reverse transcription mechanism, primed by target DNA, that is similar to group II retrohoming[10]. Perhaps these are the mobile descendants of group II introns. ■

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Nanotechnology

Heat flow through nanobridges

Leo P. Kouwenhoven and Liesbeth C. Venema

When a sample of material is heated on one side, energy will flow to the cold end. In solid material, heat can be carried either by mobile electrons or by atoms vibrating around their fixed, equilibrium positions. Insulating materials do not contain mobile electrons so only atomic vibrations can transport heat in insulators. These vibrations are not random: the atoms move collectively so that together they form waves, called phonons. Objects in everyday life, such as a ceramic cooking pot, contain many different types of phonons with varying wavelengths, which carry heat from the hot to the cold end. But by making objects smaller and smaller, today's trend in physics and engineering, properties of phonons emerge that are not evident in large materials. On page 974 of this issue, Schwab *et al.*[1] report an experiment involving an extremely narrow (nanometre-scale) bridge for phonons. A nanometre is a billionth of a metre, making the bridges about 500 atoms wide. The authors find that the amount of heat that can flow across the nanobridge is bound by an upper limit, set by the laws of quantum mechanics.

In the world of nanoscale objects, such as the nanoharp shown in Fig. 1a, heat cannot be carried by phonons of just any wavelength. Of all possible phonons, the one with the longest wavelength that just fits within the material has the lowest energy. Longer wavelengths (and hence lower-energy phonons) are not allowed. For smaller objects, the maximum wavelength decreases, and consequently the minimum phonon energy increases. When the object is so small that this minimum phonon energy exceeds the thermal energy, $k_B T$ (where k_B is the Boltzmann constant and T the temperature), quantum behaviour of the phonon motion can be expected.

Many types of phonons with different wavelengths and characters can exist. Each leads to a specific mode of wave-like motion in an object, such as twisting or bending in a wire. In the centre of the device created by Schwab *et al.*[1], various phonons are generated by heating (Fig. 1b). But only specific phonon modes can couple into the narrow wires attached at each corner. One of these possible modes is shown in colour. Because only specific modes are allowed, the phonon spectrum is quantized in these nanobridges. Similarly, oscillations in the wires of the nanoharp (Fig. 1a) can occur only at a particular set of discrete frequencies, much as the strings in a full-sized harp are restricted to resonate at certain frequencies. In the nanoharp, these frequencies form the quantized spectrum of allowed wavelengths.

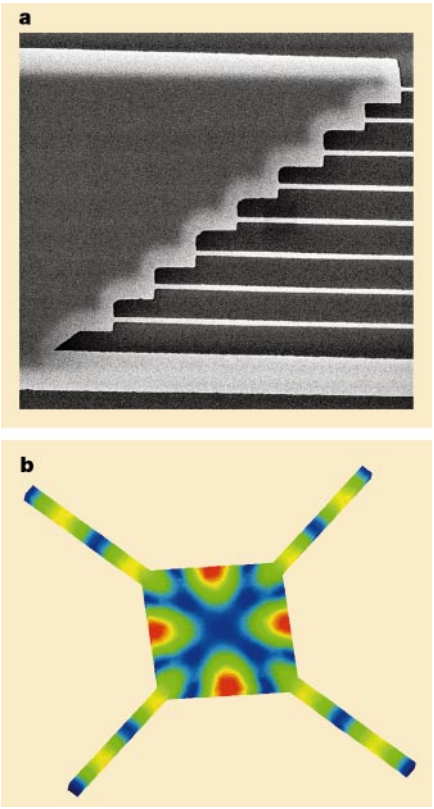

Figure 1 **The nanoscale world.** a, **Parallel nanobridges forming a nanoharp. The sound in the bridges of the nanoharp is restricted to certain resonant frequencies, as in a full-sized harp. Both sound and heat are carried through solids by phonons. The word phonon refers to the Greek word 'phon' for sound. (Photo courtesy of H. G. Craighead, Cornell University.)** b, **In the device created by Schwab *et al.*[1], phonons are generated in the central square by thermal heating. Some of these phonons can leave this region by way of the four suspended nanobridges. The colours indicate the local strain amplitude. (Simulation by D. Harrington, Caltech.)**

