

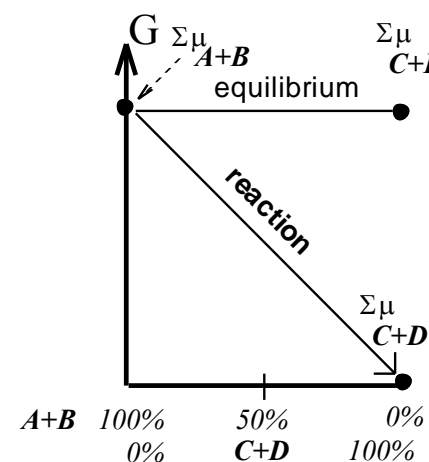
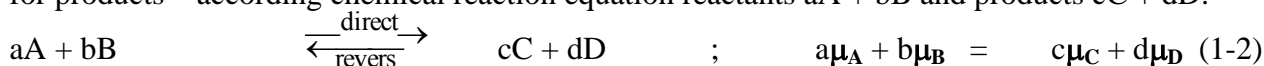
## Chemical potential $\mu$ and Homeostasis

**Chemical potential** show, how much change of **free energy**  $\Delta G_A$  brings into system-reaction adding of 1 mole amount of compound **A** . In a fact: how great amount of **free energy** belongs to one **1 mol** in mixture. It means how much free energy  $\Delta G_A$  has itself per **1 mole** compound **A** , if amount of compound in molar numbers is  $\Delta n_A = 1 \text{ mole} : \mu_A = \frac{\Delta G_A}{\Delta n_A} = \Delta G^\circ_A + R \cdot T \cdot \ln(X_A)$  (1-1)

**chemical potential** of compound **A**, where:  $\Delta G^\circ_A$ , **kJ/mol** - **standard chemical potential** at standard conditions  $T = 298.16 \text{ }^\circ\text{K}$  , pressure  $p = 101.3 \text{ kPa}$ ;  $R = 8.3144 \text{ J/mol/K}$  - universal gas constant;  $\ln(X_A)$  - natural logarithmic function from argument  $X_A$  and  $X_A$ , unless - **molar fraction** concentration of compound **A**, expressed as  $X_A = n_A/n_{\text{total}}$  and laying between  $0 < X_A \leq 1$  (absence and pure) compound **A** concentrations, where  $n_A$ , **mol** - **number of moles** for compound **A** and  $n_{\text{total}}$ , **mol** - total **number of moles** all present compounds **total** including water. Logarithmic function properties  $\ln(1) = 0$  yield that **standard chemical potential**  $\Delta G^\circ_A = \mu_A$  at  $X_A = 1$  is pure **A** compound **1 mol** free energy content  $\Delta G^\circ_A$ , assuming **standard free energy of formation**  $G^\circ_A$  from elements for compound **A** per one **1 mole**. Reaction proceeds completely forward until end only when **products** of reaction have hardly little disposition to reverse change back into **reactants**. In other words these **products** of reaction have trifling remarkable or zero value of chemical potential:  $\mu_{\text{products}} = 0$  , affinity turns back to **reactants**: **A**  $\leftarrow$  **x** **products**.

### Thermodynamical conditions of chemical equilibrium.

Provided chemical potential of reaction products is taking into consideration (it has anything remarkable level of value) , then reaction proceeds not completely until end, go not on completely 100% to reactants conversion to products, but one can observe the setting in equilibrium. In state of equilibrium sum of chemical potentials for initial compounds is equal to sum of chemical potentials for products – according chemical reaction equation reactants  $aA + bB$  and products  $cC + dD$ :



because compound factorials  $a, b, c,$  and  $d$  times  $\mu$  . For compound **A**  $(A+A+A+\dots) = aA = a\mu_A$  times  $a$ . For compounds **B, C,** and **D** as seen on equation of reaction expression(1-2), takes a part times  $b, c$  and  $d$ :  
 $(B+B+B+\dots) = bB = a\mu_B$   
 $(C+C+C+\dots) = cC = a\mu_C$   
 $(D+D+D+\dots) = dD = d\mu_D$  Chemical potential  $\mu$  like as amount of compound  $n$  in mols have additive properties, e.g. summing.

