

BCHM 463

Your Name: _____

Biochemistry and Physiology

ID #: _____

Final Exam, December 18, 2002

Prof. Jason Kahn

You have 115 minutes for this exam. It is worth 250 points, so you are getting more “points per minute” than on the hour exams.

You may use a calculator for this exam. No other study aids or materials are permitted.

Generous partial credit will be given, *i.e.*, if you don't know, guess.

Explanations should be concise and clear.

Honor Pledge: Please write out the following sentence and sign it, or talk to me about it:

“I pledge on my honor that I have not given or received any unauthorized assistance on this examination.”

Possibly useful information:

$RT = 2476 \text{ J/mole}$ today

$\Delta G = \Delta G^{\circ'} + RT \ln Q$, where Q has the form of an equilibrium constant

$\Delta G = -nF\Delta\epsilon$, where $F = 96500 \text{ J/(V}\cdot\text{mole)}$, n = number of electrons transferred

$\Delta G^{\circ'} = -30.5 \text{ kJ/mole}$ for $\text{ATP}^{4-} + \text{H}_2\text{O} \rightleftharpoons \text{ADP}^{3-} + \text{HPO}_4^{2-} + \text{H}^+$

$\Delta\epsilon^{\circ'} = 1.15\text{V}$ for $\text{NADH} + 1/2 \text{ O}_2 + \text{H}^+ \rightleftharpoons \text{NAD}^+ + \text{H}_2\text{O}$

Michaelis-Menten equation: $v_0 = V_{max}[S]/(K_M + [S])$

Type of inhibition	Apparent K_M	Apparent V_{max}	Apparent V_{max}/K_M
Competitive	αK_M	V_{max}	$(1/\alpha) V_{max}/K_M$
Uncompetitive	$(1/\alpha') K_M$	$(1/\alpha') V_{max}$	V_{max}/K_M
Mixed	$(\alpha/\alpha') K_M$	$(1/\alpha') V_{max}$	$(1/\alpha) V_{max}/K_M$
Noncompetitive ($\alpha=\alpha'$)	K_M	$(1/\alpha') V_{max}$	$(1/\alpha) V_{max}/K_M$

$$\alpha = 1 + ([I]/K_I) \quad \alpha' = 1 + ([I]/K_I')$$

$$V_{max} = k_{cat} [E]_{total}$$

The Two Towers opens tonight.

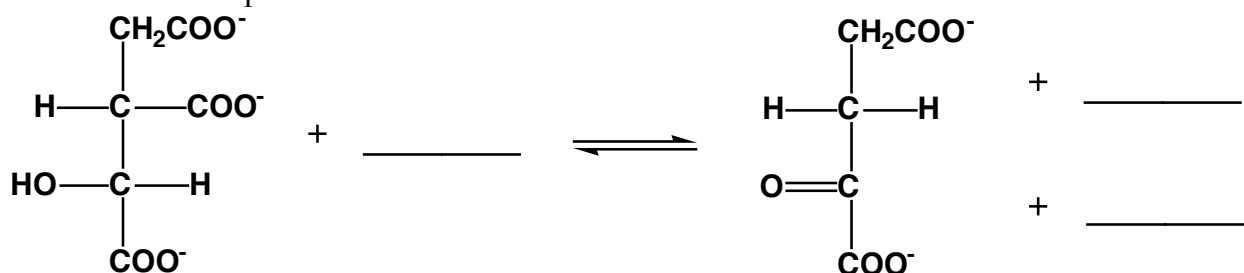
RELAX! READ THE QUESTION, THEN ANSWER!

1. (16 pts) Name the pathway whose first step is catalyzed by glucose-6-phosphate dehydrogenase, G6PDH. What is its main function in the red blood cell? Why have deleterious mutations in G6PDH arisen and been maintained in some human populations?
2. (16 pts) Most fatty acids cannot support the net synthesis of glucose (in our cells) whereas most amino acids can. Explain why in terms of the TCA cycle. Draw the structure of oxaloacetate.

