TUTORIAL 1

BB 101

MODULE: *PHYSICAL BIOLOGY*

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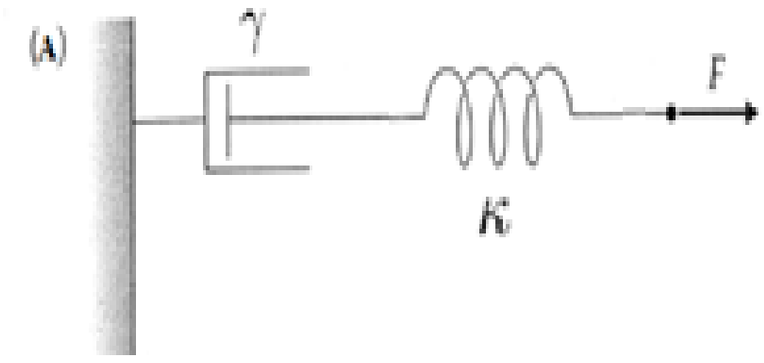
1. Consider a system consisting of a spring and a dashpot in series as shown below in (A). The stiffness or spring constant of the spring is k and drag coefficient of dashpots is γ. Initially spring and both dashpots are at rest. Suppose a constant force F is abruptly applied to this system as at t=0 and is maintained for t = T as shown below in (B), and force is then abruptly removed (i.e. F=0 for t > T), where T is an arbitrary time. Find out the expression for displacement x(t) of the system for t < T, t = T and for t > T?



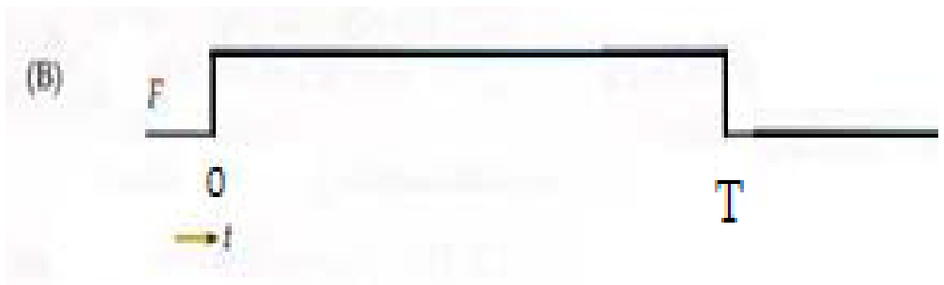
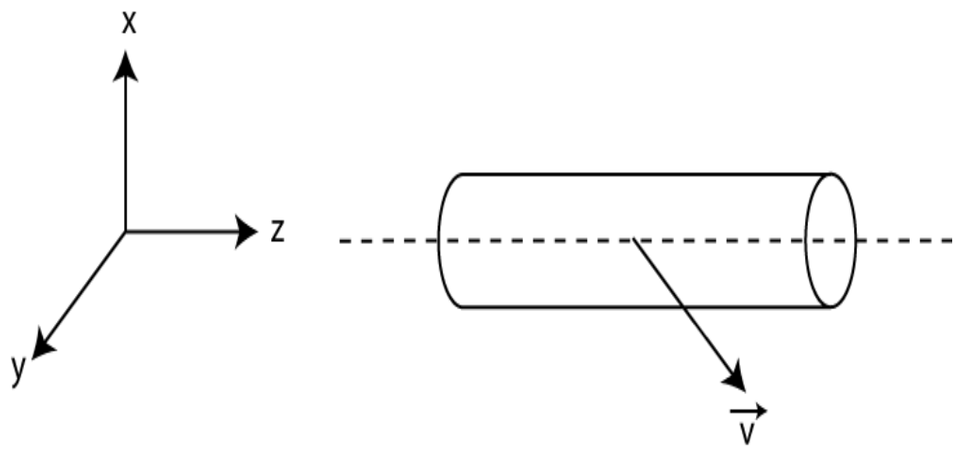


Figure Source: Mechanics of Motor Proteins and the Cytoskeleton, Jonathan Howard

2. Consider the sedimentation of a spherical bio-molecule of radius 1 nm, initially right below the surface, in an Eppendorf tube of length 2 centimeters filled with water. Suppose that density of this biomolecule is ten times that of water and this bio-molecule sediments under the effect of gravity. Further assume that this bio-molecule attains a constant velocity as soon as it starts to descend in the Eppendorf tube. Calculate the sedimentation time for this bio-molecule (Density water=1000 Kg m^{-3} and g=10m/s^2)?

