Name_____ Section_____ TA_____

7.013 Problem Set 1- 2013

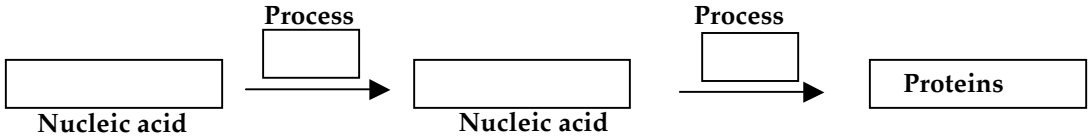
Question 1

a) With the exception of germ cells, the nucleus of all somatic cells in your body carries two copies of each DNA segment or chromosome, which together make your genome. To fit the entire DNA into a tiny nucleus, the chromosomes are highly compacted through a variety of mechanisms. If however, they were <u>not compacted</u> and you laid them out end to end, all of the chromosomes in all of your cells would travel a great distance.

Given your knowledge of the distance between base pairs in the Watson and Crick model of the DNA double helix as well as the size (in base pairs) of the human genome and the number of cells in the human body, how many round trips from the Earth to the Sun would this length of DNA travel? **Show your work.**

<u>Note:</u> *You may assume that there are 5 x 10^{13} cells in the human body and that each cell has two full copies of the genome.*

b) Fill in **all** the boxes below to explain the relationship between proteins and the two major classes of nucleic acids to which you have been introduced in 7.013.



c) Approximately 98% of all biological macromolecules are made of six major elements; carbon (C), hydrogen (H), nitrogen (N), oxygen (O), sulphur (S) and phosphorous (P).

i. Which elements (*C/ H/ O/ N/ S/ P*) are present in **<u>all</u>** biological macromolecules?

ii. Which radioactive element (*C/ H/ O/ N/ S/ P*) may be used to detect **only the proteins** in a cell? **Explain** why you selected this option.

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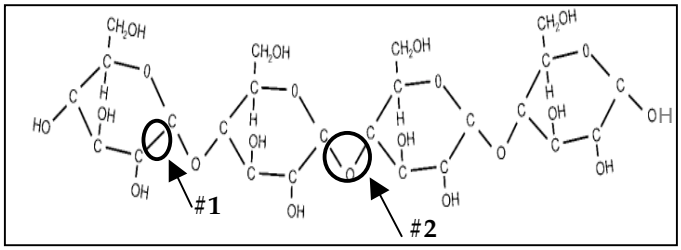
Question 2

a) Consider the structure of the following polymer.



i. Classify this polymer as a carbohydrate, lipid, protein or nucleic acid.

ii. From the following, circle **all** the options that best characterize this polymer. **Explain** why you selected these options.

Hydrophobic **Polar** **Hydrophilic** **Nonpolar** **Charged** **Uncharged**

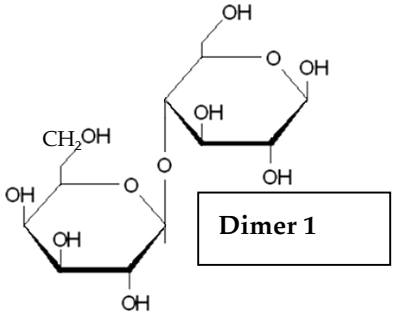
iii. Which of the above bonds (*choose either bond 1 or bond 2*) is an example of **glycosidic** bond? **Explain** why you selected this option.

iv. **Circle** the correct option(s). The breakdown of this polymer into individual monomers is an example of condensation, hydrolysis, dehydration or isomerization reaction.

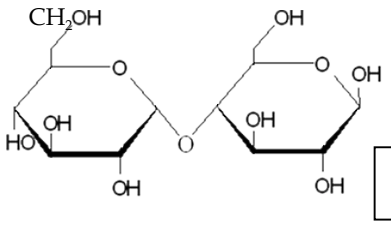
v. From the following, **circle** the type of bond or interaction that occurs between two such polymers, when they are placed in an aqueous environment. **Explain** why you selected this option(s).

