STUDY OF DIBS WITH FUNCTIONAL CHANNELS

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EXECUTIVE SUMMARY

Distinguishing the different subclasses of immunoglobulin G (IgG) antibodies in blood serum can enable breakthrough advances in mapping the immune system and the health status of the human body. In this study, using petascale-based molecular simulations (containing up to ~1,000,000 atoms) and a total aggregate simulation time of 2.7 microseconds (μs), we demonstrate that an atomically thin graphene nanopore is capable of sensing and discriminating among different subclasses of IgG antibodies despite their minor and subtle variations in atomic structure. Using machine learning, we *featurized* and clustered the ionic current and the dwell times data obtained from the device during multiple antibody translocation events. In addition, the histogram of ionic current for each segment of IgG can provide high-resolution spatial detection of antibody segments. Parallel nanofluidic studies during IgG translocation reveal distinct water flux rates for IgG subclasses facilitating an additional recognition mechanism.

DESCRIPTION OF RESULTS

DNA sequencing using nanopore technology has evolved significantly during the last few years. Oxford Nanopore Technologies Ltd. currently is fabricating a USB-stick-sized device that can sequence the DNA in a few hours. In recent years, both biological and synthetic nanopores were used for "label free," high-resolution DNA sequencing. In addition to DNA sequencing, detection of antibody proteins can lead to advances in improving human health. The challenges posed to biological molecule detection using nanopore technology are the low signal-to-noise ratio, pore degradation due to multiple uses, the identification of single bases in real time, and the high speed of translocation [1,2]. Engineering the translocation of molecules through biological/synthetic nanopores has been defined as one of the challenging problems of biotechnology. By using extensive molecular dynamics (MD) simulations, this study shows that an atomically thin graphene nanopore is capable of sensing and discriminating between different subclasses of IgG antibodies.

Protein detection via a graphene nanopore is accomplished using ionic current, dwell time, and water flux calculations. A total aggregate of 2.7 μs of simulation time has been carried out for systems containing up to ~1 million atoms. All parts of the antibody (Fig. 1) are distinguishable by ionic current measures. More specifically, the Fab, Fc, and hinge regions exhibit a unique current level when translocating through the pore. Using k-means clustering, the ionic current–dwell time and water flux–ionic current feature plots lead to clusters with distinguishable centroids. We also compared the performance of the single-layer graphene nanopore with that of a solid-state nanopore (Si_3N_4). IgG subclasses are not distinguishable when using thick nanopores of Si_3N_4 because some of the atomic details cannot be captured.

In conclusion, we have shown that ionic current, dwell time, and water flux can detect different antibodies with high precision.

WHY BLUE WATERS

We performed extensive MD simulations that involved up to 1,000,000 atoms. These expensive computations would have not been 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.

PUBLICATIONS AND DATA SETS

Farimani, A. B., M. Heiranian, K. Min, and N. R. Aluru, Antibody Subclass Detection Using Graphene Nanopores. *The Journal of Physical Chemistry Letters*, 8:7 (2017), pp. 1670–1676.

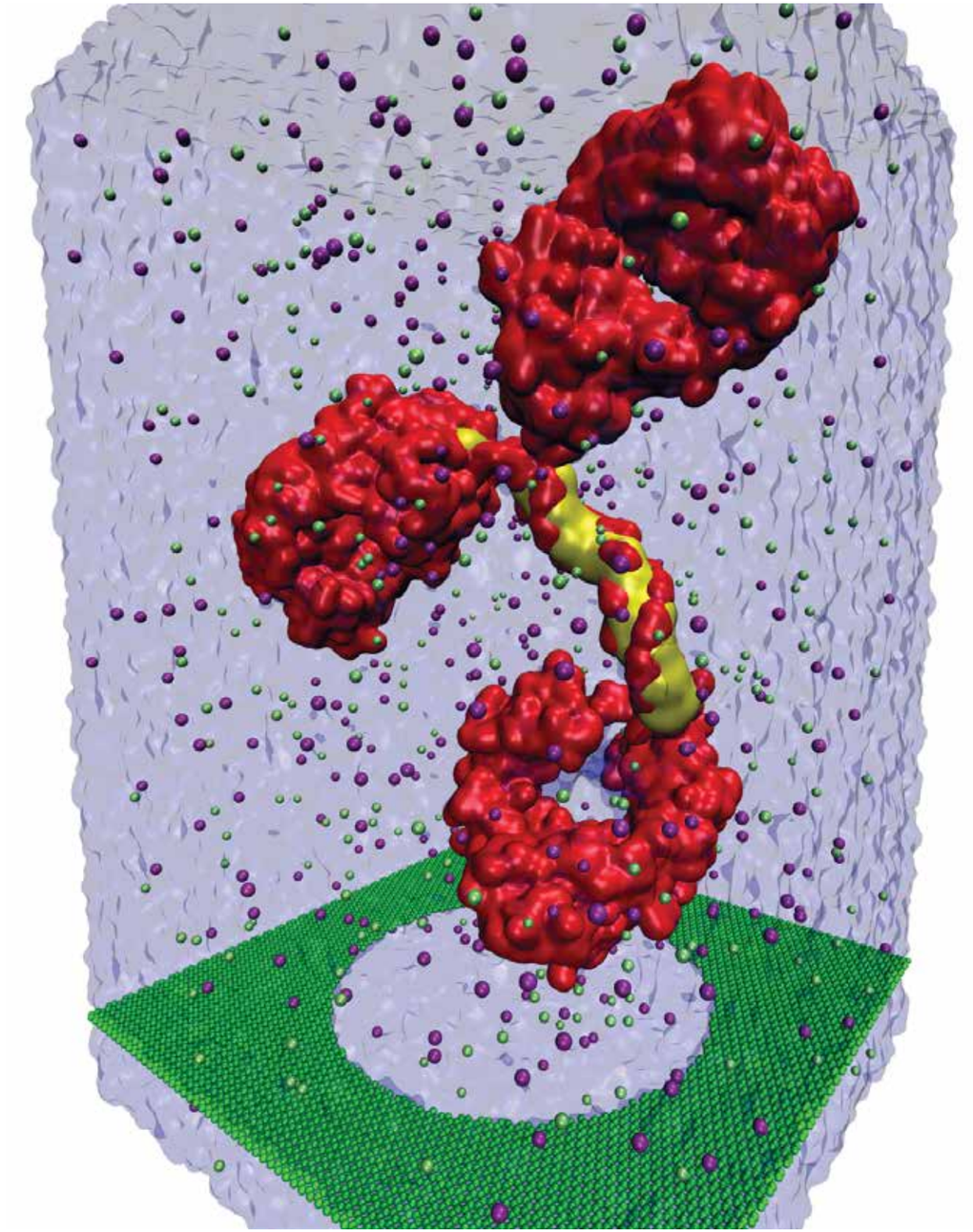

Figure 1: System consisting of IgG3 protein (red: chains; yellow: disulfide bonds), ions (pale green), and graphene sheet (green).