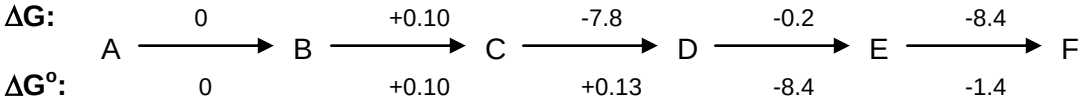
Problem Set 1

MCDB 108B

1. (10) Consider the following sequence of metabolic reactions. The value for ΔG and ΔG^o for each reaction (in kcal/mol) is given above and below the arrows, respectively, as shown:



Answer the following questions. Provide an intuitive explanation for each.

a) Which step or steps in this metabolic sequence are candidate points for regulatory control?
b) What is the K_{eq} for the reaction A ⇆ B?
c) What is the mass-action ratio* for A ⇆ B in cells during steady-state?
d) What is the mass-action ratio for B ⇆ C in cells during steady-state?
e) What is the mass-action ratio for E ⇆ F in cells during steady-state?
*mass action ratio = [product]/[reactant]

2. (10 pts) The enzyme triose phosphate isomerase catalyzes the following reaction:

glyceraldehyde-3-P ⇆ dihydroxyacetone-P

The $\Delta G°$ for this reaction is -1.83 kcal/mol. Are the following statements True or False? Give an explanation in each case.

(a) The reaction will necessarily proceed from left to right, spontaneously.
(b) The rate of the reaction in the forward direction is higher than that in the reverse direction at equilibrium.
(c) At equilibrium the concentration of dihydroxyacetone-P is greater than that of glyceraldehyde-3-P.
(d) The data given are sufficient to calculate the equilibrium constant of the reaction.
(e) Since the $\Delta G°$ for this reaction is not large, the reaction is expected to proceed slowly

3. In the following reaction: A ⇆ B, ΔG = -7.0 kcal/mol, and ΔG^o = +1.4 kcal/mol.

a) What is the ratio of [B]/[A]:
1) at equilibrium? (2)
2) during steady-state flux *in vivo*? (2)

b) If the reaction in vivo were allowed to come to equilibrium, would there be net formation of A, or B, compared to the initial conditions? Explain intuitively (2).

4. Explain in terms of free energy why the reactions catalyzed by phosphofructokinase, pyruvate dehydrogenase, acetyl-CoA carboxylase, and others are suitable points for potent metabolic control (you may need to look up the values for ΔG and ΔG^o for these reactions in Lehninger).

5. (10 pts) Indicate whether the following statements are True or False, and for each, briefly explain your answer.

a) If the change in free energy for a reaction is zero, then:
___ The changes in both entropy and enthalpy must also each be 0.
___ The equilibrium constant is 1.
___ The reaction is displaced away from equilibrium.
b) A reaction proceeds spontaneously with the liberation of heat, thus:
___ The reaction, by definition, is exclusively enthalpy driven.
c) A reaction proceeds spontaneously with the absorption of heat, thus:
___ The reaction must be entropy driven.

6. (5 pts) The hydrolysis of 2-phosphoglycerate to glycerate and phosphate has a ΔG^0= -4.1 kcal/mol. Under steady-state conditions in cells, the concentrations of reactants and products are: 2-phosphoglycerate= 10^{-5} M; glycerate= 10^{-1} M; phosphate= 10^{-1} M. Show how you arrive at your answers to the following questions:

a) To the nearest power of 10, what is the value for K_{eq} for this reaction?
b) What is the approximate change in free energy for this reaction in living cells?
c) Upon cell death, would there be net formation of glycerate or 2-phosphorglycerate?

7. (10 pts) For the following hypothetical metabolic pathway:

	ΔG^0	ΔG
A ↔ B	-0.4	-8
B ↔ C	0	-0.6
C ↔ D	-1.4	-5.6
D ↔ E	5.7	-0.3
E ↔ F	-7.8	0.6
F ↔ G	1.4	-0.4
G ↔ H	-4.5	0
H ↔ I	0.2	0.2
I ↔ J	0.4	-1.5
J ↔ K	-7.5	-4

Answer the following questions and explain your answers:
a) Indicate the steps that are rate limiting.
b) Indicate all steps that are candidate points for metabolic control.
c) Indicate the steps in which the MAR=1 during steady-state flux.
d) Indicate all steps that are essentially at equilibrium during steady-state flux.
e) Which reaction(s) has an equilibrium constant equal to 0.1?
f) What is the MAR of C ⇆ D during steady-state flux?

8) (4) Glycogen phosphorylase catalyzes the reaction:

$$\text{glycogen}_n + PO_4 \leftrightarrows \text{glucose-1-P} + \text{glycogen}_{n-1}$$

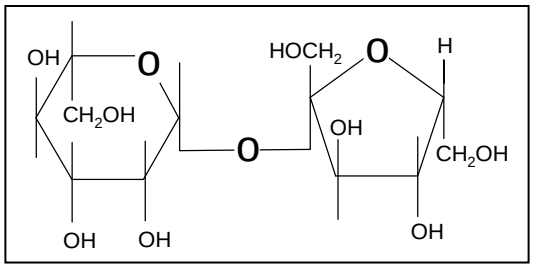
The equilibrium constant for this reaction is 0.088, meaning that at equilibrium the reactants are significantly favored. Estimate the approximate corresponding ΔG^o value for this reaaction. Under physiological conditions, how would it be possible for this reaction to exhibit a ΔG value < 0 such that glycogen can be broken down to G1P spontaneously. Explain.

9) Coupled reactions:

a) For the reaction: phosphoenolpyruvate + ADP + H^+ → pyruvate + ATP, ΔG^o = -7.5 kcal/mol. What is the value for ΔG^o for the *hydrolysis* of phosphoenolpyruvate?

b) In cells, glucose-6-P can be formed from glucose-1-P or, alternatively, from fructose-6-P:
glucose-1-P ⇆ glucose-6-P ΔG^o = -1.7 kcal/mol
fructose-6-P ⇆ glucose-6-P ΔG^o = 0.4 kcal/mol
What is the ratio of fructose-6-P to glucose-1-P at equilibrium?

10) Consider the following disaccharide (which does not necessarily occur naturally):



a) (4) Show the chemical reaction mechanism that resulted in this cyclic compound as generated from the corresponding straight chain forms of the reactants.

b) (4) Provide the name of this disaccharide indicating the correct stereoisomer and the correct linkage, by filling in the blanks:

_____- pyranosyl – (_____) - _____ -furanoside

c) (1) Would this disaccharide be detectable in the blood by Tollen's reagent?