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Mainstreaming Microbes across Biomes

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Bacteria, fungi, and other microorganisms in the environment (i.e., environmental microbiomes) provide vital ecosystem services and affect human health. Despite their importance, public awareness of environmental microbiomes has lagged behind that of human microbiomes. A key problem has been a scarcity of research demonstrating the microbial connections across environmental biomes (e.g., marine, soil) and between environmental and human microbiomes. We show in the present article, through analyses of almost 10,000 microbiome papers and three global data sets, that there are significant taxonomic similarities in microbial communities across biomes, but very little cross-biome research exists. This disconnect may be hindering advances in microbiome knowledge and translation. In this article, we highlight current and potential applications of environmental microbiome research and the benefits of an interdisciplinary, cross-biome approach. Microbiome scientists need to engage with each other, government, industry, and the public to ensure that research and applications proceed ethically, maximizing the potential benefits to society.

Keywords: microbiology, environmental science, human ecology, aquatic ecosystems, soil science

There are seemingly daily revelations about the influence that microbial communities have on human health. Such revelations have generated significant public interest in the human microbiome, highlighted by the rise of products such as gut health cookbooks, probiotic supplements, microbially enhanced yogurts, and the revival of fermented foodstuffs, such as kombucha. There is growing awareness that humans are walking ecosystems, dependent on the microbial communities living in and on our bodies.

Although public interest in the human microbiome has flourished, the awareness of environmental microbiomes—including ambient marine, freshwater, aerial, and terrestrial microbiomes—and their importance has not. Environmental microbiology has played a key role in the history and development of microbiome technology. Most clinically relevant antibiotics were isolated from soil microbes, and the majority of antimicrobial resistance genes may have originated from environmental bacteria (Cantas et al. 2013). Similarly, the first shotgun metagenomes and single-cell genomes were sequenced from marine microbes (Breitbart et al. 2002, Zhang et al. 2006). Environmental microbiomes are at the leart of nutrient cycling in both aquatic and terrestrial environments; provide essential ecosystem services, such as carbon dioxide drawdown and oxygen production, with

a central role in determining the impact of climate change (Cavicchioli et al. 2019); and are intimately linked to human microbiomes and health (Hanski et al. 2012, Stein et al. 2016). A greater awareness of the importance of environmental microbial communities is therefore critical from both ecological and human health perspectives.

In this article, we highlight the value of environmental microbiome science by describing current and potential future applications. We use global microbial data sets to explore how microbial communities are shared across human, terrestrial, and aquatic environments. We then analyze microbiome citation trends across disciplines to investigate the degree of interdisciplinarity between human and environmental microbiome research. We conclude by raising key challenges in advancing interdisciplinary microbiome science, including the emerging ethical complexities and engaging the public in the debates at the center of shared human-environment microbiome science.

Applications of environmental microbiome science

Environmental microbiome research has an extraordinary range of applications (figure 1). Early applications of environmental microbiome science included monitoring the safety of food and water supplies, and this remains an

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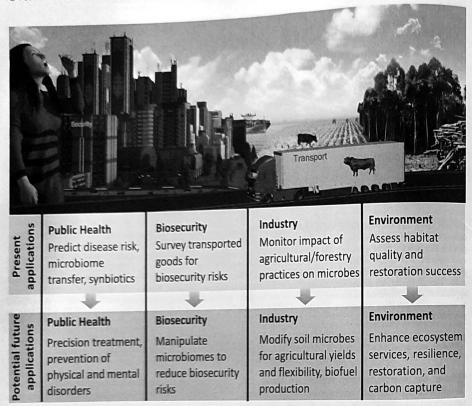


Figure 1. The applications of microbiome science span all environments and all facets of society. This figure depicts some current and possible future applications for public health, biosecurity, industry, and the environment. Potential future applications can best be realized with greater cross talk among scientific fields.

important function today. More recently, applications in areas such as agriculture, biosecurity, environmental impact assessment, and ecological restoration have vastly expanded, boosted by developments in high-throughput DNA sequencing that allow us to rapidly characterize microbial communities. Specific examples include using microbiome science to detect plant pathogens in terrestrial ecosystems (Tremblay et al. 2018), identify harmful microalgal taxa in ship ballast and marine port sediments (Shaw et al. 2019), and assess the impact of aquaculture on benthic communities (Pawlowski et al. 2014). Microbiomes have been validated as an indicator of ecosystem health: in terrestrial environments, soil bacterial communities match stages of ecological restoration (Liddicoat et al. 2019), and microbial communities can indicate the ecological condition of an estuary (Chariton et al. 2015, Raes et al. 2020).

