Brownian Motion

Reem Mokhtar
What is a Ratchet?

A device that allows a shaft to turn only one way


http://www.hpcgears.com/products/ratches_pawls.htm
Thermodynamics

2nd law, by Sadi Carnot in 1824.

- Zeroth: If two systems are in thermal equilibrium with a third system, they must be in thermal equilibrium with each other.
- First: Heat and work are forms of energy transfer.
- Second: The entropy of any isolated system not in thermal equilibrium almost always increases.
- Third: The entropy of a system approaches a constant value as the temperature approaches zero.

Why is there a maximum amount of work that can be extracted from a heat engine?

- Why is there a maximum amount of work that can be extracted from a heat engine?
- Carnot’s theorem: heat cannot be converted to work cyclically, if everything is at the same temperature → Let’s try to negate that.
The Ratchet As An Engine

Ratchet, pawl and spring.

Let us try to invent a device which will violate the Second Law of Thermodynamics, that is, a gadget which will generate work from a heat reservoir with everything at the same temperature. Let us say we have a box of gas at a certain temperature, and inside there is an axle with vanes in it. (See Fig. 46-1 but take

First, our idealized ratchet is as simple as possible, but even so, there is a pawl, and there must be a spring in the pawl. The pawl must return after coming off a tooth, so the spring is necessary.
The Ratchet As An Engine
Forward rotation

\[ \varepsilon \]
energy to lift the pawl

\[ L\theta \]
work done on load

\[ \varepsilon + L\theta \]
energy to rotate wheel by one tooth

\[ f_B^f = Z^{-1} e^{-\frac{(\varepsilon + L\theta)}{\tau_1}} \]
Boltzmann factor for work provided by vane

\[ \nu f_B^f \]
ratcheting rate with \( \nu \) attempt frequency

\[ \nu f_B^f L\theta \]
power delivered

\[ \varepsilon \]
energy provided to ratchet
Backward rotation

\[ \varepsilon \]

energy to lift the pawl

\[ L \theta \]

work provided by load

\[ \varepsilon + L \theta \]

energy given to vane

\[ f_b = Z^{-1} e^{-\varepsilon / \tau_2} \]

Boltzmann factor for tooth slip

\[ \nu f_b \]

slip rate with attempt frequency \( \nu \)
Equilibrium and reversibility

ratcheting rate = slip rate \( f^b_B = f^f_B \)

Reversible process by increasing the load infinitesimally from equilibrium \( L_{eq} \). This forces a rotation leading to heating of reservoir 1 with \( dq_1 = \varepsilon + L_{eq} \) and cooling of reservoir 2 as \( dq_2 = -\varepsilon \):

\[
\frac{dq_1}{\tau_1} = \frac{\varepsilon + L_{eq} \theta}{\varepsilon} = \frac{\tau_1}{\tau_2}
\]

\[
\frac{dq_2}{\tau_2} = \frac{\varepsilon}{\varepsilon} = \frac{\tau_1}{\tau_2}
\]

\[
dq_1 + dq_2 = dS_1 + dS_2 = 0
\]

isentropic process
Ratchet Brownian motor

Angular velocity of ratchet:
\[ \Omega = \theta \nu \left( f_B^f - f_B^b \right) = \theta \nu \left( e^{\frac{\varepsilon + L\theta}{\tau_1}} - e^{\frac{\varepsilon}{\tau_2}} \right) \]

Without load:
\[ \Omega \xrightarrow{L=0} \theta \nu \left( e^{\frac{\varepsilon}{\tau_1}} - e^{\frac{\varepsilon}{\tau_2}} \right) \]

Equal temperatures:
\[ \Omega(L) \xrightarrow{\tau_1 = \tau_2 = \tau} \theta \nu e^{\frac{\varepsilon}{\tau}} \left( e^{\frac{L\theta}{\tau}} - 1 \right) \]

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Equal temperatures:
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Kinesin

The two heads of the kinesin dimer work in a coordinated manner to move processively along the microtubule. The catalytic core (blue) is bound to a tubulin heterodimer (green, b-subunit; white, a-subunit) along a microtubule protofilament (the cylindrical microtubule is composed of 13 protofilament tracks). In solution, both kinesin heads contain ADP in the active site (ADP release is rate limiting in the absence of microtubules). The chaotic motion of the kinesin molecule reflects Brownian motion. One kinesin head makes an initial weak binding interaction with the microtubule and then rearranges to engage in a tight binding interaction. Only one kinesin head can readily make this tight interaction with the microtubule, due to constraints imposed by the coiled-coil and pre-stroke conformation of the neck linker in the bound head. Microtubule binding releases ADP from the attached head. ATP then rapidly enters the empty nucleotide binding site, which triggers the neck linker to zipper onto the catalytic core (red to yellow transition). This action throws the detached head forward and allows it to reach the next tubulin binding site, thereby creating a 2-head-bound intermediate in which the neck linkers in the trailing and leading heads are pointing forward (post-stroke; yellow) and backwards (pre-stroke; red) respectively. The trailing head hydrolyzes the ATP (yellow flash of ADP-Pi), and reverts to a weak microtubule binding state (indicated by the bouncing motion) and releases phosphate (fading Pi). Phosphate release also causes the unzipping of the neck linker (yellow to red transition). The exact timing of the strong-to-weak microtubule binding transition and the phosphate release step are not well-defined from current experimental data. During the time when the trailing head executes the previously described actions, the leading head releases ADP, binds ATP, and zippers its neck linker onto the catalytic core. This neck linker motion throws the trailing head forward by 160 Å to the vicinity of new tubulin binding site. After a random diffusional search, the new lead head docks tightly onto the binding site which comp letes the 80 Å step of the motor. The movie shows two such 80 Å steps of the kinesin motor. The surface features of the kinesin motor domains and the microtubule protofilament were rendered from X-ray and EM crystallographic structures by Graham Johnson (fiVth media: www.fiVth.com) using the programs MolView, Strata Studio Pro and Cinema 4D. PDB files used were human conventional kinesin (pre-stroke red: 1BG2) and rat conventional kinesin (post-stroke yellow: 2KIN). In human conventional kinesin the neck linker is mobile and its located in the pre-stroke state is estimated from cryo-electron microscopy data. Transitions between states were performed by performing computer-coordinated extrapolations between the pre-stroke and post-stroke positions. The durations of the events in this sequence were optimized for clarity and do not necessarily reflect the precise timing of events in the ATPase cycle.
Diffusion in asymmetric potentials

