

# Non-equilibrium applications

In the laboratory we are concerned with calculating chemical equilibrium to predict the outcome of chemical synthesis or analysis. It is of interest to know whether reactions will run in the direction that they are written and to know the extent of reaction. This is why you are taught How to calculate chemical equilibrium in much of chemistry.

However, in living systems we often calculate non-equilibrium properties. The reason is the cells are not at equilibrium. If they were they would be dead. We see in biology a collection of reactions that are linked and each running at concentrations that are not the equilibrium values. For this reason we use the non-equilibrium expression for  $\Delta G$  in these cases.

# Alternative form for free energy expression

Since

$$\Delta G = \Delta G^\circ + RT \ln Q$$

and

$$\Delta G^\circ = -RT \ln K$$

we can also write

$$\Delta G = -RT \ln K + RT \ln Q$$

which can be rearranged to

$$\Delta G = RT \ln (Q/K)$$

# Thermodynamics of glycolysis

## Reaction

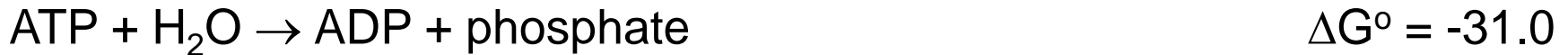
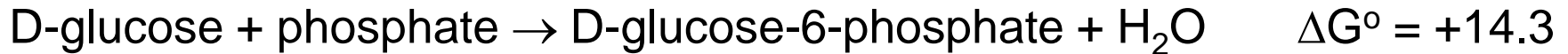
kJ/mol

D-glucose + ATP → D-glucose-6-phosphate + ADP	$\Delta G^\circ = -16.7$
D-glucose-6-phosphate → D-fructose-6-phosphate	$\Delta G^\circ = +1.7$
D-fructose-6-diphosphate + ATP → D-fructose-1,6-diphosphate + ADP	$\Delta G^\circ = -14.2$
D-fructose-1,6-diphosphate → glyceraldehyde-3-phosphate + dihydroxyacetone phosphate	$\Delta G^\circ = +23.8$
dihydroxyacetone phosphate → glyceraldehyde-3-phosphate	$\Delta G^\circ = +7.5$
glyceraldehyde-3-phosphate + phosphate + NAD <sup>+</sup> → 1,3-diphosphoglycerate + NADH + H <sup>+</sup>	$\Delta G^\circ = +6.3$
1,3-diphosphoglycerate + ADP → 3-phosphoglycerate + ATP	$\Delta G^\circ = -18.8$
3-phosphoglycerate → 2-phosphoglycerate	$\Delta G^\circ = +4.6$
2-phosphoglycerate → 2-phosphoenolpyruvate + H <sub>2</sub> O	$\Delta G^\circ = +1.7$
2-phosphoenolpyruvate + ADP → pyruvate + ATP	$\Delta G^\circ = -31.4$
pyruvate + NADH + H <sup>+</sup> → lactate + NAD <sup>+</sup>	$\Delta G^\circ = -25.1$
pyruvate → acetaldehyde + CO <sub>2</sub>	$\Delta G^\circ = -19.8$
acetaldehyde + NADH + H <sup>+</sup> → ethanol + NAD <sup>+</sup>	$\Delta G^\circ = -23.7$

# Phosphorylation of glucose



The reaction can be decomposed into two reactions.



The sum of the two reactions results in an overall negative free energy change under standard conditions. In this manner the strongly spontaneous hydrolysis of ATP is coupled to the otherwise unspontaneous glucose phosphorylation. This reaction is typical of the role played by ATP in the cell.

Note that the values for  $\Delta G^\circ$  assume a concentration of 1 M. Clearly, the concentrations in the cell are often quite different from the standard state and this will have profound consequences for the direction of spontaneous change.