Covalent bond **Ionic bond** **Hydrogen bonds** **van der Waals forces (VDW)**

b) Below is a schematic of two different dimers, Dimer 1 and Dimer 2.



Dimer 1



Dimer 2

If Enzyme X cleaves the bond that joins the two monomers of Dimer 1, will the same enzyme be able to cleave the bond that results in the formation of Dimer 2 *(Yes or No)*? **Explain** why you selected this option.

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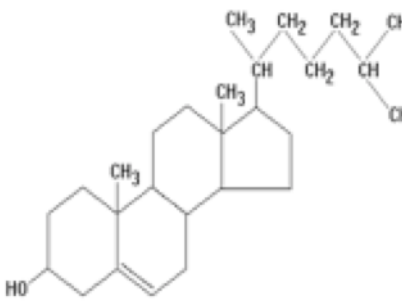
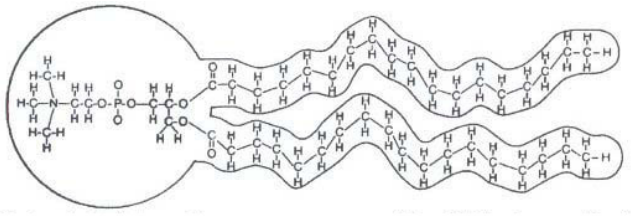
Question 2 continued

c) Consider the molecules below to answer the following questions.



#1



#2

i. Which structure *(choose either molecule #1 or #2*) is **most likely** to assemble and form a lipid bilayer? What property of the molecule that you selected allows it to form a lipid bilayer?

ii. Which bond or interaction (*choose from covalent, hydrogen, hydrophobic or ionic*) is **most likely** to stabilize the lipid bilayer?

iii. **List** the option (*choose either saturated or unsaturated*) that best characterizes Molecule 2. **Explain** why you selected this option.

iv. Draw **two** possible conformations that the molecule you selected in part (i) may assume when placed in an aqueous environment.

v. What bonds or interactions (*choose from ionic, covalent, hydrophobic and hydrogen*) are **most likely** to occur between the molecules and the surrounding **aqueous environment** when they acquire the conformations that you have drawn in part (iv) above?

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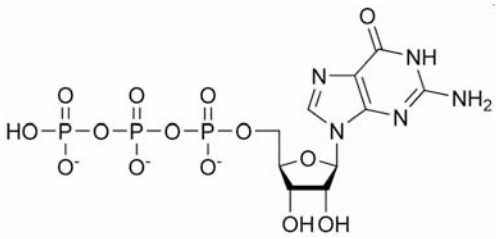
Question 3

a) The following diagram represents a nucleotide that serves as a monomer for ribonucleic acid (RNA).



i. Classify this nucleotide as purine or pyrimidine base.

ii. Besides serving as a monomer of RNA, what is the other major role of this nucleotide within a cell?

iii. Box the **group** or **atom** that you would remove, so that the nucleotide drawn above can serve as a monomer for DNA.

iv. What type of bonds would hold two such **adjacent** nucleotides together in a growing nucleic acid chain? **Circle** the group(s) that would participate in the formation of this bond if the nucleotide shown above, was added to the growing nucleic acid chain.

v. Name the type of bonds that the above nucleotide will form **with its complementary nucleotide**. How many of these bonds would you expect between this nucleotide pair?

vi. The nucleotide (N) shown above is a part of the following nucleic acid sequence.

5'GGCCA**N**ACCA3'

For the nucleic acid sequence that is given above…

- Which nucleotide base (*A*/*T*/*G*/*C*/*U*) has a free phosphate group?
- Which nucleotide base (*A*/*T*/*G*/*C*/*U*) has a free hydroxyl group?

vii. If adenosine (A) is added to the above nucleic acid sequence in a cell, would it be added to the 5′ end or the 3′ end?

viii. The nucleic acid sequence shown above interacts with a specific protein. Of the following amino acids that are a part of this protein, circle those whose **side-chains** are most likely to interact with the **phosphates** of the sugar-phosphate backbone of nucleic acids. **Explain** why you selected these amino acids.