Future applications of environmental microbiome research are certain to expand with developments in microbiome engineering—that is, actively altering microbial communities to achieve desired outcomes. Microbiome engineering for health outcomes is already apparent in

the widespread availability of pre-, pro-, and synbiotics for human use. In an environmental microbiome context, indirect microbiome engineering has been used to improve wastewater treatment (Barnard et al. 2017), whereas agricultural scientists have begun to use microbiome engineering to improve plant resilience to disease and other environmental stresses (Berg and Koskella 2018, Qin et al. 2016) and manipulate key traits such as flowering time (Panke-Buisse et al. 2015).

With further development, there is the potential for much broader applications of microbiome engineering—for example, inoculating soils or seeds to improve restoration outcomes (Muñoz-Rojas et al. 2018, Wubs et al. 2016), engineering coral microbiomes to enhance their resilience to climate change (Epstein et al. 2019), and modifying urban environmental microbiomes for human health outcomes (Flies et al. 2017, Mills et al. 2017, Watkins et al. 2020). The pinnacle of microbiome engineering may be creating synthetic microbial communities (Großkopf and Soyer 2014), which have already been developed for biotechnology applications such as biofuel production (Minty et al. 2013).

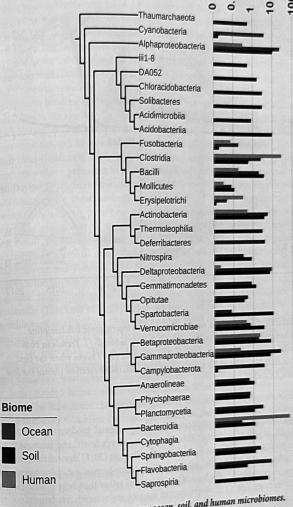


Figure 2. The shared taxonomy among ocean, soil, and human microbiomes. The plot shows the relative abundance of bacterial classes based on three large bacterial 16S ribosomal rDNA data sets representing marine, soil, and human microbiomes (Human Microbiome Project Consortium 2012, Earth Microbiome microbiomes (Human Microbiome Project, Thompson et al. 2017, International Census of Marine Microbes, Project, Thompson et al. 2017, International Census of Marine Microbes, Zinger et al. 2011). Some taxa were largely restricted to a single biome (e.g., Zinger et al. 2011). Some taxa were largely restricted to a single biome (e.g., Spartobacteria and Acidobacteriia for soil, Deferribacteres and Cyanobacteria Spartobacteria and Acidobacteriia for soil, Deferribacteres and Cyanobacteria for oceans). However, all taxa detected in the human microbiome are also for oceans). However, all taxa detected in the human microbiome are also for oceans) and ocean microbiome. A more holistic understanding of present in both the soil and ocean microbiome. A more holistic understanding of microbial communities is required to better understand, conserve, restore, and control microbial community function.

The enormous potential of environmental microbiome science to support ecological and social outcomes is therefore clear. However, if we are to harness environmental microbiome research—particularly environmental microbiome engineering—safely, and to fulfill its potential, we must ensure a solid understanding of cross-biome interactions.

Unless we know how microbes are shared across individuals, species, and ecosystems and how environmental and human microbiomes interact, we cannot best apply microbiome science for human and ecological benefit, nor can we know the potential repercussions of such microbiome manipulations.

Biomes share microbes

To demonstrate the interdependence of biomes and microbiomes, we compared the class and genus-level taxonomic composition of three large bacterial 16S ribosomal DNA data sets representing marine, soil, and human microbiomes (Human Microbiome Project Consortium 2012, Earth Microbiome Project, Thompson et al. 2017; International Census of Marine Microbes, Zinger et al. 2011; see the supplemental material for methods). The combined data set contained more than 4000 samples and over 330 million reads. Thirty-four classes of bacteria were abundant (more than 1% relative abundance) in ocean, soil or human microbiomes; of these taxa, 67.6% were shared across two or more biomes, showing the microbial connectedness of these seemingly disparate environments (figure 2). Studies examining the forces shaping the human microbiome have underlined this point, demonstrating that environmental microbes influence human microbiomes and affect our health (Hanski et al. 2012, Rothschild et al. 2018, Stein et al. 2016). Research into the cross-biome comparative function and ecology of these bacterial taxa would advance both human and environmental microbiome science.

