

Oxidation-Reduction Homeostasis

The **transfer of electron** in **oxidation-reduction RedOx** reactions is indispensable for metabolism. These reactions involve the loss of electrons $-e^-$ by one chemical species, which is thereby **oxidized**, and the gain of electrons $+e^-$ by another, which is **reduced**. The flow of electrons e^- in **RedOx** reactions is responsible, directly or indirectly, for all work W done by living organisms. In **non-photo synthetic** organisms, the sources of electrons are **reduced compounds** foods; in **photo synthetic** organisms, the initial electrons **donors** are a biochemical compounds excited by the absorbed **light** $\sim hv = E_{\text{energy}}$. Electrons e^- capture from reducing metabolites to specialized intermediates water soluble electron carriers which transfer to **enzyme** - catalyzed reactions. The carriers of e^- in turn **donate** electrons to **acceptors** with higher electron **affinities** by negative free **energy** change minimum $\Delta G_{\text{eq}} < 0$ at equilibrium. Homeostasis contain a variety of molecular **energy transducers**, which convert the electron flow into work W $W = \Delta E \cdot F \cdot n$, where ΔE potential difference $\Delta E = E^\circ_{\text{Red}} - E^\circ_{\text{Ox}}$ between Red and Ox form in volts **V**; **F=96485 C** one **mol** of electrons electric charge in units **C** coulomb, **n** number of electrons involved in to **RedOx** reactions between **reduced** form of half cell and **oxidized** form of half reactions. Electrochemical series **reduction** systems called as half cell with own **standard potential** E° ,

$$\text{Ox}^{n+} + ne^- \rightleftharpoons \text{Red};$$

$$E = E^\circ + \frac{\ln(10) \cdot R \cdot T}{F \cdot n} \cdot \log(K_{\text{eq}}); K_{\text{eq}} = \left(\frac{[\text{Ox}^{n+}]}{[\text{Red}]} \right); \frac{\ln(10) \cdot R \cdot T}{F \cdot n} = \frac{0,0591}{n}; E = E^\circ + \frac{0,0591}{n} \log \left(\frac{[\text{Ox}^{n+}]}{[\text{Red}]} \right) \quad (1)$$

where E° standard potential of given **reduction** system measured at conditions for $E = E^\circ$, as equal $[\text{Ox}^{n+}] = [\text{Red}]$ give $\log 1 = 0$; natural logarithm of ten $\ln(10) = 2.302585093$; universal gas constant **R=8.3144 J/mol/K**; absolute thermodynamics temperature on Kelvin scale **T=298.15 K (25°C)** is standard temperature conditions. Human body temperature **37°C** is **T = 310.15 K** non-standard conditions; Faraday's constant **F=96485 C** (coulomb) one **mol** of electrons e^- electric charge in **C** units; number of electrons involved in **reduction** system **n**; decimal logarithmic function $\log()$ of argument as ratio $([\text{Ox}^{n+}]/[\text{Red}])$ between **oxidized form** concentration factorial $[\text{Ox}^{n+}]$ over **reduced** form concentration $[\text{Red}]$ factorial equilibrium state constant $K_{\text{eq}} = [\text{Ox}^{n+}]/[\text{Red}]$.

Reduction - oxidation description of metabolic reactions in which electrons e^- are **transferred**. After considering Hess law and Prigogine attractors declaration for evaluation the **energy** changes ΔG in terms of **reduction** reactions **electromotive force EMF**. Reduction - oxidation potential amplitude $E^\circ_{\text{Red}} - E^\circ_{\text{Ox}}$, expressed in volts **V** and **free-energy** change at equilibrium $\Delta G_{\text{eq}} = (E^\circ_{\text{Red}} - E^\circ_{\text{Ox}}) \cdot F \cdot n$, expressed in joules over mol as Prigogine attractor free energy change minimum stay less $\Delta G_{\text{eq}} < \Delta G_{\text{Hess}}$ the difference Hess. Specialized electron carriers role in electro biochemistry have cofactors of **enzymes** designated the vitamins (life amines).

The Flow of Electrons perform Homeostasis Work

Protolytic attractors water concentration $[\text{H}_2\text{O}] = 55.3 \text{ M}$, $\text{pH} = 7.36$ concentration $[\text{H}_3\text{O}^+] = 10^{-7.36} \text{ M}$ activate functionally flow of electrons with producing positive work $W = -\Delta G_{\text{eq}}$ as irreversible molecular engine for dissipative biochemical structures to drive the processes for homeostasis. Number of moles **n** is the **electron number** moving from **reduced Red** form to **oxidized Ox** form. Free energy change stop to zero at equilibrium: $\Delta G_{\text{homeostasis}} = \Delta G_{\text{eq}} + R \cdot T \cdot \ln K_{\text{Homeostasis}}$;

$$\text{equilibrium } K_{\text{eq}} = \frac{X_{\text{Ox}^{n+}}^m \cdot X_{\text{Red}}^n}{X_{\text{Red}}^m \cdot X_{\text{Ox}^{n+}}^n} \text{ stop homeostasis to zero } 0 = \Delta G_{\text{eq}} + R \cdot T \cdot \ln K_{\text{eq}}.$$

The reduced form supply negative $(-)\text{Red}_1 - ne^- \rightleftharpoons \text{Ox}_1$ electric charge n ($n=2$) number of electrons ne^- flow to oxidized form with positive $(+)\text{Ox}_2 + ne^- \rightleftharpoons \text{Red}_2$ electron carriers acceptor. Transfer n number of electrons ne^- flow from E_{Red} to E_{Ox} for complete reaction is calculated as difference $\text{EMF} = E^\circ_{\text{Red}} - E^\circ_{\text{Ox}}$ electric-motion force in volts **V**. Because the two **2** chemical species differ in their **affinity** for electrons flow spontaneously through net reaction, driven by a **force** proportional to the difference in electron **affinity**. The **electromotive force** (typically a few volts $+1 \div 3.5 \text{ V}$) can accomplish work $W = \text{EMF} \cdot F \cdot n$ if an appropriate **energy transducer** in electrochemical reaction, which work as irreversible molecular engine for homeostasis, survival and evolution.

Living cells have an molecular network with **reduced** form **glucose** as the source of 24 electrons e^- . **Glucose** releases the 24 electrons flow spontaneously through a series of **electron-carrier** intermediates to another chemical species 6 O_2 six oxygen molecules. $\Delta G_{eq} = (E^\circ_{Red} - E^\circ_{Ox}) \cdot F \cdot n = -1.226 \cdot 96485 \cdot 24 = -2840 \text{ kJ/mol}$:



Electron flow to O_2 has a higher affinity for four electrons $4 e^-$ so it not fire safe. Protolysis attractors decreases oxygen free energy content from water $G_{O_{2(aqua)}} = 303.1 \text{ kJ/mol}$ creating safe energy level $G_{O_{2(Biochem)}} = 78.08 \text{ kJ/mol}$.

The resulting **electro-motive force** provides **energy** to the network of molecular **energy** transducers (**enzymes** and **vitamins**) that do the work. In the mitochondrion, for example, **membrane-bound enzymes** couple electron e^- flow producing the trans-membrane proton concentration gradient, generating flow of protons down concentration gradient and **electric** potential, so do the electrochemical **work**. Proton H^+ gradient down the gradient and **potential** is called the **proton-motive force** by analogy with **electro-motive force**. **Enzyme, ATP synthase** in the inner mitochondrial membrane, uses the **proton-motive force** potential $E_{membrane}$ to do electrochemical work **W**: synthesis of **ATP⁴⁻**, **ADP³⁻**, **HPO₄²⁻** and **H₃O⁺** protons H^+ flow spontaneously down the gradient. Similarly, membrane-localized **enzymes** in *E. coli* couple **electro-motive force** to **proton-motive force**, which is then used to power **ATPase motion**. Ilya Prigogine 1977 Nobel Prize attractor declaration [3,4] : Protolytic attractors equilibrium state is attractor for non-equilibrium homeostasis state irreversible continuing.

