

Thermodynamics of metabolic pathway

- Biological Energy Transformations Obey the Laws of Thermodynamics
- The first law is the principle of the conservation of energy: for any physical or chemical change, the total amount of energy in the universe remains constant; energy may change form or it may be transported from one region to another, but it cannot be created or destroyed.
- The second law of thermodynamics, which can be stated in several forms, says that the universe always tends toward increasing disorder: in all natural processes, the entropy of the universe increases.
- three thermodynamic quantities that describe the energy changes occurring in a chemical reaction are:

- **Gibbs free energy, G ,**
- expresses the amount of energy capable of doing work during a reaction at constant temperature and pressure. 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, ΔG , has a negative value and the reaction is said to be **exergonic**. In **endergonic** reactions, the system gains free energy and ΔG is positive.
- **Enthalpy, H ,**
- is the heat content of the reacting system. It reflects the number and kinds of chemical bonds in the reactants and products. When a chemical reaction releases heat, it is said to be **exothermic**; the heat content of the products is less than that of the reactants, and the change in enthalpy, ΔH , has, by convention, a negative value. Reacting systems that take up heat from their surroundings are **endothermic** and have positive values of ΔH .
- **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.

The units of ΔG and ΔH are joules/mole or calories/mole (recall that 1 cal = 4.184 J); units of entropy are joules/mole·Kelvin (J/mol·K) (Table 13-1).

TABLE 13-1 Some Physical Constants and Units Used in Thermodynamics

Boltzmann constant, k = 1.381×10^{-23} J/K
Avogadro's number, N = 6.022×10^{23} mol ⁻¹
Faraday constant, F = 96,480 J/V · mol
Gas constant, R = 8.315 J/mol · K (= 1.987 cal/mol · K)
Units of ΔG and ΔH are J/mol (or cal/mol) Units of ΔS are J/mol·K (or cal/mol·K) 1 cal = 4.184 J
Units of absolute temperature, T , are Kelvin, K 25 °C = 298 K At 25 °C, RT = 2.478 kJ/mol (= 0.592 kcal/mol)

Under the conditions existing in biological systems (including constant temperature and pressure), changes in free energy, enthalpy, and entropy are related to each other quantitatively by the equation

$$\Delta G = \Delta H - T\Delta S \quad (13-1)$$

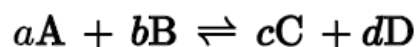
- in which ΔG is the change in Gibbs free energy of the reacting system, ΔH is the change in enthalpy of the system, T is the absolute temperature, and ΔS is the change in entropy of the system. By convention, ΔS has a positive sign when entropy increases and ΔH , as noted above, has a negative sign when heat is released by the system to its surroundings. Either of these conditions, both of which are typical of energetically favorable processes, tends to make ΔG negative. In fact, ΔG of a spontaneously reacting system is always negative.
- The second law of thermodynamics states that the entropy *of the universe* increases during all chemical and physical processes, but it does not require that the entropy increase take place *in the reacting system* itself. The order produced within cells as they grow and divide is more than compensated for by the disorder they create in their surroundings in the course of growth and division. In short, living organisms preserve their internal order by taking from the surroundings free energy in the form of nutrients or sunlight, and returning to their surroundings an equal amount of energy as heat and entropy.

Cells Require Sources of Free Energy

Cells are isothermal systems—they function at essentially constant temperature (and also function at constant pressure). Heat flow is not a source of energy for cells, because heat can do work only as it passes to a zone or object at a lower temperature. The energy that cells can and must use is free energy, described by the Gibbs free-energy function G , which allows prediction of the direction of chemical reactions, their exact equilibrium position, and the amount of work they can (in theory) perform at constant temperature and pressure. Heterotrophic cells acquire free energy from nutrient molecules, and photosynthetic cells acquire it from absorbed solar radiation. Both kinds of cells transform this free energy into ATP and other energy-rich compounds capable of providing energy for biological work at constant temperature.

Standard Free-Energy Change Is Directly Related to the Equilibrium Constant

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_{eq} (p. 25). In the general reaction



where a , b , c , and d are the number of molecules of A, B, C, and D participating, the equilibrium constant is given by

$$K_{\text{eq}} = \frac{[C]^c [D]^d}{[A]^a [B]^b} \quad (13-2)$$

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

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, ΔG . 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, ΔG° . By this definition, the standard state for reactions that involve hydrogen ions is $[H^+] = 1 \text{ M}$, or pH 0. Most biochemical reactions, however, occur in well-buffered aqueous solutions near pH 7; both the pH and the concentration of water (55.5 M) are essentially constant.

