Polymer-based network gives artificial cells a life-like cytoskeleton

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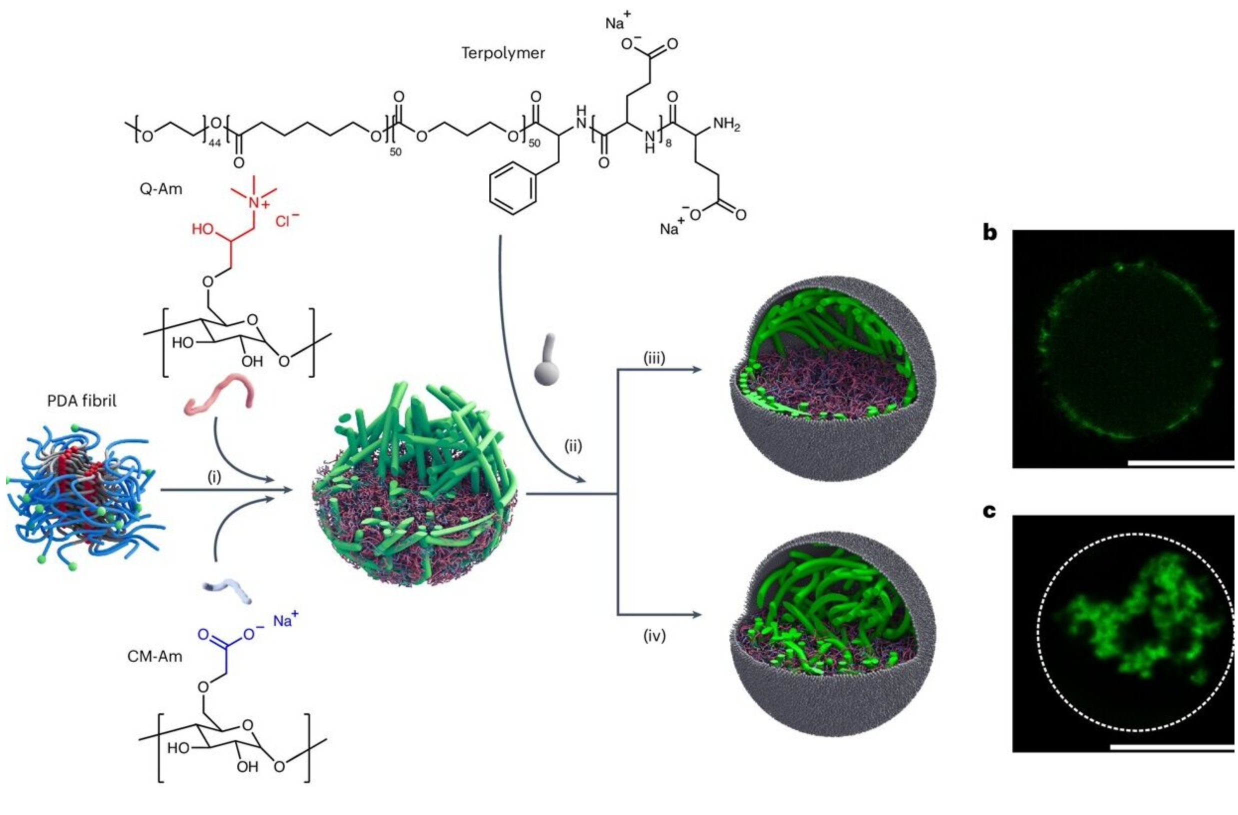


Spatial assembly of the cytoskeleton in artificial cells. Credit: *Nature Chemistry* (2025). DOI: 10.1038/s41557-024-01697-5

Just like your body has a skeleton, every cell in your body has a skeleton—a cytoskeleton to be precise. This provides cells with mechanical resilience, as well as assisting with cell division. To understand how real cells work, e.g. for drug and disease research, researchers create artificial cells in the laboratory.

However, many artificial cells to date cannot be used to study how cells respond to forces as they don't have a cytoskeleton. TU/e researchers have designed a polymer-based network for artificial cells that mimics a real cytoskeleton, thus making it possible to study with greater accuracy in artificial cells how cells respond to forces.

The research is published in the journal *Nature Chemistry*.

