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## 2007 7.013 Problem Set 1 KEY

Due before 5 PM on FRIDAY, February 16, 2007.

Turn answers in to the box outside of 68-120.

PLEASE WRITE YOUR ANSWERS ON THIS PRINTOUT.

**1.** Where in a eukaryotic cell do you think you would find the following proteins residing? Be as specific as you can in terms of subcellular location.

(a) an enzyme whose substrate is DNA

**The nucleus.** DNA is found in the nucleus of eukaryotic cells, so an enzyme that acts on DNA would have to be found inside the nucleus.

(b) an enzyme that catalyzes protein synthesis

**The cytoplasm.** Proteins are synthesized by ribosomes, which live in the cytoplasm of the cell. Some of these cytoplasmic ribosomes are associated with the membrane of the ER (i.e. the endoplasmic reticulum), the organelle that helps modify and transport any protein that is destined for the cell membrane or the outside of the cell.

(c) a protein that allows ions to pass in and out of the cell

**The cell membrane.** Many proteins are found inside the cell membrane (also called the plasma membrane). Some of these cell membrane proteins form protein pores that allow things to come inside the cell from the extracellular environment, or go outside the cell from the cytoplasm.

(d) a protein that acts as a receptor for extracellular cell-cell communication molecules that are large and hydrophilic

**The cell membrane.** Many proteins are found inside the cell membrane (also called the plasma membrane). Some of these cell membrane proteins bind to extracellular molecules and induce changes in the inside of the cell when they receive these extracellular signals.

(e) a protein that forms a channel through which RNAs can be exported into the cytoplasm

**The nuclear membrane.** Many proteins are found inside the nuclear membrane, which is the membrane that separates the inside of the nucleus from the cytoplasm. Some of these nuclear membrane proteins form nuclear pores that allow things to come inside the nucleus from the cytoplasm, or go outside the nucleus to the cytoplasm.

(f) an extracellular matrix protein

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**Outside the cell.** These proteins, which make up the majority of the dry weight of your body, are the protein glue that holds your cells together into tissues and organs.

(g) a protein that adds carbohydrate groups to proteins destined for the outside of the cell

**The ER (endoplasmic reticulum) and/or the Golgi.** The ER and the Golgi are the two organelles that help modify, sort, and transport any protein that is destined for the cell membrane or the outside of the cell. One of the most common modifications that occurs on extracellular proteins is the covalent addition of sugars/carbohydrates to the protein.

(h) a protein that synthesizes ATP

**The mitochondria.** The mitochondria are the organelles in which cellular energy (in the form of ATP) is produced.

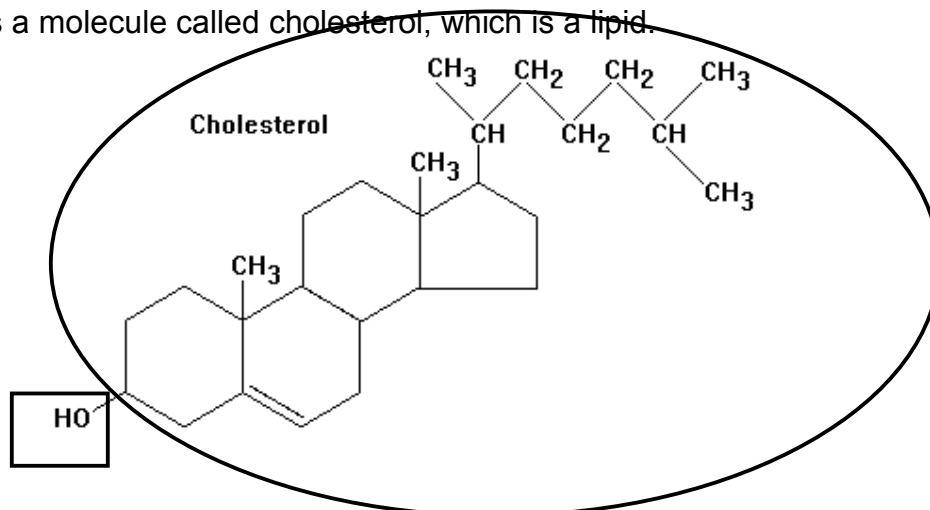
(i) the cytoskeletal protein actin

**The cytoplasm.** Actin is one of the proteins that makes up the cytoskeleton, which is a collection of large protein cables or filaments that give cells shape and structure, and confer upon cells the ability to change shape and move. Actin is the most abundant protein inside cells, and is found throughout the cytoplasm of cells.

(j) The major cytoskeletal protein actin is translated as a single polypeptide subunit. Many actins associate together to form actin filaments. These filaments can disassemble and reassemble to help cells move and change shape. During these processes, what is the highest level of actin protein structure that is changing? Your choices (from lowest to highest) are: primary, secondary, tertiary, quaternary.

