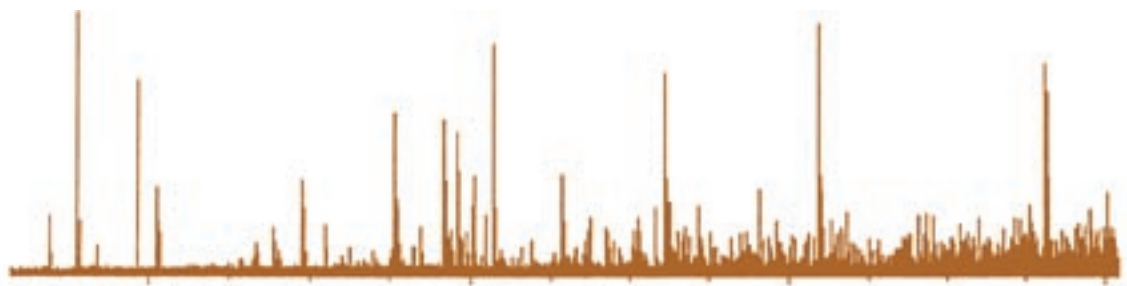


GARY L. ANDERSEN IOANNA LETSIU AND MARTINA HAUSNER

A Vista for Microbial Ecology and Environmental Biotechnology

**A consensus view
for the partnership
of microbial ecology
and environmental
biotechnology.**

BRUCE E. RITTMANN
ARIZONA STATE UNIVERSITY
MARTINA HAUSNER
NORTHWESTERN UNIVERSITY
FRANK LÖFFLER
GEORGIA INSTITUTE OF TECHNOLOGY
NANCY G. LOVE
VIRGINIA POLYTECHNIC INSTITUTE AND
STATE UNIVERSITY
GERARD MUYZER
DELFT UNIVERSITY OF TECHNOLOGY
(THE NETHERLANDS)
SATOSHI OKABE
HOKKAIDO UNIVERSITY (JAPAN)
DANIEL B. OERTHER
UNIVERSITY OF CINCINNATI
JORDAN PECCIA
YALE UNIVERSITY
LUTGARDE RASKIN
UNIVERSITY OF MICHIGAN
MICHAEL WAGNER
UNIVERSITY OF VIENNA (AUSTRIA)



Microbial ecology and environmental biotechnology are blossoming fields that are taking advantage of profound advances in biology, materials, computing, and engineering. Although traditionally microbial ecology and environmental biotechnology have been distinct disciplines, their futures are intimately linked. Together, they offer much promise for helping society deal with some of its greatest challenges in environmental quality, sustainability, security, and human health.

What are these exciting fields? How do they connect to each other? And what is their common vista? How will microbial ecologists and environmental biotechnologists invest their resources so that the two fields, working as partners, create the greatest scientific advancements and benefits to society? That was the question for the symposium held last April at Arizona State University. The symposium's 10 speakers, who are also the authors of this article, are all considered international leaders working at the interface of microbial ecology and environmental biotechnology. These experts participated in focused discussion sessions aimed at arriving at a consensus view on the most important directions for the partnership of the two fields.

This Viewpoint describes the dramatic and promising vista that the symposium's participants saw for the partnership of microbial ecology and environmental biotechnology.

Microbial ecology—The science

Microbial ecology is a long-standing scientific discipline that is undergoing remarkable, even revolutionary, changes. The core of the field aims to understand microbial communities, which are self-organizing and self-sustaining assemblages of different microorganisms, and how these communities interact with their environment.

The science of microbial ecology tries to answer four fundamental questions. First, what microorganisms are present in the community? The phylogenetic makeup (identity and number) of the microorganisms present in a community is called a *community structure*. Next, what are the capabilities of the microorganisms for carrying out reactions that transform the community's environment? The catalog of catalytic capabilities is called the community's *phenotypic potential*. Third, what reactions and transformations are the community members actually performing? The realization of phenotypic potential is called the community's *function*. Finally,

what are the interrelationships among the community's members and between them and their environment? Interrelationships involve spatial organization (i.e., who is near whom) and materials that the microorganisms exchange. Understanding these interrelationships is the ultimate goal of microbial ecology (1).

Answers to these four questions usually change over time and especially in response to perturbations to the environment. The ability of microbial communities to respond to environmental changes (natural or anthropogenic) is called community *resilience* and *stability*, and it influences each of the four questions.

