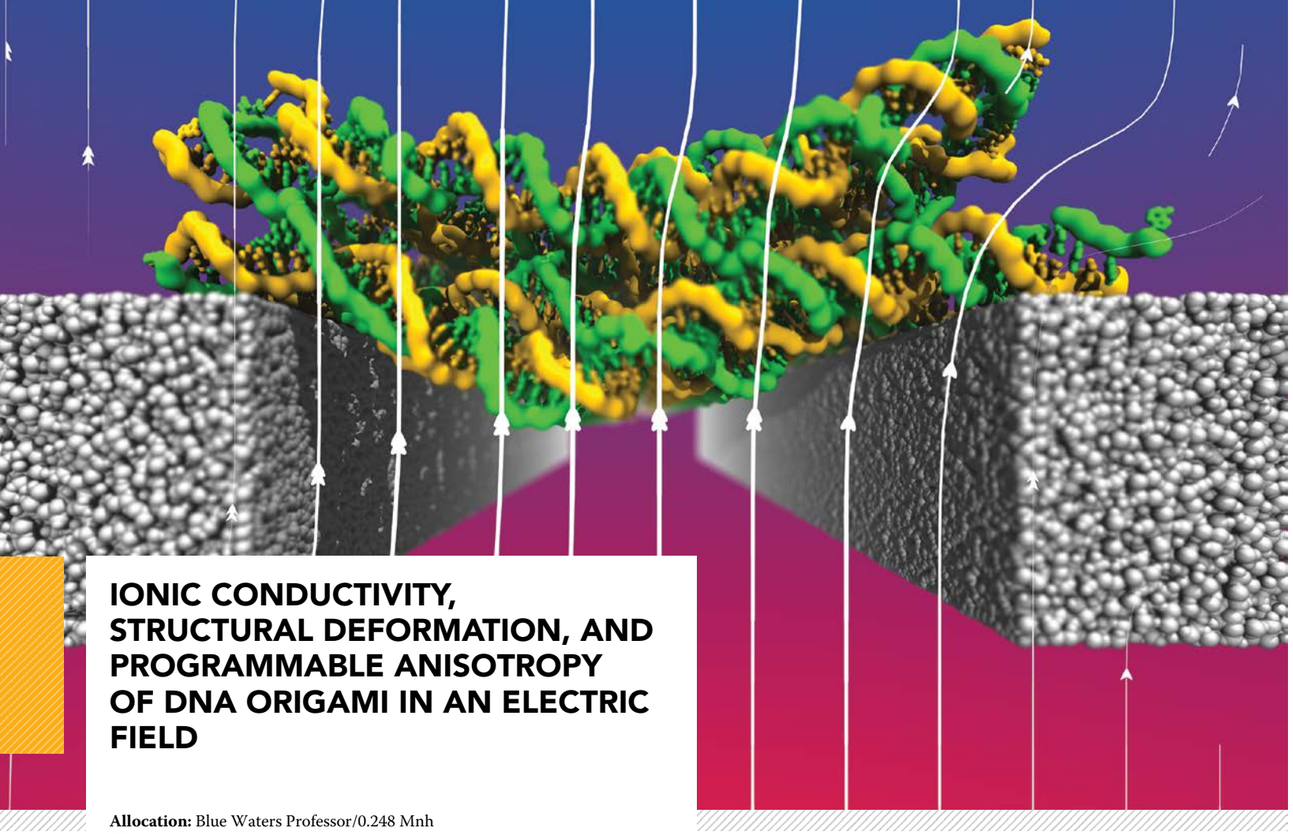

IONIC CONDUCTIVITY, STRUCTURAL DEFORMATION, AND PROGRAMMABLE ANISOTROPY OF DNA ORIGAMI IN AN ELECTRIC FIELD

Allocation: Blue Waters Professor/0.248 Mnh
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EXECUTIVE SUMMARY:

DNA origami is an experimental technique that allows folding of a long DNA molecule into an arbitrary three-dimensional shape with sub-nanometer precision. In comparison to conventional nanomanufacturing, the DNA origami method has relatively low cost, is easy to use, and has an extremely broad range of possible applications. One such application is nanopore detection, whereby measuring the ionic current flowing through a nanopore can determine the presence and/or identity of biochemical analytes.

Using Blue Waters, our group has carried out the first all-atom molecular dynamics (MD) simulations of DNA origami nanopores. We have determined how the ionic conductivity of a DNA origami plate depends on its internal structure and environmental conditions. Single molecule experiments performed in our collaborator's laboratory (Cambridge U., U.K.) confirmed our predictions. Our work demonstrates the predictive power of the MD method in characterizing DNA origami objects and the feasibility of programming the electrical properties of nanoscale self-assembled objects.

