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CONVERSATIONS WITH SCIENTISTS

David A. Leigh: Making Molecular Machines


University of Manchester

"In the field of molecular machines I think the most important development of the last 20 years is the understanding of how to get directional motion from random Brownian motion. It is the key to making molecular motors and, ultimately, all sophisticated molecular machines."

David A. Leigh is a Royal Society Research Professor and, since 2014, the Sir Samuel Hall Chair of Chemistry at the University of Manchester in the United Kingdom. Born in 1963 in Birmingham, England, Leigh earned a bachelor's degree in chemistry from the UK's University of Sheffield in 1984 and received a Ph.D from the same institution in 1987. For the next two years, Leigh worked as a postdoctoral research associate at the National Research Council of Canada in Ottawa. He returned to Britain in 1989 to lecture in organic chemistry at the University of Manchester Institute of Science and Technology. In 1998, Leigh moved on to a chair in synthetic chemistry at the University of Warwick and, in 2001 accepted a chair in organic chemistry at the University of Edinburgh. In 2012, Leigh joined the University of Manchester faculty.

Leigh is the recipient of numerous honors and awards. He has received research fellowships from the Engineering and Physical Science Research Council and from the European Research Council. His awards include the Feynman Prize for Nanotechnology, the Descartes Prize for Research, and several awards from the Royal Society of Chemistry. He is a fellow of such prestigious associations as the Royal Society of London and the Academia

Europaea. In the last three decades, Leigh has published more than 250 peer-reviewed journal articles, while serving on several editorial advisory boards.

Leigh's research focuses on "new approaches to functional molecule synthesis and the influence of non-covalent interactions on structure and function from biology to materials science." Over the last 20 years, Leigh has pioneered the development of "functional synthetic molecular level machines and motors," notably molecular knots. His goal is 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."

Below are David Leigh's February 18, 2017 responses to questions posed to him by Today's Science. *Some of the questions deal with how he became interested in science and began his career in chemistry, while others address particular issues raised by the research discussed in Tiny Knots, Untold Possibilities.*

Q. When did you realize you wanted to become a scientist?

A. I guess it was at high school. I had a great and inspiring chemistry teacher, Mr. Clarke, who made me want to study chemistry at university. I originally wanted to be a science teacher but after earning a Ph.D. and then moving from the UK to be a research scientist in Ottawa for a couple of years I realized that I wanted to tackle some research problems and so I returned to the UK and took a job as a university lecturer (the U.S. equivalent is assistant professor) and I've been running my own research group ever since.

Q. How did you choose your field?

A. The great thing about carrying out research at a university is that you can work on anything you like that you find interesting and exciting. My main research interests are learning how to make molecular machines and molecular knots (the strategies used to make both—linking together components—are remarkably similar). I got into this field by chance. One day, while working in the lab, we accidentally and unexpectedly found a way to mechanically interlock molecular rings, and I realized that this serendipitous discovery could be used as a way to link molecular components together that could be used to build molecular machines. Later on we expanded the targets to include knots.

**Q. Are there particular scientists, whether you know them in person or

not, that you find inspiring?

A.Mostly the great scientists of the 19th and 20th centuries who made extraordinary discoveries: James Clerk Maxwell, who discovered that light was electromagnetic radiation; Ernest Rutherford, who discovered the structure of the atom; Marie Curie, who discovered new radioactive elements; [James] Watson and [Francis] Crick, who discovered that DNA was a double helix and thereby revealed the way that genetic information is passed from generation to generation.