Methionine **Lysine** **Alanine** **Leucine** **Arginine**

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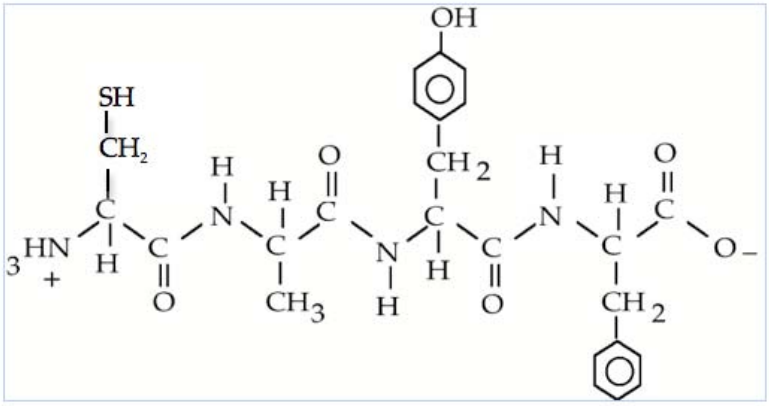
Question 3 continued

b) Consider the following amino acid sequence that is part of a protein.



i. Circle **all** the peptide bonds in the above amino acid sequence.

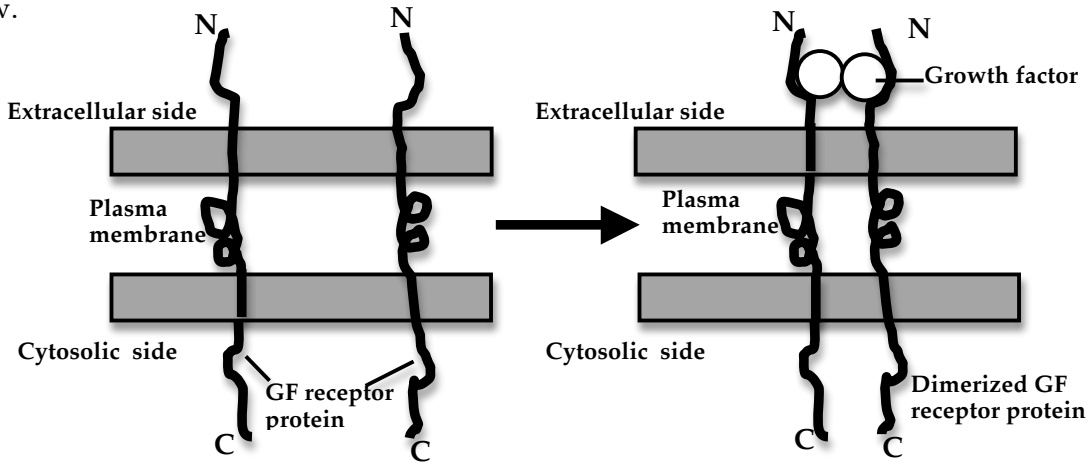
ii. Name the amino acid in this sequence that is closest to the **N- terminus** of the protein. ***Note:*** *A table of amino acids is provided on the last page of this problem set.*

iii. In the sequence above….

- Name the amino acid(s) that is **hydrophilic**.
- Name the amino acid(s) that is **hydrophobic**.
- Name the amino acid(s) that can be **phosphorylated**.
- **Box** the side-chain group (R group) of each amino acid in the sequence above.

Question 4

The following is a schematic of a plasma membrane protein that functions as a growth factor (GF) receptor. When a specific growth factor binds to the extracellular domain of this protein, the receptor protein dimerizes i.e. *two polypeptide chains, each comprised of many amino acid residues and shown by lines in the schematic, join together to make a dimerized protein*. The GF receptor is active following dimerization as shown below.



a) What is the **highest order** of this protein's structure in its **inactive** state? Choose from *primary, secondary, tertiary and quaternary* given in an ascending order. **Explain** your choice.

