Probing the metabolism of microorganisms

Modeling and genetic analyses reveal insights into microbial metabolic pathways

By Stilianos Louca

Microorganisms are the most ancient, the most abundant, and the most diverse life form on Earth. Over billions of years, their metabolic activity, coupled with geo-physical processes, has been shaping Earth’s surface chemistry (1). Today, microorganisms catalyze the bulk of biochemical fluxes in virtually every ecosystem, including the ocean, soil, and the human gut.

Unraveling the principles by which microbial communities couple with physical processes to give rise to biogeochemical fluxes is of central importance to ecology, environmental sciences, industry, and human health. Yet, our understanding of microbial communities and their role in ecosystems remains extremely limited, partly because the enormous microbial diversity poses a serious challenge to conceptual and mathematical modeling.

THE PATHWAY-CENTRIC PARADIGM

Despite the millions of extant microbial species, most elemental fluxes are driven by a core set of energy-transducing metabolic pathways, encoded by a few genes. Over time, these genes have evolved to use various energy sources, such as light for photosynthesis or various chemical compounds for respiration, and have propagated within a multitude of microbial taxa (1).

The growth of microorganisms (and, thus, of genes) is inevitably tied to the activity of these genes, which in turn is strongly constrained by current environmental conditions. It is therefore tempting to theorize that energy-transducing pathways—or more precisely, the genes encoding them—may behave as independent units of replication and selection (2) and that environmental conditions prescribe the overall biochemical fluxes catalyzed by these genes, regardless of the precise species involved. Such a “pathway-centric” paradigm, if applicable, would greatly simplify the modeling of microbial processes at ecosystem scales.

SEQUENCING THE BROMELIAD MICROBIOME

As part of my graduate work, I developed and tested the applicability of this paradigm to a multitude of environments, using experiments, DNA sequencing, and mathematical modeling. A key prediction of the pathway-centric paradigm is that similar environments will promote the growth and activity of similar energy-transducing pathways, even if the species encoding each pathway varied. To test this prediction, I examined microbial communities within the foliage of multiple bromeliad plants (3, 4).

Bromeliads are popular model systems for ecology because their cavity-shaped foli- age accumulates rainwater and detritus, the decomposition of which sustains rich food webs that can be conveniently surveyed in replicates (see the photo, left). Using DNA sequencing, I estimated the species composition of the microbial communities as well as the abundances of various pathways encoded in the microbial genomes. I discovered that each bromeliad hosted a distinct community of microbial species (see the figure, middle). Notably, less than 3% of the microbial species encountered in the study were present in all bromeliads.

In contrast, microbial communities showed a striking similarity in terms of the abundance of genes involved in various pathways, including those involved in fermentation, oxygen respiration, and carbon fixation (see the figure, right). This suggested that environmental constraints largely determined the growth of these pathways and had much less influence over which species happened to represent each pathway in a bromeliad, consistent with a pathway-centric paradigm.

SEQUENCING THE OCEAN MICROBIOME

To test the generality of my findings, I analyzed DNA sequencing data from an international ocean microbiome survey (5), in combination with oceanographic data from satellite imaging. Through extensive search of the literature, I classified over 30,000 marine microorganisms into various metabolic groups based on the pathways that they use to gain energy (6). For example, I distinguished between organisms that consume methane (a potent greenhouse gas)
and organisms that eat sulfide (a toxic gas found in parts of the ocean).

Using statistical methods, I discovered that environmental conditions strongly predicted the distribution of metabolic groups across the world’s oceans. In contrast, environmental conditions poorly predicted which microbial species were associated with each metabolic group in each location. This was perplexing, because ocean currents can transport microorganisms across large distances, and yet the same pathways were represented by different organisms in different locations of the ocean. Hence, mechanisms other than environmental selection and limitation of dispersal seem to influence which species get to perform these pathways in each location.

SIMULATING SPECIES’ STABILITY

To find out what these mechanisms may be, I borrowed statistical tools from animal ecology. I found that both in bryomedal (3) and in the ocean (6), the variation in species composition within each metabolic group was likely driven by complex interactions between organisms. Using computer simulations, I further demonstrated that such interactions—for example, predation of bacteria by viruses—could indeed cause fluctuations in species composition, even if the overall activity of metabolic pathways at the community level is constant (7, 8, 9). This realization has important implications for microbiologically catalyzed industrial processes, such as bioremediation of acid mine drainage, where a stable microbial community is often an objective of operation control. My findings suggest that taxonomic stability is neither easily achievable through control of the operating environment alone nor a pre-requisite for bioprocess stability.