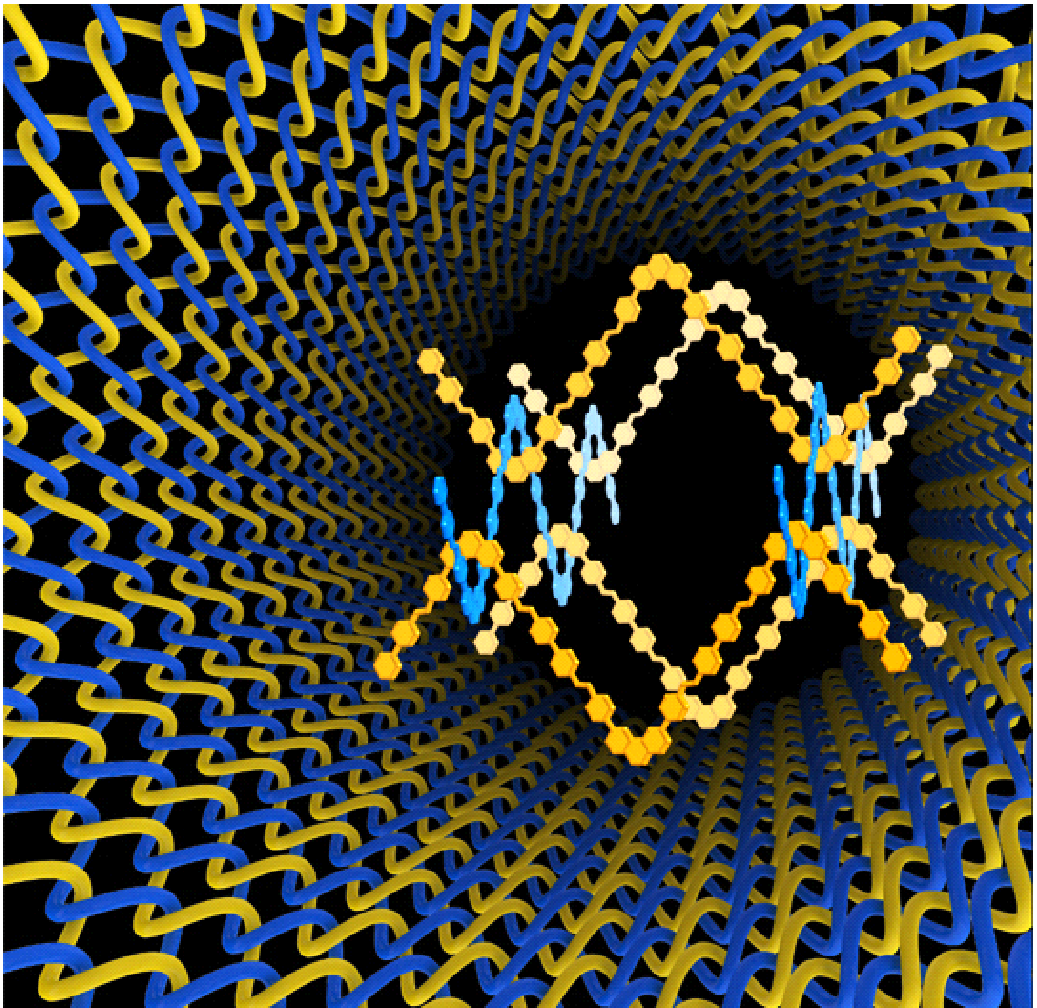
Q. What do you think is the biggest misconception about your profession?

A. That it's boring. What I and my team do, learning how to build molecular machines out of atoms, is incredibly creative and exciting. We are explorers, making molecules that no one has ever made before that in some cases do things that no one has even dreamed of before.

Q. Is it possible to offer a nontechnical explanation for why you chose to try to create the particular knot that you did? Was it easier to create than other knots of comparable complexity, or does it offer more applications, or something else?

A. Mathematicians have tabulated over six billion different types of knots, yet until we started in this area four years ago scientists had been able to make only the simplest type of knot, a trefoil knot (which has three crossings). Now, with our latest knot, scientists have made four different types of knot, of which our eight-crossing knot is the most complex. Four is still a long way from six billion, but it's a start! We chose this particular knot because it has a symmetry that makes it easier to be tackled than other eight-crossing knots.

