QnAs with Fraser Stoddart

Christopher Samoray, *Science Writer*

The design of tiny machines is not a new idea. In the 1950s, physicist Richard Feynman predicted the development of nanotechnology and embodied the idea of miniaturization in his 1959 lecture "Plenty of Room at the Bottom" (1). In recent decades, nanotechnology has come into its own and propelled the careers of many researchers. Among them is Sir Fraser Stoddart, a National Academy of Sciences member and chemist at Northwestern University. Stoddart's research focuses on mechanostereochemistry, a branch of chemistry that describes the spatial organization of atoms in mechanically bonded molecules (2). Stoddart's work has fueled a number of nanotechnology advances, including the development of molecules, called bistable rotaxanes, which can be incorporated into nano-sized machinery. For his contributions to the field, Stoddart shared the 2016 Nobel Prize in Chemistry. Stoddart spoke to PNAS about winning the Nobel Prize and the future of molecular nanotechnology.

PNAS: How did you first become interested in molecular nanotechnology?

Stoddart: I can put a date of 1991 on it. This year is the one in which we published, in the *Journal of the American Chemical Society*, a short communication entitled "A molecular shuttle" (3). It is a mechanically interlocked molecule (MIM) based on a dumbbell with two recognition sites on the rod portion for a ring to hover around. Using NMR spectroscopy, we showed that the ring darts back and forth about 1,000 times a second, at room temperature, in solution between the two recognition sites. This moment was a defining one for molecular nanotechnology: that is, the invention of MIMs, wherein we can witness translational motion between the component parts, namely rings and dumbbells. That was about the time that I started to use the term "molecular nanotechnology." I felt the time was right for chemists to join in the description of these MIMs in that context.

Fraser Stoddart. Image courtesy of Jim Prisching (photographer).

PNAS: Along with chemists Jean-Pierre Sauvage and Bernard Feringa, you were awarded the 2016 Nobel Prize in Chemistry. For your part, the selection committee recognized your work on bistable rotaxanes, the mechanically interlocked molecules that are reminiscent of a dumbbell with a ring attached around the center. Can you describe how [a] rotaxane maintains its shape, and the construction process involved in making a rotaxane molecule?

Stoddart: The dumbbell and ring components are held together by a mechanical bond. The point about this mechanical bond is that it's a new bond in chemistry. It's not a chemical bond. It doesn't involve the sharing of electrons, as in a covalent bond or a coordinative bond involving a transition metal. It is a physical bond, and to that extent it's repulsive. Of course, that repulsion is overcome by a whole gamut of weak interactions that allow us to bring the dumbbell component together with the ring component.

We have devised several different ways of making rotaxanes. The dumbbell can be made first of all, and then a ring clipped around it. We call this protocol the clipping approach. The other approach that we use commonly is "threading followed by stoppering." A rod portion with recognition sites on it traps the ring and then stoppers can be added to each end to form a dumbbell with the ring encircling it, forming a rotaxane. Put another way, we make a one-to-one complex between the rod and the ring, and then carry out chemical reactions to put the stoppers in place. A third approach that we have developed is called slippage, where—provided we get the internal diameter of the ring just right with respect to the external diameter of the stopper—we can entice the rings to go on to the dumbbells in certain solvents. Also, one ex-member of the group quite ingeniously has come up with the trick of swelling the stoppers; the ring is threaded onto the dumbbell and then some chemistry is done to make the stopper larger in diameter. That keeps the ring on

 www.pnas.org/cgi/doi/10.1073/pnas.1619654114

forever. Another approach involves the shrinking of the ring.

PNAS: You have incorporated rotaxane into devices, such as a "molecular elevator," capable of raising itself 0.7 nanometers above a surface; artificial muscles, in which the rotaxane promotes bending in the structure; and novel computer chips. Can you talk about the potential applications for these rotaxane-based creations?

Stoddart: I think the emphasis is on potential. MIMs, such as bistable rotaxanes, represent a piece of really disruptive chemistry. In terms of molecular electronic devices that are based on bistable rotaxanes, it turns out that when a congregation of these molecules is introduced into what's called a crossbar device between two terminals, hundreds or thousands of molecules can be trapped as a monolayer between the crossing point between two wires. The bistable rotaxanes can be made to switch between on and off states. This control gave us the basis for creating, ultimately, a 160-kilobit random access memory. Now we are mounting these molecular switches into metal–organic frameworks in search of more robust settings.

PNAS: In 2014 you were inducted into the National Academy of Sciences. Your Inaugural Article focused on molecular switches, which can be shifted between two or more stable states (4). Again, bistable rotaxanes played a major role and enabled the alteration of electric states in the switches. What makes bistable rotaxanes a useful design component of molecular switches and other molecular technology?

Stoddart: We put our faith in the fact that we had invented a new bond, which opens up all kinds of different movements of component parts with respect to each other within molecules. We can move components by a nanometer or two, or several nanometers, very easily using this type of bonding, whereas previously chemists were limited to torsions about single or double bonds. Azobenzene is the famous example where it is possible to attain circular motion, albeit limited. I think the mechanical bond opens up an endless amount of scope for scientists to explore switching and other mechanical properties. It has to be said, however, that motors and machines are much different from switches.

PNAS: Has your life changed after the Nobel Prize?

Stoddart: I'm still trying to work it out. It's life changing. I'm down to three hours of sleep a day at the moment. I'm racing around the world because I'm still trying to maintain some sort of program going that was in place before the announcement. It's pretty overwhelming. I've not really been trained in any way to be a celebrity, and it sort of happens to you overnight, and also to your family.

PNAS: What motivates your research?

Stoddart: I happen to be a farmer's boy. So, when people ask me, I say you need the strength of a horse and the hide of an elephant, particularly in the early days when you're doing something that's creative. People are not very accepting of new things; you've got to be able to take the hits and the barbs that come your way. In addition to the strength of a horse and the hide of an elephant, you need the work ethic of a honey bee. I'm basically on 16 hours a day, seven days a week.

PNAS: What do you see as the future of molecular nanotechnology?

Stoddart: I happen to be reading a book by Bill Bryson at the moment that zeros in on flight in the year 1927, about 20 years after the Wright brothers. Flight was a precarious pursuit in the beginning. There was still not much certainty about getting a contraption into the air without it bursting into flames or only going a few yards and dropping into a forest beyond a make-shift runway. And yet, yesterday I flew back from Frankfurt in a dream-liner, the biggest airplane I've ever been in. That's the kind of extrapolation that I think one needs to make in terms of molecular motors and machines. How fast will the transformation occur, I'm not sure, but I have no doubt it has been given an impetus by the decision the committee made in Stockholm this year. We're only scratching the surface presently. I'm hopeful the prize will give a huge fillip to the field.

1 Feynman R (1959) Plenty of room at the bottom. American Physical Society. Available at www.pa.msu.edu/~yang/RFeynman_plentySpace.pdf. Accessed November 11, 2016.

2 Barin G, Forgan RS, Fraser Stoddart J (2012) Mechanostereochemistry and the mechanical bond. *Proc R Soc A* 468(2146):2849–2880.

3 Anelli PL, Spencer N, Fraser Stoddart J (1991) A molecular shuttle. *J Am Chem Soc* 113(13):5131–5133.

4 McGonigal PR, et al. (2015) Electrochemically addressable trisradical rotaxanes organized within a metal-organic framework. *Proc Natl Acad Sci USA* 112(36):11161–11168.