Oxidation-Reductions irreversibility by Half-cell Reactions of two Ox \rightleftharpoons Red Systems

For balancing transferred electrons from **reductant** to **oxidant** must to be solved in two halves selected from electrochemical series tables.

For example, the **oxidation** of ferrous ion Fe^{2+} by cupric ion Cu^{2+} ,

$Fe^{2+} + Cu^{2+} \Rightarrow Fe^{3+} + Cu^+$ describing with two **2** half-reactions (**Ox** \rightleftharpoons **Red** systems) are used free electrons:

Red $Fe^{2+} - e^- \rightleftharpoons Fe^{3+}$. The electron-donating- e^- molecule is called Red the **reducing** agent or **reductant**;

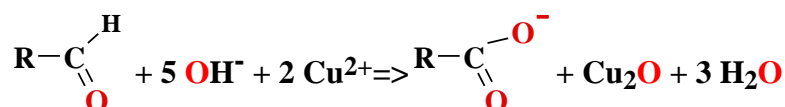
Ox $Cu^{2+} + e^- \rightleftharpoons Cu^+$. The electron-accepting $+e^-$ molecule is the Ox **oxidising** agent or **oxidant**.

Iron cations exist and functioning in Fe^{2+} or Fe^{3+} form, as conjugate **reductant** un **oxidant** pair, **RedOx** pair.

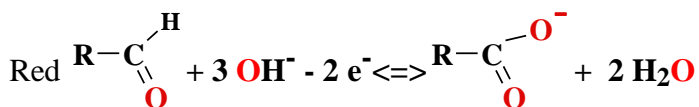
Reductant and oxidant free electrons are intermediates: electrons **donor** $\rightleftharpoons ne^-$ + electrons **acceptor**.

Similar in Brensted protolysis with one proton, however in **RedOx** system free electron number **n** is integer equal or higher as one $n \geq 1$. In the reversible half reaction Red is the electron **donor** Fe^{2+} and Ox is the electron **acceptor** Cu^{2+} .

Free electron e^- transfer in the **oxidation-reduction** reactions of organic compounds are not fundamentally different from those of inorganic species. Reducing Sugars **oxidised** about **carboxylates** an free aldehyde or ketone by cupric ion Cu^{2+} (see **reducing sugars**):



This overall reaction can be expressed as two **2** half-reactions using **RedOx** systems:



Aldehyde carbon $-(C=O)-H$ oxidation with two electrons $2 e^-$ remove is balanced through second half-reaction.

The one-electron reduction of cupric Cu^{2+} to cuprous ion Cu^+ must be doubled **2** to balance the overall reaction.

Two electrons $2 e^-$ are gained on two cupric Cu^{2+} cations converting to two cuprous ions Cu^+ in compound Cu_2O .

Dehydrogenation is Oxidation reaction

The carbon atoms on compound chains exists in eight **oxidation** states (Fig. 1). Four electron pairs covalently bind carbon atom with such atoms **H, C, S, N, O**. Paired covalent electrons belong to more **electronegative** atom. Increasing ΔREN decrease number in compound of carbon own **electron** numbers for four valence carbon atom.

$$2.2 < 2.55 < 2.58 < 3.04 < 3.44$$

$$\text{H} < \text{C} \approx \text{S} < \text{N} < \text{O}$$

$$\Delta\text{REN} = \text{X} - \text{C} \text{ in order}$$

$$-0.33 < 0.0 < 0.03 < 0.49 < 0.89$$

In four valences make sum: for CH_4 is $4 \cdot -0.33 = -1.32$ **8 e⁻**; for $\text{H}_3\text{C}-\text{CH}_3$ is $3 \cdot -0.33 + 0 = -0.99$ **7 e⁻**;
 for $\text{H}_2\text{C}=\text{CH}_2$ $\Delta\text{REN} = 2 \cdot -0.33 + 2 \cdot 0 = -0.66$ **6 e⁻**; for $\text{HC}\equiv\text{CH}$ $\Delta\text{REN} = 0.33 + 3 \cdot 0 = -0.33$ **5 e⁻**;
 for $\text{H}_3\text{C}=\text{O}$ $\Delta\text{REN} = 2 \cdot -0.33 + 0 + 2 \cdot 0.89 = -0.66 + 1.78 = 1.12$ **4 e⁻**; for $\text{H}_3\text{C}-\text{HC}=\text{O}$ $\Delta\text{REN} = -0.33 + 0 + 2 \cdot 0.89 = 1.45$ **3 e⁻**;
 for $\text{H}-\text{C}=\text{O}-\text{O}-\text{H}$ $\Delta\text{REN} = -0.33 + 3 \cdot 0.89 = -0.33 + 2.67 = 2.34$ **2 e⁻**; for $\text{H}_3\text{C}-\text{C}=\text{O}-\text{O}-\text{H}$ $\Delta\text{REN} = 0 + 3 \cdot 0.89 = 2.67$ **e⁻**;
 for $\text{O}=\text{C}=\text{O}$ $\Delta\text{REN} = 4 \cdot 0.89 = 3.56$ **0 e⁻**;

The more **electronegative** atom "owns" the bonding electrons **e⁻** from bound carbon. In methane CH_4 carbon **C** is more **electronegative** than the four **4** hydrogen **H** atoms. All eight **8** bonding electrons **8 e⁻** belong to carbon. In **ethane**, the electrons **e⁻** in the $\equiv\text{C}-\text{C}\equiv$ bond are shared equally, so each $::\text{C}:\text{C}::$ atom owns only seven **7** of its eight **8** bonding electrons **e⁻**. In **ethanol**, **C-1** is less electronegative than the **oxygen O** to which belong both electrons **2 e⁻** of the $\equiv\text{C}-$, leaving $::\text{C}-1$ with only five **5** bonding electrons **e⁻**. With each formal loss of electrons **e⁻**, the carbon **C** atom has undergone **oxidation** even when no **oxygen O** is involved, as **dehydrogenation** of an **alkane** CH_3-CH_3 (**7** bound **e⁻**) to an **alkene** $\text{CH}_2=\text{CH}_2$ (**6** bound **e⁻**) or to an **alkyne** $\text{CH}\equiv\text{CH}$ (**5** bound **e⁻**). This **oxidation** is loss of two hydrogen – **H** atoms from each of two adjacent carbon atoms: ($2 \cdot 7 = 14$, $2 \cdot 6 = 12$, $2 \cdot 5 = 10$). Many **enzymes oxidases** are **dehydrogenases** remove **-2 H** atoms.

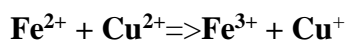
Notice: the biochemical compounds in Figure 1 are richer in hydrogen **H** than in **oxygen O**, whereas the Earth lithosphere and hydrosphere consist **oxygen O** atom number % **59.93 %** and **hydrogen H** atom % **20.34 %**.

Garrett, Grisham 2nd Ed. 1999. Biochemistry.

Not all biochemical **oxidation-reduction** reactions involve carbon **C**. For example, in the conversion of molecular **nitrogen N₂** to ammonia NH_3 : $6 \text{H}^+ + 6 \text{e}^- + \text{N}_2 \Rightarrow 2 \text{NH}_3$, the **nitrogen N** atoms are **reduced**.

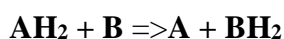
Electrons **e⁻** are transferred from one molecule **donor** to another **acceptor** in one **1** of four **4** different ways:

1. Free electrons e⁻ directly. For example, the **Fe²⁺ / Fe³⁺ Red Ox** pair can transfer an electron **e⁻** to the **Cu⁺ / Cu²⁺ RedOx** pair:



2. As **hydrogen H** atoms. Recall that a hydrogen **H** atom consists of a proton **H⁺** and a single electron **e⁻**. Often Biochemistry shows two hydrogen transfer: $\text{AH}_2 \Rightarrow \text{A} + 2\text{e}^- + 2\text{H}^+$, where **AH₂** is **hydrogen** atoms **electrons donors**.

