ducing time spent on communication with authors and reviewers, improving standards of reporting, increasing detectability of errors before publication, and ensuring that publication-related data are accessible for a long time.

Evaluation and revision. An information commons and support team at the Center for Open Science is available (top@cos.io) to assist journals in selection and adoption of standards and will track adoption across journals. Moreover, adopting journals may suggest revisions that improve the guidelines or make them more flexible or adaptable for the needs of particular subdisciplines.

The present version of the guidelines is not the last word on standards for openness in science. As with any research enterprise, the available empirical evidence will expand with application and use of these guidelines. To reflect this evolutionary process, the guidelines are accompanied by a version number and will be improved as experience with them accumulates.

Conclusion. The journal article is central to the research communication process. Guidelines for authors define what aspects of the research process should be made available to the community to evaluate, critique, reuse, and extend. Scientists recognize the value of transparency, openness, and reproducibility. Improvement of journal policies can help those values become more evident in daily practice and ultimately improve the public trust in science, and science itself. ■

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SUPPLEMENTARY MATERIALS

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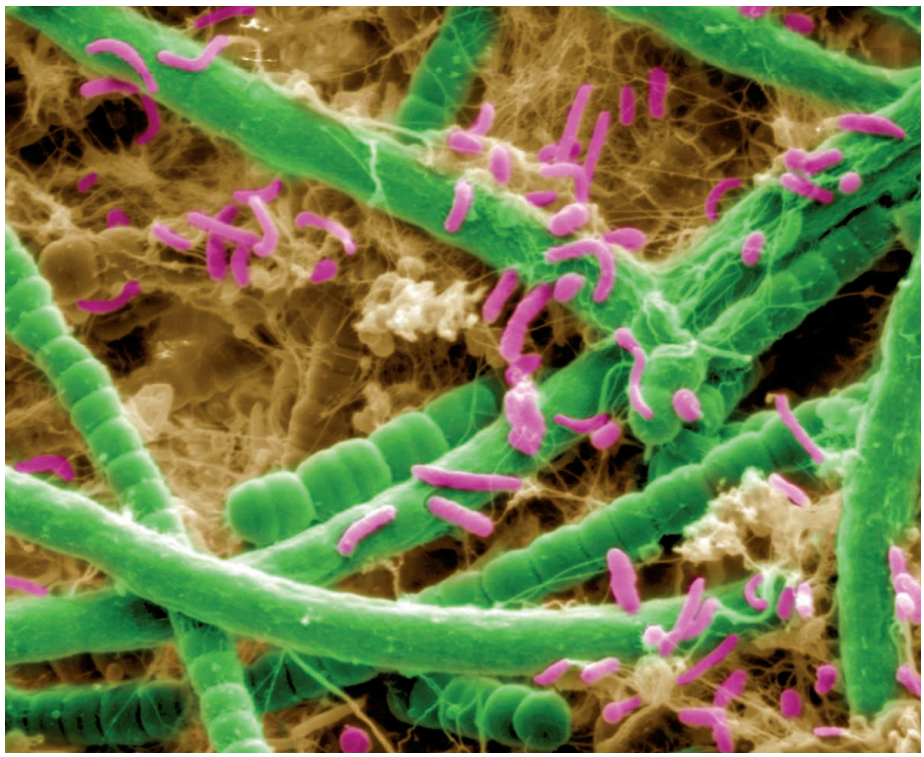


Learning from nature. Photomicrograph of cyanobacterial-heterotroph microbial consortia derived from a phototrophic microbial mat community from a saline lake. Emerging understanding of cooperative mechanisms in such communities may be helpful in the design of synthetic communities for use in biotechnology.

