

Researchers can now use molecules to build a variety of nano-scale devices and machines, including molecular shuttles, elevators and even a walking biped made from DNA

Molecular devices and machines

Vincenzo Balzani, Alberto Credi and Margherita Venturi

IT WAS ON 29 December 1959 that Richard Feynman first proposed the idea of using atoms to build nano-scale devices and machines. Speaking at a meeting of the American Physical Society at the California Institute of Technology, he gave a lecture that many now see as the trigger for nanotechnology. “The principles of physics”, he told his audience, “do not speak against the possibility of manoeuvring things atom by atom.” The idea that devices and machines could be built at a microscopic level – what we now call nanomachines – had been born.

The broad potential of such machines was first explored by Eric Drexler over 25 years later. In a fascinating book called *Engines of Creation*, he claimed that it would be possible to build a general-purpose “nanorobot” that he nicknamed an assembler. Such a device could, in principle, build almost anything – including copies of itself – atom by atom. Many scientists, however, were sceptical of this fascinating but somewhat abstract idea.

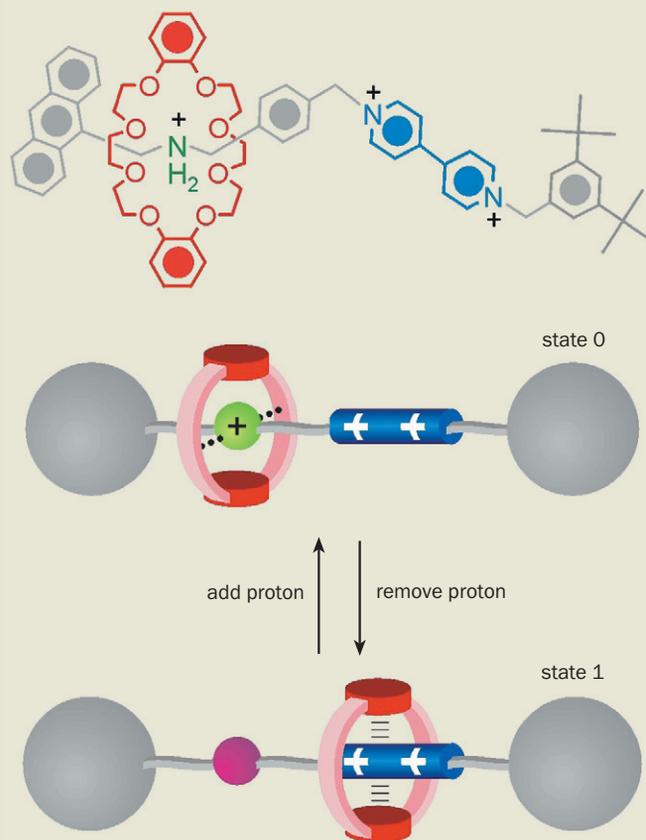
Bottom up

Chemists, in particular, were well aware that bond-making and bond-breaking – which play a key role when moving atoms around – are complex and subtle processes. Building on the work of Jean-Marie Lehn at the University of Strasbourg in the 1970s, they knew that it is much more convenient to use molecules, rather than atoms, to build nano-scale devices and machines. Indeed, molecules can be used to design an almost unlimited variety of nano-scale devices that can perform a range of specific functions.

There are several advantages to using molecules. They are stable, they have distinct shapes, and they can be manipulated, for example, using light or chemical reactions. They can also self-assemble or be linked to make larger structures. In practical terms, most laboratory chemical processes already involve molecules, not atoms. Finally, nature already uses molecules to build a vast number of nanodevices, such as the enzyme ATP synthase, to sustain life.

