NANOTECHNOLOGY

Lock-and-key PORE-igami

A nanopore built from DNA allows the controlled and selective transport of organic molecules across a lipid membrane.

Nanopores have several potential biotechnological applications in biosensing, drug delivery and nanofluidics. Although natural protein channels have been used in various nanopore applications, from sensing specific metabolites to nucleic acid sequencing, the ability to engineer protein pores with fully programmable functions has remained out of reach because of the difficulty of controlling the structure of polypeptide assemblies. To overcome this problem, Stefan Howorka and colleagues turned to DNA origami—the ability to create DNA polymers with predictable three-dimensional shapes—to build a controllable membrane-spanning nanopore.

To construct a basic pore with the approximate span of a lipid bilayer, the researchers used a simple origami design in which six concatenated 50-nucleotide-long DNA strands, each linked to two neighboring DNA duplexes at their termini through single-stranded loops, assemble to form a hollow barrel with an opening approximately two nanometers wide. To facilitate membrane insertion, cholesterol moieties were attached to the outside walls of the pore, which was then demonstrated to conduct current across the membrane with properties consistent with the pore's predicted size.

To impart gating control to the pore, the team then designed a single-stranded DNA molecule to anneal with the DNA strands located near the opening of the pore, effectively locking its entrance. Once closed, the pore could be reopened with a 'key' consisting of a sequence complementary to the 'lock' oligonucleotide, which is released from the pore upon annealing. Using this mechanism, Howorka and colleagues demonstrated the controlled release of a small-molecule cargo from lipid vesicle containers.

Transport through the pore was also affected by the charge of the cargo owing to the electrostatic properties of the DNA walls. Thus it might be possible to modify the selectivity of DNA nanopores not only by adjusting the pore geometry to allow different cargo sizes, but also by using nucleotide analogs to control the charge of the channel's interior. The ability to mechanically control the opening and closing of DNA nanopores with programmed selectivity is likely to stimulate the development of new nanobiotechnology applications.

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RESEARCH PAPERS

Burns, J.R. *et al.* A biomimetic DNA-based channel for the ligand-controlled transport of charged molecular cargo across a biological membrane. *Nat. Nanotechnol.* **11**, 152–156 (2016).