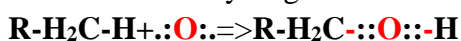
Note: Protolysis is proton jump H⁺ in water medium only but not removal of a hydrogen atom. (**H⁺ + e⁻**.) **AH₂** and **A** together constitute a conjugate **Red Ox** pair (**A / AH₂**), in which **AH₂** **reduce** another compound **B** (or **Red Ox** pair, **B / BH₂**) by transfer of hydrogen **H** atoms:



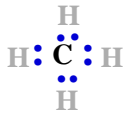
3. Transferred of **hydride ion (:H⁻)**, which has two **2** electrons **e⁻**.

occurs with the B3 vitamin as $\text{NADH} \rightleftharpoons \text{NAD}^+ + \text{H}^-$ in **dehydrogenases**, enzymes, described below.

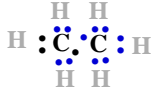
4. Through direct combination with **oxygen O₂**. In this case, **oxygen O₂** combines with an **organic reductant** and is **covalently incorporated** in the product, as in the **oxidation** of a hydrocarbon to an alcohol by **transferred 1/2 O₂** presented as **O** squeezed between carbon and hydrogen atoms $\equiv\text{C}-\text{H} \rightleftharpoons \equiv\text{C}-\text{O}-\text{H}$



Methane $8 e^-$
 $\Delta REN = -1.32$



Ethane $C7 e^-$
 $\Delta REN = -0.99$



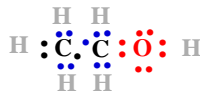
Ethene $C6 e^-$
 $\Delta REN = -0.66$



Acetylene $5 e^-$
 $\Delta REN = -0.33$



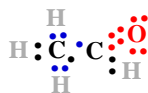
Ethanol $C5 e^-$
 $\Delta REN = 0.23$
 (alcohol)



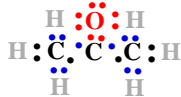
Formaldehyde $4 e^-$
 $\Delta REN = 1.12$



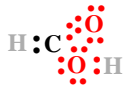
Acetaldehyde $3 e^-$
 $\Delta REN = 1.45$



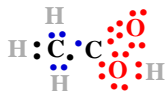
Acetone $2 e^-$
 $\Delta REN = 1.78$



Formic acid $2 e^-$
 $\Delta REN = 2.34$



Acetic acid e^-
 (carboxylic acid)
 $\Delta REN = 2.67$

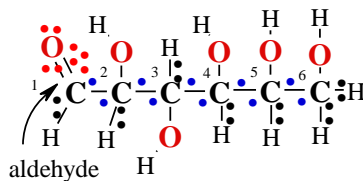


Carbon dioxide 0
 $\Delta REN = 3.56$

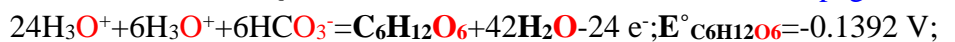
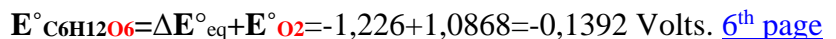
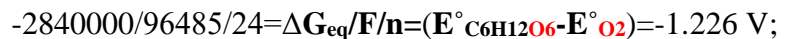
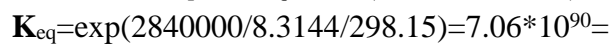


The **hydrocarbon** is the electron e^- donor and the **oxygen O** atom is the electron e^- acceptor.

All four **4** types of electron e^- transfer perform water soluble electron carriers as hydrogen H atoms with FADH₂ (vitamin B₂) or hydride ion ($:H^-$) with NADH (vitamin B₃). The neutral term **reducing equivalent** is commonly used to designate a single electron e^- valence in an **oxidation-reduction** reaction participation and no matter whether this **equivalent** is free electron e^- per se, a hydrogen H ($H^+ + e^-$) atom, or two equivalent electrons in hydride ion $:H^-$, or whether two free electron $2e^-$ transfer takes place in a reaction with **oxygen O** to yield an **oxygenated** product. Biochemical **fuel** molecules are usually **enzymatic dehydrogenated** to lose two **2 reducing equivalents** at a time, and because each **oxygen O** atom can **accept two 2 reducing equivalents**. Scientists by convention regard the unit of biochemical **oxidations** as two **2 reducing equivalents** passing from **substrate** => to **oxygen O**. Glucose Reduced form $-24 e^-$



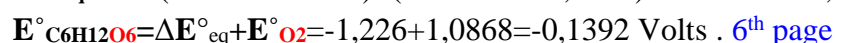
aldehyde H $7 C:-H, 5 C\bullet-O\bullet C: 7*2+5*2=24$ electrons



Hydrogen and Glucose standard reduction potentials are:



Figure 1. Oxidation states of carbon C from full eight electrons $8 e^-$ to completely lost all electrons 0 occurring in the Biochemistry: from methane CH₄ $8 e^-$ to carbon dioxide **C₂O₂ 0 e⁻**. The **oxidation** states illustrated with biorganic **compounds** representatives and with carbon relative electronegativity difference against bound atom ΔREN , summing all four covalent bonds from $-1.32 = \Delta REN$ to $3.56 = \Delta REN$. Focus on the black carbon C atom and its bonding electrons e^- . When this carbon C is bonded to the less **electro negative H** atom, both bonding electrons (blue - : •) are assigned to the carbon C. When carbon C is bonded to another carbon C, bonding electrons e^- are shared equally, so one blue • of the two 2 electrons e^- is assigned to the black carbon C. When the black carbon C of our interest is bonded to the more **electronegative O** atom, the bonding electrons e^- are assigned to the **oxygen O**. The number n black carbon C of our interest undergoes **oxidation** loses n electrons e^- , the number n gets smaller and missing number gets higher n. Thus the order of increasing **oxidation** state is missing n of full eight electrons respectively: from methane CH₄ $8 e^-$ missing n is zero $n=0$ to carbon dioxide **C₂O₂ 0** missing are eight $n=8$.



Electrons Affinity Reduction Potential concentration ratio equilibrium constant K_{eq}

Attractor pH=7.36 staying at equilibrium have true pOH=6.64 value as $pK_w=14 = pH+pOH = 7.36 + 6.64$.

Disaccount the water mass $[H_2O]=963/18=53.5$ M over liter $[H_2SO_4]=[H_3O^+]=1$ M solution with 1.061 g/mL density in Nernst equations for **hydrogen electrode** has classic standard potential $E_{o_classic}=0$ V reference zero:

$$\underline{H(Pt)} \rightleftharpoons H^+ + e^-; E_{classic} = E_{o_classic} + 0.0591 \cdot \log K^o_{classic H(Pt)} = 0 + 0.0591 \cdot \log [H^+] = 0 + 0.0591 \cdot \log(1 \text{ M}) = 0 \text{ Volts.}$$

Thermodynamic account Hydroxonium ions demand the water: $\underline{H(Pt)} + H_2O \rightleftharpoons H_3O^+ + e^-$ and $E^o_H = 0.10166$ V.

The ratio $[H_3O^+]/[H_2O] = 1 \text{ M}/52.5 \text{ M} = X_{H_3O^+}/X_{H_2O}$ is mol fraction instead molarity $[H^+] = 1$ M at classic potential expression. The water account gave thermodynamic standard $E^o_H = 0.10166$ V on potential scale.

