region was close to carbon balance during the period of the study — about as much carbon was taken up by plants for growth as was emitted from decay processes.

However, the moisture and fertility of Amazonian forests changes substantially farther south and east. Dry seasons (periods with rainfall of less than 100 millimetres per month) get progressively longer, eventually lasting for 5 months or more as the forest grades into savannah[10]. Gatti and colleagues find that the drier forests in the northeastern and southeastern regions studied were close to carbon balance during the wet season, but that carbon release from decomposition and fire tended to exceed carbon uptake by photosynthesis during the dry season. The observed regional and seasonal patterns of carbon uptake in the northwest transitioning to carbon release in the drier east were consistent with the year-to-year variability of the data — which revealed that greater carbon releases, associated with decomposition and fire, occurred during hotter and drier years.

Gatti and co-workers show that the transition of eastern Amazon forests from carbon sink to carbon source during the dry season is associated with strong regional warming trends. Eastern Amazon sites have warmed by as much as about 0.6 °C per decade during the dry season over the past 40 years. This is more than three times the rate of global warming and about the same rate as for the Arctic. Wet-season and western Amazonian forests have warmed, too, but at a much slower rate. Warming rates in the dry season for eastern Amazonia might have been amplified by deforestation and forest degradation. Gatti *et al.* conclude that increases in fires, and in physiological stress, mortality and decomposition of trees in this area, are associated with increasing carbon loss from regional ecosystems.

The authors have documented the accelerating transition of forests from carbon sinks to sources using direct measurements of large-scale gradients of atmospheric gas concentrations. The overall pattern of deforestation, warmer and drier dry seasons, drought stress, fire and carbon release in eastern Amazonia seriously threatens the Amazon carbon sink. Indeed, the results cast doubt on the ability of tropical forests to sequester large amounts of fossil-fuel-derived CO_2 in the future.

For decades, ecologists have been surprised that the fraction of fossil-fuel emissions absorbed by land ecosystems has remained fairly constant[11], even though these emissions have increased. Forests at high latitudes have continued to accumulate carbon because their growing seasons have lengthened as a result of climate change. Mid-latitude forests have done so because they have been recovering from past clearance, and because they have benefited from the increased availability of nutrients (produced as a result of human activities, or mobilized in soils by climate warming).

By contrast, increased carbon sequestration by tropical forests must be driven largely by an increase in photosynthesis associated with rising CO_2 levels — but regional atmospheric profiling[12] suggests that this carbon sink is threatened by forest degradation and warming. Another complication is that fossil-fuel emissions must be quickly reduced to meet international climate targets, but it is not clear how the CO_2-driven carbon sinks of tropical forests will respond to a rapidly warming world in which CO_2 levels are no longer rising[13]. The future of carbon accumulation in tropical forests has therefore long been uncertain. Gatti and colleagues' atmospheric profiles show that the uncertain future is happening now.

"The results cast doubt on the future ability of tropical forests to sequester large amounts of carbon dioxide."

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The author declares no competing interests.

Microbiology

Deciphering metabolism, one microbe at a time

William F. Kindschuh & Tal Korem

Small molecules produced and modified by gut microorganisms can influence human physiology. An atlas of metabolic outputs of diverse gut microbes offers new ways to decipher the microbial mechanisms behind their production. **See p.415**

The microorganisms in our gut can have far-reaching effects — on our liver[1], arteries[2] and potentially even on our behaviour[3]. One way these microbes exert their effects is through the generation or consumption of small molecules, termed metabolites. Measuring metabolite levels, an approach called metabolomics, has led to ever-increasing recognition of their importance. And yet only rarely do we understand the underlying mechanisms driving these levels: namely, which microbes, enzymes and interactions are involved in the production and uptake of a specific metabolite. This task is further hindered by the complexity of microbial communities such as the gut microbiome, studies of which have to take into account the large number of microbes, the interactions between them, their diverse metabolic capabilities and several hard-to-measure non-microbial factors, such as host diet[4]. On page 415, Han *et al.*[5] present a comprehensive approach to