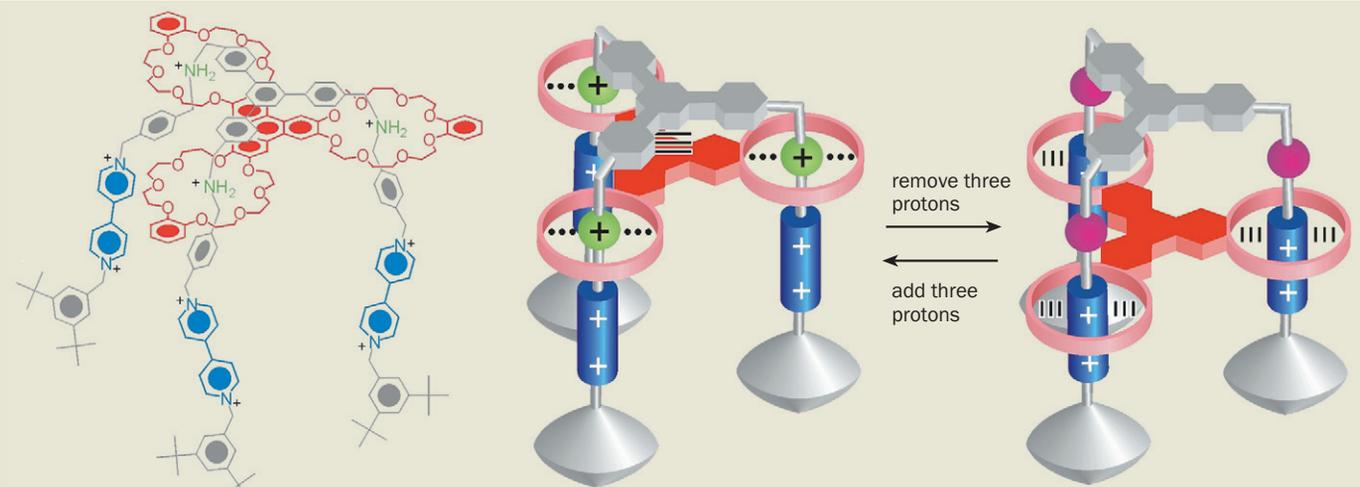
It is now clear that a “bottom-up” approach, using molecules to build nanodevices, is the way forward. Furthermore, this aspect of nanotechnology – known as “supramolecular chemistry” – can also help us to understand the extremely complex devices and machines that are found in nature.

1 Molecular shuttles



This “molecular shuttle” was built in 1998 by Fraser Stoddart from the University of California at Los Angeles. Based on a supramolecular species called a “rotaxane”, it consists of a ring and a dumb-bell-shaped component that contains a dialkylammonium unit (green) and a 4,4'-bipyridinium unit (blue). The ring normally surrounds the dialkylammonium unit because the hydrogen bond between them is much stronger than the “donor-acceptor” interaction between the ring and the bipyridinium unit. Adding a base, however, removes a proton (H^+) from the dialkylammonium centre, which weakens the hydrogen bond. The ring therefore moves to the bipyridinium unit, where it is stabilized by a donor-acceptor interaction. The addition of acid restores the ammonium centre and makes the ring to shuttle back to its original position. The fact that the ring can be in two possible positions could enable this molecular machine to process information, with the different positions representing “0” and “1”.

2 Molecular elevators



This three-legged structure (left) acts as a molecular elevator. Each leg has two “levels” in the form of a dialkylammonium unit (green) and a bipyridinium unit (blue), as well as a bulky foot (grey) to keep it stable. The central platform, consisting of three interconnected rings (red), can “stop” at either position. Initially the rings surround the dialkylammonium units because of strong hydrogen bonding. But if a base is then added, protons are removed from the dialkylammonium ions and the platform drops to the lower level, where it is stabilized by donor–acceptor interactions.

Molecular shuttles and elevators

So, what are the characteristics of a molecular machine? Like any macroscopic machine, a molecular device needs some sort of energy to make it work, which is generally fed in via a chemical reaction of some description. The nanomachine’s components can then carry out a movement that can be controlled, monitored and possibly repeated at will. These movements lead, in turn, to a particular mechanical function.

Supplying energy to an artificial molecular device is not easy. The most obvious approach is to add a chemical reactant, i.e. a fuel. This is exactly what happens in the human body, where the chemical energy from the food that we eat is used to sustain us. Indeed, several artificial machines have already been built that are driven by reactions between acids and bases – chemical species that donate and accept protons, respectively.

A classic example of such a machine was reported in 1998 by Fraser Stoddart and colleagues at the University of California at Los Angeles (UCLA). They built a device containing a dumb-bell-shaped molecular structure with a ring that encircles the bar connecting the two ends. Known as “rotaxanes”, these molecular systems are cleverly designed so that the ring sits at one of two different points along the dumb-bell (figure 1). The ring can be made to shuttle back and forth between these two points simply by changing the acidity, or pH, of the system. Initially the ring surrounds a “dialkylammonium” point. But if a base is then added, protons are removed and the ring moves to the other position. The acid/base reaction is entirely reversible, which means that the ring can be moved backwards and forwards at will – even though waste products, in the form of a salt, are created during the process. The fact that the ring can be in two possible positions could enable the machine to be used for information processing, with the different positions representing “0” and “1”.

