

## Transition Metal Rotaxanes Relevant to Molecular Machines

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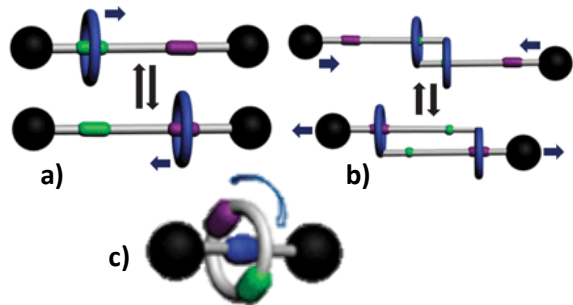
In his 1959 speech, “There’s Plenty of Room at the Bottom”, physicist Richard Feynman was the first to challenge the world’s scientists to look at machining from a miniaturized perspective.<sup>1</sup> The idea of nanoscale machines have been the subject of many historical “thought machines” from Maxwell’s Demon<sup>2</sup> to K.E. Drexler’s hypothetical nanorobot “the assembler”.<sup>3</sup> However, with the development of improved instrumentation capable of monitoring processes on an increasingly smaller scale and advances in the field of molecular synthesis, the idea of a molecular machine has become more of a reality.

There are two design philosophies in the development of these machines. The first, a “hard matter” approach, relies on a thorough understanding of macroscopic mechanics to design molecules with a structure and function similar to macroscopic machines (i.e. scissors<sup>4</sup>, wheelbarrow<sup>5</sup>, nanocars<sup>6</sup>). The second, a “soft matter” approach, seeks to adapt chemical principles to build machines from the bottom up.<sup>7</sup> The main disadvantage of the “hard matter” approach is that the environment in which macroscopic machines function is not the same as that which is encountered at the nanoscale.

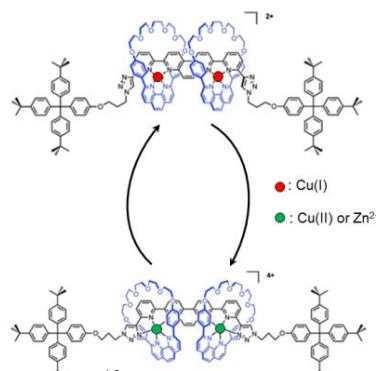
There are a number of challenges that molecular machines must surmount before they can (a) function and (b) produce useful work energy. In order to function, these machines need to overcome the effects of Brownian motion, microscopic reversibility, and viscosity. While there have been a number of molecules developed that are capable of functioning at the nano-scale, the production of useful work energy by these molecules has yet to be accomplished. To overcome this challenge these machines must interface with their environment while being capable of driving chemical systems uphill and away from their inherent equilibria.<sup>8</sup> In order to achieve this, a cooperative transition must be made from switchable molecules to the less prevalent artificial molecular machines. To make this transition, many in the scientific community feel the next logical step is to organize and integrate switching molecules into larger, rugged scaffolds that mimick the synchronization seen in many biological systems.<sup>9</sup>

While there have been a number of important pure organic systems developed over the years, transition metal-containing systems offer additional useful properties. Particularly, the electroactive nature of transition metals that leads to a stereoelectronic dependence on oxidation state allows these systems to induce large scale rearrangements via a chemical, electrochemical, or photonic signal.<sup>10</sup> A large percentage of the literature involving transition metal-containing molecular machine prototypes is focused on structures classified as mechanically interlocked molecules (MIMs). Rotaxanes belong to this class of molecules.

First synthesized in 1961 by Harrison and Harrison<sup>11</sup>, rotaxanes consist of a macrocyclic ring trapped around a dumbbell-shaped component consisting of two bulky stoppers attached at both ends of a rod-like portion. These molecules are particularly attractive because of the many types of structural modifications possible. This flexibility comes from the existence of one or two recognition sites on the dumbbell and/or macrocycle. In the case of transition metal systems, these sites typically respond to an electroactive-metal stimulus and cause characteristic motion of the ring or rod-like portion (**Figure 1**).

