

A light-fuelled nanoratchet shifts a coupled chemical equilibrium

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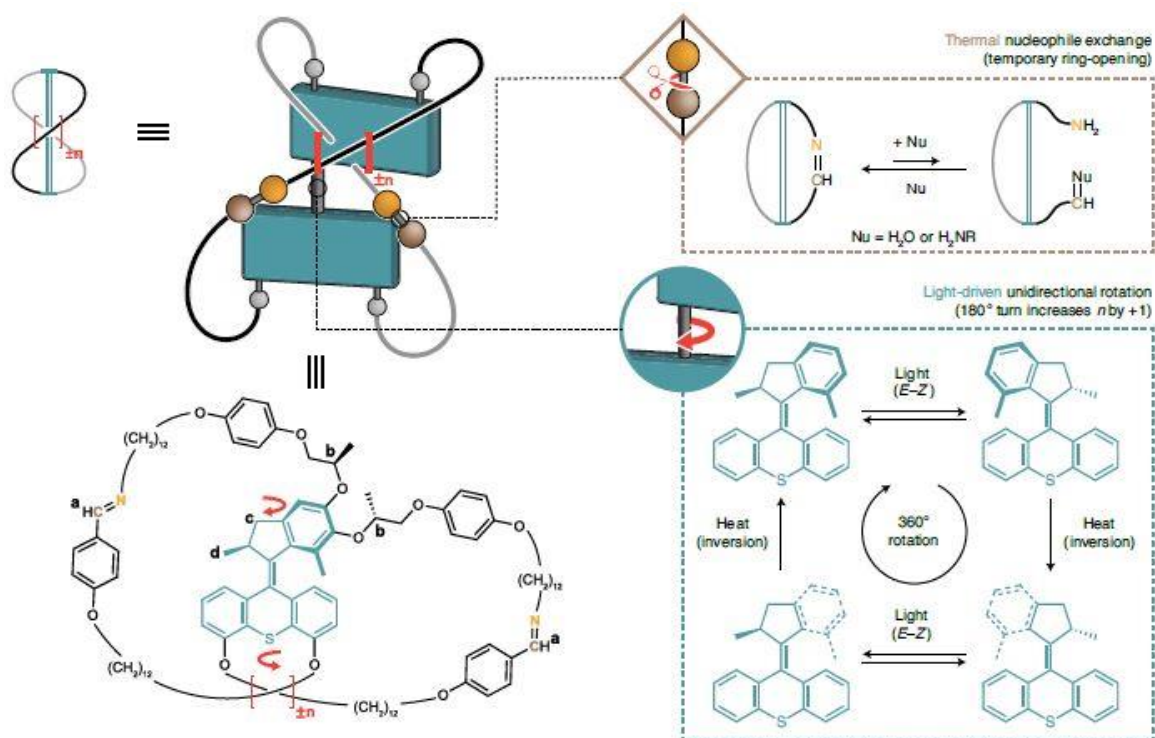


Figure 1: A photoresponsive molecular motor is constrained by two imine macrocycles, allowing AMM $\pm n$ to adopt distinct topologies by forming twists in the strands of the bicyclic molecule. Crossings can be established by either thermal nucleophile exchange of the imines (brown), leading temporary ring-opening of one macrocycle, or by light-driven unidirectional rotation (blue) via photochemical-induced E-Z isomerization and subsequent thermal helix inversion (blue).

Who are the corresponding authors and what are their research areas?

Ben L. Feringa (University of Groningen, Netherlands), Michael Kathan (University of Groningen, Netherlands), Christoph A. Schalley (Universität Berlin, Germany).

A major part of the Feringa's group research is directed towards dynamic molecular systems. The focus is on molecular nanoscience, novel responsive materials and photo-pharmacology, exploring biohybrid systems, self-assembly, molecular switches and motors. A second part of his research deals with the development (and application in chemical biology) of novel stereoselective synthesis methods and asymmetric catalysis.

