Schulz *et al.*[1] used a simple optical system to image calcium transients inside the 9.4 tesla MRI scanner: they fixed one end of a single, long, multimode optical fiber over the primary somatosensory cortex of an anesthetized rat. They placed the rat in the MRI scanner and connected the other end of the optical fiber to an optical set up located outside of the shielded magnet room. In brief, the optical setup involved a one-photon excitation beam, collimated into the fiber and a fluorescence-collecting path focused onto a photomultiplier. With this approach, a large volume of cortex was excited by light diffusing from the fiber (**Fig. 1**), and a part of backward-scattered fluorescence was collected.

By labeling both neurons and astrocytes with a calcium sensor, Shultz *et al.*[1] observed that forepaw and hindpaw stimulations elicited correlated calcium and BOLD signals in distinct cortical regions, as expected. Upon prolonged stimulation at high frequency, calcium responses showed strong adaptation, and the associated BOLD response was modeled well using the canonical impulse response function[8] after accounting for this neuronal adaptation. At that point, little was gained with regard to studies using simultaneous recording of BOLD and electrophysiological signals because calcium signals reported nonspecific neuronal and astrocytic activation in the superficial layers of the somatosensory cortex. However, Shultz *et al.*[1] next analyzed the specific sources of these sensory-evoked calcium and resulting BOLD signals.

In several rats, the authors first used two-photon fluorescence microscopy to image fluorescence signals with high spatial resolution and then correlated these signals to those obtained with the fiber placed over the same cortical region. They thus demonstrated that calcium signals measured with the fiber corresponded to whole-field calcium signals generated by the neuropil, that is, mostly dendrites of neurons of cortical superficial layers. In addition, they occasionally observed a slow and delayed calcium signal in response to prolonged stimulation. By selective astrocyte labeling with the calcium indicator Rhod 2, they could ascribe this delayed calcium response to an activation of astrocyte processes. Moreover, they found that this astrocytic activation is correlated to a specific prolongation of the BOLD response. This approach thus allowed the authors to determine that neurons and astrocytes are specifically associated with different phases of the BOLD response to sustained paw stimulation.

This work clearly demonstrates the strength of this hybrid methodology because the involvement of non-excitable cells in the generation of BOLD signals could not have been detected with electrophysiological recordings. Furthermore, with the advent of transgenic mouse models that allow conditional expression of genetically encoded calcium sensors in specific cell types, the method proposed by Shultz *et al.*[1] will enable additional investigations into the cellular mechanisms underlying BOLD responses triggered by different cellular populations and stimulation paradigms. Moreover, the single-photon fiber-optic fluorescence measurements described can easily be combined with many other MRI and fMRI sequences, such as arterial spin labeling or magnetic resonance spectroscopy, thereby providing information on hemodynamic and metabolic changes associated with cell type–specific responses to different stimuli, pathophysiological perturbations and disease models, for example, assessment of alteration of the BOLD response owing to neuronal versus astrocytic activation in models of epilepsy, stroke, Parkinson's disease or Alzheimer's disease.

COMPETING FINANCIAL INTERESTS
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Predicting microbial distributions in space and time

Noah Fierer & Joshua Ladau

Researchers describe an approach to predict microbial-community composition across broad spatial and temporal gradients, an important step to bringing microbial ecology into the 21st century.

Ever since Leeuwenhoek's discovery of 'animalcules' in the 17th century, we have known that microbes are ubiquitous and abundant on Earth. Despite this long history of research, microbiologists often cannot predict patterns in microbial diversity across time and space. In this issue of *Nature Methods*, Gilbert and colleagues[1] show that it is now possible to generate predictive maps of microbial diversity by combining environmental data and molecular analyses of marine bacterial communities. Such approaches may help us leverage the ever-increasing number of datasets being collected by microbial ecologists to build a more comprehensive understanding of microbial diversity on Earth and better understand the connections between microbial diversity, climate and biogeochemical cycling.

With respect to the modeling of taxon distributions, microbiologists lag far behind plant and animal ecologists, who began generating predictive maps of macroorganismal diversity over a century ago. In 1876, Alfred Russel Wallace published maps of animal diversity across continents[2]—essentially interpolations based on a relatively small number of observations and a keen understanding of natural history. Such maps undoubtedly inspired generations of naturalists to explore 'terra incognita' and the biological wonders promised therein. Just as importantly, these maps were critical to the development of fundamental concepts in ecology and evolutionary biology.

