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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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].

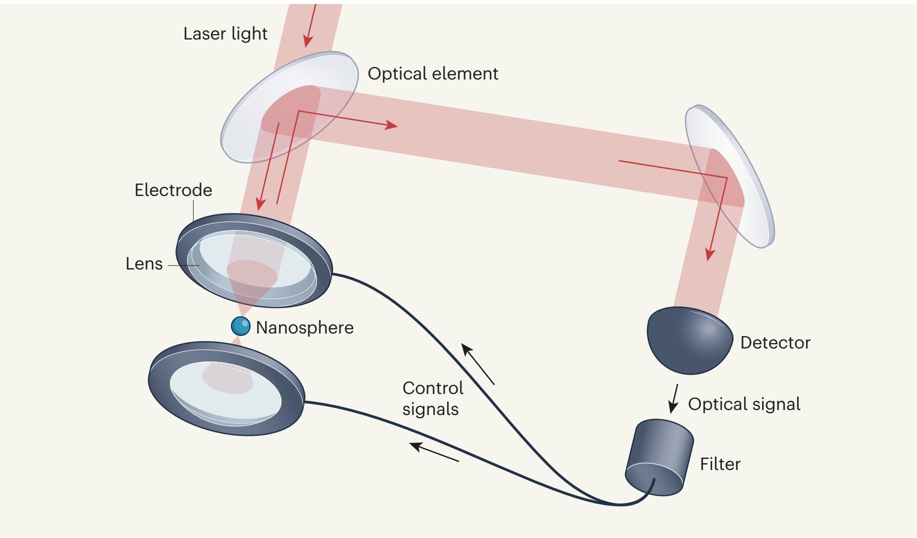

Figure 1 | A measurement-based approach for cooling nanoparticles. Magrini *et al.*[1] and Tebbenjohanns *et al.*[2] have used a system called measurement-based quantum control to damp the motion of a spherical nanoparticle. The nanosphere is captured by a tightly focused beam of laser light known as an optical trap. Light scattered from the particle is reflected by a system of optical elements to a detector, producing an optical signal that is processed by a filter to determine the nanosphere's position. This position measurement is then used to generate a signal that controls the electric field generated by a pair of electrodes around the nanosphere – thereby damping (cooling) the nanosphere's oscillatory motion.

Furthermore, the two experiments used a technique for measuring the energy of a particle[9] that not only is calibration-independent, but also involves a characteristic of particles that are approaching the quantum regime: the spectra of the light scattered by such particles have two peaks, one of which corresponds to the particle absorbing a quantum of energy and the other to the loss of one quantum. The precise ratio of the areas of the peaks corresponds to the ratio of n to $n + 1$, where n is the number of energy quanta of the nanosphere (n is 0 in the quantum ground state, for example). A version of this technique, often called sideband asymmetry, is used in optical-cavity optomechanics[4], but its applicability to experiments that use scattered light for measurements was not recognized until 2019 (ref. 9).

There are also differences between the two experiments. Magrini *et al.* cooled their particle from room temperature, which corresponds to a state in which n is in the tens of millions, down to a measured average energy of $n = 0.56$ – which means that, although the particle is not exactly in the quantum ground state, it has more than a 50% probability of being in that state, and a sharply falling probability of being in successively higher quantum states (with $n > 1$). To achieve this cooling, they used a statistical algorithm called a Kalman filter[10] to optimize the feedback forces applied in real time to the nanosphere in response to a continuous measurement. A Kalman filter is especially well suited for controlling quantum systems that have states typical of mechanical oscillators[11].

By contrast, Tebbenjohanns *et al.* used a straightforward control system that relies on the harmonic (pendulum-like) nature of the nanosphere's motion to predict the velocity of the nanosphere from its measured position, and hence to drive the feedback force. They also immersed the trapped nanosphere in a cryostat that reduced the initial temperature from about 300 to 60 kelvin. This cryogenic cooling will fulfil a crucial function in future experiments: it will ensure that the internal temperature of the nanosphere is low, thus reducing the emission of thermal radiation from the nanosphere. Such radiation is a major source of decoherence, and can potentially be produced from the relatively hot interior of a nanosphere even when the centre-of-mass motion of the object is in the quantum ground state. Tebbenjohanns and colleagues cooled nanospheres to an average energy corresponding to $n = 0.65$.

"The results are a breakthrough in the research field of optomechanics."

Measurement-based control techniques similar to those used in the two present studies were reported[12] last month to strongly damp the oscillations of a tethered 10-kilogram mirror in the 4-kilometre-long optical cavity of the Laser Interferometer Gravitational-Wave Observatory (LIGO). This achievement increased the formidable precision of the LIGO experiment, which can measure mirror displacements equivalent to a small fraction of an atomic nucleus. The mirror was cooled to an average energy corresponding to an n value of a little over 10. The big goal now is to demonstrate that cold oscillators – whether levitated or tethered – exhibit quantum behaviour in cavity-free experiments.

The new generation of table-top, optically levitated experiments[1,2,4] are relatively simple, cheaper than LIGO and open up research possibilities not available using tethered oscillators. The optical forces holding the nanoparticles are fully controllable, allowing the trapped objects to be guided in space or fully released. Because they are highly decoupled from sources of decoherence, the nanoparticles might retain their quantum coherence for long enough to exhibit the effects of quantum-wave interference. They might also exhibit a quantum effect called entanglement, possibly in experiments with multiple nanospheres. Finally, they could be used as ultrasensitive force detectors for practical applications such as accelerometry, or for testing fundamental physics such as quantum gravity.

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