform with the trends predicted by the analytical calculations and computational simulations using the classical generalized Lotka Volterra (GLV) model, which has been widely used in modeling microbial communities [9-12].

The experimental and simulation results presented in this paper are consistent with previous theoretical results that predicted the loss of stability as the community's complexity increases [13], proved the stability of feasible equilibria [14], characterized the temporal fluctuations

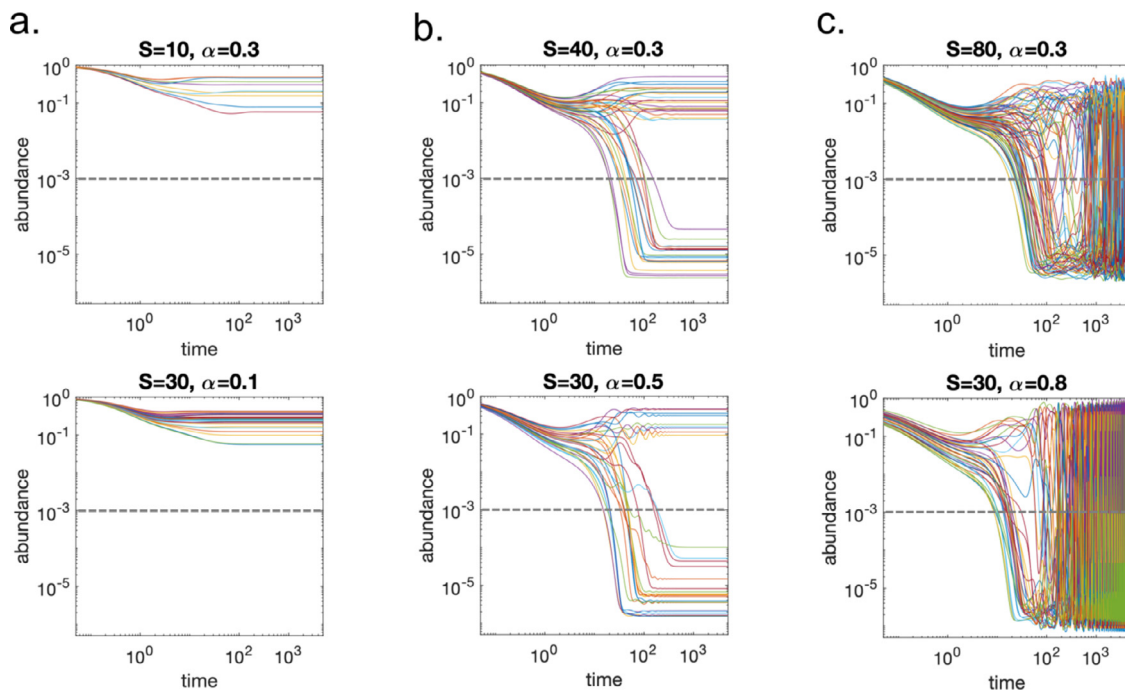
[15,16], and described the different dynamical behaviors and the transitions between them [17,18]. Previous experimental works had reproduced some of these formalisms in communities with few species [19-24]. Hu et al. took one step further and, for the first time, validated them in synthetic communities of several dozens of bacteria, controlling the characteristic inter-species and the initial species pool simultaneously and with great precision. Moreover, the authors used 16S ribosomal RNA to accurately sequence the communities' composition at the species level, advancing the observations at higher taxonomic levels of previous studies [25-28]. These new results confirm the notions that higher diversity can be achieved by allowing communities to fluctuate.

The experimental work presented in this paper has a very strong potential to fuel new efforts that can enormously advance the field of microbial ecology. For example, it sheds light on the problem of designing interventions aimed to control ecosystems' behavior and prevent their degradation, which has continually preoccupied not only the ecology community but also environmental protection groups and policy makers [29-31]. Other interesting directions in which this work will likely serve as inspiration are to test and validate the extensibility of the results to a larger ecological scale, to study their applicability to communities known to have a particular functional or interaction structure, or to expand their scope to ecosystems with spatial heterogeneity [32].

