Programming membrane transport

New in Nature Nanotechnology: A DNA origami nanosyringe introduces mechanically controlled molecular transport into synthetic cells. This opens new opportunities for synthetic biology, engineered biointerfaces and molecular therapeutics.

Transporting molecules across biological membranes is essential for life. In nature, this occurs, on the one hand, through passive transport, known as diffusion. "Biological systems often use mechanical motion to accomplish tasks that cannot be achieved by diffusion alone," says Prof. Laura Na Liu, Director of the 2nd Physics Institute at the University of Stuttgart.

For example, certain bacteria use extracellular contractile injection systems. These molecular nanomachines puncture target cells and deliver molecular cargo. At a much larger scale, intracytoplasmic sperm injection has become a widely used assisted reproductive technology by mechanically introducing a sperm cell directly into an egg. Although separated by many orders of magnitude in size, both rely on a similar principle: mechanical penetration provides direct access across biological membranes.

Researchers at the University of Stuttgart have now translated this principle into a programmable DNA nanodevice. They present their DNA origami nanosyringe in Nature Nanotechnology.

DNA origami nanosyringe: mechanical penetration into synthetic cells

The nanosyringe anchors onto lipid membranes, penetrates them through programmable mechanical motion, delivers molecular cargo into synthetic cells, and subsequently retracts to restore membrane integrity. “Rather than relying solely on passive diffusion through nanopores, the device enables membrane transport to be actively controlled in space and time”, says Laura Na Liu.

The nanosyringe consists of two modular DNA origami components: a membrane-anchoring base and a movable needle connected through a reversible sliding mechanism. DNA strand-displacement reactions drive the needle forward to penetrate the membrane and backward to retract it, enabling a fully programmable mechanical cycle. This reversible actuation allows molecular cargo attached to the needle to be transported across lipid membranes without permanently disrupting membrane integrity.

From transport to functional control

The researchers demonstrated that the nanosyringe functions as more than a molecular delivery device. "Once we established reliable and reversible transport, we could use the same platform as a programmable interface to control very different biochemical processes inside synthetic cells", says Dr. Longjiang Ding, first author of the study.

Using the platform, the team spatially initiated DNA hybridization chain reactions at the membrane, activated RNA transcription through targeted delivery of promoter activators, and introduced catalytic DNAzymes that selectively cleaved RNA substrates inside membrane-bound compartments. These demonstrations show that mechanical membrane transport can directly regulate downstream biochemical functions with precise temporal control.

Towards dynamic biointerfaces

The researchers believe that the significance of the work extends beyond membrane transport itself. "Our work introduces the mechanical principle into programmable DNA nanotechnology. Instead of relying only on molecular recognition, DNA nanodevices can now actively interact with biological membranes through controlled mechanical motion", says Laura Na Liu.

Future developments may enable programmable delivery of proteins, nucleic acids and other functional biomolecules, opening new opportunities for synthetic biology, molecular therapeutics and engineered biointerfaces.

"Living systems are dynamic, and future molecular technologies should be able to interact with them in equally dynamic ways," says Laura Na Liu. "We see programmable mechanical devices as an important addition to the DNA nanotechnology toolbox, enabling increasingly sophisticated communication between synthetic molecular systems and biological environments."

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