The concentrations  $X$  of **reactants** and **products** at **equilibrium** define the **equilibrium constant,  $K_{eq}$**  (see the Chemical Equilibrium). In the general reaction **chemical potential** sum for **reactants**  $\Sigma\mu_{\text{reactant}}$  and **products**  $\Sigma\mu_{\text{product}}$  at equilibrium are equal:  
 $\Sigma\mu_{\text{reactant}} = \Sigma\mu_{\text{product}}$  ; and **free energy change** for reaction is

$$\Delta G_{\text{reaction}} = \Sigma\mu_{\text{product}} - \Sigma\mu_{\text{reactant}} .$$

As the **chemical potential** sum at equilibrium are equal  $a\mu_A + b\mu_B = c\mu_C + d\mu_D$  ;  
 $a \cdot (\Delta G^\circ_A + R \cdot T \cdot \ln(X_A)) + b \cdot (\Delta G^\circ_B + R \cdot T \cdot \ln(X_B)) = c \cdot (\Delta G^\circ_C + R \cdot T \cdot \ln(X_C)) + d \cdot (\Delta G^\circ_D + R \cdot T \cdot \ln(X_D))$   
 $(a \cdot \Delta G^\circ_A + b \cdot \Delta G^\circ_B) - (d \cdot \Delta G^\circ_D + c \cdot \Delta G^\circ_C) = R \cdot T \cdot \{ [c \cdot \ln(X_C) + d \cdot \ln(X_D)] - [a \cdot \ln(X_A) + b \cdot \ln(X_B)] \}$   
 $-\Delta G^\circ_{\text{reaction}} = -[(d \cdot \Delta G^\circ_D + c \cdot \Delta G^\circ_C) - (a \cdot \Delta G^\circ_A + b \cdot \Delta G^\circ_B)] = R \cdot T \cdot \{ [\ln(X_D^d) + \ln(X_C^c)] - [\ln(X_A^a) + \ln(X_B^b)] \}$   
 $-\Delta G^\circ_{\text{reaction}} = - [\Sigma\Delta G^\circ_{\text{product}} - \Sigma\Delta G^\circ_{\text{reactant}}] = R \cdot T \cdot \{ \ln(X_D^d \cdot X_C^c) - \ln(X_A^a \cdot X_B^b) \}$   
 $-\Delta G^\circ_{\text{reaction}} = - [\Sigma\Delta G^\circ_{\text{product}} - \Sigma\Delta G^\circ_{\text{reactant}}] = R \cdot T \cdot \ln\left(\frac{X_C^c \cdot X_D^d}{X_A^a \cdot X_B^b}\right)$

$$-\Delta G^\circ_{\text{reaction}} = R \cdot T \cdot \ln\left(\frac{X_C^c \cdot X_D^d}{X_A^a \cdot X_B^b}\right) = R \cdot T \cdot \ln(K_{eq}) ; K_{eq} = \left(\frac{X_C^c \cdot X_D^d}{X_A^a \cdot X_B^b}\right) \quad (1-3)$$

In each sum  $a, b, c,$  and  $d$  are the number of molecules of **A, B, C,** and **D** participating, the **equilibrium constant** is expressed by (1-3) where  $X_A, X_B, X_C,$  and  $X_D$  are the **molar fraction** 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,  $\Delta G_{\text{reaction}}$ . Under

**standard conditions** (298.15 °K or 25 °C), when reactants and products are present in molar fraction concentrations or, for gases, at partial pressures for total pressure as sum  $p_{\text{total}} = 101.3$  kilo-pascals (kPa) or **1 atm**, the force driving the system toward equilibrium is defined as the **standard free-energy change**,  $\Delta G^\circ_{\text{reaction}}$ . By this definition, the **standard state** for reactions that involve hydrogen ions is  $X_{\text{H}_3\text{O}^+}$  is **pH**

maintaining equilibrium constant value in ratio  $\frac{X_C^c \cdot X_D^d}{X_A^a \cdot X_B^b} = K_{\text{eq}}$ . Most biochemical reactions occur in well-buffered aqueous solutions near **pH = 7.36** (for blood plasma); both the **pH** and the concentration of water [**H<sub>2</sub>O**] (**55.346 M**) are essentially **constant**. For convenience of calculations, biochemists therefore define a different **standard state**, in which the concentration of **H<sub>3</sub>O<sup>+</sup>** is  $10^{-7.36}$  M (**pH = 7.36**) and that of water is [**H<sub>2</sub>O**] = **55.346 M**; for reactions that involve **Mg<sup>2+</sup>** (including most reactions for which **ATP** is a substrate), its concentration in solution is commonly taken to be constant at **1 mM**, but dose not matter because magnesium **Mg<sup>2+</sup>** ion usually is a catalysts and therefore dose not affecting **equilibrium** constant  $K_{\text{eq}}$ . Physical constants based on this biochemical standard state are called **standard transformed constants** and are written with a zero index (e.g.,  $\Delta G_o$  and  $K_{\text{oeq}}$ ) to distinguish them from the **normal constants** used by chemists and physicists. (Notice that the symbol  $\Delta G_o$  is a change from the symbol  $\Delta G^\circ$  used in earlier editions of thermodynamics and in most other textbooks. The change, recommended by an international committee of chemists and biochemists, is intended to emphasize that the **transformed free energy**  $\Delta G_o$  is the criterion for **equilibrium**.) By convention, when **H<sub>2</sub>O**, **H<sub>3</sub>O<sup>+</sup>**, (**Mg<sup>2+</sup>** excepting as catalyst) are **reactants** or **products**, their concentrations could not be included in equations such as equation 1-3 but are instead incorporated into the constants  $\Delta G_o$  and  $K_{\text{oeq}}$ .