This work serves as a shining example for the perfect combination of ecological theory and experimental work. Its results will have profound implications for studies on the stability of complex ecosystems, e.g., the human microbiota — the collection of trillions of microbes that live in and on the human body. Many previous studies have reported the long-term stability of human gut, oral and skin microbiome [33,34]. In particular, most of the variance in gut microbial time series is driven

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**Fig. 1.** Two community-level parameters (size of species pool  $S$ , and inter-species interaction strength  $\alpha$ ) can determine the dynamic phase in which a microbial community exists. **a.** With a small  $S$  or  $\alpha$ , all species can coexist in a stable equilibrium, i.e., stable full coexistence (phase 1). **b.** Increasing  $S$  or  $\alpha$  leads to a loss of species (with abundances below the extinction threshold  $10^{-3}$ , indicated by the dashed line), and the survivors still coexist in a stable equilibrium, which characterizes the stable partial coexistence (phase 2). **c.** Further increasing  $S$  or  $\alpha$  induces persistent fluctuations (phase 3), in which the system loses stability, and the surviving species display persistent fluctuations in their abundances.

by external day-to-day fluctuations in host and environmental factors (e.g., diet) with occasional internal dynamics as the system recovered from larger shocks (e.g., facultative anaerobe blooms) [35]. Overall, in the absence of drastic interventions, e.g., repeated antibiotic treatments or drastic diet changes, the human gut microbiota can be considered as a dynamically stable system. But is the human gut microbiota in a phase of stable coexistence of all species, or a phase of stable coexistence of some species? If the latter, how far is the human gut microbiota from the persistent oscillation phase described in this work? Note that the notion of stability does not always apply to the microbiota of other body sites. For example, it has been reported that the vaginal microbial compositions of some healthy reproductive-age women changed markedly and rapidly over time, which has been associated with their menstrual cycle [36]. The notion of stability or equilibrium does not apply to this case. Whether the notion of persistent oscillation phase described in this work applies to this case warrants further studies. Addressing these fundamental ecological questions will help us better understand the relationship of the microbiome to human health.

#### Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

#### References

- [1] D.R. Meyer-Dombard, J.E. Bogner, J. Malas, A review of landfill microbiology and ecology: a call for modernization with 'next generation' technology, *Front. Microbiol.* 11 (2020) 1127.
- [2] A. Cydzik-Kwiatkowska, M. Zielińska, Bacterial communities in full-scale wastewater treatment systems, *World J. Microbiol. Biotechnol.* 32 (2016) 1–8.
- [3] T. Narihiro, Y. Sekiguchi, Microbial communities in anaerobic digestion processes for waste and wastewater treatment: a microbiological update, *Curr. Opin. Biotechnol.* 18 (2007) 273–278.
- [4] N.A. Bokulich, Z.T. Lewis, K. Boundy-Mills, D.A. Mills, A new perspective on microbial landscapes within food production, *Curr. Opin. Biotechnol.* 37 (2016) 182–189.
- [5] F. De Filippis, E. Parente, D. Ercolini, Metagenomics insights into food fermentations, *Microb. Biotechnol.* 10 (2017) 91–102.
- [6] E.Z. Gomma, Human gut microbiota/microbiome in health and diseases: a review, *Antonie Van Leeuwenhoek* 113 (2020) 2019–2040.
- [7] N. Zmora, D. Zeevi, T. Korem, E. Segal, E. Elinav, Taking it personally: personalized utilization of the human microbiome in health and disease, *Cell Host Microbe* 19 (2016) 12–20.
- [8] J. Hu, D.R. Amor, M. Barbier, G. Bunin, J. Gore, Emergent phases of ecological diversity and dynamics mapped in microcosms, *Science* 378 (2022) 85–89.
- [9] R.R. Stein, V. Bucci, N.C. Toussaint, C.G. Buffie, G. Rätsch, E.G. Pamer, C. Sander, J.B. Xavier, Ecological modeling from time-series inference: insight into dynamics and stability of intestinal microbiota, *PLoS Comput. Biol.* 9 (2013) e1003388.
- [10] V. Bucci, B. Tzen, N. Li, M. Simmons, T. Tanoue, E. Bogart, L. Deng, V. Yeliseyev, M.L. Delaney, Q. Liu, MDSINE: microbial Dynamical Systems INference Engine for microbiome time-series analyses, *Genome Biol.* 17 (2016) 1–17.
- [11] C.G. Buffie, V. Bucci, R.R. Stein, P.T. McKenney, L. Ling, A. Gobourne, D. No, H. Liu, M. Kinnebrew, A. Viale, Precision microbiome reconstitution restores bile acid mediated resistance to *Clostridium difficile*, *Nature* 517 (2015) 205–208.
- [12] C.K. Fisher, P. Mehta, Identifying keystone species in the human gut microbiome from metagenomic timeseries using sparse linear regression, *PLoS ONE* 9 (2014) e102451.
- [13] R.M. May, Will a large complex system be stable? *Nature* 238 (1972) 413–414.
- [14] T.J. Case, R.G. Casten, Global stability and multiple domains of attraction in ecological systems, *Am. Nat.* 113 (1979) 705–714.
- [15] F. Roy, M. Barbier, G. Biroli, G. Bunin, Complex interactions can create persistent fluctuations in high-diversity ecosystems, *PLoS Comput. Biol.* 16 (2020) e1007827.
- [16] M.T. Pearce, A. Agarwala, D.S. Fisher, Stabilization of extensive fine-scale diversity by ecologically driven spatiotemporal chaos, *Proc. Natl. Acad. Sci.* 117 (2020) 14572–14583.
- [17] M. Opper, S. Diederich, Phase transition and  $1/f$  noise in a game dynamical model, *Phys. Rev. Lett.* 69 (1992) 1616.
- [18] G. Bunin, Ecological communities with Lotka-Volterra dynamics, *Phys. Rev. E* 95 (2017) 042414.
- [19] J. Friedman, L.M. Higgins, J. Gore, Community structure follows simple assembly rules in microbial microcosms, *Nat. Ecol. Evol.* 1 (2017) 1–7.
- [20] O.S. Venturelli, A.V. Carr, G. Fisher, R.H. Hsu, R. Lau, B.P. Bowen, S. Hromada, T. Northen, A.P. Arkin, Deciphering microbial interactions in synthetic human gut microbiome communities, *Mol. Syst. Biol.* 14 (2018) e8157.
- [21] F.K. Balagaddé, H. Song, J. Ozaki, C.H. Collins, M. Barnet, F.H. Arnold, S.R. Quake, L. You, A synthetic *Escherichia coli* predator-prey ecosystem, *Mol. Syst. Biol.* 4 (2008) 187.
- [22] B. Blasius, L. Rudolf, G. Weithoff, U. Gaedke, G.F. Fussmann, Long-term cyclic persistence in an experimental predator-prey system, *Nature* 577 (2020) 226–230.

