Molecular Dynamics Study of a Rapid DNA Sequencing Device

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Outline

• Purpose of the project
• Possibilities in device analysis
• Simulation details and results using UFF for metal/non-metal interactions
• Simulation details and results using ECD for metal/non-metal interactions
• Comparison of results
• Future endeavors
Purpose

- Demonstrate through molecular dynamics that a novel nanotechnology concept developed for rapid DNA sequencing is theoretically plausible.
- Evaluate various conditions and device properties to determine their relationship with transport properties of the DNA strand.
Device Concept

- High-throughput/low-cost genomic screening device
Nucleotide Identification

• Idealized ss-DNA translocation through nanopore with gold electrodes


Analysis of Device Properties

• Use molecular dynamics to study transport properties and conformational motion of DNA
  – Using a code called LAMMPS* (Large-scale Atomic/Molecular Massively Parallel Simulator)

• “Experiment” with device properties
  – Use of electric fields to control DNA movement through detection gate
  – Length of DNA strand (possible effect on motion through detection gate)
  – Solvent viscosity effects on DNA motion
  – Gap distance between nodes (2-5nm)

Nanoscale Device

- 20.7nm x 14.4 nm x 5nm
- Mica surfaces containing copper nodes and solvated ss-DNA
- 2.87 nm gap in nodes
- 132697 atoms in total
Simulation Details

• Periodic in x and y direction, slab geometry in z direction
• Equilibration period of 1 ns
• NVT ensemble at 300 K with Nosé-Hoover thermostat
• Velocity-Verlet algorithm at 2 fs time step
• Pair potentials
  – DNA- CHARMM27 all hydrogen
  – Copper- UFF
  – Mica- CLAYFF
  – Water- TIP3P
• Mica surfaces and nodes considered rigid bodies
• Single-stranded DNA of 16 base pairs
  – 8 consecutive cytosines followed by 8 consecutive thymines
Controlling the Position of DNA

- Need to determine the magnitude and duration of an applied electric field to move the DNA strand through the electrode gap at a rate of approximately 1 base pair per nanosecond to microsecond (1-2 Å/ns to μs)
Possible Applied Fields

- Initial simulations performed with a uniform applied electric field
  - 25 pN electrical driving force experimentally sufficient (~0.02 V/Å)
- More complex applied fields, such as pulses, likely necessary to control DNA translocation through the electrode gap
  - Holding pulse to align DNA strand also necessary in practice
UFf Potential (0.005 V/Å)

QuickTime™ and a YUV420 codec decompressor are needed to see this picture.
UFF Potential (0.01 V/Å)

QuickTime™ and a YUV420 codec decompressor are needed to see this picture.
UFF Center of Mass Study
Metal/Non-metal Interactions

- A significant shortcoming of the initial simulations is the inadequate interaction potential between metal and charged atoms.
- Current implemented potentials result in hydrophobic metallic surfaces creating low density regions around the electrodes.
Electrode Charge Dynamics*

- Accounts for the varying charge density by representing the valence electrons with a diffuse negative Gaussian charge-density distribution and using a fixed positive point charge at the center to represent the nucleus and core electrons.
- Coulombic potential is supplemented by a modified Morse potential.
- Difficulty lies in integrating the ECD method into the time evolution scheme of the MD code, as the diffuse charge varies with time.

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- Mica surfaces and nodes considered rigid bodies
- Single-stranded DNA of 16 base pairs
  - 8 consecutive cytosines followed by 8 consecutive thymines
- Box size slightly shorter in the x-direction compared to UFF simulations (15.7 nm x 14.4 nm x 5 nm)
ECD Potential (0.005 V/Å)

QuickTime™ and a YUV420 codec decompressor are needed to see this picture.
ECD Center of Mass Study

![Graphs showing center of mass study results](image)
• Velocities divided into nanogate or bulk regimes within the device
• The use of the ECD method results in slower translocation through the nanogate than bulk velocity*. 
• UFF behavior at the nanogate aligns with bulk behavior.
• Large magnitude field likely in the non-linear electrophoretic response regime

• Systems equilibrated without the DNA molecule in place under same conditions as previous simulations were used for a comparison of density near the metal.

• UFF clearly resulted in an unreasonably low-density region near the nanogate.

• ECD resulted in hydrophilic electrodes; however, the center of the nanogate resembled appropriate bulk density.
Summary of Observations

- ECD has proven to be a more physically appropriate metal/charge potential though the translocation results of the applied field study are less definitive.
- Longer production runs should be performed to more accurately determine the behavior of the DNA molecule at low magnitudes, though initial results seem to indicate control of the molecule through applied fields is possible.
Future Endeavors

- Fit the ECD potential to platinum and gold
- Further investigation of transport properties resulting from device specifications
- Combine classical molecular dynamics simulations with *ab initio* calculations of differences in electron transport across the nanoscale gap as different base pairs pass through the gap
- Ultimately, the experimental fabrication of an actual detection device
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