Just as  $K_{\text{oeq}}$  is a physical constant characteristic for each reaction, so too is  $\Delta G_o$  a constant. As is noted in General Chemistry course (equilibrium and Second Law of Thermodynamics), there is a simple relationship between  $K_{\text{oeq}}$  and  $\Delta G_o$  show the energy and mass relation of compounds. The **standard free-energy**  $\Delta G^\circ$  change of a chemical reaction is simply an alternative mathematical way of expressing its equilibrium constant  $K_{\text{eq}}$ . The **equilibrium** constant for a given chemical reaction is  $K_{\text{eq}} = 1.0$ , the **standard free-energy** change of that reaction is  $\Delta G^\circ = 0.0$  (the natural logarithm of **1 ln(1) = 0** is zero). If  $K_{\text{eq}}$  of a reaction is greater than **>1.0**, its  $\Delta G^\circ < 0$  is negative. If  $K_{\text{eq}}$  is less than **<1.0**,  $\Delta G^\circ > 0$  is positive. 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  $K_{\text{eq}}$ .

It may be helpful to think of the **standard free-energy** change  $\Delta G^\circ$  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** (1-3). When  $\Delta G^\circ = G_2 - G_1 < 0$  is negative, the **products**  $G_2$  contain less  $\downarrow$  **free energy** than the **reactants** and the reaction will proceed **spontaneously** under **standard conditions**  $G_1$ ; all chemical reactions tend to go in the conversion direction that results in a decrease  $\downarrow$  in the **free energy** to  $G_2$  of the **system**. A positive value of  $\Delta G^\circ = G_2 - G_1 > 0$  means that the **products**  $G_2$  of the reaction contain more  $\uparrow$  **free energy** than the **reactants**  $G_1$  and this reaction will tend to go in the conversion reverse  $\xleftarrow{\text{reverse}}$  direction to  $G_1$ .

As an example, let us make a simple calculation of the **standard free-energy** change  $\Delta G^\circ$  of the reaction catalyzed by the enzyme **phospho-gluco-mutase** (**glucose** three letter symbols is **Glc**):

**Glc 1-phosphate**  $\rightleftharpoons$  **Glc 6-phosphate**

Chemical analysis shows that whether we start with, say, **20 mM glucose 1-phosphate** (but no **glucose 6-phosphate**) or with **20 mM glucose 6-phosphate** (but no **glucose 1-phosphate**), the final **equilibrium** mixture will contain **1 mM glucose 1-phosphate** and **19 mM glucose 6-phosphate** at **25°C**. (Remember that **enzymes** do not affect the point of **equilibrium** of a reaction; they merely hasten its attainment.) From these data we can calculate the **equilibrium** constant and **standard free-energy** change:

$$K_{\text{eq}} = [\text{Glc 6-phosphate}]/[\text{Glc 1-phosphate}] = 19 \text{ mM}/1 \text{ mM} = 19 \text{ shifted to right side ;}$$

$$\Delta G^\circ = -R \cdot T \cdot \ln(K_{\text{eq}}) = -R \cdot T \cdot \ln(19) = -7.296 \text{ kJ/mol spontaneous.}$$

Because the **standard free-energy** change  $\Delta G^\circ < 0$  is negative, when the reaction starts with **glucose 1-phosphate** and **glucose 6-phosphate**, the conversion of **glucose 1-phosphate** to **glucose 6-phosphate** proceeds with a loss  $\downarrow$  (release) of free energy.

For the reverse reaction (the conversion to **glucose 1-phosphate**  $\xleftarrow{\text{reverse}}$  from **glucose 6-phosphate**),  $\Delta G^\circ = 7.296 \text{ kJ/mol}$  has the same magnitude but the opposite sign, reverse reaction nonspontaneous.