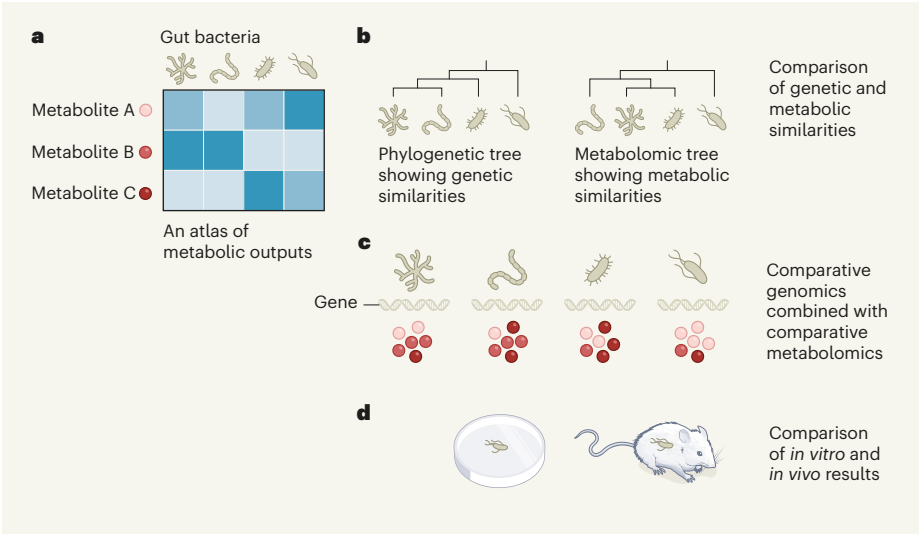

Figure 1 | An approach to studying microbial metabolism. a, Han *et al.*[5] generated a reference library of 833 small molecules (metabolites) relevant to gut-microbial metabolism, and used it to assess the metabolic output generated by 178 bacterial strains commonly found in the human gut. The authors thereby generated an atlas of metabolic outputs, as shown in this hypothetical example. Darker blue on the heat map indicates higher levels of production. **b**, The authors present a range of approaches for studying microbial metabolism using these data. They investigated the correspondence between the evolutionary relationships of different microbes (their phylogeny) and their metabolic output. Phylogeny and metabolism generally correspond; however, the authors found some exceptions and divergences. **c**, Han and colleagues further show that a parallel comparison between microbial genomes and their metabolic outputs could suggest genes responsible for unexplained metabolic capacities. **d**, The authors also investigated the correspondence between *in vitro* and *in vivo* microbial metabolism, identifying many metabolites produced in both contexts.

addressing this major challenge, by carrying out metabolic and genetic analyses of a broad set of microbes commonly found in the human gut.

The authors' approach (Fig. 1) has been facilitated by notable technical advances. Using liquid chromatography–mass spectrometry (LC–MS), a technique that quantifies metabolites on the basis of their polarity, mass and charge, Han and colleagues compiled a reference database of 833 metabolites that are relevant to microbial metabolism. They confirmed that these metabolites are detectable in biological samples, and that their measurement is consistent in several types of sample, such as faeces or blood, and quantifiable over a wide range of concentrations. The authors also developed an analysis pipeline that enables compound identification and statistical analysis. With this infrastructure in place, Han *et al.* measured metabolite levels in thousands of samples from *in vitro* cultures of 178 microbial strains grown separately in multiple media types, and from various tissues taken from mice whose intestines were colonized by the same strains, either alone or in communities of five or six species.

Having compiled an atlas of single-microbe *in vitro* metabolic outputs, Han and colleagues set out to address a long-standing question: to what degree is the evolutionary relationship between two microbes (their phylogeny) related to their metabolic capacity? The authors show that, although the two generally correspond, this correspondence is not perfect. For example, Han *et al.* report that *Clostridium sporogenes* and *Clostridium cadaveris*, two closely related species, have strikingly different metabolic profiles. By contrast, *Atopobium parvulum* and *Catenibacterium mitsuokai*, two phylogenetically distant species, have similar metabolic profiles.

