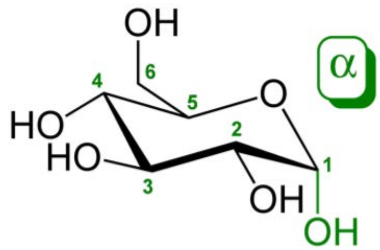
7.05 Spring 2010 Problem Set 8

Problem 1: Sugar Isomerization

a) Convert α-glucose to its furanose form.

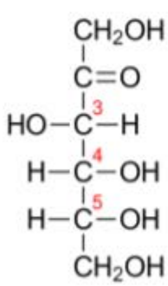


b) Is it more likely for it to be found in the cyclized or linearized form?

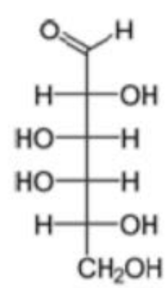
c) Draw the linear depiction of D-glucose.

Problem 2: Synthesis

I would like to make D-galactose (shown) from D-fructose (also shown). Show which steps and enzymes are necessary for this. Enzymes you can use: Ketose-aldose Isomerase, Epimerase

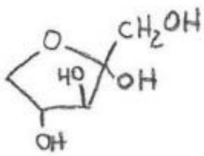


D-Fructose



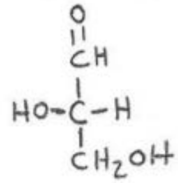
D-Galactose

Problem 3: Sugar Characteristics and Nomenclature (from previous exam)



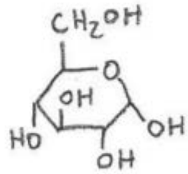
D-xylose

I



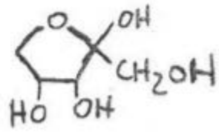
L-glyceraldehyde

II



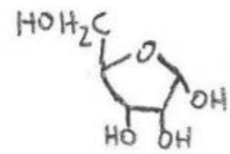
D-glucose

III



D-ribulose

IV



D-ribose

V

A) Answer the following by circling the number(s) corresponding to the sugar(s) above which best answer each question (there may be 0, 1, or >1 answer for each question). Provide BRIEF explanation only for the last question where requested.

Which sugar(s) is/(are) a pyranose? I II III IV V

Which sugar(s) is/(are) drawn as an α-pyranose <u>OR</u> as an α -furanose? I II III IV V

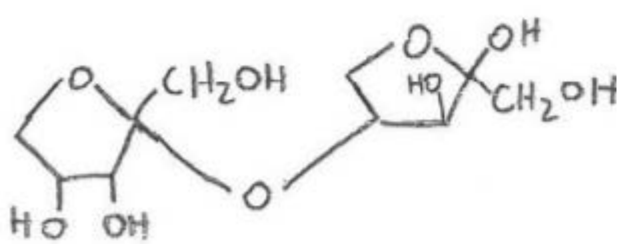
Identify all the aldose sugar(s)? I II III IV V

Identify all the reducing sugar(s)? I II III IV V

Which sugar(s) is/(are) not found in nature? I II III IV V

Briefly explain your answer:

B) Name the following sugar:



C) Draw α-D-glucopyranosyl-(1-3)-D-glyceraldehyde

D) Specify which of the sugars named/drawn in parts B and C above are reducing sugars. If neither is a reducing sugar, make this clear. Briefly explain your answer.

Problem 4: Chemistry of glycolysis

A) The reactants in the net reaction of glycolysis are given below. Complete the reaction by writing the products and balancing the equation (including charges). Assume that all inorganic phosphate (P_i) is in the form HPO_4^{2-}.

glucose ($C_6H_{12}O_6$) + 2 ADP + 2 P_i + 2 NAD^+ $\rightarrow$

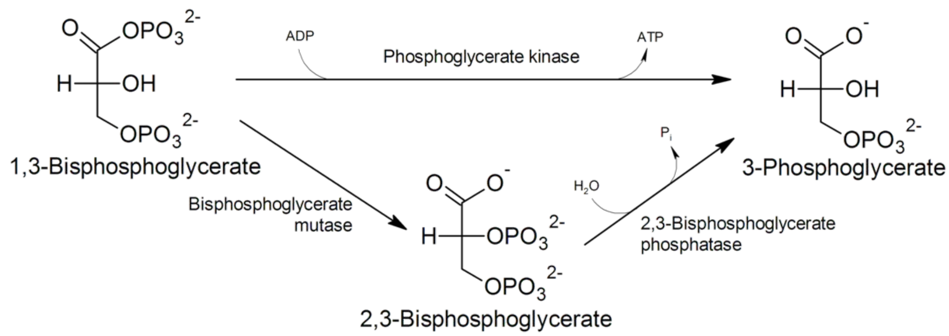
B) One component of the net reaction of glycolysis is the synthesis of ATP from ADP and P_i. For each of the following reactions, write the balanced chemical equation. Assume that all inorganic phosphate (P_i) is in the form HPO_4^{2-}. Which step of glycolysis consumes P_i? Which step uses that same P_i to generate ATP? For each step, name the enzyme and draw the balanced reaction using names, formulas, or structures of the reactants and products.

1) The synthesis of ATP from ADP and P_i (a.k.a. reverse of ATP hydrolysis):

2) The step of glycolysis that consumes P_i:

3) The step of glycolysis that makes ATP from a product in question 4B2:

C) Red blood cells express a special enzyme, **2,3-bisphosphoglycerate mutase**, that turns **1,3-bisphosphoglycerate** (**1,3-BPG**) into **2,3-bisphosphoglycerate** (**2,3-BPG**). (You may recall that **2,3-BPG** stabilizes the T state of hemoglobin and decreases its oxygen affinity.) **2,3-BPG** re-enters glycolysis when it is dephosphorylated by **2,3-BPG phosphatase** to **3-phosphoglycerate (3PG)**. These two reactions are named the **Luebering-Rapoport pathway**:



1) If a glucose molecule enters glycolysis, and *both* of the **1,3-BPG** molecules it yields go through the Leubering-Rapoport pathway *instead of* through **phosphoglycerate kinase**, what is the net number of ATP produced by glycolysis of this molecule of glucose?