Only a few taxonomic classes in this analysis were restricted to a single biome (e.g., Spartobacteria and Acidobacteriia for soil, Deferribacteres and Cyanobacteria for oceans). Interestingly, although the human microbiome data set was much less diverse at the class level than the soil or marine data sets (three classes

with more than 1% relative abundance, compared with 21 and 14 classes in the soil and marine data sets, respectively; figure 2), all classes abundant in humans—Bacteroidia, Betaproteobacteria, and Clostridia—were shared with both marine and soil biomes. At a finer taxonomic level, we found 72 genera were detected in all three biomes (supplemental

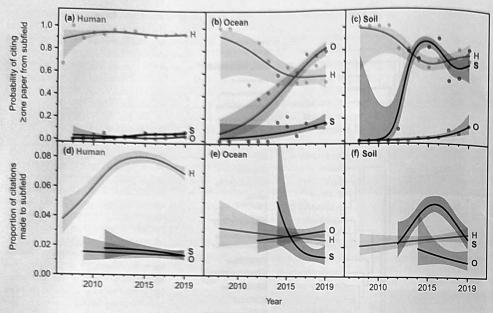


Figure 3. Citation patterns showing the probability of citing at least one paper from each microbiome subdiscipline (a-c) and the proportion of citations made from one subdiscipline to the other (excluding zeros; d-f). Trends in both citation patterns were estimated using binomial generalized additive models. The splines in (d-f) begin when the first cross-discipline citation is made and do not include papers in which there was no cross-discipline citation (hence the low proportions). Abbreviations: human, H; ocean, O; soil, S.

table S1). Most shared genera (55 out of 72, 76%) belonged to five classes: the Gammaproteobacteria and Bacilli, as well as the three classes abundant in humans. Co-occurrence patterns such as these are consistent with overlapping niche characteristics in human and environmental biomes. Species or strainlevel data is needed to confirm whether bacterial taxa are able to move between biomes.

The need for interdisciplinary microbiome research

Given the number of bacterial taxa shared between human and environmental microbiomes, do microbiome researchers also cross biomes? We conducted a citation analysis of almost 10,000 microbiome papers (see Supporting Information for methods) to investigate research links between environmental and human microbiome science (figure 3).

We found that connectivity is currently low between research in the human, soil and ocean microbiome disciplines. Despite the taxonomic crossover and growing evidence of links between human and environmental microbiomes, human microbiome papers have a low proportion and probability of citing papers from environmental microbiome disciplines (figure 3a, 3d). Some notable exceptions have highlighted links between human and environmental microbiomes: for example, Hanski and colleagues (2012)

demonstrated that environmental biodiversity affects the human skin microbiome, allergy levels, and immune function; Rothschild and colleagues (2018) showed that, surprisingly, we can better predict human gut microbiomes on the basis of environmental rather than host genetic factors. However, human microbiome research has largely not yet realized the potential for human-environmental microbiome interactions.

In contrast, soil and ocean microbiome papers are more likely to cite human microbiome papers, but this has declined over time (figure 3a-3c) as, presumably, each subdiscipline has become more established and suggests that early citations were perhaps out of necessity, rather than an awareness of the shared relevance. There is some connectivity between soil and ocean disciplines, and this does show an upward-if modest-trend (figure 3b, 3c). Human microbiome publications represent approximately 3% of the citations in papers from ocean and soil disciplines, likely for methods or context (e.g., building on the success of the Human Microbiome Project), and this proportion has remained relatively steady through time (figure 3e-3f). Similar studies of interdisciplinarity in fields such as applied ecology found much higher probabilities and proportions of cross-field citations (Staples et al. 2019).