3. A micron size cylindrical rod as shown below is moving with constant velocity $\vec{v}$ in x-z plane such that the angle between the axis of cylinder and velocity vector is 45^0. Consider the motion is dominated by viscous forces. What would be the angle between the direction of net drag force on the cylinder and axis of the cylinder, if drag coefficient for motion perpendicular to axis of cylinder is $\sqrt{3}$ times that of drag coefficient for the motion parallel to axis of cylinder? (Hint: Resolve velocity vector along the axis of cylinder and parallel to axis of cylinder)



4. Bacterial use flagella motor to rotate the helical flagellum to generate the propulsive force. Provide a qualitative explanation (using the result from Problem 3 of Tutorial 1) that if a thin, rigid helical rod as shown below is cranked about its helix axis at a certain angular speed then it can generate a net force propulsive force.

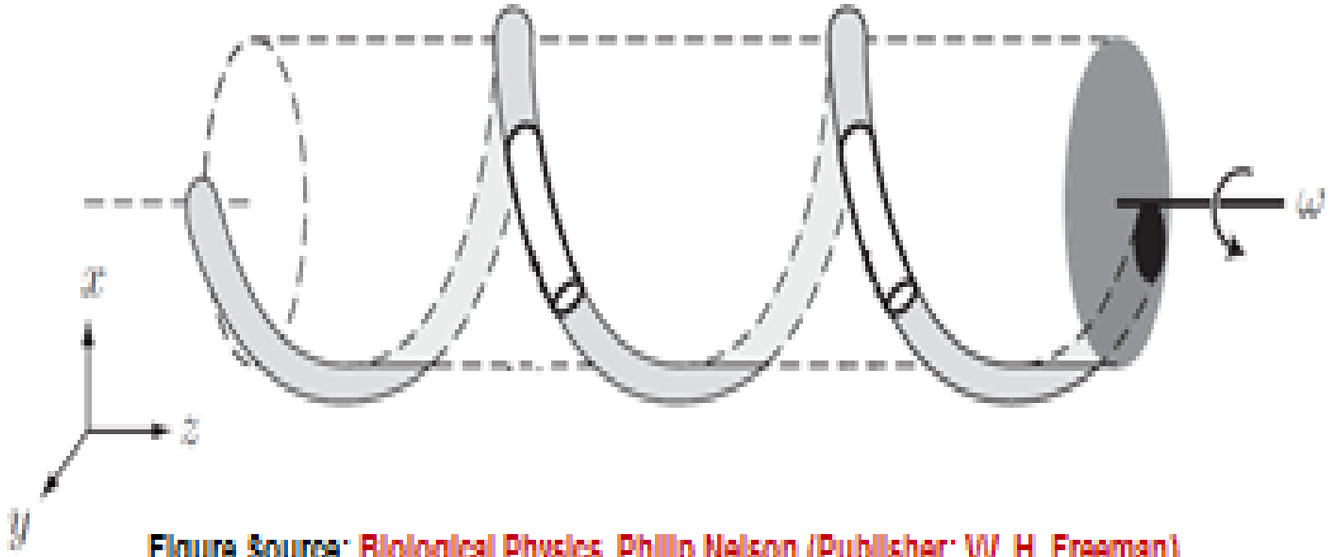


Figure Source: Biological Physics, Phillip Nelson (Publisher: W. H. Freeman)

TUTORIAL 2

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Reciprocal Motion in Newtonian Fluid

1. Consider a microscopic swimmer trying to make progress by cycling between the upward and downward strokes of its paddles as shown below. (a) On the first stroke, the paddle move downward at relative speed v, propelling the body through the fluid upward at speed u. (b) On the second stroke, the paddle move upward at relative speed v', propelling the body downward at speed u' (c) Then the cycle repeats. Assume this is low Reynolds number motion where moving the body through the fluid requires a force determined by drag coefficient γ_1 and moving the paddles through the fluid requires a force determined by a different constant γ_2. Show that reciprocal motion like this cannot give net progress in low Reynolds number environment.

