smallest device, the baseline noise level is only 39 fm $Hz^{-1/2}$, which compares very favourably with optical-based cantilever detection.

The smallest devices also have the somewhat unusual feature that they are only mininimally affected by air damping, so that the quality factor — another parameter that influences the sensitivity of the device — in air is nearly as high as it is under vacuum conditions. And as the cantilever mass is so small to begin with, the resonant frequency is a very sensitive function of any added mass, which means that these devices are excellent mass sensors. By coating the surface of a cantilever with a thin polymer film that can adsorb chemical molecules of interest, Roukes and co-workers demonstrated a mass-detection sensitivity of better than 1 attogram (10^{-18} g) under ambient conditions. Although this mass sensitivity does not yet match previous results achieved by the Roukes group in an ultrahigh vacuum at low temperatures[4], it demonstrates the remarkable benefits made possible by scaling to dimensions comparable to the mean free path in air. Overall, these devices offer a highly appealing combination of sensitivity, scalability and simplicity.

Progress in making ever smaller and more sensitive nanomechanical devices may also lead to new classes of experiments in quantum measurement. For example, mechanical detection of single nuclear spins could form the basis of a microscope that is capable of imaging molecular structure in three dimensions[5]. Such a microscope would, however, place severe demands on the cantilever and sensor, including low cantilever stiffness, megahertz frequencies, high quality factor and ultrasensitive displacement transduction.

Another class of experiments with equally ambitious goals and demanding requirements involves attempts to detect the quantum mechanical nature of the nanomechanical devices themselves[6]. To perform such experiments, the cantilever, which can be thought of as a simple harmonic oscillator, must be cooled close to its quantum mechanical ground state. Moreover, it must be possible to measure displacements with a resolution that is comparable to the magnitude of the quantum zero-point fluctuations (which are determined by the uncertainty principle).

Working towards this goal, Robert Knobel and Andrew Cleland at the University of California, Santa Barbara[7], and later Matthew LaHaye, Keith Schwab and co-workers, then at the University of Maryland[8], made suspended beams that were clamped at both ends and coupled them to displacement transducers based on single-electron transistors. LaHaye, Schwab and co-workers demonstrated position resolution down to 3.8 fm $Hz^{-1/2}$, which was only a factor of six or so away from the quantum limit for their oscillator. Although such experiments require more complex detection schemes than simple piezoresistive sensing, further development of these or other even more exotic sensors may someday allow us unprecedented access to the quantum mechanical states of matter.

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MOLECULAR MACHINES

Reinventing the wheel

The invention of the wheel was one of the most significant events in human history. Now, working out how molecules can roll across an atomic surface may have significant implications for the design and construction of nanomachines.

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For a moment, imagine taking away the ubiquitous wheel from our modern day life. We would witness an amazing retrograde spiral back to the Stone Age! Not only would it be a world without bicycles, cars, trains or airplanes, but it would be impossible to construct buildings and bridges. Most archaeologists regard the wheel — which originated in ancient Sumer in Mesopotamia in the fifth millennium BC — as one of the oldest and most important human inventions. The success of the wheel resides in its mechanical

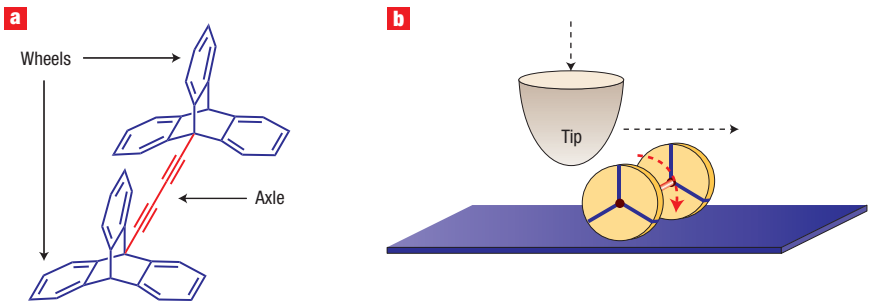

Figure 1 Wheels at the nanoscale. **a**, The chemical structure of the molecule studied by Grill and co-workers consists of two three-spoked wheels (blue) linked together with a dialkyne axle (red). **b**, The molecular wheels can be rolled along a copper surface using the tip of a scanning tunnelling microscope. The tip is first lowered toward one of the wheels and is then laterally moved across the surface. The wheel under the tip undergoes a 120° rotation while the other wheel remains at rest, and the molecule moves across the surface by rolling rather than the usual hopping mechanism.

operation, a motion that combines rotation and translation. By rolling wheels, heavy objects can be transported from one place to another — literally and physically, the very foundations on which our civilization is built.

On page 95 of this issue, the rolling of a wheel on a much smaller length scale is reported by Grill and co-workers[1] from the Freie Universität Berlin in Germany and the CEMES-CNRS in Toulouse, France. They show how a molecule with a structure that resembles two three-spoked wheels joined by a freely rotating axle can be rolled along a copper surface (Fig. 1). Unlike a macroscopic wheel, however, the rolling of a 'nanowheel' is largely governed by electrostatic interactions between its constituent atoms and those of the surface on which it rolls.