Our analysis paints a picture of unrealized research connections across biomes and a particularly stark lack of integration between human and environmental microbiome science. This lack of interdisciplinary microbiome science could be limiting advances in both human and environmental microbiome subdisciplines for two key reasons. First, the sheer degree of taxonomic crossover between biomes means that if research remains siloed within disciplines, important interactions between microbes and biomes will be missed. Second, even disregarding these ecological crossovers, interdisciplinarity is well established as a building block of innovation through its potential to connect seemingly unrelated ideas (Johansson 2006, Johnson 2010) and introduce concepts without precedent in a given discipline (Graham and Dayton 2002). In the microbiome context, there is rich potential for new understandings to arise in this way. For example, by viewing pathogens as opportunistic microorganisms most likely to successfully colonize disturbed (microbial) ecosystems, we can use ecological theory to create robust microbial communities resistant to invasion (De Schryver and Vadstein 2014, Shade et al. 2012). This approach has already seen success across disciplines including aquaculture (Attramadal et al. 2014) and ecosystem restoration (Liddicoat et al. 2019), but can also be applied in fields such as agriculture (Berg and Koskella 2018), hospital design (Kembel et al. 2012), and urban environments in general (Flies et al. 2017, Mills et al. 2017, Watkins et al. 2020). Finally, environmental microbiome science may also miss valuable opportunities to piggyback off developments in better-funded human microbiome endeavors. Overall, there can be little doubt that we must do better as a scientific community to achieve the cross-pollination needed to realize the full potential of both human and environmental microbiome science.

Ethics, risks, and interdisciplinary complications

With stronger and more holistic scientific understanding of microbial communities across biomes comes a clear responsibility to consider the ethical and social implications of environmental microbiome research and application. As with other interdisciplinary biological innovations (e.g., genetic engineering or food web biomanipulation), environmental microbiome applications can have unanticienvironmental microbiome applications can have unanticienvironmental microbiomes will affect (Dittami et al. 2019). We should therefore pause to ask how the engineering of environmental microbiomes will affect primary sector productivity, ecological services, biodiversity, and human health.

In most cases, ethical issues surrounding microbiome engineering and beneficial outcomes centers around the definition of health. In humans, health is widely understood to be a state of the absence of disease and a high level of wellbeing (WHO 2018), but its extension into other domains has been problematic. For example, in restoration ecology, an ecosystem is regarded as healthy when it has an ecological community similar to an undisturbed, reference site (SER

2004). However, there are many instances where such undisturbed, reference conditions no longer exist because of permanent, widespread or extreme anthropogenic changes. The assessment of ecosystem health according to this definition is further complicated by the natural variation in ecosystems (Hobbs et al. 2014) and, from a microbiome perspective, connectivity between microbial communities across biomes. Finally, other definitions of healthy have focused on diversity, assuming greater diversity indicates health, and, although this is often the case, the relationship between ecosystem health and biodiversity is complex (Ives and Carpenter 2007). Defining health across domains is challenging; different fields may disagree on what is healthy for a system-for example, aquaculture versus freshwater ecology. Furthermore, there can be discordance between healthy environmental states and environmental states healthiest for people. Microbes, such as Vibrio cholerae, that are a normal part of healthy, natural environmental microbial communities (Worden et al. 2006) can have negative impacts on human health. Healthy human microbiomes are also likely to be population specific. For example, the predominant health challenges in low- and middle-income countries are infectious disease, and in high-income countries, they are noncommunicable chronic disease. The optimal microbiome characteristics are likely to differ between these populations, as well as between individuals with different genotypes, phenotypes, and living environments. The concept of health underpinning any microbiome engineering intentions would need to be clearly articulated and interrogated in an interdisciplinary way to reduce the likelihood of any unintended consequences.

Risk assessments for microbiome engineering should address the potential for inadvertent, negative environmental and health effects using the precautionary principle and should strive to incorporate the numerous sources of uncertainty (Hayes et al. 2007). An example of not enacting the precautionary principle are commercial human microbiome products (probiotics, synbiotics, gut microbiome pills for travellers etc.) that are already marketed despite our incomplete understanding of the functions and interactions of even the relatively well-studied human gut microbiota. Risk assessment of environmental microbiome engineering should include environmental and health information, as well as economic and cultural considerations, combined with extensive public discussion and engagement (Stirling et al. 2018). The decision framework around microbiome engineering should evaluate the potential degree and probability of harm, and how to manage that harm. The current lack of research across biomes exposes microbiome research to unforeseen risks and inadequate frameworks for assessing risks to human health via environmental pathways.

There are also risks associated with rapid technical and analytical developments in microbiome science. For example, the sensitivity of high-throughput DNA sequencing has raised issues with detecting contaminating organisms and cross-contamination between samples (Eisenhofer et al.

2019). There is also some argument over important experimental and analytical steps, such as whether to rarefy data to control for the number of DNA sequences obtained per sample (McMurdie and Holmes 2014, Weiss et al. 2017), although several best-practice guides have recently been published (e.g., Eisenhofer et al. 2019, Knight et al. 2018, Zinger et al. 2019).