Nernst's expression with classic zero measurement demands thermodynamic standard potential $E^o_H = 0.10166$ V :

$$E = E^o_{H^+} + \frac{\ln(10) \cdot R \cdot T}{F \cdot 1} \cdot \log \frac{X_{H_3O^+}}{X_{H_2O}} = E_o + E^o_H + 0.0591 \cdot \log(1/52.5) = 0.10166 - 0.10166 = 0 \text{ V.}$$

As ratio $1 = K_{H(Pt)} = X_{H_3O^+}/X_{H_2O}$ is one than $E^o_H = 0.10166$ V is thermodynamic standard potential:

$$E = E^o_{H^+} + \frac{\ln(10) \cdot R \cdot T}{F \cdot 1} \cdot \log \frac{X_{H_3O^+}}{X_{H_2O}} = 0.10166 + 0.0591 \cdot \log(1) = 0.10166 \text{ V. Metal oxidation free energy change}$$

minimum is different endoergic $\Delta G_{eq} = E^o_H \cdot F \cdot 1 = 0.10166 \cdot 96485 \cdot 1 = 9.81$ kJ/mol instead Alberty is exoergic .

Alberty Hess value is exoergic; $\Delta G_{Hess_eq} = G_{H_3O^+} + G_{e^-} - (G_{H(Pt)} + G_{H_2O}) = 22,44 + 0 - (51,05 + 0) = -28,61$ kJ/mol .

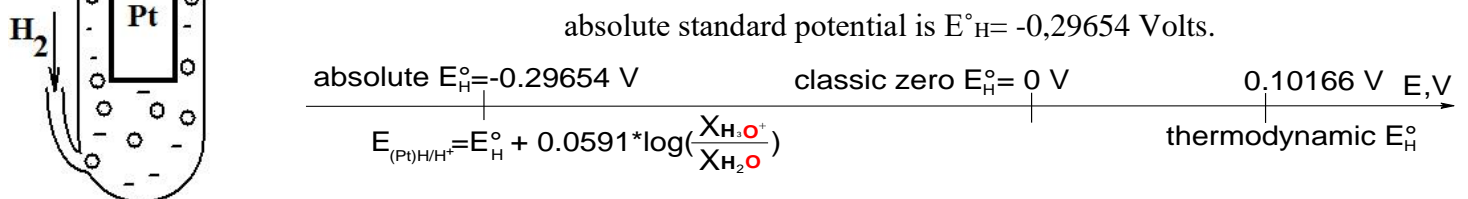
Free energy changes are determined on water and carbon dioxide gas zero $G_{H_2O} = G_{CO_2\text{gas}} = G_{e^-} = 0$ kJ/mol reference scale. Iterative found on absolute scale hydrogen standard potential is: $E^o_H = -0,29654$ V. Equilibrium free energy minimum is exoergic: $\Delta G_{eq} = E^o_H \cdot F \cdot 1 = -0,29654 \cdot 96485 \cdot 1 = -28,61$ kJ/mol coinciding with Alberty data. Absolute potential scale slips by $\Delta E = -0,29654 - 0,10166 = -0,3982$ Volts down. Nernst's hydrogen equilibrium constant is grater as one: $K_{H(Pt)_Red} = [H_3O^+] \cdot [e^-] / [H_2O] / [H(Pt)] = \text{EXP}(-\Delta G_{Alberty} / R/T) = \text{EXP}(28612 / 8.3144 / 298.15) = 102954$.

I type electrode Metal interface $\underline{H(Pt)}$ / on its cation H_3O^+ solution application.

High rate protolysis attractors $[H_3O^+] = 10^{-7.36}$ M , pH=7.36 and water mass $[H_2O] = 997/18 = 55.3$ M account in liter shows metal hydrogen strong reducing potential: $E_{pH=7.36} = -0,29654 + 0,0591 \cdot \log(10^{-7.36}/55,3) = -0,8345$ V and free energy change minimum $\Delta G_{eqpH_7.36} = E^o_H \cdot F \cdot 1 = -0,8345 \cdot 96485 \cdot 1/1000 = -80,5$ kJ/mol .

Nernst's half reaction metal reduction potential $E^o_H = -0,29654$ V energy $\Delta G_{eq} = -28,6$ kJ/mol.

Platinum sheet immersed in hydroxonium ions $[H^+] = [H_3O^+] = [H_2SO_4] = 1$ M sulfuric acid solutions $\underline{H(Pt)} \rightleftharpoons H^+ + e^-$: $E = E^o + 0.0591 \cdot \log [H^+] = 0.0 + 0.0591 \cdot \log(1 \text{ M}) = 0$ V is classic. Ratio $[H_3O^+]/[H_2O] = 1/52.5 = X_{H_3O^+}/X_{H_2O}$ give classic zero **0** insted thermodynamic standard potential: $E^o_H = 0.10166$ V and from Alberty data on absolute scale absolute standard potential is $E^o_H = -0,29654$ Volts.



Absolute standard potential $E^o_H = -0,29654$ V based on Alberty hydrogen data $G_{H_2\text{gas}} = 85,64$ kJ/mol and $G_{H_2\text{aq}} = 103,24$ kJ/mol , which was detected on water and carbon dioxide gas zero scale $G_{H_2O} = G_{CO_2\text{gas}} = G_{e^-} = 0$ kJ/mol. reducing agent at pH=7,36 , $[H_3O^+] = 10^{-7.36}$ M with potential $E = -0,2965 + 0,0591 \cdot \log(10^{(-7.36)}/55,3) = -0,8345$ V. is strong reductant. Free energy content in one mol metal hydrogen is: $G_{H(Pt)} = 51.05$ kJ/mol .

