Name Key

Chem 452 - Fall 2012 - Exam III

Some potentially useful information:

pK_a values for ionizable groups in proteins: (*α-carboxyl*, 3.1; *α-amino*, 8.0; *Asp* & *Glu* side chains, 4.1; *His* side chain, 6.0; *Cys* side chain, 8.3; *Tyr* side chain, 10.9; *Lys* side chain, 10.8; *Arg* side chain, 12.5)

R (*ideal gas constant*) = 8.314 J/mol•K = 0.08206 L•atm/mol•K

Faraday's Constant, $\mathcal{F}$ = 9.65 x 10^4 J/(mol•V)

The answer to one of the questions on this exam is -3.3 kJ/mol

1. Using a Fischer projection, draw a representative structure of a ketohexose:

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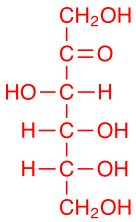
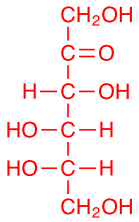


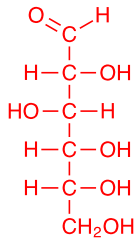
a. Ketohexoses comprise how many stereoisomers? $2^3=8$

b. Is the structure you drew a "D" or an "L" sugar? D

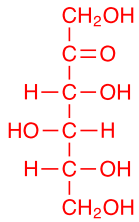
c. Draw the *enantiomer* of the structure you drew above:



e. Draw a *structural isomer* that is not a *stereoisomer* of the structure you drew above:



d. Draw a *diasteriomer* that is not an *epimer* of the structure you drew above:



2. A culture of bacteria growing at 37°C is shifted to 25°C. How might this shift alter the fatty acid composition of the bacterial membrane. Upon the shift to the lower temperature, the bacterium may look for ways to lower the melting point of its membrane phospholipids so that the membranes will remain in a liquid state at 25°C. Strategies that could be used include using a higher percentage of unsaturated fatty acids in the synthesis of the membrane phospholipids. Alternatively, the same effect could be achieved by using shorter chain fatty acids. These strategies both aim to disrupt the non-covalent vander Waals interactions that favor the solid state.

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3. Select the term from the following list that best describes each of the structures shown below

saturated fatty acid	*phosphatidylserine*	*sphingomyelin*
11-cis-retinal	*triose*	*glycosaminoglycan*
unsaturated fatty acid	*steroid*	*D-maltose*
inositol 1,4,5-trisphosphate	*D-lactose*	*serine*
D-celobios	*phosphatidylcholine*	*arachidonic acid*

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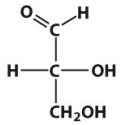
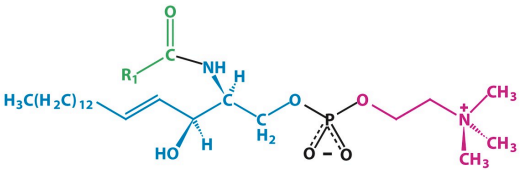
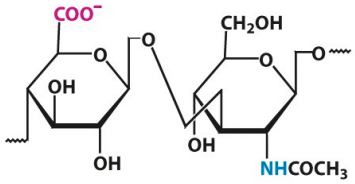
Z



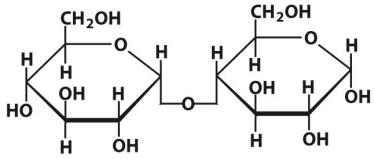
a. triose



b. sphingomyelin

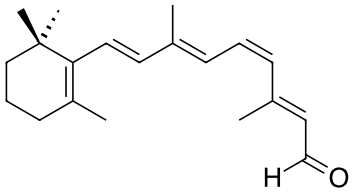


c. glycosaminoglycan

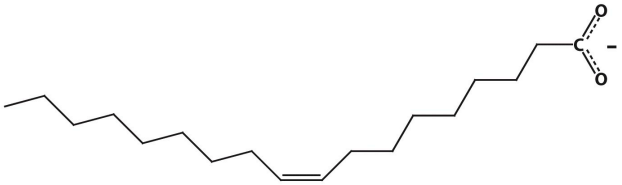


d. D-maltose

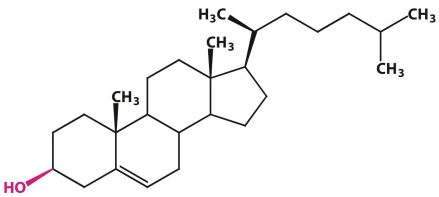
X



e. 11-*cis*-retinal

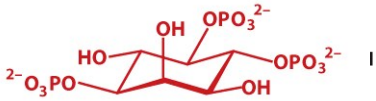


f. unsaturated fatty acid



g. steroid

Y



h. inositol 1,4,5-trisphosphate (IP_3)

i. Put an "X" next to the structure of the molecule that is allowing you to read this sentence.

j. Put a "Y" next to the structure of the molecule that is a second messenger in the angiotensin II signal transduction pathway.

k. Put a "Z" next to the structure of the molecule that is a monosaccharide.

