Exercising Demons: A Molecular Information Ratchet

Viviana Serreli, Chin-Fa Lee, Euan R. Kay and David A. Leigh, *Nature* **445**, 523-527 (2007).

'*Exercising demons*'. [High resolution image of this picture–with green or red crouching demon–and others are available on request from David.Leigh@ed.ac.uk. This illustration by Regina Fernandes – Illugraphics.]

Chemists at the University of Edinburgh have created a molecular machine that operates via a mechanism inspired by a 140 year-old thought experiment. The 'molecular information ratchet' uses light energy to fuel information transfer, a fundamentally new type of motor-mechanism for artificial nanomachines.

Nature uses molecular-sized motors and machines in virtually every important biological process and their extraordinary success is inspiring scientists to try to create synthetic devices that mimic the function of these amazing natural systems. However, it is far from obvious to see how to design such machines because mechanical behaviour at the molecular level, where everything is constantly moving (under kinetic energy supplied by the heat of the surroundings) and being buffeted by other atoms and molecules (Brownian motion), is very different to that which we observe in our everyday world. One cannot just scale down the design of a motor car to the nanoscale, for example, it simply could not operate because friction, heat dissipation and many other factors are so different. The problem of controlling motion on the molecular level is not a recent one, however, it has occupied the minds of scientists for as far back as the middle of the 19th Century.

James Clerk Maxwell

James Clerk Maxwell (1831–1879),[1] born and raised in Edinburgh, was arguably one of the three (along with Isaac Newton and Albert Einstein) most important and influential scientists of all time ["*From a long view of the history of mankind - seen from, say, ten thousand years from now - there can be little doubt that the most significant event of the 19th century will be judged as Maxwell's discovery of the laws of electrodynamics.*" — Richard Feynman; "*The work of James Clerk Maxwell changed the world forever*" —

Albert Einstein; "*Maxwell's equations have had a greater impact on human history than any ten presidents*." — Carl Sagan]. During a lifetime of contributions to science that began at age 14, two pieces of Maxwell's work are generally the most celebrated: His electromagnetic theory of light; and his contributions to the kinetic theory of gases, which for the first time explained real-world properties in terms of the statistical behaviour of atoms and molecules. These two theories have become cornerstones of modern physical science but 'Maxwell's Demon',[2] an offshoot of his work on the kinetic theory of gases, has had its own extraordinary impact.[3] Time and again it has captured the imagination and interest of scientists in different fields, profoundly influencing the development of statistical and quantum physics, information theory, computer science and cybernetics. Now, 140 years after its conception, it is the inspiration for a new motor mechanism for nanomachine systems reported by Serreli *et al* in *Nature*.[4]

Maxwell's Demon

In 1867,[2] Maxwell proposed the thought experiment which has come to be known as 'Maxwell's Demon' (Figure 1). In the original version of this imaginary system, a tiny intelligent being – a 'demon' – is able to open and close a gate connecting two boxes filled with gas so as to allow only fast ('hot') gas molecules to flow into one box and only slow ('cold') gas molecules into the other – creating a temperature difference between the two compartments (Figure 1a). If the demon can perform such a task without expending any energy (using a frictionless gate which he opens and closes very slowly), then such a result would be in violation of the Second Law of Thermodynamics ('heat cannot spontaneously pass from a colder to a hotter body' or, more generally, 'the entropy of an isolated system not at equilibrium will tend to increase over time, approaching a maximum value') which is one of the most fundamental principles of physics. Maxwell appreciated that other types of 'sorting demon' could be imagined that would also violate the Second Law, for example a system that allowed particles to pass between compartments in one direction but not the other without an energy input (Figure 1b).

