Name_____
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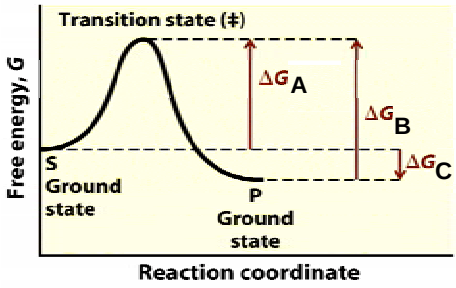
Reaction Energetics and Catalysis (8 points)



This picture is an energy diagram for the molecule S being converted into the molecule P. The vertical axis is free energy, and the horizontal axis is the progress of the reaction. Several free energy changes are represented on the curve, as ΔG A, B or C. For questions 1-5 Choose a given labeled free energy change or a function of those on the graph (eg A, B+A, C-A, whatever), to express the requested quantity. Each ΔG is in the graph is a positive number.

1) What is the free energy change for S becoming P? **write here:**

2) What is the free energy change for P becoming S? **write here**:

3) What is the activation energy for the S to P reaction? **write here:**

4) What is the activation energy for the P to S reaction? **write here:**

5) What is the component of the activation energy for the P to S reaction that can not be affected by an enzyme? **write here:**

6) Consider an enzyme that catalyzes the S to P reaction. Sketch in a little curve on the same axis that shows the effect of such an enzyme

7) Does the enzymes also catalyze the P to S reaction? Why do you say this?

8) Suppose the enzyme lowers the activation energy by 7kJ/mole. What is the activation energy for the P to S reaction when the enzyme is added?

write letter here: _____

a) 7 kJ/mole c) (A-7)kJ/mole b) (C-7)kJ/mole

d) (A+C-7) kJ/mole e) no change f) correct choice not shown

The Enzyme Apprentice (9 points)

Wallace and Grommet are each trying to get a job at Bongo Pharmaceuticals. Because many drug targets are enzymes, the people at Bongo decide to test their skills as enzymologists.. Each is given a lab for the afternoon, and each is told to measure the activity of the same batch of purified enzyme.

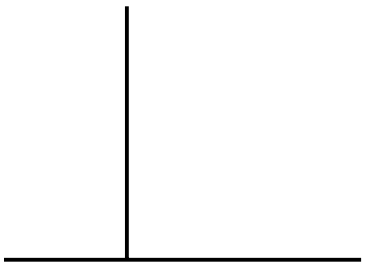
The day passes and at 5 pm, Wallace and Grommet present their data. Both report that the enzyme has Michelis-Menten behavior. They each have found the Km to be the same, 0.2mM. However, Wallace has a Vmax of 4×10^4 μmoles per second, and Grommet has a Vmax value of 8×10^4 μmoles per second.

9) What is the substrate concentration that will give half-maximal rate according to Wallace? ans:_____

10) Is the substrate concentration that causes the half-maximal rate in Grommet's experiments the same or different? Why?

11) What is the substrate concentration that will cause 2/3 the maximal rate according to Wallace? (hint: you do NOT need to use any Vmax to calculate this…) ans:_____

12 (4 pts)) Using the axis to the right, sketch the data obtained by Wallace and Grommet as a Lineweaver-Burk plot. I don't care about the actual numbers, just the comparison of the two data sets. Sketch graphs, label the axes and the intercepts. Indicte which plot is which with a W and a G.



The two contenders used the same sample of enzyme, and the same reagents to do all of their analyses. But they got different results for Vmax by a factor of two. They are baffled (they didn't take metabolic in their otherwise excellent college). The president of Bongo suggests they take their analysis one step further and calculate kcat. They do and that quantity is identical for the two enzyme samples!

13) Write the definition of kcat as a function of Vmax and the total enzyme concentration $[E]_T$

$k_{cat} =$

14) So, what is the simple explanation for why they got different values for Vmax? (One sentence)

Clinical report: β-enolase deficiency (finally, some metabolism; 8 points)

Recently Comi et al. (Comi et al., Ann Neurol. (2001) 50:202-7) reported on a new metabolic disorder: patients with a deficiency in the enzyme enolase. There are three isozymes of enolase, each encoded by a separate gene. One of these isozymes (the β isozyme) comprises the majority of enolase activity in muscle (over 90 %). In the patients described, that gene is missing, causing very low muscle enolase activity. Let's think about this situation

15) In what metabolic pathway is enolase a participant? ans:

16 (4 pts)) Write the enolase reaction. Include the structures and names of the starting and ending molecules.

17) The resulting product can transfer phosphate to ADP. What is the general name for this type of phosphate transfer? **write here:**

18) As Comi et al. report, patients missing muscle-specific enolase have all sorts of problems when they exercise. They fatigue rapidly and the muscles are prone to damage during exercise. Also, they have abnormally high levels of glucose stored as muscle glycogen. Why is the buildup of glycogen not surprising (one sentence)?