4. Which of the following membranes would be the most fluid (circle the best choice)?

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a. A bilayer made of lipids with saturated 16 carbon-fatty acids
b. A bilayer made of lipids with saturated 18 carbon-fatty acids
c. A bilayer made of lipids with polyunsaturated 18 carbon-fatty acids
(d.) A bilayer made of lipids with polyunsaturated 16 carbon-fatty acids
e. All of the above are equivalent in fluidity.

5. Which force(s) stabilize(s) lipid bilayers (circle all that apply)?

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a. Covalent bonds between the fatty acid tails
b. Covalent bonds between the lipids and membrane proteins
c. Electrostatic and hydrogen bonding between the polar heads and the surrounding water
(d.) vander Waals interactions
(e.) Electrostatic and hydrogen bonding between the fatty acid tails and the surrounding water

6. Biological membranes are able to store chemical energy. Explain how this works.

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Since membranes are impermeable to many small molecules and ions, they can be used to create regions having different concentrations of that substance on either side of the membrane. When such a concentration gradient exists it results in a free energy difference across the membrane. This can be used as a way to store chemical energy.

7. In our discussion of signal transduction pathways, we encountered a number of defined protein domains. For each of the following domains, describe their function and give one example of a signal transduction pathway that makes use of this domain.

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a. PH (Pleckstrin homology domain): The PH domain recognizes and binds to phosphotidylinositol 4,5-bisphosphosphate (PIP_2) and phosphotidylinositol 3,4,5-trisphosphosphate (PIP_3) membrane phospholipids. Examples are found on both the IRS-1 peptide and the PIP_3-dependent kinase (PDK) in the insulin signal transduction pathwathway

b. SH3 (Src homology domain 3): The SH3 domain recognizes and binds to polyproline sequences. An example can be found on Grb-2 adaptor protein in the epidermal growth factor (EGF) signal transduction pathway

8. Name a second messenger(s) for each of the following receptors and describe the reaction or processs by which it is produced.

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a. angiotensin II receptor: Inositol 1,4,5 trisphosphate (IP_3), which is produced from phosphotidylinositol 4,5-bisphoshate (PIP_2) by the enzyme Phospholipase C.

b. olfactory receptor: Cyclic-AMP (cAMP), which is produced from ATP by the enzyme adenyl cyclase.

9. It is estimated that humans possess approximately 380 different olfactory receptors, each which binds a limited number of odorants. Explain how, with this limited set of receptors that humans can detect and distinguish between odorants that produce tens of thousands of different smells.

6/6

Most odorants bind to an array of different receptors, which produces a patterned response in the brain. If, for a given odorant, it either binds or not to each of the 380 receptors, then there would be 2^{380} =2.5 x 10^{114} possible patterns. This is an astronomical number and is probably an underestimate of what is possible, since the binding of an odorant to a receptor can produce a response that varies in intensity.

10. Batrachotoxin (BTX) is a steroidal alkaloid from the skin of *Phyllobates terribilis*, a poisonous Colombian frog, and is one of the sources for the toxin used on blowgun darts. In the presence of BTX, the voltage-gated Na^+ channels in an excised patch from a nerve cell stay persistently open when the membrane is depolarized, and they only close when the membrane is depolarized again.

a. What step in the sequence that takes place during an action potential is the BTX blocking?

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The description implies that the channel is not closing properly. A reasonable suggestion is that the BTX is somehow blocking the inactivation plug domain of the voltage-gated Na^+ channel from functioning properly.

b. If placed on the tongue, predict how BTX would taste. Explain.

As an alkaloid it will be basic and therefore could be expected to produce a bitter taste.

c. Explain how in the lab a small patch of membrane can be excised from a nerve cell in order to carry out this study. In a patch clamp experiment in which the tip of a small pipet is placed on the membrane of a nerve cell and a vacuum is applied to produce a “Gigaohm” seal between the tip of the pipet ant the membrane. The pipet is then pulled back and in the process pulls away a small portion of the cell membrane, which still contains a functional Na^+ channel that can be studied in isolation.

11. To study the mechanism of the SERCA pump, you prepare membrane vesicles containing this membrane protein, oriented such that its ATP binding site is on the outer surface of the vesicle. To measure pump activity, you use an assay that detects the formation of inorganic phosphate in the medium. When you add calcium and ATP to the medium, you observe phosphate production for only a short period of time. Only after the addition of *calcimycin*, a molecule that makes membranes selectively permeable to calcium, do you observe a sustained phosphate production.