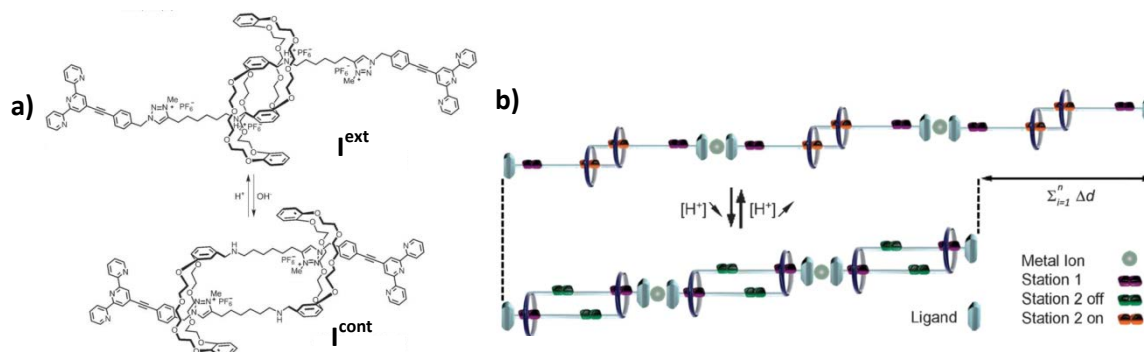


**Figure 1:**<sup>8</sup> Structure and motion of rotaxane molecules a) shuttling b) expansion/contraction c) rotation



**Figure 2:**<sup>12</sup> Motion of the two macrocycles via ion exchange or oxidation

A recent publication on rotaxane switches details a copper(I) -assembled [3]Rotaxane, which authors claim exhibits both a chemically and electrochemically induced wing flapping motion of its two macrocycles (**Figure 2**). Synthesis of this molecule utilizes a “classical copper-templated strategy followed by click chemistry” with a yield of 89% after purification. Movement is facilitated by triazole groups located on the thread fragment in such a way that when involved in the coordination sphere, as seen in the 5 coordinate case, the rings tilt to accommodate the additional triazole ligand. Chemically induced movement of this structure, characterized by  $^1\text{H}$  NMR, indicates an exchange of a four coordinate Cu(I) metal center with parallel rings for a 5 coordinate  $\text{Zn}^{2+}$  tilted ring. Additionally, the electrochemically induced oxidation of Cu(I) to Cu(II) via cyclic voltammetry causes a similar yet faster coordination change.<sup>12</sup>



**Figure 3:**<sup>13</sup> a) Structure of extended form ( $\text{I}^{\text{ext}}$ ) and contracted form ( $\text{I}^{\text{cont}}$ ) of [c2]daisy chain rotaxanes b) General principle of supramolecular polymer structure and function

There has been a growing interest in the incorporation of rotaxane switches into a solid state structure that exhibits mechanical motion via an organized network of switches. A recently published paper, “Muscle-like Supramolecular Polymers: Integrated Motion from Thousands of Molecular Machines”, details the incorporation of bistable [c2]daisy chain rotaxanes into a pH-triggered muscle-like system using a metallosupramolecular polymerization process.<sup>13</sup> The bistable nature of this rotaxane stems from two binding sites, secondary ammonium and triazolium ions, located on its axle. Upon protonation, the ammonium ion binds to the crown ether macrocycle to yield

the extended form while deprotonation yields the triazolium bound contracted form (**Figure 3a**). Molecular modeling indicates a distance of actuation between both states of 1.2 nm. Zinc and iron ions are then utilized as linkers for these switches to form a supramolecular wormlike polymer chain (**Figure 3b**). Characterization of the size and shape of these polymer chains, through a series of light scattering and small-angle neutron scattering (SANS) experiments, indicates the successful incorporation of the rotaxane switches into the iron-containing system. Furthermore, these experiments confirm the presence of an ordered mechanical output from this system, in the form of the expansion and contraction of the polymer chain with a global change in polymer contour length of  $6.4 \pm 0.7 \mu\text{m}$ . The next challenge is then bundling these single-chain polymers into stiffer fibers to elicit a macroscopic response for the development of synthetic muscles.

Despite the progress that has been made since Feynman's challenge in 1959, this field is still in its infancy and a number of challenges remain. In addition to the challenges detailed above, the limited characterization techniques available to qualify the movements of these switches leaves many current conclusions based largely on chemical intuition. There is however much that can be learned from these systems leaving a number of opportunities on the horizon for the expansion of the non-equilibrium toolbox.

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