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Question 4 continued

b) **Circle** the amino acid(s) that is part of the **extracellular domain** of the GF receptor and has a side-chain that could form a hydrogen bond with the surrounding water molecules. Include **all** that apply and **explain** why you selected this option(s).

Lysine **Tyrosine** **Tryptophan** **Glutamic acid**

c) **Circle** the amino acid(s) in the **transmembrane domain** ***(amino acid sequence of the protein that spans the plasma membrane)*** of the GF receptor whose side-chains can most likely interact with the lipid bilayer. Include **all** that apply and **explain** why you selected this option(s).

Lysine **Tyrosine** **Tryptophan** **Glutamic acid**

d) Interaction between specific amino acid residues found in two identical GF receptors is critical for their dimerization. In the table below, state the **strongest** interaction that likely occurs between the side-chains of listed amino acid pairs.

Interacting amino acid pair. ***Note:*** *In the column below Glutamic acid 155 means that the amino acid located at the 155th position in the peptide chain is Glutamic acid.*	**Strongest bonding/ interaction** *(ionic/ hydrogen/ covalent/ hydrophobic)?*
Glutamic acid^{155} and Lysine^{68}	
Tyrosine^{140} and Glutamine^{62}	
Alanine^{133} and Methionine^{54}	

e) Substitution of a single amino acid can influence the dimerization and function of the GF receptor protein. Predict whether the receptor will be able to dimerize, given the substitutions below.

i. The original amino acid bonding pair, Glutamic acid^{155} and Lysine^{68}, is changed to Glutamic acid^{155} and **Arginine**^{68}. **Explain** your answer.

ii. The original amino acid bonding pair, Alanine^{133} and methionine^{54}, is changed to **Tryptophan**^{133} and methionine^{54}. **Explain** your answer.

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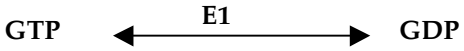
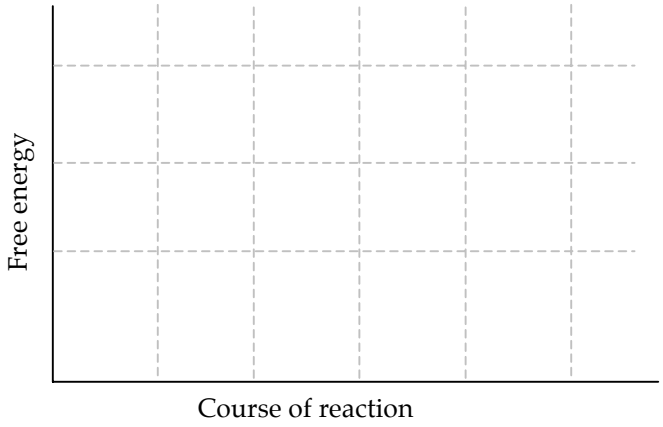
Question 5

a) The enzyme E1 catalyzes the hydrolysis of GTP to GDP (**Reaction 1**) as shown below.

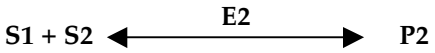


i. Draw the energy profile **of the forward E1 catalyzed reaction** on the axes below. Label the reactants and the products and indicate the overall free energy change.

ii. Draw the energy profile **of the forward reaction in the absence of E1** on the axes below. Label the reactants and the products and indicate the overall free energy change.



b) The following is a reaction (**Reaction 2**) catalyzed by a different enzyme, E2.



In a living cell, the coupling of Reaction 1 with Reaction 2 increases the rate of Reaction 2. **Explain** why this is so.

c) Enzymes enhance the rate of a reaction by decreasing the activation energy of the reactants. But they neither alter the free energy change ***(ΔG)*** of the reaction nor the reaction equilibrium (K_{eq}). Briefly explain…

i. How an enzyme may lower the activation of energy of the reactants.

ii. Why the enzymes have no effect on the ΔG and K_{eq} of the reaction.