Mainstreaming environmental microbiomes

Clearly, environmental microbiome science has much to offer a world grappling with fundamental environmental and human health challenges. However, some key questions remain: What must we do to help mainstream environmental microbiome science into sectors as diverse as biosecurity, urban planning, agriculture, and human health and across a diversity of countries and cultures? How can we best support well-informed decisions and ensure applications are grounded in a well-developed understanding of the opportunities, uncertainties and risks? How can we ensure that the benefits of microbiome science are not limited to the rich but address challenges faced by all people and are integrated into policy and practice to address some of the world's most serious human and environmental challenges?

As well as collaborating across disciplines, microbiome science will benefit from engaging with practitioners, policymakers, regulators, and a diverse range of human communities to achieve the greatest possible impact. Human microbiome science provides the best examples to date of achieving this engagement, helping to explain the growing public awareness of this field and the comparative lag in environmental microbiome science. The American Gut Project (http://humanfoodproject.com/americangut) exemplifies successful public engagement, having crowdsourced funding and samples from over 11,000 participants from more than 40 countries (McDonald et al. 2018). Microbiome science is now available to the general public via print and electronic media in popular science TV shows, TED talks, podcasts, and books, many of which are presented or authored by leading scientists in the field. Greater collaboration between scientists and the media also reduces the potential for sensationalized science reporting, which would facilitate communication, understanding, and trust between the public and microbiomes researchers.

Projects such as the Healthy Urban Microbiome Initiative (www.HUMIglobal.org) that integrate the natural, social, and health sciences show the potential for international, transdisciplinary collaboration, but how can we encourage more transdisciplinary microbiome science collaboration? There are well-known barriers to transdisciplinary activity in any field (Rogers 2010), ranging from tension over appropriate methods of inquiry to differences in lexicon and communication practices used by scientists within disciplines. A unified microbiome vocabulary has been proposed that may help overcome these barriers and reduce misunderstandings among both the scientific

and broader community (Marchesi and Ravel 2015). An emphasis on accessible data and analysis code, as well as minimum metadata standards (http://gensc.org/mixs) help facilitate connectivity and reproducible science-all of which we strongly encourage. Bacterial and archaeal full-length 16S ribosomal RNA gene reference sequence databases are biased toward host-associated organisms. with less than 25% of sequences originating from soil or aquatic environments (Schloss et al. 2016). Integrating future sequencing efforts with multibiome data storage options for both sequences and metadata will make connecting across biomes easier. For example, expanding the Human Microbiome Project repository to include environmental data from both soil and ocean biomes is likely to foster cross-discipline connections (Tasnim et al. 2017). Furthermore, multiagency funding to develop broadly applicable tools can help reduce redundancy and facilitate cross-biome comparisons (Alivisatos et al. 2015).

Conclusions

Microbiome science is shifting the social perception of microbes from disease causing, unhygienic organisms to potential partners vital for human and ecosystem health (Cavicchioli et al. 2019). Scientists now recognize the importance of microorganisms for ecosystem function. However, our understanding of the contributions made by microbes within a system and how they are shared and interact across ecosystems and biomes is incomplete, hindering our ability to translate microbiome science into safe applications for the greatest environmental and human

We are not the first to suggest that a coordinated, intensely collaborative research effort is needed to fill these gaps. For example, the interdisciplinary Unified Microbiome Initiative was proposed to develop cross-cutting microbiome technologies in order to facilitate translation into applications (Alivisatos et al. 2015). Furthermore, we should codevelop research with environmental and health practitioners and work across disciplines to understand how microbiome technology can be safely applied. We must be ready to help national and international watchdogs grapple with novel regulatory challenges and support policymakers to breach silos and build bridges between traditionally disparate sectors. It is highly important that we also engage the public with integrity, clarity and skill to maintain public trust and support the development of a microbiome-literate community (Shamarina et al. 2017)—taking heed, as well as we can, of the lessons from climate change science communication (Bostrom et al. 2013). Microbiome research and discourse should include people from a range of national, cultural, genetic and socioeconomic backgrounds to ensure the applications are distributed equitably. These are no small challenges, but ones that we must overcome to ensure that we are collectively equipped to develop, understand and translate microbiome science for maximal global benefit.

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Supplemental material

Supplemental data are available at BIOSCI online.

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