Reports about Feringa making molecular 'nanocars' have appeared everywhere in recent months. But how did these cars come about? And what else is his lab producing?

RENÉ FRANSEN ILLUSTRATIONS PAUL DE VREEDE/UG FERINGA AND RESEARCH

Ben Feringa's left hands

No, University of Groningen chemist Ben Feringa isn't a car freak, although he was given a toy Ferrari during celebrations on 5 October when his Nobel Prize was announced. The nanomotor is just one of the many molecules that he has made, and probably not the most significant. Nor are motors his only research area. In fact, catalysts, which are what first brought Feringa to the world's attention, were something completely different. He is also working with the UMCG on antibiotics and new materials for radiologists.

The common thread in Feringa's work is the concept of chirality, whereby certain molecules appear in two forms that mirror each other, as with our right and left hands. Although both our hands are made up of exactly the same components (fingers and palm), they are not the same. In the same way, there are molecules consisting of exactly the same atoms, also attached in exactly the same way, and yet they are each other's mirror image.

The desired form

That's an important difference because all living cells have a preference for one of the two variants, the L or left-handed form. Although there are medicines that exist in both mirrored forms, one of the two is usually biologically active whereas the other 'does nothing'. Unfortunately, this isn't always the case, as we saw with the thalidomide disaster (trade name Softenon). It was discovered too late that it was the right-handed form of the drug that had the desired medical effect, whereas the left-handed variant caused birth defects when taken by pregnant women.

Chemists have therefore been trying for decades to come up with reactions that produce the desired variant. It is in this field, asymmetric synthesis, that Feringa began his career. Whereas most chemical reactions neatly produce left-handed and right-handed variants in equal numbers, Feringa looked for methods that would mainly produce just one of the forms.

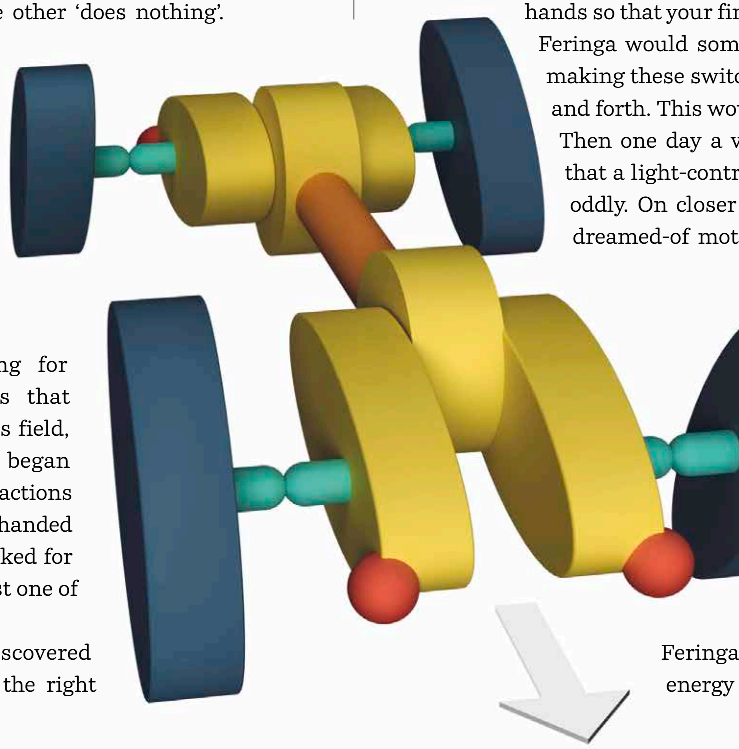
In the early 1990s researchers discovered that this could be achieved by using the right catalysts. Catalysts accelerate certain chemical reactions and researchers found that a cleverly designed catalyst could specifically produce the L or R form. The discoverers of this technique (Knowles, Noyori and Sharpless) were awarded the Nobel Prize in Chemistry in 2001.

International prestige

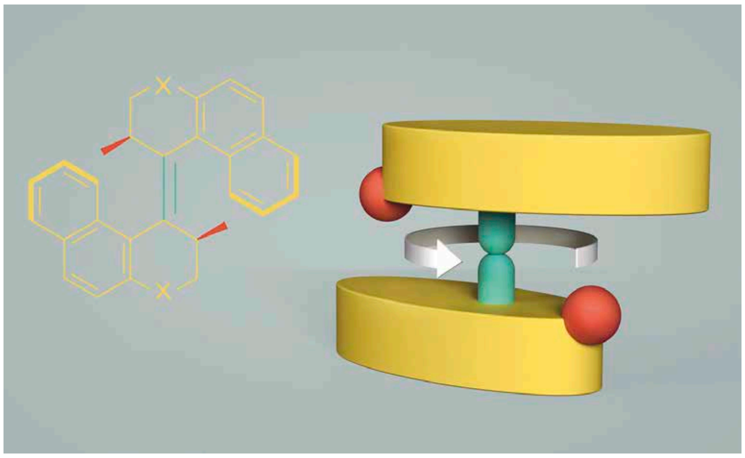
Feringa was also hard at work on catalysts for 'chiral synthesis', the selective production of left- and right-handed forms. He succeeded: in 1996 he discovered a compound that would be the cornerstone of an entirely new class of catalysts based on a metal atom attached to 'phosphoramidites'. If you look up phosphoramidites in Wikipedia, you'll see that the name Feringa features in the four key publications. His international prestige was assured.

