

Climate change microbiology — problems and perspectives

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Abstract | The signs of climate change are undeniable, and the inevitable impact for Earth and all its inhabitants is a serious concern. Ice is melting, sea levels are rising, biodiversity is declining, precipitation has increased, atmospheric levels of carbon dioxide and greenhouse gases are alarmingly high, and extreme weather conditions are becoming increasingly common. But what role do microorganisms have in this global challenge? In this Viewpoint article, several experts in the field discuss the microbial contributions to climate change and consider the effects of global warming, extreme weather, flooding and other consequences of climate change on microbial communities in the ocean and soil, on host–microbiota interactions and on the global burden of infectious diseases and ecosystem processes, and they explore open questions and research needs.

Q *How does climate change affect the diversity and function of the microorganisms in the environment you study? What are the consequences of this change?*

David A. Hutchins. Some drivers of global change that influence microbial assemblages, such as warming, are common to both marine and terrestrial ecosystems. However, some environmental changes in the ocean also include ocean acidification, deoxygenation and altered circulation of seawater, which are processes that are unique to this environment. These multiple stressors pose a daunting obstacle to predicting the net responses of the planktonic microorganisms that control ocean biological productivity and elemental cycling^{1,2}.

Nevertheless, some generalizations are possible. Ocean acidification frequently inhibits nitrification by archaea and bacteria, whereas deoxygenation promotes microbial denitrification. Nitrogen-fixing cyanobacteria should also thrive in a changing ocean, as their growth and fixation rates often benefit from increased carbon dioxide levels and rising temperatures. Taken together,

these projected future trends indicate a fundamentally restructured marine nitrogen cycle¹.

Ocean-warming experiments sometimes reveal losses of biodiversity in microbial communities, leading to dominance by a few previously inconspicuous taxa. Many plankton assemblages seem to include such ‘rare biosphere’ thermophiles that are poised to quickly take advantage of rising temperatures. Unfortunately, the species favoured under future warmer, acidified conditions may include toxin-producing phytoplankton that can cause ecologically and economically devastating harmful algal blooms¹.

Increased temperature and/or decreased pH commonly shifts the size range of plankton communities towards smaller species, which sink much more slowly than larger ones do. Ocean acidification is also detrimental to calcifying protists such as coccolithophores, which have heavy mineral shells that act as ballast for sinking particles. Both of these responses make it likely that global change will lead to less biologically mediated storage of fossil-fuel-derived carbon in the deep ocean, one of the major ecosystem functions currently provided by marine microorganisms¹.

Janet K. Jansson. We are studying two climate-sensitive soil ecosystems: Arctic permafrost and grasslands. Permafrost soil is thawing in large regions of the Arctic, and this has major impacts on functions carried out by the soil microbiome³. In a frozen state, the stored carbon in permafrost is largely preserved owing to low activity of microorganisms. However, when it thaws, the microorganisms become more active and start to decompose the organic carbon, releasing greenhouse gases such as carbon dioxide and methane to the atmosphere as a result⁴. Grassland ecosystems are being affected by changes in precipitation patterns, such as increased, intense rainfall events and/or increasing drought. Soil moisture is paramount for determining the connectivity between spatially discrete soil microorganisms, and, therefore, changes in soil moisture will have a large impact on the ability of soil microorganisms to cycle carbon and other nutrients, including plant-derived compounds that are key inputs into grassland ecosystems.

Justin V. Remais. We study pathogens in the environment — including those present in soil, water and air — and how their transmission responds to environmental changes such as those driven by global climate change. Classic research in this area focused on changes in rates of replication, senescence and dispersal as meteorological conditions change and established that there is considerable heterogeneity in the responses of pathogenic bacteria, protozoa, viruses and fungi. In the case of diseases caused by waterborne pathogens, current knowledge suggests a decrease in the burden of viral infections, for instance, owing to decreased environmental persistence as temperatures rise. Changes to microbial diversity and function also result from shifts in environmental conditions. For example, exposure of certain waterborne bacterial pathogens to increased temperatures can lead both to the increased expression of genes associated with virulence and to faster die-off. Increasing local temperature has also been found to be positively associated with increasing antibiotic resistance in common pathogens. Meanwhile, pathogens can be strongly affected by changes in microbial community ecology. As an

example, we are studying the fungal soil pathogen *Coccidioides immitis* in California, USA, which causes coccidioidomycosis (also known as valley fever) and benefits from extreme shifts in precipitation. High temperatures and prolonged dry conditions are thought to remove *C. immitis* competitors from the surface community, and subsequent precipitation enables *C. immitis* that persists in the subsurface to grow uninhibited by competitors and to colonize the soil surface. Subsequent dry periods then facilitate the airborne phase of the pathogen (arthroconidia), which causes human and wildlife infections. We are only beginning to understand how the dynamics of pathogen transmission, virulence and antibiotic resistance change in response to the complex effects of environmental change.

