CHEM 330 **Exam #2** **Dr. Brandt**
Fall 2012-13

Read each question carefully. Please answer the questions asked.

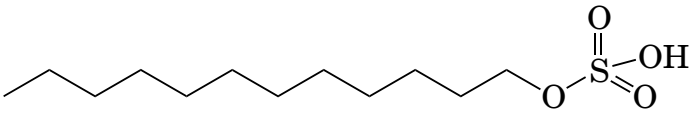
Rules:

1. **You may use any inanimate source you like. *Note, however, that neglecting to cite your sources appropriately is unethical and is potentially an instance of Academic Misconduct*.**
2. **You may work in groups of up to three.**
3. **You may discuss the questions with your partner(s) or with your instructor (don't count on answers, but you might get hints).**
4. **You may not discuss (neither verbally, via email, nor using any other method, including mental telepathy) the exam questions with anyone not currently enrolled in the class.**
5. **Please submit your text in *typed* form (equations/drawings may be *neatly* drawn by hand in ink). (You may submit one set of answers per group).**
6. **Due Date: Tuesday, October 23, 2011 *in class*.**
7. **Good luck!**

1. Who won the 2012 Nobel Prize in Chemistry? What was their contribution? Was this worthy of being recognized with the Nobel Prize? Please justify your answer.

2. You begin to study a simple reversible reaction that interconverts compound S and compound P, catalyzed by enzyme X. You observe that the $\Delta G'^{\circ}$ for the S to P conversion to be –15 kJ/mol, and that compound S has a dissociation constant (K_d) of 15 mM for Enzyme X, while compound P has a K_d of 5 mM.
    a. What are the $\Delta G'^{\circ}$ values for the binding of compound S and P to enzyme X?
    b. Is it likely that both S and P bind to the same site on enzyme X? Why?
    c. Please explain the effect of enzyme X on conversion of S to P. (A graph of energy *versus* reaction progress is likely to be quite helpful, in illustrating your explanation; however, you ***still*** need to explain your answer in words!)
    d. Please explain what will happen if 5 mM compound S and 5 mM compound P are mixed with a small amount of enzyme X. (Hints: are binding of S and P to enzyme X thermodynamically favorable processes? Is this a problem? Will net amounts of S or P be produced? ***More generally, demonstrate that you understand how a simple enzyme actually functions***.)

3. Membranes are found in all organisms.
    a. What environmental features are necessary for membranes to be stable structures? Please justify your answer in thermodynamic terms.
    b. How does a detergent (such as dodecyl sulfuric acid, below) alter membrane stability?



Dodecyl sulfuric acid

    c. Can water cross a lipid bilayer? Is the bilayer a kinetic or a thermodynamic barrier? Why? (Hint: be explicit about the starting and ending states for the process you are describing and consider any transition states before attempting to answer this question.)
    d. Do active transporters alter kinetics, thermodynamics, or both? Please justify your answer. (Hint: be explicit about the starting and ending states for the process you are describing and consider any transition states before attempting to answer this question.)

4. *Staphylococcus aureus* secretes the polypeptides that comprise the mushroom-shaped protein α-hemolysin (Protein DataBank file 7AHL), a structurally aesthetically pleasing but lethal toxin.
    a. Is α-hemolysin a transmembrane protein? Please use relevant measurements as part of the process for assessing this, and please justify your answer.
    b. Examine the tubular portion of the protein (the "stem" of the "mushroom"). Is there a pattern to the amino acid side-chains in this

part of the protein? If so, what is the purpose of the side-chain pattern? Please rationalize your answer.

c. Is there a functional reason for the secondary structure that comprises the "stem" of the molecule? Why this secondary structure, rather than another one? Why a regular secondary structure rather than a non-repeating set of Φ/Ψ angles? Please rationalize your answer.
d. How does the structure of this protein allow it to be lethal to cells? (In other words, look at the structure, and give a ***mechanistic explanation*** as to how it might be capable of killing a cell. Note that simply stating that α-hemolysin causes cells to lyse without giving a mechanism is ***not*** a good answer.)
e. What is the role of the "cap" for the protein interaction with cells? What relevant amino acid side-chains are present in the "cap", and what is their purpose?