Currently, artificial cells are being created to understand how living cells work. This may sound perplexing at first, but there is a logic to the approach.

"This is not only of interest from a fundamental point of view but can also be very useful when it comes to more effective drug screening, the design of better drug delivery technologies, and for tissue regeneration," says Jan van Hest, full professor at the Department of Chemical Engineering and Chemistry and Department of Biomedical Engineering.

"Artificial cells can be used to study biological processes in cells without the need for living cells, and it can be done in a controlled fashion too. This is beneficial if you want to study what type of molecules affect certain processes in cells."

Until now, scientists have mainly focused on including the key functions of cells in artificial cells.

"In other words, researchers have made artificial cells that can communicate with each other and the environment around them, as well as moving like real cells," notes van Hest. "But, to date, most artificial cells can't be used to study how forces affect cells because they don't have a cytoskeleton."

Why artificial over real?

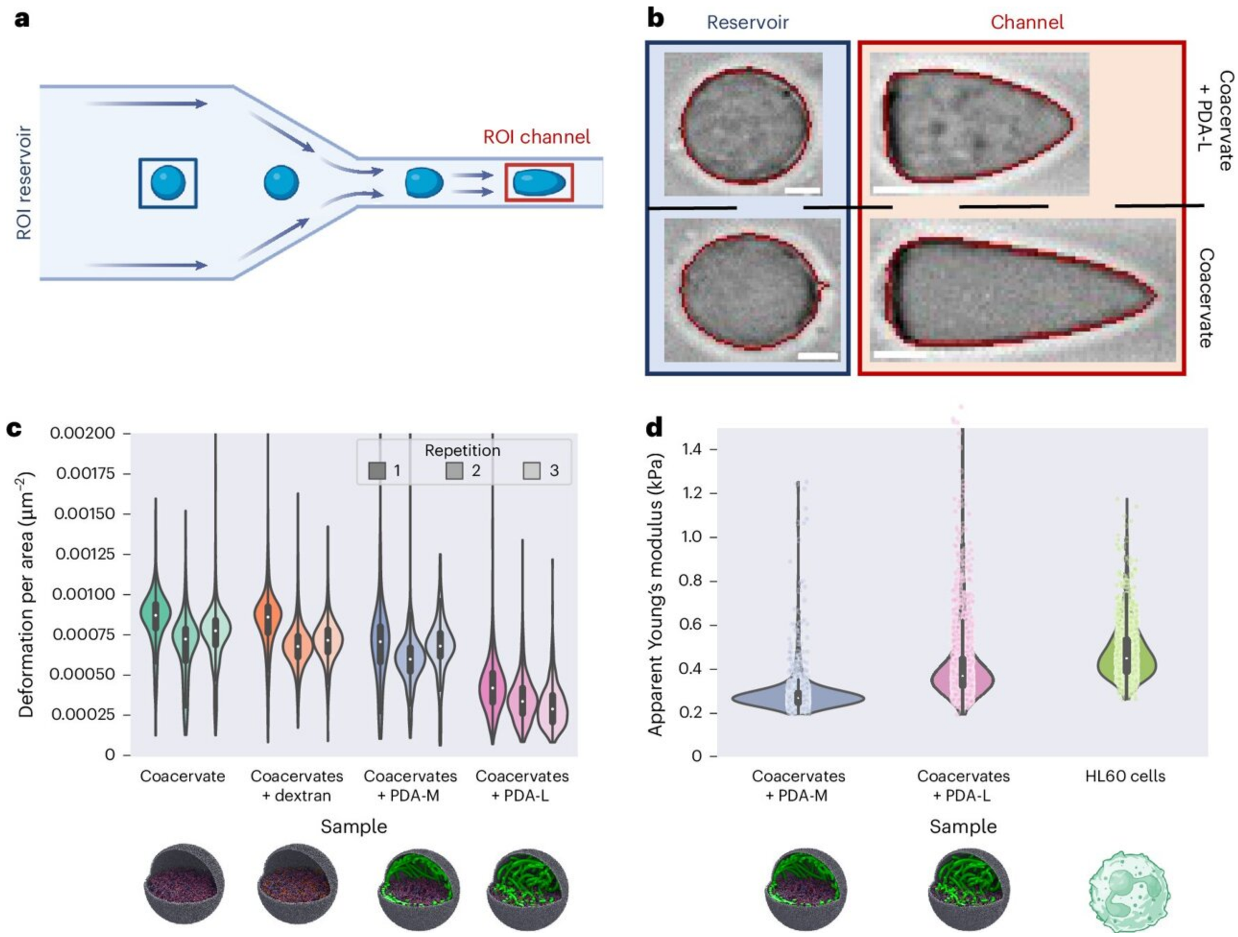
The human body contains a large skeleton, which is made up of around 206 bones. It performs a host of tasks in the body, ranging from structural support to storage of key minerals.