Virginia I. Rich. How will the thaw of permafrost ecosystems impact climate? I co-lead the IsoGenie Project, an international consortium of microbiologists, biogeochemists and modellers, in characterizing microbial carbon cycling and climate feedbacks along a permafrost thaw gradient and its interconnected postglacial lakes in Arctic Sweden. Here, climate change is causing extensive habitat shifts, as permafrost-underlain palsas sink into partially thawed bogs and fully thawed fens, each with differing hydrology⁵, vegetation⁵, geochemistry⁶, microbiology^{7,8} and carbon gas emissions⁹.

Thaw initially decreases microbial diversity, owing to the harsher conditions created in the bog by sphagnum mosses (for example, low pH and inhibitory compounds), but diversity then peaks in the sedge-dominated fens⁷ as the geochemistry becomes more favourable. Thaw also shifts community functions: high-affinity methanotrophs drive slight methane uptake in the palsas; a mixture of methane cyclers mediates low emissions in the bogs; and in the fens, diverse hydrogenotrophic and acetoclastic methanogens outpace methanotrophs to produce high (and isotopically heavier) emissions^{7,9}. A single novel methanogen best predicts the methane isotopic signatures (a value used to link emissions to their sources) of bogs — better than environmental drivers or other aggregations of microorganisms and over multiple years and methods^{7,9}.

Genomes recovered from metagenomes now represent ~60% of the mire microorganisms at the genus level and reveal that thaw subtly shifts the microbial repertoire for carbon processing ‘upstream’

of methanogenesis, towards simpler polysaccharide degradation, fermentation and acetogenesis⁷. Resident viruses, in turn, infect diverse carbon-cycling microbial hosts, covarying with them in response to thaw, and carry active ‘host’ carbon-cycling genes¹⁰. The interconnected lakes are a critical part of the mire complex, emitting half of its total methane¹¹ and much of the ‘old carbon’ mobilized from thawing permafrost. Methane production in the warmer areas of the lakes is less temperature-sensitive than it is in the cooler areas, highlighting the key role of microbial acclimation or adaptation in determining future fluxes.

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Throughout the history of Earth, microbial communities have been changing the climate and have been changed by the climate. An understanding of how environmental microbiomes respond, adapt and evolve to climate change is central to our ability to identify climate–ecosystem feedbacks. Climate change can have a direct effect (for example, warming and aridity) or an indirect effect (for example, increased carbon dioxide levels) on soil microbiomes through changes in plant growth, physiology and community structure¹². Climate change can lead to shifts in the geographical range of microbial species; affect their distribution, diversity and abundance; and influence microorganism–microorganism and plant–microorganism interactions. Current knowledge indicates that microbial diversity, community composition and abundance are negatively affected by increasing aridity in global drylands¹³. Similar effects have been observed under warming and drought conditions¹⁴.

Given that microorganisms have a critical role in most ecosystem functions, the potential consequences of diversity and biomass loss, local extinction and composition shift are enormous. There is increasing evidence that climate-change-induced (for example, aridity and warming) loss in microbial diversity and abundance is linked to reduced ecosystem multifunctionality, low stability of ecosystem functions and increased ecological succession with unknown consequences^{15,16}. Even low-level changes (for example, community composition shifts, whereas diversity remains unchanged) can have a large impact on functions owing to the altered metabolic capabilities of the ecosystem. If a keystone species becomes locally extinct or replaced (for example, nitrogen-fixing symbionts or a species

providing protection against drought or pathogens), the consequences will be substantial and can result in the loss of above-ground diversity and productivity, which can feed back to desertification with severe economic, environmental and social consequences.

