

LARGE-SCALE SIMULATIONS OF BIOLOGICAL–SYNTHETIC INTERFACE MATERIALS FOR SENSING APPLICATIONS

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EXECUTIVE SUMMARY:

Sensing and detecting biological molecules is of utmost importance in DNA mapping for human health. DNA base detection using nanopore technology has paved the way towards designing high-speed, high-precision sequencing devices. The high speed of DNA translocation and low signal-to-noise ratio are two challenges in DNA nanopore technology. For the first time, we introduce the mechano-sensitive channel (MscL) for DNA sequencing. MscL can produce two distinct tension and ionic current signals, making it an attractive pore for DNA sequencing technology. Moreover, MscL slows down DNA translocation by about one order of magnitude compared to traditional biological channels used for DNA sequencing. In another project, we found that single-layer MoS₂ is a promising material for DNA detection, exhibiting distinct signals for different types of DNA bases with a high signal-to-noise ratio.

INTRODUCTION

DNA sequencing using nanopore technology evolved greatly during the last few years. Oxford Nanopore Technologies is currently fabricating a USB-stick-size device that can sequence DNA 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 signal-to-noise ratio, pore degradation due to multiple uses, the identification of a single base in real time, and the high speed of translocation [1,2]. Engineering the translocation of the DNA through a biological/synthetic nanopore is a challenging problem in biotechnology. Although a number of studies

have been performed on different types of pores in terms of translocation speed and ionic current blockade, fundamental understanding of the effect of pore architecture (the material and size of the pore) on the quality of DNA sequencing and speed of translocation is still lacking. In this study, we investigate both synthetic and biological nanopores by comparing the quality of the signals obtained during DNA translocation in nanopores using molecular dynamics (MD) simulations.

METHODS & RESULTS

Recently, we simulated all-atom MD of the translocation of DNA through a mechano-sensitive channel to distinguish different DNA base types according to the mechanical response of the channel [3]. In this study, a new type of signal, namely mechanical tension (in addition to ionic current signal), was introduced for DNA sequencing. We showed that the initially closed mechano-sensitive channel of large conductance (MscL) protein pore opens for single-stranded DNA translocation under an applied electric field. As each nucleotide translocates through the pore, a unique mechanical signal was observed; specifically, the tension in the membrane containing the MscL pore was different for each nucleotide. In addition to the membrane tension, we found that the ionic current was also different for the four nucleotide types. The initially closed MscL adapted its opening for nucleotide translocation due to the flexibility of the pore. This unique operation of MscL provided single-nucleotide resolution in both electrical and mechanical signals. Finally, we also showed that the speed of DNA translocation was roughly one order of magnitude slower in MscL compared to MspA (the membrane porin from *Mycobacterium smegmatis* which has been shown to be suitable for DNA sequencing), suggesting MscL to be an attractive protein pore for DNA sequencing.

In another study, which gained attention through many news outlets, we simulated DNA translocation through a MoS₂ nanopore [4]. Using atomistic and quantum simulations, we found that single-layer MoS₂ is an extraordinary material (with a signal-to-noise ratio >15) for DNA sequencing by two competing technologies (i.e. nanopore and nanochannel). A MoS₂

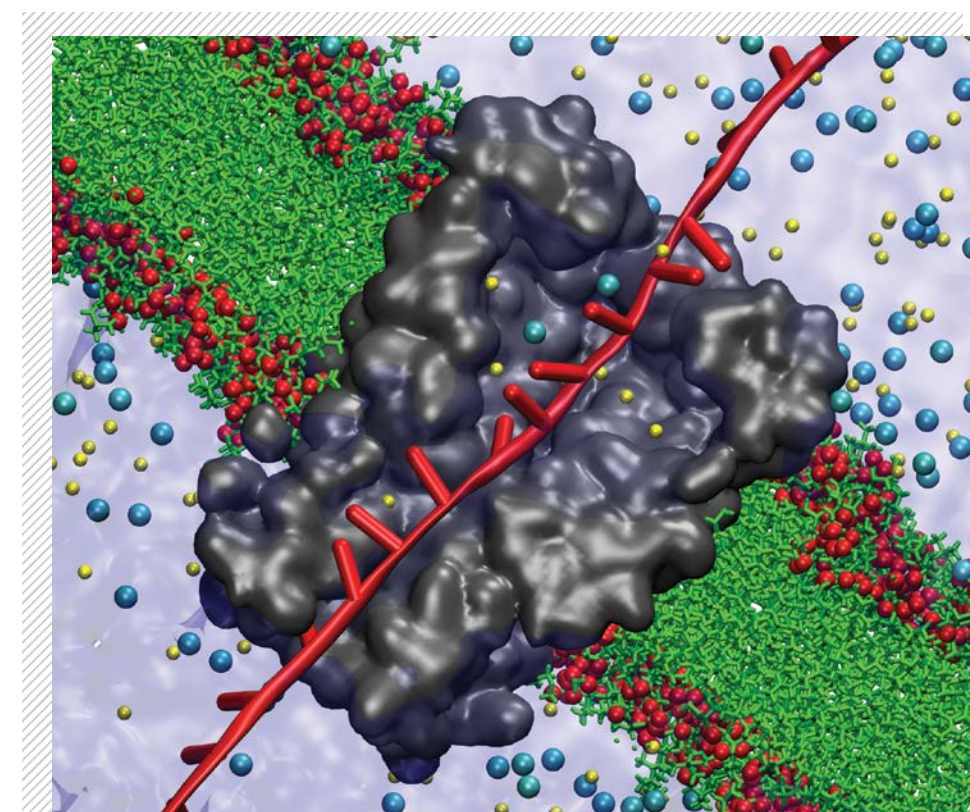


FIGURE 1: Single-strand DNA translocation through a mechano-sensitive channel.

nanopore showed four distinct ionic current signals for single-nucleobase detection with low noise. In addition, single-layer MoS₂ showed a characteristic change in the total density of states for each base. The band gap of MoS₂ was significantly changed compared to other nanomaterials (e.g., graphene, h-BN, and silicon nanowire) when bases were placed on top of the pristine MoS₂ or armchair MoS₂ nanoribbon, thus making MoS₂ a promising material for base detection via transverse current tunneling measurement. MoS₂ nanopores benefit from a pore architecture (combination of Mo and S atoms at the edge) that can be engineered to obtain the optimum sequencing signals.

WHY BLUE WATERS?

For both projects, we performed extensive MD simulations that involved up to 600,000 atoms.

These expensive computations are not possible without a petascale supercomputer. Also, the MD package we used (NAMD) scales almost linearly with the number of cores up to 1,000 cores in our test on Blue Waters.

PUBLICATIONS

Farimani, A. B., M. Heiranian, and N. R. Aluru, Electromechanical Signatures for DNA Sequencing through a Mechano-sensitive Nanopore. *J. Phys. Chem. Lett.*, 6 (2015), pp. 650–657, doi:10.1021/jz5025417.

Farimani, A. B., K. Min, and N. R. Aluru, DNA Base Detection Using a Single-Layer MoS₂. *ACS Nano.*, 8 (2014), pp. 7914–7922, doi:10.1021/nn5029295.