dissect the differences between subgroups.

Pyramidal tract neurons located primarily in the upper part of layer 5 send signals to a brain region called the thalamus that sends projections back to the cortex, forming a loop involved in preparing for motor activity. Tasic *et al.* demonstrated that these neurons are molecularly distinct from those located in a lower portion of layer 5 that project to the medulla, which is associated with the execution of movement. Economo *et al.* engineered each subpopulation of neurons to express the protein channelrhodopsin — a light-sensitive ion channel. This enables neuronal activity to be precisely controlled using light (a method known as optogenetics), and so allowed the authors to dissect the roles of the upper and the lower layer-5 neurons in different types of motor function.

Economo and colleagues used light to independently activate the pyramidal tract populations in mice, and simultaneously monitored both the activity patterns of the cells and the behaviour of the animals as they engaged in a motor-learning exercise. These experiments confirmed that the two populations of pyramidal tract neurons have separate roles: one in preparing for motor activity and the other in initiating movement. The authors' results also provide a compelling demonstration of how understanding the molecular taxonomy of the brain can lead us to an understanding of how neurons connect and function.

Together, the two studies highlight the transformative potential of atlas-scale data sets in modern neuroscience[6,7]. They make a strong case for conducting similar studies of more cell types and of the brains of animals of different species, including humans, at various ages. In support of the need for data from different species, a recent single-cell sequencing study[8] has reported a greater diversity of neurons in a cognition-associated region of the human cortex than has been described for mice — this might explain our ability for higher-order cognition. Further characterization of both neuronal and non-neuronal cell classes could also yield fresh insights into their selective vulnerabilities to disease states, and instruct the development of protocols to generate these cell types from stem cells *in vitro*, for use as disease models and for drug testing.

In the future, researchers will undoubtedly make use of the genetic markers of specific neuronal populations identified by Tasic and colleagues' cell atlas. For example, these markers could be used to design more optogenetic experiments that target specific neuronal populations; to investigate whether 'area-specific' cell types can be found in other cortical regions; and to isolate populations of cells for further functional characterization.

However, translating the cellular composition of the brain into biologically meaningful insights will require new strategies for interrogating neuronal function. Technologies to manipulate cell types currently being developed through the support of the US National Institutes of Health BRAIN Initiative[9] might enable these analyses. In doing so, they could allow us to fully appreciate the portrait gallery of cells that control brain function. ■

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QUANTUM PHYSICS

Mechanical quantum systems controlled

The control of quantum systems offers great potential for advanced information-processing and sensing applications. An approach has been demonstrated that enables such control over the motion of mechanical oscillators. SEE ARTICLE P.53

MICHAEL R. VANNER

People tend to behave differently when they are being watched. It turns out that objects in the quantum world do, too, and that the very act of measurement can modify their behaviour. This effect is a consequence of Heisenberg's uncertainty principle, which states that, if we measure the position of a moving object precisely, we cannot simultaneously know the object's momentum. On page 53, Rossi *et al.*[1] report an experiment that beautifully demonstrates this tenet of quantum physics. The authors use their measurements to apply a feedback force to a mechanical oscillator — an object akin to a vibrating drumhead — to greatly suppress the oscillator's motion. The work opens up an avenue for controlling mechanical quantum systems by continuously monitoring and manipulating their dynamics.

The use of measurements and feedback to stabilize a system is a well-developed technique in engineering and is applied in many everyday technologies. For example, the technique is used to stabilize the motion of lifts, and is also used to reduce the effects of turbulence during flights in many types of aircraft. Researchers have now extended these concepts so that measurement and feedback can be used to control the properties of individual quantum systems[2].

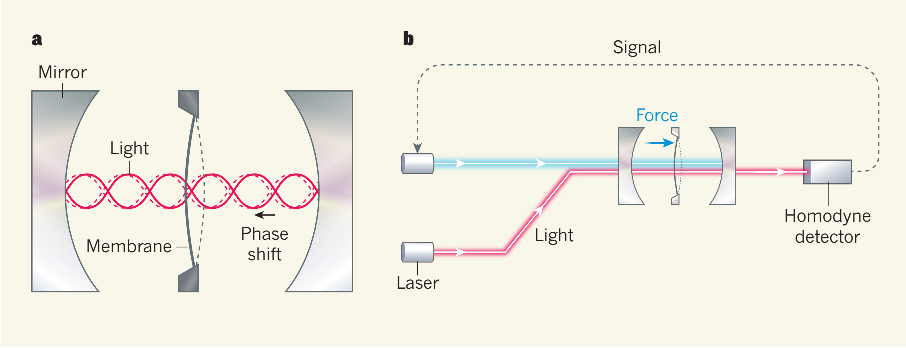

Figure 1 | Quantum measurement and feedback. a, Rossi *et al.*[1] report an experiment in which a millimetre-sized mechanical membrane interacts with light that bounces back and forth between a pair of mirrors known as an optical cavity. The drumhead-like motion of the membrane causes the light to acquire a phase shift that depends on the position of the membrane. The black and red dashed lines indicate a mechanical displacement and such a phase shift, respectively. **b**, The authors continuously supplied the cavity with light (red) from a laser. They monitored the phase shift of light that was transmitted through the cavity using a device called a homodyne detector, thus enabling a continuous measurement of the membrane's position. The signal from the detector was then used to control the intensity of a second laser. The light (blue) from this laser applied a feedback force to the membrane that brought the membrane's motion close to its ground state — a convenient starting point for future quantum experiments.