Half-reaction - RedOx systems	Data from [16-24]	Water disaccount classic zero E _o	Thermodynamic. scale 0.10166 V	Absolute scale -0.3982 V
OH⁻ = H₂O + e⁻	CRC	2.020	2,1217	1,7235
4 H₂O = H₂O_{2(aqua)} + 2 H₃O⁺ + 2 e⁻	Suchotina	1.776	2,0837	1,6855
H₂O₂ + 2 H₂O = O_{2(aqua)}⁻ + 2 H₃O⁺ + e⁻	David Harris	1.276	1,4811	1,0829
6 H₂O = O_{2(aqua)} + 4 H₃O⁺ + 4 e⁻	Suchotina	1.229	1,4850	1,0868
HNO₂ + 4H₂O = NO₃⁻ + 3H₃O⁺ + 2e⁻	University Alberta	0.928	1,2352	0,8370
NO₂ + 3 H₂O = NO₃⁻ + 2 H₃O⁺ + 2e⁻	David Harris	0.835	1,0913	0,6931
Hydroquinone + 2H₂O = p-quinone + 2H₃O⁺ + 2e⁻		0.699	0,9041	0,5059
H₂O_{2(aqua)} + 2H₂O = O_{2(aqua)} + 2H₃O⁺ + 2e⁻	University Alberta	0.695	0,8477	0,4495
H₂O_{2(aqua)} + H₂O = O_{2(aqua)} + H₃O⁺ + H⁻(H⁺ + 2e⁻)	University Alberta	0.695	0,8477	0,4495
Fe²⁺ = Fe³⁺ + e⁻	University Alberta	0.769	0,8707	0,4725
Ubiquinol + 2H₂O = Ubiquinone + 2H₃O⁺ + 2e⁻		0.459	0,6638	0,2656
Succinate²⁻ + 2H₂O = Fumarate²⁻ + 2H₃O⁺ + 2e⁻	Lehninger pH=7 E _o =0.031	0.4447	0,6494	0,2512
ButyrylCoA + 2H₂O = CrotonylCoA + 2H₃O⁺ + 2e⁻		0.399	0,6038	0,2056
AscorbicAcid + 2H₂O = C₆H₆O₆ + 2H₃O⁺ + 2e⁻	DC. Harris	0.390	0,5947	0,1965
glycolate + 2H₂O = Glyoxylate + H⁻(H⁺ + 2e⁻) + H₃O⁺	D.C.Harris 25°C	0.324	0,5287	0,1305
Fe²⁺ = Cytochrome F Fe³⁺ + e⁻	David Harris	0.365	0,4667	0,0685
[Fe^{II}(CN)₆]⁴⁻ = [Fe^{III}(CN)₆]³⁻ + e⁻	University Alberta	0.356	0,4574	0,0592
Malate²⁻ + 2H₂O = Oxalo-acetate²⁻ + 2H₃O⁺ + 2e⁻		0.248	0,4528	0,0546
Fe²⁺ = Cytochrome a3 Fe³⁺ + e⁻		0.350	0,4517	0,0535
Lactate⁻ + H₂O = Pyruvate⁻ + H₃O⁺ + H⁻(H⁺ + 2e⁻)		0.229	0,3823	-0,0159
FADH₂ + 2H₂O = FADfree + 2H₃O⁺ + 2e⁻		0.195	0,3998	0,0016
CH₃COO⁻ + 2H₂O = glycolate + H⁻(H⁺ + 2e⁻) + H₃O⁺	D.C.Harris 25°C	0.161	0,3652	-0,0330
C₆H₁₂O₆ + 4H₂O = 2H₃O⁺ + 6H₃O⁺ + 6HCO₃⁻ + 24 e⁻	5 th page.	0,0701	0,2590	-0,1392
H₂S_{aq} + 2 H₂O = S_{rombic} + 2 H₃O⁺ + 2e⁻	CRC 2010	0.142	0,3467	-0,0515
CH₃CH₂OH + H₂O = CH₃CHO + H₃O⁺ + H⁻(H⁺ + 2e⁻)	KortlyShucha	0.190	0,3432	-0,0550
Fe²⁺ = Cytochrome a Fe³⁺ + e⁻		0.2900	0,3917	-0,0065
2GlutathSH + 2H₂O = GlutaS-Sthione + 2H₃O⁺ + 2e⁻		0.1841	0,3888	-0,0094
HSH + 2H₂O = S_{rhb} + 2H₃O⁺ + 2e⁻	University Alberta	0.1739	0,3786	-0,0196
Fe²⁺ = Cytochrome c Fe³⁺ + e⁻		0.2540	0,3557	-0,0425
LipSHSH + 2H₂O = LipoicAcidS-S + 2H₃O⁺ + 2e⁻		0.1241	0,3288	-0,0694
Fe²⁺ = Cytochrome c1 Fe³⁺ + e⁻		0.2200	0,3217	-0,0765
β-OH Butyrate⁻ + 2H₂O = AcetoAcetate⁻ + 2H₃O⁺ + 2e⁻		0.0681	0,2728	-0,1254
isocitrate²⁻ + 2H₂O = α-Ketoglutarate²⁻ + CO₂ + 2H₃O⁺ + 2e⁻		0.0341	0,2388	-0,1594
Nernst's H_{2aq} + 2H₂O ⇌ 2H₃O⁺ + H₂O + 2e⁻ ; ΔG _{Hess, H3O+} = 58.12 kJ/mol		-	-	0,3020
Ox inverse: 2H₃O⁺ + 2e⁻ ⇌ H_{2aq} + 2H₂O ; ΔG _{Hess, H2aq} = -58.12 kJ/mol		--	-	-0,3020
2H(Pt) + H₂O ⇌ H_{2aq} ; ΔG _{Alberty_sp_H(Pt)}} = G _{H2aq} - 2G _{H(Pt)}} - G _{H2O} = 1,14 kJ/mol		-	-	-
H(Pt) + H₂O = H₃O⁺ + (Pt) + e⁻ ; [H ₃ O ⁺] = 1 M pH=0 classic zero		0.0 ; [H ₂ SO ₄] = 1 M	0.10166	-0.2965
Luciferin + OH⁻ = ?luciferin + CO_{2(aqua)} + OH⁻ + 3H(3H⁺ + 3e⁻) + e⁻		0.0000	0,1017	-0,2965
Fe²⁺ = Cytochrome b Fe³⁺ + e⁻		0.0770	0,1787	-0,2195
CH₃CHO + 3H₂O = CH₃COOH + 2H₃O⁺ + 2e⁻	Suchotina	-0,1180	0,1382	-0,2600
Glycaldeh3-P²⁻ + H₂O + HPO₄²⁻ = 13PGlycerate⁴⁻ + H₃O⁺ + H⁻(H⁺ + 2e⁻)		-0,1314	0,0218	-0,3764
NADPH = NADP⁺ + H⁻(H⁺ + 2e⁻)		-0,1170	-0,0153	-0,4135
NADH = NAD⁺ + H⁻(H⁺ + 2e⁻)	David Harris	-0,1130	-0,0113	-0,4095
O_{2(aqua)} = O_{2(aqua)} + e⁻	Suchotina	-0,2450	-0,1433	-0,5415
Ferredoxin Fe²⁺ = Ferredoxin Fe³⁺ + e⁻		-0,4320	-0,3303	-0,7285
C₆H₁₂O₆ + 4H₂O = 2C₃H₄O₃ + 4H₃O⁺ + 4e⁻	Stryer	-0,5427	-0,3380	-0,7362
S²⁻ = S_{rombic} + 2 e⁻	CRC 2010	-0,4763	-0,3746	-0,7728
HS⁻ + OH⁻ = S_{rombic} + H₂O + 2e⁻	CRC 2010	-0,4780	-0,3248	-0,7230
H(Pt) + OH⁻ = H₂O + (Pt) + e⁻	Suchotina	-0,8280	-0,6233	-1,0215
Ubiquinol6 + 2H₂O = Ubiquinone6 + 2H₃O⁺ + 2e⁻	CRC 2012	-1,0500	-0,8453	-1,2435

Proton reduction at hydroxonium capture electron from crystal lattice (Pt)+e⁻. Hess free energy change negative (Pt)H+H₂O ⇌ H₃O⁺+e⁻ is ΔG_{Alberty(Pt)H}} = G_{H3O+} + G_{e-} - (G_{H2O} + G_{H(Pt)}) = 22,44 + 0 - (0 + 51) = -28,61 kJ/mol. Absolute scale E^o_{Habsolute} = ΔG_{Alberty(Pt)H}}/F/1 = -28610/96485/1 = -0,29654 V. High rate protolysis Attractor [H₃O⁺] = 10^{-7.36} M on zero scale G_{H2O} = G_{CO2gas} = 0 kJ/mol activate metallic Hydrogen (Pt)H and Glucose C₆H₁₂O₆ to strong reduction potential .}

Ox: $O_{2(aq)} + 4H_3O^+ + 4e^- \rightleftharpoons 6H_2O$; $E^\circ_{O_2} = 1,0868$ Volti; Red: $4(Pt)H + 4H_2O \rightleftharpoons 4H_3O^+ + 4e^-$; $E^\circ_H = -0.2965$ V

$O_{2(aq)} + 4(Pt)H \rightarrow 2H_2O$; $\Delta G_{eq2H_2O} = (E^\circ_H - E^\circ_{O_2}) \cdot F \cdot 1 \cdot 4 = (-0.2965 - 1.0868) \cdot 96485 \cdot 4 = 2 \cdot -266,94$ kJ/mol;

$\Delta G_{eq2H_2O} = 2G_{H_2O} - 4G_{H(Pt)} - G_{O_{2(aq)}} = 2 \cdot 0 - (4 \cdot G_{H(Pt)} + 330) = -533,9 = 2 \cdot -267$ kJ/mol;

$G_{H(Pt)} = (2G_{H_2O} - \Delta G_{eq2H_2O} - G_{O_{2(aq)}}) / 4 = (2 \cdot 0 + 533,886 - 330) / 4 = 51.05$ kJ/mol; $G_{(Pt)H} = 51.05$ kJ/mol;

If homeostasis zero are $G_{H_2O} = G_{CO_{2(gas)}} = 0$ kJ/mol.