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a. Provide and explanation for this observation. The SERCA pump is coupling the free energy derived from the hydrolysis of ATP to pump Ca^{2+} ions into the vesicle. This produces both a concentration gradient and a membrane potential across the vesicle membrane that will resist the pumping of additional Ca^{2+} ions, and at the same time will halt further hydrolysis of the ATP and the concomitant production of phosphate ions. The calcimycin allows the Ca^{2+} ions to flow back out of the vesicle.

b. Characterize the transport mechanism used by calcimycin to transport calcium ions across the membrane. This is an an example of facilitated passive transport.

c. What is the source of free energy used to transport the Ca^{2+} into the vesicle?

As indicated above, it the free energy derived from the hydrolysis of a phosphate from ATP.

d. What is the source of free energy used to transport Ca^{2+} back out of the vesicles?

The free energy comes from the ion moving down both a concentration and electrical potential gradient.

12. A major theme of the signal transduction pathways is *signal amplification*. Describe what this means and how it works. In addition, give one specific example that is drawn from the plethora of signal transduction pathways that we discussed in class.

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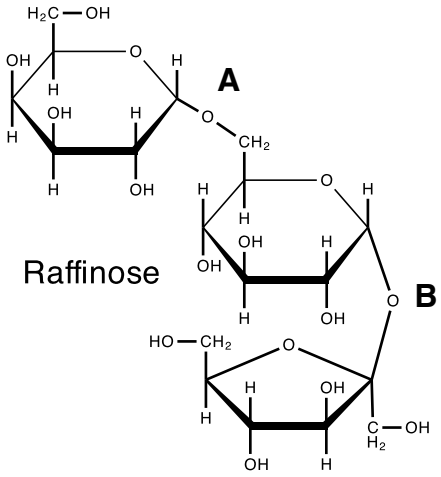
A signal transduction pathway contains a series of steps, some of which lead to an amplification of the signal. Taking the β-adrenergic receptor as an example, when epinephrin binds to the β-adrenergic receptor it converts it to an active form, which in tern converts the hetertrimeric G-protein to its active form. but one activated β-adrenergic receptor can activate a number of G-proteins so this leads to an amplification of the signal. The active G_α subunit of the G-protein then goes on to activate the enzyme adenylate cyclase, which catalyzes the conversion of ATP to cyclic-AMP, which is a second messenger in the β-adrenergic signal transduction pathway. Each activated adenylate cyclase enzyme can catalyze the product of a large number of cyclic-AMP molecule and provides another example of signal amplification.

13. Raffinose is a trisaccharide that is found in beans, cabbage, broccoli and other vegetables. When eaten, humans lack the enzyme needed to hydrolyze one of the glycosidic bonds found in this trisaccharide. As a consequence, the sugar passes undigested from the stomach and upper intestine to the lower intestine, where gas-producing bacteria that possess this enzyme go on to ferment the raffinose. This is the cause of the excessive flatulence that you may have experienced after eating hearty helping of beans.

7/7



a. What three monosaccharides comprise raffinose?

α-D-galactopyranose α-D-glucopyranose β-D-fructofuranose

b. Characterize the two types of glycosidic bonds that are used to connect the three monosaccharide units together.

A α(1-6) **B** α1-β2

c. The enzyme that humans lack that is needed to digest raffinose, is the one that hydrolyzes the glycosidic bond that is labeled **A** in the figure shown above. What is the name of the dissacharide that is produced after the bacteria successfully hydrolyze this bond? D-sucrose

d. Is raffinose a *reducing* sugar? No

14. When phospholipids are mixed with water they spontaneously self-assemble into lipid bilayers. How is this self-assembly process similar to that for polypeptides when they fold to form protein tertiary structures, and DNA polynucleotides when they combine to form double helices?

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All of these structures form in response to the same driving forces. Non-polar regions are looking for ways to minimize their exposure to water while at the same time the polar, hydrophilic regions with to remain in contact with water. This is called the *hydrophobic effect*. In the formation of lipid bilayers, the non-polar fatty acid side chains are buried in the interior of the bilayer, in protein folding, the non-polar amino acid side chains are buried in the interior of the tertiary fold, and in DNA double helices, the faces of the non-polar nucleotide bases are buried and stacked in the center of the double helix. Conversely, the hydrophilic groups are left exposed to water: the polar head-groups of membrane lipids, the hydrophilic amino acid side chains of proteins, and the phosphate-ribose backbone along with the edges of the nucleotide bases of DNA, are all found on the water-exposed surfaces of the the corresponding structures that they form.

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