Actual Free-Energy Changes Depend on Reactant and Product Concentrations in **Homeostasis**

Table 1-1 gives the **standard free-energy** changes  $\Delta G^\circ$  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  $\Delta G^\circ$ , whereas **hydrolysis** of **acid anhydrides** occurs with relatively large decreases  $\downarrow$  in **standard free-energy**  $\Delta G^\circ$ . The complete **oxidation** of organic compounds such as **glucose** or **palmitate** to **CO<sub>2</sub>** and **H<sub>2</sub>O**, which in cells requires many steps, results in very large decreases  $\downarrow$  in **standard free energy**  $\Delta G^\circ$ . However, **standard free-energy** changes  $\Delta G^\circ$  such as those in Table 1-1 indicate how much **free energy** is available from a reaction under **standard conditions** for one **1 mol** of compound. To describe the energy released under the **homeostasis (stationary) conditions** existing in real cells, an expression for the **actual free-energy** change  $\Delta G_{\text{reaction}}$  calculation is essential.

$$\Delta G_{\text{reaction}} = \Delta G^\circ_{\text{reaction}} + R \cdot T \cdot \ln \left( \frac{X_C^c \cdot X_D^d}{X_A^a \cdot X_B^b} \right) \neq 0; \quad 0 = \Delta G^\circ_{\text{reaction}} + R \cdot T \cdot \ln(K_{\text{eq}}) \text{ at equilibrium zero} \quad (1-4)$$

We must be careful to distinguish between two **2** different quantities: the **free-energy** change,  $\Delta G$ , and the **standard free-energy** change,  $\Delta G^\circ$ . Each chemical reaction has a characteristic **standard free-energy** change per one **1 mol** of **reactant**, which maybe positive  $\Delta G^\circ > 0$ , negative  $\Delta G^\circ < 0$ , or some times zero  $\Delta G^\circ = 0$ , depending on the equilibrium constant  $K_{\text{eq}}$  of the reaction. The **standard free-energy** change  $\Delta G^\circ$  tells us in which direction and how far a given reaction must go to reach **equilibrium** when the temperature is **25 °C** or  $T_0 = 298.15 \text{ °K}$ , and the pressure **p** is **101.3 kPa (1 atm)** and component concentrations at **equilibrium** are **X**. Thus  $\Delta G^\circ$  is a constant: it has a characteristic, unchanging value for a given reaction. But the actual **free-energy** change,  $\Delta G$ , is a function of **reactant** and **product** concentrations **X** and of the temperature  $T = 310.15 \text{ °K}$  prevailing during the reaction in human body, which will not necessarily match the **standard conditions** as defined above. Moreover, the  $\Delta G$  of any reaction proceeding  $\Rightarrow$  spontaneously toward its **equilibrium** state is always negative  $\Delta G < 0$ , becomes less negative as the reverse  $\leftarrow$  reaction proceeds, and is zero  $\Delta G = 0$  at the point of **equilibrium**  $(X_D^d \cdot X_C^c) / (X_A^a \cdot X_B^b) = K_{\text{eq}}$ , indicating that no more work  $W = -\Delta G = 0$  can be done by the reaction:  $aA + bB = cC + dD$  according expression (1-4)

$\Delta G$  and  $\Delta G^\circ$  for any reaction are related by the equation (1-4). in which the terms in **red** are those actually prevailing in the system under observation. The concentration **X** terms in this equation express the effects commonly called **mass action**. As an example, let us suppose that the reaction  $aA + bB = cC + dD$  is taking place at the **standard conditions** of temperature  $T_0 = 298.15 \text{ °K (25 °C)}$  and pressure (**101.3 kPa**) but that the concentrations of  $X_A$ ,  $X_B$ ,  $X_C$ , and  $X_D$  into reaction mixture are not equal and that none of the components is present at the standard concentration **X** of **1.0** like pure compounds. To determine the actual **free-energy** change,  $\Delta G$ , under these **nonstandard conditions** of concentration **X** as the reaction proceeds from left  $\Rightarrow$  to right, we simply enter the actual concentrations of  $X_A$ ,  $X_B$ ,  $X_C$ , and  $X_D$  in Equation 1-4; the values of **R**,  $T_0$ , and  $\Delta G^\circ$  are the standard values.  $\Delta G$  is negative  $\Delta G < 0$  and approaches zero  $\Delta G \Rightarrow 0$  as the reaction proceeds because the actual reactants concentrations of  $X_A$  and  $X_B$  decrease  $\downarrow$  and products concentrations of  $X_C$ , and  $X_D$  increase  $\uparrow$ . Notice that when a reaction is at **equilibrium**-when there is no **force** driving the reaction in either direction and  $\Delta G$  is zero-Equation 1-4 reduces to  $\Delta G^\circ = -R \cdot T \cdot \ln(K_{\text{eq}})$  and  $0 = \Delta G^\circ + R \cdot T \cdot \ln(K_{\text{eq}})$  the equation relating the **standard free-energy** change and **equilibrium** constant  $K_{\text{eq}}$  as noted above (1-4).