>> Key Convention: For convenience of calculations, biochemists define a standard state different from that used in chemistry and physics: in the biochemical standard state, $[H^+]$ is 10^{-7} M (pH 7) and $[H_2O]$ is 55.5 M. For reactions that involve Mg^{2+} (which include most of those with ATP as a reactant), $[Mg^{2+}]$ in solution is commonly taken to be constant at 1 mM. <<

Physical constants based on this biochemical standard state are called **standard transformed constants** and are written with a prime (such as $\Delta G'^\circ$ and K'_{eq}) to distinguish them from the untransformed constants used by chemists and physicists. (Note that most other textbooks use the symbol $\Delta G^{\circ'}$ rather than $\Delta G'^\circ$. Our use of $\Delta G'^\circ$, recommended by an international committee of chemists and biochemists, is intended to emphasize that the transformed free-energy change, $\Delta G'^\circ$, is the criterion for equilibrium.) For simplicity, we will hereafter refer to these transformed constants as **standard free-energy changes** and **standard equilibrium constants**.

>> Key Convention: In another simplifying convention used by biochemists, when H_2O , H^+ , and/or Mg^{2+} are reactants or products, their concentrations are not included in equations such as Equation 13-2 but are instead incorporated into the constants K'_{eq} and $\Delta G'^\circ$. <<

Just as K'_{eq} is a physical constant characteristic for each reaction, so too is $\Delta G'^\circ$ a constant. As we noted in Chapter 6, there is a simple relationship between K'_{eq} and $\Delta G'^\circ$:

$$\Delta G'^\circ = -RT \ln K'_{\text{eq}} \quad (13-3)$$

The standard free-energy change of a chemical reaction is simply an alternative mathematical way of expressing its equilibrium constant. Table 13-2 shows the relationship between $\Delta G'^{\circ}$ and K'_{eq} . If the equilibrium constant for a given chemical reaction is 1.0, the standard free-energy change of that reaction is 0.0 (the natural logarithm of 1.0 is zero). If K'_{eq} of a reaction is greater than 1.0, its $\Delta G'^{\circ}$ is negative. If K'_{eq} is less than 1.0, $\Delta G'^{\circ}$ is positive. Because the relationship between $\Delta G'^{\circ}$ and K'_{eq} is exponential, relatively small changes in $\Delta G'^{\circ}$ correspond to large changes in K'_{eq} .

TABLE 13-2 Relationship between Equilibrium Constants and Standard Free-Energy Changes of Chemical Reactions

K'_{eq}	(kJ/mol)	$\Delta G'^{\circ}$ (kcal/mol) ^a
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

^a Although joules and kilojoules are the standard units of energy and are used throughout this text, biochemists and nutritionists sometimes express $\Delta G'^{\circ}$ values in kilocalories per mole. We have therefore included values in both kilojoules and kilocalories in this table and in Tables 13-4 and 13-6. To convert kilojoules to kilocalories, divide the number of kilojoules by 4.184.

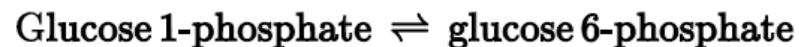
TABLE 13-3 Relationships among K'_{eq} , $\Delta G'^{\circ}$, and the Direction of Chemical Reactions

When K'_{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

It may be helpful to think of the standard free-energy change in another way. $\Delta G'^{\circ}$ 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). Table 13-3 summarizes these points.

WORKED EXAMPLE 13-1 Calculation of $\Delta G'^{\circ}$

Calculate the standard free-energy change of the reaction catalyzed by the enzyme phosphoglucomutase,



given that, starting with 20 mM glucose 1-phosphate and no glucose 6-phosphate, the final equilibrium mixture at 25 °C and pH 7.0 contains 1.0 mM glucose 1-phosphate and 19 mM glucose 6-phosphate. Does the reaction in the direction of glucose 6-phosphate formation proceed with a loss or a gain of free energy?

