DNA ORIGAMI MEMBRANE CHANNELS

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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 [1] and largest [2] 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 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 with high fidelity, allowing researchers to fully characterize their structural fluctuations and transport properties. 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.

PUBLICATIONS AND DATA SETS


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).