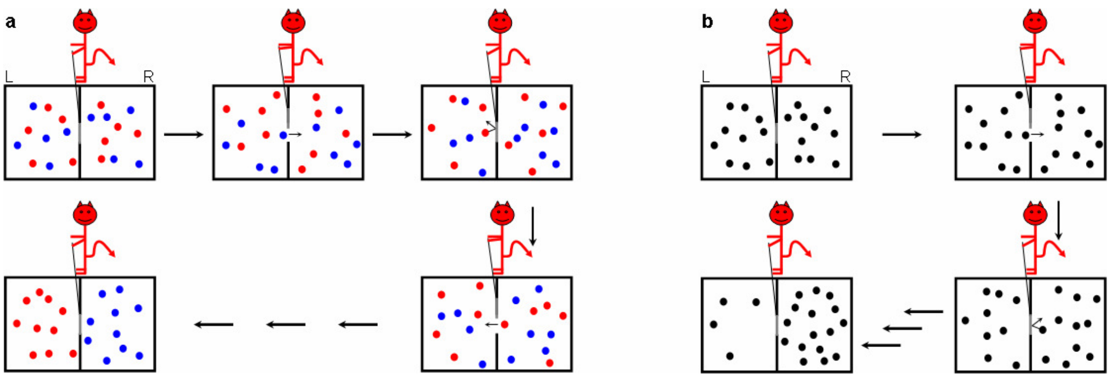

Figure 1. The Maxwell Demon thought experiments. **a** Maxwell's 'temperature demon'[2a,b] in which a gas at uniform temperature is sorted into 'hot' (red) and 'cold' (blue) molecules. The demon opens the gate between the compartments when it detects a cold particle approaching the gate from the left or a hot particle coming from the right, thus separating the particles according to their thermal energy and creating a temperature differential between the compartments. **b** A Maxwellian 'pressure demon'[2c] in which a concentration gradient is established by the gate being opened only when a particle approaches it from the left. In both versions of the thought experiment the idea is that the demon's actions involve no work being done, but as the end-result is a reduction in the entropy of the gas this is in conflict with the Second Law of Thermodynamics. Maxwell appreciated that the successful operation of the demon in the thought experiment somehow relied on its intelligence as an animate being. Subsequent analysis by several generations of scientists revealed a fundamental link between entropy and information, significantly influencing the development of statistical and quantum physics and chemistry, information theory and computer science.

Exorcising Demons

In formulating his thought experiment, Maxwell was only interested in illustrating the statistical nature of the Second Law, but subsequent generations of inventors and philosophers have been fascinated by its implications for the creation of a perpetual motion machine. A temperature or pressure differential between two compartments can be used to do work, so if one could be established without expending any energy it could form the basis for a 'something-for-nothing' device which does work without requiring fuel! Such a machine is impossible, of course, and is NOT what Serreli *et al* were trying to achieve through the work described in *Nature*. But why is it not possible for a demon do the necessary sorting task without an input of energy? The solution to this paradox took more than a century to fully resolve[5] but it was eventually understood through the discovery that no matter how you design your 'demon' component, any device that is able to process and act upon information has an inherent energy requirement that always saves the Second Law. This is due to the fundamental relationship between information and entropy – the link that, for example, requires memory erasure in computers to feed entropy into the environment (Landauer's principle[6]).

Exercising Demons

Now, chemists at the University of Edinburgh have actually made[4] a molecular machine that performs the sorting task envisaged for Maxwell's pressure demon (Figure 1b) but, crucially, it requires an input of external energy to do so and so does not challenge the Second Law of Thermodynamics. Using light energy, the molecule is able to transmit information about the position of a molecular fragment in a manner that allows transport of the same fragment in a particular direction (Figure 2). This information-based system represents a fundamentally new type of motor-mechanism for synthetic nanomachines.

The new nanomachine belongs to a class of molecules known as 'rotaxanes'. These structures consist of a molecular ring ('macrocycle') trapped on a linear molecular thread by bulky 'stoppers' at either end. Molecules of this kind have proved popular with synthetic molecular machine designers over the past decade because their architecture restricts significant submolecular motions to only two modes, namely random movement of the ring back and forth along the thread ('shuttling') and nondirectional rotation around the thread ('pirouetting'). But random motion–even cleverly restricted random motion–is not enough to create a molecular machine. An input of energy is required to control how the motion occurs. Various methods for the net transport of macrocycles between different regions in rotaxanes have previously been demonstrated in molecules called 'stimuli-responsive molecular shuttles'.[7] However, these are simple two-state switches, the most basic and functionally limited type of machine mechanism[8] in which the ring distribution is always at, or relaxing towards, equilibrium. In contrast, biological motors and machines are able to drive chemical systems away from equilibrium,[9] just like Maxwell's Demon. Only a handful of synthetic molecular machines have been made that can claim to do that.[10-12] Yet, although these structures are relatively diverse (they do not all use rotaxane architectures, for example), they all use similar mechanistic principles in their operation. The latest nanomachine from the Edinburgh group operates using a new and entirely different type of mechanism involving information transfer between the substrate and the molecular machine.

