BCH 4053 **FINAL EXAM** **NAME_____**
May 1, 2003

There are 9 pages and 9 questions on the exam.
Only five are to be answered, each worth 20 points.

Page	Points
1	____
2	____
3	____
4	____
5	____
6	____
7	____
8	____
9	____
Total	_____

Answer two from questions 1, 2, 3, and 4

Answer three from questions 5, 6, 7, 8, and 9.

(Only five questions total will be graded. If you answer more than the required number from either group, please indicate which ones are to be graded.)

1. Following is an alphabetical list of the glycolytic and TCA cycle enzymes plus a few other enzymes we have discussed. Choose enzymes from this list that are described by the statements below, and place the number or numbers of the enzyme in the blank to the left of the statement. In most cases, more than one enzyme will apply. Given in parenthesis after the statement is the **target number** of enzymes for you to identify.

(1) aconitase
(2) aldolase
(3) citrate synthase
(4) enolase
(5) fumarase
(6) glucose-6-phosphate isomerase (phosphoglucoisomerase)
(7) glyceraldehyde-3-phosphate dehydrogenase
(8) hexokinase
(9) isocitrate dehydrogenase
(10) a-ketoglutarate dehydrogenase complex
(11) malate dehydrogenase
(12) malic enzyme
(13) phosphoenolpyruvate carboxykinase
(14) phosphofructokinase
(15) phosphoglycerate mutase
(16) phosphoglycerate kinase
(17) pyruvate carboxylase
(18) pyruvate dehydrogenase complex
(19) pyruvate kinase
(20) succinate dehydrogenase
(21) succinyl-CoA synthetase
(22) triose phosphate isomerase

(a) _____ CO_2 is a substrate or a product. (six enzymes)

(b) _____ ATP or GTP is a substrate or a product. (six enzymes)

(c) _____ Coenzyme A is a substrate or a product. (four enzymes)

(d) _____ NADH is a substrate or a product. (five enzymes)

(e) _____ Thiamine pyrophosphate is a prosthetic group. (two enzymes)

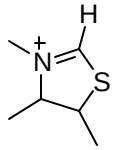
(f) _____ Possible anaplerotic reactions. (three enzymes)

(g) _____ An oxidoreductase (seven enzymes)

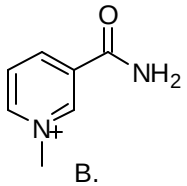
(h) _____ Operates removed from equilibrium (eight enzymes)

2. Below are the **partial** structures of seven coenzymes you have studied.

(a) Below each structure, draw an alternative form of the coenzyme to which it is converted during the course of a reaction.



A.



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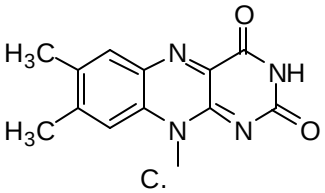

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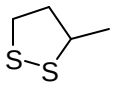

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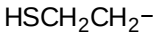
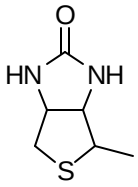


E.



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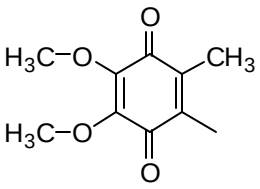


G.

(b) Complete the following table by giving the name of the coenzyme, identifying it as a **cosubstrate** or **prosthetic group**, and give the name of an enzyme that it reacts with.

Structure	Coenzyme	Cosubstrate or Prosthetic Group?	Enzyme
A			
B			
C			
D			
E			
F			
G			

3. Glycerol, formed from hydrolysis of triglycerides, can be provide energy by oxidation via glycolysis and the TCA cycle. It must first be activated by the enzyme **glycerol kinase**, which catalyzes:

glycerol + ATP $\rightarrow$ glycerol-3-phosphate + ADP

Glycerol phosphate dehydrogenase converts glycerol-3-phosphate to dihydroxyacetone phosphate.

(a) Starting with [2-^{14}C]-glycerol (the middle carbon), trace the radioactive carbon through glycolysis and the **first turn** of the citric acid cycle, showing how oxaloacetate would be labeled at the end of the first turn. To do so, give the structure of each intermediate in the pathway, and circle the carbon atom(s) of each intermediate which derive from carbon-2 of glucose.

(b) Indicate each step that **uses** or **produces** an NADH, $CoQH_2$, ATP, or GTP, and calculate the overall stoichiometry for the reaction:

glycerol $\rightarrow$ 3 CO_2

(c) Assuming 2.5 ATP per NADH, 1.5 ATP per $CoQH_2$, and 1.5 ATP per cytoplasmic NADH, what is the total ATP yield from oxidation of 1 mole of glycerol?

4(A) Following is an alphabetical list of the intermediate electron carriers found in the mitochondrial electron transport chain. Identify the carriers that fit each description on the right by placing the letter of the carrier(s) in the blank next to the description. A carrier may be used more than once.

Electron Carrier	**Description**
(a) Coenzyme Q	A component of Complex I _____
(b) Cu_A	A component of Complex II _____
(c) Cu_B	A component of Complex III _____
(d) cytochrome a	A component of Complex IV _____
(e) cytochrome a_3	Carries electrons from Complex II to Complex III _____
(f) cytochrome b_H	Carries electrons from Complex III to Complex IV _____
(g) cytochrome b_L	Forms a binuclear center for oxygen reduction _____
(h) cytochrome c	Accepts electrons directly from succinate _____
(i) cytochrome c_1	Accepts electrons directly from NADH _____
(j) FAD	
(k) Fe/S center	
(l) FMN	

4(B). Mitochondria or submitochondrial particles can carry out the following coupled reaction:

$$2 \text{ cyt c (red)} + \tfrac{1}{2} O_2 + ADP + P_i \rightarrow 2 \text{ cyt c (ox)} + H_2O + ATP$$

(a) Calculate the overall $\Delta G^{o'}$ for this coupled process. (E_o' for cyt $c_{(ox)}$/cyt $c_{(red)}$ is +0.25 V, E_o' for ½ O_2/H_2O is +0.82 V, R = 8.314 J-mol^{-1}-K^{-1}, F = 96.5 kJ-mol^{-1}V^{-1}, T = 298 K $\Delta G^{o'}$ for ATP hydrolysis = -30.5 kJ-mol^{-1})

(b) Diagram the orientation of the two complexes in the inner mitochondrial membrane that carry out this coupled reaction, illustrating in the diagram how the coupling occurs.