19) Humans also express a distinct, neuron-specific isozyme of enolase, called NSE. This version of enolase provides all of the activity of this enzyme in the nerve cell. Would you expect the patients in Comi's paper to have normal or abnormal neuronal metabolism? Justify your answer. (One sentence)

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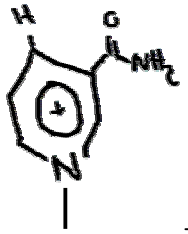
Functional Group Junction: ripped from the headlines! (8 points)

20-27) The functional groups below are directly from lecture slides. Each is found in a cofactor that serves a specific biochemical function. Write the cofactor (eg: CoA) where each is found, and in the box write (WORDS ONLY) a few words about the **chemical function** of each. Example: accepts electrons in pairs. I have filled in a few to get you started. 1 pt for names, 2 pts for function.



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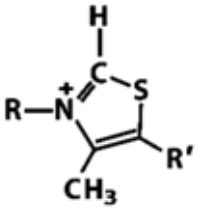
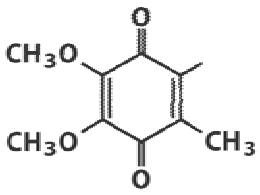


TPP

_____



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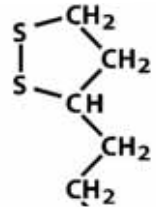
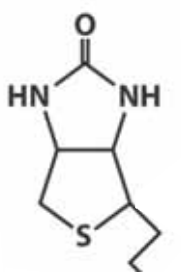


transfers acetyl groups and electrons

_____



_____

PFK-1: The Minister of Glycolysis (11 points)

Phosphofructokinase 1 is regulated by both citrate and AMP. That's A-*M*-P. Now you know enough about these things to understand why they regulate this key enzyme.

28 (4pts)) What is the reaction catalyzed by PFK-1? Write the structures of the glucose-derived molecules. (no, I am not going to be freaky about stereochemistry). Name the molecules.

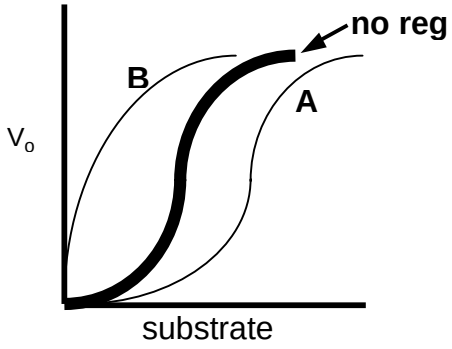
29) What feature of this reaction in cellular conditions makes PFK-1 a reasonable regulation point for the control of glycolysis? (sentence or phrase)

30) What is the general name for the kind of regulation that PFK-1 undergoes by things like citrate and AMP?

answer:

This is a graph of the PFK-1 reaction kinetics in the presence and absence of nothing, citrate or AMP. The "no regulator" curve is bold and labeled. Answer the following questions

31) What is the shape of the "no-regulator" curve called?



32-35) From what you know about PFK-1, decide which curve represents the "plus citrate" curve and which represents the "plus AMP" curve, and write one sentence describing why each particular effect is metabolically useful to the cell.

_____ is the plus citrate curve

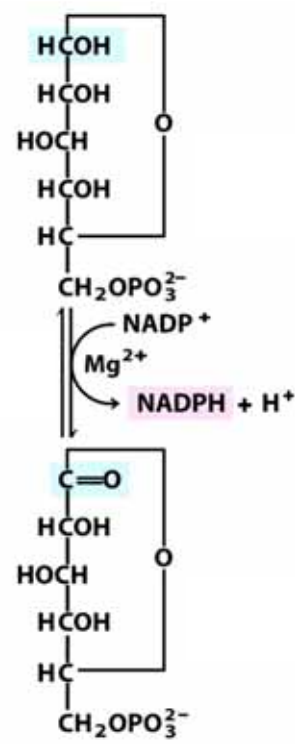
why useful:

_____ is the plus AMP curve

why useful:

The other glucose pathway (12 points)

This is a reaction we covered in class. Look familiar?



36 (2 pts)) Write the names of the 6-carbon reactant and product in the space below

reactant:

product:

37) What is the enzyme that catalyzes the depicted reaction?

38) What is the name of the pathway that includes this reaction?

39 (2 pts) What are the two most important products of that pathway?

This is a redox reaction, and so can be understood in terms of electron giving and taking. Lets think about this reaction in that way. If you need them, just say"R" for the reactant or "P" for product.

40) What is the oxidizing agent for the forward reaction? _____

41) What is the reducing agent for the forward reaction?_____

42) What is the reducing agent for the reverse reaction?:

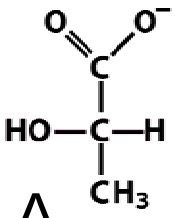
43) The half-cell potential for NADP/NADPH is E'^{o} = -0.324. At equilibrium which form is favored? **ans:**

44) What is the $\Delta G'^{o}$ for the NADP half-cell reaction? Set up an equation for calculating this quantity in the space to the right.