The above strategy has been extended recently by Stoddart and one of us (AC) to design and build a molecular machine that behaves like a nanometre-scale elevator. This device – roughly 2.5 nm in height – consists of a three-legged rig that supports a platform made of three interconnected rings (figure 2). Each leg has a bulky foot to keep the structure stable, as

well as two “notches” at different heights. In an acid medium, the platform sits at the upper position, where each ring surrounds a dialkylammonium unit on the legs. But if a base is added, the platform moves to the lower position with the rings now surrounding “bipyridinium” units.

Using simple thermodynamics, it can be calculated that moving the platform from the lower to the upper level requires an energy of about 21 kcal per mol, while moving the platform back down again requires about 4 kcal per mol. Since the platform travels about 0.7 nm, the device can potentially generate a force of about 200 pN on the forward stroke. This is about 10 times greater than the force generated by natural motors like myosin – a protein that forms part of muscle fibre.

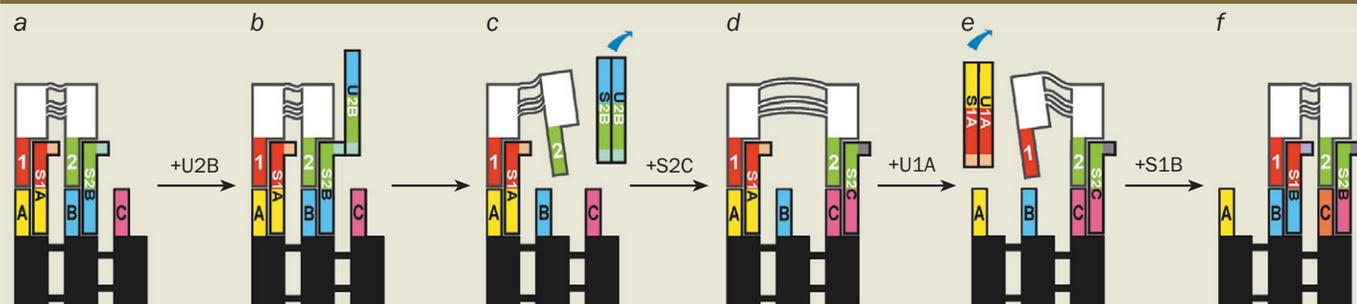
This three-legged elevator could also be used to host large “guest” molecules in the cavity that opens up when the platform moves to the lower position. Roughly 0.8×1.5 nm in size, the cavity disappears when the platform moves back up again by adding acid. In other words, the ability of the structure to host a molecule can be turned on and off at will. Another advantage is that the elevator could host a molecule that would otherwise be insoluble; by encapsulating the molecule in the cavity, it becomes soluble.

What is also interesting about the structure is that when the platform is at the upper level, the bipyridinium units on the lower half of each leg do not interact with anything. They are therefore free to capture any electron-donating chemical species. But when the platform moves to the lower position, the bipyridinium units are now surrounded by the platform’s rings and can no longer capture any electron donors.

A biped walking device made from DNA

Perhaps the most useful molecule for nano-scale applications is DNA (see Turberfield in further reading). Carrying the genetic information of all living things, DNA typically consists of two deoxyribonucleic-acid strands that are entwined in a double helix. Attached to each strand are a series of side groups, or “bases”, that come in four different types – adenine (A), cytosine (C), guanine (G) and thymine (T). Hydrogen bonds between complementary base pairs (A and T; C and

3 Walking with DNA



Nadrian Seeman at New York University has used DNA to build a molecular “biped” that can “walk” along a track. The biped consists of two legs (white), each of which ends in a “foot” composed of a single strand of DNA (1 and 2). The track has three stations (black), each of which ends in a “foothold” that is also made from a single strand of DNA (A, B and C). (a) The biped initially has foothold A connected to foot 1 via set strand S1A, and foothold B linked to foot 2 via set strand S2B. (b) Foot 2 can be released by adding unset strand U2B, which binds to S2B. (c) S2B and U2B pair up completely, leaving foot 2 free to dangle. (d) By adding set strand S2C, foot 2 can now be fixed to foothold C. (e) In the penultimate step, foot 1 is freed by adding unset strand U1A. (f) Finally, foot 1 lands on foothold B when set strand S1B is added.

G) keep the two strands entwined.

