

# Genesis of the Nanomachines: The 2016 Nobel Prize in Chemistry

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catenanes · molecular machines · molecular motors ·  
rotaxanes

Perhaps the best way to appreciate the technological potential of molecular machines is to recognize that they lie at the heart of every significant biological process.<sup>[1]</sup> In stark contrast to biology, none of mankind's present-day technologies exploit controlled molecular-level motion in any way at all: every catalyst, every material, every polymer, every pharmaceutical, every reagent, all function through their static or equilibrium dynamic properties. When we learn how to build artificial structures that can control and exploit molecular-level motion, and interface their effects directly with other molecular-level substructures and the outside world, it will surely impact on every aspect of functional-molecule and materials design. It is this staggering potential, famously discussed by Richard Feynman in his 1959 lecture “*There's Plenty of Room at the Bottom*”,<sup>[2]</sup> that is recognized through the award of the 2016 Nobel Prize in Chemistry to three of the pioneers of the field of synthetic molecular machines, Jean-Pierre Sauvage, Sir J. Fraser Stoddart, and Ben L. Feringa. The Scientific Background Report<sup>[3]</sup> of the Nobel Committee reveals the Prize to be chiefly recognition for the ingenious tools and strategies the awardees invented for the construction of molecular architectures (mechanically interlocked molecules and over-crowded alkenes) that are particularly well suited for molecular machine design, during a remarkable period from the mid-1980s to the turn of the Millennium.

A substantial part of the progress made in molecular machinery is a result of the invention of effective synthetic routes to mechanically interlocked molecules: catenanes and rotaxanes. Prior to the early 1980s, rotaxanes and catenanes could only be made in miniscule amounts, often through lengthy synthetic routes. In 1983 a stroke of genius from Sauvage began a revolution in the synthesis of interlocked molecules through the use of template synthesis.<sup>[4]</sup> By assembling two phenanthroline ligands tetrahedrally around a Cu<sup>I</sup> ion prior to macrocyclization of the end groups his

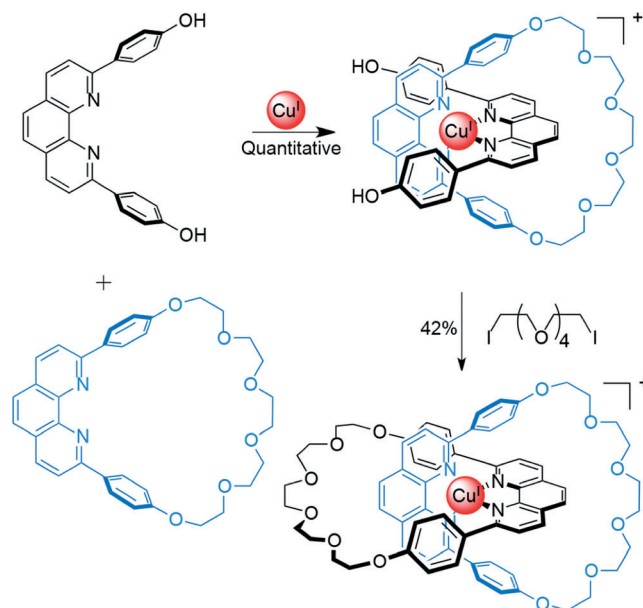


Figure 1. First template synthesis of a [2]catenane by Sauvage et al.<sup>[4]</sup>

group assembled a [2]catenane in just two steps (Figure 1). Suddenly, mechanically interlocked architectures became accessible. A few years later Stoddart used the association of electron-rich and electron-poor aromatic rings—depicted in his publications as red rings and blue boxes, respectively, that rapidly became his trademark—to thread molecular components to form catenanes and rotaxanes.<sup>[5]</sup> In a landmark 1991 report<sup>[6]</sup> he described his first studies on the well-defined large-amplitude motions in “molecular shuttles”, rotaxanes with two macrocycle binding sites on the axle. By the mid-1990s both the Sauvage and Stoddart groups had shown that the components of rotaxanes and catenanes could be switched, from one position to another, in response to electrochemical or chemical changes (Figure 2).<sup>[7,8]</sup>

Other groups started to enter the field, developing new interlocking systems (either by accident or through design) and alternative ways to control the switching of the components, and investigating how to use the change in the position of the components to perform simple tasks.<sup>[1]</sup> The late 1990s was a time of great excitement and rapid proliferation of different “molecular machine systems”, but the rate of

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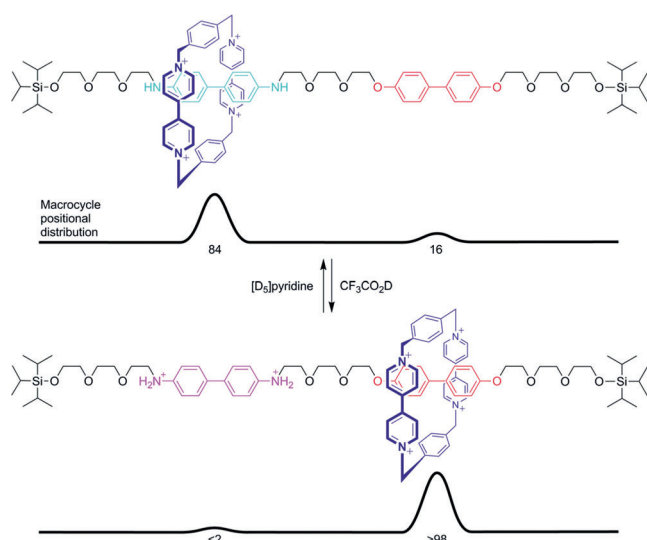