Biological mediums usually have some certain hydrogen ion  $[H_3O^+]$  concentrations expressed as **pH =  $-\log([H_3O^+])$**  for: blood plasma and cytosol **pH = 7.36**; mitochondria matrix **pH = 8.37**; mitochondria inter membrane space **pH = 5.0**; saliva juice **pH = 6.8**; stomach juice **pH = 1.2** (before meals). Extracting from **equilibrium** mixture constant  $K_{\text{eq}}$  as expression  $R \cdot T \cdot \ln(X_{H_3O^+}^n)$  by mathematical separation

**Table 1-1. Standard Free-Energy Changes of Some Chemical Reactions at 25 °C (298.15 °K)**

Hydrolysis reactions types	$\Delta G^\circ$ (kJ/mol)(kcal/mol)	
Acetic acid and phosphoric acid anhydrides		
$\text{CH}_3\text{CO-O-OCCH}_3 + \text{H}_2\text{O} \Rightarrow 2 \text{CH}_3\text{COO}^- \text{H}^+$	-91.100	-21.80
$\text{CH}_3\text{CO-O-OCCH}_3 + 3 \text{H}_2\text{O} \Rightarrow 2 \text{CH}_3\text{COO}^- + 2 \text{H}_3\text{O}^+$	-3.317	-0.793
$\text{ATP}^{4-} + \text{H}_2\text{O} \Rightarrow \text{ADP}^{3-} + \text{H}_2\text{PO}_4^-$	-30.500	-7.30
$\text{ATP}^{4-} + 2 \text{H}_2\text{O} \Rightarrow \text{ADP}^{3-} + \text{HPO}_4^{2-} + \text{H}_3\text{O}^+$	34.4605	8.24
$\text{ATP}^{4-} + \text{H}_2\text{O} \Rightarrow \text{AMP}^{2-} + \text{HOPO}_2\text{-O-O}_2\text{POH}^-$	-45.600	-10.90
$\text{HOPO}_2\text{-O-O}_2\text{POH}^- + \text{H}_2\text{O} \Rightarrow 2 \text{H}_2\text{PO}_4^-$	-19.200	-4.60
$\text{HOPO}_2\text{-O-O}_2\text{POH}^- + \text{H}_2\text{O} \Rightarrow 2 \text{HPO}_4^{2-} + 2 \text{H}_3\text{O}^+$	110.721	26.46
$\text{UDP-Glc}^{2-} + \text{H}_2\text{O} \Rightarrow \text{UMP}^- + \text{Glc 1-phosphate}^-$	-43.000	-10.30
Esters		
$\text{CH}_3\text{CH}_2\text{-O-OCCH}_3 + \text{H}_2\text{O} \Rightarrow \text{CH}_3\text{CH}_2\text{-OH} + \text{HO-OCCH}_3$	-19.600	-4.70
$\text{CH}_3\text{CH}_2\text{-O-OCCH}_3 + 2 \text{H}_2\text{O} \Rightarrow \text{CH}_3\text{CH}_2\text{-OH} + \text{O-OCCH}_3^- + \text{H}_3\text{O}^+$	24.2905	5.806
$\text{Glc 6-phosphate}^- + \text{H}_2\text{O} \Rightarrow \text{Glc} + \text{H}_2\text{PO}_4^-$	-13.800	-3.30
$\text{Glc 6-phosphate}^- + 2 \text{H}_2\text{O} \Rightarrow \text{Glc} + \text{HPO}_4^{2-} + \text{H}_3\text{O}^+$	51.1605	12.23
Amides and peptides <small>Chem. Phys. CRC, 2010-2005, p.876,882,1220,1223</small>		
$\text{Glutamine} + \text{H}_2\text{O} \Rightarrow \text{glutamate}^- + \text{NH}_4^+$	-14.200	-3.40
$\text{Glycylglycine} + \text{H}_2\text{O} \Rightarrow 2 \text{glycine} \quad \Delta G_r =$	-80.99	-19.36
Glycosides $\Delta G_r =$		
$\text{Maltose} + \text{H}_2\text{O} \Rightarrow 2 \text{glucose}$	-15.500	-3.70
$\text{Lactose} + \text{H}_2\text{O} \Rightarrow \text{glucose} + \text{galactose}$	-15.900	-3.80
Rearrangements		
$\text{Glucose 1-phosphate}^- \Rightarrow \text{glucose 6-phosphate}^-$	-7.300	-1.70
$\text{Fructose 6-phosphate}^- \Rightarrow \text{glucose 6-phosphate}^-$	-1.700	-0.40
Elimination of water $\text{H}_2\text{O}$		
$\text{Malate} \Rightarrow \text{Fumarate} + \text{H}_2\text{O}$	3.1	0.8
Oxidations with molecular oxygen $\text{O}_2$		
$\text{Glucose} + 6 \text{O}_2 \Rightarrow 6 \text{CO}_2 + 6 \text{H}_2\text{O}$	-2 840	-686
$\text{Palmitic Acid} + 23 \text{O}_2 \Rightarrow 16 \text{CO}_2 + 16 \text{H}_2\text{O}$	-9 770	-2 338

