CSCI 4314/5314 Dynamic Models in Biology
Homework Set 1

Coarse Grained Simulation of a Protein (50 points)

This homework will illustrate a simple example of protein structure prediction through a dynamics simulation. In the simulation, you will implement a two dimensional coarse grained model of a protein which consists of a chain of N amino acids. Each amino acid a_i is represented by a circle connected to amino acids a_{i-1} and a_{i+1} via an harmonic spring potential:

$$U_{ij,S}(r) = \frac{k}{2}(r_{ij} - r_0)^2 \tag{1}$$

where $U_{ij,S}$ is the spring potential for a pair of amino acids i and j separated by a distance r_{ij}, k is the spring coefficient, r is the current distance between the connected pair of amino acids, and r_0 is the equilibrium distance for the spring potential. Additionally, each pair of amino acids a_i and a_j interact via the Lennard-Jones potential

$$U_{ij,LJ} = 4\epsilon \left[\left(\frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}} \right)^{6} \right] \tag{2}$$

where $U_{ij,LJ}$ is the Lennard-Jones potential for a pair of amino acids i and j separated by a distance r_{ij}, σ_{ij} is the distance at which the potential reaches its minimum, and ϵ is the depth of the potential well. An initial velocity is assigned to each atom, and Newton's laws are applied at the atomic level to propagate the system's motion through time:

$$x_i(t+1) = x_i(t) + \Delta t F_x(t) + T\zeta \tag{3}$$

where $x_i(t+1)$ is the x position of an amino acid at time $t+1$, $F_x(t)$ is the force acting along the x position at time t, Δt is the integration time step, T is the temperature and ζ is random number taken from a uniform distribution between 0 and 1. Similarly, the new y positions of each amino acid are calculated as:

$$y_i(t+1) = y_i(t) + \Delta t F_y(t) + T\zeta \tag{4}$$

The following starter code can be found on Canvas; Feel free to modify the code in any way you prefer:

- Matlab version, file name polymer_MD_Matlab.m
- Python version, file name polymer_MD_Python.py

(1) Calculate the size of the folded protein as a function of time, using the radius of gyration property:

$$R_g(t) = \frac{1}{2N^2} \sum_{i=1}^{N} \sum_{j=1, j\neq i}^{N} (\mathbf{r}_i - \mathbf{r}_j)^2 \tag{5}$$

where N is the number of amino acids in the protein chain, $\mathbf{r}_i$ and $\mathbf{r}_j$ are vectors describing the position or amino acids a_i and a_j, respectively. Prepare a plot of the radius of gyration $R_g(t)$ as a function of time t, for each one of the chain lengths: $N = 25$, $N = 10$, and $N = 5$. Set the rest of the parameters to: $T = 0.05, \Delta t = 0.0005, k = 5, r_0 = 1.122, \epsilon = 1$ and run your simulation for 200000 steps. (25 points)

(2) Set $N = 25$ and explore the following LJ potential strengths: $\epsilon = 1$, $\epsilon = 0.5$, $\epsilon = 0$. Prepare a plot of the radius of gyration $R_g(t)$ as a function of time t, for each ϵ value. Set the rest of the parameters to: $T = 0.05, \Delta t = 0.0005, k = 5, r_0 = 1.122$ and run your simulation for 200000 steps. (25 points)

Paper Review (50 points)

The paper "Design and self-assembly of two-dimensional DNA crystals" by Winfree *et. al* published in Nature more than 20 years ago, was a seminal approach to molecular structure design. The paper can be found on Canvas under Files/Paper Reviews/Winfree_Nature_1998.pdf.

For this part of the homework set, download the paper from Canvas, read it carefully and write a couple of sentences on each of the following items:

- What do you feel the main contribution of this paper is? (10 points)
- What's the essential principle that the paper exploits? (10 points)
- Describe one major strength of the paper. (10 points)
- Describe weakness of the paper. (10 points)
- Describe one future work direction you think should be followed. (10 points)

The point of the reviews is demonstrate your understanding of the paper. It is not to regurgitate the paper but to identify what *you think* is the key concept to learn from the paper and what your opinion is of the strength/weakness of the idea and or paper. We are looking for thoughtful and insightful reviews, that demonstrate depth in your reading and thinking about the paper.