How does a quantized phonon spectrum affect the flow of heat? Dimensionality plays an important role here. Each nanobridge shown in Fig. 1a is a one-dimensional (1D) system, in which phonons are free to move only in the longitudinal direction. In general, 1D systems display many quantized transport phenomena, irrespective of what is being transported (electrons, photons or other carriers)[2]. For instance, the flow of electrons through a narrow constriction between two large conductors leads to a quantized conductance in units of $2e^2/h$ (where h is the Planck constant and e is the charge on an electron). In other words, each mode of electrical transport contributes a maximum value (independent of the material involved) of $2e^2/h$ to the conductance.

Quantized electrical conductance has turned out to be a very general phenomenon. It was first discovered in sub-micrometre-scale semiconductor transistors[3,4]. Later, quantized conductance was also found in systems of two metals connected by a single atom[5] and subsequently in carbon nanotubes that are dipped in a conducting solution[6]. Besides electrons, analogous 1D quantum transport phenomena have been observed for photons, for pairs of electrons in superconductors, and for heat carried by electrons[2].

Phonon transport is predicted to show similar quantized behaviour. This may seem surprising, because an electric current transports charge and mass, whereas a heat current carried by phonons transports no mass. Moreover, electrons and phonons obey different quantum statistics. Nonetheless, one single formula describes it all: the Landauer formula treats conduction as a general transmission problem between two reservoirs and is applicable to both electrons and phonons[7].

Notwithstanding the theoretical similarity, the experimental requirements are hugely different. Commercial batteries and ampere meters are sufficiently sensitive to measure quantized electrical conductance. (Note that $(2e^2/h)^{-1}$ is equal to 13 kΩ, and is therefore an easy resistance to measure.) In contrast, for the observation of quantized phonon transport between two heat reservoirs, various technical difficulties have to be solved. First, to achieve good thermal isolation of the phonon wires they have to be freely suspended (Fig. 1a). This is not an easy

task on the scale of a hundred nanometres. In addition, a sensitive technique is needed to heat one end of the wire and measure the temperature difference between the two ends with millikelvin resolution. Schwab *et al.*[1] have managed to construct such a nanobridge device and have performed measurements at ultra-low-power levels. They find that a single phonon mode can at most contribute a quantum of $\pi^2 k_B^2 T/3h$ to the thermal conductance.

In experiments with quantized electron transport, a sequence of conductance steps is observed as the electronic states fill up. With phonons, in contrast, the authors find a single plateau at low temperatures, which then rises linearly with temperature at higher temperatures. The reason is that electronic states are either full or empty — the change in occupation occurs in a sharp, discontinuous step. The occupation of phonon states is actually regulated by the temperature (as indicated by the linear dependence of $\pi^2 k_B^2 T/3h$ on T). When the temperature is increased, more phonon states become occupied. But instead of a series of steps, the hallmark of 1D quantum transport of phonons is saturation of the thermal conductance at very low temperatures, precisely at the quantum value $\pi^2 k_B^2 T/3h$.

This observation by Schwab *et al.* is the first demonstration of quantum physics in nanomechanical structures. We can now look forward to measurements of phonon counting, double-slit interference experiments with single phonons, and many other experiments on phonons in quantum systems. ■

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Huntington's disease

In reverse gear

Gillian Bates

Yamamoto and colleagues[1], writing in *Cell*, describe a mouse model of Huntington's disease with a difference: the pathological features and symptoms of the disease can be reversed. These findings are both dramatic and unexpected, and indicate — with the obvious caveat that we do not yet know how these results will translate to humans — that it may be possible to treat this devastating disease after symptoms appear.

Huntington's disease is an inherited, late-onset neurodegenerative disease for which there is no known cure. In the Western world it affects about 1 in 10,000 people, with a slightly larger number than this being at risk of developing the disease. Symptoms include changes in personality, cognitive decline and a movement disorder (such as uncontrollable, jerky movements, called chorea)[2].