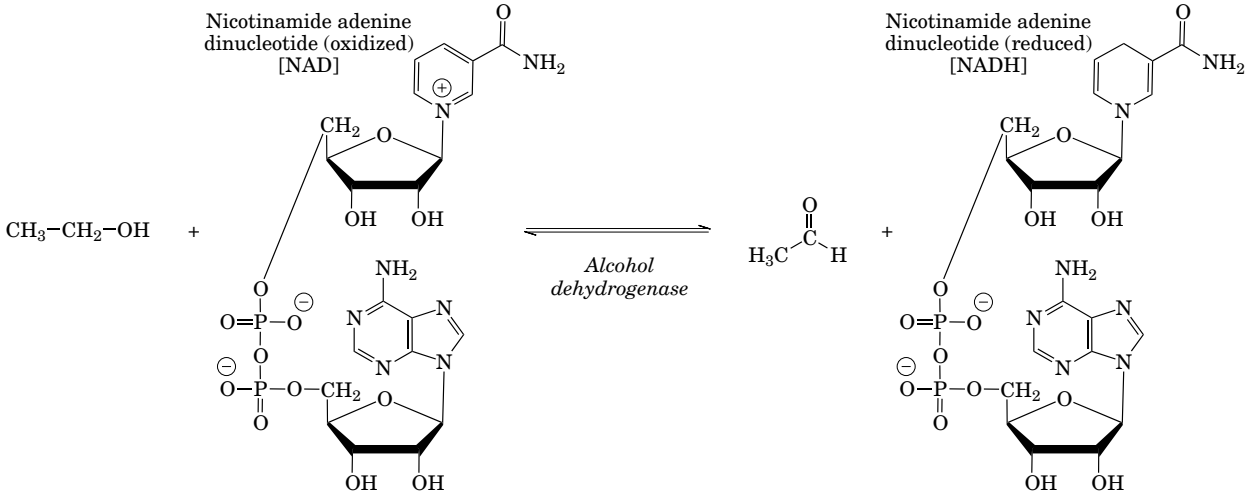
5. In the *Star Trek* (original series) episode "The Naked Time", members of the *Enterprise* crew became infected with a novel transmissible agent that altered brain functioning[1]. While working as part of Dr. McCoy's science team, you discovered that affected individuals have elevated levels of enzyme Z, which catalyzes a reaction involving compound B, and that compounds O and U affect enzyme Z activity in different ways. The enzyme data you obtained are in a spreadsheet posted on the course website.
    a. Based on your analysis of the enzyme Z data, what are the enzyme parameters for enzyme Z? Does enzyme Z exhibit cooperativity? (Please justify your answer.)
    b. How do compounds O and U affect enzyme Z activity?
    c. Assuming that elevated enzyme Z activity is a cause of the altered brain functioning, describe (in qualitative terms!) how you might develop a compound to help the affected individuals.

6. Hemoglobin, the oxygen transport protein in vertebrates, provides a useful example of many issues related to the understanding of biochemical processes and protein structure-function relationships.
    a. Why is hemoglobin necessary for oxygen transport in vertebrates? Please explain, using the principles of thermodynamics and kinetics, the mechanism by which hemoglobin allows oxygen transport. (Hint: this question is ***not*** as simple as it sounds; a statement that hemoglobin carries oxygen is insufficient without an explanation for the reasons that the carrier is necessary.)
    b. A company develops an effector compound, Q, which enters red blood cells, binds to hemoglobin, and stabilizes the R state of the protein. Would compound Q be an effective performance-enhancing drug for athletic competition? Please justify your answer.
    c. Many animals can function normally in an atmosphere with 50% of the oxygen partial pressure of observed at sea-level. However, sufficient carbon monoxide to occupy 50% of the oxygen binding sites on

[1] Note: it is ***not*** necessary to be a fan of *Star Trek* or to have seen "The Naked Time" to answer this question.

hemoglobin is usually lethal. Why is this true? (Hint: you may ignore any effects of carbon monoxide on mechanisms other than oxygen transport.)

7. In the alcohol dehydrogenase reaction (an important metabolic reaction in yeast, and, in the opposite direction, in humans consuming liquid beverages containing yeast metabolic byproducts), the enzyme uses a vitamin-derived coenzyme as part of the reaction.



   a. What is the purpose of the coenzyme in this process? (In other words, why is the coenzyme used, instead of simply using amino acid side chains?)
   b. (Extra credit: in which direction (forward or reverse, relative to the reaction shown above) should the process have a negative value of $\Delta G'^{\circ}$? Use **Spartan calculations** and a clear explanation to justify your conclusion.)

8. One class of signaling compounds includes several related molecules, all of which are protein dimers comprised of two subunits. The dissociation constant for these dimers is about 10^{-6} M; in circulation the concentration is usually about 10^{-8} M. The vast majority of these hormones exist as the intact dimer in circulation. Is this expected? Why? If not, please account for the observation that, in spite of the dimer being the only functional form, the hormone is active in animals.

9. The "RNA World" hypothesis states that the earliest organism used RNA for all of the roles currently filled by RNA, DNA, and proteins. (Reading the chapter on nucleotide and nucleic acid structure might assist in answering this question.)
   a. Why is RNA, rather than DNA or proteins, thought to be the first significant biological molecule?
   b. RNA, regardless of sequence, is intrinsically less stable than DNA. What type of reaction underlies this lower stability? (Hint: a reaction mechanism, with electron movement arrows should be part of your answer.)