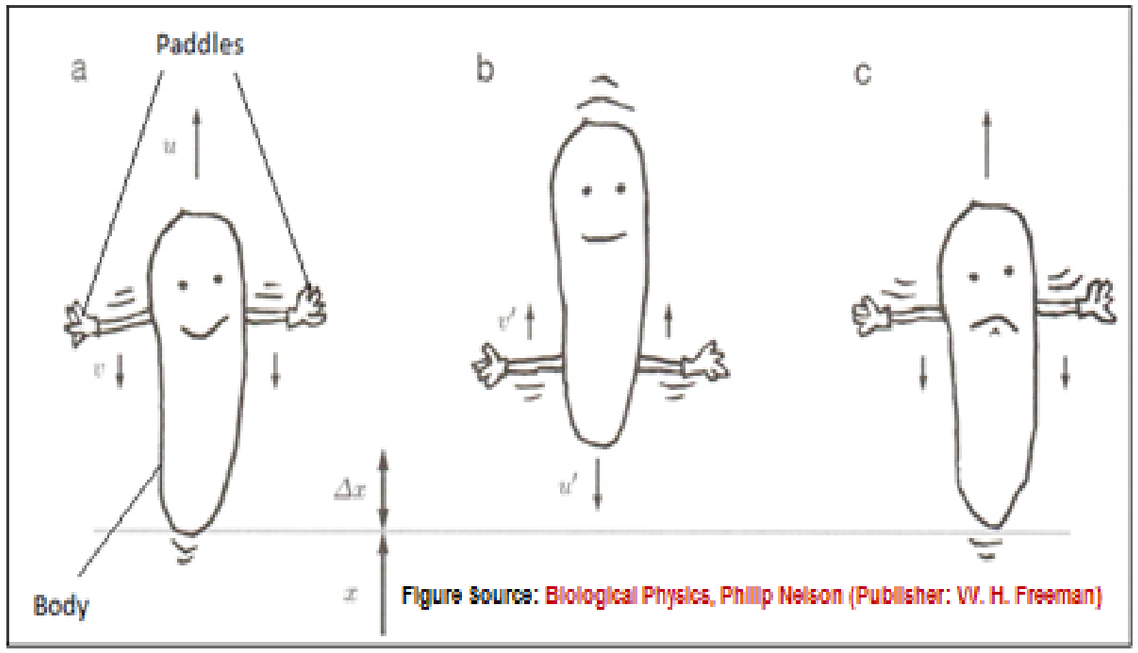

Figure Source: Biological Physics, Philip Nelson (Publisher: W. H. Freeman)

Concentration Profile

2. Solution of one dimensional diffusion equation for a substance freely diffusing with initial condition $C(x,0) = C_0\delta(x - x_0)$ is given by $C(x,t) = \frac{C_0}{\sqrt{4\pi Dt}} e^{-\frac{(x-x_0)^2}{4Dt}}$. Write down the solution of diffusion equation for a substance diffusing in presence of a perfectly reflecting wall located at $x = 0$ i.e. $\vec{J}(0,t) = 0$. Draw the resulting concentration profile in presence of perfectly reflecting wall located at $x = 0$ for $t > 0$. (Hint: Consider an imaginary source located at $-x_0$ and make required adjustment to real source).

Diffusion of drug molecules

3. Suppose that drug molecules diffuse out of a tablet (which is modelled as a thin plane wall) into a solution. In addition to diffusion, the drug molecules also undergo a chemical reaction which causes drug to deplete with time in proportion to its present concentration. The constant rate of the chemical reaction which depletes the drug molecules with time is k and D is the diffusion constant of the drug. Find out the concentration profile for the drug as a function of distance x away from the tablet wall in the solution in the steady state i.e. when concentration doesn't change with time. Show that drug will be drawn out of the tablet rapidly if it has high diffusion constant or has a high reaction rate in solution. (*Hint: Add one extra term to diffusion equation to include the effect of depletion of drug due to chemical reaction*)

