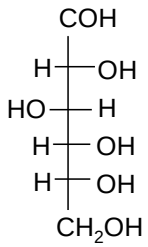
Problem Set 2
MCDB 108B

1. a) Draw the structure of the disaccharide D-glucose (α1,6) D-galactose in the β-anomeric form. The straight chain structure of D-glucose is given. Galactose is the 4-epimer of glucose.



b) The glycogen main chain is a polymer of D-glucose linked in α(1,4) linkage. Branch points in glycogen occur, in which main chains are linked to each other via a single α(1,6) linkage. 0.4 g of glycogen was incubated with methyl iodide, which results in methylation of all free primary or secondary alcohol groups. Subsequent acid hydrolysis resulted in cleavage all glycosidic linkages. The amount of 2,3 dimethylglucose was then determined.

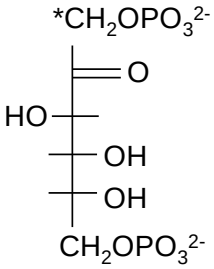
i) Why is 2,3 dimethylglucose produced from branch points in glycogen?

ii) It was found that the yield of 2,3 dimethylglucose was 0.247 mmol. What fraction of the total number of residues are branch pts? (MW of a glycosyl residue = 162).

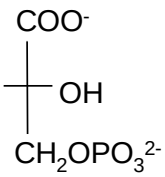
2. The systematic name of *melezitose* is α-D-glucopyranosyl-(1,3)-β-D-fructofuranosyl-(2,1)-β-L-glucopyranoside. Draw its molecular structure. Will it reduce Tollen's reagent?

3. (6) The glucose transporter of liver has different kinetic properties compared to those of brain. On the same graph, draw the curves that relate transport velocity to glucose concentration (y vs x) for both types of transporters. Explain the physiological significance behind the kinetic differences.

4. (6) Compounds A and B are intermediates in glycolysis. If A is labeled with ^{14}C as shown (by the asterisk), indicate which carbon in compound B will become labeled during glycolytic flux. Show the intermediates formed between structures A and B based on your knowledge of the chemical reactions involved. Indicate which carbon in each structure becomes labeled.



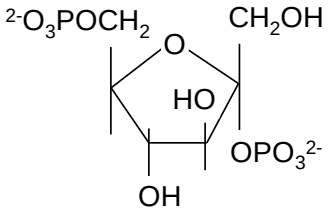
A



B

5. (8) When blood glucose levels are low, glucagon and epinephrine are secreted. Are the following statements True or False? If true, explain the physiological rationale for this phenomenon. If false explain why, and describe what happens in reality.

a) Compound A increases and glycolysis is turned on in liver.
b) Compound A increases and glycolysis is turned on in muscle.



A

6. Among the following compounds are metabolic intermediates in glycolysis. Answer the following questions referring to the structures by their corresponding letters. Do not provide the names of the structures.

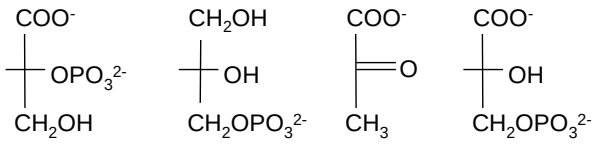
a) Organize the relevant structures in the order in which they appear in the conversion of glyceraldehyde-3-phosphate to pyruvate. _____ (4)

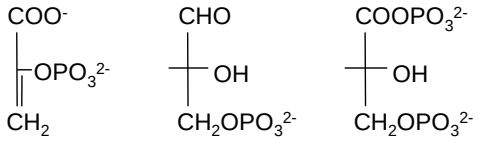
b) Which step(s) require(s) P_i? (1)

c) Which step(s) require(s) NAD^+? (1)

d) The generation of ATP is driven by keto-enol isomerization in which step? (1)

e) The generation of ATP is driven by oxidation in which step? (1)



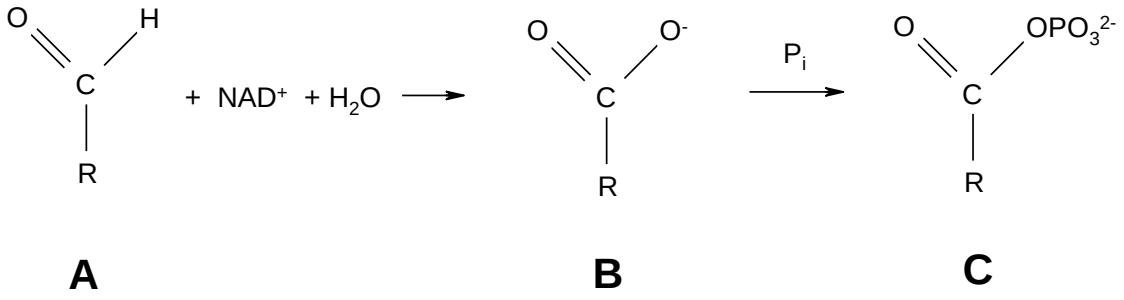


7. Fermentation can occur in cell-free extracts of yeast, because these extracts contain all the enzymes and cofactors necessary for glycolysis. The addition of glucose to these extracts initiates the fermentation process, which can be monitored by the evolution of CO_2.

a) (1) Draw a graph of the expected relationship between CO_2 produced (on the y-axis) and time (on the x-axis), after addition of glucose.
b) (2) Indicate the expected effect if phosphate were added approximately 1 hr after glucose. Explain.
c) (4) Indicate the expected effects of adding an ATPase (an enzyme that hydrolyzes ATP to ADP + P_i) *before* addition of glucose and, alternatively, 1 hr *after* glucose addition. Explain why.
d) (6) Compound X inhibits the enzyme that converts acetaldehyde to ethanol. When X is added, the production of CO_2 slows down. What would be the effects of subsequently adding: P_i, ADP, NAD^+, or pyruvate. For each answer, explain.

8. A hypothetical enzyme catalyzes the rate-determining step of an energy-producing metabolic pathway. At high energy charge it is desirable that the enzyme is off at low substrate concentrations, while at low energy charge the enzyme should be turned on. How would you engineer such an enzyme? Draw the graphs of enzyme velocity (on the y-axis) vs substrate concentration (on the x-axis) corresponding to both high and low energy charge. Explain your answer. If this enzyme were a kinase, how would the graph of enzyme velocity vs [ATP] look like? Draw the graph and explain (8).

9. a) (5 pts) The following compound, A, can be phosphorylated to form C through an intermediate B, with thermodynamics that are slightly favorable under standard conditions (ΔG^0= -0.2 kcal/mol, for A to C). The non-catalyzed reaction is found to be *extremely* slow, while the enzymatic reaction, as you'd expect, is greatly accelerated. Show the chemistry of the enzymatic reaction versus the reaction in water.



A **B** **C**

b) (5 pts) What is the critical reason why the enzyme-catalyzed reaction is so much faster. Speculate on the chemical basis for this rate acceleration.

10. Shown below is a hypothetical 6-carbon compound. You wish to design a simple strategy by which this compound can be enzymatically cleaved into two 3-carbon compounds. Based on the reactions of glycolysis, what chemistry would you incorporate into a simple metabolic scheme? Considering the step in which actual cleavage occurs, what features would you design into the active site of an enzyme to efficiently catalyze the cleavage reaction, and why? Show each step and the organic chemical mechanism involved. (8)