INTRODUCTION

Nanopores have emerged as versatile tools for single-molecule manipulation and analysis. In a typical nanopore experiment, an analyte (e.g., DNA or protein) is driven through a nanometer-sized pore in an insulating membrane by applying an external electric field. The presence and, in some cases, the chemical structure of the DNA or proteins can be determined by measuring the ionic current change produced by the analyte blocking the nanopore. Solid-state inorganic materials are commonly used to create nanopore membranes. However, the dimensions and surface chemistry of such solid-state nanopores are difficult to control experimentally. A hybrid nanopore system consisting of a solid-state nanopore and a DNA origami plate can overcome the above shortcomings; however, the electrical conductivity of DNA origami objects has not been systematically characterized until now. The goal of this study was to elucidate the mechanism of ionic conductance through DNA origami objects and the means to control the conductance of such objects.

METHODS & RESULTS

To predict the structural and electrical properties of DNA origami materials, we performed molecular dynamics (MD) simulations of DNA origami plates, varying the number of DNA layers in an origami lattice, the lattice type, the nucleotide content, the orientation of the object with respect to the applied electric field, and the ionic conditions [1]. Tens of different DNA origami systems were built using a protocol our group developed [2]. The systems were simulated using the all-atom MD method and the NAMD2 package, which was optimized for Blue Waters.

Our MD simulations revealed how the current of ions through the DNA origami plate—the leakage current—depends on the internal design of the plate. First, the leakage current through the origami plate monotonically decreases as the number of DNA layers in the origami plate increases. The ionic conductivity of a DNA origami plate also depends on the lattice type of the DNA helices in the DNA origami structure (square, honeycomb, or hexagon). In addition, the plate's nucleotide content can have a nontrivial influence on its ionic conductivity. For example, a DNA origami plate made entirely of adenine (A) and thymine (T) nucleotides is about two times more conductive than a plate made entirely of guanidine (G) and cytosine (C) nucleotides.

The ionic environment (i.e. the magnitude and direction of the applied electric field) can considerably affect the ionic conductivity. Our simulations predicted that the ionic conductivity of DNA origami objects decreases as the solution concentration of Mg^{2+} increases. The simulations also revealed the mechanism of the dependence: higher amounts of Mg^{2+} lower the strength of DNA–DNA repulsion, making the structure of DNA origami more compact, reducing the ionic current through it. Experimental measurements of the ionic current through nanocapillaries blocked by different DNA origami plates and the Förster resonance energy transfer measurements directly confirmed the results of our MD simulations. The DNA origami objects were also found to have anisotropic electric properties: the objects conduct electricity better along the direction of the DNA helices than perpendicular to them. By controlling the orientation of the plates in the corresponding single-molecule experiments, our collaborators in the Keyser group (U.K.) directly confirmed this prediction as well. Finally, our MD simulation of a hybrid structure, where the DNA origami plate is placed on top of a solid-state nanogap, revealed considerable yet reversible deformations of the DNA origami structure, providing a mechanistic explanation for reduced conductance in the hybrid systems with voltage that has been observed in experiment.

The results of our study demonstrate the utility of the MD method in predicting material properties of DNA origami objects. The study has immediate consequences on the design of the next generation of DNA origami nanopore sensors, where the effect of nucleotide composition and the ionic environment will be combined to minimize the leakage current through the plates. Furthermore, the structural responses of DNA origami to the changes in ionic and electrical environments suggest possible applications of DNA origami systems as electro-mechanic switches and other components of nanofluidic electronics.

FIGURE 1 (BACKGROUND): DNA origami plate (in orange and green) on top of a solid-state nanogap. Streamlines indicate the magnitude and direction of local water flux through the hybrid nanopore system. DNA origami is a deformable material with programmable electrical properties.

WHY BLUE WATERS?

Characterizing a given material property of a DNA origami object requires a MD simulation from 100 to 1,000 nanoseconds in length. Performing many such simulations in parallel was necessary to systematically evaluate the behavior of DNA origami as a function of its design or environmental conditions. Using Blue Waters allowed us to complete the study in less than one year, which would not have been possible using other supercomputer systems.

PUBLICATIONS

Li, C., et al., Ionic Conductivity, Structural Deformation, and Programmable Anisotropy of DNA Origami in Electric Field. *ACS Nano,* 9:2 (2015), pp. 1420–1433, doi:10.1021/nn505825z.