RedOx half reaction at 298 K (25 °C) and at 310.15 K (37 °C), expression (1) reduces to expressions with K_{eq} :

$$E = E^\circ + \frac{0,0591}{n} \cdot \log(K_{eq}); E = E^\circ + \frac{0,0615V}{n} \cdot \log(K_{eq}); K_{eq} = \left(\frac{[Ox^{n+}]}{[Red]} \right);$$

Half-reactions involve high rate protolysis equilibrium attractors pH=7.36 concentration $[H_3O^+] = 10^{-7.36}$ M and water concentration $[H_2O] = 55.3$ M. Water protonation H^+ form **hydroxonium** ions H_3O^+ and rule the homeostasis reactions promotion. Thermodynamic calculations demand use in expressions the **standard reduction potential** $E^\circ_{H_2O}$ and K_{eq} . Therefore the **standard reduction potentials** $E^\circ_{H_2O}$ given in

Table 1 are indispensable used throughout this book: classic standard E° and thermodynamic $E^\circ_{H_2O}$ or E°_{37} ;

Notice: For complete calculations at standard temperature are used standard potential $E^\circ_{H_2O}$ (V) and at body temperature 310.15 K (37 °C) are used standard potential values E°_{37} (V).

Standard Reduction Potentials used for Prigogine attractor Free-Energy Change minimum

High rate protolysis attractors equilibriums let experimental determine the **reduction potentials** E_{Red} and E_{Ox} for two **half-cells** reactions. Therefore $EMF = E_{Red} - E_{Ox}$ values are difference reductants minus oxidants.

Electrons will flow to side **half-cell** with more positive E°_{Ox2} and the trend strength is proportional to negative $\Delta E^\circ < 0$ value because always $E^\circ_{Red1} < E^\circ_{Ox2}$:

$$\Delta E^\circ = E^\circ_{Red1} - E^\circ_{Ox2}.$$

The energy ΔG_{eq} made available by this favored electron e^- flow from **Red1** reductant to **Ox2** oxidant. Hess law products sum minus reactants sum $\Delta G_{Hess} = \sum \Delta G^\circ_{products} - \sum \Delta G^\circ_{reactant}$ is greater as minimised ΔG_{eq} .

$-W$ is proportional \sim to ΔE° . **Oxidized** form Ox^{n+} formed with lost electrons ne^- flows. In this process **RedOx** system are accomplished the chemical work $W = -\Delta E^\circ \cdot F \cdot n$ by spending given **RedOx** system **free energy** in conversion of **reduced** form **Red1** and Ox^{2n+} to **oxidized** form Ox^{n+} and **Red2**:

Red1 - $ne^- \rightleftharpoons Ox^{n+}$; $Ox^{2n+} + ne^- \rightleftharpoons Red2$; $W = -\Delta E^\circ \cdot F \cdot n = -(E^\circ_{Red1} - E^\circ_{Ox2}) \cdot F \cdot n = -\Delta G_{eq} = -(G_{Red1} - G_{Ox2})$ (4)

Here n represents the number of electrons ne^- transferred in the reaction.

Chemical Potential of Species μ

Professor Ilya Prigogine **chemical potential** μ of compound A shows, how much change of **free energy** ΔG_A brings into system of our interest when adding the **1 mol** amount of compound A in the mixture.

In a fact: how great amount of free energy belongs to one **1 mol** of compound in mixture. Free energy ΔG°_A has the pure compound A itself per **1 mol** amount, no mixture of compounds, the **chemical potential** μ_A of compound A if amount with in mixture others for molar number is $\Delta n_A = 1$ mol

$$\mu_A = \frac{\Delta G_A}{\Delta n_A} = \Delta G^\circ_A + R \cdot T \cdot \ln(X_A), \text{ where } X_A \text{ is concentration of A unit less } \mathbf{mol\ fraction } X_A = \frac{n_A}{n_{total}} \quad (5)$$

For pure compound A when $n_A = n_{total}$ **mol fraction** is $X_A = 1$ so $\ln(1) = 0$ and

$\mu = \Delta G^\circ_A$ that present **standard free energy** of formation the **1 mol** pure compound A from elements.

Conflict in consideration pure compound ΔG°_A greater as mixture amount for one mole $|\mu_A| < |\Delta G^\circ_A|$.

Minimisation in mixture I. Prigogine, R. Defey. "Chemical Thermodynamics".1954, Longmans Green & co ©.

Prigogine attractor the free energy change minimum.

Chemical potentials sum of reactants is equal to products reaching **equilibrium** mixture.

Red $\rightleftharpoons Ox^{n+} + ne^-$; $W = -E \cdot F \cdot n = G_{Red}$; $\sum \mu_{Red} + E \cdot F \cdot n = \sum \mu_{Ox^{n+}} + n \mu_{e^-}$ (6)

Compounds work accomplished, moving positive ($n+$) charged Ox^{n+} from metal surface to solution, so leaving in metal lattice electron ne^- gas. For **RedOx** system due to electric work of charged Ox^{n+} movement between metal and solution sides are not equal $\mu_{Red} \neq \mu_{Ox^{n+}} + n \mu_{e^-}$, what compensate work $W = -E \cdot F \cdot n = G_{Red}$ and left numbers

of electrons ne^- on metal as is seen in expression (6). Free energy change G_{Red} for chemical reaction is to calculate as **chemical potential** sum subtraction: the product $\Sigma\mu_{product}$ minus reactants $\Sigma\mu_{reactant}$:

$G_{Red} = (\Sigma\mu_{Ox^{n+}} + n \mu_{e^-}) - \Sigma\mu_{Red} = E \cdot F \cdot n$, and **equilibrium** establishes when electric work is compensated by free energy change $-W = G_{Red} = E \cdot F \cdot n$ and on electrode absolute **potential** E forms which remains unknown.

At **equilibrium** the **chemical potential** sum of reactants and products are equal and **reduced** form includes the compensating free energy change $-W = G_{Red} = E \cdot F \cdot n$ but is unknown absolute **potential** E . Becomes obvious that **chemical potential** sum of **oxidized** form has the number n additional **chemical potential** of free electrons $n \mu_{e^-}$ those values for all known **RedOx** systems are different and mostly laying in side interval between $-90 \div +90$ kJ/mol. Electrons ne^- are occupied metal (**Pt**) free electron gas solid phase and as pure solid compound has mol fraction concentration $X_{e^-} = 1$. Expressing above mentioned meaning of **chemical potentials** (7) we calculate the free energy change G_{Red} but still with uncertainty unknown absolute values E and G_{e^-} :

$$G_{Red} + R \cdot T \cdot \ln(X_{Red}) + E \cdot F \cdot n = G_{Ox^{n+}} + R \cdot T \cdot \ln(X_{Ox^{n+}}) + n G_{e^-} + n \cdot R \cdot T \cdot \ln(X_{e^-}) \quad (7)$$

$$\Delta G_{eq} = E \cdot F \cdot n = G_{Ox^{n+}} + n G_{e^-} - G_{Red} + R \cdot T \cdot \ln(X_{Ox^{n+}} / X_{Red})$$

Hess law conditions make greater absolute value of free energy change as at Prigogine attractor equilibriums:

$$|G_{HessRed}| = |\Delta G^{\circ}_{Ox^{n+}} + n \Delta G^{\circ}_{e^-} - \Delta G^{\circ}_{Red}| > |E^{\circ}_{Red} \cdot F \cdot n| = |G_{Red}| \quad \text{and} \quad (8)$$

equilibrium free energy change for **oxidized** form: $|G_{Ox}| = |-E^{\circ}_{Ox} \cdot F \cdot n| < |-(\Delta G^{\circ}_{Ox^{n+}} + n \Delta G^{\circ}_{e^-} - \Delta G^{\circ}_{Red})|$ however separately for Red and Ox relative to reference potential scale absolute values G_{eq} remains unknown

nor reductant: $G_{RedHomeostasis} = E_{Red} \cdot F \cdot n = E^{\circ}_{Red} \cdot F \cdot n + R \cdot T \cdot \ln(X_{Ox^{n+}} / X_{Red})$,

nor oxidant: $G_{OxHomeostasis} = -E_{Ox} \cdot F \cdot n = -E^{\circ}_{Ox} \cdot F \cdot n - R \cdot T \cdot \ln(X_{Ox^{n+}} / X_{Red}) \quad (9)$

Uncertainty is compensate for balanced RedOx reactions in two half reactions sum. Considerable **oxidation-reduction** reaction is composed from two **2 RedOx** systems (half-reactions) using compounds reaction

equivalence law $|+m' \cdot ne^-| = |-n' \cdot me^-|$ we have balanced **oxidation-reduction** reaction and can get the summary

reaction of both half-reactions : $(-) Red_1 \Leftrightarrow Ox_1^{n'+} + ne^- \cdot m'$; $(+) Ox_2^{m'+} + me^- \Leftrightarrow Red_2 \cdot n'$

$m' \cdot Red_1 + n' \cdot Ox_2^{m'+} \Rightarrow m' \cdot Ox_1^{n'+} + n' \cdot Red_2$; reactants forming products direction of reaction.