The beginnings of microbial ecology can be traced back at least to the late 1940s and 1950s; great conceptual advancements were made in the 1960s and early 1970s (1, 2). However, microbial ecology struggled as a scientific discipline for decades because of a simple reality: Tools to address the four fundamental questions either did not exist at all or were unreliable. The small sizes and simple shapes of microorganisms made morphology a tedious and insufficient gauge of identity. Selective culturing on the basis of metabolic function was a giant step forward, conceptually and in practice, but often failed or gave biased results (3). Thus, brilliant microbiologists labored to gain the faintest glimpse of the diversity and organization of microbial communities. They knew that so much more could be learned, if they only had the tools.

The use of molecular biology tools, beginning around 1985, started to change the prospects for microbial ecologists. Selective and reliable amplification of defined DNA with the polymerase chain reaction (PCR) and hybridization with DNA oligonucleotides made it possible to interrogate directly the genetic information of individual microorganisms and entire communities. The small-subunit ribosomal RNA (SSU rRNA, also known as 16S rRNA for prokaryotes) was the first target for hybridization

and is still the most widely used. This rRNA gives information on the phylogenetic identity of the microorganisms (4), and this addresses the first fundamental question of microbial ecology.

Other targets within the genetic system of microorganisms answer different questions (5). For example, amplifying and detecting specific genes in the genome of microorganisms in the community defines the phenotypic potential (6), and this addresses the second question about the capability of microorganisms. Messenger RNA (mRNA) reveals which genes are being expressed and, therefore, which functional proteins likely are formed (7). This gives information on the expressed phenotypic potential, or the third question about the community's function. Assessing RNA targets by using microscopic visualization, such as with fluorescence in situ hybridization (FISH) (8), (see top photo, p 1096) adds information on spatial organization. Recently, microbial ecologists have begun to clone and sequence large genome fragments from various microbial communities (9); therefore, it is now possible, at least for low-diversity communities, to reconstruct entire genomes of uncultured community members (10). In addition, microautoradiography, coupled with FISH (i.e., MAR-FISH) (11) and stable-isotope probing (12), makes it possible to detect the function in the community, even when the researcher has no idea what genes or mRNA should be detected.

Criteria for a successful environmental biotechnology for detoxification or resource capture

The technology must be practical at a large scale. Relevant units normally are thousands of cubic meters per day for flow or tons for mass.

It must operate reliably and continuously around the clock. The concept of a "time-out" normally is not relevant. The technology must be relatively simple to operate and largely self-correcting without much human intervention.

It must be economical to build and operate. The services provided are so essential to society that they cannot be priced out of the reach of those on the lowest rung of society's economic ladder.

Environmental biotechnology—The service

Environmental biotechnology manages microbial communities that provide services to society. Prominent and emerging services include removing contaminants from water, wastewater, sludge, sediment, or soil; capturing valuable products from renewable resources (e.g., biomass), particularly energy carriers but also nutrients, metals, and water; sensing contaminants or pathogens in the environment or, perhaps, in humans; and protecting the public from dangerous exposure to pathogens.

These services are essential if modern human society is to be safe, sustainable, and secure. Microbiological communities, properly managed, can provide these services reliably, continuously, economically, and without creating other hazards.

Environmental biotechnology is almost a century old, although this name is relatively new. Past names include biological treatment, biological processes, bioprocess engineering, bioremediation, and bioenvironmental systems. The new name reflects that environmental biotechnology is adapting and benefiting from the modern tools of molecular biology, as well as from other advances in science and technology.

The scientific foundation of environmental biotechnology is microbial ecology. Because environmental biotechnology ultimately aims to manage microbial communities for the good of society, a deep understanding of microbial communities—that is, microbial ecology—is essential. Environmental biotechnology addresses real-world goals by managing microbial communities, rather than finding or creating the solves-all-problems "superbug".

The box at left lists criteria for a successful environmental biotechnology for removing contaminants or resource capture. These criteria demand a robust, self-organizing, and self-sustaining microbial community; they do not cater to a highly specialized or pampered superbug. Thus, the goal is to understand microbial communities so that the system's conditions lead to robust communities that provide the desired service.

Needs pull, science pushes

A field that has been around for a century usually does not show a burst of creativity, but environmental biotechnology is doing just that today. The reason is the convergence of a strong "needs pull" with a strong "science push". Today, environmental biotechnology gets a powerful pull from the needs of human society arising from increasing challenges to achieve sustainability, environmental quality, security, and human health.

The sustainability of modern human society depends on extracting essential materials from renewable resources and reducing reliance on non-renewable resources. At the top of the list of at-risk resources are two that environmental biotechnology addresses directly: water and energy. Today, water providers are forced to tap sources of lower quality: polluted ground and river water, eutrophic lake and reservoir water, and wastewater. These poor-quality sources need substantial treatment to eliminate public-health risks, unpleasant taste and odor, and discoloration. Experts on the Middle East predict that water—not oil—will be the greatest future cause of strife in this region.

