

# Energy and catalysis

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# Enthalpy and Entropy

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**Enthalpy**, H, is the heat content of the reacting system. It reflects the number and kinds of chemical bonds in the reactants and products.

Exothermic reactions: Reaction proceeding with release of heat.

The heat content of the products is less than that of the reactants.

$\Delta H$  has a negative value.

Endothermic reactions: Reacting systems that take up heat from their surroundings.

The heat content of the products is more than that of the reactants .

$\Delta H$  has a positive value.

**Entropy**, S, is a quantitative expression for the randomness or disorder in a system. When the products of a reaction are less complex and more disordered than the reactants, the reaction is said to proceed with a gain in entropy.

# Gibbs free energy

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Gibbs free energy, G, expresses the amount of energy capable of doing work during a reaction at constant temperature and pressure

$$G = H - TS$$

The units of G and H are joules/mole or calories/mole (1 cal = 4.184 J)

The units of entropy are joules/mole.Kelvin (J/mol.K)

When a chemical reaction occurs at constant temperature, we get free energy change,  $\Delta G$ , determined by the enthalpy change,  $\Delta H$ , reflecting the kinds and numbers of chemical bonds and non-covalent interactions broken and formed, and the entropy change,  $\Delta S$ , describing the change in the system's randomness.

$$\Delta G = \Delta H - T \Delta S$$

# Gibbs free energy

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- Exergonic reactions: When a reaction proceeds with the release of free energy (that is, when the system changes so as to possess less free energy), the free-energy change,  $\Delta G$ , has a negative value.
- Endergonic reactions: The system gains free energy and  $\Delta G$  is positive.
- A process tends to occur spontaneously only if  $\Delta G$  is negative.

# Energy Coupling Links Reactions in Biology

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- Cell function depends largely on molecules, such as proteins and nucleic acids, for which the free energy of formation is positive: the molecules are less stable and more highly ordered than a mixture of their monomeric components.
- To carry out these thermodynamically unfavorable, energy-requiring (endergonic) reactions, cells couple them to other reactions that liberate free energy (exergonic reactions), so that the overall process is exergonic: the sum of the free energy changes is negative.

Amino acids  $\longrightarrow$  polymer       $\Delta G_1$  is positive (endergonic)



- When these reactions are coupled, the sum of  $\Delta G_1$  and  $\Delta G_2$  is negative—the overall process is exergonic.

# State of equilibrium

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- The composition of a reacting system (a mixture of chemical reactants and products) tends to continue changing until equilibrium is reached.
- At the equilibrium concentration of reactants and products, the rates of the forward and reverse reactions are exactly equal and no further net change occurs in the system.
- The concentrations of reactants and products at equilibrium define the equilibrium constant,  $K_{\text{eq}}$

$$aA + bB \rightleftharpoons cC + dD \quad K_{\text{eq}} = \frac{[C]^c[D]^d}{[A]^a[B]^b}$$

where,

a, b, c, and d are the number of molecules of A, B, C, and D

[A], [B], [C], and [D] are the molar concentrations of the reaction components at the point of equilibrium

# Standard free-energy change

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- When a reacting system is not at equilibrium, the tendency to move toward equilibrium represents a driving force, the magnitude of which can be expressed as the free-energy change for the reaction,  $\Delta G$ .
- Under standard conditions (298 K = 25°C), when reactants and products are initially present at 1 M concentrations or, for gases, at partial pressures of 101.3 kilopascals (kPa), or 1 atm, the force driving the system toward equilibrium is defined as the standard free-energy change,  $\Delta G^\circ$ .
- Just as  $K'_{\text{eq}}$  is a physical constant characteristic for each reaction,  $\Delta G^\circ$  is also a constant.

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

Gas constant, R = 8.315 J/mol.K (1.987 cal/mol .K)

# Standard free-energy change

- The standard free-energy change of a chemical reaction is simply an alternative mathematical way of expressing its equilibrium constant.

Relationships among  $K'_{\text{eq}}$ ,  $\Delta G'^{\circ}$ , and the Direction of Chemical Reactions under Standard Conditions

When $K'_{\text{eq}}$ is ...	$\Delta G'^{\circ}$ is ...	Starting with all components at 1 M, the reaction ...
>1.0	negative	proceeds forward
1.0	zero	is at equilibrium
<1.0	positive	proceeds in reverse

Relationship between the Equilibrium Constants and Standard Free-Energy Changes of Chemical Reactions

$K'_{\text{eq}}$	$\Delta G'^{\circ}$	
	(kJ/mol)	(kcal/mol)*
$10^3$	-17.1	-4.1
$10^2$	-11.4	-2.7
$10^1$	-5.7	-1.4
1	0.0	0.0
$10^{-1}$	5.7	1.4
$10^{-2}$	11.4	2.7
$10^{-3}$	17.1	4.1
$10^{-4}$	22.8	5.5
$10^{-5}$	28.5	6.8
$10^{-6}$	34.2	8.2

- Because the relationship between  $\Delta G'^{\circ}$  and  $K'_{\text{eq}}$  is exponential, relatively small changes in  $\Delta G'^{\circ}$  correspond to large changes in  $K'_{\text{eq}}$ .