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Question 5 continued

d) You perform the coupled reactions in two separate test tubes (Tube 1 and Tube 2). Both these tubes contain GTP, substrates S1 and S2, enzymes E1 and E2 and either Drug 1 or Drug 2 as described below.

- *Tube 1 contains Drug 1 that is a **manufactured chemical** and inhibits the hydrolysis of GTP but it does not prevent the binding of GTP to the active site of E1. This drug has no effect on E2. Furthermore, you observe that the effect of this drug is irreversible.*

- *In comparison, Tube 2 contains Drug 2 under appropriate reaction conditions. This drug is **found naturally in a cell** and it inhibits the binding of S1 to the active site of E2 but has no effect on E1. The inhibitory effect of this drug can be reversed by the excess amount of S1.*

You perform the reactions under optimal conditions and measure the amount of P2 formed after 30 minutes in both the tubes.

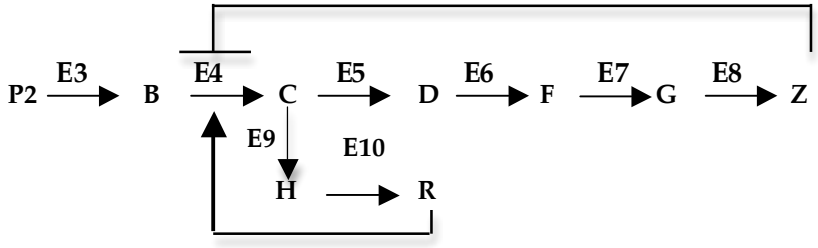
i. **Circle** the option(s), from the choices below, that best characterizes Drug 1 and **explain** why you selected this option(s).

Competitive inhibitor **Non-competitive inhibitor** **Allosteric inhibitor**

ii. **Circle** the option(s), from the choices below, that best characterizes Drug 2 and **explain** why you selected this option(s).

Competitive inhibitor **Non-competitive inhibitor** **Allosteric inhibitor**

e) The product P2 can be converted either to product 'Z" or product "R" through a biochemical pathway where each step is catalyzed by a specific enzyme (E3 –E10) as shown below. The metabolites (products) at each step are indicated. ***Note:*** *An arrow means activation and a "T" means inhibition of the reaction.*



What is the effect of **Compound Z** on Enzyme E4? Of what is this an example? Briefly **explain** why the cell may need such a regulatory mechanism.

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Question 6

An eye lens is comprised of cells that are created when an eye is formed and are retained for its lifetime. These cells lack organelles and can be regarded as "sacs" that are filled with a loose uniform arrangement of water-soluble structural proteins called crystallins. The uniform distribution of crystallins in a cell prevents light scattering, maintains lens transparency and allows us to see. With age, the crystallins undergo different modifications that increase the opacity of a lens and may lead to the onset of cataracts.

Biologists are currently using computer-modeling programs to view the structure and function of various proteins in both normal and diseased states. For this problem you will use a computer to view the structure of γ–crystallin. To begin, go to http://web.mit.edu/star/biochem, click on the **"Start** and allow the link to open**.** You may have to **install JAVA** to open this program. This can be downloaded free from the JAVA website. Click on **"Samples-> Select from samples ->Amino acids/ Proteins ->1HK0 -> open"**. You will see a schematic of γ- crystallin on the right and a menu on the left.

a) Does the current view of **1HK0** show a monomeric (*single polypeptide chain*) or multimeric (*more that one polypeptide chain*) protein?