After water, energy is the most precious resource, and future sources must shift from fossil fuels to renewable ones. Environmental biotechnology is at the heart of upgrading poor water sources for human use and for converting renewable energy sources—particularly biomass and sunlight—to useful forms, including natural gas, hydrogen, and electricity.

Organics, nutrients, and metals that are not captured but are instead discharged to the environment become pollutants, not resources. Environmental biotechnology has a long-standing role in treating wastewater and other contaminated water, air, and solids (13, 14). Increasing population, urbanization,

and economic activity heighten the need to apply environmental biotechnology to preserve (or improve) environmental quality, along with capturing valuable resources. Innovative environmental biotechnology approaches appear to be well suited for improving environmental quality in developed and developing countries alike (15). The readiness of developing countries to use these technologies lies in their improved reliability and operability in a decentralized setting.

Security and human health also relate to environmental biotechnology. Infectious diseases from pathogenic microorganisms remain the main cause of death worldwide, and terrorist threats to disseminate pathogens heighten the danger. Microbial systems can monitor for pathogens or chemical toxins in hospitals, water supplies, the air, and, perhaps, even humans. Microbial systems also contribute to cures or therapies by producing drugs or enzymes to fight diseases.

Environmental biotechnology can contribute in all these ways because microbial communities have seemingly infinite ways to live, even in environments that appear to be bizarre or hostile. Their ability to organize and sustain themselves provides human society with a cornucopia of metabolic potential to find services to benefit society. Microbial ecology, the core scientific discipline, allows us to understand microorganisms as part of their communities: "to think like the microorganisms." Armed with this deep insight, the environmental microbiologist can create sustainable systems that "work for the microorganisms so that they work for us."

On the science side, the great advances in microbial ecology, previously summarized, stand at the head of the science push and tend to garner the greatest credit. However, microbial ecology is not the only strong science push behind environmental biotechnology at the beginning of the 21st century.

The products of modern materials science provide another hearty push, perhaps as important as from microbial ecology. The materials push began around 1970, when lightweight, high-strength plastics made possible biological towers for wastewater treatment, which were the first biofilm processes with high surface areas and small footprints (14). From the 1980s through the 1990s, lightweight biofilm carriers in the form of gravel-sized pellets made even more compact, high-rate processes possible (14). From the late 1990s to today, microfiltration membranes have been replacing gravity separators for activated sludge, improving effluent quality, reliability, and compactness (15). More recently, the membrane biofilm reactor makes it possible to use H_2 to reduce NO_3^- , ClO_4^- , and a large range of oxidized contaminants in drinking water, groundwater, and wastewater (16). Recent advancements in nanoscale (1–100-nm) materials (17) and biomicroelectromechanical systems (bioMEMS) technologies (18) surely will provide similar opportunities.

Another science push comes from mathematical modeling, the ultimate tool for integrating the large number of microbiological, chemical, and physical processes that occur in any microbial community

of environmental significance. A model uses mass-balance equations to represent the significant components in the community (19). Creating a model demands that the modeler identify the important system components, for example, the critical types of microorganisms, the substrates they consume, and the products they produce. Likewise, the modeler must represent the important reactions, such as the synthesis of new biomass, consumption of

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substrates, and generation of products, with mathematical expressions that capture what is known about the microorganisms and how they function. On the one hand, modeling is an exercise in integrating all that we know about microorganisms so that we can test and exploit our understanding of how the microbial communities work as a functioning ecosystem. On the other hand, modeling is the best way to find out what we do not understand about the microorganisms and their interrelationships with each other and their environment. When we cannot model a system, we can identify what we do not understand, and this helps us direct fundamental research to the most important questions.

Whether the goal is gaining scientific understanding or applying that understanding to create high-value services or products, the most fundamental questions are at the interface of microbial ecology and environmental biotechnology. Perhaps the overarching question is, "How do microbial communities self-assemble to achieve and maintain a function?"

The environmental biotechnologist depends on self-assembly once the proper conditions are in place. Therefore, self-assembly needs to be based on identifiable principles that can be put into practice. The overarching question then leads to corollary questions: What are the underlying principles of self-assembly? What community structure is optimal for a biotechnological application? What environmental conditions trigger assembly of the desired community with its desired function? Are the conditions and outcomes predictable, reproducible, and controllable?

