DNA Sequencing using nanopores

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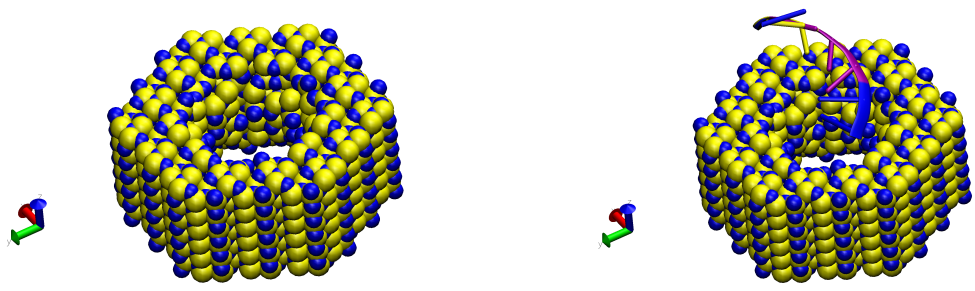
1 Introduction and motivation

Nanopores, nanoscale holes that allow the passage of single molecules, have emerged as a powerful tool in the field of molecular biology and nanotechnology. These tiny structures are particularly valuable for their application in DNA sequencing, where the passage of DNA molecules through a nanopore can be monitored by measuring ionic currents. This report presents a detailed analysis of the ionic current passing through a nanopore in two different scenarios: with a DNA chain present and without a DNA chain. By comparing these scenarios, we aim to elucidate the impact of the DNA molecule on the ionic current, which is critical for understanding the fundamental mechanisms of nanopore-based DNA sensing.

To achieve this, we utilize data provided by an official tutorial and conduct our analysis using two state-of-the-art molecular dynamics software packages, VMD (Visual Molecular Dynamics) and NAMD (Nanoscale Molecular Dynamics). These tools enable us to perform comprehensive simulations and visualizations, providing insights into the behavior of the system at an atomic level. Furthermore, we extend our analysis to investigate how variations in temperature affect the system under different electric field strengths. This aspect is crucial as it mimics real-world conditions where temperature fluctuations can influence the performance and accuracy of nanopore-based devices.

2 Simulation parameters and equations

As commented before, we are going to perform all the simulations in two different scenarios. The system will be the same for both cases, but in the first scenario, there will be a nanopore with no molecule passing trhough it, and in the second scenario there will be a DNA chain passing trhough the nanopore. We can see both cases on Figure 1.



(a) (b)

Figure 1: (a) Empty pore. (b) Pore with DNA chain.

To prepare both systems, the tutorials gives all the files needed. First, we create the base material, where the pore is going to be "drilled". This material will be silicon nitride (Si_3N_4). In order to buil this material, the tutorial starts from its unit cell, then repeating it to create a membrane, and finally drilling the pore onto this created membrane.

For the pore, we first generate the coordinates file (`.pdb`) and the we generate the structure file (`.psf`) using topology parameters, also given by the tutorial.
Then, a solvation box is added and cut to the system to match the pore hexagonal geometry. Also, the tutorial calibrates the force field for getting our Si_3N_4 model to reproduce experimental data for just one property: the dielectric constant. To determine the dielectric constant, the tutorial applies an electric field to a block of Si_3N_4 with no free surfaces and measure the electric dipole moment.
For the case where the nanopore is not filled we have our `.pdb` and `.psf` files ready to do the simulations. Nonetheless, for the case where there is a DNA chain crossing the nanopore, we may add this chain to the files.
This process consists on adding a DNA structure to the nanopore, then separating the chains to have a single-straned DNA (ssDNA).
With `.pdb` and `.psf` files ready, we may start preparing our system in order to perform our desired current measurements. For achieving this, we will run some NAMD scripts with different purposes:

- The first NAMD script minimizes the energy of the system. This is achieved by doing a 201 steps simulation with a 1 fs time step.
- The second NAMD script raises the temperature of the system from OK to 295K, keeping the system at a constant voltage. This is achieved by doing a 500 steps simulation with a 1 fs time step.
- The third NAMD script is the one use for the system equilibration, maintaining a constant pressure and using a Langevin thermostat. This is achieved by doing a 1000 steps simulation with a 1 fs time step.

Now we have our system ready to perform the simulation in order to calculate the current passing through the nanopore.
Before doing that, we have to calculate the value of the electric field we want to apply during the simulation. The tutorial tells us to use a 20V potential difference, but for this value the temperature of the system is expected to increase constantly and not stabilize. For the sake of completeness in this study, The values on Table 1 of electric field were used during the simulations:

ΔV, $[V]$	empty nanopore E_z, $[V/\text{Å}]$	DNA nanopore E_z, $[V/\text{Å}]$
2	1,030	0,711
10	5,152	5,557
20	10,304	7,114

Table 1: Electric Field values used on simulations for the two scenarios.

The values above have been calculated using the following equation, provided by the tutorial:

$$E_z = -23,060549 \frac{\Delta V}{l_z} \left[\frac{V}{\text{Å}}\right],$$

where $l_z = -c_z$, a parameter that we can check on `.xsc` files for both situations ($l_z^{empty} = -44,7598\text{Å}$ and $l_z^{DNA} = -64,8282\text{Å}$.