Driven Brownian ratchets

\[ U_{on} = U_{bare} - xF_{ext} \]

\[ U_{on} = -xF_{ext} \]

\[ \Delta U \]

\[ \frac{B}{m} \]

\[ f_{off} \]

\[ \text{Large particles} \]

\[ \text{Small particles} \]

\[ F_{gray} \sin \theta \]
DNA transport by a micromachined Brownian ratchet device

Joel S. Bader et al., PNAS 96. 13165 (1999)

Fig. 3. Three images are shown from a typical experiment using a device with 2-\(\mu\)m electrodes and a 0.7-Hz switching frequency to transport a rhodamine-labeled DNA 50-mer. These images were saved during the trapping phase of the cycle, and fluorescence maxima are clearly seen from DNA molecules captured on the positive electrodes. At the start of the experiment, the DNA oligomers are focused on left-most three electrodes. As the potential cycles between on- and off-states, the packet moves to the right and broadens.
A. van Oudenaarden and S. G. Boxer,
DNA transport by a micromachined Brownian ratchet device

Joel S. Bader et al., PNAS 96, 13165 (1999)


Geometrical Brownian ratchet I

Geometrical Brownian ratchet II

Unidirectional molecular rotation

T. Ross Kelly et al., Nature 401 (1999) 150

Chemically driven rotation

Light driven rotation

N. Koumura et al., Nature 401 (1999) 152
Unidirectional molecular rotation

T. Ross Kelly et al.,
Nature 401 (1999) 150
Chemically driven rotation

From molecular ratchet...

Spokes

Spindle

Brake

... to molecular motor

1

2

3

4

5

(corresponds to Fig. 2c)

urethane formation

NaBH(OEt)_3, (cleaves urethane)

rotate over E_{act}

(corresponds to Fig. 2d)

1. [Chemical structures and reactions]

2. [Chemical structures and reactions]

3. [Chemical structures and reactions]

4. [Chemical structures and reactions]

5. [Chemical structures and reactions]
Light driven rotation

N. Koumura et al., Nature 401 (1999) 152
Maxwell’s demon

W. Smoluchowski (1941):
No automatic, permanently effective perpetual motion machine can violate the second law by taking advantage of statistical fluctuations (Feynman: the demon is getting hot). Such device might perhaps function if operated by intelligent beings.

The second law is safe from intelligent beings as long as their abilities to process information are subject to the same laws as these of universal Turing machines.
Quantum demon? (ask Milena Grifoni)

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Quantum demon? (ask Milena Grifoni)

Fluctuations of µm-sized trapped colloidal particles


\[ \text{Entropy production} = \int_0^\tau \Sigma dt \]

Noise ratchet
Maxwell’s demon

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Fluctuations of µm-sized trapped colloidal particles


\[ \Sigma_t = \frac{1}{\tau} \int_0^t v_{opt} \cdot F_{opt}(s) \, ds \]

Entropy production

physics.okstate.edu/ackerson/vackerson/
The Feynman Thermal Ratchet

\[ P_{\text{forward}} \sim \exp\left(-\frac{\Delta \varepsilon}{kT_1}\right) \]
\[ P_{\text{backward}} \sim \exp\left(-\frac{\Delta \varepsilon}{kT_2}\right) \]

works only if \( T_1 > T_2 \) !!

motor protein conformational change: \( \mu s \)

decay of temperature gradient over 10 nm: \( \text{ns} \)

\[ \tau_{\text{rel}} \approx \frac{C l^2}{4 \pi^2 \kappa} \]
Brownian Ratchet
(A.F. Huxley ‘57)

perpetuum mobile? Not if ATP is used to switch the off-rate.
Three-bead assay with ncd
Myosin: averaged power strokes
(Veigel et al. Nature ‘99, 398, 530)
Myosin Power Stroke

Mechano-chemical cycle:

- **attach**
- **working stroke**
- **detach**
- **recovery stroke**

- M$^*$ATP → M$^*$ADP*Pi → M → ADP + P$_i$ → ADP + P$_i$
Conformational Change of Single ncd Molecule

Single Molecule Bead Assay

0.5 μm bead

dimeric kinesin motor

Microtubule

ATPase rate: ~45/head*sec.
Max. velocity: ~ 1 μm/sec.
Stepping and Stalling of a Single Kinesin Molecule

~ 6 pN stall force

~ 8 nm steps

Randomness parameter

\[ r := \lim_{t \to \infty} \frac{\langle x^2(t) \rangle - \langle x(t) \rangle^2}{d \langle x(t) \rangle} \]

\[ \Delta t = \text{const.} \]

“clockwork”

\[ r = 0 \]

1 \( \rightarrow \) 2 \( \rightarrow \) 3 \( \rightarrow \) 4 \( \rightarrow \) 5 \( \rightarrow \) 6

\[ k \quad k \quad k \quad k \quad k \quad k \quad k \]

\[ \Delta t \text{ exponentially distributed} \]

Poisson process

\[ r = 1 \]

1 \( \rightarrow \) 2
Randomness parameter for single kinesin

(Visscher, Schnitzer, Block (‘99), Nature 400, 184)
Thermal Motion of a Trapped/Tethered Particle

Time series:

\[
\text{var}(x) = \langle x^2 \rangle - \langle x \rangle^2 = \frac{k_B T}{\kappa}
\]

Spectrum:

\[
S(f) = \frac{k_B T}{\pi^2 \gamma (f_c^2 + f^2)}
\]

\[
f_c = \frac{\kappa}{2\pi \gamma}, \quad S_0 = \frac{4\gamma k_B T}{\kappa^2}
\]

Trapped bead attached to motor:

\[
\text{var}(x) = \frac{k_B T}{\kappa_{\text{trap}} + \kappa_{\text{motor}}}
\]
Efficiency, Invertability and Processivity of Molecular Motors