- [23] G.F. Fussmann, S.P. Ellner, K.W. Shertzer, N.G. Hairston Jr, Crossing the Hopf bifurcation in a live predator-prey system, *Science* 290 (2000) 1358–1360.
- [24] W. Shou, S. Ram, J.M.G. Vilar, Synthetic cooperation in engineered yeast populations, *Proc. Natl. Acad. Sci.* 104 (2007) 1877–1882.
- [25] E. Benincà, B. Ballantine, S.P. Ellner, J. Huisman, Species fluctuations sustained by a cyclic succession at the edge of chaos, *Proc. Natl. Acad. Sci.* 112 (2015) 6389–6394.
- [26] E. Benincà, J. Huisman, R. Heerkloss, K.D. Jöhnk, P. Branco, E.H. Van Nes, M. Scheffer, S.P. Ellner, Chaos in a long-term experiment with a plankton community, *Nature* 451 (2008) 822–825.
- [27] C. Ratzke, J. Barrere, J. Gore, Strength of species interactions determines biodiversity and stability in microbial communities, *Nat. Ecol. Evol.* 4 (2020) 376–383.
- [28] J.E. Goldford, N. Lu, D. Bajić, S. Estrela, M. Tikhonov, A. Sanchez-Gorostiaga, D. Segrè, P. Mehta, A. Sanchez, Emergent simplicity in microbial community assembly, *Science* 361 (2018) 469–474.
- [29] C.S. Holling, G.K. Meffe, Command and control and the pathology of natural resource management, *Conserv. Biol.* 10 (1996) 328–337.
- [30] C. Folke, S. Carpenter, B. Walker, M. Scheffer, T. Elmqvist, L. Gunderson, C.S. Holling, Regime shifts, resilience, and biodiversity in ecosystem management, *Annu. Rev. Ecol. Syst.* (2004) 557–581.
- [31] W.C. Clark, D.D. Jones, C.S. Holling, Lessons for ecological policy design: a case study of ecosystem management, *Ecol. Modell.* 7 (1979) 1–53.
- [32] S. Widder, R.J. Allen, T. Pfeiffer, T.P. Curtis, C. Wiuf, W.T. Sloan, O.X. Cordero, S.P. Brown, B. Momeni, W. Shou, Challenges in microbial ecology: building predictive understanding of community function and dynamics, *ISME J.* 10 (2016) 2557–2568.
- [33] J. Grilli, Macroecological laws describe variation and diversity in microbial communities, *Nat. Commun.* 11 (2020) 1–11.
- [34] K. Faust, F. Bauchinger, B. Laroche, S. De Buyl, L. Lahti, A.D. Washburne, D. Gonze, S. Widder, Signatures of ecological processes in microbial community time series, *Microbiome* 6 (2018) 1–13.
- [35] S.M. Gibbons, S.M. Kearney, C.S. Smillie, E.J. Alm, Two dynamic regimes in the human gut microbiome, *PLoS Comput. Biol.* 13 (2017) e1005364.
- [36] P. Gajer, R.M. Brotman, G. Bai, J. Sakamoto, U.M.E. Schütte, X. Zhong, S.S.K. Koenig, L. Fu, Z. Ma, X. Zhou, Temporal dynamics of the human vaginal microbiota, *Sci. Transl. Med.* 4 (2012) 132ra52–132ra52.