Isha Saini & Cesar Sotero

Project 1A: DNA biopolymer confinement and escape (molecular dynamics)

1) one paragraph on scientific background/motivation

Importance of molecular dynamics:
Understanding the importance of molecular dynamics (MD) gives us insight into how molecules behave such as proteins, DNA, RNA, and lipids. Molecular dynamics allows us to understand their structure, conformational changes, biological function, and interactions. MD simulations provide detailed information of target proteins that can be used for drug delivery by identifying binding sites,and binding affinities, which is important for drug delivery. This accelerates the drug development process and reduces the need for costly experimental screening (Bunker, A., & Róg, T. 2020). This article expands the role of MD as a design tool in drug delivery. Molecular dynamics is valuable for understanding enzyme mechanisms, drug delivery, and understanding disease pathways.

2) two to three objectives of increasing complexity

- Understand MD simulations of DNA
- Understand the parameters that affect the mechanisms of how our MD simulations will behave, such as ligand binding. As well as how certain parameters may shift when protein folding occurs.

3) a description of the methods you will use for each objective.

- To understand MD simulations of DNA we will initially run a code that was provided by Dr. Kinjal Dasbiswas, this is to get us started with a base line and understand the parameters affecting DNA MD simulation and play around with these. This is to understand the mechanics and behavioral changes in DNA.
- To understand how parameters shift when protein folding occurs we want to observe how our simulated DNA/RNA affects parameters when DNA/RNA escapes a confinement, whether there are any changes in length or bonds. One example that can be used for RNA could be MD simulations of tRNA (McDowell, Elizabeth S., etc. 2007) where they observe at Yeast tRNA stability of a 500 ps simulation of tRNA molecule. Some limitations by MD simulations that can be considered are sampling limitations which if we run longer simulations there may be force field deficiencies, as well as only having approximations of force fields.

Backup Plan:

A backup plan would be to simplify the parameter that we want to control. Which is going to be the hardest part. Once we learn how these parameters affect DNA MD simulations, the obstacle we might run into the parameters we chose. If we face this, we might change these parameters.

Cited Papers:

Bunker, A., & Róg, T. (2020). Mechanistic Understanding From Molecular Dynamics Simulation in Pharmaceutical Research 1: Drug Delivery. *Frontiers in molecular biosciences*, *7*, 604770. https://doi.org/10.3389/fmolb.2020.604770

McDowell, S. E., Spacková, N., Sponer, J., & Walter, N. G. (2007). Molecular dynamics simulations of RNA: an in silico single molecule approach. *Biopolymers*, *85*(2), 169–184. https://doi.org/10.1002/bip.20620

We used ChatGPT to get a quick background of what we need to do in the project. This guided us in the direction that we might take as well as using Dr. Kinjal Dasbiswas poly1.lam script that can be found in catcourses.
Part 1: Setting up the DNA double helix in LAMMPS

To set up the DNA double helix in LAMMPS, we'll first define the parameters of the system, such as bead types, spring constants, dimensions, and the slit width. Then, we'll create the input file for LAMMPS to simulate the system.

```bash
# LAMMPS input script for simulating DNA escape from confinement

# Define bead types
atom_style bond
bond_style harmonic
pair_style lj/cut/coul/cut 10.0

# Set up dimensions
boundary p p p
units lj
atom_modify sort 0 0.0

# Define parameters
variable N equal 100  # Number of beads per helix
variable slit_width equal 1.5  # Width of the slit

# Create atoms for the double helix
region box block 0 10 0 10 0 20
create_box 2 box
lattice fcc 0.85
region helix1 cylinder z 0 0 5 5 units lattice
region helix2 cylinder z 0 0 5 5 units lattice
create_atoms 1 region helix1
create_atoms 2 region helix2

# Define bonds for the double helix
bond_coeff 1 harmonic 100.0 1.0
bond_coeff 2 harmonic 100.0 1.0

# Create walls with a slit
region slit block INF INF INF INF INF ${slit_width}
```

```
group slit_region region slit
fix 1 slit_region wall/reflect zlo EDGE zhi EDGE

# Define interactions
pair_coeff 1 1 1.0 1.0
pair_coeff 2 2 1.0 1.0
pair_coeff 1 2 1.0 1.0

# Output settings
thermo_style custom step atoms
thermo 100
dump 1 all custom 100 dump.lammpstrj id type x y z

# Run simulation
timestep 0.01
run 1000
```

Part 2: Running the MD simulation and analyzing DNA escape
After setting up the simulation, you can run it using LAMMPS. Once the simulation is complete, you can analyze the trajectory files to determine what fraction of the DNA polymer escaped confinement. This analysis can involve tracking the position of the DNA polymer over time and comparing it to the position of the slit to determine if any part of the polymer has crossed the slit.

Part 3: Adding solvent for more realistic simulations
To make the simulation more realistic, you can add solvent molecules around the DNA polymer. This can be achieved by randomly placing solvent particles (e.g., water molecules) around the DNA double helix and simulating their interactions using appropriate force fields. This addition allows for the consideration of hydrodynamic effects, such as the stirring of water by the fluctuating DNA polymer, which can influence the dynamics of the system.
To include solvent molecules, you would modify the LAMMPS input script to create solvent particles, define their interactions with the DNA polymer (e.g., using Lennard-Jones and Coulomb potentials), and potentially simulate fluid flow using techniques such as dissipative particle dynamics or smoothed particle hydrodynamics. This would provide a more realistic representation of the behavior of DNA in an aqueous environment.