F. Jülicher, Institut Curie, Paris

A. Parmeggiani
L. Peliti (Naples)
A. Ajdari (Paris)
J. Prost (Paris)

http://www.curie.fr/~julicher
Mechano-chemical coupling

\[ \frac{\partial}{\partial t} P_i + \frac{\partial}{\partial x} J_i = - \sum_{j \neq i} \omega_{ij} P_i + \sum_{j \neq i} \omega_{ji} P_j \]

\[ J_i = -\mu(k_B T \frac{\partial}{\partial x} P_i + P_i \frac{\partial}{\partial x} W_i - f_{ext} P_i) \]

mean velocity

\[ v = \int_0^l dx \sum_i J_i \]
Example: weakly bound state

weakly bound

strongly bound

ATP

ADP

ADP-P

ADP

actin

myosin

position
Example: identical shifted states

\[ \omega_{12} = \omega e^{(\Delta \mu - \Delta W)/kT} \]
\[ \omega_{21} = \omega \]

chemical free energy of hydrolysis:

\[ \Delta \mu = \mu_{ATP} - \mu_{ADP} - \mu_P \]
\[ \mu_i \approx \mu_i^0 + kT \ln(C_i / C_i^0) \]
Dissipation rates

motion within a state:

\[ \dot{Q}_i = \int_0^l dx \; J_i \partial_x H_i \geq 0 \]

\[ H_i = W_i - f_{ext} x + k_B T \ln(P_i) \]

chemical transitions:

\[ \dot{Q}_\alpha = \int_0^l dx \left( \omega_{12} P_1 - \omega_{21} P_2 \right) (H_1 - H_2 + \Delta \mu) \geq 0 \]

total internal dissipation of the motor:

\[ \dot{Q} = \dot{Q}_1 + \dot{Q}_2 + Q_\alpha \geq 0 \]
Efficiency of energy transduction

Energy conservation:

\[ \dot{Q} = r \Delta \mu + f_{\text{ext}} v \]

\( \eta = -\frac{f_{\text{ext}} v}{r \Delta \mu} \)

\( f_{\text{ext}} \) force
\( \nabla \) velocity
\( \Delta \mu \) chemical energy
\( r \) chemical rate

A. Parmeggiani, F. Jülicher, A. Ajdari and J. Prost, PRE 60, 2127 (1999)
remarkable that any form of controlled motion is possible. It is the result of random collisions. In a near-vacuum, for example, although there would be few molecules to influence a system as a function of scale, not of the nature of the surroundings. It cannot be avoided by putting a molecular-level structure in place; the effect of a switch is undone by resetting the machine.

In 1905, the Scottish physicist James Clerk Maxwell played a major role (along with Ludwig Boltzmann) in developing the kinetic theory of gases, which established the relationship between heat and particle motion and gave birth to the concept of statistical mechanics. In doing so, Maxwell realized the importance of the stochastic nature of molecular-level motion even at room temperature, thus providing a foundation for understanding Brownian motion.

Scientists have been fascinated by the implications of his three celebrated papers of 1905 and 1906, which were proven experimentally by Einstein in one of his many thought experiments. The phenomenon—random collisions to set such a Brownian particle in motion, in the absence of any other molecules, heat would still be transmitted from the hot walls of the container to the particle by electromagnetic radiation, with the random emission and absorption of the photons producing the particle's Brownian motion. In fact, even temperature is not a particularly effective modulator of Brownian motion since the velocity of the particles depends on the square root of the kinetic energy of the particle and only the mean-free path between collisions is affected by the concentration of molecules in solution. This was proven experimentally by Einstein in his thought experiment which has come to be known as the Maxwell Demon.

When designing molecular machines it is important to remember that the presence of Brownian motion is a consequence of scale, not of the nature of the surroundings. Scientists have been fascinated by the implications of the second law of thermodynamics which had recently been formulated by Rudolf Clausius and William Thomson (later Lord Kelvin). In 1871, Rudolf Clausius and William Thomson (later Lord Kelvin) published a paper in which they asked “What prevents cold bodies from becoming colder?”. They conjectured that energy could flow spontaneously from cold objects to hot objects, but not the other way around. This is the second law of thermodynamics which states that the total entropy of an isolated system never decreases over time. In 1873, Clausius realized that this law could be restated in terms of the average kinetic energy of the particles in a system: the higher the temperature, the greater the average kinetic energy of the particles. This is the first law of thermodynamics which states that the total energy of a system remains constant. The third law sets the limits against which absolute measurement of temperature can be made. Whenever energy changes hands, the zeroth law of thermodynamics tells us about the nature of equilibrium, the first law is concerned with the total energy of a system, while the second law determines the direction and rate of the energy changes.

In the absence of any other molecules, heat would always cancel each other out, and as long as a temperature can be defined for an object it will undergo Brownian motion even though there would be little viscosity to slow it down. These effects dominate mechanical behavior in the molecular world. Even doing work was the subject of several celebrated historical "thought-machines" intended to test the very nature of the laws of thermodynamics which had recently been formulated. Indeed, the design of tiny machines capable of harnessing Brownian motion to make molecular-level "motor" at the molecular level. Both translational and rotary switches influence a system as a function of the switch state. They switch between two or more, often equilibrium, states. Motors, however, influence a system as a function of the trajectory of their components or a substrate. Motors function repetitively and progressively on a system; the affect of a switch is undone by resetting the machine. a) Rotary switch. b) Rotary motor. c) Translational switch. d) Translational motor or pump.

Reviews

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term "demon" for Maxwell thermal fluctuations. The term "Maxwell an attempt to construct a perpetual motion machine driven by subsequent investigators, who have perceived the demon as nature. This, however, has not been the view of many illustration of its limitations—an exposition of its statistical threat to the second law of thermodynamics, but rather an Indeed, neither Maxwell nor Thomson saw the demon as a supernatural being of a nature between gods and humans. Greek roots of the word (more usually daemon) as a Thomson apparently did not intend to suggest a malicious expanded upon Maxwell and "cold" molecules.

