Problem Set 9 (**Due April 14th**)

1. Describe the process of delivering amino acids to the liver from:
    a. Dietary proteins
    b. Degraded cellular proteins

2. Ammonia is transported through the blood from extrahepatic cells to the liver as glutamine or alanine.
    a. Why is this necessary?
    b. How are these two molecules generated in other tissues?

3. The first step in the degradation of most amino acids is removal of the amine group.
    a. What is the class of molecules that are produced when amino acids are deaminated?
    b. How is aspartic acid deaminated? Please show a mechanism describing this process.
    c. In addition to aspartic acid metabolism, Aspartate transaminase has a special role in nitrogen metabolism. What is this role?

4. Glutamate Dehydrogenase is allosterically inhibited by GTP.
    a. How does this process occur?
    b. Using the crystal structure of GDH (pdbID 1HWX), discuss the inhibition graph found in your lecture notes (Lecture 18, slide 8) based on what you seen in the structure Note that the numbering of amino acids in the pdb is off by 4 relative to the book (H454 = H450, S448 = S444, and R463 = R459). **Please include an image of ONE subunit of this protein with GTP and these three residues shown as stick images.**

5. Although mammals can synthesize Arginine, it is often considered an essential amino acid. Why is this?

6. Oxaloacetate, α-Ketoglutarate, pyruvate and 3-phosphoglycerate are all metabolic precursors for amino acid biosynthesis. Please determine the energetic cost (e.g. how much ATP is sacrificed) of using one of each of these molecules. For the two TCA cycle intermediates, recall that the product of the pyruvate carboxylase catalyzed reaction is in equilibrium with some, but not all TCA intermediates.

7. How much energy is required to biosynthesize arginine?

8. Please compare the energetic cost vs. yield of proline anabolism and catabolism.

9. Using KEGG Pathways, navigate to the page that describes the degradation of branched chain amino acids.
    a. As you can see, the first steps in each case are the same. Once transamination occurs, the next step (or 3, depending on how you look at it) should look very familiar to you. What reaction does this resemble? Hint: looking closely at the cofactors should be very helpful here.
    b. Based on your answer to 9a, propose a mechanism for the oxidative decarboxylation steps in the L-leucine degradation pathway.
    c. Show a reaction scheme for the rest of the degradation of L-Leucine. Make sure to include the steps that convert acetoacetate to Acetyl-CoA.
    d. Determine the energy yield for the complete oxidation of L-Leucine. You may ignore any energetic cost or yield associated with the fate of NH_3.

10. Determine the net reaction for the Urea Cycle.

11. Please show a mechanism for the enzyme-catalyzed steps of the Urea Cycle.

12. How is flux through the Urea Cycle regulated?

13. How are the biosynthesis of arginine and glutamine linked? Please show a reaction scheme to reinforce your answer.

14. Please draw the fully reduced form of folic acid (tetrahydrofolate) and discuss how this essential cofactor plays a role in glycine and serine metabolism.