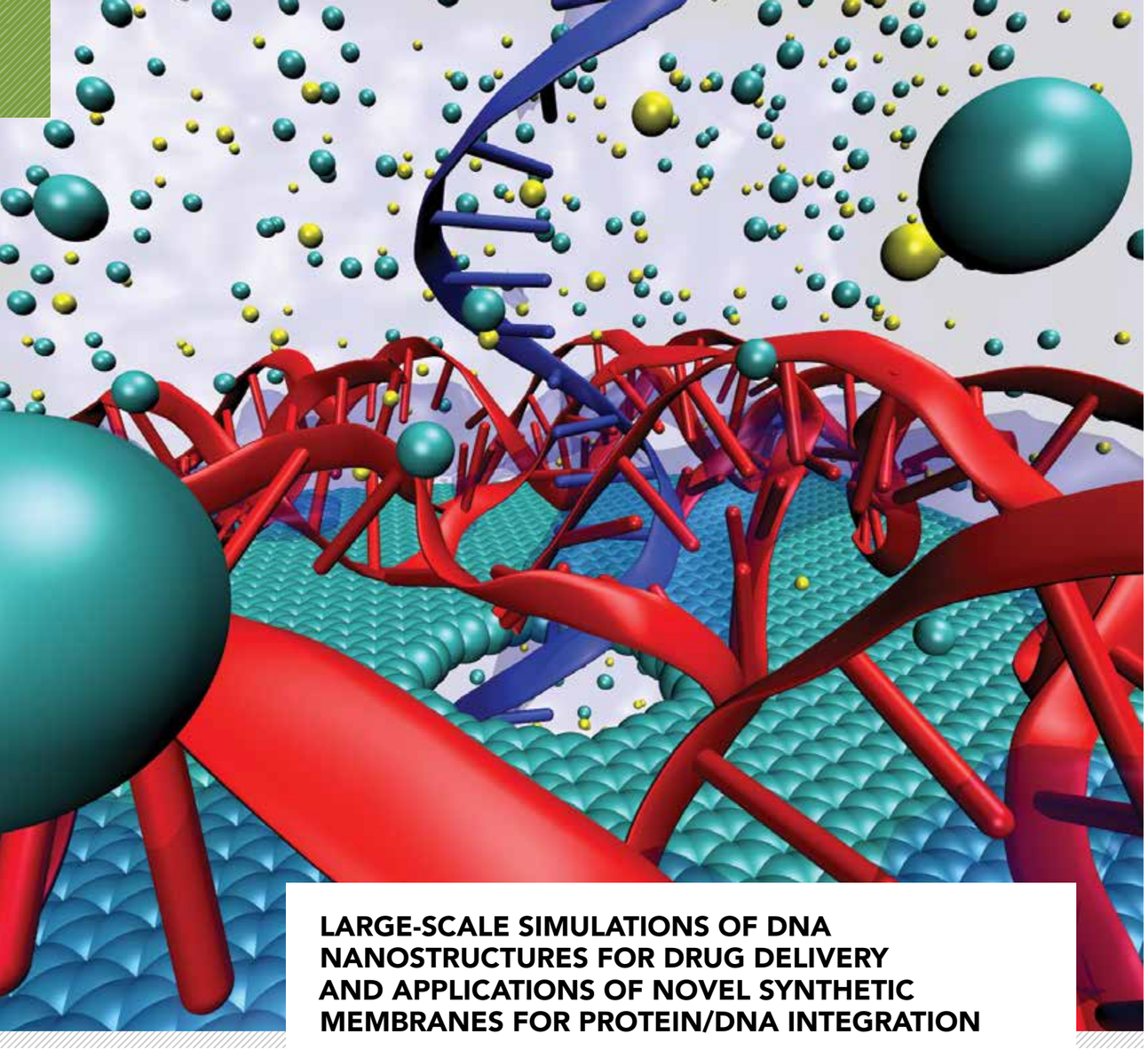

FIGURE 1: Single strand of DNA (blue) translocating through a single layer DNA origami (red) mounted on a graphene sheet (cyan).

LARGE-SCALE SIMULATIONS OF DNA NANOSTRUCTURES FOR DRUG DELIVERY AND APPLICATIONS OF NOVEL SYNTHETIC MEMBRANES FOR PROTEIN/DNA INTEGRATION

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EXECUTIVE SUMMARY

DNA nanostructures have the advantage of being biocompatible and programmable. The self-assembly features of DNA can be used to design nanopores within the DNA structure for sensing and detecting biological molecules. DNA base detection, which is important in mapping human health, faces a key challenge of high translocation speed in nanopores. Here, we propose a DNA origami-graphene nanopore for DNA sequencing. The DNA origami sits on top of a graphene sheet acting as a substrate. We show that the translocation speed of DNA strands inside the DNA origami nanopore is reduced due to the attractive interactions of nucleotides of the pore and the DNA strands. We also find that the proposed nanopore leads to distinct signals for different types of DNA bases making it a **promising** hybrid material (DNA origami-graphene) for DNA detection.

METHODS AND RESULTS

DNA sequencing using nanopore technology has evolved significantly during the last few years. Oxford nanopore technology is currently fabricating a USB-stick size device that can sequence the DNA rapidly—in a couple of hours. In recent years, both biological and synthetic nanopores were used for "label-free," high-resolution DNA sequencing. The challenges posed to DNA sequencing using nanopore technology are the low signal to noise ratio, pore degradation due to multiple uses, the identification of single base in real time and the high speed of translocation [1,2]. Engineering the translocation of DNA through biological/synthetic nanopore has been defined as one of the challenging problems of biotechnology. Although a number of studies have been performed on different types of pores regarding translocation speed and ionic current blockade, the fundamental understanding of the pore architecture, material and size of the pore on the quality of DNA sequencing and speed of translocation is still lacking. In this study, we will examine DNA origami-graphene hybrid nanopores for DNA sequencing by using extensive molecular dynamics (MD) simulations.

The self-assembly properties of atoms and molecules have frequently been used to create arbitrary 3D nanostructures. The DNA origami technique is a **novel** method, which takes advantage of self-organization properties of DNA molecules and allows folding DNA single strands to construct a complex shape at nanoscale. DNA origami sheets can be created via self-assembly process. Here, we introduce a nanopore in a DNA origami nano sheet mounted on top of a graphene sheet acting as a substrate (Fig. 1). Using extensive MD simulations, this nanopore is shown to be able to detect and sense DNA bases. The DNA origami nanopore is designed in such a way that the edge of the pore carries a specific nucleotide type. We show that the nanopore in DNA origami-graphene results in distinct dwell times for the four DNA base types, while a bare graphene nanopore gives rise to almost identical dwell times for the four DNA base types. The difference in dwell times is due to the strength of attractive interaction between the nanopore and DNA translocating strand. Depending on the nanopore edge functionalization, the base pairing between the bases of the pore and strand is different for different translocating bases. In addition to these distinguishable dwell times, this base pairing results in high residence time of the DNA strand inside the pore or lower speed of translocation.

WHY BLUE WATERS

We performed extensive molecular dynamics simulations which involve up to 120,000 atoms. These expensive computations are not possible to perform without a petascale supercomputer. Also, the MD package (NAMD) we used scales almost linearly with the number of cores up to 1,000 in our test on Blue Waters.