Figure 2.

a) Maxwell’s “temperature demon” in which a gas at uniform temperature is sorted into “hot” and “cold” molecules.\cite{15} Particles with energy higher than the average are represented by red dots while blue dots represent particles with energies lower than the average. All mechanical operations carried out by the demon involve no work—that is, the door is frictionless and it is opened and closed infinitely slowly. The depiction of the demon outside the vessel is arbitrary and was not explicitly specified by Maxwell. b) A Maxwellian “pressure demon” in which a pressure gradient is established by the door being opened only when a particle in the left compartment approaches it.\cite{15c}

a) Initially a single Brownian particle occupies a cylinder with a piston at either end. A frictionless partition is put in place to divide the container into two compartments (a→b). b) The demon then detects the particle and determines in which compartment it resides. c) Using this information, the demon is able to move the opposite piston into position without meeting any resistance from the particle. d) The partition is removed, allowing the “gas” to expand against the piston, doing work against any attached load (e). To replenish the energy used by the piston and maintain a constant temperature, heat must flow into the system. To complete the thermodynamic cycle and reset the machine, the demon’s memory of where the particle was must be erased (f→a). To fully justify the application of a thermodynamic concept such as entropy to a single-particle model, a population of Szilard devices is required. The average for the ensemble over each of these devices can then be considered to represent the state of the system, which is comparable to the time average of a single multiparticle system at equilibrium, in a fashion similar to the statistical mechanics derivation of thermodynamic quantities.

Figure 4. a) Smoluchowski’s trapdoor: an “automatic” pressure demon (the directionally discriminating behavior is carried out by a wholly mechanical device, a trapdoor which is intended to open when hit from one direction but not the other).\cite{16} Like the pressure demon shown in Figure 2b, Smoluchowski’s trapdoor aims to transport particles selectively from the left compartment to the right. However, in the absence of a mechanism whereby the trapdoor can dissipate energy it will be at thermal equilibrium with its surroundings. This means it must spend much of its time open, unable to influence the transport of particles. Rarely, it will be closed when a particle approaches from the right and will open on collision with a particle coming from the left, thus doing its job as intended. Such events are balanced, however, by the door snapping shut on a particle from the right, pushing it into the left chamber. Overall, the probability of a particle moving from left to right is equal to that for moving right to left and so the trapdoor cannot accomplish its intended function adiabatically. b) Feynman’s ratchet and pawl.\cite{18} It might appear that Brownian motion of the gas molecules on the paddle wheel in the right-hand compartment can do work by exploiting the asymmetry of the teeth on the cog of the ratchet in the left-hand compartment. While the spring holds the pawl between the teeth of the cog, it does indeed turn selectively in the desired direction. However, when the pawl is disengaged, the cog wheel need only randomly rotate a tiny amount in the other direction to move back one tooth whereas it must rotate randomly a long way to move to the next tooth forward. If the paddle wheel and ratchet are at the same temperature (that is, $T_1=T_2$) these rates cancel out. However, if $T_1 \neq T_2$ then the system will directionally rotate, driven solely by the Brownian motion of the gas molecules. Part (b) reprinted with permission from Ref. [18].

Figure 8. A temperature (or diffusion) ratchet.\textsuperscript{[39f]} a) The Brownian particles start out in energy minima on the potential-energy surface with the energy barriers $\gg k_B T_1$. b) The temperature is increased so that the height of the barriers is $\ll k_B T_2$ and effectively free diffusion is allowed to occur for a short time period (much less than required to reach global equilibrium). c) The temperature is lowered to $T_1$ once more, and the asymmetry of the potential means that each particle is statistically more likely to be captured by the adjacent well to the right rather than the well to the left. d) Relaxation to the local energy minimum (during which heat is emitted) leads to the average position of the particles moving to the right. Repeating steps (b)–(d), progressively moves the Brownian particles further and further to the right. Note the similarities between this mechanism and that of the on–off ratchet shown in Figure 6.

Figure 6. An example of a pulsating ratchet mechanism—an on–off ratchet.\textsuperscript{[39f]} a) The Brownian particles start out in energy minima on the potential-energy surface with the energy barriers $\gg k_B T$. b) The potential is turned off so that free Brownian motion powered diffusion is allowed to occur for a short time period (much less than required to reach global equilibrium). c) On turning the potential back on again, the asymmetry of the potential means that the particles have a greater probability of being trapped in the adjacent well to the right rather than the adjacent well to the left. Note this step involves raising the energy of the particles. d) Relaxation to the local energy minima (during which heat is emitted) leads to the average position of the particles moving to the right. Repeating steps (b)–(d) progressively moves the Brownian particles further and further to the right.

into two basic types—pulsating ratchets and tilting ratchets—and are the subject of a recent major review by Reimann, and information ratchets, which are much less common in the physics literature, but have been discussed by Parrondo, Astumian, and others.

Both energy ratchets and information ratchets bias the movement of a Brownian substrate. However, we will also show (Sections 1.4.3 and 4.4) that they offer clues for how to go beyond a simple switch with a chemical machine to enable tasks to be performed through the non-equilibrium control of conformational and co-conformational changes within molecular structures.

1.4.2.1. Pulsating Ratchets

Pulsating ratchets are a general category of energy ratchet in which potential-energy minima and maxima are varied in a periodic or stochastic fashion, independent of the position of the particle on the potential-energy surface. In its simplest form this can be considered as an asymmetric sawtooth potential being repetitively turned on and off faster than Brownian particles can diffuse over more than a small fraction of the potential energy surface (an “on–off” ratchet, Figure 6). The result is net directional transport of the particles across the surface (left to right in Figure 6).

More general than the special case of an on–off ratchet, any asymmetric periodic potential may be regularly or stochastically varied to give a ratchet effect (such mechanisms are generally termed “fluctuating potential” ratchets). As with the simple on–off ratchet, most commonly encountered examples involve switching between two different potentials and are therefore often termed “flashing” ratchets. A classic example, which has particular relevance for explaining a number of biological processes as well as being the basis for a catenane rotary motor (see Section 4.6.3), is illustrated in Figure 7. It consists in physical terms of an asymmetric potential-energy surface (comprising a periodic series of two different minima and two different maxima) along which a Brownian particle is directionally transported by sequentially raising and lowering each set of minima and maxima. The particle starts in a green or orange well (Figure 7a or c). Raising that energy minimum while lowering those in adjacent wells provides the impetus for the particle to change position by Brownian motion (Figure 7b–7c or 7d–7e). By simultaneously (or beforehand) changing the relative heights of the energy barrier to the next energy well, the kinetics of the Brownian motion in each direction are different and the particle is transported from left to right. Note that the position of the particle does not influence the sequence in which (or when, or if) the energy minima and maxima are changed. Furthermore, the switching of the

Figure 6. An example of a pulsating ratchet mechanism—an on–off ratchet.