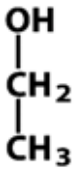
45) Besides all the constants, what information do you need to calculate the true $\Delta G'$ for the NADP half reaction at standard temperature and pressure in cellular conditions? Just words, one sentence.

In vino (or lactis), veritas…(11 points)

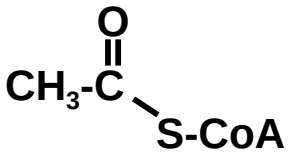
Here are three molecular structures. We have learned about each of these. Answer the following questions by filling in the blanks with the appropriate letter or combination of letters associated with each structure. If none apply, write "none".



A



B



C

Examples:

Produced from pyruvate: A, B, C Has a visible OH group B
Has uranium in the structure: none

46) (freebie!) Produced from pyruvate _____

47) Can be converted to pyruvate by lactate dehydrogenase _____

48) TPP cofactor is required for this structure's production from pyruvate _____

49) Made from pyruvate by a large multi-enzyme complex _____

50) Produced from pyruvate by two enzymes _____

51) Has two carbon functional unit that is directly transferred to alpha ketoglutarate _____

52) Synthesis from pyruvate yields free $C0_2$ _____

53) Production results in restoration of NAD for glycolysis _____

54) Synthesis from pyruvate directly involves the FAD cofactor _____

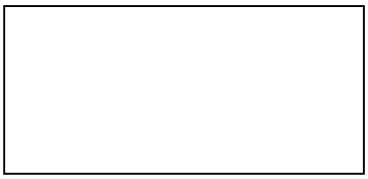
55) Tends to build up during intense exercise _____

56) Tends to be drunk when watching intense exercise _____

You got me straight trippin', chymotrypsin…(6 points)

The peptide in the picture is processed by chymotrypsin, the protease that we learned about in class. Note that some of the atoms are numbered so you can refer to them without having to draw elaborate pictures.

57) The amino acid serine, shown in the little box, plays a key role in the action of chymotrypsin. *In one sentence*, describe its role in the chymotrypsin reaction. Refer to the numbered atom(s) to help your description



58 (2 pts)) Which numbered atom has the most intimate association with the chymotrypsin "oxyanion hole"? What is the function of the oxyanion hole? One sentence.

59) Which one of the depicted products is released first during the hydrolysis of the peptide above?

choose_____

60) Why are two separate products released from the enzyme at different times?

61) What chemical reaction allows the release of the second product?

A cycle so nice they named it thrice (15 points; guest author S. Mason)

62 (4 pts)) The primary way carbon enters the Krebs cycle is through combination of a 2-carbon unit with oxaloacetate. Draw that reaction, showing the 2-carbon molecule that combines with oxaloacetate, the carrier cofactor, and the resulting products. Include the names of the enzyme, structures of substrates and products.

63-68) The following are some molecules that control Krebs cycle enzymes. Each acts as would be expected for useful regulation. Knowing this, mark the regulator with an I if you expect it to be an inhibitor, or an A if you expect it to be an activator.

____NADH ____ ATP ____ succinyl-CoA

____ADP ____citrate ____ Ca^{2+}

69) Sometimes intermediates of the Krebs cycle are removed or lost, and must be replenished. What is the general name for the reactions that carry out replenishing?

70 (4 pts)) A lack of oxaloacetate would really slow down the Krebs cycle. Write a reaction that produces oxaloacetate from a non-Krebs cycle molecule – no structures needed, but the names of all molecules, cofactors, and the enzyme name must be present.

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Truth or Dare! T/F questions below (12 points)

_____ **71)** All spontaneous reactions have a negative ΔH, that is, heat is generated

_____ **72)** Each reaction in a metabolic pathway has a negative ΔG'o

_____ **73)** The hydrolysis of pyrophosphate provides the driving force for the synthesis of polynucleotides such as RNA and DNA

_____ **74)** Cytochromes accept electrons one at a time, by reduction of Fe^{2+}

_____ **75)** Aconitase demonstrates that a prochiral carbon can be processed sterospecifically by an enzyme

_____ **76)** The Krebs cycle only operates in conditions where O_2 is available

_____ **77)** Both glycolysis and Krebs cycle occur in the cytosol of the eukaryotic cell

_____ **78)** All reactions in a metabolic pathway are normally in equilibrium

_____ **79)** Allosteric regulation requires covalent modification of an enzyme

_____ **80)** Glycogen breakdown is regulated by free glucose

_____ **81)** The respiratory chain enzymes are on the outer membrane of the mitochondrion

_____ **82)** Somewhere in Tokyo, there is a squid living in constant fear….