of logarithm ratio in (1-4) may correct **standard free-energy**  $\Delta G^\circ$  value to non-standard conditions for pH of medium of  $[\text{H}_3\text{O}^+] = 10^{-\text{pH}} \text{ M}$  solution where **n** is the number of hydrogen ions  $\text{H}_3\text{O}^+$  involved in reaction **equilibrium** mixture according given reaction equation. Addition or subtraction to **standard free-energy**  $\Delta G^\circ$  value yield  $\Delta G_o = \Delta G^\circ \pm \text{R} \cdot \text{T} \cdot \ln(\text{X}_{\text{H}_3\text{O}^+}^{\text{n}})$  non-standard free-energy at given medium pH conditions ( $-\text{R} \cdot \text{T} \cdot \ln(\text{X}_{\text{H}_3\text{O}^+}^{\text{n}})$  agree for reactant and  $+\text{R} \cdot \text{T} \cdot \ln(\text{X}_{\text{H}_3\text{O}^+}^{\text{n}})$  for product).

The criterion for spontaneity of a reaction is the value of  $\Delta G$ , not  $\Delta G^\circ$ . A reaction with a positive  $\Delta G^\circ > 0$  can go in the forward direction if  $\Delta G < 0$  is negative. This is possible if the term  $\text{R} \cdot \text{T} \cdot \ln([\text{products}]/[\text{reactants}])$  in equation 1-4 is negative (-) and has a larger absolute value greater > 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  $\text{R} \cdot \text{T} \cdot \ln([\text{products}]/[\text{reactants}])$  has a large, negative (-) value.

$\Delta G^\circ$  and  $\Delta G$  are expressions of the maximum amount of **free energy** per one **1 mol** of compound 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 **free energy**  $\Delta G$  is always lost to **bound energy**  $\text{T} \cdot \Delta \text{S}$  or entropy **S** during any process), the amount of work  $\text{W} < -\Delta G$  done by the reaction at constant temperature **T = const** and pressure is always less than the theoretical amount  $\Delta G$ .

Another important point is that some thermodynamically favorable reactions (that is, reactions for which  $\Delta G^\circ < 0$  is large and negative) do not occur at measurable rates. For example, **combustion** of firewood to  $\text{CO}_2$  and  $\text{H}_2\text{O}$  is very favorable thermodynamically, but firewood remains stable for years because the activation energy  $\text{E}_a$  (see Reaction Rate (Velocity) and Kinetics) for the **combustion** reaction is higher  $\uparrow$  than the energy  $\text{E}_r$  available at room temperature. If the necessary activation energy  $\text{E}_a$  is provided (with a lighted match, for example), combustion will begin, converting the wood to the more stable products  $\text{CO}_2$  and  $\text{H}_2\text{O}$  and releasing energy as **heat**  $-\Delta \text{H}$  and light  $\sim \text{h}\nu$ . The **heat**  $-\Delta \text{H}$  released by this **exothermic** reaction provides the activation energy  $\text{E}_a$  for **combustion** of neighboring regions of the firewood; the process is self-perpetuating.



In living cells, reactions that would be extremely slow and long time if uncatalyzed are caused to occur, not by supplying additional **heat**  $-\Delta H$ , but by lowering  $\downarrow$  the activation energy  $E_a$  with an **enzyme**. An **enzyme** provides an **alternative reaction pathway** with a lower  $\downarrow$  activation energy  $E_a$  than the uncatalyzed reaction, so that at room temperature a large fraction of the **substrate** molecules have enough thermal energy  $-\Delta H$  to overcome the **activation barrier**, and the reaction rate increases dramatically  $10^6$ . The **free-energy change**  $\Delta G$  for a reaction is independent of the **pathway** by which the reaction occurs; it depends only on the nature  $\Delta G^\circ$  and concentration **X** of **reactants** and the final **products**. **Enzymes** cannot, therefore, change equilibrium constants  $K_{eq}$ ; but they can and do increase  $\uparrow$  the rate **v** at which a reaction proceeds in the direction dictated by **thermodynamics homeostasis** (stationary) conditions.

