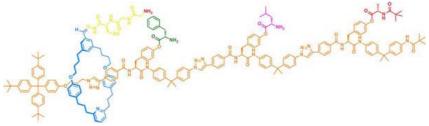


Rotaxane mimics ribosome to spin out peptides

10 January 2013 Laura Howes

The field of molecular machines has taken a <u>new bio-inspired turn to assemble another molecule</u>, in this case linking up individual amino acids into a peptide. While this molecular peptide synthesiser isn't going to rival a ribosome for speed any time soon, it does suggest a way to make multicomponent polymers.



Is the assembly of the peptide mechanical or chemical? $\ensuremath{\textcircled{\sc b}}$ David Leigh

The project involved <u>David Leigh</u>'s groups at the University of Edinburgh and then at the University of Manchester, where he is now based. His group decided to mimic the ribosome, a cellular machine that can build proteins. 'The ribosome uses a track where a machine moves along it processively,' Leigh says. So when the group started thinking about how to build a synthetic version they naturally thought of the rotaxane architecture of a ring on a track. However, Leigh is keen to stress this is not intended as an artificial alternative for the ribosome, especially as his machine is much slower than its biological counterpart – it took 36 hours to synthesise a three amino acid peptide. Instead, Leigh says the work is a proof-of-concept for a molecular machine.

That's something that <u>Fraser Stoddart</u>, father of rotaxane-based machines at Northwestern University in California, US, agrees with. Stoddart describes the work as 'way out there in conception', but that the idea of using molecules to build other molecules is 'the direction that chemistry has got to go in'. But while Leigh and Stoddart focus on the applications of the approach, <u>Dean Astumian</u> of the University of Maine, US, cautions against simple descriptions of molecular mechanical machines. 'One of the big controversies is whether we should look for a mechanical description or whether it is predominantly a chemical phenomenon,' he says.

For Astumian, the exciting thing about this work is the potential insights the molecule might bring to the workings of molecular machines. Does the ring move along the track smoothly, Astumian wonders, or is it a stochastic process with the ring moving back and forth until it overcomes an energy barrier and moves to the next amino acid on the track?

Whatever the answer, Leigh has a number of plans for the device, including increasing the number of amino acids that can be strung together. As the peptide sequence grows, says Leigh, 'it will be very interesting to, at the single molecule level, see how these things fold as they are made'. There are also different chemistries and polymers to try, and Leigh also says he'd like to investigate keeping the information on the track so that it can be read again, just as RNA can be read more than once by a ribosome.

But Stoddart is clear that whilst molecular machines are starting to find applications this is just the beginning. 'Chemistry is by far the youngest of the sciences and we haven't scraped the surface yet. There's so much we have to learn,' he says.

REFERENCES

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