Solution: First we calculate the equilibrium constant:

$$K'_{\text{eq}} = \frac{[\text{glucose 6-phosphate}]}{[\text{glucose 1-phosphate}]} = \frac{19 \text{ mM}}{1.0 \text{ mM}} = 19$$

We can now calculate the standard free-energy change:

$$\begin{aligned}\Delta G'' &= -RT \ln K'_{\text{eq}} \\ &= -(8.315 \text{ J/mol} \cdot \text{K}) (298 \text{ K}) (\ln 19) \\ &= -7.3 \text{ kJ/mol}\end{aligned}$$

Because the standard free-energy change is negative, the conversion of glucose 1-phosphate to glucose 6-phosphate proceeds with a loss (release) of free energy. (For the reverse reaction, $\Delta G'^{\circ}$ has the same magnitude but the *opposite* sign.)

Table 13-4 gives the standard free-energy changes for some representative chemical reactions. Note that hydrolysis of simple esters, amides, peptides, and glycosides, as well as rearrangements and eliminations, proceed with relatively small standard free-energy changes, whereas hydrolysis of acid anhydrides is accompanied by relatively large decreases in standard free energy. The complete oxidation of organic compounds such as glucose or palmitate to CO_2 and H_2O , which in cells requires many steps, results in very large decreases in standard free energy. However, standard free-energy changes such as those in Table 13-4 indicate how much free energy is available from a reaction under *standard conditions*. To describe the energy released under the conditions existing in cells, an expression for the *actual* free-energy change is essential.

TABLE 13-4 Standard Free-Energy Changes of Some Chemical Reactions

Reaction type	$\Delta G'^{\circ}$	
	(kJ/mol)	(kcal/mol)
Hydrolysis reactions		
Acid anhydrides		
Acetic anhydride + $\text{H}_2\text{O} \rightarrow 2$ acetate	-91.1	-21.8
	-30.5	-7.3
ATP + $\text{H}_2\text{O} \rightarrow$ ADP + P_i		
ATP + $\text{H}_2\text{O} \rightarrow$ AMP + PP_i	-45.6	-10.9
$\text{PP}_i + \text{H}_2\text{O} \rightarrow 2\text{P}_i$	-19.2	-4.6
UDP-glucose + $\text{H}_2\text{O} \rightarrow$ UMP + glucose 1-phosphate	-43.0	-10.3
Esters		
Ethyl acetate + $\text{H}_2\text{O} \rightarrow$ ethanol + acetate	-19.6	-4.7
Glucose 6-phosphate + $\text{H}_2\text{O} \rightarrow$ glucose + P_i	-13.8	-3.3
Amides and peptides		
Glutamine + $\text{H}_2\text{O} \rightarrow$ glutamate + NH_4^+	-14.2	-3.4
Glycylglycine + $\text{H}_2\text{O} \rightarrow 2$ glycine	-9.2	-2.2
Glycosides		
Maltose + $\text{H}_2\text{O} \rightarrow 2$ glucose	-15.5	-3.7
Lactose + $\text{H}_2\text{O} \rightarrow$ glucose + galactose	-15.9	-3.8
Rearrangements		
Glucose 1-phosphate \rightarrow glucose 6-phosphate	-7.3	-1.7
Fructose 6-phosphate \rightarrow glucose 6-phosphate	-1.7	-0.4
Elimination of water		
Malate \rightarrow fumarate + H_2O	3.1	0.8
Oxidations with molecular oxygen		
Glucose + $6\text{O}_2 \rightarrow 6\text{CO}_2 + 6\text{H}_2\text{O}$	-2,840	-686
Palmitate + $23\text{O}_2 \rightarrow 16\text{CO}_2 + 16\text{H}_2\text{O}$	-9,770	-2,338

Actual Free-Energy Changes Depend on Reactant and Product Concentrations

We must be careful to distinguish between two different quantities: the actual free-energy change, ΔG , and the standard free-energy change, $\Delta G'^{\circ}$. Each chemical reaction has a characteristic standard free-energy change, which may be positive, negative, or zero, depending on the equilibrium constant of the reaction. The standard free-energy change tells us in which direction and how far a given reaction must go to reach equilibrium *when the initial concentration of each component is 1.0 M*, the pH is 7.0, the temperature is 25 °C, and the pressure is 101.3 kPa (1 atm). Thus $\Delta G'^{\circ}$ is a constant: it has a characteristic, unchanging value for a given reaction. But the *actual* free-energy change, ΔG , is a function of reactant and product concentrations and of the temperature prevailing during the reaction, none of which will necessarily match the standard conditions as defined above. Moreover, the ΔG 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.

