Mitocheck website[2]. In particular, the authors provide a very high-resolution picture of mitosis, exploiting the advantage that time-lapse movies offer over the canonical endpoint assays typically used. Moreover, their event-order maps, generated by observations over a specific time window, provide an excellent overview of the patterns of temporal coupling of different mitotic perturbations.

The advantage of such a fine and articulated classification[1] is that it allows predictions to be made about the reason behind new perturbations — for example, those caused by drugs, treatment conditions or disease states — by comparing their phenotypic signatures with those of known genes. This data set, however, could be complemented in various ways. The creation of a transcription profile of the relevant genes, the use of high-confidence protein–protein interaction databases, and an analysis of signal transduction by the proteins encoded, mapped onto Neumann and colleagues' data set, would allow a more comprehensive study and understanding of the phenotypes the authors observed.

The use of this data set and of the experimental pipeline developed by Neumann *et al.* will be particularly useful for discovering new drug targets and for defining the action mechanism of different drugs. This is particularly relevant to cancer, because many cancer drugs perturb the cell cycle, precisely the area that Neumann *et al.* investigated in detail. Linking their data[1] to a drug's phenotypic signature could help to identify targets and mechanisms of action in much the same way as has been proposed for the 'connectivity' project[6], in which researchers developed a map linking gene-expression patterns to corresponding patterns of gene expression produced by various drugs and genetic manipulations.

One concern about the authors' work is that it was performed in only one cell line, potentially missing — or overemphasizing — certain pathways. It would be beneficial to complete the same analysis using cancer cell lines and normal cells to see if different cell types show different hierarchical clusters of gene expression.

We believe that, as more such genome-wide screens are performed, a future challenge will be not only the creation of new data sets and the amplification of existing ones, but also the establishment of a flexible platform that will cross-reference and integrate different screens to facilitate the collection of information and to create an overall picture of protein function. ■

Cecilia Cotta-Ramusino and Stephen J. Elledge are in the Department of Genetics, Harvard University Medical School, and Division of Genetics, Brigham and Women's Hospital, Boston, Massachusetts 02115, USA.
e-mail: selledge@genetics.med.harvard.edu

1. Neumann, B. *et al. Nature* **464,** 721–727 (2010).
2. www.mitocheck.org
3. Poser, I. *et al. Nature Meth.* **5,** 409–415 (2008).
4. Bramsen, J. B. *et al. Nucleic Acids Res.* **37,** 2867–2881 (2009).
5. Hübner, N. C. *et al. Chromosoma* **119,** 149–165 (2010).
6. Lamb, J. *et al. Science* **313,** 1929–1935 (2006).

QUANTUM MECHANICS

The surf is up

Markus Aspelmeyer

Researchers have long wanted to be able to control macroscopic mechanical objects in their smallest possible state of motion. Success in achieving that goal heralds a new generation of quantum experiments.

Dead silence — and then roaring applause. I still remember that brief moment that revealed the astonishment of everyone in the audience. Andrew Cleland had just concluded his talk at the conference 'Quantum Optics of Nano- and Micromechanical Systems', which was held last July in Bad Honnef, Germany. He had taken us all by surprise. Andrew's talk had begun as a review of recent results[1] of his and John Martinis' team — they had achieved an unprecedented degree of control over individual electromagnetic quanta (photons) in a microwave resonator by coupling the resonator to a superconducting two-state quantum system, or qubit. But the awe came with his last slide: in it, he showed that if the microwave resonator could possibly be replaced with a mechanical oscillator of similar resonance frequency, then the same qubit device could be used to attain quantum control over individual mechanical quanta (phonons). Just eight months later, Cleland, Martinis and their colleagues (O'Connell *et al.*, page 697 of this issue)[2] report that they have done just that*.

Over the past few years, impressive progress has been made in studying nano- and micromechanical resonators, and the common aim of exploring the quantum regime of mechanical systems has generated a thriving field that continues to attract an eclectic mix of researchers[3]. O'Connell and colleagues' results[2] are a remarkable achievement because they involved overcoming two outstanding challenges in the field. The first is bringing the mechanical device reliably to its quantum ground state of motion, and the second is coupling it strongly to a different quantum system. With these challenges met, the future is ripe to use these systems both to test the principles of quantum mechanics and in applications such as quantum information processing.

The difficulty in bringing a mechanical device to its quantum ground state lies in the environmental temperatures (T) needed. To suppress residual thermal phonons in the device requires $T < hf_m/k_B$, where f_m is the device's resonance frequency and h and k_B are Planck's and Boltzmann's constants, respectively. Typical mechanical resonators involve the motion of the device's centre of mass and have resonance frequencies smaller than hundreds of megahertz. The required ground-state temperatures of such devices are below those achievable with standard cryogenic refrigerators. One solution is to use additional cooling schemes analogous to the laser cooling of atoms. This technique has allowed the preparation of mechanical states of mean phonon occupation, n, close to the quantum ground state ($n = 0$), for both nanomechanical[4] ($n \approx 4$) and micromechanical[5,6] ($n \approx 30$) resonators.