Figure 7. Another example of a pulsating ratchet mechanism—a flashing ratchet. For details of its operation, see the text.

periodic force cases (imagine applying the electric field discussed above for longer in one direction than the other), but is less so for stochastic driving forces. In general, these mechanisms are known as “asymmetrically tilting” ratchets.

1.4.2.3. Information Ratchets

In the pulsating and tilting types of energy ratchet mechanisms, perturbations of the potential-energy surface—or of the particle's interaction with it—are applied globally and independent of the particle's position, while the periodicity of the potential is unchanged. Information ratchets (Figure 10) transport a Brownian particle by changing the effective kinetic barriers to Brownian motion depending on the position of the particle on the surface. In other words, the heights of the maxima on the potential-energy surface change according to the location of the particle (this requires information to be transferred from the particle to the surface) whereas the potential-energy minima do not necessarily need to change at all. This switching does not require raising the potential energy of the particle at any stage, rather the motion can be powered with energy taken entirely from the thermal bath by using information about the position of the particle. This is directly analogous to the mechanism required of Maxwell's pressure demon (Figure 2 b, Section 1.2.1.1), but does not break the second law of thermodynamics as the required information transfer (actually, information era-$$\text{[48]}$$sure) has an intrinsic energy cost that has to be met externally.

It appears to us that information-ratchet mechanisms of relevance to chemical systems can arise in at least three ways: 1) a localized change to the intrinsic potential-energy surface depending on the position of the particle (Figure 10); 2) a position-dependent change in the state of the particle which alters its interaction with the potential-energy surface at that point; or 3) switching between two different intrinsic periodic potentials according to the position of the particle.

An example of the first of these types, in which the system responds to the “information” from the particle by lowering the energy barrier to the right-hand side (and only to the right-hand side) of the particle, is shown in Figure 10. The particle starts in one of the identical-minima energy wells (Figure 10 a). The position of the particle lowers the kinetic barrier for passage to the adjacent right-hand well and it moves there by Brownian motion (10 b–10 c). At this point it can sample two energy wells by Brownian motion, and a random reinstatement of the barrier has a 50 % chance of returning the particle to its starting position and a 50 % chance of trapping it in the newly accessed well to the right.

Figure 9. A rocking ratchet.$^{[39]}$ a) The Brownian particles start out in energy minima on the potential-energy surface with the energy barriers $$\gg k_BT$$. b) A directional force is applied to the left. c) An equal and opposite directional force is applied to the right. d) Removal of the force and relaxation to the local energy minimum leads to the average position of the particles moving to the right. Repeating steps (b)–(d) progressively moves the Brownian particles further and further to the right.

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1.4.2.3. Information Ratchets

In the pulsating and tilting types of energy ratchet mechanisms, perturbations of the potential-energy surface—or of the particle/s interaction with it—are applied globally and independent of the particle’s position, while the periodicity of the potential is unchanged. Information ratchets (Figure 10) transport a Brownian particle by changing the effective kinetic barriers to Brownian motion depending on the position of the particle on the surface. In other words, the heights of the maxima on the potential-energy surface change according to the location of the particle (this requires information to be transferred from the particle to the surface) whereas the potential-energy minima do not necessarily need to change at all. This switching does not require raising the potential energy of the particle at any stage, rather the motion can be powered with energy taken entirely from the thermal bath by using information about the position of the particle. This is directly analogous to the mechanism required of Maxwell’s pressure demon (Figure 2 b, Section 1.2.1.1), but does not break the second law of thermodynamics as the required information transfer (actually, information erasure [48]) has an intrinsic energy cost that has to be met externally.

It appears to us that information-ratchet mechanisms of relevance to chemical systems can arise in at least three ways: 1) a localized change to the intrinsic potential-energy surface depending on the position of the particle (Figure 10); 2) a position-dependent change in the state of the particle which alters its interaction with the potential-energy surface at that point; or 3) switching between two different intrinsic periodic potentials according to the position of the particle. An example of the first of these types, in which the system responds to the "information" from the particle by lowering the energy barrier to the right-hand side (and only to the right-hand side) of the particle, is shown in Figure 10. The particle starts in one of the identical-minima energy wells (Figure 10 a). The position of the particle lowers the kinetic barrier for passage to the adjacent right-hand well and it moves there by Brownian motion (10 b ! 10 c). At this point it can sample two energy wells by Brownian motion, and a random reinstatement of the barrier has a 50 % chance of returning the particle to its starting position and a 50 % chance of trapping it in the newly accessed well to the right.

Figure 10. A type of information ratchet mechanism for transport of a Brownian particle along a potential-energy surface.[39h,42b,45] Dotted arrows indicate the transfer of information that signals the position of the particle. If the signal is distance-dependent—say, energy transfer from an excited state which causes lowering of an energy barrier—then the asymmetry in the particle's position between two barriers provides the “information” which transports the particle directionally along the potential energy surface.

Correlated disrotation maintains the phase relationship between the labeled blades (shown here in red) for each isomer. Interconversion between isomers ("gear slippage") requires correlated conrotation or uncorrelated rotation. Molecular gear train 2. Molecular gear 3 (shown as the racemic residual diastereomer) and a molecular gear 4 with a 2:3 gearing ratio, and a molecular gear 5 based on revolution around a metallocene and with a 3:4 gearing ratio. The arrows show correlated motions but are not meant to imply intrinsic directionality.

The same comparison can be applied to a more recent series of trinuclear sandwich complexes in which multiple correlated motions have been demonstrated. Each silver cation in \([\text{Ag}_3(6)_2]\) has a linear coordination geometry, bound to one nitrogen donor from each tris-monodentate disk-shaped ligand (red)—the resulting complex is helical, with all the thiazolyl rings tilted in the same direction (Figure 11b). Random helix inversion is a low-energy process, which occurs through a nondissociative "flip" motion whereby rotation of the heteroaromatic rings so that they point in the opposite direction is accompanied by a 120° relative rotation of the two large disks (illustrated for \([\text{Ag}_3(6)_2]\) in Figure 11 c).