Furthermore, although the authors could identify some strong species-specific associations with the production of particular metabolites, such as production of the molecule tyramine by *Enterococcus faecalis*, metabolomic profiles were insufficient to independently distinguish between members of different species. A machine-learning algorithm trained to identify a species on the basis of its metabolomic profile was correct only about 30% of the time, and even members of different genera or families were not well separated by the algorithm (in such analyses, it achieved an accuracy of approximately 70%). These results raise a note of caution regarding typical microbiome analyses, which often rely on microbial-abundance estimates at the genus and species levels, and thus might miss crucial metabolic aspects of the microbial community.

"To what degree is the evolutionary relationship between two microbes related to their metabolic capacity?"

Although the correspondence between phylogeny and metabolism is imperfect, the authors present an analytical approach using the association between specific genes and metabolic outputs to obtain insights into microbial metabolism. Han and colleagues paired their metabolomic analyses with analyses of bacterial genomes to uncover the genes responsible for unexplained metabolic capacities. The authors identify a previously unknown mechanism by which microbes of the phylum Bacteroidetes utilize the amino acids glutamine and asparagine. Nevertheless, the *spe* genes responsible for producing the molecules putrescine and agmatine in several species are not present in three species of *Fusobacterium* that the authors found to produce these molecules – a result that demonstrates the limitations of this analytical method.

Han and colleagues conclude by turning to the most challenging aspect of their approach: assessing the correspondence between *in vitro* and *in vivo* metabolic output. Strains with a prominent metabolic capacity, such as *Citrobacter portucalensis*, which produces agmatine from the amino acid arginine, maintained some of this capacity both in culture and in mice. In some cases, this led to effects reaching beyond the gut (systemic effects). For example, agmatine levels were increased in the urine of mice if the animals were colonized by *C. portucalensis*.

However, such a high level of correspondence between *in vitro* and *in vivo* data was not observed for the overall metabolic output, as tested by the authors for two strains. For these strains, there was only a moderate correlation between the *in vitro* metabolic profile of the strain and the profile measured from the intestines or faeces of a mouse colonized by it. Furthermore, no correlation was found between the *in vitro* profiles of these strains and the blood or urine profiles of mice colonized by them. This was the case despite the simplified 'mono-colonization' scenario, in which each mouse harboured only a single microbial strain, without other members of the bacterial community and the complex effects that arise from the interactions between them[6].

These results highlight a major challenge left in the wake of this impressive endeavour, which is to use this extensive atlas of metabolic measurements, taken in simplified settings, to provide accurate models of complex community metabolism. This could be done experimentally – for example, by extending the work performed by Han *et al.* to assess combinatorial co-cultures – or by harnessing

various computational and mathematical methods[7,8]. Future work could further validate the utility of this data set for studying the human gut microbiome; extend the data set to strains that are found in, and have probably adapted to, a specific host[9]; and expand the data set to microbes and metabolites that are relevant to other human-associated microbial communities, such as the vaginal and skin microbiomes.

Han and colleagues provide useful resources for the research community, including an extensive metabolomics data set consisting of thousands of samples, web resources with which to explore it and analytical approaches for studying microbial metabolism. Moreover, this work provides a truly open-source technical resource, with protocols, analysis pipelines and an extensive metabolite reference library, which the authors demonstrate to be applicable, with minimal calibration, to different machines. This resource could be used by others as they pursue similar experimental set-ups, thereby promoting the democratization of metabolomics. Altogether, this work lays a foundation for future work seeking to decipher microbial metabolism — an important step towards new therapeutics that target the microbiome.

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The authors declare no competing interests.