Using techniques from modern biotechnology, it is possible to make DNA molecules with a sequence of base pairs chosen at will – opening the door to new paths that nature has never before taken. For example, Nadrian Seeman and colleagues at New York University have used DNA to build a two-legged walking motor or “biped”. This is a complex device, in which both legs have a “foot” that is made from a single strand of DNA (figure 3). The feet can be made to “walk” along a track that consists of three stations, each of which also ends in a single strand of DNA called a “foothold”.

The sequence of bases on the feet and footholds are carefully selected so that they actually match up very little. The only way in which a foot can attach itself to a foothold is if a separate strand of DNA – called a set strand – with appropriate bases is added. The foot can later be detached by adding another strand of DNA – called an unset strand – that pairs up with a special sequence of eight bases on the set strand, nicknamed a “toehold”. The paired set and unset strands can then be removed from the solution.

By adding set strands and unset strands in an appropriate sequence, the two feet of the device can be detached and attached to the footholds in turn, thereby allowing the device to walk (figure 3). Because the flexible links that connect the two legs are relatively short, the biped moves rather like an inchworm, with one foot edging forward and the other then being dragged up to the same position. In contrast, natural walking proteins like kinesin move more like humans, with each foot passing ahead of the other in turn.

The state of the system can be monitored by taking some of the solution and exposing it to ultraviolet light, which creates crosslinks between different strands of the feet and foothold. It is then possible to work out which feet were attached to which strands by unravelling the paired strands and subjecting them to chemical analyses. Walking molecular devices of this type, which can move in a single direction along a pre-defined nano-scale route, could be used in nanorobotics, medicine or computing. They could, for example, be used to carry molecules from one point in space to another.

Photochemically and electrochemically driven machines

Any artificial molecular device or machine that requires chemical energy to operate will require fresh reactants – or fuel – at every step of its operation. It will also produce waste

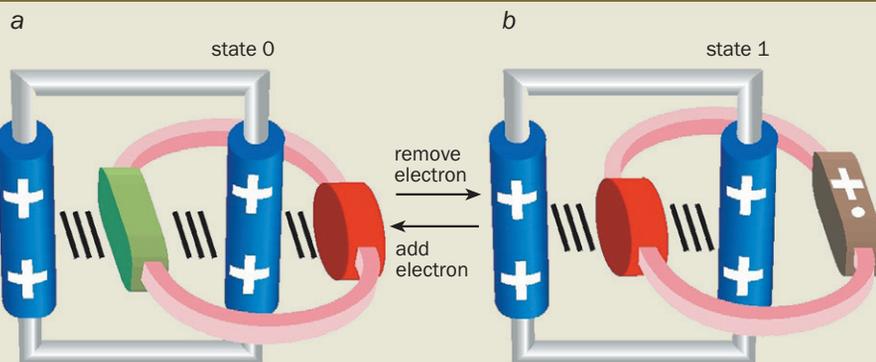
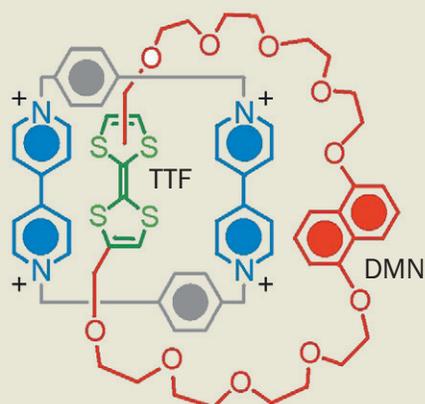
products that can compromise the performance of the system unless they are removed. This need for waste disposal limits the design and construction of artificial molecular-level machines based on chemical-fuel inputs. However, some molecular devices have been built that are powered instead by light or electrical energy and so do not create any waste.

For example, in 1999 Ben Feringa at the University of Groningen in the Netherlands constructed a light-driven rotary motor. It is based on a carefully designed molecule that consists of two halves joined by a carbon-carbon double bond. Shining light on the device causes one half of the molecule to rotate about the double bond with respect to the other half. Once again, this nanomotor could be used to carry molecules from one point in space to another. Meanwhile, Stoddart at UCLA and Jean-Pierre Sauvage at Strasbourg have studied, also in collaboration with our group, several electrochemically driven molecular shuttles.

