Science imitating life

Researchers are taking inspiration from the dynamic nature of life to create synthetic systems that behave in new ways. ***Dr Maria Cardona*** *spent her PhD developing a structure that imitates parts of a biological cell. Words by* ***Emma Clarke****.*

Chemistry doesn't only happen in the lab. Right now your body is home to countless reactions that are working together to keep you alive. The cells that make up your tissues and organs are not static, but changing continually in response to their surroundings and to signals from other cells. Our biology is always adapting. Now, chemists are taking inspiration from life's dynamic properties to create lab-made systems that can behave in new and innovative ways. By mimicking nature, these researchers are trying to push the boundaries of what synthetic chemistry can achieve.

FROM NATURAL CELLS...

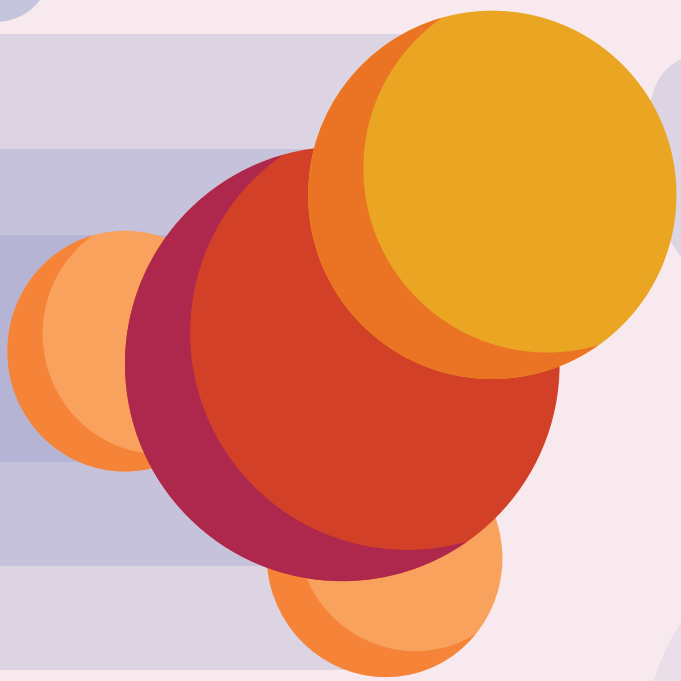
Cells are the living units of our biology, and to function they need to move and communicate. Within their jelly-like centre, cells contain a mesh of protein called a 'cytoskeleton'. It is the cytoskeleton that forms the shape of the cell and drives the mechanics of movement. The cytoskeleton is not rigid but constantly in flux, disintegrating and reforming to meet the cell's changing demands. This fluidity is possible because of how it uses energy.'

In the same way that a car is fueled by petrol, the cytoskeleton is fueled by a type of energy called ATP (Adenosine triphosphate). When ATP is present, protein's building blocks can gather the energy they need to join together into strands, like towers of lego pieces. As soon as the ATP is used up, these strands disintegrate into their parts. This energy-dependent system means that the individual strands of the cytoskeleton can form temporarily, as and when they are needed. What results is an adaptable network that can quickly change the direction of the cell's movement or modify its shape.

Though researchers are a long way off from replicating the sophisticated inner workings of a cell, they are keen to imitate some properties of life in synthetic systems. During her PhD at the University of Padova in Italy, Dr Maria Cardona began to create a chemical structure that could assemble dynamically, inspired by processes in biology.

TO SYNTHETIC CREATIONS

Cardona was working to create a very small 'nanosized' container. To put this scale into perspective, a nanometer is around a billion times smaller than a meter, so Cardona was working with structures far too small to be seen by the human eye. These containers can hold chemicals inside them, a bit like miniature reactors. They are unique



because, just like the strands of the cytoskeleton, their existence is dependent on the presence of energy. When the energy is used up, the containers self-destruct.

This property is exciting because it gives researchers a precise level of control over the system. By changing the supply of energy, they can determine the number and duration of these containers that exist. This could be useful in many contexts, but one potential future application is in drug delivery. The nanoscale containers could be used to transport the components of a drug to a certain place, then self destruct and allow the release of the chemicals they hold. Reactions can take place within them, like minute chemical factories, or they could keep chemicals separate for a set length of time, for example if a chemist needs to time a reaction precisely. An example could be if a drug needed to be released only at a certain time or in a certain place. This kind of system would allow the researcher to control the release of the drug and direct the treatment.

PRECISE AS A SWISS WATCH

Building on the work of her supervisor, Professor Leonard J. Prins, Cardona developed the containers so that they would only form in response to ATP, one of the fuels naturally found within cells. By showing how her reactions absorbed light, she demonstrated that the containers would disintegrate when the molecule of ATP was used up, and that adding ATP again would allow them to reform.

Cardona's second hurdle was to control the exact amount of energy to pump into the system. In nature, ATP is consumed by an enzyme called alkaline phosphatase. Like a car engine burning through fuel, the enzyme processes ATP, using it up. By adding alkaline phosphatase to the reaction at a set time point, Cardona saw that she could quickly use up the ATP in the system, triggering the destruction of the containers. Like a stop button, this system allows a precise level of control over the chemical reaction.

With some hard work and persistence, Cardona managed to refine her system so that it behaved how she wanted it to. By adding different amounts of ATP and alkaline phosphatase, she was watching the containers form and degrade in controlled cycles. She had managed to create a synthetic structure that could behave dynamically.

Next, to study the system, Cardona took advantage of the fact that the containers could hold small amounts of fluorescent dye. Cardona needed to be able to see whether the structures were intact or not, so she used a specific type of dye that glows brighter when enclosed within the containers. Using a fluorescence microscope, Cardona could see exactly how the containers were behaving by measuring how strong the signal was from the dye. Less fluorescence meant that more of the containers had disintegrated and released the dye into the solution. This handy strategy provides one way that the containers could be monitored if they were to be used commercially. It also allowed Cardona to carefully investigate her system and gather more information about how it reacted to different conditions, for example different concentrations of the enzyme.

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Dr Maria Cardona

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these could one day improve drug delivery to treat disease more effectively. It will be fascinating to see what other ideas take root as synthetic chemists look to the world around them for inspiration.

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Further reading:

Cardona, M., & Prins, L. (2020). ATP-fuelled self-assembly to regulate chemical reactivity in the time domain. Chemical Science, 11(6), 1518-1522. https://doi.org/10.1039/c9sc05188k

Cardona, M., Chen, R., Maiti, S., Fortunati, I., Ferrante, C., & Gabrielli, L. et al. (2020). Time-gated fluorescence signalling under dissipative conditions. Chemical Communications, 56(90), 13979-13982. https://doi.org/10.1039/d0cc05993e