Another solution is simply to avoid the difficulty, as O'Connell *et al.*[2] do. Their micromechanical resonator consists of a suspended slab that, owing to its piezoelectric nature (it changes its volume when subjected to an external electric field), can undergo oscillations in its thickness when the two metal electrodes between which it is sandwiched are subjected to a voltage. This acoustic vibration does not involve any centre-of-mass motion and hence allows the authors to achieve ultra-high mechanical frequencies of $f_m \sim 6$ gigahertz, for which they could prepare their system's ground state using a conventional dilution refrigerator: at temperatures of about 25 millikelvin they obtained $n < 0.07$.

After meeting the first challenge, the authors were set to meet the second: to couple a resonator and another quantum system sufficiently strongly for quantum effects to be observed. Recent experiments have demonstrated mechanical coupling to qubits[7] and strong coupling to optical cavities[8]. However, decoherence mechanisms have thus far prevented quantum effects from being observed.

In their experiment, O'Connell *et al.*[2] overcome this problem. Their mechanical resonator is connected via a capacitor to a Josephson phase qubit, which consists of two superconductors coupled by an insulating (Josephson) junction. The qubit's ground and excited states represent the two lowest energy states of the superconductors' wavefunction phase difference across the tunnel junction. By using the piezoelectric nature of the resonator, the electromagnetic energy of the qubit can be converted into the mechanical energy of the resonator, or vice versa. In principle, this interaction allows the authors to coherently transfer an arbitrary state of the qubit to the resonator, and even to generate entanglement — a quantum effect in which the states of the qubit and the resonator are linked together in an inseparable way.

To demonstrate coherent quantum-state transfer, O'Connell *et al.* prepared the qubit in the excited state and switched on the interaction between the qubit and the resonator. They then

*This article and the paper under discussion[2] were published online on 17 March 2010.

measured the occupancy of the qubit's excited state as a function of the interaction time. The observed oscillatory behaviour of this occupancy is a clear quantum effect and indicates reversible qubit–resonator exchange of a single quantum of energy. The typical transfer times for single quanta (the Rabi swap time) was 4 nanoseconds, which is smaller than the energy decay times of 17 ns and 6 ns for the qubit and resonator, respectively. The authors observed a similar oscillatory behaviour in the excited-state occupancy when they transferred a qubit's superposition state, one in which the system is in the ground and excited states at the same time, hence preparing a quantum superposition of the mechanical system. It is also worth noting that, after half the Rabi swap time, the authors' transfer interaction should create an entangled state between the qubit and the mechanical resonator. They point out, however, that their current experimental performance excludes a direct test of entanglement.

Although today it is routine to control the quantum-mechanical motion of individual atoms[9], controlling that of a nano- or micrometre-sized system is not. Quantum mechanics on such scales has been envisaged[10,11] since the 1990s. With their experiment, O'Connell *et al.* have not only set foot firmly in this quantum regime but have also opened the door for quantum control of truly macroscopic mechanical devices. And the prospects are exciting. One in particular is quantum information processing. In this, a key ingredient is the coherent control of many quantum systems, ideally in a scalable architecture. There have been proposals[12,13] to achieve such control by using arrays of mechanical resonators. Although actual implementations will require minimizing the effect of detrimental decoherence mechanisms, the authors[2] have undoubtedly set the stage for such a future.

Another long-term prospect is testing the foundations of quantum physics. For example, superposition states of massive mechanical objects may be used to test possible deviations from quantum mechanics, which have been suggested to eliminate the 'Schrödinger's cat' paradox (in which a cat concealed in a box can be both dead and alive in a superposition of states)[14,15]. Such tests require quantum superpositions of macroscopic spatial separation between two states of an object, literally of an object being both 'here' and 'there'. In O'Connell and colleagues' experiment[2], access to this regime is still hampered by the resonator's high mechanical frequency: the actual displacement between the two motional states of the prepared superposition is on the order of 10^{-16} metres — that is, six orders of magnitude smaller than the size of the unit cells of the resonator's structural lattice.