Patients suffering from Huntington's disease bear alterations in the *HD* gene[3]. Close to the beginning of this gene — in a protein-coding part, exon 1 — is a region that includes a variable number of a trinucleotide motif (the cytosine/adenine/guanine, or CAG, motif). The only difference between the *HD* gene in unaffected and affected individuals is the number of copies of this motif. The CAG trinucleotide encodes the amino acid glutamine, and so the huntingtin protein encoded by the *HD* gene contains a polyglutamine tract of varying length. When the tract is 38 glutamines long or more, the protein gains toxic properties. On autopsy, the brains of Huntington's patients show a selective death of neuronal cells (mainly in the striatum)[4] and the deposition of polyglutamine aggregates both within and outside nuclei (primarily in neurons of the brain's cortex)[5,6]. The precise relationship between the aggregation process and the malfunction and death of nerve cells is uncertain.

Mice that have been engineered to express exon 1 of the *HD* gene with long CAG repeats develop a phenotype with many features reminiscent of Huntington's disease[7]. In this model, a late-onset, progressively worsening movement disorder is preceded by the formation of the characteristic polyglutamine aggregates[8,9]. At the same time that symptoms appear, the binding of a particular neurotransmitter (dopamine) to dopamine receptors on neurons decreases, as do levels of the messenger RNA encoding that receptor[10]. The brains of Huntington's patients show a similar pattern[11].

Yamamoto *et al.*[1] have built on this work, taking advantage of a conditional regulatory system[12] that allows the mutant exon 1 *HD* gene to be switched on or off. They found that, when the gene was switched on in mice, it was expressed throughout the animals' lifetime. The mice developed a progressive neurological phenotype: onset of a motor disorder was seen at 4 weeks of age; a mild tremor was present by 20 weeks; and mice were clearly underactive by 36 weeks. Yamamoto *et al.* detected nuclear staining specific to the mutant *HD* gene, as well as intranuclear and extranuclear polyglutamine aggregates, in brain sections of mice at 8 weeks. The brains of the mice were smaller than normal, with a marked reduction in the size of the striatum. A reduction in binding of dopamine to its receptors was also seen. This is all in line with what would

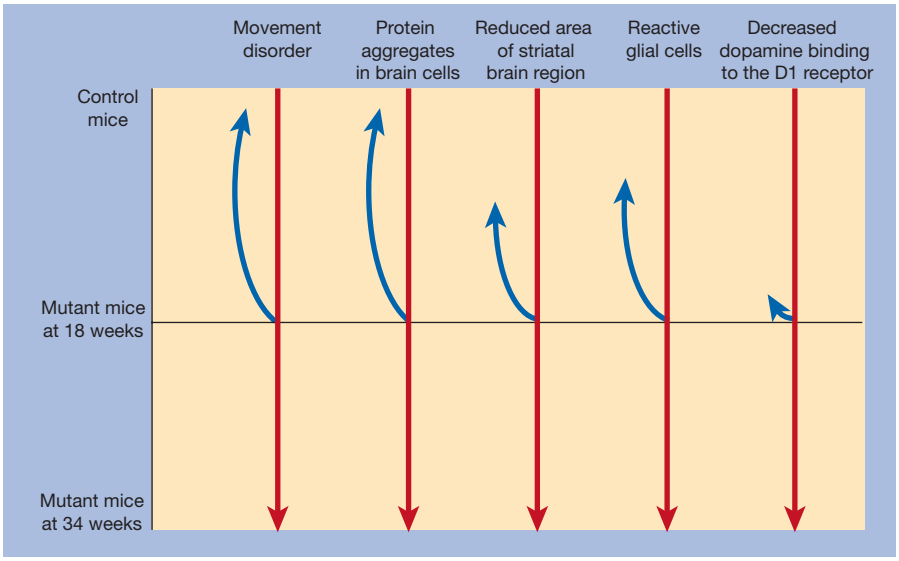

Figure 1 **Progression and reversal of Huntington's disease in a mouse model. Red lines represent the relative progression of the various characteristics of Yamamoto *et al.*'s mutant mice[1] over a 34-week period. In one set of mice, the mutant gene was turned off at 18 weeks of age by adding the antibiotic doxycycline to the animals' drinking water. The blue lines represent the degree to which each of the characteristics shown was either halted or reversed when the gene was no longer expressed. Dopamine is a neurotransmitter; reactive glial cells are generally indicative of nerve cell loss.**