Kathan joined the group of Prof. Stefan Hecht as a PhD student, focusing on the control of chemical reactivity and adaptive materials with light. After receiving his PhD in 2019, he moved to Groningen to work on molecular motors in the group of Prof. Ben Feringa.

The group of Schalley works in supramolecular chemistry with current projects in the gas-phase chemistry of non-covalent complexes, surface chemistry, low-molecular weight gelators, and the analysis of the thermochemistry and kinetics of multivalent binding in multiply threaded (pseudo)rotaxanes.

What is the main claim of the article?

They describe the design and operation of an artificial, light-fuelled molecular rotary motor that can drive a coupled chemical equilibrium energetically uphill.

Their AMM $\pm n$ (Fig. 1; n represents the number of twists, while \pm describes the chirality of the crossing) consists of two complementary parts: two imine macrocycles bridged by a light-driven molecular rotary motor, connecting the contrarotating top and bottom halves of the central motor unit.

This bridged bicyclic system can adopt several topologies by forming n crossings between the two macrocycles via two orthogonal pathways: a photochemical and a thermal one (Fig. 1). While the former will relax the machine towards the global energetic minimum, the latter increases the number of crossings in the system above the equilibrium value.

In the thermal pathway, the imine bonds can undergo a reversible intermolecular exchange reaction with a nucleophile, leading to a temporary ring-opening of the bicyclic compound (Fig. 1, brown). In this open form, the side arms can slip through or undergo an intramolecular imine exchange with the other macrocycle to generate an entangled structure. Subsequent ring-closure by intramolecular imine formation fixes the twists in the system, thus reforming the bicyclic molecule and leading to the formation of distinct topological isomers. Since the imine exchange is a dynamic and reversible process that is constrained by microscopic reversibility, the minimization of the Gibbs free energy of the system dictates the population of distinct topological states.

The population of these distinct states at thermal equilibrium is shown in Fig. 2, top, with the expected abundance indicated in brown.

In the photochemical pathway, the motor unit performs a unidirectional 360° rotation around its central double bond, which is solely driven by light energy and therefore not constrained by microscopic reversibility but by the Bose–Einstein relations for absorption and emission of photons. This involves a four-step rotary cycle, that is, two photochemical $E-Z$ isomerizations converting a stable to a metastable isomer each followed by a thermal helix inversion (Fig. 1 blue).

Upon illumination with UV light, its direction of rotation is governed by the methyl group at the stereogenic centre (Fig. 1). A positive (+) crossing is induced by every 180° turn of the motor until winding is hindered by mechanical resistance in the system. The molecular motor increases the number of entanglements (strain build-up) in the bicyclic system far from its equilibrium level, performing chemical work on a coupled chemical equilibrium in a topologically stereoconvergent manner, thereby acting as a light-fuelled ratchet.

The far-from-equilibrium distribution upon light-driven winding is shown in Fig. 2, bottom, with the expected abundance indicated in blue.