Although future experiments will need to find a working regime at lower frequencies, O'Connell *et al.* have taken a decisive first step towards an exciting future in mechanical quantum physics. This reminds me of the closing remark of another intriguing talk that was given at the same conference by Pierre Meystre, one of the early pioneers in the field: "Thirty years ago I thought that it was a dead field. Now I think that the surf is up!" ■

Markus Aspelmeyer is at the Faculty of Physics, University of Vienna, Vienna 1090, Austria.
e-mail: markus.aspelmeyer@univie.ac.at

1. Hofheinz, M. *et al. Nature* **459,** 546–549 (2009).
2. O'Connell, A. D. *et al. Nature* **464,** 697–703 (2010).
3. Cho, A. *Science* **327,** 516–518 (2010).
4. Rocheleau, T. *et al. Nature* **463,** 72–75 (2009).
5. Gröblacher, S. *et al. Nature Phys.* **5,** 485–488 (2009).
6. Schliesser, A. *et al. Nature Phys.* **5,** 509–514 (2009).
7. LaHaye, M. D. *et al. Nature* **459,** 960–964 (2009).
8. Gröblacher, S. *et al. Nature* **460,** 724–727 (2009).
9. Blatt, R. & Wineland, D. J. *Nature* **453,** 1008–1015 (2008).
10. Cleland, A. N. & Roukes, M. L. *Nature* **392,** 160–162 (1998).
11. Schwab, K. C. & Roukes, M. L. *Phys. Today* **58**(7)**,** 36–42 (2005).
12. Cleland, A. N. & Geller, M. R. *Phys. Rev. Lett.* **93,** 070501 (2004).
13. Rabl, P. *et al.* Preprint at http://lanl.arxiv.org/abs/0908.0316v1 (2009).
14. Marshall, W., Simon. C., Penrose, R. & Bouwmeester, D. *Phys. Rev. Lett.* **91,** 130401 (2003).
15. Leggett, A. J. *Science* **307,** 871–872 (2005).

STEM CELLS

Skin regeneration and repair

Cédric Blanpain

Different types of stem cell maintain the skin's epidermis and contribute to its healing after damage. The identity of a stem-cell type that gives rise to different epidermal-cell lineages has just been revealed.

Skin acts as an essential barrier, protecting organisms from their environment. It is composed of two parts: the epidermis, the cells of which form the barrier; and the dermis, which provides support and nutrition to the epidermis. The epidermis also produces appendages, including sweat glands, and hair follicles and their associated sebaceous glands. The different epidermal compartments undergo constant cellular turnover to replace the dead or damaged cells. This homeostatic process is thought to involve several types of stem cell, each located in a specific epidermal region and contributing to the maintenance of a discrete compartment of the skin[1] (Fig. 1a). In a paper published in *Science*, Snippert *et al.*[2] identify the Lgr6 protein as the marker of progenitors that can differentiate into different cell lineages of the skin epidermis.

The first evidence that skin stem cells can differentiate into interfollicular epidermis, sebaceous gland and hair follicle lineages came from transplantation of bulge stem cells[3,4] — a cell population located at the base of hair follicles. Further experiments revealed that, during both embryonic development and normal adult skin homeostasis, bulge stem cells and their progeny contribute to hair-follicle regeneration but not to the maintenance of the interfollicular epidermis[4–6]. In conditions such as wounding, however, bulge stem cells rapidly migrate towards the interfollicular epidermis to help with the rapid regeneration of the wounded skin[5,7,8].

Later findings also showed that sebaceous-gland cells are maintained by progenitors located above the bulge, which express the Blimp1 protein during morphogenesis[9]. Maintenance of the interfollicular epidermis, meanwhile, involves many small units of proliferation scattered throughout this skin layer, called epidermal proliferative units[10,11]. The infundibulum — the upper part of the hair follicle, which interfaces with the interfollicular epidermis — is thought to be maintained by progenitors located in a hair-follicle region known as the isthmus; these cells, which express the marker proteins MTS24 and Lrig1 (refs 12–14), can differentiate into all epidermal cell lineages after transplantation[13,14].

Snippert *et al.*[2] set out to identify the 'mother' of these epidermal stem cells. They find that, during skin formation in mice, the transmembrane receptor Lgr6 is expressed in both the hair follicle and the interfollicular epidermis. In adult animals, however, Lgr6 expression becomes restricted to the isthmus, where about one-third of Lgr6-marked cells also express MTS24 and a few co-express Blimp1.

To more precisely define the differentiation potential of Lgr6-expressing cells, the authors used genetic wizardry to permanently label Lgr6-expressing cells and their progeny. As expected from the first set of results[2], as well as previous data[6,8], Lgr6-expressing cells gave rise to cells of both the hair follicle and the sebaceous gland during embryonic development. Moreover, some cells of the interfollicular epidermis were derived from Lgr6-expressing cells (Fig. 1b).

The authors' lineage tracing of adult skin shows that Lgr6 labelling was initially restricted mainly to the cells of the isthmus region, with some labelling of cells in the interfollicular epidermis and other parts of the hair follicles, albeit at lower frequency. Two months later, Lgr6 progeny were found mainly in the isthmus and sebaceous gland, with some in the interfollicular epidermis, and more rarely elsewhere in the hair follicle. These findings suggest that Lgr6-expressing cells contribute mostly to the homeostasis of the isthmus region and the