From the start of his professorship he worked concurrently on another project involving molecular switches. These are also chiral molecules, which can be converted into a different state by giving them a little 'push' (e.g. with light). These switches usually consist of two similar structures linked by a kind of axle, or pivot. You can get a rough idea by placing the thumbs of both hands against one another (the axle) and turning your hands so that your fingers go up and/or down. In his team Feringa would sometimes talk about the possibility of making these switches go right around, instead of back and forth. This would then give you a motor.

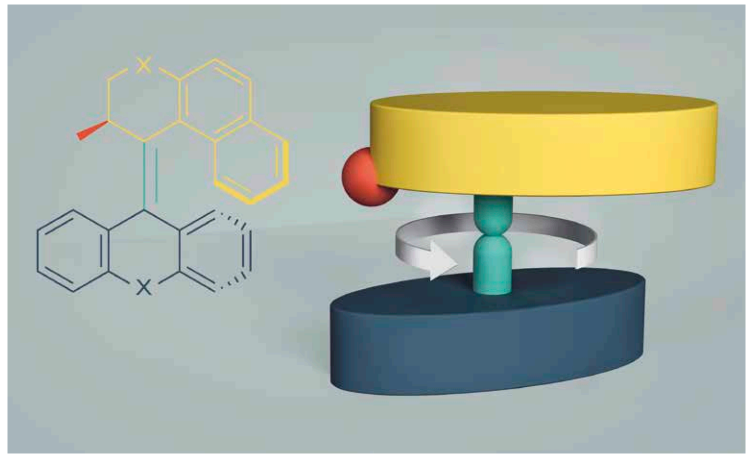
Then one day a visiting Japanese researcher noticed that a light-controlled switch molecule was behaving oddly. On closer inspection it proved to be the long dreamed-of motor. This became the first molecular motor that Feringa showed to the world in *Nature* in 1999. In 2011 four of these motors produced the now iconic nanocar, which was developed primarily to demonstrate that his motors could indeed be used to propel something. And in 2005 Feringa presented a motor that didn't run on energy from light but on chemical fuel. All



Models of molecular motors



Ben Feringa's first nanomotor published in Nature in 1999: two identical halves (yellow) attached to a double C=C compound (green). A side chain (red) ensures that rotation is unidirectional.



Second-generation nanomotor: the top half (yellow) rotates on a generic base (blue). Only one side chain (red) is needed to ensure unidirectional rotation. This molecule is the light-driven 'wheel' of Feringa's nanocar.

instances involve a comparable structure: a molecule that consists of two large 'flaps' attached by a small axle made up of two carbon molecules. The flaps are in each other's way a little, but if you add a small amount of energy to the axle, one flap shoots past the other, making a half turn. A bit more energy and they shoot past each other again, completing the rotation.

Drugs

After the phosphoramidites, Feringa hit the international jackpot for a second time with this motor. He now began concentrating increasingly on catalysis and motors, but he didn't lose sight of switches. Recently, he added a switch to an antibiotic so that the antibiotic could be turned 'on' or off' with the help of light. This means you can target the antibiotic exactly where it is needed, which prevents side effects. And he is conducting similar research on drugs to combat cancer. Meanwhile, Feringa has been working for some thirty years with UMCG radiologists who are looking for improved compounds (tracers) to show the interior of the body – in particular, disease areas such as tumours. As these are mainly organic compounds, Feringa's expertise is much appreciated. He and two colleagues head the UMCG/UG 'tracerlab'.

The nanocar is just one of the many molecules created by Feringa

Concrete applications

These switches and motors, as well as catalysts and tracers, are all chiral molecules. Whereas the motors are still awaiting concrete applications, the switches have made great advances. Feringa is now incorporating them into drugs and tracers. The catalysts he has developed are helping industry to create the right molecules, usually in a cleaner process than with classic chemical synthesis.

A special sideline is his research into how life has developed a preference for 'left-handedness'. As stated earlier, chemical processes generally produce exactly the same number of L and R forms. Somewhere in the development of life, a preference for left-handed molecules must have evolved. But just how this happened is one of the great scientific mysteries.

In late November, Anne Schoonen was awarded her PhD under Feringa's supervision – the first PhD conferral since the Nobel Prize was awarded. She investigated whether certain reactions can lead to a preference for one type of 'handedness'. The findings were not conclusive, but if follow-up research does provide an answer, Feringa could be firmly in the running for a second Nobel Prize. Two left hands can take you a long way!