Quantum physics

Feedback offers quantum control of nanoparticles

Tania S. Monteiro

Precise measurements of the position of a levitating nanosphere have been used to control forces that damp the nanosphere's motion — potentially opening the way to quantum control of larger objects. **See p.373 & p.378**

The Heisenberg uncertainty principle states that certain incompatible pairs of properties of a particle cannot be determined simultaneously with unlimited precision. It is often taught using a thought experiment for the case involving position and momentum: if the position of an atom is measured with light, the back-action of the scattered photons on the atom invariably disturbs the atom's momentum. The back-action can be reduced by using less-energetic or fewer photons, but this also reduces the precision of the measurement. More specifically, the Heisenberg uncertainty principle stipulates that the product of the uncertainties in measurements of position and momentum must be greater than or equal to half of Planck's constant, $\hbar$. But this constant is so tiny (1.05×10^{-34} joule seconds) that the trade-offs between the back-action and imprecision can be observed only in carefully controlled experiments, typically using objects at the size scale of atoms.

Now, Magrini *et al.*[1] (page 373) and Tebbenjohanns *et al.*[2] (page 378) report independent studies in which they were able to track the position not of a single atom, but of a nanosphere containing billions of atoms, with a precision close to the Heisenberg limit (the minimum possible product of the uncertainties of the measured quantities). This enabled them to use a technique called measurement-based quantum control to cool the nanosphere from highly excited thermal states down to average energies that are close to the lowest energy state of the particle (the quantum ground state).

The results of the two studies are a breakthrough in optomechanics, the research field that aims to bring small mechanical oscillators into quantum regimes through their interaction with light. In the subfield of levitated quantum optomechanics, the oscillator is a silica particle about the size of a virus (100–200 nanometres in diameter), and is trapped and controlled by light. This minimizes both unwanted heating of the particle and decoherence — the loss of the particle's quantum behaviour through interactions with the environment. Decoherence typically occurs much faster in experiments with oscillators that are directly tethered to their environment than in levitated systems.

After a decade of effort by several groups worldwide[3], light-induced cooling of a levitated nanoparticle to the quantum ground state was finally reported[4] in 2020. But that experiment relied on the quantum mode of light bouncing between two highly reflective mirrors, a set-up known as an optical cavity. This approach comes with limitations: only particles with certain ranges of oscillation frequency can be cooled in each set-up. Moreover, it is challenging to control the operation of an optical cavity sufficiently well to hold a particle stably, and then to cool it.

Magrini *et al.* and Tebbenjohanns *et al.* used a completely different approach, dispensing with the optical cavity, and thus evading the associated problems. Their technique might therefore offer a more robust and straightforward way to prepare quantum states of mesoscopic objects (those between about 100 nanometres and one micrometre in size) .

The authors' approach (Fig. 1) is an extension of a method termed feedback cooling, in which continuous measurement of an oscillator's position enables a force (the feedback) to be applied that counters and damps the oscillator's motion. Although feedback cooling has been extensively investigated, for some years there was considerable scepticism as to whether this approach alone, without cavity cooling, could reach the milestone of cooling a levitated particle to an average energy that corresponds to less than a single quantum of energy above the fundamental zero-point motion (the residual motion that an oscillator retains in the quantum ground state). The current studies demonstrate that this milestone can indeed be reached using this method.

Several advances have paved the way to this achievement. A feedback technique known as cold damping, which applies a force that is proportional to the velocity of the particle, was in the past few years[5,6] shown to yield highly efficient cooling. Importantly, the nanospheres are naturally charged, which means that the feedback force can be applied using an electric field[7], rather than light — thus avoiding extra photon back-action being exerted on the nanospheres. The experimental set-ups in the two new studies also operate at ultrahigh-vacuum levels (about 10^{-12} of normal air pressure), largely eliminating heating and decoherence associated with collisions of the nanosphere with surrounding gas molecules. And both studies benefited from improvements in the efficiency with which scattered photons are collected to measure the position of the nanosphere[8].