### Free-Energy Changes $\Delta G$ Are Additive

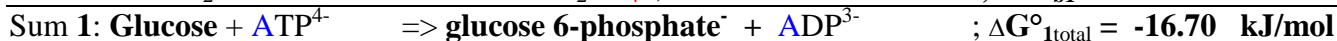
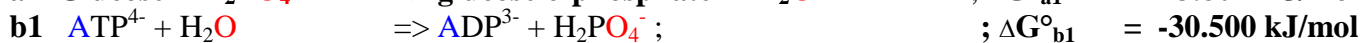
In the case of two **2** sequential chemical reactions,  $A \rightleftharpoons B$  and  $B \rightleftharpoons C$ , each reaction has its own **equilibrium** constant  $K_{eq1}$ ,  $K_{eq2}$  and each has its characteristic **standard free-energy change**,  $\Delta G^\circ_1$  and  $\Delta G^\circ_2$ . As the two reactions are sequential, **B** cancels out to give the overall reaction  $A \rightleftharpoons C$ , which has its own **equilibrium** constant  $K_{eq}$  and thus its own **standard free-energy change**,  $\Delta G^\circ_{total}$ . The  $\Delta G^\circ$  values of sequential chemical reactions are additive. For the overall reaction  $A \rightleftharpoons C$ ,  $\Delta G^\circ_{total} = \Delta G^\circ_1 + \Delta G^\circ_2$  is the algebraic sum of the individual **standard free-energy changes**,  $\Delta G^\circ_1$  and  $\Delta G^\circ_2$ , and the overall **equilibrium** constant  $K_{eq} = K_{eq1} \cdot K_{eq2}$  is the factorial of the individual **equilibrium** constant  $K_{eq1}$  and  $K_{eq2}$  of the two **2** separate sequential reactions. The principle of biochemical thermodynamics explains how unfavorable (**endergonic**) reaction can be driven in the forward  $\Rightarrow$  direction by coupling it to a highly **exergonic** reaction through a **common intermediate**. For example, many organisms thru synthesis of **glucose 6-phosphate** as the first **1st** step in the utilization of **glucose** maintains gradient blood **5 mM**  $\Rightarrow$  to cytosol **0,01  $\mu$ M**:



The positive value of  $\Delta G_{a1}^\circ > 0$  predicts that under **standard conditions** the reaction **a1** will tend not to proceed spontaneously in the direction  $\leftarrow$  written. In accounting reaction **a2** with  $\text{HPO}_4^{2-} + \text{H}_3\text{O}^+$  is affecting by **pH** of medium and can be derived by appropriate **pH** value. Another cellular reaction, the **hydrolysis** of **ATP<sup>4-</sup>** to **ADP<sup>3-</sup>** and **H<sub>2</sub>PO<sub>4</sub><sup>-</sup>** or  $\text{HPO}_4^{2-} + \text{H}_3\text{O}^+$ , is very **exergonic b1** or **endergonic b2**:



These two **2** reactions share the common intermediates  $\text{H}_2\text{PO}_4^-$  or  $\text{HPO}_4^{2-} + \text{H}_3\text{O}^+$  and  $\text{H}_2\text{O}$  or  $2 \text{H}_2\text{O}$  and may be expressed as sequential reactions **1** and **2**:



The overall **standard free-energy change**  $\Delta G^\circ_{\text{total}} = -16.7 \text{ kJ/mol}$  is obtained by adding the  $\Delta G^\circ$  values for individual reactions...

The overall reaction is **exergonic**. In this case, energy stored in the bonds of  $\text{ATP}^{4-}$  is used to drive the synthesis of **glucose 6-phosphate**, even though its formation from **glucose** and **phosphate a1** is **endergonic** or **pH** affected hydrolyze **b2** is **endergonic**. Any way the **pathway** of **glucose 6-phosphate** formation by **phosphate transfer** from  $\text{ATP}^{4-}$  is different from reactions (a) and (b) above in both cases **1** and **2**, but the net result is the same as the sum of the two **2** reactions. In thermodynamic calculations, all that matters is the **state** of the **system** at the **beginning (reactants)** of the process, and its **state** at the **end (products)**, the route between the **initial** and **final states** is immaterial.

We have said that  $\Delta G^\circ$  is a way of expressing the **equilibrium** constants  $K_{a1eq}$  and  $K_{a2eq}$  for a reaction. For reaction (a) **1** and **2** above at standard  $T=298.15^\circ\text{K}$  and  $T=310.15^\circ\text{K}$ ,

$$K_{a1eq298} = \frac{[\text{Glu6P}^-] \cdot [\text{H}_2\text{O}]}{[\text{Glu}] \cdot [\text{H}_2\text{PO}_4^-]} = 3.823 \cdot 10^{-3} \quad \& \quad K_{a1eq310} = \frac{[\text{Glu6P}^-] \cdot [\text{H}_2\text{O}]}{[\text{Glu}] \cdot [\text{H}_2\text{PO}_4^-]} = 4.7418 \cdot 10^{-3} ;$$

$$K_{a2eq298} = \frac{[\text{Glu6P}^-] \cdot [\text{H}_2\text{O}]^2}{[\text{Glu}] \cdot [\text{HPO}_4^{2-}] \cdot [\text{H}_3\text{O}^+]} = 9.177 \cdot 10^8 \quad \& \quad K_{a2eq310} = \frac{[\text{Glu6P}^-] \cdot [\text{H}_2\text{O}]^2}{[\text{Glu}] \cdot [\text{HPO}_4^{2-}] \cdot [\text{H}_3\text{O}^+]} = 4.1299 \cdot 10^8$$