ECOLOGY

Ecological communities by design

Synthetic ecology requires knowledge of how microbial communities function

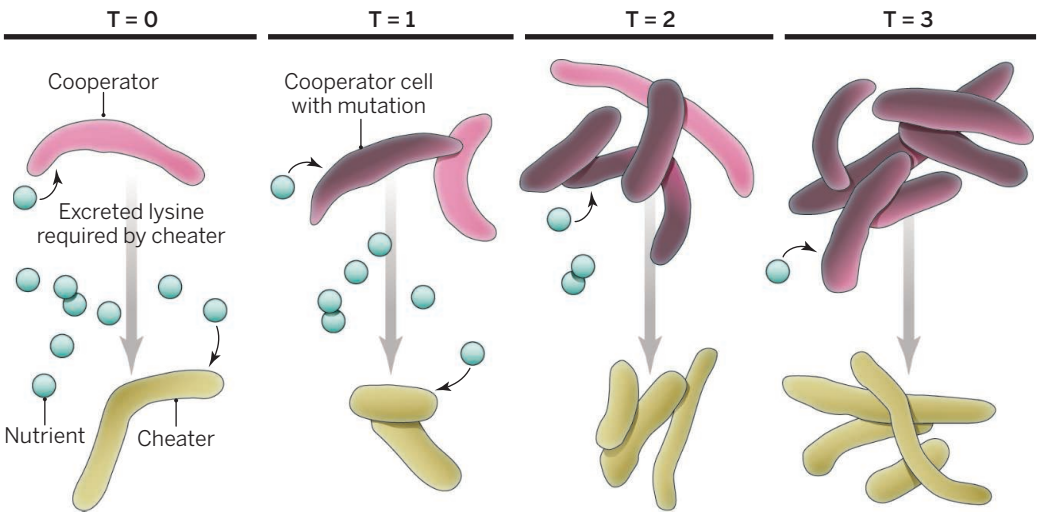
By **James K. Fredrickson**

In synthetic ecology, a nascent offshoot of synthetic biology, scientists aim to design and construct microbial communities with desirable properties. Such mixed populations of microorganisms can simultaneously perform otherwise incompatible functions (*1*). Compared with individual organisms, they can also better resist losses in function as a result of environmental perturbation or invasion by other species (*2*). Synthetic ecology may thus be a promising approach for developing robust, stable biotechnological processes, such as the conversion of cellulosic biomass to biofuels (*3*). However, achieving this will require detailed knowledge of the principles that guide the structure and function of microbial communities (see the image).

Recent work with synthetic communities is shedding light on microbial interactions that may lead to new principles for community design and engineering. In game theory, cooperators provide publicly available goods that benefit all, whereas cheaters exploit those goods without reciprocation. The tragedy of the commons predicts that cheaters are more fit than cooperators, eventually destroying the cooperation. Yet, this is not borne out by observations. For example, using a synthetic consortium of genetically modified yeast to represent cooperators and cheaters, Waite and Shou (*4*) found that, although initially less fit than cheaters, cooperators rapidly dominated in a fraction of the cultures. The evolved cooperators harbored mutations allowing them to grow at much lower nutrient concentrations than their ancestor. This suggests that the tragedy of the commons can be avoided

if, during adaptation, the fitness gain of cooperators exceeds that of the cheaters by at least the cost of cooperation (see the figure).

The work by Asfahl *et al.* provides another example of deferring the tragedy of the commons via nonsocial adaptation (*5*). The opportunistic pathogen *Pseudomonas aeruginosa* uses diffusible signaling molecules, in a process known as quorum sensing (QS), to regulate public goods—resources that can benefit the entire community. Under growth conditions that require QS-regulated public goods, mutations in the transcriptional regulator *psdR* give rise to a nonsocial adaptation. This mutation has no effect on public goods expression; rather, it increases the fitness of individuals harboring the mutation by improving intracellular metabolism of the goods. Although the adapted population is still subject to invasion by cheaters, the mutation affords a higher fitness (growth rate) that increases the population's tolerance of cheaters, thus maintaining cooperative behavior. This suggests that fitness adaptations are a fundamental mechanism by which cooperative communities can be maintained under the persistent threat of cheaters.



Adaptive race. In cooperative communities, cheaters use common goods without paying the cost to produce them. In the absence of adaptation or adaptive mutations, the cheaters eventually win out but cause the system to collapse. In synthetic communities of cooperators that excrete lysine and cheaters that require lysine, both species adapt to cope with limited resources. In the example shown, a mutation in a cooperator allows the mutated strain to outcompete its ancestors over time. This mechanism explains why cooperating microbial communities can persist in changing environments. For further details, see (*4*).

