Name:____________________________

Physics 400 Biophysics
Exam 1 – Ch. 1-7

You will have two hours to take this exam. Take the exam using only your calculator, pencil, scratch paper, and 1 sheet of notes. Do not consult any other resources. STOP at the end of the two hours. Turn in your completed exam to the table at the front of the class. Turn in your sheet of notes as well.

Note: It is always important to cite your work. These problems are adapted from a variety of sources. If you are interested I will give you the full source list after the exam.

Problem 1 – Atomic Structure→ Grade:______ out of 5 pts

One thing we would like you to remember from this class is the size of a typical atom. This size, along with the size of a cell will be immensely useful for determining the relative sizes of biological objects.

A. What is the size of an atom? 2 Angstroms in diameter

B. What is the size of a cell? ~1-10 microns

C. If you don't remember what the size of an atom is then you are in luck, because we are going to calculate it using dimensional analysis. Let's assume we want to find the size of hydrogen – interestingly the sizes of the other atoms are about the same so this will be a good estimate. The size of the hydrogen atom is set by the electron cloud around the atom, which for hydrogen consists of one electron with mass m_e=9 x 10^{-31} kg and electric charge e=1.6 x 10^{-19} C. The force that "holds" the electron cloud to the nucleus is the electrostatic force and that has an electric permittivity of free space of ε0=8.85 x 10^{-12} $C^2N^{-1}m^{-2}$. We also know that the hydrogen atom is very small so quantum mechanics are important and the value of Planck's constant will be needed; h=6.6 x 10^{-34} Js. Given that 1 J = 1 Nm and 1 N = 1 kgm/s^2, what is the size of a hydrogen atom?

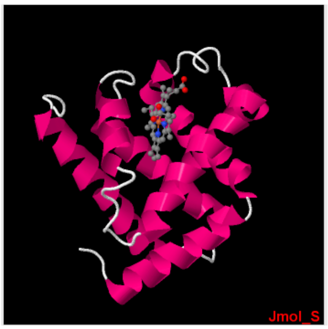
$m_e \rightarrow M$
$e \rightarrow C$
$\varepsilon 0 \rightarrow C^2T^2/(ML^3)$
$h \rightarrow ML^2/T$

$h^2\varepsilon 0/(m_e e^2) = [(ML^2/T)^2]\,[C^2T^2/(ML^3)]/([M]\,[C^2]) = L$
$h^2\varepsilon 0/(m_e e^2)$ = order of 1 Angstrom

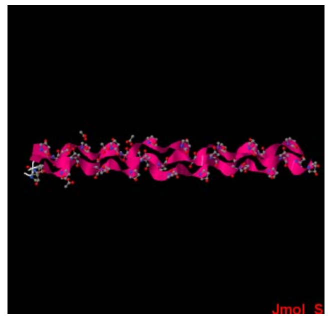
Problem 3 – Biomolecular Structure→ Grade:_____ out of 40 pts

The first biophysicists used the tools of physics to determine the structures of biological molecules. In 1958 John Kendrew found the first protein structure using x-ray crystallography; the protein is shown in (α). Now about 70,000 structures are located in the Protein Data Bank (PDB) and the field is overseen mostly by structural biology or biochemistry instead of biophysics. There are three molecules from the PDB shown below.

(α)



(β)



(γ)

A. For each of the molecules listed above describe what you know about the molecules from their structures and using this structural data make a guess as to the function. Specifically list the type of molecule(s), the structural motifs present, the size of the molecule(s), and your best guess as to the molecule's function.

α – protein with several alpha helices and a small molecule bound in its core. There is only one subunit and it is a globular protein not fibrous. It is probably some sort of enzyme that coordinates the small molecule bound in its core. It looks like it is about 3 nm across given the size of the atoms in the small molecule bound in the core. FYI - Protein is actually myoglobin and the small molecule is a heme molecule. Myoglobin is responsible for binding and carrying iron and oxygen in the muscles.

β – protein ribbon with what appears to be some small molecules around it. There appears to be three strands in the ribbon. They are not in an alpha helix, beta sheet, or loop. The structure appears to have the three strands twisted around. The molecule is about 10 times longer than it is wide, with a width of about 1 nm. The molecule is fibrous rather than globular and so my guess is that it is structural. FYI – The molecule is collagen and it is the main protein found in connective tissue.

γ – It is a nucleic acid that forms a 3D structure so it must RNA. It is probably used for catalyzing a reaction rather than storage of the genetic code given the shape. There also appear to be atoms or ions in the structure (small green dots). It appears to be about ~5 nm across given the size of the double helix regions. FYI – it is a riboswitch that binds to metal ions.