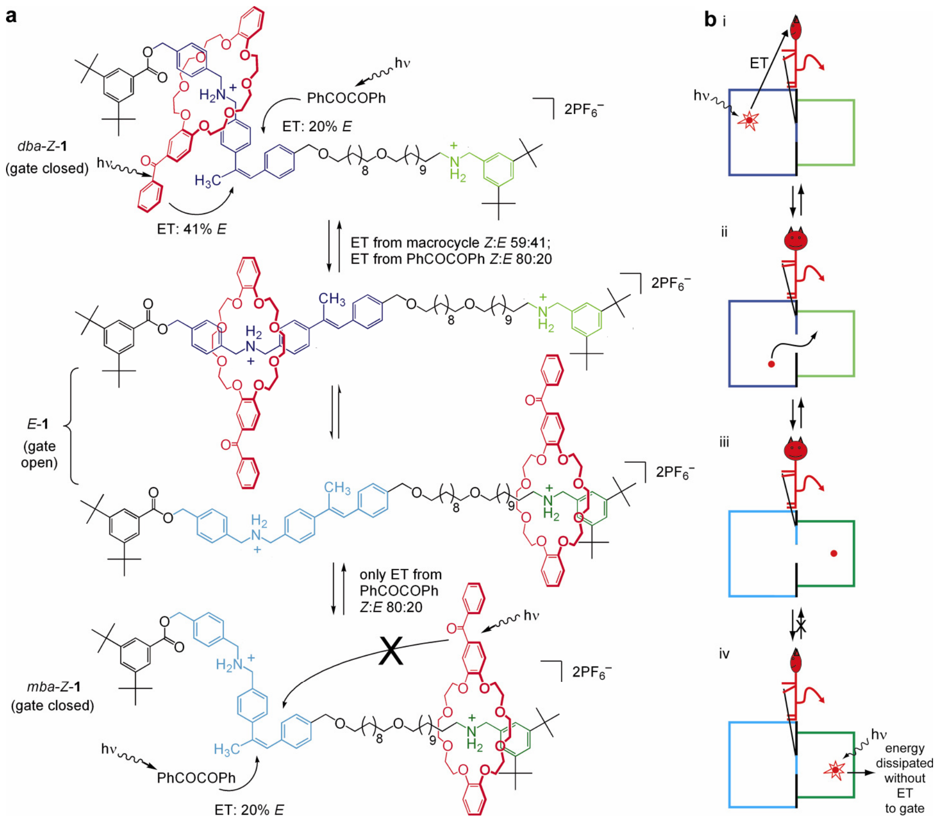

Figure 2. A photo-operated molecular information ratchet. **a** Irradiation of rotaxane **1** at 350 nm in CD_3OD at 298 K interconverts the different forms of **1** and, in the presence of benzil (PhCOCOPh), drives the ring distribution away from its thermodynamic minimum without ever changing the binding strengths of the macrocycle or ammonium binding sites. When the macrocycle is on the *mba* binding site (green), intramolecular energy transfer (ET) from the macrocycle is inefficient and intermolecular ET from benzil dominates. When the macrocycle is on the *dba* binding site (blue), both ET mechanisms can operate. The amount of benzil present determines the relative contributions of the two ET pathways and thus the nanomachine's effectiveness in pumping the macrocycle distribution away from equilibrium. **b** Cartoon illustration of the operation of **1** as a Maxwellian pressure demon[2c]: **i** Photo-induced excitation of a particle signals its position in the blue compartment by energy transfer to the demon operating the gate (the demon uses information from the asymmetry in the compartments to distinguish where the excited particles are most likely to be, here through their average distance from the gate). **ii** & **iii** The demon opens the gate and the particle shuttles incessantly between the two compartments by Brownian motion until the gate shuts trapping the particle at random in one of them. **iv** Photo-induced excitation of the particle in the green compartment is ignored by the demon and the energy of the excited state is dissipated as heat.