ΔG and $\Delta G'^{\circ}$ for any reaction $aA + bB \rightleftharpoons cC + dD$ are related by the equation

$$\Delta G = \Delta G'^{\circ} + RT \ln \frac{[C]^c [D]^d}{[A]^a [B]^b} \quad (13-4)$$

in which the terms in red are those *actually prevailing* in the system under observation. The concentration terms in this equation express the effects commonly called mass action, and the term $[C]^c [D]^d / [A]^a [B]^b$ is called the **mass-action ratio, Q** . Thus Equation 13-4 can be expressed as $\Delta G = \Delta G'^{\circ} + RT \ln Q$. As an example, let us suppose that the reaction $A + B \rightleftharpoons C + D$ is taking place under the standard conditions of temperature (25 °C) and pressure (101.3 kPa) but that the concentrations of A, B, C, and D are *not* equal and none of the components is present at the standard concentration of 1.0 M. To determine the actual free-energy change, ΔG , under these nonstandard conditions of concentration as the reaction proceeds from left to right, we simply enter the *actual* concentrations of A, B, C, and D in Equation 13-4; the values of R , T , and $\Delta G'^{\circ}$ are the standard values. ΔG is negative and approaches zero as the reaction proceeds, because the actual

concentrations of A and B decrease and the concentrations of C and D increase. Notice that when a reaction is at equilibrium—when there is no force driving the reaction in either direction and ΔG is zero—Equation 13-4 reduces to

$$0 = \Delta G = \Delta G'^{\circ} + RT \ln \frac{[C]_{\text{eq}} [D]_{\text{eq}}}{[A]_{\text{eq}} [B]_{\text{eq}}}$$

or

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

which is the equation relating the standard free-energy change and equilibrium constant (Eqn 13-3).

The criterion for spontaneity of a reaction is the value of ΔG , not $\Delta G'^{\circ}$. A reaction with a positive $\Delta G'^{\circ}$ can go in the forward direction *if ΔG is negative*. This is possible if the term $RT \ln ([\text{products}]/[\text{reactants}])$ in Equation 13-4 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 $[\text{products}]/[\text{reactants}]$ well below 1, such that the term $RT \ln ([\text{products}]/[\text{reactants}])$ has a large, negative value. $\Delta G'^{\circ}$ and ΔG are expressions of the *maximum* amount of free energy that a given reaction can *theoretically* deliver—an amount of energy that could be realized only if a perfectly efficient device were available to trap or harness it. Given that no such device is possible (some energy is always lost to entropy during any process), the amount of work done by the reaction at constant temperature and pressure is always less than the theoretical amount.

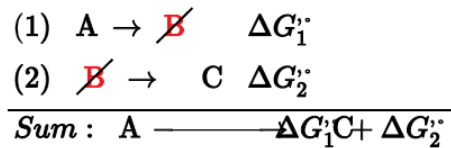
Another important point is that some thermodynamically favorable reactions (that is, reactions for which $\Delta G'^{\circ}$ is large and negative) do not occur at measurable rates. For example, combustion of firewood to CO_2 and H_2O is very favorable thermodynamically, but firewood remains stable for years because the activation energy (see Figs 6-2, 6-3) for the combustion reaction is higher than the energy available at room temperature. If the necessary activation energy is provided (with a lighted match, for example), combustion will begin, converting the wood to the more stable products CO_2 and H_2O and releasing energy as heat and light. The heat released by this

exothermic reaction provides the activation energy for combustion of neighboring regions of the firewood; the process is self-perpetuating.

In living cells, reactions that would be extremely slow *if uncatalyzed* are caused to proceed not by supplying additional heat but by lowering the activation energy through use of an enzyme. An enzyme provides an alternative reaction pathway with a lower activation energy than the uncatalyzed reaction, so that at room temperature a large fraction of the substrate molecules have enough thermal energy to overcome the activation barrier, and the reaction rate increases dramatically. *The free-energy change for a reaction is independent of the pathway by which the reaction occurs; it depends only on the nature and concentration of the initial reactants and the final products. Enzymes cannot, therefore, change equilibrium constants; but they can and do increase the rate at which a reaction proceeds in the direction dictated by thermodynamics (see Section 6.2).*