When a large molecule moves across a surface, it can adapt to the surface landscape by changing its shape. This change depends on a number of factors, such as the strength and geometry of the chemical bonds that hold together the atoms in the molecule (which govern its mechanical strength), as well as interactions between the molecule and the surface. Since the rolling process of a nanowheel involves both rotational and translational motions, it is more complicated than just a lateral movement or a rotation. For example, the rotation of a single molecule on a surface has previously been demonstrated with decacylene — a large flat propeller-like organic molecule[2]. However, this molecule lies flat on the surface, so even though it rotates, it does not roll.

In some visions of nanotechnology, construction at the nanoscale will be analogous to the real world, where vehicles — just a few nanometres in size — will be required to transport materials from one place to another. These vehicles will need wheels that actually roll. Molecules designed to function as 'nanocarts' or 'nanocars' may be the ideal candidates for this purpose and the first tentative steps in this direction have been taken. Triptycene molecules — which are reminiscent of paddle-wheels — have been connected together to make a wheelbarrow-like molecule[3], but this 'nanocart' could not be moved along a surface. In contrast, a nanocar built by attaching four spherical C_{60} molecules as wheels to a non-rigid molecular board[4] could be pushed across a surface. As this molecule hops from one position to the next, however, no direct evidence for the rotation of the fullerene wheels was detected.

To investigate the rolling of a molecular wheel at the atomic level, first we need to be able to roll the wheel in a controlled way. Second, it is necessary to detect that the nanowheel is actually rolling, rather than hopping or sliding. Neither of these tasks are simple, but Grill and co-workers successfully use the tip of a scanning tunnelling microscope (STM) to perform both of them. Although the STM was initially used to image the electronic density of surfaces and atoms sitting on them, since the early 1990s it has also been used as a stick to move or to manipulate them[5] whilst simultaneously recording their electronic and vibrational signatures. Therefore, the STM can be considered as the 'eyes', 'hands', and 'ears' of the scientists connecting our macroscopic world to the nanoscopic one[6].

In their experiment, Grill and co-workers begin by depositing their molecules on a Cu (110) surface under ultrahigh vacuum conditions. Each molecule (Fig. 1a) contains two triptycene wheels joined together by a rigid axle, which is composed of alternating single and triple carbon–carbon bonds. This design allows either wheel to rotate independently about the central axis. Initially, the researchers take STM images to visualize the nanowheels and identify different relative orientations between the molecules and the ordered copper surface. The Cu (110) surface is corrugated with a series of parallel atomic troughs running across it. The researchers then choose a nanowheel that has its axle aligned with a trough.

The nanowheel lies on the surface, supported by two of its spokes with the centre spoke pointing upwards, resembling an inverted 'Y' shape (Fig 1b). The STM tip is lowered towards a wheel in order to increase the tip–molecule interaction, and the tip is then moved laterally along a direction perpendicular to the axle. During this process, the tunnelling current is recorded and shows a unique hat-shaped signature (Fig. 2a) that indicates the molecule is rolling rather than hopping. The shape of the signal can be explained by considering how the interaction between the tip and the wheel changes as the rolling occurs.

The STM tip first passes over a spoke resting on the surface and gives rise to the less intense left hand side of the hat-shape profile. When the tip reaches the central spoke, it pushes the wheel to roll 60° into an upright 'Y'-shaped position, bringing it closer to the tip and resulting in a greater tunnelling current. The tip continues to move over the wheel in this position, producing the top (higher) part of the hat-shaped profile. Finally, the wheel is tipped over and rotates another 60°, regaining the inverted 'Y' shape — like its initial position — and the intensity of the manipulation signal suddenly drops. The STM tip, which continues moving, now provides the last part of the hat-shape signal as it passes over the final spoke that is now resting on the surface.

The beauty of this experiment lies in the fact that the STM tip is used as a stick to mechanically roll the wheel while simultaneously recording the rolling mechanism. During this process, only one wheel is rotated — the wheel on the other end of the axle remains in its original position.