Self-assembly also implies that microbial communities behave as a kind of multicellular organism, one in which the whole is more than the sum of its parts. Corollary questions along this line of inquiry include: Does the community have a multicellular

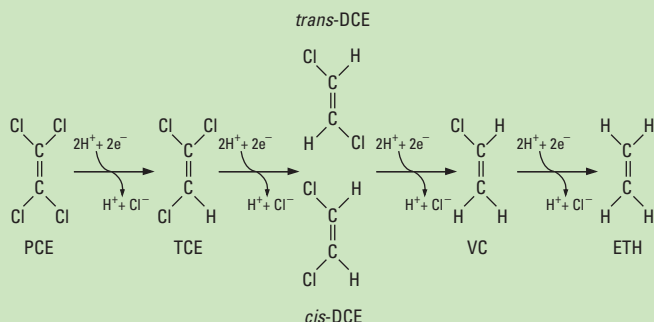
“life of its own”? How do the microorganisms communicate and coordinate to gain the advantages of a multicellular state? What are the advantages, if any, to the community and to humans?

A three-peak vista

The consensus vista for the partnership of microbial ecology and environmental biotechnology shows three “peaks” in the distance, representing different themes: more powerful analytical tools, integrated “—omics” approaches, and research that is more theory- or process-driven.

Complete biodegradation of PCE

Tetrachloroethene (PCE) and trichloroethene (TCE) are all-too-common groundwater contaminants that threaten human health. Basic research over the past decade brought to light a novel group of microbes, the *Dehalococcoides*, that can detoxify the troublesome chloroethenes (28, 29). *Dehalococcoides* capture energy from reductive dechlorination reactions, thus making a living by reducing toxic groundwater contaminants. The reductive dechlorination pathway that leads to the complete detoxification of PCE and TCE to nonhazardous ethane (ETH) is shown below.



A critical aspect is removing all chlorine substituents from the ethene backbone, because the last chlorinated intermediate, vinyl chloride (VC), is more toxic than the parent compounds. Some *Dehalococcoides* organisms, such as strain BAV1, efficiently detoxify dichloroethene (DCE) and VC, thereby producing environmentally benign ETH and inorganic chloride (28).

Consortia containing *Dehalococcoides* organisms have been successfully applied at field sites where the intrinsic microbiology was insufficient to sustain acceptable degradation rates (27). Knowing the key players (i.e., *Dehalococcoides*) and understanding the microorganisms' ecology were critical for successful technology implementation. For example, nucleic-acid-based tools (e.g., quantitative real-time [qRTm] PCR) were designed to specifically detect and quantify *Dehalococcoides* 16S rRNA genes (29) and genes implicated in VC reductive dechlorination (30). These diagnostic and prognostic tools changed chloroethene bioremediation to a predictable science with obvious benefits to society.

More powerful analytical tools. The strongest science push in microbial ecology comes from the explosion of new molecular tools (see box above). These tools have propelled the field forward, which makes it possible to answer questions that we could not think to ask in the not-so-distant past. Nonetheless, existing tools are inadequate for studying the complexity of microbial ecosystems and supporting the design and operation of innovative environmen-

tal biotechnology approaches. Shortcomings include methods that produce results too slowly and with too much effort, have biases, are too expensive, offer insufficient quantification, and lack coverage over the ranges of structure and function that are important in relevant microbial communities.

To overcome these shortcomings, developers of new molecular tools need to meet four criteria. First, the methods must be high-throughput, generating relevant data in minutes to a few hours. Second, the outputs must be quantitative enough to provide the information that sorts out the “lead actors” from the “bit players” for a given function and sufficiently sensitive to find the important microorganisms or reactions even when others dominate in numbers. Third, the outputs must provide the type of information that reveals structure and function in parallel, because they are intimately connected. Finally, methods must put more emphasis on the structure and function of eukaryotes and phages in order to yield a more complete picture of community structure and function. Ideally, more than one method should be applied to generate data (e.g., PCR-based and PCR-independent approaches).

Integrate the “—omics” approaches. Most molecular interrogation has been directed toward DNA, focused on selected genes (4, 7, 8), or (recently) aimed at high-throughput genomics (9, 10). Although the potential for expanding capabilities in environmental genomics is enormous and must be pursued with vigor, resources also need to be invested in developing and using tools on the basis of the other molecules within the cells, or the other —omics disciplines. The primary other —omics are transcriptomics, which is the study of mRNA as an indicator of gene expression; proteomics, which focuses on protein (enzyme) identification, characterization, and quantification as they relate to cellular function; lipomics, which targets the study of membrane lipids; and metabolomics, which studies the metabolic intermediates of cellular functions.

Each of the several —omics approaches provides different but complementary information that reveals distinct information about communities. Information from genomic and proteomic studies forms a comprehensive picture of the cellular response to perturbations or other changes in the environment; however, metabolomics reveals the ultimate functional response and is most likely to predict community phenotype (20).