(c) Explain how the proposed coupling leads to the proposed stoichiometry in the equation (1 ATP made per two cyt c's reduced).

5. One of the proton dissociations of hemoglobin occurs near neutral pH. This dissociation is affected by the binding of oxygen to Hb. Assume that the dissociations for oxyhemoglobin (HbO_2) and deoxyhemoglobin (Hb) can be treated as a simple monoprotic acids as follows:

$$HHbO_2 \rightleftarrows H^+ + HbO_2 \text{ , } pK = 6.6; \quad \text{and} \quad HHb \rightleftarrows H^+ + Hb \text{ , } pK = 8.2;$$

(a) Assume that blood is 3.0 mM in hemoglobin. At the plasma pH of 7.4, and the hemoglobin in the lungs fully oxygenated, what are the concentrations of the protonated ($HHbO_2$) and unprotonated (HbO_2) forms?

(b) In tissues, the pressure of O_2 drops, and the oxygen dissociates from hemoglobin. The deoxyhemoglobin is a stronger base, and must be titrated with protons for the pH to remain constant at 7.4. Assuming the oxygen were completely dissociated, how many protons would be required per liter to produce the proper Hb/HHb ratio for pH 7.4?

6. In 2010 the Mars shuttle returned to earth with a sample of a Martian single-celled organism. Not surprisingly, extracts of the organism catalyzed the hydrolysis of ATP, showing Michaelis-Menten kinetics with a $\mathbf{K_m}$ of 3.5 x 10^{-5} M and a $\mathbf{V_m}$ of 90 µmoles-min^{-1}-mg $protein^{-1}$.
   (a) Give the **Michaelis-Menten** equation.
   (b) Calculate the velocity of the ATPase reaction at the following ATP concentrations:
   S = 0.75 x 10^{-6} M; S = 2.5 x 10^{-4} M; S = 0.035 M
   (c) What would $\mathbf{V_m}$ be in the presence of 0.0015 M concentration of a competitive inhibitor of ATPase that had a $\mathbf{K_I}$ of 0.0015 M?
   (d) The ATPase activity was stimulated by the addition of Ca^{2+} ions. What does this suggest about the function of the ATPase?
   (e) Using GTP as a substrate, the kinetic parameters were a $\mathbf{K_m}$ of 4.9 x 10^{-3} M and a $\mathbf{V_m}$ of 230 µmoles-min^{-1}-mg $protein^{-1}$. Would you consider GTP or ATP the "better" substrate? Why?

7. Aldolase catalyses the following reaction of glycolysis:

fructose-1,6-bisphosphate $\rightleftharpoons$ dihydroxyacetone phosphate + glyceraldehyde-3-phosphate

(a) Give the structures of the reactant and products of this reaction.

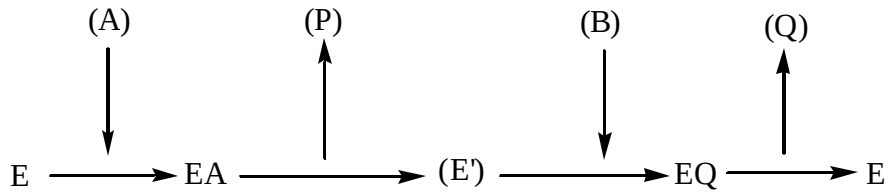
(b) **?G°'** for this reaction is +23.9 kJ mol^{-1}. Calculate **K'**, the equilibrium constant. (R=8.314 J/mol-K; assume T = 37 °C or 310 K)

(c) Calculate **Q'** and **?G** for the reaction when fructose-1,6-diphosphate is $1.0x10^{-4}$ M, dihydroxyacetone phosphate is $4.0x10^{-5}$ M, and glyceraldehyde-3-phosphate is 2.5×10^{-6} M.

(d) Fructose metabolism bypasses this reaction of glycolysis. Describe how Fructose is metabolized to glycolytic intermediates.

8. The mechanism of chymotrypsin illustrates several of the factors that are believed to contribute to the rate acceleration obtained by enzymes. Describe each of the following aspects of the chymotrypsin mechanism.

(a) A reaction model that shows ping-pong kinetics. (i.e., specify the identity of A, B, P, Q, E, and E', in the following scheme:)



(b) Transition state stabilization by bonds formed between the enzyme and the transition state that are not found in the binding of substrate or product.

(c) Acid-base catalysis mediated through a "catalytic triad". Describe how the triad assists in the formation of the covalently bound intermediate.

(d) Substrate specificity provided by the nature of the substrate binding site. (Explain how chymotrypsin differs from trypsin in the binding site.)

(e) Regulation of chymotrypsin activity in the digestive tract.

9. Draw the structure of **5** of the following:

(a). Guanosine

(b). Arachidonic acid

(c). Mannose (Haworth projection)

(d). Phosphatidyl choline

(e). AT base pair

(f). Sucrose (Haworth projection)

(g). Stearic acid

(h). Cholesterol