In terms of climate feedback and carbon cycling, soils store more organic carbon (soil organic carbon (SOC) of ~2,000 billion tonnes) than the atmosphere and vegetative carbon pool combined; this SOC is under the direct control of microbial activities. Microorganisms also indirectly influence carbon storage in vegetation via the provision of plant nutrients. Microbial respiration accounts for 50% of global respiration (~60 billion tonnes of annual carbon release), and the loss of SOC via microbial respiration will increase under projected climate change conditions. However, the magnitude and mechanisms of SOC loss remain debatable. Moreover, the effect of climate change on microbial communities and their functions may vary between different ecosystems and regions. For example, increasing temperature is likely to have a pronounced effect on SOC in boreal and temperate regions¹⁷ (where most SOC is stored) because, in these ecosystems, microbial growth and activities are limited by temperature.

Q How can the effects of climate change on microbial communities be mitigated? Are there any microorganism-targeted and/or microbially mediated interventions in your area of study?

D.A.H. In the absence of effective action to curtail global greenhouse gas emissions, some marine scientists have advocated measures to mitigate local anthropogenic stressors, such as reducing pollution and nutrient overenrichment. Such small-scale interventions undoubtedly benefit reefs, seaweeds and resident fish stocks but may be of more limited value to most oceanic microorganisms, except in very nearshore environments. The sheer size of the open ocean and the nature of the free-floating transient planktonic lifestyle mean that many of the most ecologically and biogeochemically important marine microorganisms will almost certainly require global solutions to global stressors.

Marine microorganisms have themselves been suggested as a global climate change mitigation tool. In large parts of the open ocean, phytoplankton growth is limited by low concentrations of the micronutrient iron, and in situ experimental iron

additions have shown that an impressive phytoplankton bloom can be produced that strongly stimulates photosynthetic carbon dioxide drawdown¹⁸. Whether this well-established observation can serve as the basis for a safe and effective large-scale climate mitigation effort has been the subject of an impassioned debate. Proponents suggest that artificial iron-fuelled blooms could store large amounts of carbon in deep waters, in a manner that closely resembles natural phytoplankton blooms. Opponents of ocean iron fertilization point to substantial uncertainties regarding ecological consequences, carbon storage effectiveness and economic viability. The United Nations has proscribed commercial-scale iron fertilization attempts in international waters, and today, many (but not all) marine microbiologists feel that the risks of this proposed microbial geoengineering scheme outweigh the potential benefits.

J.K.J. There are several research options that are being explored to harness soil microorganisms to mitigate the negative consequences of climate change. One possibility is to exploit the metabolic capabilities of soil microbiomes to sequester carbon, either through uptake and immobilization of plant-derived carbon compounds or through direct uptake and metabolism of carbon dioxide and/or methane. Synthetic biology tools could be used to custom design plant-soil-microorganism combinations that facilitate uptake and sequestration of carbon dioxide in forms that are resistant to decomposition in soil. Another possibility is to harness the ability of soil microorganisms to promote growth of plants under stress conditions, such as caused by drought. Of particular interest is the use of naturally interacting combinations of soil microbiomes (that is, consortia, rather than single microbial inoculants) to provide enhanced beneficial ecosystem services, such as promoting plant growth in degraded soils.

J.V.R. Opportunities to mitigate the effects of climate change that favour or disseminate environmental pathogens include traditional measures to disrupt contact between pathogens and human hosts, such as strengthening sanitation systems to reduce pathogen loading to environmental media, vegetative buffers to control agricultural run-off of pathogens and emerging strategies to control the abundance of pathogen-carrying animal hosts and vectors. Although it is challenging to directly target pathogen populations,