A great challenge is to borrow strategies that were developed for the analysis of single organisms and apply them to complex microbial communities containing many and often unknown species (21). Initial success stories of monitoring gene expression (22) and protein formation (23) are encouraging and provide important guidance for future designs.

The hallmark of high-value —omics technology is the integration of the high-throughput data. An essential element is bioinformatics tools, which offer database support for data management and mining and biostatistics to maximize the benefit of these expensive and labor-intensive methods. Our current format for disseminating scientific results (e.g., ref-

ered journal papers) is not ideally suited to handle the massive data sets of—omics-based experiments. Long-term stewardship and maintenance of these data over time must be addressed.

Make the research more theory- or process-driven. Molecular-based research in microbial ecology has developed an image of “stamp collecting”, or the gathering of a lot of data because it is possible with the available tools. This enthusiasm for data collection is natural in an emerging field and was necessary when so little information was available before. Having any information is a giant leap forward, and no one knows a priori what will be the most interesting findings. Therefore, collecting microbiological stamps has been essential and will never disappear.

After 15 or so years of profitable stamp collecting, microbial ecology and environmental biotechnology are poised to advance to a higher plane of molecular-based research. This next step will emphasize research driven by ecological theory, process needs, or both.

Molecular-based research in microbial ecology has developed an image of “stamp collecting”.

The field of macroecology has developed elaborate theories about ecosystem succession, diversity, invasion, and stability, such as the hypothesis that highly diverse ecosystems are more stable (24). Statistical and deterministic modeling tools have been developed to design experiments and interpret results (25). For the most part, these theories have not penetrated microbial ecology. Without a doubt, the application of ecological theory from macroecology will demand a major modification to take into account the fundamental differences between systems of macroecology and microbial ecology (14). For example, microbial ecosystems deal with huge numbers of cells (e.g., more than trillions of bacteria per liter of water) that often cannot be differentiated as individuals; this contrasts with much smaller numbers of identifiable individuals in a macroecosystem. In addition, macroecosystems are based to a large degree on specific prey–predator relationships, whereas microbial ecosystems more often target the parallel metabolism and exchange of materials, despite predation being important (albeit poorly understood). Thus, the simplistic application of macroecology theory to microbial ecosystems would likely backfire. Nonetheless, proper application of ecological concepts—such as diversity, stability, competition, redundancy, and allied tools—provides a powerful intellectual framework for designing research and understanding the meaning of the results (26).

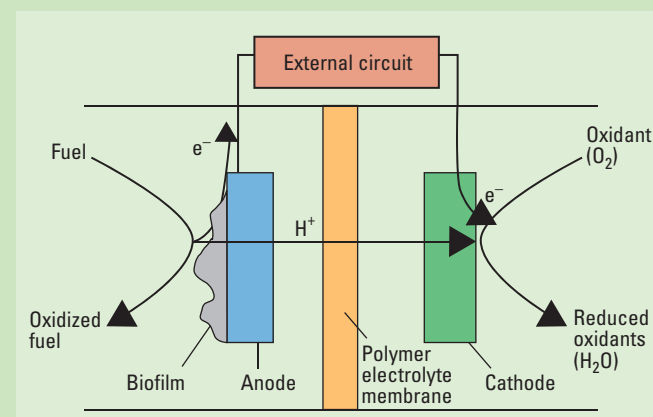
The next plane of research also needs to be process-driven rather than tools-driven. Now that a wide array of tools is available and continuing to expand, the researcher can ask critical questions about

the process and then pick the right tools to find the answers. This approach allows researchers to take a more holistic approach toward understanding community structure and function. The researcher can form a hypothesis and bring in a range of molecular, modeling, and other tools to gain information that tests the hypothesis. A powerful research tool is to perturb the microbial community and then observe whether the organisms respond in the predict-

Bioelectricity from the microbial fuel cell

More than 20 years ago, researchers noticed that a fuel cell containing microorganisms could generate electricity (31), but how it occurred was a mystery. Several years later, researchers started discovering that certain bacteria could transfer electrons to solid-phase acceptors, such as iron oxides (32). If they could reduce a solid-phase acceptor, could they also transfer electrons to a solid-phase electrode acting as an anode in a fuel cell? The answer was a resounding “yes” (33, 34). Thus, the revolutionary concept of a microbial fuel cell (MFC) was born.

