Physics 452: Biophysics
Midterm Exam
100 points

Problem 1: Biochemistry (15 points)

a. (3 points) List 3 organelles

Many answers are possible. Organelles on the list on our website are: Nucleus,Mitochondria,Endoplasmic Reticulum,Golgi,Lysosome

b. (4 points) List the following bonds in order of increasing strength, and give the approximate strength of the bonds in water using units of KT: Hydrogen, Covalent, Ionic, Van der Walls.

Van der Walls (0.2 KT), Hydrogen (2 KT), Ionic (6 KT), Covalent (180 KT)

c. (3 points) What type of structure are alpha helices and beta sheets? (Primary,Secondary,Tertiary, Quaternary)

Theses are Secondary Structures.

d. (2 points) How many different types of amino acids are found in proteins?

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e. (3 points) Show or describe the chemistry of how amino acids link to form a polypeptide chain.

The amine group of one amino acid binds with the carboxyl group on the second amino acid in a condensation reaction (losing an H_2O). This is a peptide bond.

Problem 2: Reading (15 points)

a. (5 points) Give a description of the helix-coil transition.

The helix-coil transition is the transition from an alpha helix structure to a random coil in a polypeptide. The energy of H-bonds holding the alpha-helix together competes with conformational entropy. The large number of H-bonds holding the alpha helix are cooperative, and lead to sharp transitions from helix to random coil as a function of temperature or environment. (Nelson 9.5)

b. (5 points) Why can't bacteria swim with a purely oscillatory motion?

At low Reynolds number, which is the regime of bacteria motion, the motion produced by a force can be canceled completely with an inverse force (Nelson 5.23,5.3)

c. (5 points) What are micelles?

Small spheres made of dozens of lipids with the hydrophobic tails in the center. (Nelson 8.4.2)

Problem 3 (20 points)

Laplace's formula relates the surface tension of a spherical object to the pressure difference across the boundary, $\Sigma = Rp/2$. A cell bursts when $\Sigma = 10^{-3}$ N m^{-1}. Given a filtration coefficient of $L_p = 10^{-5}$cm s^{-1} atm^{-1} for the membrane, estimate how long it will take before a 10 μm diameter cell containing 10 mM of NaCl will burst when it is suddenly transported from an osmotically balanced media to pure water. The membrane can be stretched with a Young's modulus of 10^7 Pa.

The osmotic pressure is p=(Δc)KT $= 10 \times 10^{-3} * 6 \times 10^{23}/(10^{-3}\text{m}^3) * 4.1 * 10^{-21}\text{Nm} = 2.5\times 10^4$ Pa
The rupture pressure is p=2Σ/R $= 2 * 10^{-3}$ N m$^{-1}/(5 * 10^{-6}\text{m}) = 400$ Pa
So the cell will rupture.

Because the cell membrane is "stretchy" it will increasingly resist expansion and the membrane will produce an increasing back pressure as it fills with water. The cell ruptures when the pressure produced by the membrane matches the rupture pressure.

Consider a small square portion on a spherical shell membrane with the size of $L \times L$. The pressure inside the cell gives rise to an overall stretching of the bilayer. The small square element will feel that it is being stretched in all directions parallel to the membrane. The young's modulus, Y, defines the relation between an applied force per unit area and the relative extension away from equilibrium. When considering stress from more than one direction, the Poisson ratio, ν, must be taken into account giving a generalized Hooke formula:

$$\frac{\Delta L_x}{L} = \frac{1}{Y} * [\sigma_x - \nu(\sigma_y + \sigma_z)]$$

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$\sigma = \frac{F}{hL}$ where h is the thickness of the membrane (5 nm). In our case we take $\sigma_x = \sigma_y$ and $\sigma_z = 0$ giving:

$$\frac{\Delta L}{L} = \frac{1}{Y}[1-\nu]\sigma$$

Since $\frac{\Delta R}{R} = \frac{\Delta L}{L}$

$$\frac{\Delta R}{R} = \frac{1}{Y}[1-\nu]\sigma$$

Using $\sigma = \frac{Rp}{2h}$, which is just Laplace's equation and taking R as R_0

$$p = \frac{\Delta R}{R_0^2}\frac{Yh}{1-\nu} = \frac{2\Sigma}{R_0}$$

$$\Delta R = \frac{2R_0\Sigma(1-\nu)}{Yh}$$

Now we need to find how long it takes for the cell to expand from R_0 to R. To estimate a time, make an approximation that the total volume flow rate into the cell is a constant and given by $Aj = 4\pi R_0^2 L_p(\Delta c)KT$.
The change in volume of the cell is:

$$\Delta V = 4/3\pi(R^3 - R_0^3) = 4/3\pi((R + \Delta R_0)^3 - R_0^3) = 4\pi\Delta R R_0^3$$

where the right most term keeps only the most significant term in the expansion. The time is then:

$$t = \Delta V/Aj = \frac{\Delta R}{j} = \frac{2R_0\Sigma(1-\nu)}{Yh}\frac{1}{L_p(\Delta c)KT}$$

