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Motorised molecules

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The conversion of chemical energy to mechanical motion drives movement in living things from bacteria to whales. An intricate array of molecular ratchets (such as the actin/myosin system that drives muscle contraction) and motors (including the rotary motors that twist bacterial flagella) allows cells to extract mechanical work from chemical reactions. Two recent papers, one in *Nature*¹ and one in *Nature Chemistry*,² report the design and construction of artificial molecular motors that achieve the same outcome using much simpler, and purely synthetic, structures. Both pieces of work show that chemical reagents can be used to drive the unidirectional motion of one part of a molecule (the rotor) relative to another (the stator), and thus provide direct functional analogues of the biological motors.

It is not easy to design a synthetic molecular motor.³ As pointed out nearly 20 years ago,^{4,5} molecular motors are characterized by movement that must be more than mere Brownian motion. Angular momentum cannot be used to maintain a constant directionality on the molecular scale as it can in motors of more familiar construction. To design a molecule that undergoes unidirectional motion needs the thermodynamic landscape of the system to be repeatedly altered to force concerted movement in a single direction, rather than mere forward and backwards shuttling between two states. The greatest successes in the field to date have employed light energy to drive a molecular system away from equilibrium, followed by a directionally-defined thermal relaxation—by this means motors have been designed with megahertz rotational speeds.⁶

Both of the recent papers make use of chemical energy to drive the rotation. The work by Feringa et al.² is remarkably simple in conception. The rotor and stator are each a benzene ring, connected together by a single bond, which forms a rotatable axle. Such biaryls can be free to rotate about this axle, but if the two benzene rings carry substituents adjacent to the bond joining them, the rotation is restricted to some degree. Addition of alternating sets of reagents allows first one side and then the other side of one ring to slip past a sulfur substituent (–SOR) bonded to the other ring (Figure 1). The alternating reagents allow insertion of a palladium atom into first a C–H and then a C–Br bond. Palladium's affinity for a sulfur atom of a sulfoxide (SOR) group located on the other ring forms a bridge between the rings that lowers the barrier to rotation. On its own, this shuttling between C–H and C–Br activation would simply cause random rotation in a clockwise or anticlockwise direction, but because of the chirality of the sulfoxide group, a handedness is imparted to the slippage mechanism, and the resulting motion exhibits a directional preference.

The alternating C–H and C–Br activation needed to drive this switchback process requires Pd in respectively the +2 and 0 oxidation states, and this motor, in its current form, cannot be autonomous because different reaction conditions are needed to shuttle the Pd between these states. However, since metal redox processes can be driven electrochemically, the intriguing possibility arises that future versions of this motor could be electrically powered.

The chemically-powered motor reported by Leigh et al. ¹ overcomes this problem of autonomy by using a rather different, and somewhat more complex design. In Leigh's motor, one small ring travels around another larger one by constantly advancing in the same direction from one of two 'stations' to the other, but crucially—and unlike in the Feringa work—only one set of reaction conditions is needed to drive the motor forward (Figure 2). A reactive 'fuel' known as FmocCl is continuously broken down to CO₂ and other by-products as the motor runs.

The motion of the ring is powered by an ingenious mechanism which channels random kinetic motion in a single direction. Immediately after each station, a removable carbonate substituent provides a 'stop signal'. Making or breaking the carbonate bond allows the signal to switch between 'stop' and 'go'. The chemistry of the system is designed such that the signal switches from 'stop' to 'go' at a more or less constant rate at both stations, but changes from 'go' to 'stop' only *after* the train has passed through to the more remote station. Thus the stop signal tends to follow the train round the track, ensuring that forward motion is always faster than reverse. Using Fmoc, a well known blocking group from peptide chemistry, cleverly ensures the chemical mechanisms switching from 'stop' to 'go' and vice versa are different, meaning their rates are under independent control. The energy needed for the constant forward movement of the train is provided by the consumption of FmocCl, and the train keeps moving until the FmocCl is all consumed.

The work constitutes an important step in the construction of a chemically-propelled autonomous molecular device, but there is still a long way to go. The ring typically takes twelve hours to travel round the track, and the FmocCl 'fuel' that powers it is used rather inefficiently – parallel decomposition of the fuel occurs at a significant rate. Both motors currently function in solution, with around 10²⁰ molecules working in tandem. Translation of chemical energy into macroscopic motion is likely to require the components to be constructed in the solid phase and to be controllable in the form of single molecules.

The story of artificial molecular motors is still in its opening pages, but chemists' attempts to mimic this core biological process reveal clearly just how many challenges biological systems have overcome in order to evolve the cellular motors that power movement. The design principles that work are becoming clearer, and the possibility that we may see molecular motors routinely powering artificial devices at some point in the future is distinct, if still distant for the time being.

Figure captions:

Fig 1: (a) Two benzene rings connected by an axle lie perpendicular; (b) Addition of a Pd(II) reagent allows the C–H substituent to pass the sulfoxide (SOR) substituent; (c) The rings relax to the alternative perpendicular arrangement; (d) A Pd(0) reagent allows the C–Br substituent to pass the SOR group. Alternative conditions are required to switch between Pd(0) and Pd(II).

Fig 2. (a) The motor consists of a track with two stations and two 'signals' that can be set to 'stop' or 'go', with a ring that can travel between the two stations.

(b) The proximity of the ring to the nearer signal forces the signal to stay in the 'go' position, allowing the ring to travel round the to second station; (c) The first signal now moves to 'stop', preventing reversal of the direction of travel, while the second signal now switches to 'go', allowing the ring to return to the first station. The signals are switched from 'go' to 'stop' by formation of a carbonate group using the reagent FmocCl.

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