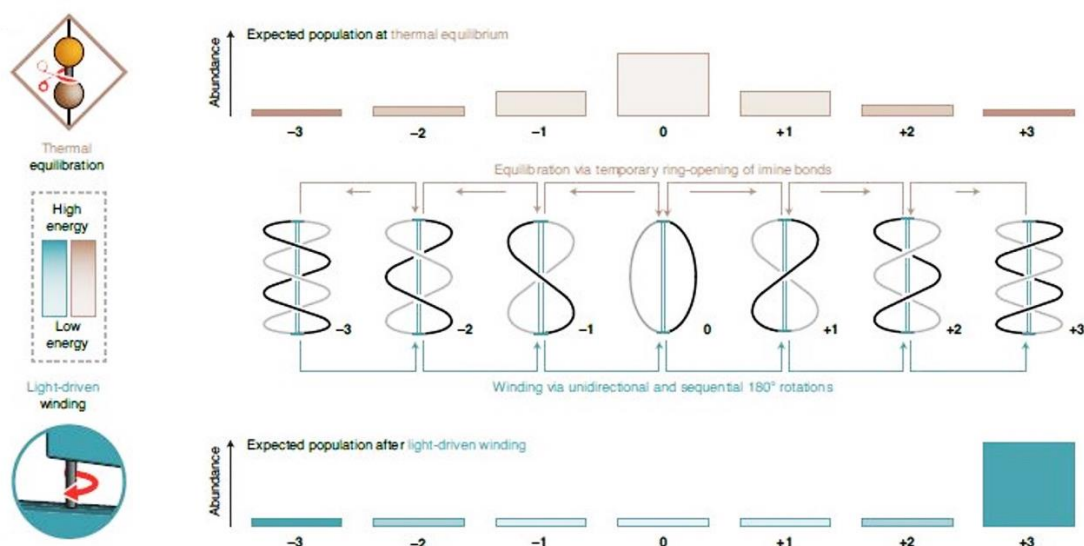


Figure 2: Thermal equilibration (brown) takes place by temporary ring-opening of the imines and will populate all accessible, distinct topological states so that the Gibbs free energy of the system is minimized. The expected population is indicated by the brown bar diagram.

Light-driven winding (blue) twists the bicyclic molecule in a unidirectional and sequential manner, increasing the number of crossings in the system above its equilibrium level until mechanical resistance in the system hinders further winding. The expected population is indicated by the blue bar diagram.

How is it demonstrated?

First, they valued the conversion to the imine by $^1\text{H-NMR}$ spectroscopy.

Then, they studied the light-driven winding process of $\text{AMM} \pm n$.

Following with $^1\text{H-NMR}$ spectroscopy the compositional change of a fully equilibrated sample upon illumination with UV light, they saw that in thermal equilibrium, $\text{AMM} \pm n$ can adopt up to one crossing and therefore exists as a mixture of distinct topological isomers -1 , 0 and $+1$. The crossings in the bicyclic molecule are increased stepwise by one, until the system selectively reaches its final state $+3$ via intermediate $+2$.

The formation of topological isomer $+3$ from an equilibrium mixture of -1 , 0 and $+1$ was also observed using ion mobility interfaced with mass spectrometry (IM-MS).

Next, they examined the unwinding of the system both under thermal and nucleophile-assisted conditions. Full relaxation of the system at $10\text{--}40\text{ }^\circ\text{C}$ can only be achieved in the presence of an external nucleophile, such as catalytic amounts of *n*-butyl amine. The competing nucleophile can induce temporary ring-opening of the imine macrocycles, leading to a topological reshuffling of the wound-up machine in a non-sequence-specific manner thus re-establishing the initial topological equilibrium. The ring-opening of $+3$ and $+2$ with $n\text{BuNH}_2$ is an irreversible process and indicates that both topological isomers are high energy, strained species that are not populated in thermal equilibrium.

The fact that species $+2$ and $+3$ were not detected in the relaxed reaction mixture, was also confirmed by the computational studies that predicted a strong increase in the potential energy per half-turn.

What are the typical experimental conditions?

The $\text{AMM} \pm n$ samples were prepared in situ by reducing the corresponding bisaldehyde and bisazide (1mg) previously lyophilized in a J. Young NMR tube.

The unwinding experiment was performed with catalytic amounts (20%) of nucleophile.

For the UV experiment, typically, a J. Young NMR tube containing a 1 mM solution of $\pm n$ in 0.6 ml C_6D_6 was illuminated for eight minutes with a hand-held UV lamp (365 nm).

Which are the key related papers?

1. Li, Q. *et al. Nat. Nanotechnol.* **10**, 161–165 (2015).
2. Kathan, M. *et al. Nat. Chem.* **10**, 1031–1036 (2018).