Taking $\nu = 0.5$ and putting in values gives t=4s

Problem 4 (20 points)

A system contains a set of stationary receptors with a concentration of freely diffusing ligands.

a. (5 points) The ligands have a diameter of 5 nm, what is their diffusion constant? Express in $\mu m^2 s^{-1}$

$$D=\frac{KT}{6\pi\eta R} = \frac{4.1*10^{-21}J}{6\pi\times10^{-3}kgm^{-1}s^{-1}\times2.5\times10^{-9}} = 8.7\times10^{-14}m^2s^{-1} = 8.7\times10^{2}\mu m^2 s^{-1}$$

b. (5 points) There is 1 mM of NaCl present. How close must the ligand get to the receptor before there is any significant attraction?

The screening length for a salt solution is given by the Debye length, $\lambda_D = (8\pi l_B c_\infty)^{1/2}$ where l_B is the Bjerrum length, $l_B = e^2/(4\pi\epsilon k_B T)$. At room temperature l_B=0.71 nm.

At room temperature λ_D=0.31 nm/([NaCl])$^{1/2}$, therefore λ_D=10 nm.

c. (5 points) The system is contained in a 10 μm diameter cell. If a ligand is localized somewhere at t=0, how long before it is almost equally likely to find the ligand anywhere in the cell? Give your definition of "almost equally likely".

The probability of finding a particle with diffusion constant D, to be found at a distance r from it original positions after time t is $P(r,t) = (4\pi Dt)^{-3/2}e^{-r^2/(4Dt)}$. Taking, somewhat arbitrarily, the condition to be found anywhere with equal probability to be $4Dt = (2*R)^2$ where R is the radius of the cell, $t = R^2/D = \frac{(5\times10^{-7}m)^2}{8.7\times10^{-14}m^2s^{-1}} = 3$ s.

d. (5 points) K_d is 1 nM. What percentage of receptors are occupied when there is a 2 nM concentration of unbound ligand?

$K_d = \frac{[L][R]}{[LR]}$

Ratio of bound receptor to total receptor is $\frac{[LR]}{[R]+[LR]} = \frac{1}{1+\frac{[LR]}{[R]}} = \frac{1}{1+\frac{[L]}{K_d}}$

When [L] is 2 nM, ratio is 2/3 and bound percentage is 66 percent.

Problem 5 (20 points)

a. (2 points) For what is FCS an acronym?

Fluorescence Correlation Spectroscopy

b. (8 points) Draw the optical setup of an FCS system and label all the components.

see next page.

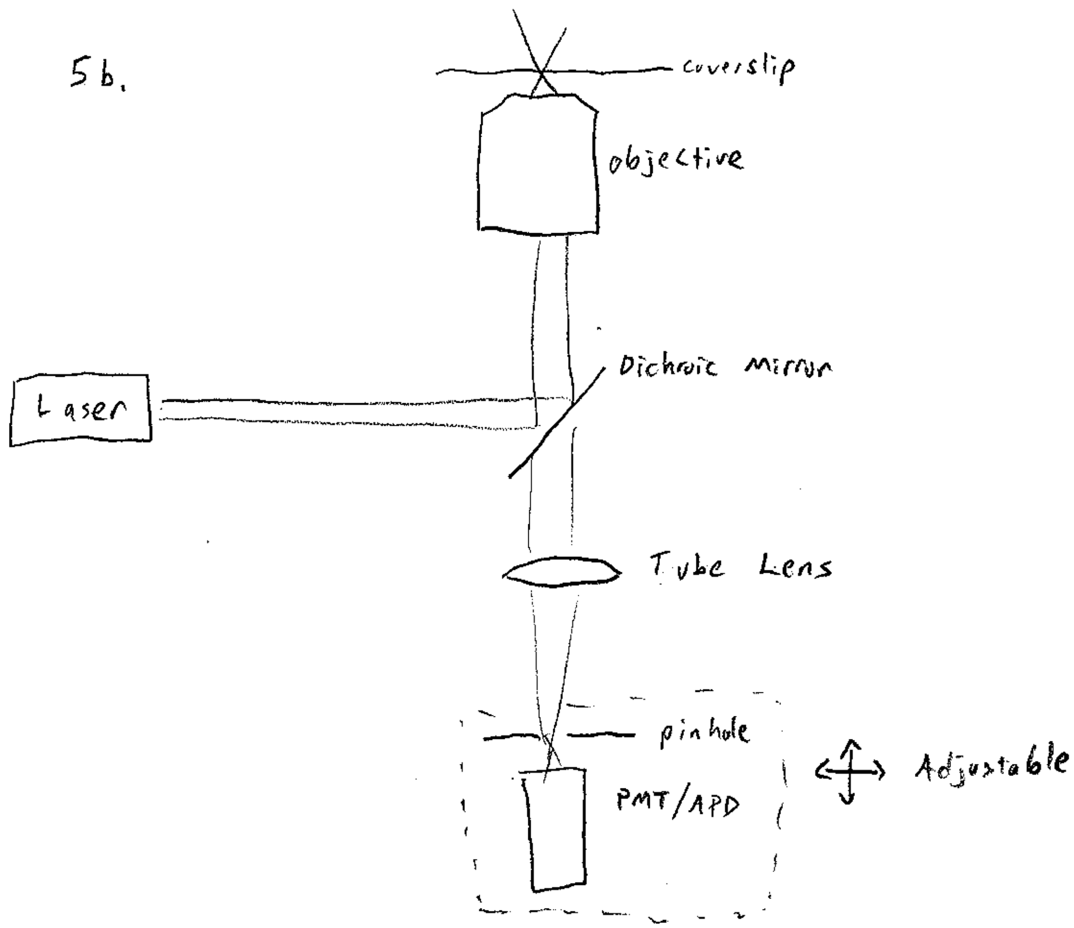
c. (10 points) The concentration of dye labeled protein in the system under study is c, the detection volume is V, and the diffusion constant of the proteins is D. Without doing a calculation, draw a rough curve of the auto-correlation. Label and discuss the parts of curve corresponding to short, long and intermediate values of τ. Draw a second curve for a system with half the concentration and twice the diffusion constant.

