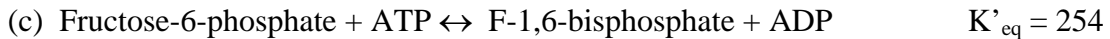
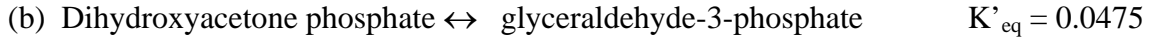
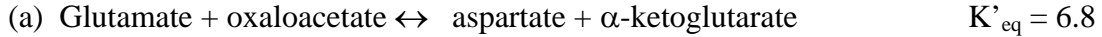


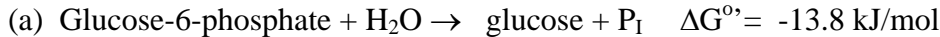
PRACTICE SET 1

Free energy changes and equilibrium constants

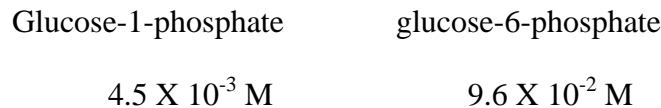
1. Calculate the standard free-energy changes of the following metabolically important enzyme-catalyzed reactions at 25°C and pH 7.0 from the equilibrium constants given.



2. Calculate the equilibrium constants K'_{eq} for each of the following reactions at pH 7.0 and 25°C, using the $\Delta G^{o'}$ values given:

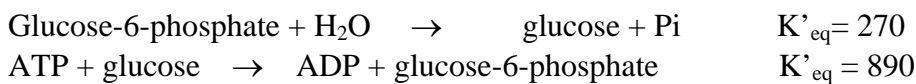


3. If a 0.1 M solution of glucose-1-phosphate is incubated with a catalytic amount of phosphoglucomutase, the glucose-1-phosphate is transformed to glucose-6-phosphate until equilibrium is established. The equilibrium concentrations are:



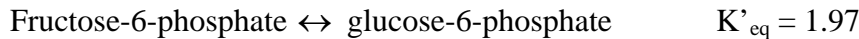
Calculate K'_{eq} and $\Delta G^{o'}$ for this reaction at 25 °C.

4. A direct measurement of the standard free-energy change associated with the hydrolysis of ATP is technically demanding because the minute amount of ATP remaining at equilibrium is difficult to measure accurately. The value of $\Delta G^{o'}$ can be calculated indirectly, however, from the equilibrium constants of two other enzymatic reactions having less favorable equilibrium constants:



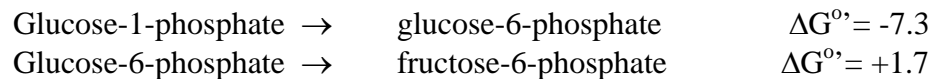
Using this information, calculate the standard free energy of hydrolysis of ATP. Assume a temperature of 25°C.

5. Consider the following interconversion, which occurs in glycolysis:

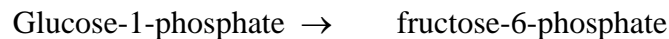


- (a) What is ΔG° for the reaction (assuming that the temperature is 25°C)?
- (b) If the concentration of fructose-6-phosphate is adjusted to 1.5 M and that of glucose-6-phosphate is adjusted to 0.5M, what is ΔG ?
- (c) Why are ΔG° and ΔG different?

6. Glucose-1-phosphate is converted into fructose-6-phosphate in two successive reactions:



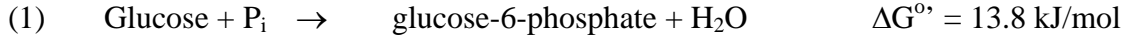
Calculate the equilibrium constant, K'_{eq} , for the sum of the two reactions at 25°C:



7. *ATP-Dependent Chemical Coupling* The phosphorylation of glucose to glucose-6-phosphate is the initial step in the catabolism of glucose. The direct phosphorylation of glucose by P_i is described by the equation



- (a) Calculate the equilibrium constant for the above reaction. In the rat hepatocyte, the physiological concentrations of glucose and P_i are maintained at approximately 4.8 mM. What is the equilibrium concentration of glucose-6-phosphate obtained by the direct phosphorylation of glucose by P_i ? Does this route represent a reasonable metabolic route for the catabolism of glucose? Explain.
- (b) In principle, at least, one way to increase the concentration of glucose-6-phosphate is to drive the equilibrium reaction to the right by increasing the intracellular concentrations of glucose and P_i . Assuming a fixed concentration of P_i at 4.8 mM, how high would the intracellular concentration of glucose have to be to have an equilibrium concentration of glucose-6-phosphate of 250 μM (normal physiological concentration)? Would this route be a physiologically reasonable approach, given that the maximum solubility of glucose is less than 1M?
- (c) The phosphorylation of glucose in the cell is coupled to the hydrolysis of ATP; that is, part of the free energy of ATP hydrolysis is utilized to effect the endergonic phosphorylation of glucose:



Calculate K'_{eq} for the overall reaction. When the ATP-dependent phosphorylation of glucose is carried out, what concentration of glucose is needed to achieve a 250 mM intracellular concentration of glucose-6-phosphate when the concentration of ATP and ADP are 3.38 and 1.32 μM , respectively?