Figure 2. First switchable molecular shuttle by Stoddart et al.<sup>[8]</sup>

development sometimes outpaced appreciation of the design principles necessary for different types of machine, leading to criticisms of hype from some quarters.<sup>[9]</sup> In particular the concepts surrounding directionality and molecular motors took time to be understood by chemists, and for several years we did not know how to make motors, and we didn't even know that we did not know!<sup>[1]</sup>

That situation began to change in 1999 when Ben Feringa's group produced the first rotary molecular motor, using an overcrowded alkene (Figure 3).<sup>[10]</sup> Irradiation with light while holding the molecule above a certain temperature was sufficient to drive the rotor component repeatedly 360° in one direction around a stator. The issue of directionality at the molecular level had been addressed for the first time, and so elegantly too. Faster motor-molecules followed from the Feringa lab that were used to perform feats such as rotating

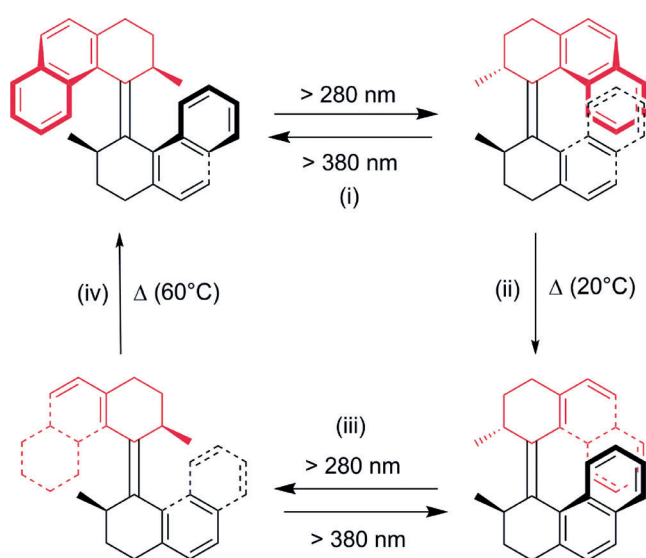


Figure 3. First light-driven rotary molecular motor by Feringa et al.<sup>[10]</sup>

a glass bar on a liquid crystalline film<sup>[11]</sup> and as wheels to propel a “nanocar” on a surface.<sup>[12]</sup>

Post-millennium Stoddart's group applied their molecular switches to areas such as molecular electronics<sup>[13]</sup> and nano-container-release systems<sup>[14]</sup> and also made eye-catching molecular objects that resemble in some aspects their counterparts from the macroscopic world, such as a “molecular elevator”.<sup>[15]</sup> Along with other groups they helped tackle the issue of performing mechanical work with molecular machines. The group of Sauvage made “molecular muscles” that could contract and expand in size,<sup>[16]</sup> while the Feringa group showed that the switching function of their motor-molecules could be exploited in numerous tasks from mechanical work to catalysis.<sup>[17]</sup> Other groups introduced ratchet mechanisms (the general solutions for directional motion), developed the first pumps and linear molecular motors, made machines from DNA and self-propelled nanomotors from metal strips, and began to build multicomponent molecular machines that could perform tasks in chemical synthesis.<sup>[1]</sup>

As Euan Kay and I recently summarized,<sup>[18]</sup> there have been many other developments over the past 15 years that are leading us towards the dawn of an era of useful molecular nanotechnology. But we are not there yet. Indeed, in contrast to biology, there is as yet no task that can be performed by a synthetic molecular machine that cannot be done more effectively another way. However, when we do get there it will be by standing on the shoulders of three giants who have given us some of the tools necessary to build truly useful molecular machines. The Nobel Committee Report<sup>[3]</sup> ends: “In a sense, we are at the dawn of a new industrial revolution of the twenty-first century, and the future will show how molecular machinery can become an integral part of our lives. The advances made have also led to the first steps towards creating truly programmable machines, and it can be envisaged that *molecular robotics* will be one of the next major scientific areas.” It is a vision of a story waiting to be written by the next generation of molecular machine researchers.

This Nobel Prize is not about curing cancer (not yet), nor making wonder materials (not yet), nor harvesting energy from the sun (not yet). It is a Nobel Prize given for tremendous scientific creativity, inspirational science, science that makes you dream “what if”. It is a Nobel Prize about what the future may bring and a call to arms to all those who wish to accept the challenge to invent it. Feynman would surely have approved.

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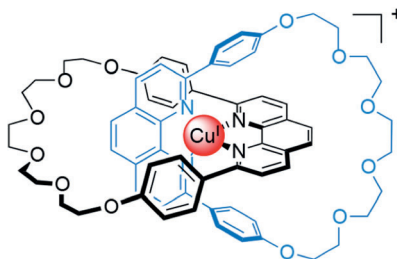


## Highlights

### Molecular Machines

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Genesis of the Nanomachines: The 2016 Nobel Prize in Chemistry



**In the beginning...** The Nobel Prize in Chemistry 2016 goes to three of the pioneers of the field of synthetic molecular machines, Jean-Pierre Sauvage, Sir J. Fraser Stoddart, and Ben L. Feringa. Their work has led from the reliable synthesis of rotaxanes and catenanes (see picture) to molecular rotary motors, shuttles, muscles, and other devices.