A GENE-CENTRIC MODEL OF BIOGEOCHEMISTRY EMERGES

If the dynamics of individual genes become decoupled from particular species assemblages, then we may be able to directly model the dynamics of these genes within an ecosystem. Motivated by my previous findings, I developed a gene-centric mathematical model for the biogeochemistry in Saanich Inlet, a fjord off Vancouver Island (10). In Saanich Inlet, annual oxygen depletion leads to dramatic shifts in microbiologically mediated biochemical fluxes, and much research on ocean biochemistry uses Saanich Inlet as a model ecosystem.

My model integrated DNA, RNA, and protein sequence data, as well as chemical measurements, into a single framework. Using this model, I found that genes indeed displayed population dynamics that resembled self-replicating organisms that are feeding on each other’s metabolic waste products. The model also revealed an important and previously unsuspected microbial process that removes toxic sulfide and transforms ammonia into nitrogen gas, with potentially strong implications for ocean productivity.

In conclusion, environmental conditions appear to be directly coupled to the dynamics of certain energy-transducing microbial pathways, whereas complex species interactions influence which taxa get to perform each pathway. Disentangling the pathway structure of microbial communities from their taxonomic structure, as advanced by my work (4, 6, 10), will be an important component of future research in microbial ecology.

REFERENCES


10.1126/science.aar2000

PHOTOS: TOP TO BOTTOM: COURTESY OF STILIANO LOUCA; ALENA HEATH; WILLY JOHNSON; COURTESY OF MIJO SIMUNOVIC

GRAND PRIZE WINNER: ECOLOGY AND ENVIRONMENT
Stilianos Louca
As an undergraduate, Stilianos Louca studied physics and mathematics at the Friedrich-Schiller-Universität, Germany, before going on to attain a Ph.D. in applied mathematics at the University of British Columbia, Canada. During his doctoral research, he investigated how microorganisms, in particular their genes, interact with the environment and with each other to drive elemental fluxes at ecosystem scales. Louca is currently a postdoctoral researcher at the Biodiversity Research Centre in Vancouver, where he continues to investigate the ecology and evolution of microbial metabolism using mathematical modeling, molecular sequencing, and laboratory experiments. www.sciencemag.org/content/358/6368/1264

FINALIST: TRANSLATIONAL MEDICINE
Jared Mayers
Jared Mayers is a resident in internal medicine at Brigham and Women’s Hospital in Boston, MA, working toward a career that balances basic science research with clinical practice. After completing his undergraduate degree at Williams College, he earned an M.D. from Harvard Medical School and a Ph.D. in biology from the Massachusetts Institute of Technology. His research interests center on identifying and understanding the mechanisms driving whole-body metabolic alterations and tissue interactions in early disease states. Outside of the hospital and lab, he enjoys running and spending time with his family. www.sciencemag.org/content/358/6368/1265.1

FINALIST: GENOMICS AND PROTEOMICS
Kelley Harris
Kelley Harris studied mathematics as an undergraduate at Harvard and transitioned into genomics during a postgraduate year at the Wellcome Trust Sanger Institute. She then earned a Ph.D. in mathematics at the University of California, Berkeley, with a designated emphasis in computational biology, where she continued building statistical methods that describe how genome sequences evolve. In January 2018, Harris will finish her postdoctoral fellowship at Stanford and will become an assistant professor of genome sciences at the University of Washington. www.sciencemag.org/content/358/6368/1265.2

FINALIST: CELL AND MOLECULAR BIOLOGY
Mijo Simunovic
A native of Europe, Mijo Simunovic sought higher education in the United States and in France, earning a Ph.D. in theoretical chemistry from the University of Chicago and a Ph.D. in experimental physics from the University of Paris. In his scientific work, he pursues complex biological problems that are fundamentally driven by physics. Currently, he is at The Rockefeller University where, as a junior fellow of the Simons Society, he uses stem cells to build experimental models of the human embryo, aimed at elucidating the earliest events in human development. Simunovic is passionate about teaching, having served as a teaching consultant at the University of Chicago and instructed undergraduate biophysics courses in Chicago and New York. www.sciencemag.org/content/358/6368/1265.3
Probing the metabolism of microorganisms
Stilianos Louca

Science 358 (6368), 1264-1265.
DOI: 10.1126/science.aar2000