For more than 20 years, it has been possible to survey the microbial diversity contained in environmental samples[3], but such data have rarely been used to generate predictive models of how communities, or the abundances of individual taxa, vary across broad

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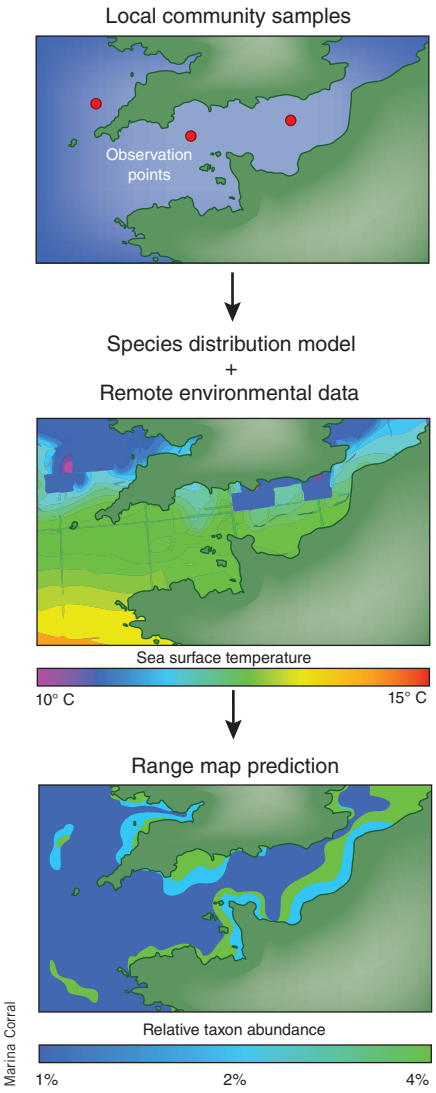

Figure 1 | Species-distribution modeling and prediction. A variety of possible statistical approaches are used to model how diversity depends on environmental conditions (top). Models are projected into geographic space or through time using rasters of environmental data (center) to generate predictions of taxon distributions (bottom).

spatial or temporal scales (but see ref. 4). One reason for this is that individual samples can harbor thousands of taxa, and surveying diversity across enough samples to build predictive models can be a daunting task. However, advances in high-throughput DNA sequencing now allow the identification of thousands of individual microbes living in each of thousands of samples in a single sequencing run[5]. Microbial ecologists have begun using such approaches to capture microbial diversity patterns across broad spatial and temporal gradients in a wide range of environments including soil[6], seawater[7] and human intestine[8]. This pace of exploration will only increase as large-scale projects such as the Earth Microbiome Project (http://www.earthmicrobiome.org/) apply these tools to characterize the microbial diversity found in habitats across the globe.

Of course, high-throughput sequencing is, by itself, no panacea. Tools are needed to move beyond simple descriptions of observed patterns and start predicting microbial diversity patterns. The paper by Larsen *et al.*[1] describes one approach for doing exactly that. They developed a species distribution model (SDM; **Fig. 1**) that models how the relative abundances of microbial taxa depend on environmental conditions and the relative abundances of other taxa. The model can be used to interpolate and extrapolate taxon abundances in conditions that were not directly observed. They used a unique dataset, a 6-year time series of bacterial communities at a single location in the English Channel, to predict the population dynamics of individual bacterial taxa over time. In addition, they could incorporate spatial measurements of surface water conditions into their model and predict microbial distributions across the western English Channel.

The modeling approach they developed is not entirely new. Plant and animal ecologists have developed similar SDM methods, and many of these could be applied to microbial-community data. The broad range of SDM methods developed in ecology use a range of statistical tools, from general linear models to machine-learning approaches such as boosted regression trees. They work with data ranging from relative organismal abundances to counts of presence and absence, or just presence[9]. It will be interesting to see how these pre-existing methods compare in their ability to predict the distributions of microbes. Regardless, Gilbert and colleagues[1] demonstrate that microbial-community dynamics can be surprisingly easy to predict via SDM models, provided there is a sufficiently rich dataset to train the model.

The approach described by Larsen *et al.*[1] and other related SDM methods yield more than just maps or predictions of taxon abundance over time. One can use such approaches to document new microbial interactions, identify shared niche spaces, reveal the natural histories of microbial taxa and possibly predict how global climate change (for example) may impact microbial communities. Although their model focused on predicting taxon distributions, a similar approach using shotgun metagenomic data could be leveraged to predict the abundance of functional genes that are critical to global biogeochemical cycles.

Can this modeling approach be used in other microbial habitats? It depends. To build the model, it is necessary to have microbial-community data from a large number of sites or from many time points at a single site. Second, it is necessary to have solid data on environmental characteristics that may impact the communities. For some microbial habitats, such data may be difficult to acquire (for example, the human gut), or we may simply not know which characteristics we need to measure. Third, the Larsen *et al.*[1] model, along with many SDMs, assumes that community composition is related to measurable environmental conditions rather than dispersal constraints, priority effects or stochastic processes[9]. This may not always be the case as we know that both microbial and macroorganismal communities can be strongly influenced by these factors.

These caveats aside, there is no doubt that microbial ecologists will increasingly have to rely on the types of approaches described by Larsen *et al.*[1] to take full advantage of their datasets. Advances in high-throughput sequencing have been a blessing in disguise: microbial ecologists now need to apply analytical tools to keep from drowning in the flood of data. Gilbert and colleagues[1] offer one such life preserver and an important way forward. Microbial ecologists no longer have to lag behind plant and animal ecologists; we can start exploring microbial communities across time and space to an extent that was unimaginable only a few months ago.

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