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Artificial molecular manufacturing machine mimics nature

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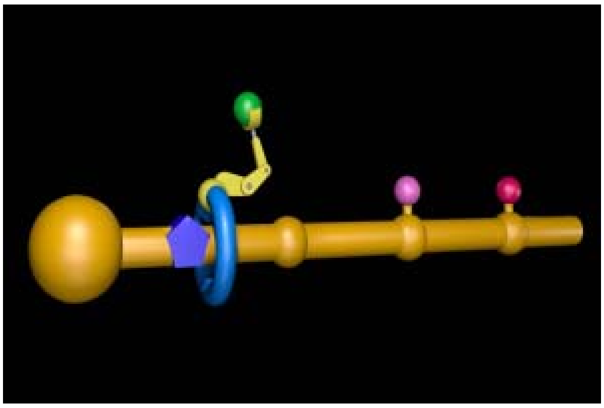

Illustration of artificial molecular machine (Credit: University of Manchester)

An industrial revolution at the nanoscale is taking place in laboratories at The University of Manchester with the development of a highly complex machine that mimics how molecules are made in nature.

The artificial molecular machine developed by Professor David Leigh FRS and his team in the School of Chemistry is the most advanced molecular machine of its type in the world.

Leigh explains: "The development of this machine, which uses molecules to make molecules in a synthetic process, is similar to the robotic assembly line in car plants. Such machines could ultimately lead to the process of making molecules becoming much more efficient and cost effective.

"This will benefit all sorts of manufacturing areas, as many manmade products begin at a molecular level. For example, we're currently modifying our machine to make drugs such as penicillin."

The rotaxane-based machine is just a few nanometers long (a few millionths of a millimeter) and can only be seen using special instruments. Its creation was inspired by natural complex molecular factories where information from DNA is used to program the linking of molecular building blocks in the correct order.

The most extraordinary of these factories is the ribosome, a massive molecular machine found in all living cells that links amino acids together in the order specified by messenger RNA (mRNA) molecules. Leigh's machine is based on the ribosome.

How it works

A nanometer-sized ring moves along a molecular track, picking up up building blocks (amino acids) in its path, to synthesize a desired peptide in a specific order.

- First the ring is threaded onto a molecular strand using copper ions to direct the assembly process.
- Then a "reactive arm" is attached to the rest of the machine and it starts to operate. The ring moves up and down the strand until its path is blocked by a bulky group.
- The reactive arm then detaches the obstruction from the track and passes it to another site on the machine, regenerating the active site on the arm.
- The ring is then free to move further along the strand until its path is obstructed by the next building block.
- This, in turn, is removed and passed to the elongation site on the ring, thus building up a new molecular structure on the ring.
- Once all the building blocks are removed from the track, the ring de-threads and the synthesis is over.

Leigh says the current prototype is still far from being as efficient as the ribosome: “The ribosome can put together 20 building blocks a second until up to 150 are linked. So far we have only used our machine to link together 4 blocks and it takes 12 hours to connect each block. But you can massively parallel the assembly process: We are already using a million million million (10^{18}) of these machines working in parallel in the laboratory to build milligram quantities of a peptide molecule.

“The next step is to start using the machine to make sophisticated molecules with more building blocks. The potential is for it to be able to make molecules that have never been seen before. They’re not made in nature and can’t be made synthetically because of the processes currently used. This is a very exciting possibility for the future.”

References:

- Bartosz Lewandowski et al., Sequence-Specific Peptide Synthesis by an Artificial Small-Molecule Machine, *Science*, 2013, DOI: 10.1126/science.1229753