In the heteroleptic analogue \([\text{Ag}_3(6)_2]\), a similar coordination geometry is adopted so that only every alternate thiazolyl ring in the hexakis-monodentate disk ligand (blue) is bound at any one time. The "flip" helix reversal, during which the ligand and metal partners do not change, can clearly still occur. Ligand exchange is also rapid, however, and most likely occurs via the trigonal transition state illustrated in Figure 11 c. The overall result is a correlated rotation of the heteroaromatic rings together with a 60° relative rotation of the two disks. If a ligand exchange and a flip step occur concurrently, the sense of rotation in each step is opposite, so that overall a 60° relative rotation of the disk-shaped ligands occurs.

While all these and other related studies clearly demonstrate the role steric interactions can play, at equilibrium the submolecular motions are nondirectional even within a partial rotational event. Simply restricting the thermal rotary motion of one unit by a larger blocking group or by the similarly random motion of another unit cannot, in itself, lead to directionality. A molecular machine requires some form of external modulation over the dynamic processes to drive the system away from equilibrium and break detailed balance.

2.1.2. Stimuli-Induced Conformational Control around a Single Covalent Bond

As a first step towards achieving controlled and externally initiated rotation around \(C_1/C_0\) single bonds, Kelly and co-workers combined triptycene structures with a molecular-recognition event. In the resulting "molecular brake" Figure 11. a) Chemical structure of tris-monodentate disk-shaped ligand 6 and hexakis-monodentate ligand 7. b) Schematic representation of complex \([\text{Ag}_3(6)_2]\) arbitrarily shown as its \(M\)-helical enantiomer. c) Description of the two correlated rotation processes occurring in \([\text{Ag}_3(6)\](7)]. The direction of rotation for an \(M\rightarrow P\) transition through ligand exchange is opposite to that for the potentially subsequent \(P\rightarrow M'\) transition by the nondissociative flip mechanism. Schematic representations reprinted with permission from Refs. [65a,c]. Carter, N. J., & Cross, R. A. (2005). Mechanics of the kinesin step. Nature, 435(7040), 308–312.
The same comparison can be applied to a more recent series of trinuclear sandwich complexes in which multiple correlated motions have been demonstrated.

Each silver cation in $[\text{Ag}_3(6)\text{]}^2_2$ has a linear coordination geometry, bound to one nitrogen donor from each trismonodentate disk-shaped ligand (red)—the resulting complex is helical, with all the thiazolyl rings tilted in the same direction (Figure 11b).

Random helix inversion is a low-energy process, which occurs through a nondissociative "flip" motion whereby rotation of the heteroaromatic rings so that they point in the opposite direction is accompanied by a $120^\circ$ relative rotation of the two large disks (illustrated for $[\text{Ag}_3(6)(7)]$ in Figure 11c).

In the heteroleptic analogue $[\text{Ag}_3(6)(7)]$, a similar coordination geometry is adopted so that only every alternate thiazolyl ring in the hexakis-monodentate disk ligand (blue) is bound at any one time. The "flip" helix reversal, during which the ligand and metal partners do not change, can clearly still occur. Ligand exchange is also rapid, however, and most likely occurs via the trigonal transition state illustrated in Figure 11c. The overall result is a correlated rotation of the heteroaromatic rings together with a $60^\circ$ relative rotation of the two disks. If a ligand exchange and a flip step occur concurrently, the sense of rotation in each step is opposite, so that overall a $60^\circ$ relative rotation of the disk-shaped ligands occurs.

While all these and other related studies clearly demonstrate the role steric interactions can play, at equilibrium the submolecular motions are nondirectional even within a partial rotational event. Simply restricting the thermal rotary motion of one unit by a larger blocking group or by the similarly random motion of another unit cannot, in itself, lead to directionality. A molecular machine requires some form of external modulation over the dynamic processes to drive the system away from equilibrium and break detailed balance.

2.1.2. Stimuli-Induced Conformational Control around a Single Covalent Bond

As a first step towards achieving controlled and externally initiated rotation around $\text{C}_/\text{C}_0\text{C}$ single bonds, Kelly and co-workers combined triptycene structures with a molecular-recognition event.

$\text{Scheme 2.} \quad \text{"Molecular brakes" induced by a) metal-ion binding}^{[68]} \text{and b) redox chemistry}^{[70]} \text{. EDTA = ethylenediaminetetraacetate, mCPBA = meta-chloroperbenzoic acid.}$

Figure 12. a) Kelly’s molecular realization (10) of Feynman’s adiabatic ratchet and pawl which does not rotate directionally at equilibrium.\cite{[72]} b) Schematic representation of the calculated enthalpy changes for rotation around the single degree of internal rotational freedom in 10.
Scheme 3. A chemically powered unidirectional rotor. Priming of the rotor in its initial state with phosgene (11a→12a) allows a chemical reaction to take place when the helicene rotates far enough up its potential well towards the blocking triptycene arm (12b). This gives a tethered state 13a, for which rotation over the barrier to 13b is an exergonic process that occurs under thermal activation. Finally, the urethane linker can be cleaved to give the original molecule with the components rotated by 120° with respect to each other (11b).

This cycle produces the opposite enantiomer, which undergoes an analogous cycle in which rotation must be biased in the opposite direction. A number of potential side reactions (not illustrated) which would divert the system from the catalytic cycle were found to be kinetically insignificant under the reaction conditions employed.

removal of one of the protecting groups on the enantiotopic phenols results in spontaneous lactonization when thermally driven axial rotation brings the two reactive groups together—again probably a net directional process because of the steric hindrance of the \textit{ortho} substituents (although this is not demonstrated because the chirality is destroyed in this step). Figure 13b illustrates the unidirectional process achieved using the (\textit{S})-Corey–Bakshi–Shibata (\textit{S}-CBS) catalyst; rotation in the opposite sense can be achieved by employing the opposite borolidine enantiomer and swapping the order of phenol protection and deprotection steps.