B. In class we discussed that while the structure of the molecule was important in determining its function, we needed other data (biochemical, etc.) to really tell what the protein did. In particular we highlighted that the forces within the molecule were important for determining the molecule's function. The protein in (β) consists of three strands that are held together through covalent bonds. Estimate the relative strength of a covalent bond vs. a hydrogen bond. If the molecule contained hydrogen bonds instead of covalent bonds how would that change the molecule's properties or function?

Covalent bond is ~400 kJ/mole = ~160 k_BT
Hydrogen bond is ~8 kJ/mol = ~3 k_BT
about 100 times stronger
If the ribbon was held together by hydrogen bonds instead of covalent bonds then a force that acted on the ribbon would cause more stretching, bending, or shearing than if the ribbon was held together by covalent bonds. Since the covalent bond is 100 times stronger the ribbon is much stiffer and is therefore a much stronger "building material".

C. Given that the Young's modulus for the protein in (β) is 2 GPa, what is the extension of the molecule given a 50 pN force? Your estimates of the molecular dimensions will be useful here.

(F/A) = E(dL/L) → dL=(F/A)(L/E)
F= 50 pN
A=pi*r^2, where r =1 nm
E= 2 GPa
L= 10 nm
dL =(50E-12/(pi*1E-9^2))(10E-9)/(2E9)=8E-11 m = 0.8 Angstroms = 1 Angstrom

D. Use estimation to tell me whether the molecule has an elasticity closest to rubber, plastic, or steel.

The deformation was: dL/L= 1 Angstrom/100 Angstroms = 1% deformation, given a pressure of (F/A) = 16 MPa. Let's say a rod of rubber, plastic, or steel is an inch in diameter then 16 MPa would be a force of 30 kN. A 3000 kg car weighs 30 kN. You could probably hang a car by a steel rod without stretching it… Rubber rod would definitely stretch a bunch. Let's go with plastic.

E. Protein structures can be obtained from other methods than just x-ray crystallography. List two other methods and tell me the limitations for those two methods as well as for x-ray crystallography.

x-ray – protein has to crystallize. This means that it is not in its natural environment or aqueous solution. Floppy parts of protein are hard to resolve and get only rigid structure – not dynamic
NMR – There has to be a lot of protein, but is in aqueous solution, still not in native environment though. Protein can move around. Protein has to be small (200 a.a.'s or so) and the sequence has to be known.

AFM – The cantilever can change the protein structure when it pushes on it. AFM resolution in aqueous environment is not angstrom-scale.

Problem 4 – Membrane Structure → Grade:______ out of 30 pts

Answers will vary. See lecture notes and textbook for full discussion. Comments are written on your exam.

Problem 5 – Cellular Structure → Grade:_____ out of 15 pts

Physicist's like to make simple models of systems and then modify the original model based on experimental data. In this section we talked a lot about modeling a minimal cell.

A. Let's say you want to model the minimal neuron. What cellular "pieces" would you need to keep in your model, what could you throw away? Draw a picture of your minimal neuron and label or list the parts you would need. Remember to ask the right questions!!! What does a neuron need to be a neuron?

Answers will vary. For a neuron you need the reproductive parts found in the minimal cell (see notes), but you also need a sensor (chemical receptor), an output (flagellar motion), and possibly some sort of feedback.

B. Prof. Loinaz and the book talked at length about using E. coli as a minimal cell. Would E. coli work as a minimal neuron? List some reasons for why it might work, and some reasons for why it wouldn't, and then make your determination.

Yes, it will work and is one of the reasons given for studying its chemotactic behavior. The E. coli has a chemical receptor as its sensor and its output is the flagellar motion. The larger output is that E. coli can navigate up a chemical gradient or chemotax. Also, E. coli is a "simple" cell that is able to reproduce – a key concern for a minimal cell. A reason that it might not be a good minimal neuron is that multiple E. coli do not form a neural network. In addition, E. coli in some ways may be too sophisticated (with one neuron it can sense both temperature and chemical gradients) or may be too narrowly defined (it doesn't have an action potential) to be a general neuron. E. coli doesn't have the general structure seen for typical neurons – axon, soma, dendrite – given it is not carrying the message to other cells.

C. If the experimental data showed that E. coli did not chemotax, would this affect your answer to part B?

No, as long as E. coli was still able to thermotax. Yes, if we were to remove all the navigation abilities of E. coli. If it does not navigate then it is not required to sense it's environment or formulate a behavioral output – In my mind the things that a neuron or neural network need to do.