With this equation we can calculate the **equilibrium free-energy** change ΔG_{eq} for equi-molar amount of **oxidation-reduction** reaction from the values of E° in a table of **reduction potentials** (Table 1) :

$$\Delta G_{eq} = m' \cdot G_{Red1} - n' \cdot G_{2Ox^{n+}} = m' \cdot E^{\circ}_{Red1} \cdot F \cdot n - n' \cdot E^{\circ}_{2Ox^{n+}} \cdot F \cdot m = (E^{\circ}_{Red1} - E^{\circ}_{2Ox^{n+}}) \cdot F \cdot (m' \cdot n = n' \cdot m)$$

where n'/N $m'/N = nm$ is equivalent - common number of electrons e^- involved in **RedOx** reaction $n' \cdot m' \leq n \cdot m$. can be less by number N of common divider **Red1** or **Ox2^{m+}**. The **free-energy** content G according (9) at known concentrations

X_{Red} and $X_{Ox^{n+}}$ of the each species (G_{red} and $G_{Ox^{n+}}$) participating in the reaction.

$$\Delta G_{eq} = m' \cdot G_{Red1} + n' \cdot G_{2Ox^{n+}} = m' \cdot E_{Red1} \cdot F \cdot n - n' \cdot E_{2Ox^{n+}} \cdot F \cdot m = (E_{Red1} - E_{2Ox^{n+}}) \cdot F \cdot (m' \cdot n = n' \cdot m) = (E^{\circ}_{Red1} - E^{\circ}_{2Ox^{n+}}) \cdot F \cdot (m' \cdot n = n' \cdot m) + R \cdot T \cdot \ln((X_{1Ox^{n+}} \cdot X_{2Red}) / (X_{1Red} \cdot X_{2Ox^{n+}})), \quad \text{where} \quad (10)$$

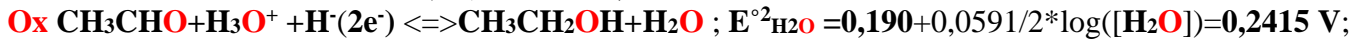
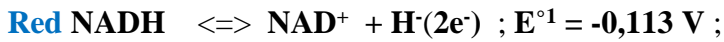
$$K_{homeostasis} = \frac{X_{1Ox^{n+}}^m \cdot X_{2Red}^n}{X_{1Red}^m \cdot X_{2Ox^{n+}}^n} \quad \left| \begin{array}{l} \text{is homeostasis ratio as a multiple products over reactants concentrations.} \\ \text{Equilibrium free energy change } \Delta G_{eq} = \Delta G_{min} \text{ is Prigogine attractor constant} \\ \text{K}_{eq} \text{ calculation } \Delta G_{eq} = (E^{\circ}_{Red1} - E^{\circ}_{2Ox^{n+}}) \cdot F \cdot (m' \cdot n = n' \cdot m) ; K_{eq} = \exp(-\Delta G_{eq} / R / T) \end{array} \right.$$

Acetaldehyde reduced by NADH hydride $H^-(2e^-)$ tunneling and protolysis.



$\Delta G_{Hess} = \Delta G^\circ_{CH_3CH_2OH} + \Delta G^\circ_{H_2O} + \Delta G^\circ_{NAD^+} - \Delta G^\circ_{H_3O^+} - \Delta G^\circ_{CH_3CHO} - \Delta G^\circ_{NADH} = -159 \text{ kJ/mol}$ exoergic by Hess law as well CRC Handbook of Chemistry and Physics 2010, 90th Edition David R. Lide

Free energy change minimum $\Delta G_{min} = \Delta G_{eq}$ equilibrium K_{eq} based **Red-Ox** half reactions standard potentials Half-reactions and standard potential E° sources David Harris and KortlyShucha water concentration including:



By convention (10) balanced $n = 2 = m$ number of electrons $2e^- \Delta E^\circ$ is expressed as E° of the electron **donor** minus $E^\circ_{H_2O}$ of the electron **acceptor**. **Acetaldehyde** is **accepting** hydride H^- from NADH in tunneling, n is 2:

$\Delta E^\circ = E^\circ_{H_2O} - E^\circ = 0,2415 - (-0,113) = 0,3545 \text{ V}$. Equilibrium free energy change is favored Homeostasis joined $\Delta G_{AnaerobicRed} = \Delta E^\circ \cdot F \cdot n = 0,3545 * 2 * 96485 \text{ C/mol} = -R \cdot T \cdot \ln(K_{eq}) = -68,4 \text{ kJ/mol}$. Oxidation reduction free-energy change at equilibrium is zero $\Delta G = 0$ oposit for Homeostazis $\Delta G_{Homeostasis} \neq 0$ negative for anaerobic :

$$\Delta G_{AnaerobicRed} = -R \cdot T \cdot \ln(K_{eq}); \frac{[NAD^+][CH_3CH_2OH][H_2O]}{[NADH][CH_3CHO][H_3O^+]} = K_{eq} = e^{-\frac{\Delta G_{Anaerobic}}{R \cdot T}} = e^{-\frac{-68400}{8.314 \cdot 298.15}} = 10^{12}$$

Constant $K_{AnaerobicRed} = 10^{12}$ shows position far to **products**. Anaerobic fermentation conditions $[NADH]/[NAD^+] = 10/1$ times at **pH = 7.36**. At presence of air oxygen O_2 ratio $[NAD^+]/[NADH]$ is 700/1 times higher over concentration NADH, what cause reaction condition to oxidize **ethanol** and **acetaldehyde** as well known aerobic fermentation forms acetic acid. If **ethanol ratio** of concentrations is 10/1 to **acetaldehyde** amount 1/1 in aerobic fermentation: than calculated free energy change is negaive $\Delta G = -0,2 \text{ J/mol}$ but anaerobic with $NAD^+/NADH = 1/10$ $\Delta G = -27,8 \text{ J/mol} = -68,4 + 40,5$ produces ethanol ten times over acetaldehyde 10% practical efficiency and reaction shifted toward ethanol negative $-27,9 \text{ kJ/mol}$. Anaerobic shifted to **ethanol** negative:

$$[CH_3CHO]/[CH_3CH_2OH] = 1/10; \Delta G_{AnaerobicRed} = (E^\circ_{Red1} - E^\circ_{2Ox}) \cdot F \cdot (m' \cdot n = n' \cdot m) + R \cdot T \cdot \ln \frac{X_{1Ox}^m \cdot X_{2Red}^n}{X_{1Red}^m \cdot X_{2Ox}^n} = \text{page 8};$$

$$= -68,4 + 8,3144 \cdot 298,15 \cdot \ln \frac{[NAD^+][CH_3CH_2OH][H_2O]}{[NADH][CH_3CHO][H_3O^+]} = \left(\frac{1}{10} \cdot \frac{1}{10} \cdot \frac{55.3}{10^{-7.36}} \right) = -68,35 + 40,5 = -27,9 \text{ kJ/mol};$$

$$\text{Oxidation of ethanol: } \Delta G_{AnaerobicRed} = -68,4 + 8,3144 \cdot 298,15 \cdot \ln \left(\frac{700}{1} \cdot \frac{1}{10} \cdot \frac{55.3}{10^{-7.36}} \right) = (8,875 \cdot 10^{10}) = -0,2 \text{ kJ/mol};$$

$$\Delta G_{AnaerobicRed} = -68,4 + 8,3144 \cdot 298,15 \cdot \ln(700/1 * 1/10 * 55,3457/10^{(-7,36)})/1000 = -68,4 + 68,2 = -0,2 \text{ kJ/mol}$$
 negative.