The new rotaxane molecule has some key novel components in its design. Firstly, the axle is divided into two compartments by a chemical 'gate' known as a stilbene. This can exist in two forms: one, the 'gate-open' form, allows the macrocycle to pass over it; the other 'gate-closed' form blocks motion of the ring. The operating conditions are chosen such that the gate tends to be closed. Each compartment on the axle also contains a 'binding site' for the ring – a zone which the ring finds sticky, and so this is where it spends most of its time. In one compartment the sticky region is close to the gate, in the other compartment the binding site is far away from the stilbene. The rings are also special in that an input of light energy gives them the ability to signal their presence to the gate by 'energy transfer' (ET, figure 2). This signalling triggers a process that opens the gate, momentarily allowing the rings to pass, before the gate is returned to its closed state. Because the rings in one compartment spend much more time close to the gate than those in the other, the gate is more likely to be opened by rings moving in one direction than the other. The result is that the number of rings in one compartment increases upon the shining of light on the molecules. We end up with many more rings in this compartment than is statistically expected given its stickiness – the system has been driven away from equilibrium.

Of course, because the information transfer process is powered by the input of light energy this system is certainly not a perpetual motion machine. In fact, modern theoretical physicists had become aware of the possibility of moving Brownian objects by using energy to cause a transfer of information in a mechanism dubbed an 'information ratchet'.[8b] The molecule reported in *Nature*[4] represents the first time chemists have designed and made such a device in the laboratory.

Nanomachines and nanotechnology

Designing molecular-level systems that employ motion in a useful manner teaches us much about the fundamental mechanical behaviour of matter at small length scales. This in turn helps scientists to unravel how the sophisticated and complicated biomachines of the cell work – crucially important because of the central role they play in many disease states. But the ultimate goal for synthetic molecular machines is to harness their abilities for our own technological use; the creation of artificial nanotechnology. Many believe that a working artificial nanotechnology will ultimately have an impact on our economy and our society that is comparable in scale and scope to the steam engine, electricity, the transistor, and the internet. The realisation of that vision is still some way off, but this new motor-mechanism represents a useful step along the road towards it.[8]

Footnotes and references

[1] (a) B. Mahon, *The Man Who Changed Everything: The Life of James Clerk Maxwell*, John Wiley & Sons, Chichester, **2004**. (b) The year 2006 marked the 175th anniversary of Maxwell's birth, see http://www.maxwellyear2006.org/index.html.

[2] The first (a) private and (b) public written discussions of the 'temperature demon' were: a) J. C. Maxwell, *Letter to P. G. Tait, 11 December 1867*. Quoted in C. G. Knott, *Life and Scientific Work of Peter Guthrie Tait*, Cambridge University Press, London, **1911**, pp. 213-214; and reproduced in *The Scientific Letters and Papers of James Clerk Maxwell Vol. II 1862-1873* (Ed.: P. M. Harman), Cambridge University Press, Cambridge, **1995**, pp. 331-332. b) J. C. Maxwell, *Theory of Heat*, Longmans, Green and Co., London, **1871**, Chapter 22. c) Maxwell introduced the idea of a 'pressure demon' in a later letter to Tait (believed to date from early 1875). Quoted in C. G. Knott, *Life and Scientific Work of Peter Guthrie Tait*, Cambridge University Press, London, **1911**, pp. 214-215; and reproduced in *The Scientific Letters and Papers of James Clerk Maxwell Vol. III 1874-1879* (Ed.: P. M. Harman), Cambridge University Press, Cambridge, **2002**, pp. 185-187. "*Concerning Demons.... Is the production of an inequality of temperature their only occupation? No, for less intelligent demons can produce a difference in pressure as well as temperature by merely allowing all particles going in one direction while stopping all those going the other way. This reduces the demon to a valve.*". More formally, a pressure demon would operate in a system linked to a constant-temperature reservoir with the sole effect of using energy transferred as heat from that reservoir to do work. This is in conflict with the Kelvin–Planck form of the Second Law whereas the temperature demon challenges the Clausius definition.

[3] For reprints of key papers and commentary on some of the main issues regarding Maxwell's Demon, see: *Maxwell's Demon 2. Entropy, Classical and Quantum Information, Computing* (Eds.: H. S. Leff, A. F. Rex), Institute of Physics Publishing, Bristol, **2003**.