re-engineering organisms and applying gene-editing techniques, including the CRISPR-Cas9 system, provide key opportunities, as does reproductive manipulation of disease-carrying vectors and hosts through manipulation of their microbiota, such as deployment of *Wolbachia* (the intracellular bacterium of mosquitoes and other invertebrates). As these technologies advance, an improved understanding of the factors that amplify the effects of climate change on pathogen persistence, virulence and transmission would enable targeted actions to limit the effect on infectious diseases. For instance, introduced iron can affect the expression of virulence genes in *Vibrio cholerae*; such an increase in gene expression has also been observed in response to increased incident sunlight, which can be prompted by climatic changes that lead to reduced cloud formation. Thus, mitigating micronutrient pollution provides an opportunity to limit the pathway by which climate factors affect pathogen virulence. As another example, nutrient pollution can also interact with warmer temperatures to create conditions that support colonization of zooplankton by *Vibrio* spp., and, therefore, improved nutrient management and control may counteract some risks associated with a warming climate. Thus, there are opportunities to investigate and act on the modifiers that enhance the effects of climate change, limiting the proliferation and virulence of climate-sensitive environmental pathogens. Finally, mitigating effects of climate change that facilitate transmission of environmental pathogens will also require that we are able to detect and enumerate pathogens in environmental media. For many environmental pathogens of global significance — including *Schistosoma* spp., certain soil-transmitted helminths, airborne and soil-borne fungi and certain viruses that cause gastroenteritis — we lack reliable and widely accepted methods for capturing, recovering, determining the viability of and quantifying the concentration of pathogens in soil, water or air. A recommitment to developing such tools would lead to an improved ability to characterize, understand and mitigate shifting spatial and temporal distributions of pathogens as the climate changes.

V.I.R. One general strategy for mitigating climate change is the identification and utilization of key microbial lineages to reduce methane emissions. Advanced statistical analyses integrating microbial

and biogeochemical data, empowered by our growing libraries of assembled genomes and meta-omes, can identify those lineages most associated with high or low methane emission. These may include not only methane cyclers but also syntrophs or key upstream carbon processors. These lineages provide experimental targets to modulate methane emissions. One control mechanism that we are excited to pursue is 'ecosystem-aware phage therapy', whereby thawing sites would be 'treated' with a phage cocktail against target microorganisms such as methanogens. Another control mechanism focuses on methane consumption: while diverse methanotrophs are present at our site in Arctic Sweden, only a few are typically active; supplying genome-inferred growth-limiting nutrients could increase methane consumption by the 'workhorse' methanotrophs or by normally less-active lineages.

Ecosystem engineering presents another strategy for mitigating methane emissions: inducing a state change to a less-methanogenic state. This approach has been successful in rice paddies, where emissions mitigation practices include complete drying of paddies between planting seasons and the addition of substrates such as biochar, which decrease methanogenesis and increase methanotrophy. In thawing Arctic peatlands, methanogenesis might be thermodynamically bypassed by sulfate application (as sulfur reducers typically outcompete methanogens) or ecologically impeded by promotion of sphagnum mosses, which inhibit both methanogens and upstream organic matter breakdown by lowering pH and producing antimicrobial compounds.

It is vital to consider the inherent risks of intervention (think microbial-scale cane toads and mongooses), and the surest way to mitigate emissions from thawing Arctic peatlands is to slow their rate of thaw by stabilizing planetary warming. However, given the rapid changes already underway, the risks of interventions must be weighed against the risks of climate change itself.

B.K.S. and P.T. The manipulation of terrestrial ecosystems offers an effective means to mitigate anthropogenic climate change. Changes in land use (for example, changing from arable land to forestry) and management practices (for example, using low-nitrogen inputs or no-till systems) are known to affect soil microbiome functionality and in increased carbon sequestration. Recent research demonstrated that a small amount of

'donor' microbiome from healthy soil helped to restore degraded ecosystems¹⁹.

The use of microalgae and cyanobacteria to generate biofuel and for carbon dioxide sequestration has been demonstrated and can be effective for removing atmospheric carbon dioxide. Such approaches are efficient because photosynthetic microorganisms are estimated to grow 100 times faster than plants. Using carbonic anhydrase from cyanobacteria (which converts atmospheric carbon dioxide to calcium carbonate) is a viable approach because calcium carbonate is common and thermodynamically stable and as such can provide a long-term carbon dioxide sequestration option²⁰. However, to achieve this at industrial scales and to make the process economically feasible, substantial additional research and investment will be required. Another option includes restoring degraded lands (desert and less-productive drylands) using cyanobacteria (natural or synthetic), which have an important role in ecosystem functions in global drylands (accounting for ~41% of terrestrial ecosystems). Restoring land will increase soil carbon and fertility and will promote increased carbon storage above ground by increasing plant productivity. In addition, the microbiomes of the bioenergy feedstock plants, including sugarcane and *Populus* spp., are being studied to potentially harness plant–microbiome interactions to enhance nutrient acquisition, stress tolerance and biomass yield. This knowledge could lead to strategies for sustainable production of biomass feedstocks for bioenergy in marginal lands.