As shown in the diagram, an MFC operates in the same manner as does a conventional fuel cell, except that bacteria living as a biofilm on the anode catalyze the oxidation of the fuel. The MFC is still at an early research stage, but it can be a revolutionary breakthrough for capturing renewable energy sources. The bacterial catalysis at the anode makes it possible, for the first time, to use renewable organic material (biomass) as a fuel for fuel cells. In contrast, conventional fuels cells use an expensive platinum catalyst on the anode and still can use only high-grade H_2 , which is obtained by reforming petroleum, a nonrenewable energy resource. By operating at ambient temperature and without combustion, an MFC can more than double energy-capture efficiency while eliminating air pollution. Recent work shows that specialized bacteria are not necessary to generate electricity from organics in an MFC (35), but inspiration comes from the fundamental studies on physiology, ecology, and genomics of particular metal-reducing bacteria.



ed manner. In this hypothesis-driven approach, the questions lead to selection of the tools; this is a welcome reversal from the common situation in which tools dictate what questions can be addressed.

Theory- and process-driven research must recognize the role of scale—spatial and temporal. Microorganisms are generally on the order of a few micrometers in size, and microbial aggregates are only occasionally >1 mm. The technological pro-

cesses in which microbial communities are used are very much larger. Even a bench-scale bioreactor has dimensions in centimeters, and full-scale systems measure in meters, often in tens of meters. Research that focuses on the micrometer-to-millimeter scale relates to what happens at the scale of meters, but the application is not always simple.

Detecting airborne infectious diseases

The recognition of emerging airborne infectious diseases, such as avian influenza and severe acute respiratory syndrome (SARS), as well as heightened concerns over bioterrorism, has put a spotlight on the persistent public-health problem of airborne infectious disease. For decades, public-health professionals were poorly equipped to measure or identify pathogens in air. Now, the application of microbial ecology principles and techniques to aerosols holds tremendous promise for explaining airborne disease epidemiology and designing systems that minimize our exposure to allergens, cold viruses, and other current and emerging infectious airborne agents.

For example, although >1.5 million people die from tuberculosis each year and one-third of the world's population has been exposed to *Mycobacterium tuberculosis*, viable bacteria have never been cultured from an ambient air sample. *M. tuberculosis* cells were recently detected in indoor air by a polymerase chain



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reaction (PCR) assay (36). PCR-based measurement of rhinoviruses in office-building air, in conjunction with human epidemiology studies and measurement of ventilation rates, has led to a rethinking of how humans catch colds (37).

The photograph shows a DNA microarray with the potential for describing >9000 taxonomic groups (38).

In such a situation, modeling can be of special value, because it takes into account transport processes and heterogeneity. In parallel with spatial scales, the range of temporal scales is extreme. A classic microbiology experiment might last 1 day, and an experiment on microbial ecology might last for a few months and have controlled operating conditions; however, a real-world process operates continuously for years and with unpredictable changes in temperature, substrate loading, and other factors. It seems logical that increasing time horizons and variability affect community structure and, perhaps, function. These effects need to be addressed directly in research design and how results are interpreted.

Where are the benefits and roadblocks?

Skeptics demanding proof that “molecular research is really improving environmental technology” have confronted all of the participants in the vista symposium. Skeptics want specific examples of cause and effect in which research led directly to a new or improved process. Perhaps they seek a single “magic bullet”. Up to now, direct, incontrovertible proof has been scarce, but it is beginning to emerge (27).

The demand to see cause and effect is justifiable, and the partnership of microbial ecology and environmental biotechnology needs to satisfy the demand. Achieving the three-peak vista will go a long way toward satisfying critics and attracting new supporters of the partnership. The immediate and direct payout from the science research is thinking like the microorganisms. Then, good engineering and modern materials can translate the understanding into systems that manage the microbial communities to provide new and better services: working for the microorganisms so that they work for us. It is a two-part process that grows and harvests the fruit of microbial ecology and environmental biotechnology. Although the partnership of microbial ecology and environmental biotechnology may not have such dramatic results yet, the boxes on pages 1100–1102 give concrete examples that fruits are beginning to be harvested.

Despite these impressive achievements that are beginning to emerge and the high potential for the partnership, roadblocks are inevitable because of the inherent complexities of environmental microbial ecosystems. First, the numbers of different microbial strains are enormous—de facto infinity. Furthermore, only a tiny fraction of the strains have been cultured and characterized. Second, microorganisms can evolve rapidly—we face a perennial “moving target”. Third, environmental microbial ecosystems are physically complex aggregates that change in time and space. Fourth, the environmental matrices of sludge, wastewater, sediment, and soil are “dirty”—a special problem for extracting cellular material and avoiding interferences. Fifth, a microbial ecosystem needs to be understood in terms of its structure, function, and interactions with other ecosystems in order to achieve society's goals. In summary, the study of microbial ecology in the context of environmental biotechnology is substantially more difficult than its study in medical settings, where many of the tools originated. Thus, connecting microbial ecology to environmental biotechnology always will demand a lot of hard work, persistence, and creativity as roadblocks are identified and overcome.