Notice if  $\text{H}_2\text{O}$  is not included in this expression one should deviate the **standard equilibrium** constants by water concentration  $[\text{H}_2\text{O}] = 55.1398 \text{ M}$  at cell temperature  $T = 310.15^\circ\text{K}$  to get non-standard equilibrium constant. The **equilibrium** constants  $K_{b1}$  and  $K_{b2}$  for the **hydrolysis** of  $\text{ATP}^{4-}$  are

$$K_{b1298} = \frac{[\text{ADP}^{3-}] \cdot [\text{H}_2\text{PO}_4^-]}{[\text{ATP}^{4-}] \cdot [\text{H}_2\text{O}]} = 2.2041 \cdot 10^5 \quad \& \quad K_{b1310} = \frac{[\text{ADP}^{3-}] \cdot [\text{H}_2\text{PO}_4^-]}{[\text{ATP}^{4-}] \cdot [\text{H}_2\text{O}]} = 1.3693 \cdot 10^5 ;$$

$$K_{b2298} = \frac{[\text{ADP}^{3-}] \cdot [\text{HPO}_4^{2-}] \cdot [\text{H}_3\text{O}^+]}{[\text{ATP}^{4-}] \cdot [\text{H}_2\text{O}]^2} = 9.1821 \cdot 10^{-7} \quad \text{or} \quad K_{b2310} = \frac{[\text{ADP}^{3-}] \cdot [\text{HPO}_4^{2-}] \cdot [\text{H}_3\text{O}^+]}{[\text{ATP}^{4-}] \cdot [\text{H}_2\text{O}]^2} = 1.5722 \cdot 10^{-6}$$

The equilibrium constant for the two coupled reactions is

$$K_{eq1} = \frac{[\text{Glu6P}^-] \cdot [\text{H}_2\text{O}]}{[\text{Glu}] \cdot [\text{H}_2\text{PO}_4^-]} \cdot \frac{[\text{ADP}^{3-}] \cdot [\text{H}_2\text{PO}_4^-]}{[\text{ATP}^{4-}] \cdot [\text{H}_2\text{O}]} = \frac{[\text{Glu6P}^-] \cdot [\text{ADP}^{3-}]}{[\text{Glu}] \cdot [\text{ATP}^{4-}]} = K_{a1eq} \cdot K_{b1} = 842.63 \quad \text{or} \quad 649.3$$

$$K_{eq2} = \frac{[\text{Glu6P}^-] \cdot [\text{H}_2\text{O}]^2}{[\text{Glu}] \cdot [\text{HPO}_4^{2-}] \cdot [\text{H}_3\text{O}^+]} \cdot \frac{[\text{ADP}^{3-}] \cdot [\text{HPO}_4^{2-}] \cdot [\text{H}_3\text{O}^+]}{[\text{ATP}^{4-}] \cdot [\text{H}_2\text{O}]^2} = \frac{[\text{Glu6P}^-] \cdot [\text{ADP}^{3-}]}{[\text{Glu}] \cdot [\text{ATP}^{4-}]} = 842.64 \quad \text{or} \quad 649.3$$

This calculation illustrates an important point about **equilibrium** constants  $K_{eq}$ , although the  $\Delta G^\circ$  values for two **2** reactions that sum to a third **3rd** are additive, the  $K_{eq}$  for a reaction that is the sum of two **2** reactions is the product of their individual  $K_{a1eq} \cdot K_{b1}$  or  $K_{a2eq} \cdot K_{b2}$  values yielding  $K_{eq1} = 649.3$  or  $K_{eq2} = 649.3$  at human body temperature  $T=310.15^\circ\text{K}$  ( $37^\circ\text{C}$ ) respectively. **Equilibrium** constants are multiplicative. By coupling  $\text{ATP}^{4-}$  **hydrolysis** to glucose 6-phosphate<sup>-</sup> synthesis, the  $K_{eq}$  for formation of glucose 6-phosphate<sup>-</sup> has been raised by a factor of about  $\sim 10^5 = 136931.7$  factor ( $K_{a1eq} \cdot K_{b1} = 649.3 / K_{a1eq310} = 4.7418 \cdot 10^{-3}$ ). 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  $\text{ATP}^{4-}$  are continuously available. In the following chapters we consider several of the most important cellular pathways for producing  $\text{ATP}^{4-}$ .