3 Results and Discussion

First, we can plot the results for the current measurements when applying a $\Delta V = 20V$, $\Delta V = 10V$ and $\Delta V = 2V$. We can see it on Figure 3.

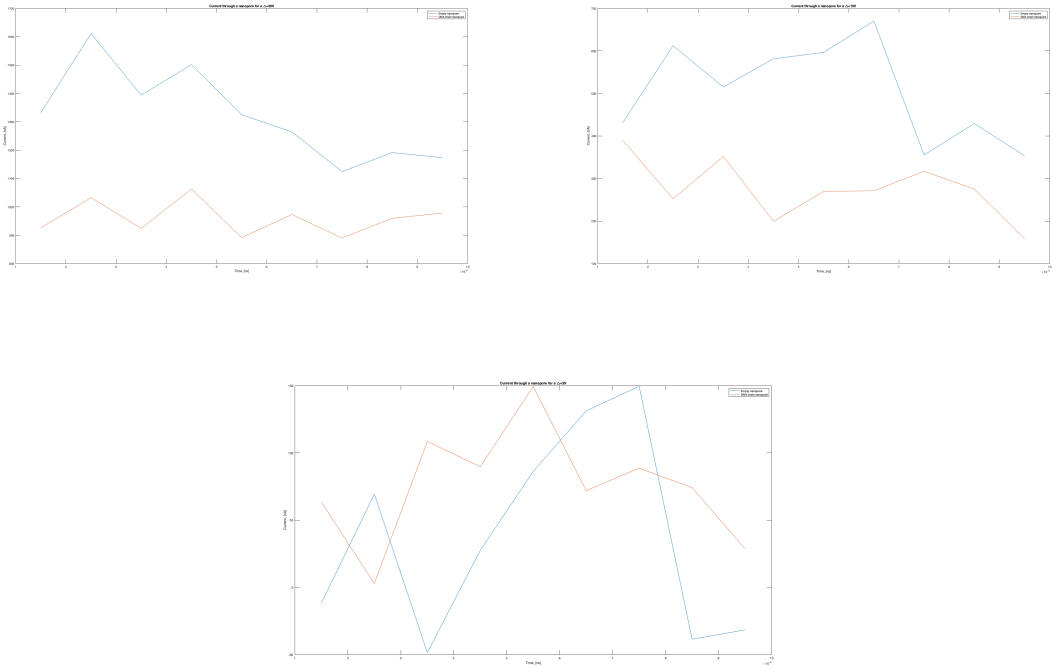
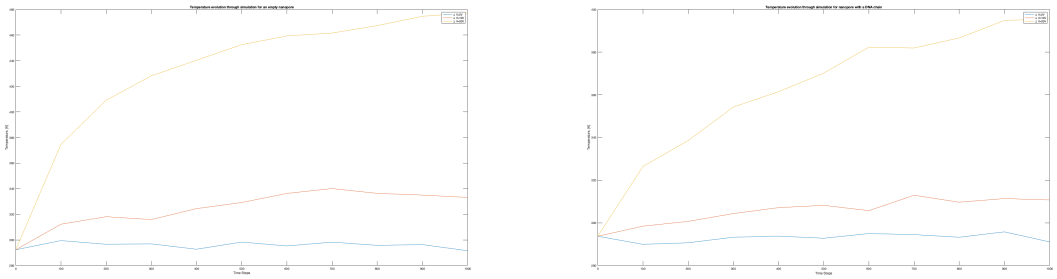


Figure 3: Current through a nanopore for (a) $\Delta V = 20V$, (a) $\Delta V = 10V$ and (a) $\Delta V = 2V$

We can clearly see that, for the first two cases ($\Delta V = 20V$ and $\Delta V = 10V$) the mean value of the current ($I_{20}^{empty} = 1324,4nA$, $I_{20}^{DNA} = 959,9nA$, $I_{10}^{empty} = 505,2nA$, $I_{10}^{DNA} = 276,2nA$) is higher when the nanopore is empty. Nonetheless, for the case where $\Delta V = 2V$ the mean value of the current ($I_{2}^{empty} = 37,1nA$, $I_{2}^{DNA} = 75,3nA$) is higher when there is a DNA chain in the nanopore.
Now, we can see how the temperature changes throughout the simulation. We can compare the temperature evolution for the three different values of ΔV and for our two different scenarios. We see that in Figure 4



(a) (b)

Figure 4: Temperature evolution for (a) empty nanopore and (b) nanpore with DNA chain.

It is notorious how temperature evolution stabilises when the applied potential difference is lower for both scenarios, as we can see above.

4 Conclusions

Once the analysis has been done, we can stand out two main conclusions about the results:

- The current through a nanopore is higher when the nanopore is empty than when there is a DNA chain inside it. Although, some results may outstand different conclusions, more simulations should be done with more different values of ΔV.
- The temperature of the system, with or without the DNA chain on the nanopore, tends to be more constant when the potential difference is lower, which may sound obvious, because for high ΔV the system atoms move more rapidly and the vibrations of its electron makes the temperature to raise.

5 References

[1] Aksimentiev, A., & Comer, J. (2007, May). Bionanotechnology Tutorial. Theoretical and Computational Biophysics Group.