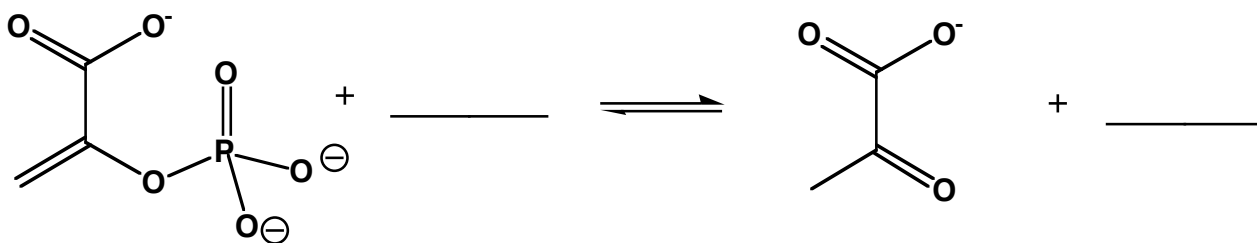
2. (16 pts) Most fatty acids cannot support the net synthesis of glucose (in our cells) whereas most amino acids can. Explain why in terms of the TCA cycle. Draw the structure of oxaloacetate.

- (12 pts) We have made the analogy that fat is like gasoline, an efficient means of storing chemical energy. Give two fundamental reasons that fat stores energy more densely than glucose, both on an ATP per carbon basis and a kJ/cm^3 basis. Following the analogy, if fat is gasoline then what is glucose?
- (15 pts) Draw the structure of a Cys-Lys dipeptide at pH 7.
- (15 pts) Diabetes is a disease of cellular starvation in the midst of plenty. What is the difference between Type I and Type II diabetes? Briefly describe one metabolic consequence of non-responsiveness to insulin (for example, decreased glucose transport into cells but pick another one), and one disease symptom arising from the presence of excess glucose in the blood or other tissues.

6. (12 pts) For the reactions below, name the enzyme that catalyzes the reaction and add the other necessary reactants and products (things like ATP, ADP, CO₂, etc) on the lines given. Don't worry about water or protons.



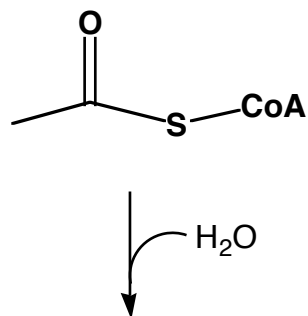
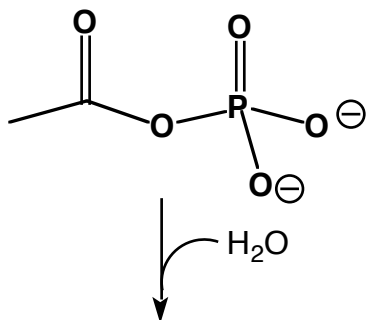
Enzyme:



Enzyme: _____

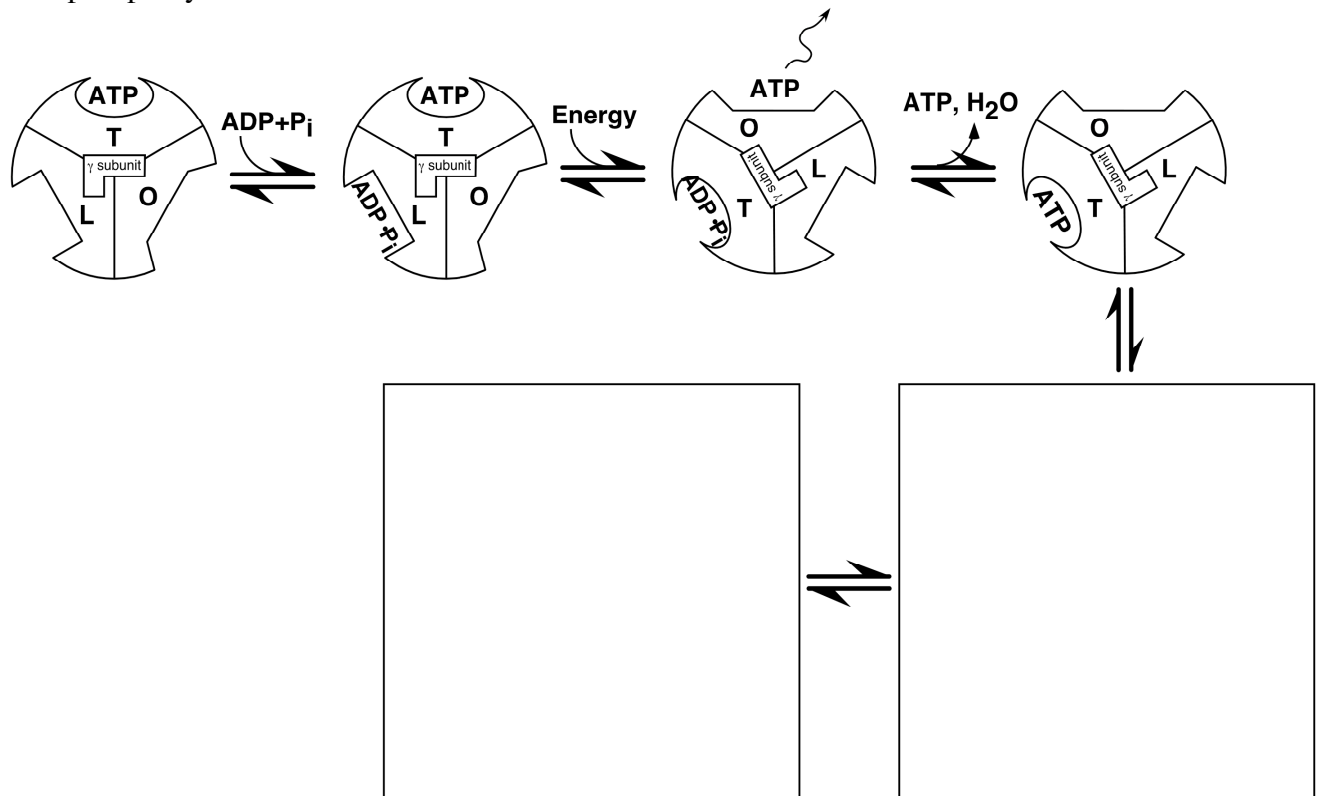
7. (12 pts) It is often observed that enzymes that catalyze near-equilibrium reactions in a given pathway are present in much larger amounts than those that catalyze strongly exergonic steps. Why might this be necessary in terms of maintaining flux? Why are the enzymes of anaerobic glycolysis present in larger quantities than TCA cycle enzymes in skeletal muscle?

8. (16 pts) Why are acetyl phosphate and Acetyl-CoA (shown below) each “high-energy” molecules (two separate explanations with a common thread)? Draw the products of (thio)ester hydrolysis for each.



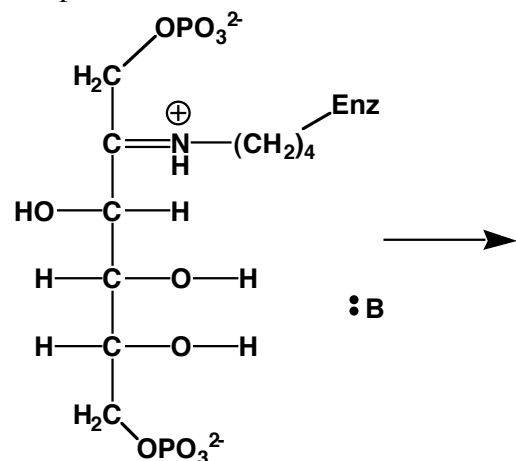
9. (13 pts) Briefly speculate on the metabolic consequences of a hemoglobin mutant with reduced oxygen-binding cooperativity (a lower Hill coefficient than normal) but a normal $p50$. What might one cellular response to hypoxia be? [These are important in solid tumors, which often are relatively anaerobic.]

10. (12 pts) Draw the next two steps in the binding change mechanism for ATP synthesis in oxidative phosphorylation:



11. (16 pts) Briefly describe the key steps of the phosphorylation cascade that activates glycogen breakdown in response to glucagon.

12. (20 pts) One intermediate in the Class I aldolase reaction is shown below. Draw the arrow pushing and the next structure (going toward GAP + DHAP) in the reaction mechanism. Draw the DHAP product of the reaction. What kinds of catalysis are illustrated by this mechanism?



- 13. (25 pts)** Name the electron donors and acceptors for electron transport by Complexes I, II, III, and IV (just initial and final for each one). Why does FADH₂ oxidation provide less ATP than NADH reduction?