Short time range: The position of diffusing molecules change very little, thus the signal is nearly constant, leading to a large correlation between intensity measurements.

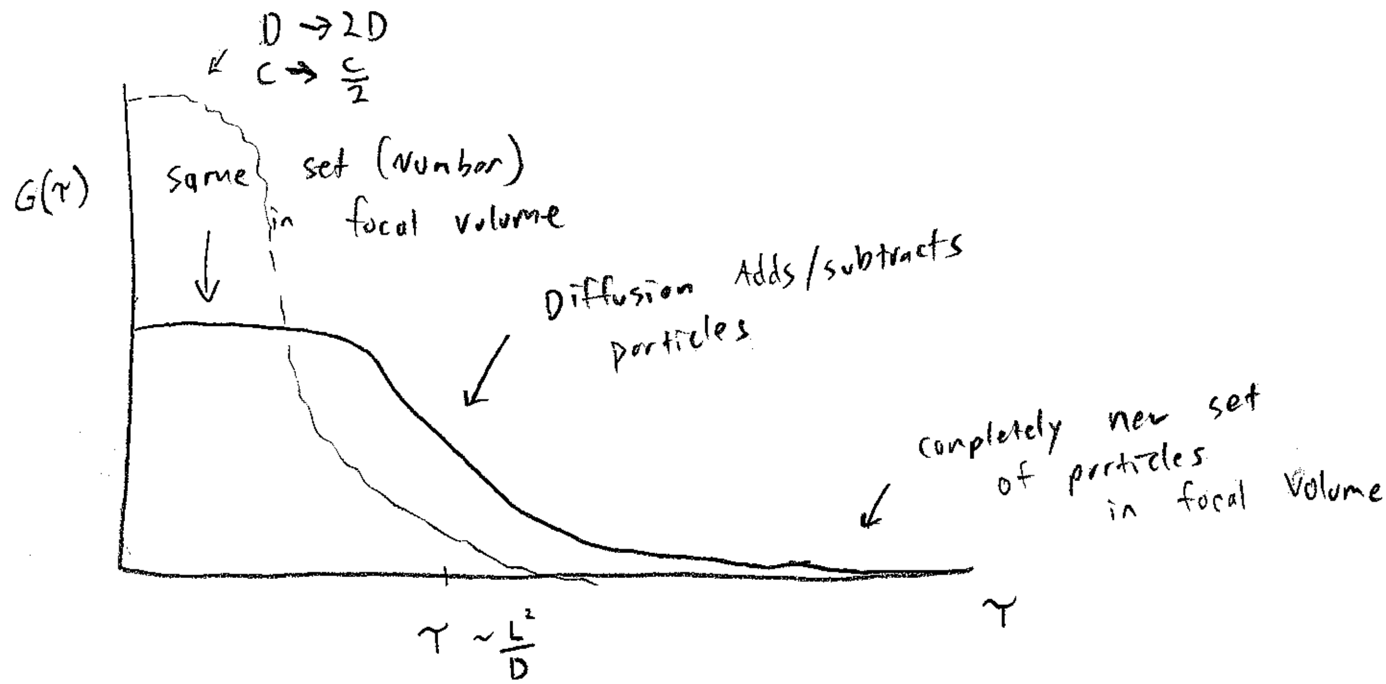
Long time range: A completely new set of particles are in the detection volume, so there is no correlation expected at long times.

Intermediate range: The approximate time it takes for a particle to diffuse out of the detection volume. Some correlation as some particles still remain in detection volume.

5b.



5c,



where L is focal volume length scale