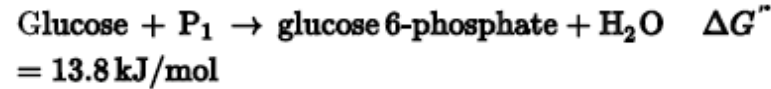
Standard Free-Energy Changes Are Additive

In the case of two sequential chemical reactions, $A \rightleftharpoons B$ and $B \rightleftharpoons C$, each reaction has its own equilibrium constant and each has its characteristic standard free-energy change, ΔG_1° and ΔG_2° . As the two reactions are sequential, B cancels out to give the overall reaction $A \rightleftharpoons C$, which has its own equilibrium constant and thus its own standard free-energy change, $\Delta G_{\text{sum}}^{\circ}$. *The ΔG° values of sequential chemical reactions are additive.* For the overall reaction $A \rightleftharpoons C$, $\Delta G_{\text{sum}}^{\circ}$ is the sum of the individual standard free-energy changes, ΔG_1° and ΔG_2° , of the two reactions: $\Delta G_{\text{sum}}^{\circ} = \Delta G_1^{\circ} + \Delta G_2^{\circ}$

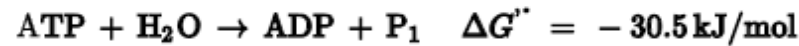


This principle of bioenergetics explains how a thermodynamically unfavorable (endergonic) reaction can be driven in the forward direction by coupling it to a highly exergonic reaction through a common intermediate. For example, in many organisms, the synthesis of glucose 6-phosphate is the

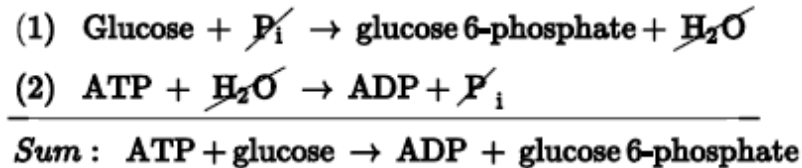
first step in the utilization of glucose. In principle, the synthesis could be accomplished by this reaction:



But the positive value of ΔG° predicts that under standard conditions the reaction will tend not to proceed spontaneously in the direction written. Another cellular reaction, the hydrolysis of ATP to ADP and P_1 , is highly exergonic:



These two reactions share the common intermediates P_1 and H_2O and may be expressed as sequential reactions:



The overall standard free-energy change is obtained by adding the ΔG° values for individual reactions:

$$\Delta G_{\text{sum}}^{\circ} = 13.8 \text{ kJ/mol} + (-30.5 \text{ kJ/mol}) = -16.7 \text{ kJ/mol}$$

The overall reaction is exergonic. In this case, energy stored in ATP is used to drive the synthesis of glucose 6-phosphate, even though its formation from glucose and inorganic phosphate (P_1) is endergonic. The *pathway* of glucose 6-phosphate formation from glucose by phosphoryl transfer from ATP is different from reactions (1) and (2) above, but the net result is the same as the sum of the two reactions. In thermodynamic calculations, all that matters is the state of the system at the beginning of the process and its state at the end; the route between the initial and final states is immaterial.

We have said that ΔG° is a way of expressing the equilibrium constant for a reaction. For reaction (1) above,

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

Notice that H_2O is not included in this expression, as its concentration (55.5 M) is assumed to remain unchanged by the reaction. The equilibrium constant for the hydrolysis of ATP is

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

The equilibrium constant for the two coupled reactions is

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

This calculation illustrates an important point about equilibrium constants: although the ΔG° values for two reactions that sum to a third, overall reaction are *additive*, the K'_{eq} for the overall reaction is the *product* of the individual K'_{eq} values for the two reactions. Equilibrium constants are *multiplicative*. By coupling ATP hydrolysis to glucose 6-phosphate synthesis, the K'_{eq} for formation of glucose 6-phosphate from glucose has been raised by a factor of about 2×10^5 .

This common-intermediate strategy is employed by all living cells in the synthesis of metabolic intermediates and cellular components. Obviously, the strategy works only if compounds such as ATP are continuously available. In the following chapters we consider several of the most important cellular pathways for producing ATP. For more practice in dealing with free-energy changes and equilibrium constants for coupled reactions, see the worked examples in [Chapter 1 \(pp. 25–27\)](#).