**Quaternary.** Actin is a monomeric protein, and proteins that are monomers (i.e. consist of only one chain of amino acids) have primary, secondary, and tertiary structure. However monomeric proteins do not have quaternary structure by definition. Quaternary structure is the level of structure that tells you how multiple protein chains interact with each other. Thus, when protein cables or filaments are being formed by the association of many actin monomers, quaternary structure is changing.

2. Below is a molecule called cholesterol, which is a lipid.



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(a) Put a circle around the part of this molecule that is hydrophobic.

**Circle the entire molecule except the OH.** Cholesterol (other than the one OH group) is made entirely of carbons and hydrogens. Hydrocarbons are hydrophobic because they are not polar and thus cannot form Hydrogen bonds with water.

(b) Draw a box around the part of this molecule that is hydrophilic.

**Box the OH group.** An OH group is polar and thus can form Hydrogen bonds with water.

(c) Cholesterol is transported through your blood. Do you think that cholesterol molecules can be transported in your blood freely, i.e. without requiring any sort of transport protein? Why or why not?

**No.** Blood is aqueous and cholesterol is very hydrophobic. Thus cholesterol cannot be dissolved in blood. Thus cholesterol must be packaged into protein structures (called, for example, HDL and LDL particles) that hide the cholesterol on the inside of the particles, shielding the hydrophobic cholesterol from the aqueous blood.

**3.** \*\*For this problem, you will need to use a computer program to view the structure of a protein and of DNA.\*\*

To begin, go to the site:

<http://web.mit.edu/star/biochem/index.html>

and click on “Click here to start Star Biochem.”

Once the program Star Biochem has been downloaded onto your computer, go to the site:

<http://web.mit.edu/viz/7.01x/>

This website has several links. Those marked “The Amino Acids,” “The Peptide Bond,” “Secondary Structure,” and “Nucleotides and DNA” contain models of each of these things that will help you understand protein and DNA structure.

To do the graded problem, click on “7.013 Problems” and do “**Problem 1 (pdf with live links)**.” To help you learn how to use the program, a tutorial is available under “*StarBiochem Tutorial Problem (pdf with live links)*.”

**If you do not have a computer easily available, or if you would like to do this problem in the presence of technical staff who are familiar with this computer program, there will be staff present on Thursday 2/15/07 from 4-9pm in a room TBA (see the course website).**

**You are welcome to stop by anytime during that interval to use one of the computers in that room to do the problem, or to ask the staff questions about the program.**

**Please write your answers to the question entitled “Problem 1” in the space below.**

Once you have Star Biochem open, go to “File” and then “Open” and choose the file 1CF7. To begin, go to “Structure” and then to “Quaternary” and click on the box such that there is now a check-mark present in the box. This action will color each chain of either DNA or protein a different color. Now go to “Secondary” and click on the box next

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to “All Ribbons.” This action will allow you to see the protein as a ribbon diagram. Once you have done this, answer the questions below.

We examine the structure of a segment of DNA bound to a transcription factor (named 1CF7). A transcription factor is defined as a protein that binds to a DNA sequence of a gene and influences whether or not a protein product will be made from that gene. (We will learn more about transcription factors later in the semester, and we will learn about how transcription factors achieve this goal by regulating the process of transcription, i.e. the production of mRNA from DNA.)

- (a) The transcription factor shown here is in a complex with the DNA molecule.  
(i) Examine the ribbon structure of the protein and the DNA complex. How many protein chains are involved in this complex?

**Two.** Each protein chain is colored in a different color, and there are two different colored chains. Thus 1CF7 works as a dimer, or a protein which functions using two separate subunits.

- (ii) List in order the 10 amino acids numbered #16 through #25 in the first protein chain listed, and state which level of protein structure this list represents.

**Ser-Arg-His-Glu-Lys-Ser-Leu-Gly-Leu-Leu, which is primary structure. Primary structure is just the list of the amino acids found in a protein chain. Primary structure tells you the sequence of the protein but not anything about its 3D structure.**

- (b) Write out the entire double-stranded DNA sequence (and label the 5' and 3' ends) of the piece of DNA to which this 1CF7 protein complex is bound.

5' -TTTTTCGCGCGGTTTT-3'  
3' -AAAAGCGCGCCAAAA-5'

This can be read from under “Primary Structure,” just as the protein sequence can be read.

- (c) Examine one interaction site by selecting Residues 121 and 122 of chain B.  
(i) Which amino acids are residues 121 and 122?

AA#121 = Arginine

AA#122 = Arginine

- (ii) What kind of amino acids are residues 121 and 122 (hydrophobic, polar, acidic or basic)?

