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DNA ORIGAMI MEMBRANE CHANNELS

Allocation: Blue Waters Professor/240 Knh
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EXECUTIVE SUMMARY

DNA nanotechnology utilizes self-assembly with nanometer precision for the high-throughput construction of sub-micron-size objects. In comparison to conventional nanofabrication approaches, the DNA origami method is relatively low cost, easy to use, and has an infinite number of possible applications. Using Blue Waters, we have performed landmark molecular dynamics (MD) simulations to characterize the structure and transport properties of two biomimetic DNA origami channels—the smallest [1] and largest [2] DNA channels ever made—working in collaboration with the experimental Keyser lab (University of Cambridge). Once the technology is perfected, the DNA channels could be used to replace biological membrane channels or to deliver drugs across cellular membranes.

RESEARCH CHALLENGE

Membrane protein channels are biological sensors with high selectivity and efficiency. One important avenue of medical research is building a synthetic channel that has the same functionality as a biological channel or that performs a user-defined role. Recently, researchers demonstrated that DNA origami-based channels could mimic the ionic conductance and transport properties of membrane protein channels [3–8]. Only after characterizing their structural and electrical properties can these DNA channels be applied to biosensing and drug delivery.

METHODS & CODES

We performed explicit-solvent all-atom MD simulations with the latest version of NAMD2 [9–10] of the smallest and largest synthetic DNA channels ever designed, complementing the experimental work of our collaborators in the Keyser Lab. The smallest DNA channel was built using a single DNA helix, and the largest was a megadalton funnel-shaped DNA origami porin (a protein channel that allows passive diffusion). Chemical tags were added to stably embed the channels in a lipid bilayer. Simulations with an applied electric field were then performed to measure the ionic conductance of each channel.

RESULTS & IMPACT

Through all-atom MD simulations, we have shown that a membrane-spanning single DNA helix decorated with chemical tags can provide a pathway for ions across the lipid membrane despite the lack of an internal physical channel. Lipid molecules were found to rearrange around the helix, forming a narrow water-filled passage at its circumference, allowing ions and water molecules to pass through the membrane. The average conductance calculated from simulation was in excellent agreement with experiment, and the simulations provided a microscopic explanation for the large variation in ionic conductance measured in experiment and simulation. Results of the single-DNA helix channel were published in *Nano Letters* [1].

Following the same all-atom MD approach, the conductance of the large funnel-shaped DNA channel was measured to be an order of magnitude larger than any previous man-made channel, and its cross-sectional area was similar to that of the nuclear pore complex. Consistent with the results of the single DNA helix, the ion current was found to flow through both the central pore of the channel and along the channel's walls. Results of the large funnel-shaped DNA channel were published in *ACS Nano* [2].

This work could lead to important applications at the frontier of medical science. Researchers could use synthetic DNA channels as a syringe for specific drug molecules by modifying the channels to recognize selective tissues and to open up the membrane. Furthermore, synthetic channels could be used in artificial tissues to give neighboring cells a new way to communicate.

WHY BLUE WATERS

Explicit-solvent all-atom MD simulation is the only computational method that can treat DNA origami objects enhanced by nonstandard functional groups and accurately characterize their structural fluctuations and transport properties [11]. Because of the size of the DNA origami structures, such MD simulations are computationally demanding. The large number of XK nodes on Blue Waters with graphics processing unit accelerators connected by the fast Gemini interconnect make it one of the best publicly available systems for performing DNA origami simulations. Over the past several years, our group has used Blue Waters to carry out a set of landmark simulations in the area of DNA nanotechnology, bringing high-performance simulations to the forefront of this research field.

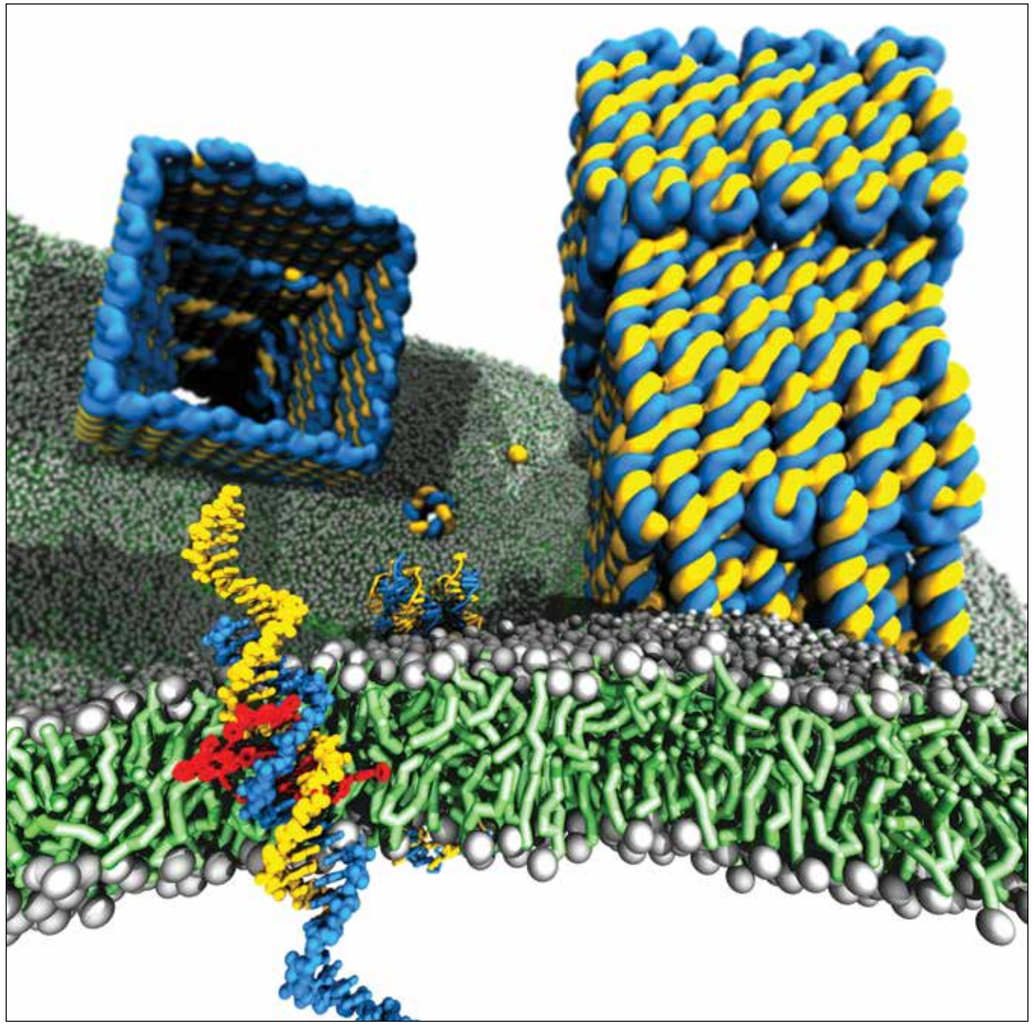

Figure 1: The smallest and largest synthetic DNA channels (in blue and yellow) embedded in a lipid bilayer (in green and gray). Chemical tags were used to anchor the channels in place (shown in red).

PUBLICATIONS AND DATA SETS

Göpfrich, K., et al., Ion channels made from a single membrane-spanning DNA duplex. *Nano Letters* 16:7 (2016), pp. 4665–4669.

Göpfrich, K. and Li, C., et al., Large-conductance transmembrane porin made from DNA origami. *ACS Nano* 10:9 (2016), pp. 8207–8214.