Unlike a human skeleton, though, the cytoskeleton in cells doesn't contain bones. Instead, it's made up of microtubules (long polymer tubes of the tubulin protein) and microfilaments made from the protein actin.

"The building blocks might be different, but the cytoskeleton does many of the things that the human skeleton does, just on a much smaller scale," says van Hest.

Numerous studies are available on the mechanical properties and response of the human skeleton, but the same cannot be said for studies on cytoskeletons in artificial cells.

"People study artificial cells to gain better insight into the biological workings of living cells. But if there's no cytoskeleton in the artificial cells, it's harder to draw concrete comparisons as to how real cells respond to forces," adds van Hest.



Mechanical properties of cytoskeleton-functionalized coacervates. Credit: *Nature Chemistry* (2025). DOI: 10.1038/s41557-024-01697-5

Artificial becomes more real

So, working with colleagues at the Max Planck Institute in Erlangen, Germany, van Hest and his team at TU/e have now included a cytoskeleton in an artificial cell that provides it with mechanical properties like those of living mammalian cells.

The team makes the artificial cytoskeleton using a polydiacetylene-based (PDA) polymer.

"PDA is an excellent material from which to make an artificial cytoskeleton. It captures the key aspects of a natural cytoskeleton, it bundles up to form fibrous structures which are about the same size as the filaments in a natural cytoskeleton, and it can deform when subjected to external forces," says van Hest.

Mechanical testing

Ph.D. researcher Sebastian Novosedlik (lead author for the *Nature Chemistry* paper) performed most of the work and designed the cytoskeleton. However, to test the mechanical properties of the artificial cytoskeleton in a reliable way, van Hest and the TU/e team sought help from further afield.

"Jochen Guck and Felix Reichel in Germany provided a way to test the mechanical properties of individual artificial cells in real-time," says van Hest.

The researchers used a technique known as real-time deformability cytometry (RT-DC) to study how artificial cells with and without a cytoskeleton deformed as they were pushed down a narrow channel.

"When we included a cytoskeleton made from PDA in the cells, we noted that the deformation of the cells decreased. In other words, they became stiffer. In addition, their compressive stiffness—as measured by the Young's modulus—was shown to be like certain human cells," says van Hest.

When it comes to the future, artificial cells with cytoskeletons will prove very important, as van Hest explains: "The inclusion of a cytoskeleton in artificial cells allows us to account for both chemical and mechanical signals when artificial cells interact with living ones in future studies, such as those where you want to modulate immune cells."

Poignant study

The next step for van Hest and the researchers is to explore the combined functional and mechanical properties of their system when cells interact with other cells, which could be significant for new research using artificial cells in cases where living cells are integral.

On a personal note, this research is also impactful in terms of collaboration and personal connection to van Hest.

"This project was a collaboration with the company SyMO-Chem, and especially Henk Janssen, who is the co-corresponding author of the paper. Henk was a dear friend of mine, and he passed away recently. Henk's exceptional knowledge of synthetic organic chemistry and his stimulatory mentoring skills have greatly contributed to the success of this investigation. I have fond memories of the lively discussions Sebastian, Henk, and I had over the course of Sebastian's Ph.D. research," explains van Hest.

Jan van Hest and his team dedicate this paper to the memory of Henk Janssen.

More information: Sebastian Novosedlik et al, Cytoskeleton-functionalized synthetic cells with life-like mechanical features and regulated membrane dynamicity, *Nature Chemistry* (2025). DOI: 10.1038/s41557-024-01697-5

Provided by Eindhoven University of Technology

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