# Role of enzymes as catalysts

All of the reactions in the glycolytic pathway are catalyzed by enzymes. For example, the phosphorylation of glucose is catalyzed by hexokinase. The role of the enzyme is to speed up the reaction, but the enzyme does not change thermodynamics of the process. The role of enzymes is the same as that of any catalyst. Catalysts affect the kinetics of the reaction, but not the thermodynamics. We will consider the role of catalysts in the section on kinetics.

# Equilibrium can be important even when $\Delta G^\circ > 0$

Notice that  $\Delta G^\circ$  for certain steps is positive. For example,  
D-glucose-6-phosphate  $\rightarrow$  D-fructose-6-phosphate

$$\Delta G^\circ = +1.7$$

is catalyzed by phosphoglucose isomerase.

The equilibrium constant for this process is

$$K = \exp\{-\Delta G^\circ/RT\} = \exp\{-1700/8.31/310\} \sim 0.5$$

The concentration of D-fructose-6-phosphate at equilibrium  
will be less than that of D-glucose-6-phosphate.

# Question

Given that  $K \sim 0.5$  for the reaction



Calculate the concentration of D-fructose-6-phosphate at equilibrium under standard conditions (i.e. for initial concentrations of 1 M).

A. 1 M

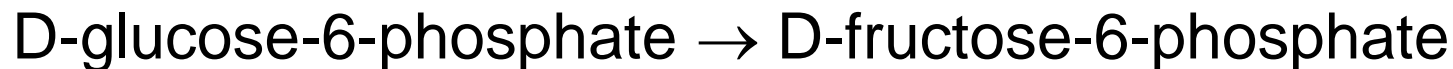
B. 0.5 M

C. 0.667 M

D. 0.15 M

# Question

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Calculate the concentration of D-fructose-6-phosphate at equilibrium under standard conditions (i.e. for initial concentrations of 1 M).

A. 1 M

$$K = \frac{1 + x}{1 - x}, \quad K(1 - x) = 1 + x, \quad K - 1 = (1 + K)x$$

B. 0.5 M

$$x = \frac{K - 1}{1 + K} = \frac{-0.5}{1.5} = -0.333$$

C. 0.667 M

$$[\text{D-gluc-6-phos}] = 1 - x = 1.33$$

$$[\text{D-fruc-6-phos}] = 1 + x = 0.67$$

D. 0.15 M



# Intracellular conditions are not equilibrium conditions

If the subsequent step in a series of reactions is spontaneous this will tend to deplete the product for the previous reaction. Thus, more of the product will form by L'Chateliers principle.

We can observe this quantitatively by considering the value of Q, the reaction quotient. Since,

$$\Delta G = \Delta G^{\circ} + RT \ln Q$$

the value of  $\Delta G$  may not be zero. In other words, the coupled Series of reactions in the cell are not at equilibrium. Rather, they proceed under steady state conditions where the concentrations are not at 1 M, but are poised so that the overall of effect on a series of reactions is to produce a net spontaneous change.

# Sample Problem in Metabolism

The enzyme aldolase catalyzes the conversion of fructose 1,6-diphosphate (FDP) to dihydroxyacetone phosphate (DHAP) and glyceraldehyde-3-phosphate (GAP). Under physiological conditions the concentrations of these species in red blood cells (erythrocytes) are  $[FDP] = 35 \mu\text{M}$ ,  $[DHAP] = 130 \mu\text{M}$  and  $[GAP] = 15 \mu\text{M}$ . Will the conversion occur spontaneously under these conditions?

Solution: The standard free energy change for the reaction is



and

$$Q = \frac{[\text{DHAP}][\text{GAP}]}{[\text{FDP}]} = \frac{(130 \times 10^{-6})(15 \times 10^{-6})}{(35 \times 10^{-6})} \\ = 5.57 \times 10^{-5}$$

$$\Delta G = \Delta G^\circ + RT \ln Q = 23800 \text{ J/mol} + (8.31 \text{ J/mol}\cdot\text{K})(310 \text{ K})\ln(5.57 \times 10^{-5}) \\ = -1434 \text{ J/mol or } -1.43 \text{ kJ/mol}$$

The reaction will occur spontaneously under the conditions of the cell.