The study of microbial ecology in the context of environmental biotechnology is substantially more difficult than its study in medical settings.

Modern-day microbial ecology and environmental biotechnology are young disciplines, still finding their identities separately and as partners. As with any emerging field, its researchers and the society that supports them must have a degree of faith that

an investment of resources will yield a large benefit, because this is the way breakthrough advances in science and technology often have been made. Scientists first construct a “cathedral of knowledge”, which inspires and enables creativity that leads to the great technological breakthroughs. Perhaps microbial ecology and environmental biotechnology are putting up the buttresses of the cathedral now.

Bruce E. Rittmann is a professor and director of the Center for Environmental Biotechnology at Arizona State University. Martina Hausner is an assistant professor in the Department of Civil and Environmental Engineering at Northwestern University. Frank Löffler is an associate professor in the School of Civil and Environmental Engineering at the Georgia Institute of Technology. Nancy G. Love is a professor in the Department of Civil and Environmental Engineering at Virginia Polytechnic Institute and State University. Gerard Muyzer is an associate professor in the Department of Biotechnology at the Delft University of Technology. Satoshi Okabe is an associate professor in the Department of Urban and Environmental Engineering at Hokkaido University. Daniel B. Oerther is an assistant professor in the Department of Civil and Environmental Engineering at the University of Cincinnati. Jordan Peccia is an assistant professor in the Department of Chemical Engineering at Yale University. Lutgarde Raskin is a professor in the Department of Civil and Environmental Engineering at the University of Michigan. Michael Wagner is a professor and director of the Department of Microbial Ecology at the University of Vienna. Address correspondence to Rittmann (Rittmann@asu.edu).

