

## Abstracts



### LAST AUTHOR

One of the largest natural product molecules, vitamin B<sub>12</sub>, is a molecular marvel and an enzymatic enigma. The biosynthetic enzymes responsible for the formation of one of its components, dubbed DMB, have remained elusive — until now. On page 449, biologist Graham Walker at the Massachusetts Institute of Technology and his colleagues identify a role for the bacterial enzyme BluB in DMB formation and show that this enzyme catalyses complex and novel chemistry — including the cannibalization of flavin.

### How did you finally identify the enzymes in the DMB biosynthetic pathway?

Our success has its roots in an undergraduate lab experiment with the soil microbe, *Sinorhizobium meliloti*, which led years later to identification of the *bluB* mutant, which cannot form a symbiotic relationship with its plant host. It was some time before we recognized the clues implicating *bluB* in vitamin B<sub>12</sub> biosynthesis. Other workers unearthed a *bluB* homologue in a cluster of vitamin B<sub>12</sub> genes in another bacterium, and a colleague discovered that *bluB* was regulated in response to vitamin B<sub>12</sub>. Determining the function of the BluB protein then required expertise in basic biology, enzyme mechanisms and crystallography.

### What was most surprising about the enzyme?

We knew that three bonds were cut and one new bond formed during DMB synthesis, but it was not obvious that one enzyme could do this. My postdoc Michiko Taga conducted clever genetic screens for other genes involved in DMB biosynthesis, but found nothing. Then she discovered that purified BluB protein could make DMB all by itself.

### What makes the reaction so unusual?

BluB has a structure similar to an oxidoreductase but has a different function. Many enzymes use flavin as a coenzyme to help a reaction proceed, but the flavin is not consumed or changed. This is the first example we know of in which flavin is destroyed by the enzyme and transformed into part of another coenzyme. That's what we're calling cannibalization.

### How will this help us understand soil microorganisms and symbiosis better?

We're investigating how making vitamin B<sub>12</sub> could enable the bacterium to carry out symbiosis. If you can grow fine without vitamin B<sub>12</sub>, why carry around 30 genes to make it? We're testing whether B<sub>12</sub>-containing forms of these enzymes are more resistant to the oxidative stress that microbes undergo when trying to get into a plant. ■

## MAKING THE PAPER

Jeffrey Moore

### A molecule that undergoes chemical reaction in response to stress.

'Self-healing' materials that can automatically repair their daily wear and tear could produce lenses that never scratch or cars that always look new. In 2001, Jeffrey Moore and his colleagues Scott White and Nancy Sottos at the University of Illinois at Urbana-Champaign, described one such self-healing polymer. Into the basic polymer material were embedded tiny capsules filled with liquid monomer. When the material was broken, the capsules ruptured, releasing monomers into the crack, where a catalyst induced their formation into new polymer to repair the break.

Moore and his colleagues wanted to find ways of promoting this repair without having to add a catalyst. They thought they could create molecules that would undergo the desired reaction in response to the physical stress itself. The idea that mechanical force can induce a chemical reaction has been around for years, but so far scientists had only used such force to break bonds. "If you can use mechanical force to break bonds, why not do something more interesting, like creating a reactive intermediate that might alter the material in useful ways," says Moore. "We did not see any fundamental limitations."

In what turned out to be a five-year chemical *tour-de-force*, the team has synthesized the first mechanophore — a molecule that changes structure in response to mechanical force (see page 423). They first designed a mechanically sensitive molecule consisting of a small carbon ring. To be able to target force to this small molecule it was linked to long polymer chains on each side. "We had many designs that did not work. Eventually we came up with the one in the paper," says Moore.

The next step was to find a way to pull on the tiny molecule. "We explored different ways



and what worked first was ultrasound," says Sottos. Ultrasound applied to a solution containing the construct sends shockwaves through it that apply force to the polymer chains, which in turn pull on the mechanophore. But the researchers had a hard time detecting what was happening. "We were trying to detect a very small change in a tiny portion of a giant polymer," explains Sottos.

To overcome this final hurdle, they captured the mechanophore with a <sup>13</sup>C-enriched molecular label and compared the <sup>13</sup>C nuclear magnetic resonance spectrum of the molecule before and after ultrasound treatment. The results showed that ultrasound caused the ring to open to its reactive form.

Thermal energy (heat) is usually used to drive chemical reactions forward, but heat makes molecules move faster in random directions. "Mechanical force gives directionality," says Moore. "By pulling atoms you can cause chemical change to follow a more intentional route."

Moore and his colleagues expect that the work will eventually have practical applications in self-repair. "We are not sure that the same molecule and analytical tools we developed will map to solid materials, like fibres and films," says White. He adds that they are already designing new mechanophores and ways of detecting reaction. "They should be done next week," he jokes. ■

## KEY COLLABORATION

After a month-long expedition in 1997 to the East Pacific Rise — a ridge in the ocean floor that stretches from California to near Antarctica — as well as several years worth of data crunching, geologist Douglas Toomey at the University of Oregon and an international team came up with some startling results.

At first they assumed they had miscalculated, but after multiple reanalyses to pinpoint the apparent error, the

conclusions were still the same. Toomey and co-author William Wilcock of the University of Washington had to consider that the results were legitimate. "Even among the group, there was scepticism initially," Toomey says. "It took some convincing, but eventually we all got on board."

Their seismic data suggested that areas of the ridge are volcanically or hydrothermally active not because of a surplus supply of magma

pushing its way to the surface (the generally accepted hypothesis), but because magma is coming from the mantle directly underneath active vents (see page 409).

In areas on the ridge where this is not the case, Toomey explains, the Earth's 'plumbing system' redirects the magma underground along the Moho, the boundary between Earth's crust and the upper mantle, which makes volcanic eruptions less likely. ■