Q. Are there any applications of molecular knots that you see as particularly easy to develop, or particularly exciting?



Omar Yaghi/University of California at Berkeley

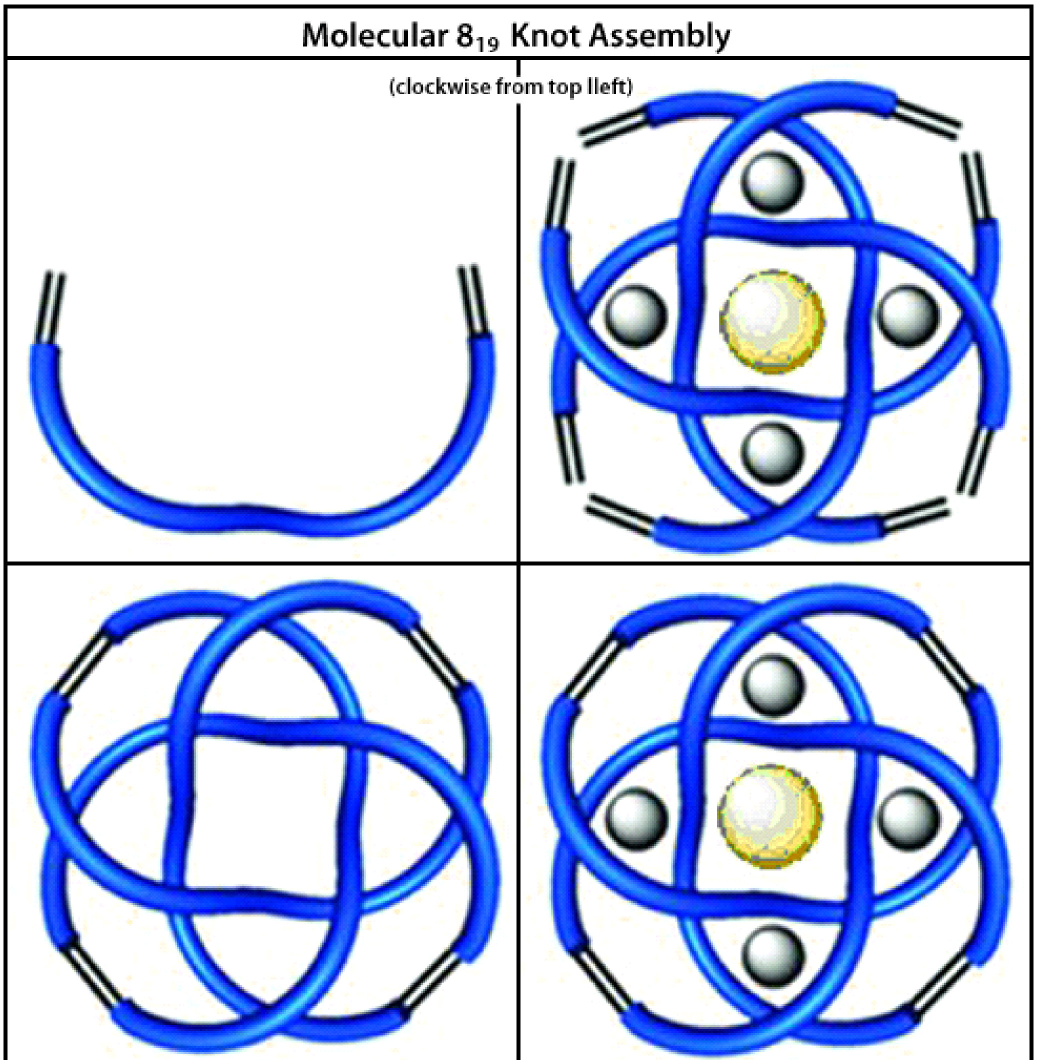
"The principles of knotting are very similar to those of weaving, so it should be possible to use what we're learning about knotting molecules to weave molecular strands to make new sorts of materials."