AA#121 is (circle one):    hydrophobic            polar            acidic            basic

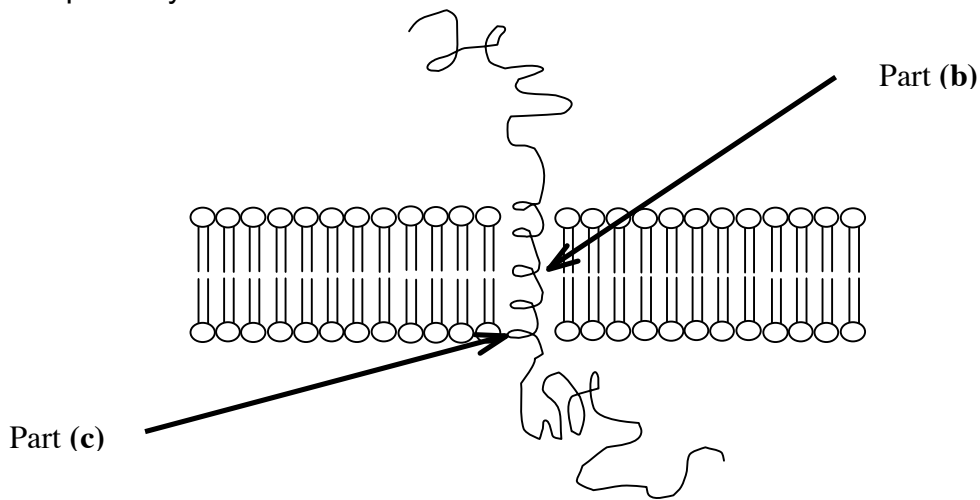


See the drawing above. There is one peptide bond, where the two amino acids are joined together by a covalent bond.

(d) Rank the following amino acids from most hydrophobic to least hydrophobic: alanine, arginine, asparagine, phenylalanine.

**Phenylalanine, alanine, asparagine, arginine.** Phenylalanine is the most hydrophobic because it has a lot of CH groups and is bulky and non-polar. Alanine's R group is also made of Cs and Hs, but its R group is smaller than phenylalanine. Asparagine is polar but uncharged. Arginine is charged, making it the most hydrophilic.

5. Below is a schematic of a transmembrane protein, which is a protein that crosses a lipid bilayer.



(a) If a protein crosses the membrane, it usually does so using a secondary structure called an alpha helix, as depicted in the diagram above. In an alpha helix, the R groups point out of the helix and the peptide bonds point into the helix. Why do you think the peptide bonds have to be hidden inside an alpha helix, away from the lipids in the membrane?

**Peptide bonds are polar.** Peptide bonds are a carboxyl group joined to an amino group. The O in a carboxyl group and the N in an amino group make these groups very polar, as O and N are electronegative. The inside of a lipid membrane is non-polar, because the long tails of phospholipids are long hydrocarbon tails. Thus the polar peptide bonds must be hidden from the non-polar tails of the lipids in a membrane.

(b) Which one of the following amino acids would most likely be found in the portion of an alpha helix that crosses the membrane? (See the arrow labeled part (b).)

alanine

serine

lysine

glutamic acid

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**Alanine** has a non-polar R group, and all the R groups that point out into a lipid membrane must be non-polar in order to interact favorably with the non-polar tails of the lipids used to make up a membrane.

(c) Which one of the following amino acids would most likely be found at the very edge of an alpha helix that crosses the membrane? ? (See the arrow labeled part (c).)