Does this coupling process provide a feasible route, at least in principle, for the phosphorylation of glucose as it occurs in the cell? Explain.

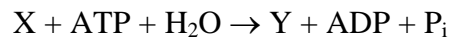
8. From data in the Handbook, calculate the $\Delta G^{\circ'}$ value for the reactions;



9. This problem explores the consequences of coupling ATP hydrolysis under physiological conditions to a thermodynamically unfavorable biochemical reaction. Because we want to explore these consequences in stages, we shall consider the hypothetical transformation, $\text{X} \rightarrow \text{Y}$, a reaction for which $\Delta G^{\circ'} = 20 \text{ kJ/mol}$.

(a) What is the ratio $[\text{Y}]/[\text{X}]$ at equilibrium?

(b) Suppose X and Y participate in a sequence of reactions during which ATP is hydrolyzed to ADP and P_i . The overall reaction is



Calculate $[\text{Y}]/[\text{X}]$ for this reaction at equilibrium. Assume for the purposes of this calculation that the concentrations of ATP, ADP, and P_i are all 1 M when the reaction is at equilibrium.

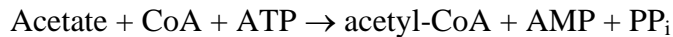
(c) We know that $[\text{ATP}]$, $[\text{ADP}]$, and $[\text{P}_i]$ are not 1 M under physiological conditions. Calculate the ratio $[\text{Y}]/[\text{X}]$ for the ATP-coupled reaction when the values of $[\text{ATP}]$, $[\text{ADP}]$, and $[\text{P}_i]$ are 8.05 mM, 0.93 mM, and 8.05 mM, respectively.

10. Calculate the physiological ΔG (not $\Delta G^{\circ'}$) for the reaction:

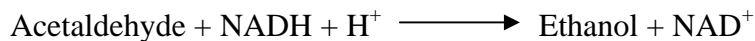


at 25°C as it occurs in the cytosol of neurons, in which phosphocreatine is present at 4.7 mM, creatine at 1.0 mM, ADP at 0.20 mM, and ATP at 2.6 mM.

11. The synthesis of the activated form of acetate (acetyl-CoA) is carried out in an ATP-dependent process:



- (a) The ΔG° for the hydrolysis of acetyl-CoA to acetate and CoA is -32.2 kJ/mol and that for hydrolysis of ATP to AMP and PP_i is -30.5 kJ/mol. Calculate ΔG° for the ATP-dependent synthesis of acetyl-CoA.
- (b) Almost all cells contain the enzyme inorganic pyrophosphatase, which catalyzes the hydrolysis of PP_i to P_i . What effect does the presence of this enzyme have on the synthesis of acetyl-CoA? Explain.
12. *Are All Metabolic Reactions at Equilibrium?*
- (a) Phosphoenolpyruvate is one of the two phosphate donors in the synthesis of ATP during glycolysis. In human erythrocytes, the steady-state concentration of ATP is 2.24 mM, that of ADP is 0.25 mM, and that of pyruvate is 0.051 mM. Calculate the concentration of phosphoenolpyruvate at 25°C , assuming that the pyruvate kinase reaction is at equilibrium in the cell.
- (b) The physiological concentration of phosphoenolpyruvate in human erythrocytes is 0.023 mM. Compare this with the value obtained in (a). What is the significance of this difference? Explain.
13. Calculate the free energy change at standard conditions for the following reaction:



Answer Key

1. $\Delta G^{\circ} = -RT \ln K'_{eq}$ $R=8.315 \text{ J/mol}^{\circ}\text{K}$ $T=298^{\circ}\text{K}$

a. $-8.315 (298) (\ln 6.8)$
 $-4757 \text{ J/mol} = -4.76 \text{ kJ/mol}$

b. $-8.315 (298) (\ln 0.0475)$
 7.5 kJ/mol

c. $-8.315 (298) (\ln 254)$
 -13.7 kJ/mol

2. a. $-13,800 = -8.315 (298) \ln K'_{eq}$
 $K'_{eq} = 262$

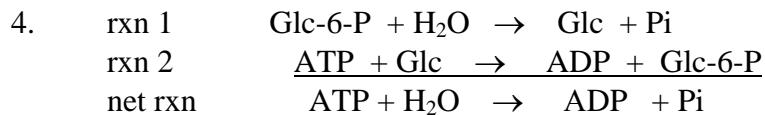
b. $-15,900 = -8.315 (298) \ln K'_{eq}$
 $K'_{eq} = 612$

c. $+3,100 = -8.315 (298) \ln K'_{eq}$
 $K'_{eq} = 0.286$

3. $K_{eq} = \frac{[\text{Glc-6-P}]}{[\text{Glc-1-P}]} = \frac{9.6 \cdot 10^{-2}}{4.5 \cdot 10^{-3}} = 21.3$

$\Delta G^{\circ} = -RT \ln K'_{eq}$ $R=8.315 \text{ J/mol}^{\circ}\text{K}$ $T=298^{\circ}\text{K}$

$\Delta G^{\circ} = -8.315 (298) \ln 21$
 $= -7.5 \text{ kJ/mol}$



ΔG° for rxn 1 = $-8.315 (298) \ln 270 = -13.9 \text{ kJ/mol}$

ΔG° for rxn 2 = $-8.315 (298) \ln 890 = -16.8 \text{ kJ/mol}$

ΔG° for net rxn = $-13.9 + (-16.8) = -30.7 \text{ kJ/mol}$

5. a. $\Delta G = -8.315 (298) \ln 1.97$
 $= -1.68 \text{ kJ/mol}$

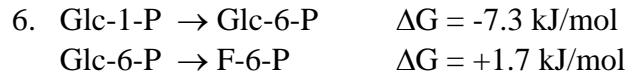
b. Since concentrations are not 1M, use

$$\Delta G = \Delta G^{\circ'} + RT \ln \frac{[\text{Glc-6-P}]}{[\text{F-6-P}]}$$

$$\Delta G = -1,680 + 8.315 (298) \ln \frac{0.5}{1.5}$$

$$= -4.4 \text{ kJ/mol}$$

c. $\Delta G^{\circ'}$ is used for “standard” conditions, ΔG is used for other concentrations.



$$-7.3 + 1.7 = -5.6 \text{ kJ/mol}$$

$$\Delta G^{\circ'} = -RT \ln K'_{\text{eq}}$$

$$-5,600 = -8.315 (298) \ln K'_{\text{eq}}$$

$$K'_{\text{eq}} = 9.6$$

7. a. $13,800 = -8.315 (298) \ln K_{\text{eq}}$
 $K_{\text{eq}} = 3.8 \times 10^{-3}$

$$3.8 \times 10^{-3} = \frac{[\text{Glc-6-P}]}{[0.0048] [0.0048]}$$

$$[\text{Glc-6-P}] = 8.8 \times 10^{-8} \text{ M} \quad \text{Concentration too low, not physiological}$$

b. $3.8 \times 10^{-3} = \frac{[250 \times 10^{-6}]}{[0.0048] [\text{Glc}]}$

$$[\text{Glc}] = 13.7 \text{ M}$$

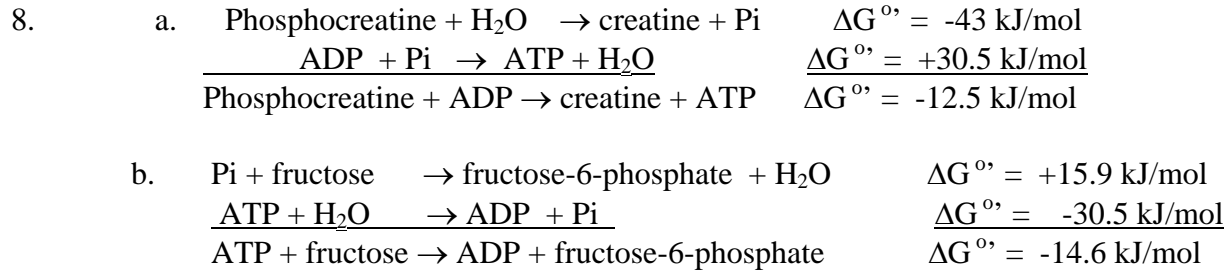
Not soluble at this concentration!

c. $\Delta G^{\circ'} = 13.8 + (-30.5) = -16.7 \text{ kJ/mol}$
 $-16,700 = -8.315 (298) \ln K_{\text{eq}} \quad K = 845$

$$845 = \frac{[250 \times 10^{-3}] [1.32 \times 10^{-6}]}{[3.38 \times 10^{-6}] [\text{Glc}]}$$

