Identifying DNA Mononucleotides based upon Flight Times Using Molecular Dynamics Simulations

Katie Gamble[1], Dorel Moldovan[2], Dimitris Nikitopoulos[2], Brian Novak [2]
[1]Stevens Institute of Technology, [2] Louisiana State University

LA-SiGMA
Louisiana Alliance for Simulation-Guided Materials Applications

Abstract:

While the field of genealogy is growing rapidly, our ability to decode the genome has had little progression. Thus, a push to develop a more time and cost efficient method of genome identification has began. The research presented in this poster uses Molecular Dynamics (MD) Simulations to investigate a probable technique for genome identification which determines the identities of mononucleotides based upon their flight times over a specified length of a nanochannel. These flight times differ due to the chemical properties of mononucleotide bases being sent through the channel. Through manipulation of the properties and variables, a realistic simulation is developed depicting results which can be later transferred physically and investigated in physical laboratory experiments. While the simulation provided viable results, the wall properties are simulated for simplification instead of reflection of properties of poly (methyl methacrylate), or PMMA (the material which will likely be used if an actual laboratory experiment occurs). Therefore, the chemical variables of the simulation must be tailored to determine realistic and effective nanochannel wall properties. Thus, producing more effective and accurate simulation results and data.

Goals:

1. Correctly decipher a genome by sending mononucleotides using their flight times through a section of a nanoslit of determined length.
2. Understand the continuum hydrodynamics behind the interactions and determine nanoslit wall properties that satisfy goal one best (produce desired wall/mononucleotide interactions).

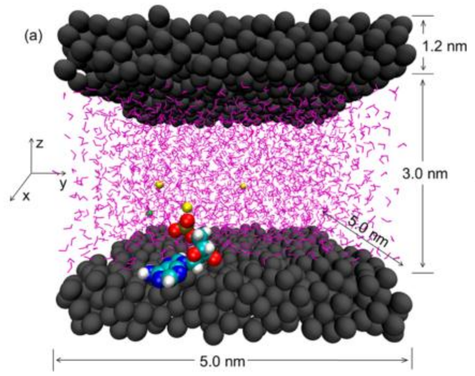

Figure 3: Simulation of DNA mononucleotide traveling through nanochannel

Materials:

- Computer Systems/Programs- Ubuntu, GROMACS MD package, VMD
- Simulation:
  - Simulated DNA strand
  - Enzyme (possibly λ-exonuclease)- used to cut the strands of DNA into mononucleotides
  - Simulated wall polymer material- poly(methyl methacrylate), PMMA
  - Simulated electrodes in polymer- used to identify passing of mononucleotide

Results/Things Learned:

- The goal of using a model of a mononucleotides being sent through a nanoslit is viable to decipher a selected segment of the genome.
- The mononucleotides flight times are directly related to their hydrophobic properties;
  * The more hydrophobic, the less adsorption and interaction with the wall will occur, resulting in a shorter flight time.
- The order of flight times of the mononucleotides from shortest to longest was found to be: C,G, A, T
- The simplified wall parameters simulated in the original research occasionally result in misordering of the genome sequence and are not able to be replicated in a lab setting (due to high velocity/ simplified walls)

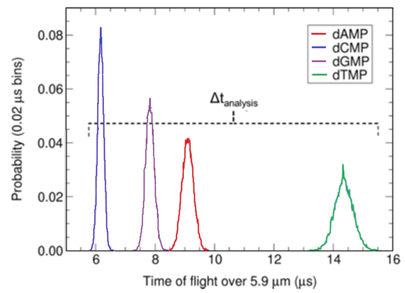

Figure 4: Plot displaying the flight times of each mononucleotide over 5.9 micrometers

Background:

- Proven theorems define the physical and chemical interactions that exist and define a liquid's motion (specifically Stoke's law and the Fluctuation-Dissipation theorem)
- At a molecular level the interactions that exist between nanoparticles and walls do not correlate with the general continuum hydrodynamic theorems
- While moving in the proximity of a wall, nanoparticles suspended in liquid experience a drag force (shown in Fig. 1)
  - In proximity of less than one molecular radius, the drag force values calculated through molecular simulations diverge from predicted hydrodynamic equation results
  - Simulations performed by researchers including Andreas Fuchs and Sivakumar Challa have demonstrated that :
    * Divergence in force values are due to the rapid dissipation of fluid molecules in the space between the wall and nanoparticle
    * Relations exist between specific simulation properties (wall type and particle velocity) and the resulting fluid drag properties
- Simulation properties must be repeatedly tested to produce accurate and realistic testing data
- Mononucleotides being sent through the nanochannel in simulation experience physical interactions due to both general hydrodynamics and their chemical composition
    * Specifically their hydrophobic properties attributed to the chemical properties of the nitrogenous base: *Adenine, Guanine, Thymine, and Cytosine* (shown in fig 2)
- Nucleotides travel through the channel at different rates due to their varying levels of hydrophobicity

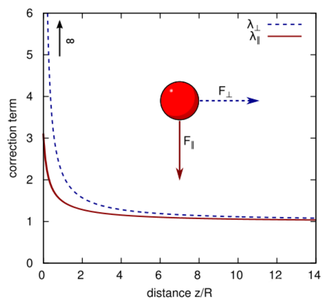

Figure 1: drag forces displayed during motion with respect to a wall (perpendicular and perpendicular) [2]

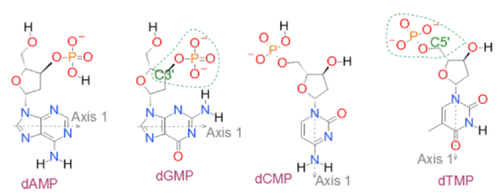

Figure 2: Chemical composition of nucleotides sent through channel [1]

Conclusion:

- The simulations can, on average, correctly identify small segments of a simulated genome in simplified form
- Numerous simulation trials must still be performed to construct a simulated wall materials which not only provide the desired adsorption and desorption, but also can be replicated in a real life lab situation.
- The process of developing an effective and manufacturable wall will likely result in further extensive testing and manipulation of the wall properties.

References:

1. *Distinguishing Single DNA Nucleotides Based on Flight through Nonoslites*, Brian R. Novak, Dorel Moldovan, Dimitris Nikitopoulos, Steven A. Soper, Journal of Physical Chemistry"
2.*Molecular Dynamics Simulations of Nanoparticle Interations with a Planar wall,* Andreas Fuchs, David Kauzlaric, Andreas Greiner
3.*Molecular Simulations of Lubrication and Solvation Forces,* Sivakumar R. Challa, Frank Van Swol, "Physical Review E. 73"

Acknowledgements:

NSF EPSCoR Cooperative Agreement EPS-1003897, Louisiana Board of Regents, NSF Career Award CBET-1253075