2.1.3. Stimuli-Induced Conformational Control in Organometallic Systems

Controlling the facile rotary motion of ligands in metal sandwich or double-decker complexes (introduced in Section 2.1.1) is conceptually similar to controlling rotation around covalent single bonds, and stimuli-induced control in such metal complexes has also been demonstrated. In metal bisporphyrinate complexes such as \([\text{Ce(21)}]\) (Scheme 6) rotary motion corresponds to enantiomerization when the ligands possess \(D_{2h}\) symmetry. This situation provides a convenient handle for monitoring the kinetics of rotation. \[82\]

In complex \([\text{Ce(21)}]\), rotation around the metal center is slow enough to permit isolation of the two enantiomers by chiral HPLC. However, reduction of the metal center (\([\text{Ce}^{IV}(21)] \rightarrow [\text{Ce}^{III}(21)] / C_{0}\)) increases the rate of racemization by over 300-fold. \[82c\] This effect is thought to derive from a reduced \(p–p\) interaction between the two ligands as a consequence of the larger ionic radius of the metal center in the lower oxidation state. Similarly, complexes formed around the smaller \(\text{Zr}^{IV}\) ion show very slow rotational dynamics at pH 7, \[83\] yet protonation results in facile racemization. \[82a\] The effect is retarded by oxidation of the porphyrin ligands, probably as a result of electrostatic repulsion of incoming protons, but also because of the fact that the highest occupied molecular orbital (HOMO) of the complex is antibonding, so removal of electrons should...

Scheme 9. a) Negative heterotropic allosteric receptor 25 binds alkali metal ions, with selectivity for K⁺.\textsuperscript{100} Chelation of tungsten to the bipyridyl moiety forces this unit to adopt a rigid conformation in which the 3 and 3' substituents are brought close together. The resulting conformation of the crown ether does not favor binding through all the oxygen atoms and so affinity for K⁺ ions is reduced. In fact [W(CO)₃(25)] shows a preference for binding the smaller Na⁺ ion. b) Positive homotropic allosteric allosteric receptor 26.\textsuperscript{101}

shows the incidence and the amplitude of forward and backward (step) and amplitude (the distance moved) for each step. Figure 2a time (the time interval between the previous step and the current steps within a data set of multiple records, and to determine the dwell activation energy barrier in accordance with Kramers theory about 3 pN both at 1 mM ATP and at 10

The load–dwell-time curve for forward steps is exponential above
23–25

The load–dwell-time curve for forward steps is exponential above

2

Two successive experiments on the same molecule are shown. For automated dwell time calculations and step-averaging, a t-test step finder was applied to the bead position data. The inset shows the t-test profile for the first part of record 1. Steps are defined where the t-value exceeds a preset threshold value (dotted line). The located steps are shown offset just above record 1. In all records, detachment events (steps larger than 12 nm recognized by the step finder) are marked with D. Conditions: single kinesin molecules on 560-nm polystyrene beads, 1 mM ATP. The trap stiffnesses for the beads in these records were 0.064, 0.067 and 0.064 pN nm\(^{-1}\), respectively. The force scale represents a trap stiffness of 0.065 pN nm\(^{-1}\). Stage movements (arrows) were typically complete within 200 ms. The data shown are 1-ms boxcar filtered.

which backward stepping synthesizes ATP and specifically exclude models that forbid backward steps. Models in the probability of forward stepping is equal to that of backward probability of a forward step decreases exponentially with increasing Vol 435 shown: the fit time constant for 500-nm beads (black) was faster than that by a least-squares exponential fit for step position refinement. The averaged positions were determined automatically with a test step finder, followed against models that predict substeps arising from rapidly equilibrating mechanical substates step averaging were recorded at 1 mM ATP.

There are previous reports of substeps to 30–32 | NATURE 30–32 m 6,7, and several current data gainsay models in which kinesin steps along the 4-nm load, whereas the probability of a backward step is constant. At stall, mechanical states linked by strain-dependent conformational behaviour and was modified to include multiple bound this original scheme proved inadequate to account for the mechanical excursions in the progress direction. This excursion can then be locked in by irreversible ADP release from the lead head.

Figure 4 | Model. Before ATP binding, the motor is parked (state 0): the holdfast head remains stably bound to the microtubule and the ADP-containing tethered head cannot access its new site. Straining this state either forwards or backwards does not induce stepping. ATP (T) binding to the holdfast head sanctions ADP (D) release from the tethered head. Forward steps (+1, +2, +3, 0) occur when the tethered head binds in front of the holdfast head, backward steps (−1, −2, −3, 0) when it binds behind. The choice between forward and backward stepping depends on the applied load (the spring). In the figure, the central state 0 represents stall, in which the backward load applied by the trap (represented by the stretched spring) is such that the tethered head has an equal probability of stepping forwards or backwards. To make a forward step, the motor needs to make a diffusional excursion in the progress direction. This excursion can then be locked in by irreversible ADP release from the lead head.

The same data sets are shown on two timescales: fine (a) and coarse (b). Step positions were determined automatically with a t-test step finder, followed by a least-squares exponential fit for step position refinement. The averaged forward steps (circles) and backward steps (squares) for two bead sizes are shown: the fit time constant for 500-nm beads (black) was faster than that for 800-nm beads (red). For 500-nm beads, forward steps (n = 1,693) had time constant 15.3 μs, amplitude 7.39 nm and average force 5.0 pN; for backward steps (n = 316) these were 19.4 μs, 7.34 nm and 6.1 pN, respectively. For 800-nm beads, forward steps (n = 565) had time constant 35.9 μs, amplitude 7.6 nm and force 4.7 pN; for backward steps (n = 68) these were 37.3 μs, 7.8 nm and 5.6 pN, respectively. All records used for the step averaging were recorded at 1 mM ATP.

Non-linear effects, which form the basis of this particular parameter 

\[ \text{current versus the amplitude of the rocking voltage for various temperatures at constant side-gate voltage.} \]

In Fig. 2 we show measurements of the net adiabatically rock the device, and the resulting net current, averaged over many periods of rocking, was a low-frequency square-wave voltage of amplitude smaller than the length scales for elastic (smaller than the length scales for elastic (6.24 m)).

The crucial guide. The left point contact, which is not influenced by the side gates, plays no significant role in creating an asymmetric energy barrier which is experienced by the electrons as they traverse the wave-guide (marked SG in the SEM image). The side gate voltage tunes the energy of the 2DEG areas above and below the right point contact that serve as side gates created an asymmetric one-dimensional (1D) wave-guide connecting 2D electron reservoirs. The crucial parameter (7040), 308–312.

The boldness of the arrows is indicative of the relative strengths of the contributions of high and low energy electrons to the current across the barrier under negative (a) and positive (b) voltages. The dashed lines indicate the spatial distribution of the assumed voltage drop over the barrier, which is scaled with the local potential gradient of the barrier at zero voltage.