Prominent experimental examples of quantum control include preparing and stabilizing quantum states of a microwave signal that bounces between a pair of mirrors known as an optical cavity[3], and controlling the state of a superconducting quantum bit of information[4]. Progress in quantum control has been rapid during the past few decades, and researchers have been extending these techniques to other physical systems to exploit the advantages that different systems provide.

One such area under development is cavity quantum optomechanics, in which laser light inside an optical cavity is used to control the motion of a mechanical oscillator. Central to this field of research is the radiation–pressure interaction, whereby the reflection of light from an object modifies the object's momentum and, concurrently, causes the light to acquire a phase shift — a shift in the crests and troughs of the light's electric field — that depends on the object's position. Using this interaction, physicists can both precisely measure and control mechanical motion.

A key goal in optomechanics research has been to bring mechanical motion close to its ground state — the state that describes the tiny amount of jiggling that is imposed by quantum mechanics, even at absolute zero temperature. Realizing this state is a convenient starting point for future quantum experiments that would otherwise be unfeasible because of random heat-induced fluctuations of the mechanical motion.

A common route to achieving this goal is sideband cooling — a technique that uses light to reduce mechanical fluctuations and that was previously applied to trapped ions. The method requires the light in the optical cavity to have a lifetime that is much longer than the period of the mechanical motion. This configuration of experimental parameters is known as the resolved-sideband regime, and precludes fast measurements of the mechanical motion because the cavity accumulates a signal of such motion over a relatively long timescale.

Rossi and colleagues developed an optomechanical experiment that operates well outside the resolved-sideband regime. The authors placed a millimetre-sized mechanical membrane inside an optical cavity that was continuously supplied with light from a laser (Fig. 1). They monitored the resulting phase shifts in the light using a device known as a homodyne detector, which enabled the membrane's position to be measured continuously.

The authors then passed the signal from the detector through a filter, which essentially converted the information about the membrane's position into information about its momentum, and used this new signal to control the intensity of a second laser. The light from the second laser applied a feedback force to the membrane that greatly suppressed the membrane's motion. Using this approach, the team achieved a mean thermal occupation of approximately 0.3, which means that the oscillator was in the ground state for more than 75% of the time.

Rossi and co-workers' achievement can be viewed as the culmination of decades of research in engineering and quantum physics, and it builds on the work of several other groups around the globe that are too numerous to list here. The use of laser light to both monitor mechanical motion and apply a feedback force was first studied theoretically[5] in the late 1990s, and a proof-of-concept experiment was carried out shortly thereafter[6]. Since then, improvements in optomechanical experiments have enabled researchers[7] to achieve a thermal occupation of about 5.3, which is equivalent to a ground-state probability of 16%. The technique has also been used to stabilize the mirrors in gravitational-wave detectors[8].

Key to the present work's success was the fact that the speed with which the experiment precisely measured the position of the membrane was much faster than the rate at which the membrane returns to thermal equilibrium. Such a regime is said to have high 'quantum cooperativity', and allowed the physics of the Heisenberg uncertainty principle to be clearly visible in Rossi and colleagues' experimental results.

The authors' work not only demonstrates the utility of quantum measurement and feedback, but also highlights the richness of optomechanical experiments that operate well outside the resolved-sideband regime. Among many applications, working in this regime allows optomechanical interactions to be carried out that, when combined with the authors' control method, offer a route towards producing 'quantum-superposition' states of mechanical motion[9]. Such states would be useful to both develop quantum technologies and probe the foundations of physics. ■

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MICROBIOLOGY

Chromatin clues to a parasite's coat switch

The parasite *Trypanosoma brucei* causes sleeping sickness. It evades human defences by changing the version of a protein that coats its surface. Analysis of its genome and nuclear structure clarifies this variation process. SEE LETTER P.121

STEVE KELLY & MARK CARRINGTON

Most infections don't usually cause prolonged illness in humans because the body's immune system recognizes the presence of a molecular fragment made by the pathogen, termed an antigen, as alien, and triggers a defence response that eliminates the pathogen. However, pathogens use a range of strategies to evade such destruction. One approach is called antigenic variation, whereby a pathogen population keeps changing the antigens that are expressed. If antigenic variation occurs more rapidly than the host can respond to a newly expressed antigen, infection can persist. Müller *et al.*[1] report on page 121 that in the parasite *Trypanosoma brucei*, the structure of the DNA–protein complex known as chromatin has a role in how antigenic variation occurs in this organism.

The process of antigenic variation has evolved independently in many organisms[2–5]. It has certain common features, such as the presence of a reservoir of many versions of a particular gene, and hence the possibility that many different antigens can be expressed that correspond to that gene or gene family. Another aspect central to infection persistence is the presence of mechanisms to ensure that only one version of such a gene is expressed at a time, with all the other versions existing in a silenced state that might later be reversed[6].

Antigenic variation has been studied intensively in *T. brucei*, which causes African trypanosomiasis, historically known as sleeping sickness, in humans, and a range of diseases in livestock. The disease can be fatal if trypanosomes enter the brain, causing a range of neurological symptoms that including the disturbance of sleep patterns[7]. Although the incidence of the human disease is in decline[8], the animal illness remains a major cause of poverty among farmers in sub-Saharan Africa[9].

The surface of a *T. brucei* trypanosome is