alanine

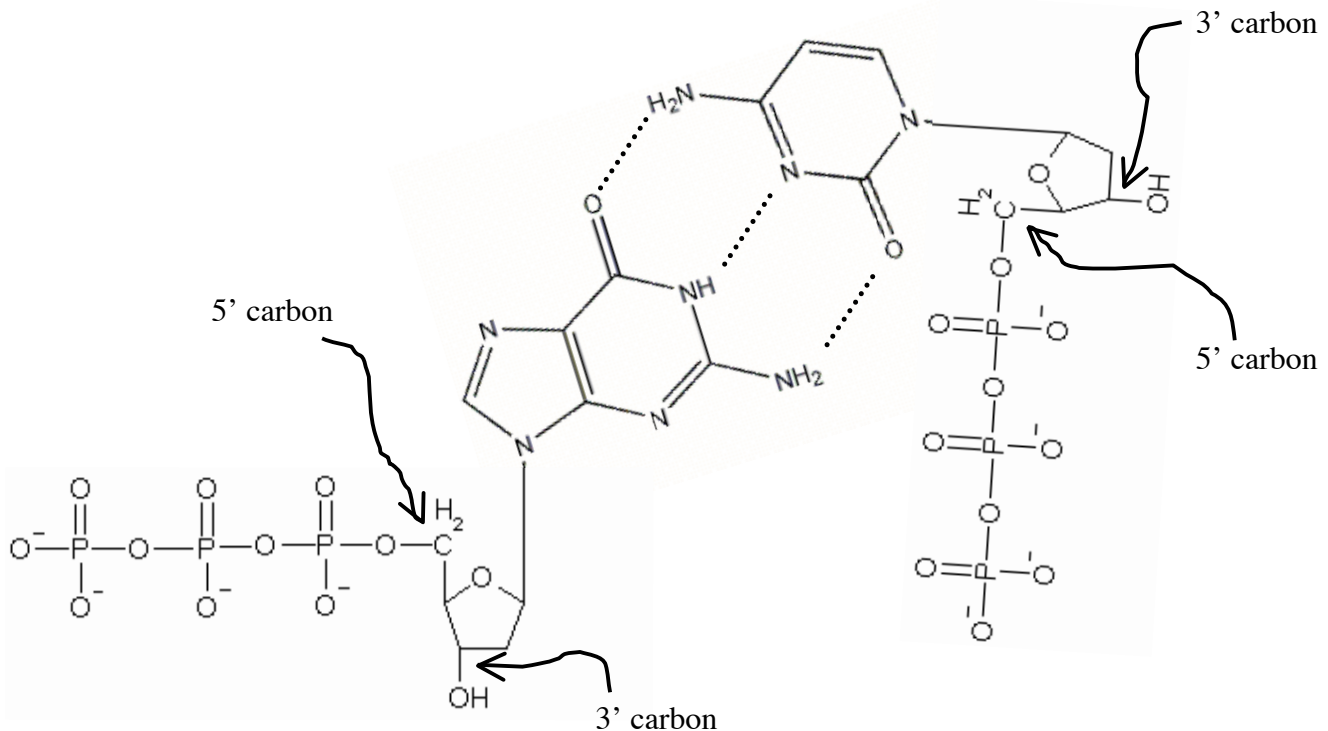
serine

lysine

glutamic acid

**Lysine** is positively charged, and the polar heads of phospholipids are negatively charged, so the opposite charges of the polar head groups of the lipids and the amino acids of the protein attract each other.

6. (a) Draw a G nucleotide triphosphate (dGTP) base-pairing with a C nucleotide triphosphate (dCTP).



(b) Label all 5' and 3' carbons in your drawing above.

See the above drawing. Each nucleotide has a 5' carbon and a 3' carbon in its sugar (deoxyribose). The 5' carbon is attached to the phosphate group and the 3' carbon is attached to the OH group.

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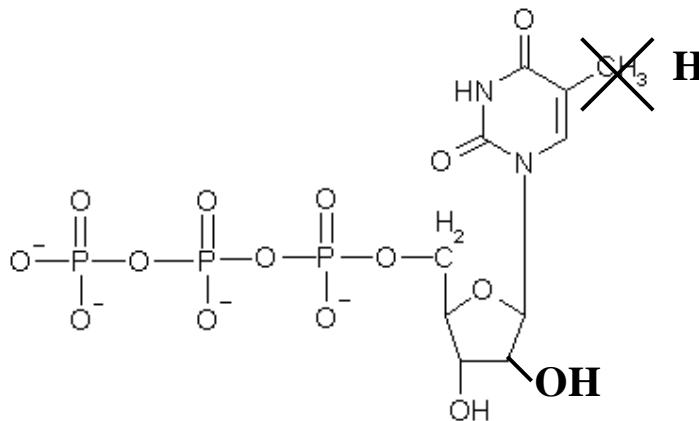
(c) How many phosphodiester bonds are present in your drawing above?

**None.** Phosphodiester bonds are the covalent linkages between nucleotides, and there are no covalent linkages between these two nucleotides.

(d) How many hydrogen bonds are present in your drawing above?

**Three.** G and C basepair with each other via three hydrogen bonds, shown as dashed lines above.

(e) Below is the structure of a nucleotide triphosphate that is used to make DNA. Change this structure in two ways so as to make it into a nucleotide that could be used to make RNA.



The above nucleotide as it was originally drawn is dTTP. To make this into UTP, one must change the sugar from deoxyribose into ribose by adding an OH group from the 2' carbon, and one must change the CH<sub>3</sub> to an H coming off of the pyrimidine base.

(f) Is the overall charge on a DNA double helix at pH7 neutral, negative, positive, or inconclusive?

**Negative.** The sugar and base in a nucleotide are uncharged, but the phosphate group is negatively charged. Thus the backbone of DNA is very negatively charged.

(g) Is the overall charge on a protein at pH7 neutral, negative, positive, or inconclusive?

**Inconclusive.** The charge of a protein is based on its amino acid sequence, and how many positively charged and negatively charged amino acids are contained therein. Thus you cannot make a generalization about the charge on all proteins. Every different protein in your cell has a different total charge on it.