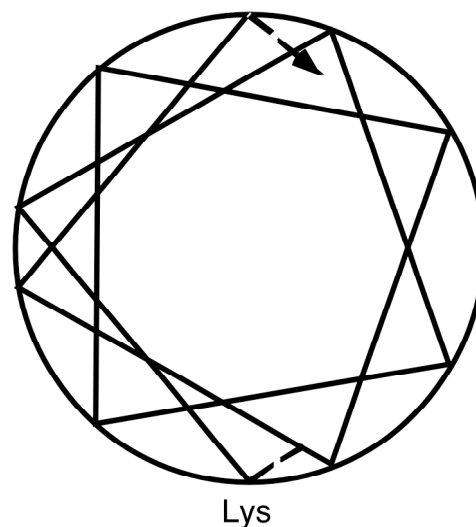
14. (12 pts) It is occasionally observed that an enzyme with a mutation of a serine to glutamate acts as if it were always phosphorylated at the serine. Draw the phosphoserine and glutamate side chains, and speculate on the structural origin of the functional change.

15. (20 pts) Use the following sequence for this problem: Lys-Val-Glu-Glu-Leu-Leu-Ser-Lys-Asn-Tyr

On the helical wheel representation to the right, enter the amino acid from the above sequence which would be at each position. The N-terminal Lysine is entered for you, and the helix runs from N-term to C-term away from you, into the page.

Does this α -helix have an amphipathic moment (i.e. one hydrophobic side and one hydrophilic side)? If it does, indicate which side is which on the helical wheel.

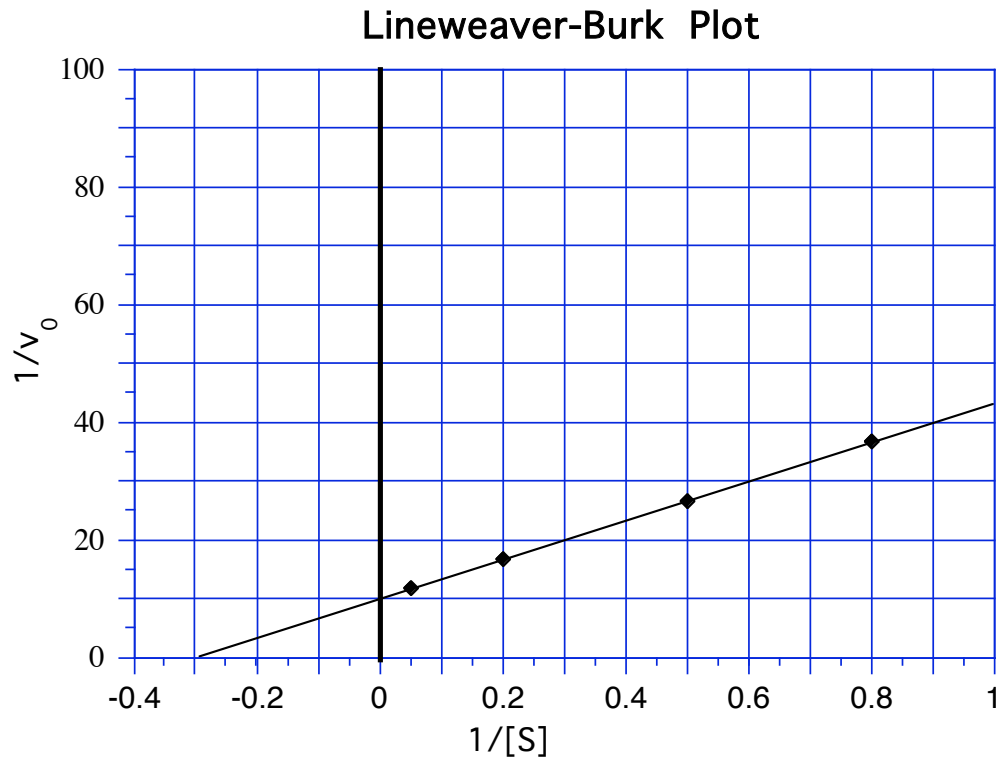
Circle one: Yes No



Which side of the helix is most likely to face the inside of the protein, and why?

It is observed that phosphorylation at serine destabilizes the folding of this α -helix. Why might this be the case?

16. (18 points) Pure non-competitive inhibition, as we have discussed, is quite rare. However, it is still a useful idea. Sketch the lines on the Lineweaver-Burk plot below corresponding to noncompetitive inhibition at increasing inhibitor concentrations.



It turns out that irreversible inhibition of an enzyme at different reagent concentrations has the same kinetic signature as non-competitive inhibition. With reference to the definition of V_{max} , explain why.

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