balance between lipophilicity and charge distribution. In a previous application[5] by the same group of researchers, an antibody–rifabutin conjugate was shown to be superior to vancomycin *in vivo*, suggesting that antibody–antibiotic conjugates are viable for enriching the current therapeutic armamentarium.

As the team recognize, this is not a universal solution for drug delivery and a more comprehensive number of drugs and protein carriers will need to be assessed. Despite the potential to enrich the current chemistry toolbox in chemical biology, there are several important pending questions, including the suitability of the technology to expand the tractable drug space and address unmet medical needs in other disease areas, such as inflammation and immunomodulation. Moreover, the imine methide by-product resulting from the linker self-immolation deserves a comprehensive toxicological study given its similarity to quinone methides, which are members of the so-called pan assay interference compounds[6] — a group of molecules containing dreaded substructures that are notorious for their uncontrolled polypharmacology and associated toxicity. That said, despite the nucleophile acceptor potential of the imine methide motif, and any possible toxicity profile, it may still be compatible with the delivery of drugs for a disease — for instance, if the therapeutic benefit is high, or if this approach enables a lower dose of a cytotoxic drug to be used. Nonetheless, this report represents a disclosure that promises to enable the inclusion of new drugs in the realm of antibody– and carrier–drug conjugates in general, is highly welcomed and will certainly spur further studies in the future. ❐

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2016 NOBEL PRIZE IN CHEMISTRY

Molecular machines


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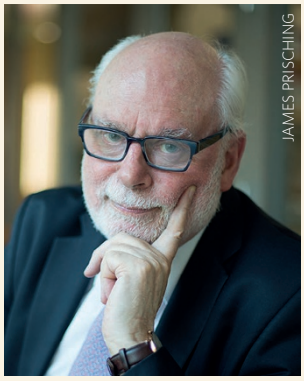
JAMES PRISCHING


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In what has been a giant leap forward for fundamental chemistry, researchers have spent the past two decades creating tiny machines that can perform tasks in response to external stimuli. These machines can synthesize or transport small molecules, and some have been shown to come together in large numbers to accomplish macroscopic work such as making objects bend, rotate or contract. In recognition of their pioneering efforts in this field, Jean-Pierre Sauvage, Fraser Stoddart and Ben Feringa (left to right) have been jointly awarded the 2016 Nobel Prize in Chemistry "for the design and synthesis of molecular machines".

The first real breakthrough came in 1983 when Jean-Pierre Sauvage, from the University of Strasbourg, devised a high-yielding metal-templated strategy to synthesize a catenane: an assembly of two molecular rings that are mechanically interlocked but can move freely with respect to one another. In 1991, Fraser Stoddart, now at Northwestern University, was responsible for the next major development: a rotaxane shuttle consisting of a macrocyclic ring that can move between two different 'stations' along the axle component on which it is threaded, trapped there by virtue of a bulky stopper at each end.

By creating entangled assemblies, Sauvage and Stoddart were armed with the tools they needed to build nanoscale machines — molecules with moveable parts that undergo reversible, positional displacements. The next step was to gain motional control, which they each achieved in 1994 when they introduced chemically distinct redox-active units into these systems and controlled the relative positions of catenane or rotaxane rings using electrochemistry. Between them they have since developed molecular muscles, logic gates, elevators and pumps, with Stoddart in particular having contributed significantly to the catalogue of available machinery.

Ben Feringa from the University of Groningen made significant contributions to the design of rotary molecular motors. In 1999 his team reported a molecule that possesses two blades that undergo 360° rotation in a single direction by photoisomerization of the double bond through which they are connected. Feringa has since introduced reversible directionality to his motor and increased the rotational frequency to over 12 MHz. His group also synthesized a molecule based on four rotors that can propel itself across a surface in a straight line in response to electronic excitation. The development of molecular motors has led to enormous progression in the field, with researchers now designing machines that function in high-energy states away from equilibrium — a state completely familiar to the biologist, but one that was relatively uncharted territory for the chemist.

VICTORIA RICHARDS