Inoculation with nitrate reductase and methanotroph microorganisms can reduce emission of nitrogen oxide and methane from soils and animal husbandry. The emerging tool of *in situ* microbiome engineering (using ecological, microbial, biochemical and molecular approaches) provides a viable option to minimize greenhouse gas emission at farm scales²¹. A recent report that quorum-sensing molecules (biochemical approach) can influence production and consumption of nitrogen oxide gases²² provides evidence and potential for such approaches. The use of plant species or varieties (ecological approach) to promote the growth and activities of methanotrophs and nitrogen oxide reductase communities can be an effective tool to manipulate microbiomes along with biochemical approaches to mitigate greenhouse gas emissions for large-scale uses.

Q *What are the current open questions and research needs and priorities? How can we deal with both the spatial and temporal scales of research questions arising in climate change microbiology?*

D.A.H. National and global ocean-observing networks are in place to measure the progression of acidification and warming, and regional time series stations have assembled decade-long records of changing physical, chemical and biological parameters. Progress has also been rapid in developing new quantitative frameworks to model future shifts in marine plankton communities and biogeochemistry. Given the complex multivariate nature of ocean environmental change, one of the biggest current challenges for biological oceanographers is being able to mechanistically predict the integrated responses of marine microorganisms. Fully meeting this challenge requires an entirely different approach: targeted experiments in the laboratory and the field².

Such experiments need to examine microbial responses to multiple climate stressors over timescales ranging from rapid physiological acclimation to extended adaptive evolution. Not surprisingly, descriptions of short-term acclimation experiments are far more common in the literature, and only a few long-term studies have tested the evolutionary responses of marine bacteria, cyanobacteria and phytoplankton to ocean acidification or warming. These experiments suggest that these two drivers can indeed be potent selective agents for many marine microorganisms, but more challenging experiments are needed that examine adaptation to simultaneous, interacting climate change stressors^{1,2}. Likewise, formidable logistical difficulties have so far precluded unenclosed pH or temperature manipulations in the open ocean, despite the unique insights gained from such mesoscale *in situ* experiments in the ocean iron limitation field. These experimental frontiers are among those that remain to be explored by the next generation of ocean global-change microbiology studies.

J.K.J. Key research needs include going beyond sequencing to use of other emerging technologies, including proteomics, metabolomics and imaging, to determine the functions carried out by interacting microbial members of natural soil ecosystems and how those functions are perturbed by climate change²³. We need to understand how soil microorganisms

(including bacteria, archaea, fungi, protists and viruses) interact across trophic levels to decompose soil carbon, cycle nutrients and support or hinder the growth of plants. We also need to understand how resilient different soil microbiomes are to stress perturbations and whether there are tipping points beyond which they can no longer carry out key functions. Currently, there is a disconnect between the fine-scale detail arising from microbiome studies and the larger 'landscape' scale resolution of most climate models. Therefore, a priority is to incorporate knowledge about soil microbial biogeochemical pathways and interactions into predictive models of the impact of climate change on important ecosystem functions carried out by the soil microbiome.

J.V.R. Major gaps remain in our understanding of how the spatiotemporal distribution, epidemiology and environmental microbiology of pathogens and the infectious diseases they cause may shift under climate change. Much of our current understanding is inferred from observed correlations between environmental conditions and the incidence of human infections, with the underlying causal pathways and population dynamics of environmental pathogens relatively understudied. We need to move beyond correlation and develop experimental designs and analytical frameworks capable of discriminating the causal links between short-term and long-term environmental perturbations, community structure and function among microbiota, and health outcomes. Strengthening our mechanistic understanding would provide a stronger foundation for the prediction and mitigation of changes in disease burden as microbial community structure and diversity respond to changes in the abiotic environment.

An additional barrier to causal understanding is our limited knowledge on the relative contributions of host-associated and environmental factors to pathogen persistence, proliferation and disease in many parts of the world; we need to resolve when and under what circumstances host susceptibility, exposure and pathogen shedding, for instance, govern pathogen population dynamics versus when environmental factors dominate and why. Doing so would enable a more rigorous estimation of the burden of infectious disease attributable to environmental change, particularly in low-resource settings where epidemiological data may be limited. Finally, owing to the pronounced heterogeneity

in response to climate variability among pathogens — and acknowledging that many infections are polymicrobial rather than restricted to single agents — a community perspective will be increasingly important for understanding the influence of the climate on pathogens and disease, including through the application of metagenomic sequencing and other approaches for understanding microbial assemblages.

