BMT-72106 Cellular Biophysics

Project Work 1 Option 1: Intracellular Diffusion Model

Deadline 7.4.2019 at midnight

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In this project work, you will study molecular diffusion. The project consists of two parts: theoretical consideration of diffusion and implementation of model of diffusion by writing a small simulation program. There is no requested format for the report or minimum length, as long as you answer the questions and include the requested things. Remember to cite your references in the text if you use them!

Task 1. *Theory of Diffusion*

Diffusion in molecular scale can be described as a random walk process. The mean-square diffusion distance or displacement of a molecule in two dimensions after time t can be calculated from equation

$$\langle x^2 \rangle = 4Dt, \tag{1}$$

where $\langle x^2 \rangle$ is the mean-square diffusion distance and D is the diffusion coefficient. For a small molecule (under 1 kDa) the diffusion coefficient at body temperature is around 5×10^{-10} m^2/s. The most well known equation to relate the molecular size and diffusion coefficient is the Stokes-Einstein equation:

$$D = \frac{k_B T}{6\pi\eta R}, \tag{2}$$

where k_B is Boltzmann's constant, T is the absolute temperature, η is the dynamic viscosity and R is the radius of the molecule. This equation works quite well for large spherical molecules.

Consider the following questions:

a) What can you say about the importance of diffusion inside a cell based on the time scale of diffusion from one side of the cell to the other? What about over large distances (> 1 cm)? What are the advantages and disadvantages of diffusion in comparison with the active intracellular transport processes?

b) What drives diffusion and why is the motion random? Why does the temperature affect diffusion as shown in equation 2?

Task 2. *Diffusion Simulation*

In this part, you will write a Monte Carlo simulation code to study diffusion of a ligand while it is trying to find enzymes inside a cell.

The simulated system consists of one ligand and multiple enzyme molecules in a 3 dimensional box of the size of $50 \times 50 \times 50$ nm^3. The starting position for the ligand is in the middle of the box, and the enzyme molecules are located randomly within the box. The enzymes are static as the ligand diffuses. In 3D, the ligand can diffuse into 6 different directions with the same probabilities: 2 in each dimension, each having the probability of 1/6. The diffusion length for each diffusion step can be assumed to be 1 nm. Basically, the ligand diffuses in a 3D grid randomly step by step until the simulation stops. This happens either when the ligand diffuses to a neighboring position to an enzyme (distance between the ligand and any of the enzymes is 1 nm) or when the ligand diffuses to the edge of the box.

The aim of the simulation is to find the number of enzymes there has to be in a box so that the probability of the ligand finding an enzyme is higher than it hitting the box edge. I.e. start with one enzyme molecule and increase their number until in most simulations the ligand finds an enzyme molecule.

You can use any programming language you wish. Note that you will have to run the simulation multiple times to get statistically reliable results (few thousands). This is because of the randomness of the motion; one simulation is only one possible outcome.

Provide a plot showing the number of ligands that find an enzyme and the number of those hitting the edge as a function of enzyme molecule number. Please include your code in your report as an appendix.