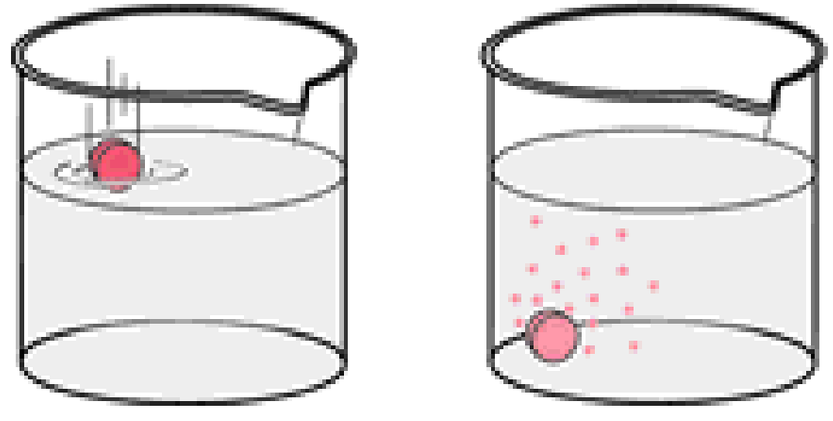

Figure Source: https://www.embibe.com/exams/diffusion

TUTORIAL 3

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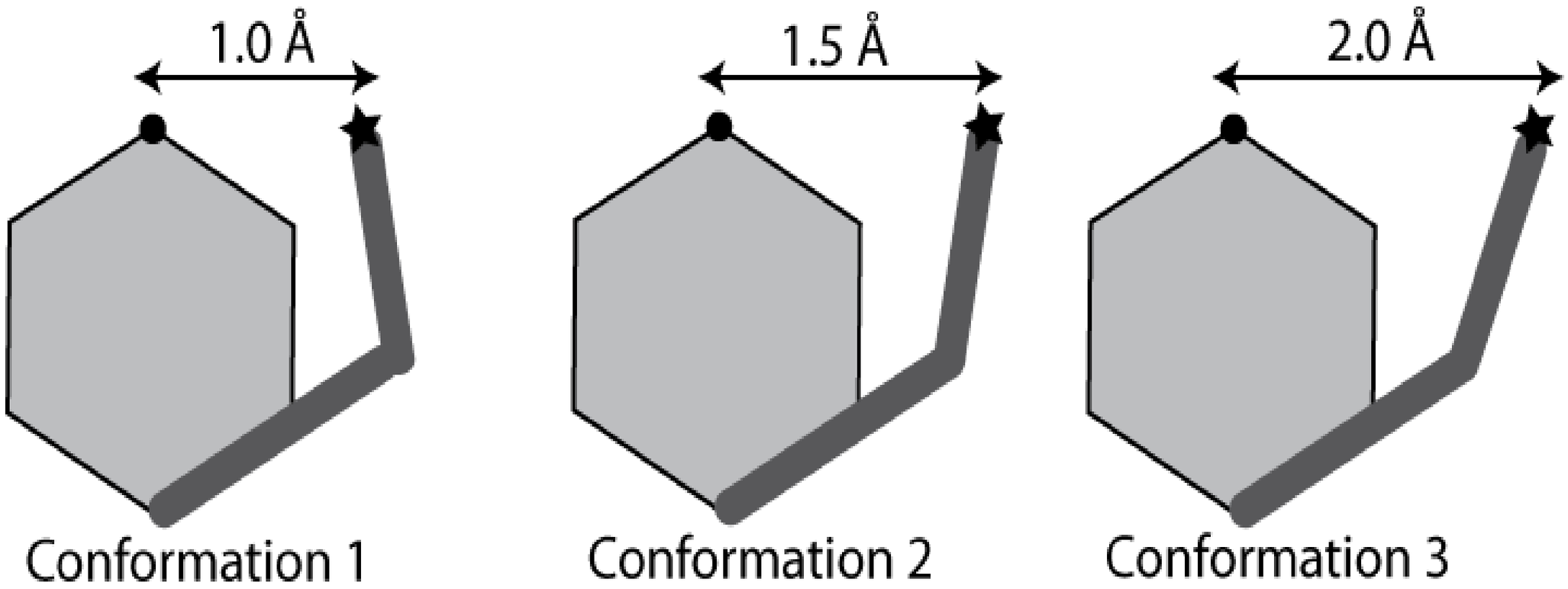
Application of Boltzmann Law and Partition Function

1. A peptide loop on a protein molecule was probed using fluorescence spectroscopy to measure the separation l from a point on the loop to a point on the protein as shown in figure below. After experiment you decide to model the loop as having following three different conformations:



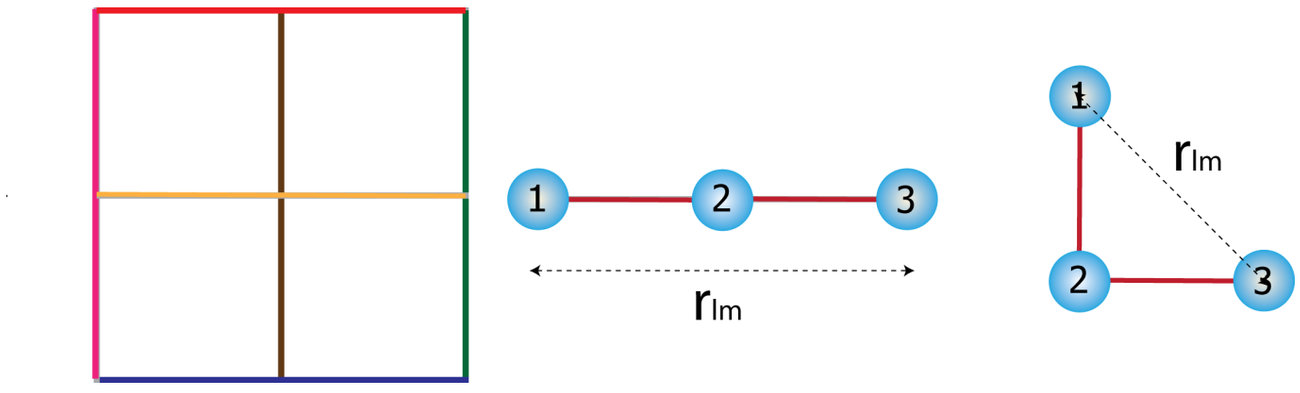
Application of Boltzmann Law and Partition Function

(1) In first conformation, the loop sticks to the side of the loop with separation l=1.0 Å; and you define this as the ground state, with energy ϵ=0 pN nm
(2) In second conformation, the loop is more distant from the protein with separation l=1.5 Å; you define this as first excited state with energy ϵ=4.14 pN nm
(3) In third conformation, the loop is far away from the protein with separation l=2.0 Å; and you define this as second excited state with energy ϵ=8.28 pN nm

Using above model, calculate following at T=300 0K:

(a) Partition function for the loop
(b) (b) Average separation i.e. $\langle l \rangle$
(c) (c) Average energy of the loop $\langle \epsilon \rangle$

2. Imagine a protein made of three identical/indistinguishable connected positive charges. The length of the bond between two neighboring charges of protein is $1\,nm$. This three-charge protein is lying on a 3×3 square lattice in 2D (or a 2D grid connecting 9 lattice sites) as shown below. Color of the grid line denote the spatial inhomogeneity such that all possible conformations/microstates become unique and are not related by rotational symmetry



The Coulomb energy of the protein, in a conformation/microstate i is given by the typical formula for energy,

$$U_i = \sum_{l=1}^{2} \sum_{m=l+1}^{3} \frac{A}{r_{lm}}$$

Where r_{lm} is the distance between charges l and m. Assume $A = 1\ k_B T\ nm$. Note that the charges can only lie on the sites of the lattice and the bonds on the edges.

(a) What is the energy of the protein in the conformation/microstate when all the three charges on a straight line?

(b) What is the energy of the protein in the conformation/microstate that is bent (non-straight; when one bond is making 90^o angle with the other one)?

(c) How many straight conformations are possible on this square lattice?

(d) How many bent conformations are possible on this square lattice?

(e) What is the probability that you will find the protein in a straight structural state or straight macrostate?

(f) What is the probability that you will find the protein in a bent structural state/macrostate?

3. Show that expression for entropy $S = k_B ln W$ is equivalent to $S = -k \sum_i p_i \, ln p_i$ if k_B is replaced by k.

4. During evolution, some genes get mutated and the resulting proteins get altered. In biology, it is very useful (and often important) to find out the DNA sequence that is “conserved" during evolution. Entropy can be a simple measure of this conservation (or the lack of it) during evolution. Let us imagine you got 10 DNA sequences (say, from 10 different organism). Each of these sequences have 3 bases as shown below.

AAT

AGT

ATA

ACG

ATT

AGT

ACT

AAC

ATT

AGT

(i) Calculate the entropy (disorder) at each position (column) using following relation

$$S = -k_B \sum_{i=1}^{M} p_i \ln p_i$$

where M is the number of different letters in each position (column) and $p_i = n_i$/N, where n_i is the number of letters of type i in the column, and N is the total number of letters in that position (column).

(ii) Calculating entropy for each position (column)? Find out which position is more “conserved" over evolution and which position is least conserved over evolution

Notes: Those highly conserved positions are likely to have some crucial role in the function/folding of the protein. This also tells you how to use information theory {theory used for communication by electrical engineers} to understand information content in biological sequences.