Microbial communities also cooperate through metabolic cross-feeding or syntrophy, where one organism synthesizes a compound that another organism requires but cannot produce. For example, amino acids and sugar exchange are common mutualistic interactions in co-occurring subcommunities from different habitats (*6*). In a recent study, Mee *et al.* (*7*) explored the basic principles of syntrophic exchange in synthetic communities consisting of *Escherichia coli* mutants auxotrophic for different amino acids. They found that stronger cooperative interactions were promoted between cells exchanging metabolically expensive amino acids compared to those that are cheaper to synthesize. Hence, amino acid auxotrophy may be a common strategy by which microbial communities lessen the collective metabolic burden of biosynthesis and stabilize cooperation. Further evidence for this comes from the persistence of metabolic cooperation between different *E. coli* amino acid auxotrophs in adaptively evolved cocultures (*8*).

Inherent to community productivity is the question of what maintains cross-feeding in the presence of metabolically independent noncooperators. Pande *et al.* (*9*) addressed this question with synthetic communities of *E. coli* that had been genetically modified to require uptake of certain amino acids for growth and to release other amino acids into the environment. Most cross-feeding consortia grew more rapidly than the parental bacterium that could synthesize all the amino acids needed for growth; this was the case even when the consortia were cultivated with the parent and therefore in direct competition for nutrients. The authors attributed the greater fitness of the cooperating consortia to a metabolic division of labor. Here, the added costs of producing an excess of one or more amino acids to benefit the community were more than compensated for by the reduced costs incurred by not having to synthesize all amino acids de novo. The loss of specific biosynthetic functions can give rise to stable metabolic interactions that benefit the interacting organisms. This likely explains why amino acid exchange is common among members of microbial communities throughout the biosphere (*7*).

In some cases, the interactions between community members that give rise to higher-order properties emerge only when distinct physical structures are formed. A coculture of *P. aeruginosa*, *Pseudomonas protegens*, and *Klebsiella pneumoniae* forms a mixed-species biofilm that collectively exhibits greater resistance to antimicrobials (tobramycin and sodium dodecyl sulfate) than do biofilms of the individual species (*10*). Furthermore, when the mixed culture is grown planktonically and treated with tobramycim, only the more resistant *P. protegens* survive. The results indicate that species composition and spatial organization can affect higher-order properties such as stress resistance. It remains unclear how the spatial organization of different species in mixed biofilms helps to make them resilient.

Model systems derived from natural communities have tremendous untapped potential to uncover the genetic, biochemical, and evolutionary bases for ecological interactions at play in more complex systems (*11*). Microbial oxygenic phototrophs are ubiquitous worldwide and host diverse microbes that can influence the physiology and ecology of the host. Sison-Mangus *et al.* (*12*) investigated how coadaptation affects the interactions between *Pseudo-nitzschia*, a genus of marine diatoms, and the bacteria associated with them. They discovered that individual species of the diatom harbor phylogenetically distinct bacterial communities and that the communities associated with species that produce the toxin domoic acid are less diverse. Transplant experiments to assess coevolution effects on host fitness revealed that bacteria conferred stronger fitness to their natural host than to non-native diatoms. That some organisms may select for specific microbes they host, possibly through metabolite secretion, suggests this may be an effective approach for designing synthetic communities.

Colonization resistance, defined as the capacity for the native community to resist invasion, is thought to be a major function of the microbiome. To explore mecha-

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nisms of colonization resistance, He *et al.* (*13*) investigated a community cultivated from mouse oral cavity that could detect the presence of *E. coli* and enhance its lethality toward the invader by elevating H_2O_2 production (*14*). Using information from the simplified oral microbiome, the authors constructed a synthetic consortia consisting of three mice oral bacterial species from previous studies and used it to investigate colonization resistance mechanisms. Their results revealed the roles of the three species: *Streptococcus saprophyticus* functions as a sensor by detecting *E. coli* lipopolysaccharide, whereas *Streptococcus infantis* serves as a mediator that detects a diffusible signal from the sensor and relays information to the killer (*Staphylococcus sanguinus*), which turns on H_2O_2 production. These mechanistic details of interactions provide insight into how microbiomes might be designed and engineered to resist invasion.