# Standard free-energy change

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- $\Delta G^\circ$  is the difference between the free-energy content of the products and the free-energy content of the reactants, under standard conditions.
- When  $\Delta G^\circ$  is negative, the products contain less free energy than the reactants and the reaction will proceed spontaneously under standard conditions; all chemical reactions tend to go in the direction that results in a decrease in the free energy of the system.
- A positive value of  $\Delta G^\circ$  means that the products of the reaction contain more free energy than the reactants, and this reaction will tend to go in the reverse direction if we start with 1.0 M concentrations of all components (standard conditions).

# Actual free-energy change

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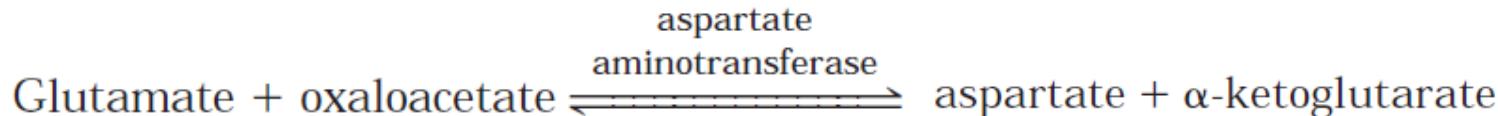
- The actual free-energy change,  $\Delta G$ , is a function of reactant and product concentrations and of the temperature prevailing during the reaction.  $\Delta G$  of any reaction proceeding spontaneously toward its equilibrium is always negative, becomes less negative as the reaction proceeds, and is zero at the point of equilibrium, indicating that no more work can be done by the reaction.

So, for reaction  $A + B \rightleftharpoons C + D$ ,  $\Delta G = \Delta G^\circ + RT \ln \frac{[C][D]}{[A][B]}$

- The criterion for spontaneity of a reaction is the value of  $\Delta G$ , not  $\Delta G^\circ$ .
- A reaction with a positive  $\Delta G^\circ$  can go in the forward direction *if  $\Delta G$  is negative*. This is possible if the term  $RT \ln([products]/[reactants])$  is negative and has a larger absolute value than  $\Delta G^\circ$ . For example, the immediate removal of the products of a reaction can keep the ratio [products]/[reactants] well below 1, such that the term  $RT \ln([products]/[reactants])$  has a large, negative value.

# Problems to solve

1. Calculate the standard free-energy changes of the following metabolically important enzyme-catalyzed reaction at 25°C and pH 7.0, using the equilibrium constant ( $K'_{\text{eq}}$ ) to be 6.8.



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

and  $[\text{products}]/[\text{reactants}]$  is the mass-action ratio,  $Q$ . At equilibrium,  $\Delta G = 0$  and  $Q = K'_{\text{eq}}$ , so

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

where  $R = 8.315 \text{ J/mol} \cdot \text{K}$  and  $T = 25 \text{ }^{\circ}\text{C} = 298 \text{ K}$ . Using the value  $RT = 2.48 \text{ kJ/mol}$ , we can calculate the  $\Delta G'^{\circ}$  values from the  $K'_{\text{eq}}$  for each reaction.

$$\Delta G'^{\circ} = -(2.48 \text{ kJ/mol}) \ln 6.8 = -4.8 \text{ kJ/mol}$$

## Problems to solve

2. Calculate the equilibrium constants  $K'_{\text{eq}}$  for the reaction, Malate  $\rightleftharpoons^{\text{fumarase}}$  fumarate + H<sub>2</sub>O at pH 7.0 and 25°C, provided that its  $\Delta G'^{\circ}$  is 3.1 kJ/mol.

$\Delta G = \Delta G'^{\circ} + RT \ln Q$ , and at equilibrium,  $Q = K'_{\text{eq}}$ ,  $\Delta G = 0$ , and

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

So, at equilibrium,  $\ln K'_{\text{eq}} = -\Delta G'^{\circ}/RT$ , or  $K'_{\text{eq}} = e^{-(\Delta G'^{\circ}/RT)}$ ; at 25 °C,  $RT = 2.48$  kJ/mol.