b) What is the highest order of protein structure that you observe for **1HK0**? **Explain** why you selected this level. ***Note:*** *In the sequence window, click on* ***"Structure-> Protein -> Quaternary"****. Increase the* ***"Size slide bar"*** *in the* ***"Surfaces"*** *window. Each polypeptide chain in this program is shown by a different color.*

c) The crystal structure of **1HK0** exhibits two homologous domains that are joined intra-molecularly by a six amino acid linker. What is the secondary structure of this amino acid linker (*choose from helices, sheets and coils*)? ***Note*** *Click on "****Reset - > Reset structure****". Then click on "****Structure -> Protein-> Secondary".*** *Select helices, sheets and ribbons one at a time and look at the amino acid sequences that get highlighted in the "****sequence window****". For better reviewing of protein structure you can increase the "****Size slide bar****" within in the "****Secondary structure window****".*

d) Open another protein structure by going to "***Samples-> Select from samples ->Amino acids/ Proteins ->1BLB -> open"***. What is the overall difference between structure of **1HKO** and **1BLB**?

e) Based on what you have learned from this exercise, hypothesize how the change in crystallin structure, as seen in **1BLB**, may lead to the development of cataract.

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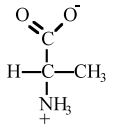
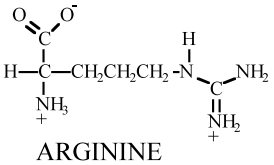
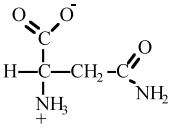
STRUCTURES OF AMINO ACIDS at pH 7.0



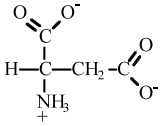
ALANINE
(ala)



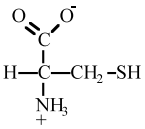
ARGININE
(arg)



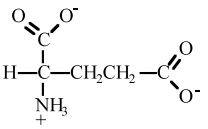
ASPARAGINE
(asn)



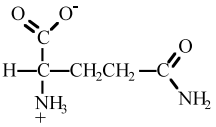
ASPARTIC ACID
(asp)



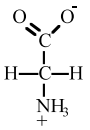
CYSTEINE
(cys)



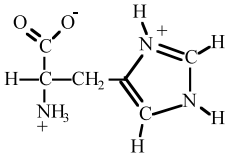
GLUTAMIC ACID
(glu)



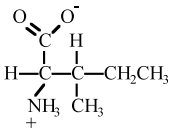
GLUTAMINE
(gln)



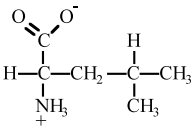
GLYCINE
(gly)



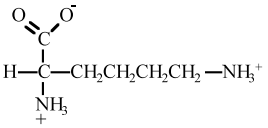
HISTIDINE
(his)



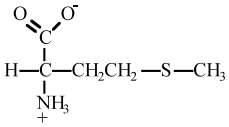
ISOLEUCINE
(ile)



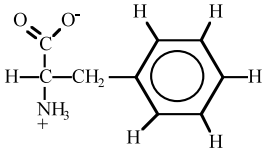
LEUCINE
(leu)



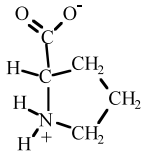
LYSINE
(lys)



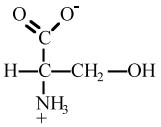
METHIONINE
(met)



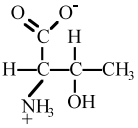
PHENYLALANINE
(phe)



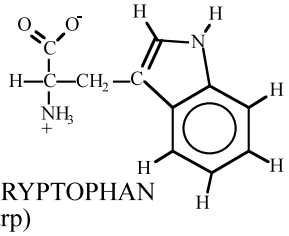
PROLINE
(pro)



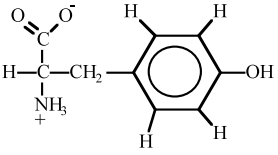
SERINE
(ser)



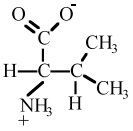
THREONINE
(thr)



TRYPTOPHAN
(trp)



TYROSINE
(tyr)



VALINE
(val)

7.013 Introductory Biology
Spring 2013