2) Genetic defects in glycolysis can disrupt levels of **2,3-PBG** and diminish the ability of red blood cells to transport oxygen. How would **2,3-BPG** level and hemoglobin oxygen affinity be affected by defects in the following enzymes?

Enzyme	**2,3-BPG (+ / - / 0)**	**Hb O_2 affinity (+ / - / 0)**
hexokinase		
pyruvate kinase		

3) In 2006, scientists discovered that cells in the outermost layer of the placenta also express **2,3-bisphosphoglycerate mutase**. **2,3-BPG** binds more tightly to adult hemoglobin than to fetal hemoglobin. Why would expressing this enzyme in the placenta help the fetus get oxygen?

D) Organisms growing anaerobically cannot perform glycolysis for long without reducing the pyruvate from glycolysis into another compound, most commonly to lactate or to ethanol plus CO_2. Both of these reactions are given below in their unbalanced forms. Explain in one sentence why one of these reducing steps is needed to sustain anaerobic glycolysis.
   1) pyruvate + NADH → lactate + NAD^+
   2) pyruvate + NADH → ethanol + CO_2 + NAD^+

E) In mammals, muscles produce lactate during intense exercise because glucose availability for glycolysis is in excess of oxygen delivery to support complete glucose oxidation. Lactate is transported via the bloodstream to the liver, where it is converted back to pyruvate and then to glucose via gluconeogenesis, which returns to the muscles (the Cori Cycle). Write the balanced reaction that converts lactate back into pyruvate in the liver.

Problem 5: Energetics of glycolysis

A) The complete combustion of glucose ($C_6H_{12}O_6$) in oxygen (O_2) yields water and CO_2. Write the balanced reaction for the combustion of glucose.

B) The free energy ($\Delta G°'$) of this reaction under standard conditions (25°C, each species at 1M) is -2930.4 kJ/mol [equilibrator.weizmann.ac.il]. Calculate the free energy under physiological conditions, assuming that T = 37°C, [glucose] = 1.0 mM, [O_2] = 2.0 mM, [CO_2] = 2.5 mM.

C) Assume that under physiological conditions, hydrolysis of ATP has a ΔG of -46 kJ/mol. What percentage of the chemical energy in glucose (your answer to 5B) gets stored in the molecules of ATP produced from glycolysis? Does glycolysis by itself seem like an efficient way to get energy from glucose?

D) The free energy change of each step of glycolysis is given in the table below. $\Delta G°'$ is the free energy under standard conditions (25°C, 1M each reactant, pH 7), while ΔG is the free energy change at presumed physiological conditions.

Step	**Enzyme**	**$\Delta G°'$ (kJ/mol)**	**ΔG (kJ/mol)**
1	HK	- 20.9	- 27.2
2	PGI	2.2	- 1.4
3	PFK	- 17.2	- 25.9
4	aldolase	22.8	- 5.9
5	TIM	7.9	~ 0.0
6 + 7	GAPDH + PGK	- 16.7	-1.1
8	PGM	4.7	- 0.6
9	enolase	- 3.2	- 2.4
10	PK	- 23.0	- 13.9

a. Why must no step have a positive ΔG under physiological conditions?

b. Conversion of F1,6BP to GA3P and DHAP by aldolase is striking in that it is strongly unfavorable when all species are at 1 M ($\Delta G°'$ = +22.8 kJ/mol) but favorable when the species are at their physiological conditions (ΔG = -5.9 kJ/mol). Based on $\Delta G°'$ and ΔG of aldolase and TIM, and using a reasonable physiological value of 15 mM for the concentration of F1,6BP, calculate the concentrations of GA3P and DHAP under physiological conditions (use T = 37°C). Why is the reaction so much more favorable under these conditions than when all species are at 1 M?

E) The step of glycolysis catalyzed by PFK is called the committed step because it is the first reaction in glycolysis that is practically irreversible and doesn't produce a product that is used for anything else. As such, PFK activity is regulated to control the rate of glycolysis. If the products of glycolysis accumulate, PFK is inhibited; if the products begin to deplete, PFK is activated. This type of regulation is negative feedback. Based on this, propose whether each of the following chemicals activates (+), inhibits (-), or has no effect (0) on PFK activity:

Chemical	**Effect (+ / - / 0)**
ATP	
AMP	
H^+ (i.e. low pH)	
hexokinase	
phosphoenolpyruvate (PEP)	
fructose 2,6-bisphosphate (made from F6P by phosphofructokinase 2)	

F) Humans actually use different versions of hexokinase in different tissues. For example, muscle cells express a form known simply as hexokinase, while liver cells express a form known as glucokinase. There are many notable differences between hexokinase and glucokinase:

a. The phosphorylation of glucose by hexokinase or glucokinase traps it inside cells. Muscle cells may need to absorb glucose no matter its concentration in the blood. Liver cells store glucose but do not use it as a main fuel source, so they only take up glucose when concentrations in the blood are high. Based on this, which enzyme (hexokinase or glucokinase) do you predict has a higher Michaelis constant (K_M), and why?

b. Like PFK, some hexokinases can be inhibited by their product, G6P. One role of the liver is to store large quantities of glucose (in the form of glycogen), while muscle cells metabolize glucose only when they have a large need for ATP. Do you predict that hexokinase is inhibited by G6P? What about glucokinase?