For fumarase:

$$\Delta G'^{\circ} = 3.1 \text{ kJ/mol}$$

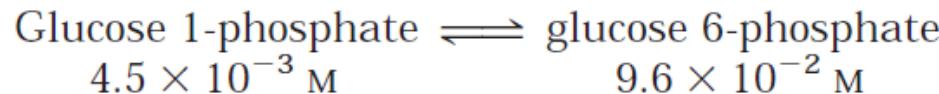
$$\ln K'_{\text{eq}} = -(3.1 \text{ kJ/mol})/(2.48 \text{ kJ/mol}) = -1.25$$

$$K'_{\text{eq}} = e^{-1.25} = 0.28$$

## Problems to solve

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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. At equilibrium, the concentrations of the reaction components are



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

$$K'_{\text{eq}} = [\text{G6P}]/[\text{G1P}] = (9.6 \times 10^{-2} \text{ M})/(4.5 \times 10^{-3} \text{ M})$$
$$= 21.3$$

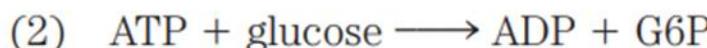
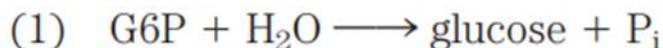
$$\Delta G'^{\circ} = -RT \ln K'_{\text{eq}}$$
$$= -(2.48 \text{ kJ/mol})(\ln 21.3) = -7.56 \text{ kJ/mol}$$

## Problems to solve

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  $\Delta G^\circ$  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 at 25°C.



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

$$\Delta G'_1^\circ = (-2.48 \text{ kJ/mol})(\ln 270) = -13.89 \text{ kJ/mol}$$

$$\Delta G'_2^\circ = (-2.48 \text{ kJ/mol})(\ln 890) = -16.86 \text{ kJ/mol}$$

$$\Delta G'_{\text{sum}}^\circ = \Delta G'_1^\circ + \Delta G'_2^\circ = -30.75 \text{ kJ/mol}$$

# Problems to solve

5. Consider the following interconversion, which occurs in glycolysis



- a) What is  $\Delta G^\circ$  for the reaction (at 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 0.50 M, what is  $\Delta G$ ?
- c) Why are  $\Delta G^\circ$  and  $\Delta G$  different?

(a) At equilibrium,  $\Delta G'^\circ = -RT \ln K'_{\text{eq}}$

$$\begin{aligned} &= -(2.48 \text{ kJ/mol}) \ln 1.97 \\ &= -1.68 \text{ kJ/mol} \end{aligned}$$

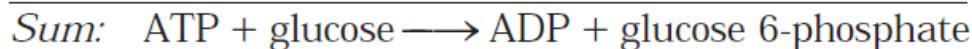
(b)  $\Delta G = \Delta G'^\circ + RT \ln Q$

$$\begin{aligned} Q &= [\text{G6P}]/[\text{F6P}] = 0.5 \text{ M}/1.5 \text{ M} = 0.33 \\ \Delta G &= -1.68 \text{ kJ/mol} + (2.48 \text{ kJ/mol}) \ln 0.33 \\ &= -4.4 \text{ kJ/mol} \end{aligned}$$

- (c)  $\Delta G'^\circ$  for any reaction is a fixed parameter because it is defined for standard conditions of temperature (25 °C = 298 K) and concentration (both F6P and G6P = 1 M). In contrast,  $\Delta G$  is a variable and can be calculated for any set of product and reactant concentrations.  $\Delta G$  is defined as  $\Delta G'^\circ$  (standard conditions) plus whatever difference occurs in  $\Delta G$  on moving to nonstandard conditions.

# Problems to solve

6. Consider the following sequential reactions and their respective  $K'_{\text{eq}}$ :



Calculate the equilibrium constant for the two coupled reactions.

$$K'_{\text{eq}_1} = \frac{[\text{glucose 6-phosphate}]}{[\text{glucose}][\text{P}_i]} = 3.9 \times 10^{-3} \text{ M}^{-1}$$

$$K'_{\text{eq}_2} = \frac{[\text{ADP}][\text{P}_i]}{[\text{ATP}]} = 2.0 \times 10^5 \text{ M}$$

$$\begin{aligned} K'_{\text{eq}_3} &= \frac{[\text{glucose 6-phosphate}][\text{ADP}][\text{P}_i]}{[\text{glucose}][\text{P}_i][\text{ATP}]} \\ &= (K'_{\text{eq}_1})(K'_{\text{eq}_2}) = (3.9 \times 10^{-3} \text{ M}^{-1})(2.0 \times 10^5 \text{ M}) \\ &= 7.8 \times 10^2 \end{aligned}$$