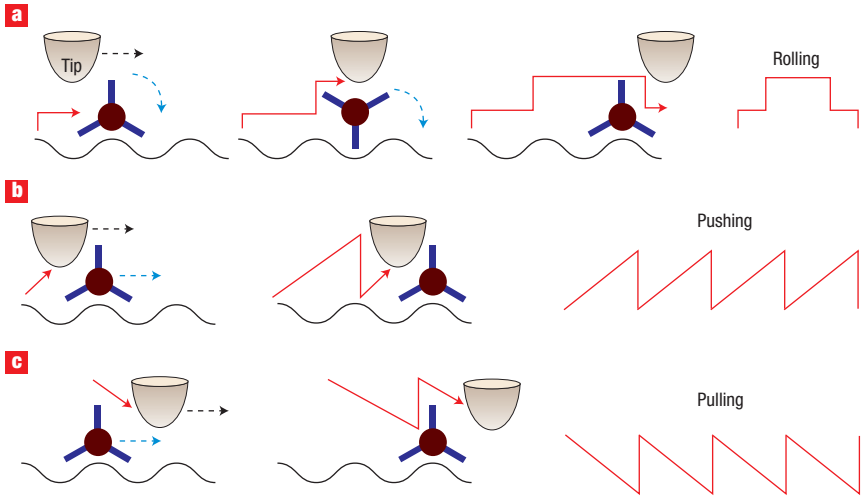

Figure 2 The manner in which the wheel is translated across the copper surface can be determined by measuring the tunnelling current. A rolling mechanism (**a**) results in a symmetric hat-shaped signal, whereas pushing (**b**) and pulling (**c**) processes give rise to asymmetric saw-tooth currents[7] as the wheel hops across the surface in a discontinuous manner. During pushing, the molecule moves in front of the tip because of a repulsive electrostatic interaction between them, whereas the molecule follows the tip during pulling because of an attractive interaction arising from the overlapping of their electronic wavefunctions[6].

This experiment elegantly demonstrates the effect of surface corrugation on wheel rotation. When the nanowheel is laterally manipulated along a direction parallel to the surface troughs or on an atomically smooth surface, such as Cu (100), no rolling motion is achieved. Instead, the entire molecule hops onto the next adsorption site. This results in characteristic 'pushing' or 'pulling' signals[7] being recorded during the STM manipulation. The authors also show that the wheel can be rolled only at larger tip–molecule distances (above 4 Å) and is pushed or pulled (Fig. 2b,c) at smaller separations. Therefore, to roll a nanowheel we need an appropriate surface (an 'atomic road') and a means of pushing the wheel in the correct direction.

A detailed grasp of this rolling mechanism of a nanowheel at the atomic limit may allow scientists to design and build better and smarter nanovehicles using individual molecules, with implications for the transport of materials on the nanoscale. It also impacts the development of nanomachines in general as wheels form the basis of many parts of machines, not just the means by which transport occurs. For instance, rotation of a nano-pinion against a molecular rack was recently demonstrated by Chiaravalloti and co-workers[8]. The rotation of the pinion is similar to the rolling of a nanowheel, but the pinion lies flat on the surface and moves along a serrated edge of an island-like structure.

The invention of the wheel revolutionized our civilization. It can be expected that nanowheels will follow suit in revolutionizing the nanoscopic world.

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BIOTECHNOLOGY

Logic goes *in vitro*

Since its earliest inception, the computer has evolved with the development of faster and smaller electronics. Now, DNA logic circuits tread in water — where no electronic circuit can.

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The first universal computer, described by Alan Turing in 1936, was a rather abstract mathematical device. It consisted of symbols written on a potentially unlimited length of tape and a simple device that could move along the tape and process and rewrite each symbol, one at a time, according to a finite set of rules. A decade later, John von Neumann and colleagues conceived and implemented the first practical programmable computer, representing Boolean logic '1's and '0's through the presence or absence of electrical signals. Since then practically all computers have been built according to the von Neumann design.

In retrospect, the similarity of Turing's conceptual machine to the enzymes and ribosomes that process DNA and RNA according to well defined chemical rules is quite astonishing, considering that his ideas predated our current understanding of the structure and function of these basic biological molecules. The idea driving research in DNA computing is to use DNA and enzymes, rather than electronic circuits, to implement mathematical models of computation. Early attempts at DNA computing included conceptual and experimental implementations of Turing machines[1–2], combinatorial algorithms[3–6] and finite automata[7].

Writing in *Science*, Eric Winfree and colleagues[8] at the California Institute of Technology come full circle by demonstrating DNA-based logic circuits that follow the same design principles as modern electronic computing. Why implement logic circuits from DNA if electronic computers have been doing so well for several decades now? We believe the answer is that logical circuits made of biological molecules will have an important advantage compared with electronic circuits in their ability to interact with other biological molecules. DNA computing will likely occur initially *in vitro*, in biotechnology applications; eventually *ex vivo*, facilitating the analysis and manipulation of living cells for biological and biomedical research; and ultimately *in vivo*, as so-called 'smart drugs'[7] that can activate a medical treatment *in situ* by releasing a drug molecule based on a positive logical diagnosis of a disease.

Winfree and colleagues report the implementation of logic circuits using only DNA and demonstrate AND, OR and NOT gates, which are sufficient to effectively compute any Boolean function. The authors show that their application can handle noisy signals and incorporate feedback and cascading, in which the output of one gate is the input of another gate. The latter is trivial in this system thanks to the fact that inputs and outputs are designed to be of the same form. In addition, they show that complex circuits can be made from simpler ones in a modular and scalable way.

The core of the DNA logical operations is strand-displacement. Figure 1a shows the starting components of a basic process: an 'input' strand, A, and a duplex of bound strands, B and C. Strand A, binds by a base pair complementary to the unbound 'toe-hold' of strand B, ultimately displacing strand C. The process ends with the free C strand forming the 'output' and a new, more stable, AB duplex. This process occurs spontaneously because the duplex formed between strands A and B is longer and contains more hydrogen bonds. The end product is therefore thermodynamically more stable. As the single-stranded toe-hold initiates the process, changing its length may change the process speed[9].

The '1's and '0's of Boolean logic are represented by the presence or