The experimentally determined net current as a function of rocking amplitude at a number of temperatures as indicated. Reversals in the direction of the net current as a function of rocking amplitude, and implicitly as a function of temperature, are observed. Data taken from [6]. Inset: A scanning electron microscope image of the ratchet device (top view). The dark regions are etched trenches that electrically deplete a two-dimensional electron gas located at the AlGaAs/GaAs interface beneath the surface, forming a one-dimensional wave-guide. Due to quantum confinement inside the waveguide, an electron moving from left to right will experience an asymmetric potential barrier similar to that shown in Fig. 1. Note the side gates (marked SG) which are used to tune the height of the potential barrier which is experienced by electrons moving though the ratchet. The left point contact does not play a significant role in the behaviour of the device as a ratchet.

3 The Landauer model

The Landauer equation expresses the current flowing through a mesoscopic device between two reservoirs as a function of the Fermi distribution of electrons in the reservoirs and of the energy dependent probability that an electron will be transmitted through the device [7]. It may be written as:

\[ I = \frac{2e}{h} \int_{-\mu_{av}}^{\infty} [f_R(\varepsilon, V) - f_L(\varepsilon, V)]d\varepsilon, \tag{1} \]

where

\[ f_{L/R}(\varepsilon, V) = \frac{1}{1 + \exp \left( \frac{-\varepsilon \pm eV/2}{k_B T} \right)} \tag{2} \]

**Fig. 3:** The bold curve (corresponding to the left vertical axis) is the difference between the transmission probabilities for +0.5mV and −0.5mV tilting voltages as a function of electron energy. The dotted and dashed curves (corresponding to the right vertical axis) are the Fermi ‘windows’, \( \Delta f(\varepsilon, V_0 = 0.5 \text{ mV}) \), centred on an equilibrium Fermi energy, \( \mu_0 = 11.7 \text{meV} \), for temperatures of 0.3K and 2K respectively. As the temperature is changed from 0.3K to 2K, note that the integral of the product of \( \Delta f \) and \( \Delta t \) will make a transition from positive to negative, leading to a reversal in the direction of the net particle current (Eq. 4). Small oscillations in \( \Delta t \) exist for \( \varepsilon > 1 \text{ meV} \).

To obtain an intuitive understanding of the action of the ratchet as a heat pump at parameter values where the net particle current goes through zero, it is helpful to rewrite Eq. (7) as:

$$q_{L/R}^{\text{net}} = \mp \frac{1}{h} \int_{-\mu_{av}}^{\infty} \varepsilon \Delta E d\varepsilon + \frac{1}{h} \frac{eV_0}{2} \int_{-\mu_{av}}^{\infty} \tau \Delta E d\varepsilon = \frac{\mp 1}{2} \Delta E + \frac{1}{2} \Omega \tag{8}$$

Here $\tau(e,V_0) = \left( 1/2 \left[ \tau(e,+V_0) + \tau(e,-V_0) \right] \right)$ is the average transmission probability for an electron under positive and negative bias voltage. $\Delta E = q_{L}^{\text{net}} - q_{R}^{\text{net}}$ is the heat pumped from the left to the right sides of the device due to the energy sorting properties of the ratchet, and can be non-zero only for asymmetric barriers. $\Omega = \left( V_0/2 \right) \left[ |I(+V_0)| + |I(-V_0)| \right]$ is the ohmic heating, averaged over one cycle of rocking. $\Delta E$ can be interpreted as the heat pumping power of the ratchet, averaged over a period of rocking, while $\Omega = q_{L}^{\text{net}} + q_{R}^{\text{net}}$ is the electrical power input, averaged over a period of rocking. We therefore define a coefficient of performance for the ratchet as a heat pump as:

$$\chi(T,V_0) = \frac{\Delta E}{\Omega} = \frac{q_{R}^{\text{net}} - q_{L}^{\text{net}}}{q_{R}^{\text{net}} + q_{L}^{\text{net}}} \tag{9}$$

**Fig. 4:** The heat-pumping coefficient of performance of the ratchet model shown in Fig. 1, plotted as a function of rocking voltage and temperature. Each point on the surface corresponds to a set of values of rocking voltage, temperature and Fermi energy for which the net particle current goes through zero.

4 Energy current

The heat change associated with the transfer of one electron to a reservoir with chemical potential $\mu$ is given by [10]:

$$\Delta Q = \Delta U - \mu$$  \hspace{1cm} (5)

The heat current entering the left and right reservoirs associated with the particle current generated by a voltage $V$ across the device is then obtained from the equation for the electrical current (Eq. 1). This is done by replacing the electron charge, $-e$, by a factor of $\Delta Q_{L/R}$ inside the integral. The heat current can then be written as

$$q_{L/R} = \mp \frac{2}{h} \int_{-\mu_{av}}^{\infty} (\varepsilon \pm eV/2) \tau(\varepsilon, V) \Delta f(\varepsilon, V) d\varepsilon$$  \hspace{1cm} (6)

The net heat current into the left and right reservoirs over a full cycle of square-wave rocking, $q_{L/R}^{net} = (1/2)[q_{L/R}(V_0) + q_{L/R}(-V_0)]$, is then:

$$q_{L/R}^{net} = \mp \frac{1}{h} \int_{-\mu_{av}}^{\infty} [(\varepsilon \pm eV_0/2) \tau(\varepsilon, \pm V_0) \Delta f(\varepsilon, \pm V_0) + (\varepsilon \mp eV_0/2) \tau(\varepsilon, \mp V_0) \Delta f(\varepsilon, \mp V_0)] d\varepsilon$$  \hspace{1cm} (7)

To obtain an intuitive understanding of the action of the ratchet as a heat pump at parameter values where the net particle current goes through zero, it is helpful to rewrite Eq. (7) as:

$$q_{L/R}^{net} = \mp \frac{1}{h} \int_{-\mu_{av}}^{\infty} \varepsilon \Delta t \Delta f d\varepsilon + \frac{1}{h} \frac{eV_0}{2} \int_{-\mu_{av}}^{\infty} \tau \Delta f d\varepsilon = \mp \frac{1}{2} \Delta E + \frac{1}{2} \Omega$$  \hspace{1cm} (8)