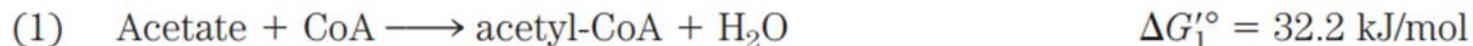
Although the  $\Delta G^\circ$  values for two reactions that sum to a third are *additive*, the  $K'_{\text{eq}}$  for a reaction that is the sum of two reactions is the product of their individual  $K'_{\text{eq}}$  values. Equilibrium constants are *multiplicative*. By coupling ATP hydrolysis to glucose 6-phosphate synthesis, the  $K'_{\text{eq}}$  for formation of glucose 6-phosphate has been raised by a factor of about  $2 \times 10^5$ .

# Problems to solve

7. The synthesis of the activated form of acetate (acetyl-CoA) is carried out in an ATP-dependent process:  $\text{Acetate} + \text{CoA} + \text{ATP} \longrightarrow \text{acetyl-CoA} + \text{AMP} + \text{PP}_i$

- The  $\Delta G^\circ$  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<sub>i</sub> is -30.5 kJ/mol. Calculate  $\Delta G^\circ$  for the ATP dependent synthesis of acetyl-CoA.
- Almost all cells contain the enzyme inorganic pyrophosphatase, which catalyzes the hydrolysis of PP<sub>i</sub> to Pi. What effect does the presence of this enzyme have on the synthesis of acetyl-CoA? Explain.

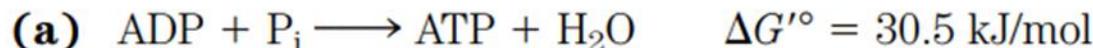
(a) The  $\Delta G'^\circ$  can be determined for the coupled reactions:



(b) Hydrolysis of PP<sub>i</sub> would drive the reaction forward, favoring the synthesis of acetyl-CoA.

## Problems to solve

8 (a). A total of 30.5 kJ/mol of free energy is needed to synthesize ATP from ADP and Pi when the reactants and products are at 1 M concentrations (standard state). Because the actual physiological concentrations of ATP, ADP, and Pi are not 1 M, the free energy required to synthesize ATP under physiological conditions is different from  $\Delta G^\circ$ . Calculate the free energy required to synthesize ATP in the human hepatocyte when the physiological concentrations of ATP, ADP, and Pi are 3.5, 1.50, and 5.0 mM, respectively.



$$\text{Mass action ratio, } Q = \frac{[\text{ATP}]}{[\text{P}_i][\text{ADP}]} = \frac{[3.5 \times 10^{-3} \text{ M}]}{[1.5 \times 10^{-3} \text{ M}] [5.0 \times 10^{-3} \text{ M}]} = 4.7 \times 10^2 \text{ M}^{-1}$$

$$\begin{aligned}\Delta G &= \Delta G^\circ + RT \ln Q \\ &= 30.5 \text{ kJ/mol} + (2.58 \text{ kJ/mol}) \ln (4.7 \times 10^2 \text{ M}^{-1}) \\ &= 46.37 \text{ kJ/mol}\end{aligned}$$

## Problems to solve

8 (b). A 68 kg (150 lb) adult requires a caloric intake of 2,000 kcal (8,360 kJ) of food per day (24 h). The food is metabolized and the free energy is used to synthesize ATP, which then provides energy for the body's daily chemical and mechanical work. Assuming that the efficiency of converting food energy into ATP is 50%, calculate the weight of ATP used by a human adult in 24 h. What percentage of the body weight does this represent?

*Hint: Molecular weight of ATP is 503*

- (b) The energy going into ATP synthesis in 24 hr is  $8,360 \text{ kJ} \times 50\% = 4,180 \text{ kJ}$ . Using the value of  $\Delta G$  from (a), the amount of ATP synthesized is

$$(4,180 \text{ kJ})/(46 \text{ kJ/mol}) = 91 \text{ mol}$$

The molecular weight of ATP is 503 (calculated by summing atomic weights). Thus, the weight of ATP synthesized is

$$(91 \text{ mol ATP})(503 \text{ g/mol}) = 46 \text{ kg}$$

As a percentage of body weight:

$$100\%(46 \text{ kg ATP})/(68 \text{ kg body weight}) = 68\%$$

## Problems to solve

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8 (c). Although adults synthesize large amounts of ATP daily, their body weight, structure, and composition do not change significantly during this period. Explain this apparent contradiction.

- (c) The concentration of ATP in a healthy body is maintained in a steady state; this is an example of homeostasis, a condition in which the body synthesizes and breaks down ATP as needed.