Reactions Far from Equilibrium in Cells Are Common Points of Regulation

- For some steps in a metabolic pathway the reaction is close to equilibrium, with the cell in its dynamic steady state (Fig. 15–4).
- these near-equilibrium reactions in a cell by comparing the **mass action ratio**, Q , with the equilibrium constant for the reaction, K_{eq} . Recall that for the reaction $A + B \rightarrow C + D$, $Q = [C][D]/[A][B]$.

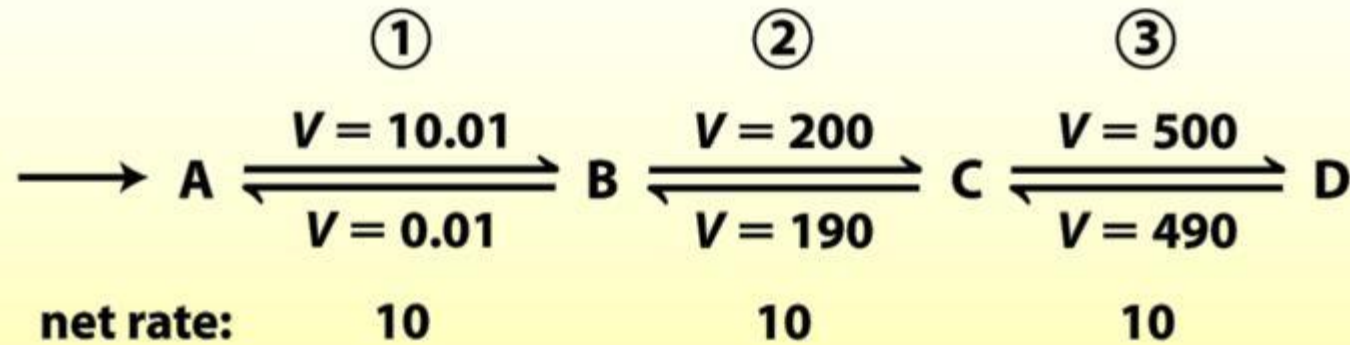
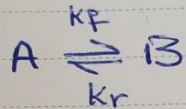


FIGURE 15–4 Near-equilibrium and nonequilibrium steps in a metabolic pathway.

$$\Delta G = -RT \ln K_{eq} + RT \ln Q$$

$$\Delta G = RT \ln \left(\frac{Q}{K_{eq}} \right) \rightarrow \rho$$

(disequilibrium ratio)



equilibrium

$$v_f = k_f [A]$$

forward

$$v_r = k_r [B]$$

reverse

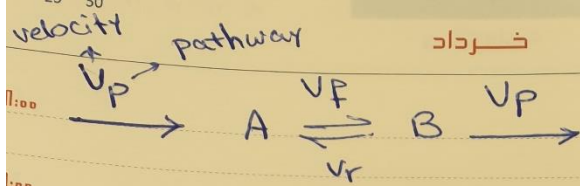
$$v_f = v_r$$

$$k_f [A] = k_r [B]$$

$$\frac{[B]}{[A]} = \frac{k_f}{k_r} = K_{eq}$$

Far from equilibrium

$$\frac{v_r}{v_f} = \frac{k_r [B]}{k_f [A]} = \frac{Q}{K_{eq}} = \rho$$



$$v_f - v_r = v_p \Rightarrow v_f - v_p = v_r$$

$$\frac{v_r}{v_f} = \frac{v_f - v_p}{v_f} = 1 - \frac{v_p}{v_f} = \rho$$

$$\frac{v_p}{v_f} = 1 - \rho \left\{ \begin{array}{l} \rho = 1 \Rightarrow \frac{v_p}{v_f} = 0 \Rightarrow \left. \begin{array}{l} v_f \gg v_p \\ \Downarrow \\ v_f = v_r \end{array} \right\} \text{equilibrium} \end{array} \right.$$

$$\rho = 0.2 \Rightarrow \frac{v_p}{v_f} = 0.8 = \frac{8}{10} \left\{ \begin{array}{l} \text{Far} \\ \text{From} \\ \text{equilibrium} \end{array} \right.$$

$$v_p = 8 \text{ mol/sec}$$

$$v_f = 10 \text{ mol/sec}$$

$$\rho = 0.9 \Rightarrow \frac{v_p}{v_f} = \frac{1}{10} \left\{ \begin{array}{l} \text{near} \\ \text{equilibrium} \end{array} \right.$$

$$v_p = 1 \text{ mol/sec}$$

$$v_f = 10 \text{ mol/sec}$$