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[8] (a) E. R. Kay, D. A. Leigh. Lighting Up Nanomachines. *Nature* **440**, 286-287 (2006). (b) E. R. Kay, D. A. Leigh and F. Zerbetto. Synthetic molecular motors and mechanical machines. *Angew. Chem. Int. Ed*. **46**, 72-191 (2007).
[9] M. Schliwa (ed) *Molecular Motors* (Wiley-VCH, Weinheim, **2003**).
[10] (a) D. A. Leigh, J. K. Y. Wong, F. Dehez and F. Zerbetto. Unidirectional rotation in a mechanically interlocked molecular rotor. *Nature* **424**, 174−179 (2003). (b) J. V. Hernández, E. R. Kay, and D. A. Leigh. A reversible synthetic rotary molecular motor. *Science* **306**, 1532−1537 (2004). (c) M. N. Chatterjee, E. R. Kay and D. A. Leigh. Beyond switches: ratcheting a particle energetically uphill with a compartmentalized molecular machine. *J. Am. Chem. Soc*. **128**, 4058−4073 (2006).
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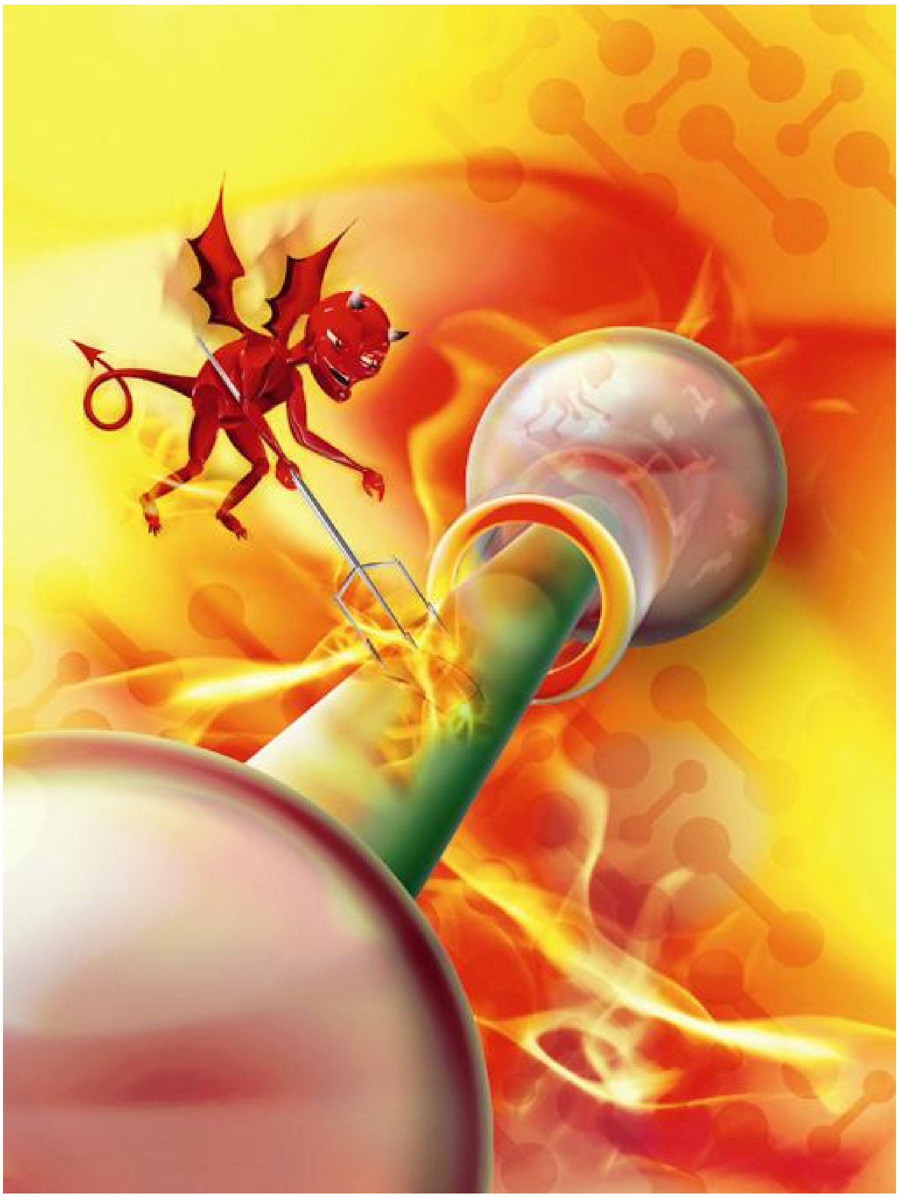

'*A demonic rotaxane*'. [High resolution image of this and other pictures are available on request from David.Leigh@ed.ac.uk. This illustration by Peter Macdonald – Edmonds UK.]