V.I.R. A key research priority in global-change microbiology is the grand challenge of ecogenomics itself: scaling from genes to ecosystems. As central dogma relationships

between transcripts, proteins and enzymatic transformations vary among lineages and climate-relevant microbial processes, no universal rule of thumb can solve scaling. Which components of a diverse natural system are most consequential to its particular climate-relevant services?

There are two promising approaches. First, as we develop increasingly rich paired microbial and biogeochemical characterizations of natural systems, we can use advanced statistical approaches to identify the lineages and pathways most predictive of a given ecosystem output (for example, methane emission), letting the data

reveal the essential system components for scaling, under current conditions. Then, these lineages or functional guilds can be experimentally targeted in cultures and low-complexity microcosms and informatically targeted in high-complexity natural systems with additional measurements (for example, samples spanning high and low abundances of those members or a range of conditions) to characterize the specific scaling parameters — and underlying mechanisms — under both current and predicted future conditions.

Second, in a parallel and iterative approach, the genome-informed representation of microorganisms in biogeochemistry models can identify those most consequential to predicted outputs and can distil community insights into tractable additions or adjustments to larger-scale climate models.

In addition, scaling relationships are likely to be dynamic themselves. For each climate-critical natural system and process, what will be the relative importance of microbial acclimation, adaptation and assembly as they move further from current states?

Global change microbiology is tackling a number of important open questions and research priorities beyond those cited above, from accurate multiscale representation of *in situ* thermodynamic constraints (the importance of which is demonstrated by discoveries like that of '*Candidatus Methanothrix paradoxum*'²⁴) to reaching beyond ecosystems to scale to entire biomes via remote sensing of microbial system types. It is a compelling time to be engaged in this research.

B.K.S. and P.T. Understanding microbial responses and harnessing the potential of microbiomes into practical solutions for climate change mitigation will require creative insight and problem solving from multiple disciplines. Several open questions require prioritizing. Do microorganisms respond consistently (functionally and taxonomically) to climate change treatments? How do above-ground and below-ground interactions influence microbial responses to climate change? Can the functional consequences be predicted on the basis of climate-change-induced shifts in microbial communities across ecosystems? What is the dominant mechanism for acclimation of microbial respiration (for example, resource availability versus physiology)? Which attributes of the microbiome (for example, diversity or abundance) can improve prediction of simulation models?

To tackle these questions, we require large-scale, long-term field studies to generate cross-biome temporal data for

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examining the microbial response to climate change. We also need to develop technologies in single-cell genomics, high-throughput 'omics', bioinformatics and modelling to generate insights into climate–microbiome feedbacks and to improve access of microbiome data across ecosystems. Further, we need to develop robust predictive models to interpolate or extrapolate observed microbial interactions with their environment and require interdisciplinary, collaborative research to enable a predictive understanding of microbiome functions in diverse ecosystems. The new global-change ecology should generate systematic, open-access data sets for probing the morphological and molecular diversity, evolution and ecology of environmental microbiomes in a changing world. Incorporation of microbial attributes in ecological models could reduce uncertainties associated with model predictions of the impact of climate change and enable the manipulation of the microbiome in the future for mitigation.

In the past decades, some multifactorial climate change field experiments have been established to examine the temporal succession of terrestrial ecosystems in response to climate change across multiple ecosystems. Support for these experiments and further expansion in other biomes along with studying environmental gradients across ecosystems that experience rapid climate change may identify the legacy effects of microbiome disturbances in the current climate. Technology development is required to enable experimental manipulation of the environmental microbiome, determine mechanisms underpinning microbial interactions and predict the influence of environmental gradients on microbial functions with

precise spatiotemporal control. With integrated systems biology approaches and powerful analytical and modelling techniques, it should be possible to predict the links between microbiome functions and climate change. Defining the core environmental microbiome components, dynamics, functions and interactions and integrating this knowledge with emerging digital and precision agricultural tools will assist in developing microbiome solutions to create healthy, resilient and sustainable climate-smart ecosystems.

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Competing interests

The authors declare no competing interests.

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