Substantial challenges remain before synthetic ecology can be successfully applied to biotechnologies such as consolidated bioprocessing of lignocellulosic biomass for biofuel production. For example, it remains to be shown how interactions among community members drive assembly and structure and how these interactions give rise to higher-order properties. To gain a better understanding of these processes, scientists must identify and quantify the numerous biomolecules produced and secreted by microbes in communities and link the exchanges of these molecules to specific organisms and the genes involved in production and consumption. ■

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MICROBIOTA

Mother's littlest helpers

Breastmilk nourishes the microbes colonizing the neonatal intestinal tract

By **Katie Hinde**[1] *and* **Zachery T. Lewis**[2]

Commensal bacteria underlie, in part, our nutritional status, immune function, and psychological well-being. The trillions of beneficial microbes within our intestinal tract convert dietary nutrients, inhibit pathogen colonization, regulate immune processes, and produce neural signals (*1*, *2*). Advances in our understanding of the importance of microbes have motivated the commercial development of products intended to boost "good" commensals and confer health benefits. Probiotic dietary supplements contain live beneficial microbes hoped to subsequently colonize the gut. Prebiotic nutrients are thought to enhance good gastrointestinal microflora by preferentially nourishing beneficial microbes. Even "psychobiotics" are being explored to ameliorate symptoms of psychiatric illness. These live organisms influence the brain through metabolites and neuroactive compounds in rodent models and preliminary human studies (*3*). How to most effectively be the landscape architects of our microbial community, however, often remains unclear. An opportunity to gain insights into how natural selection has shaped the coevolution of hosts and microbes can be found in mammalian mother-infant dyads, as our microbiota are ecologically engineered by mothers and breastmilk. Such insights can be leveraged to improve clinical management and nutritional technologies, enhancing human health not just in infancy, but across the life course (*4*, *5*).

Establishment and maintenance of the microbial community within the human infant gut vary as a function of bacterial exposure, successful colonization, and sustained nutrition. Perinatal exposure is a function of highly variable birth experiences within and across cultures, from Cesarian delivery in a hospital surgical suite to a vaginal birth in a traditional village home (*1*, *2*, *5*). As such, microbial transfer from the surrounding people, animals, and surfaces to the neonate varies substantially. Microbes are also present in breastmilk and may contribute to the developing infant gut microbiome, but this is currently an open question. The origin of these milk microbes may lie in the established pathways of surface skin contamination and retrograde flow (salivary backwash) as a result of the intra-oral vacuum dynamics of suckling (*6*), or via the more speculative translocation to milk through a gut-mammary route (*5*, *7*).

Once breastmilk is in the intestinal environment of an infant, intense microbial competition exists for both space and nutrients. The major available carbon source, human milk glycans, are complex oligosaccharide and glycoconjugate compounds that typically pass undigested from the infant stomach because eutherian mammals (those with a placenta) lack enzymes to cleave them (*8*, *9*). Investigations of the structure of milk oligosaccharides reveal that human milk has a greater diversity (>200 isomers), more complexity, and higher abundance than the milk of other primates, including all of the great apes (*4*, *8*). Importantly, certain oligosaccharides that dominate human milk, but are absent or rare in other primates, are the preferred food of *Bifidobacterium*, the most prevalent microbial clade in the healthy infant gut (*8*).

> ***"...our microbiota are ecologically engineered by mothers and breastmilk."***

Bifidobacterium was first described as a major member of the infant gut community over 40 years ago. More recently, it was demonstrated that the model "breastfed-infant-type" bifidobacteria, *B. longum* subsp. *infantis,* has genes encoding proteins predicted to bind, import, cleave, and metabolize the major oligosaccharides present in human milk (*10*). Variation in the oligosaccharide profile in breast milk (within and among mothers) influences the timing and type of microbial community established in an infant, both at the level of broad microbial clades and among bifidobacterial species (*11*). Bifidobacterial consumption of oligosaccharides produces short-chain fatty acids such as acetate and butyrate, some of which are used as a fuel source by infant

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Ecological communities by design

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