References

- Alexander, M. *Microbial Ecology*; Wiley: New York, 1971.
- Alexander, M. *Introduction to Soil Microbiology*; Wiley: New York, 1961.
- Amann, R.; Ludwig, W.; Schleifer, K. H. Phylogenetic Identification and *In Situ* Detection of Individual Microbial Cells without Cultivation. *Microbiol. Rev.* **1995**, *59*, 143–169.
- Pace, N. R.; et al. The Analysis of Natural Microbial Populations by Ribosomal RNA Sequences. *Adv. Microb. Ecol.* **1985**, *9*, 1–55.
- Rittmann, B. E. The Role of Molecular Methods in Evaluating Processes Used in Environmental Biotechnology. *Water Environ. Res.* **2002**, *74*, 421–427.
- Wagner, M.; Loy, A. Bacterial Community Composition and Function in Sewage Treatment Systems. *Curr. Opin. Biotechnol.* **2002**, *13*, 218–227.
- Sharkey, F. H.; Banat, I. M.; Marchant, R. Detection and Quantification of Gene Expression in Environmental Bacteriology. *Appl. Environ. Microbiol.* **2004**, *70*, 3795–3806.
- Wagner, M.; Horn, M.; Daims, H. Fluorescence *In Situ* Hybridisation for the Identification and Characterisation of Prokaryotes. *Curr. Opin. Microbiol.* **2003**, *6*, 302–309.
- Handelsman, J. Metagenomics: Application of Genomics to Uncultured Microorganisms. *Microbiol. Mol. Biol. Rev.* **2004**, *68*, 669–685.
- Venter, J. C.; et al. Environmental Genome Shotgun Sequencing of the Sargasso Sea. *Science* **2004**, *304*, 66–74.
- Lee, N.; et al. Combination of Fluorescent *In Situ* Hybridization and Microautoradiography. *Appl. Environ. Microbiol.* **1999**, *65*, 1289–1297.
- Manefield, M.; et al. RNA Stable Isotope Probing, a Novel Means of Linking Microbial Community Function to Phylogeny. *Appl. Environ. Microbiol.* **2002**, *68*, 5367–5373.
- Fair, G. M.; Geyer, J. C.; Okun, D. A. *Water and Wastewater Engineering*; Wiley: New York, 1971.
- Rittmann, B. E.; McCarty, P. L. *Environmental Biotechnology: Principles and Applications*; McGraw-Hill: New York, 2001.
- Daigger, G. T.; et al. Are Membrane Bioreactors Ready for Widespread Application? *Environ. Sci. Technol.* **2005**, *39*, 399A–406A.
- Rittmann, B. E.; et al. The Hydrogen-Based Hollow-Fiber Membrane Biofilm Reactor (HFMBfR) for Reducing Oxidized Contaminants. *Water Science and Technology: Water Supply* **2004**, *4* (1), 127–133.
- Wiesner, M. R.; Colvin, V. L. Environmental Implications of Emerging Nanotechnologies. In *Environmentalism & the Technologies of Tomorrow: Shaping the Next Industrial Revolution*; Olson, R. L., Rejeski, D., Eds. Island Press: Washington, DC, 2003.
- Sakamoto, C.; Yamaguchi, N.; Nasu, M. Rapid and Simple Quantification of Bacterial Cells by Using a Microfluidic Device. *Appl. Environ. Microbiol.* **2005**, *71*, 1117–1121.
- Wanner, O.; et al. *Mathematical Modeling of Biofilms*; IWA Publishing: London, 2005.
- Dettmer, K.; Hammock, B. D. Metabolomics—A New Exciting Field within the “omics” Sciences. *Environ. Health Perspec.* **2004**, *112*, A396–A397.
- Wagner, M. Crystal Ball: The Community Level: Physiology and Interactions of Prokaryotes in the Wilderness. *Environ. Microbiol.* **2005**, *7*, 472–485.
- Dennis, P.; et al. Monitoring Gene Expression in Mixed Microbial Communities by Using DNA Microarrays. *Appl. Environ. Microbiol.* **2004**, *69*, 769–778.
- Ram, R. J.; et al. Community Proteomics of a Natural Microbial Biofilm. *Science* **2005**, *308*, 1915–1920.
- Johnson, K. H.; et al. Biodiversity and the Productivity and Stability of Ecosystems. *Trends in Ecology and Evolution* **1996**, *11*, 372–377.
- Horner-Devine, M. C.; Carney, K.; Bohannon, B. J. M. An Ecological Perspective on Bacterial Biodiversity. *Proc. R. Soc. B* **2004**, *271*, 113–122.
- Curtis, T. P.; Head, I. M.; Graham, D. W. Theoretical Ecology for Engineering Biology. *Environ. Sci. Technol.* **2004**, *37*, 64A–70A.
- Major, D. W.; et al. Field Demonstration of Successful Bioaugmentation to Achieve Dechlorination of Tetrachloroethene to Ethene. *Environ. Sci. Technol.* **2002**, *36*, 5106–5116.
- He, J.; et al. Isolation and Characterization of *Dehalococcoides* sp. Strain FL2, a Trichloroethene (TCE) and 1,2-Dichloroethene-Respiring Anaerobe. *Environ. Microbiol.* **2005**, *7*, 1442–1450.
- He, J.; et al. Detoxification of Vinyl Chloride to Ethene Coupled to Growth of an Anaerobic Bacterium. *Nature* **2003**, *424*, 62–65.
- Krajmalnik-Brown, R.; et al. Genetic Identification of a Putative Vinyl Chloride Reductase in *Dehalococcoides* sp. Strain BAV1. *Appl. Environ. Microbiol.* **2004**, *70*, 6347–6351.
- Wingard, L. B.; Shaw, C. H.; Castner, J. F. Bioelectrochemical Fuel Cells. *Enzyme Microb. Technol.* **1982**, *4*, 137–142.
- Lovley, D. R.; Phillips, E. J. P. Novel Mode of Energy Metabolism: Organic Carbon Oxidation Coupled to Dissimilatory Reduction of Iron or Manganese. *Appl. Environ. Microbiol.* **1988**, *54*, 1472–1480.
- Bond, D. R.; Lovley, D. R. Electricity Production by *Geobacter sulfurreducens* Attached to Electrodes. *Appl. Environ. Microbiol.* **2003**, *69*, 1548–1555.
- Kim, H. J.; et al. A Mediator-Less Microbial Fuel Cell Using a Metal-Reducing Bacterium, *Shewanella putrefaciens*. *Enzyme Microb. Technol.* **2002**, *30*, 145–152.
- Liu, H.; Ramnarayanan, R.; Logan, B. E. Production of Electricity During Wastewater Treatment Using a Single-Chamber Microbial Fuel Cell. *Environ. Sci. Technol.* **2004**, *38*, 2281–2285.
- Chen, P. S.; Li, C. S. Quantification of Airborne *Mycobacterium tuberculosis* in Health Care Setting Using Real-Time qPCR Coupled to an Air-Sampling Filter Method. *Aerosol Sci. Technol.* **2004**, *39*, 371–376.
- Myatt, T.; et al. Detection of Airborne *Rhinovirus* and Its Relation to Outdoor Air Supply in Office Environments. *Am. J. Resp. Crit. Care* **2004**, *169*, 1187–1190.
- Wilson, K. H.; et al. High-Density Microarray of Small-Subunit Ribosomal DNA Probes. *Appl. Environ. Microbiol.* **2002**, *68*, 2535–2541.