A. The principles of knotting are very similar to those of weaving, so it should be possible to use what we're learning about knotting molecules to weave molecular strands to make new sorts of materials. In our everyday world we know the benefits of weaving fabrics—you get materials that can stretch in different directions, hold their shape, are light and strong and flexible. Hopefully we will be able to use these concepts to weave molecular strands to make plastics and polymers with similarly advantageous properties. For example, Kevlar, used in bulletproof vests and body armor but also car brakes and parts of aircraft bodies, is a super-tough polymer with a chemical structure that consists of tiny straight molecular rods that pack close together, like pencils packed tightly in a pencil case. If we can weave molecular strands into molecular fabrics, maybe we will be able to get the same sort of strength with a lighter and more flexible material.

Q. From a mathematical point of view, a knot is characterized by its geometry. But your molecular knot employs particular molecules, and

these are combined using particular reactants. If it were possible to make the same (mathematical) knot as a molecule using different molecules, would it have different properties? Is it possible to give a not-too-technical explanation of why you chose the particular materials you used in making the knot?

A. Actually, knots are characterized by their topology—how points are connected—not geometry, which concerns shape. Yes, it should be possible to make knots with different molecules—this has already been done with the simplest type of knot, the trefoil knot (three crossings). Knots made out of different molecules would, indeed, have different properties. We chose building blocks for the current knot that we could design to form the knot. It will be difficult to tie knots in molecules without designing building blocks that have suitable shapes and properties that help the knots form.



Danon, J.J., et al./*Science*

"We chose building blocks for the current knot that we could design to form the knot. It will be difficult to tie knots in molecules without designing building blocks that have suitable shapes and properties that help the knots form."

Q. Where do you spend most of your workday? Who are the people you work with?

A. I spend about a third of my time traveling; I'm writing this in Shanghai and earlier in the week I was at a conference in New Zealand. About a third of the time I work from home, where I can switch off email and get work done! The other third of the time I'm with my students and research scientists in my laboratory at the University of Manchester. They are a great bunch of young people, great fun and inspiring to be around.

Q. What do you find most rewarding about your job? What do you find most challenging about your job?

A. The most rewarding thing is when my students and research students discover something new in the lab or make a molecule or molecular machine we've been working towards for several years and we find that it does what we want. That's a great day! The most challenging aspect is the constant email requests for things. I probably get 100-200 emails most days, many of which require a response and do not actually advance any science being done.

Q. What has been the most exciting development in your field in the last 20 years? What do you think will be the most exciting development in your field in the next 20 years?

A. In the field of molecular machines I think the most important development of the last 20 years is the understanding of how to get directional motion from random Brownian motion. It is the key to making molecular motors and, ultimately, all sophisticated molecular machines.

In the next 20 years I believe that it will be possible to design programmable molecular robots that will be able to carry out sophisticated tasks in the construction of new molecules and materials, in the same way that robots are used today in factories to build cars and other pieces of machinery.

Q. How does the research in your field affect our daily lives?

A. Not too much yet, but watch this space!

Q. For young people interested in pursuing a career in science, what are some helpful things to do in school? What are some helpful things to do outside of school?

A. The most important reason that young people should study science, whether it is for a career or not, is because science tells us the truth about why the world we live in is the way it is. It explains why the sky is blue, why the sea is green, why there are mountains and islands, and how we come to have lions and birds and people in the present day, while we had dinosaurs 200 million years ago. We only have one life and I think it’s important that we base our choices of what we do during that life on facts.

For young people interested in pursuing a career in science I say congratulations, you have chosen a vocation which will be endlessly fascinating, often exciting and always awe-inspiring to uncover how the universe really is. The best thing to do to have a career in science is study science subjects and mathematics at school, but also do something creative—art, music, dance, whatever you take pleasure from—because creativity and imagination are actually two of the most important characteristics of great science and great scientists, who need to be able to look beyond the simple experimental observation and see the possibilities that that discovery can lead to.

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