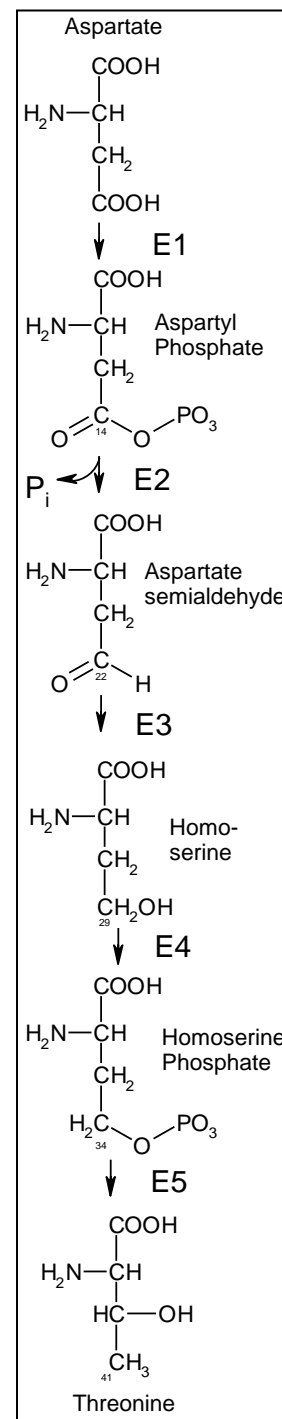


Due Tuesday, November 19

Estimated time: ~ 75 minutes

1. (10 pts, 15 min) The metabolic pathway for the *synthesis* of threonine is shown on the right. Note that not all reactants/products are shown for each reaction.

- The first step in this pathway is phosphorylation of a carboxylic acid. The phosphorylation of a carboxylic acid by inorganic phosphate is unfavorable, with a ΔG° of approximately +30 kJ/mol yet the reaction proceeds spontaneously in the forward direction. How can the Gibbs energy, ΔG , become negative for this step in the pathway (2 pts).
- Provide a name for the enzyme (E1) that catalyzes the first step of this reaction, based on your answer to part i) (2 pts).
- How would you describe the chemical changes that occur between aspartyl phosphate and aspartate semialdehyde (catalyzed by enzyme E2)? What cofactor/co-substrate is likely involved in this step? Sample *incorrect* answer: This step is catalyzed by a phosphatase because a phosphate is released from the substrate). [Hint: a similar reaction occurs in glycolysis, but in reverse. You can consider the reaction to be a change between a protonated carboxylic acid and an aldehyde – i.e. pretend the phosphate is not there.] (2 pts)
- Show, by balancing the reaction (or counting electrons on the relevant atoms in the reactant and product), that the step catalyzed by E3 is a redox reaction. Is it an oxidation or a reduction? (2 pts)
- What *general* conclusion can you draw about synthetic pathways? Do they produce or consume energy? Do they contain oxidative or reductive steps? Briefly justify your answer with reference to the pathway for threonine biosynthesis (2 pts)

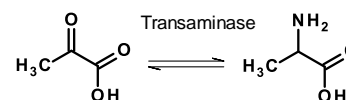


- (5 pts, 5 min) Glyceraldehyde-3-phosphate dehydrogenase catalyzes the oxidation of glyceraldehyde to a phosphorylated carboxylic acid in glycolysis. Briefly discuss how changing the cysteine residue to serine would affect the mechanism.
- (5 pts, 5 min) Is the hypothetical conversion of hexanoic acid (a 6 carbon fatty acid) to glucose an oxidation or a reduction? Show by either balancing or electron counting. Which compound is higher in energy?
- (6 pts, 10 min) Fill in the steps in the conversion of an alkane (e.g. ethane) to a carboxylic acid (e.g. acetic acid) using a series of two electron oxidations, plus any additional reactions that might be required. Give the generic name (e.g. type of reaction catalyzed) by each enzyme in each step. A skeleton outline is given below:



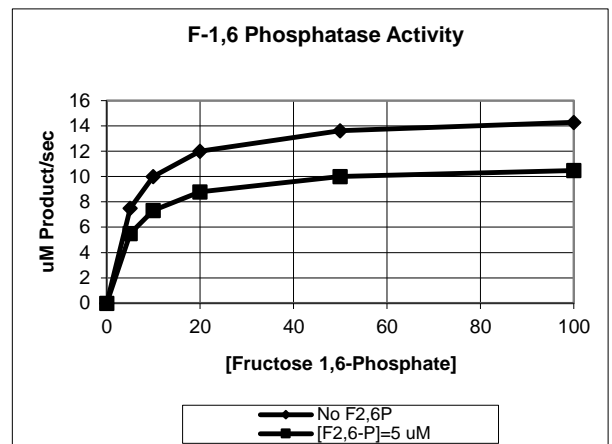
- (8 pts, 10 min) In recitation we investigated how PFK was controlled by ATP and ADP.
 - Does the regulation make physiological sense? Briefly justify your answer (4 pts).
 - Propose a mechanism by which this occurs, based on the **structure** of PFK (4 pts)

6. (5 pts, 10 min) Transaminases are enzymes that reversibly convert α -keto acids to α -amino acids by the replacement of a ketone group by an amide group, thus providing a way to both synthesize and degrade amino acids. Discuss how the amino acids alanine and aspartic acid could be used to synthesize glucose.



7. (10 pts, 20 min) The curves to the right show the effect of fructose-2,6-bisphosphate (5 μ M) on the activity of fructose-1,6-bisphosphatase. The data that was used to generate this plot is given in the table below:

[F-1,6-Phosphate] (μ M)	uM Product/sec	
		+F-2,6P
0	0	0
5	7.5	5.5
10	10	7.3
20	12	8.8
50	13.6	10.0
100	14.3	10.5



Please answer the following questions (most of these are straightforward and are designed to draw your attention to differences in F16P and F26P).

- Draw the substrate and product of the reaction catalyzed by fructose-1,6-bisphosphatase. Include any cofactors/co-substrates that may be involved in the reaction (e.g. ATP, NADH, etc.) (1 pt)
- In which metabolic pathway does fructose-1,6 bisphosphatase operate (1 pt)?
- What is the structural difference between F-1,6-Phosphate and F-2,6-Phosphate (1 pt)?
- Would you characterize F-2,6-P as which of the following: (1 pt)
 - Competitive inhibitor of F-1,6-bisphosphatase
 - Allosteric activator of F-1,6-bisphosphatase
 - Allosteric inhibitor of F-1,6-bisphosphatase

Briefly justify your answer on the basis of the experimental data (3 pts).

- Based on your answer to part iv, draw a *simple*, cartoon-like diagram of fructose-1,6-bisphosphatase. In your diagram should indicate the binding sites for F-1,6-P and F-2,6-P and indicate the active site region on the enzyme (3 pts).