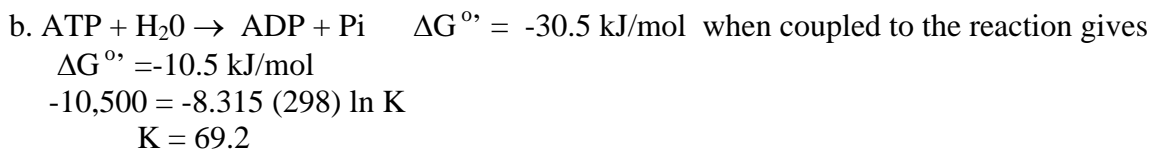
$$[\text{Glc}] = 1.16 \times 10^{-4} = 116 \mu\text{M}$$

Yes, concentration is physiologically reasonable.



9. a. $20,000 = -8.315 (298) \ln K_{eq}$

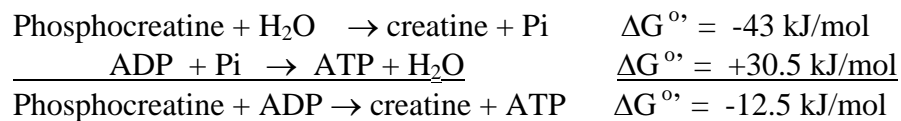
$$K_{eq} = 3.2 \cdot 10^{-4} \text{ M}$$



c.
$$K_{eq} = \frac{[\text{ADP}][\text{Pi}][\text{Y}]}{[\text{ATP}][\text{X}]} \quad 69.2 = \frac{[0.93 \cdot 10^{-3}][8.05 \cdot 10^{-3}][\text{Y}]}{[8.05 \cdot 10^{-3}][\text{X}]}$$

$$\frac{[\text{Y}]}{[\text{X}]} = 7.44 \cdot 10^4$$

10. get ΔG° from the handbook

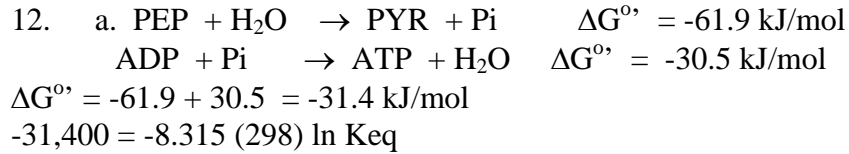


$$\Delta G = \Delta G^{\circ} + RT \ln \frac{[\text{products}]}{[\text{reactants}]}$$

$$= -12,500 + 8.315 (298) \ln \frac{[1 \times 10^{-3}][2.6 \times 10^{-3}]}{[4.7 \times 10^{-3}][0.2 \times 10^{-3}]}$$

$$= -10 \text{ kJ/mol}$$

11. a. $\Delta G = -30.5 + 32.2 = +1.7 \text{ J/mol}$
 b. It catalyzes the hydrolysis of pyrophosphate and drives the reaction towards the formation of acetyl CoA.



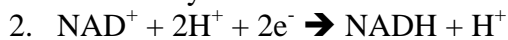
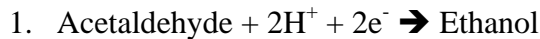
$$K_{eq} = 3.19 \times 10^5$$

$$K_{eq} = \frac{[\text{pyruvate}] [\text{ATP}]}{[\text{PEP}] [\text{ADP}]}$$

$$3.19 \times 10^5 = \frac{[0.051 \times 10^{-3}] [2.24 \times 10^{-3}]}{[\text{PEP}] [0.25 \times 10^{-3}]} \quad \text{PEP} = 1.43 \times 10^{-9}$$

b. 0.023 mM is 16,000 x higher - Reaction is not at equilibrium.

13. The redox reaction can be written as two half-reactions:



See Table 3 for reduction potentials E^o.

$$\Delta E^{\circ} = E^{\circ}_{\text{Oxidant}} - E^{\circ}_{\text{Reductant}}$$

$$\Delta E^{\circ} = -0.20 \text{ V} - (-0.32 \text{ V})$$

$$\Delta E^{\circ} = +0.12 \text{ V}$$

$$\Delta G^{\circ} = -nF\Delta E^{\circ}$$

$$\Delta G^{\circ} = -2 \cdot 96.5 \text{ kJ mol}^{-1} \text{ V}^{-1} \cdot 0.12 \text{ V}$$

$$\Delta G^{\circ} = -23.16 \text{ kJ mol}^{-1}$$