One interesting type of molecular device is made from a “catenane” – a chemical compound that consists of two (and sometimes more) interlocked rings. By using an external input it is possible to control the relative position of the two rings. For example, Stoddart and the current authors have designed a catenane that consists of a symmetric ring interlocked with an asymmetric ring (figure 4). The asymmetric ring has been designed so that it contains two different “recognition sites”, one of which is much better at donating electrons than the other. The molecule is thermodynamically stable when the strong electron-donating site lies inside the electron-accepting symmetric ring. But if an electron is removed from that site, it becomes positively charged and loses its electron-donating power. The original site is therefore expelled from the cavity of the ring and is replaced by the other site. In other words, the asymmetric ring has rotated through 180°. Adding an electron rotates the ring by another 180° back to its original position, which means that we have a primitive way of rotating the ring back and forth between two states that can be designated “0” and “1”.

Stoddart, Heath and co-workers have incorporated this compound in a solid-state device that could potentially be used for random access memory (RAM) storage, in which data could be read and written using either electrical or optical means. It should be pointed out, however, that repeated 180° rotations between the two states do not need to occur through a full 360° rotation. In fact, because of the intrinsic

4 Rotating rings



Catenanes are chemical compounds consisting of two (or more) interlocked rings. This example consists of a symmetric positively charged ring (silver) containing two “electron-hungry” bipyridinium units (blue). It is interlocked with an asymmetric ring (pink) that has two different electron-donating units in the form of a tetrathiafulvalene (TTF) group (green) and a 1,5-dioxynaphthalene (DMN) unit (red). The TTF unit is, however, much better at donating electrons than the DMN unit, which means that the molecule is thermodynamically stable when the symmetric ring encircles the TTF unit (a). But if an electron is removed from the asymmetric ring, the TTF becomes positively charged and loses its electron-donating power. It is expelled from the cavity of the ring and is replaced by the DMN unit (b). Adding an electron sends the ring back to its original position.

symmetry of the system, both the movement from state 0 to state 1 and back again can take place, with equal probabilities, either in a clockwise or anticlockwise direction. A full rotation, however, would be much more interesting from a mechanical point of view.

A clever – albeit complex – way of obtaining full unidirectional rotation has been devised by David Leigh and co-workers at Edinburgh University. Their system consists of two identical small rings that are interlocked with a larger ring. The large ring contains four different binding sites that the small rings can surround. By changing the chemical nature of the four sites through light- or heat-driven reactions, the small rings can be made to move in discrete steps around the larger ring. The rotation processes can be followed using nuclear magnetic resonance.

Future directions

When Feynman spoke to the American Physical Society in 1959, he finished his talk by speculating on the possible applications of molecular-level machines. “Who knows?” he concluded. “I cannot see exactly what would happen, but I can hardly doubt that when we have some control of the rearrangement of things on a molecular scale we will get an enormously greater range of possible properties that substances can have, and of different things we can do.” Over 50 years later, his comments are still appropriate for the work described here.

Still, the results that have so far been achieved with rotaxanes and catenanes are opening up new developments that we – and other researchers – are examining. Three goals stand out. First, we would like to design and build more sophisti-

cated machines that are more stable, can switch faster, and can perform even more complex motions. Second, we would like to see if such machines can open and close molecular-sized channels, which would allow (or prevent) ions or molecules from being transported through membranes. Finally, we would like to use such machines as tiny information-processing devices and – ultimately – to build an ultra-miniature chemical computer.

Will this happen, and, if so, when? These are questions that are just as hard to answer now as they were in Feynman’s day.

Further reading

- J D Badjic *et al.* 2004 A molecular elevator *Science* **303** 1845–1849
- V Balzani *et al.* 2003 *Molecular Devices and Machines: A Journey into the Nanoworld* (Wiley-VCH, Weinheim)
- D A Leigh *et al.* 2003 Unidirectional rotation in a mechanically interlocked molecular rotor *Nature* **424** 174–179
- M Schliwa (ed) 2003 *Molecular Motors* (Wiley-VCH, Weinheim)
- W B Sherman and N C Seeman 2004 A precisely controlled DNA biped walking device *Nano Lett.* **4** 1203–1207
- A Turberfield 2003 DNA as an engineering material *Physics World* March pp43–46

Links

- Vincenzo Balzani: www.ciam.unibo.it/photochem
- David Leigh: www.chem.ed.ac.uk/staff/leigh.html
- Nadrian Seeman: seemanlab4.chem.nyu.edu
- Fraser Stoddart: www.chem.ucla.edu/dept/Faculty/stoddart/new/index.php

Vincenzo Balzani, Alberto Credi and Margherita Venturi are in the Dipartimento di Chimica “G Ciamician”, Università di Bologna, Italy, e-mail vincenzo.balzani@unibo.it