$$\Delta G_{AerobicOx} = 68,4 + 8,3144 \cdot 298,15 \cdot \ln(1/700 * 1/10 * 10^{(-7,36)}/55,3457)/1000 = 68,4 - 73,91 = -5,51 \text{ kJ/mol}.$$

Oxidation of Glucose with water soluble Electron Carriers produce $6HCO_3^- + 6H_3O^+$

The principles of **oxidation-reduction energetic** described above apply to the many metabolic reactions that involve electron e^- transfers. For example, the **oxidation** of **glucose** supplies **energy** for the production of **ATP**. The **glucose oxidation**: $C_6H_{12}O_6 + 6O_{2aqua} + 6H_2O \Rightarrow 6HCO_3^- + 6H_3O^+ + \Delta G + Q$ is exoergic $\Delta G_{Hess} = -3049,55 \text{ kJ/mol}$. This is a much larger release of free energy than is required for **ATP** synthesis erythrocyte mitochondria at **pH = 7.36** use $-55,16 \text{ kJ/mol}$ 45,9% of 100% **120,23 kJ/mol**. Cells do not convert **glucose** to CO_{2aqua} in a single, high-**energy**-releasing reaction, but rather in a series of controlled reactions, some of which are **oxidations**. The **free energy** released in these **oxidation** steps is of the same order of magnitude as that required for **ATP** synthesis from **ADP**, with some **energy** to spare. Electrons e^- removed in these **oxidation** steps are transferred to water soluble **coenzymes** for carrying two electrons $2e^-$, such as **NADH** with tunneling hydrid $H^-(2e^-)$ and/or **FADH₂** with transfer two hydrogen atoms **2H** ($2H^+ + 2e^-$) (vitamins B₃ and B₂).

The clusters of **enzyme complexes** **oxidation** electrons e^- transfer **channel** from their hundreds **100** of different **substrates** electrons wove into just a few types of universal **electron carriers**. The **reduction** of these **carriers** in catabolic processes results in the conservation of **free energy** released by **substrate oxidation**. **NAD⁺**, **NADP⁺**, **FMN**, and **FAD** are water-soluble **coenzymes** that undergo reversible **oxidation** \rightleftharpoons **reduction** in many of the electron-transfer e^- reactions of metabolism. The **nucleotides** **NAD⁺** and **NADP⁺** move readily in transfer **channels** from one **enzyme** to another; the **flavin nucleotides** **FMN** and **FAD** are usually very tightly bound to

the **enzymes**, called **flavo-proteins**, for which they serve as **prosthetic** groups. **Lipid-soluble quinones** such as **ubiquinone** and **plastoquinone** act as **electron carriers** and **proton donors** in the non-aqueous environment of membranes. **Iron-sulfur proteins** and **cytochromes**, which have tightly bound **prosthetic** groups that undergo reversible \rightleftharpoons **oxidation** and **reduction**, also serve as electron e^- carriers in many **oxidation-reduction** reactions. Some of these **proteins** are **water-soluble**, but others are **peripheral** or **integral membrane proteins**.

We conclude this chapter by describing some chemical features of **nucleotide coenzymes** and some of the **enzymes** (**dehydrogenases** and **flavo-proteins**) that use them. The **oxidation- reduction** chemistry of **quinones**, **iron-sulfur proteins**, and **cytochromes** is discussed in Oxidative Phosphorylation and Photo-Phosphorylation.

NADH and NADPH Act with Dehydrogenases as water soluble Electron Carriers

Nicotin-amide adenine dinucleotide NAD⁺ in its **oxidized** form and its close analog **nicotin-amide adenine dinucleotide phosphate NADP⁺** are composed of two **2nucleotides** joined through their **phosphate** groups by a **phospho-anhydride** bond (Fig. 3). Because the **nicotinamide** ring resembles **pyridine**, these compounds are sometimes called **pyridine nucleotides**. The vitamin **niacin** is the source of the **nicotin-amide** moiety in **nicotin-amide nucleotides**.

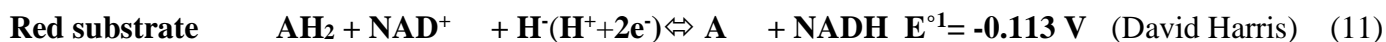
Both **coenzymes** undergo reversible \rightleftharpoons **reduction** of the **nicotinamide ring** (Fig. 3). As a **substrate** molecule undergoes **oxidation (dehydratation)**, giving up two $2e^-$ in hydride H^- , the **oxidized** form of the **nucleotide NAD⁺** or **NADP⁺** **accepts a hydride ion** ($:H^-$ the equivalent of a proton H^+ and two 2 electrons e^-) and is transformed into the **reduced** form **NADH** or **NADPH**. The second proton H^+ departure the **substrate** reach water molecule H_2O converts to hydronium ion H_3O^+ . The **half-reactions** for each type of **nucleotide** are similar:



Reduction of **NAD⁺** or **NADP⁺** converts the **benzenoid ring** of the **nicotin-amide** moiety (with a fixed positive (+) charge on the ring **nitrogen N**) to the **quinonoid** form (with neutral **nitrogen N**). Note that the **reduced nucleotides** absorb light at **340 nm**: the **oxidized** forms do not (Fig. 13). The plus sign in the abbreviations **NAD⁺** and **NADP⁺** does not indicate the no charge on these molecules (they are each negative (-) ions), but rather that the **nicotin-amide ring** is in its **oxidized** form, with a positive (+) charge on the **nitrogen N⁺** atom. In the abbreviations **NADH** and **NADPH**, the "H" denotes the added **hydride** ion.

The total concentration of **NAD⁺ + NADH** in most tissues is about $10^{-5}M$; that of **NADP⁺ + NADPH** is about **10** times lower. In many cells and tissues, the ratio of **NAD⁺(oxidized)** to **NADH (reduced)** is high, **favoring hydride H⁻** transfer from a **substrate** to **NAD⁺** to form **NADH**. By contrast, **NADPH (reduced)** is generally present in greater \square amounts than its **oxidized** form, **NADP⁺**, favoring **hydride H⁻** transfer from **NADPH** to a **substrate**. This reflects the specialized **metabolic** roles of the two **2 coenzymes**: **NAD⁺** generally functions in **oxidations** - usually as part of a **catabolic** reaction; and **NADPH** is the usual coenzyme in **reductions** nearly always as part of **anabolic** reaction. A few **enzymes** can use either **coenzyme**. but most show a strong preference for one over the other. This functional specialization allows a cell to maintain two **2** distinct pools of **electron carrier**, switch two **2** distinct functions, in the same cellular compartment.

More than **200 enzymes** are known to catalyze reactions in which **NAD⁺** (or **NADP⁺**) **accepts a hydride :H⁻** ion from a **reduced substrate AH₂**, or **NADPH** (or **NADH**) **donates a hydride :H⁻** ion to an **oxidized substrate A**. Balanced sum reactions is $H_3C-CH_2-OH + NAD^+ + H_2O \rightleftharpoons H_3C-CH=O + NADH + H_3O^+$ (11) where **AH₂** is the **reduced substrate** and **A** the **oxidized substrate**. The general name for first class **enzymes** is **oxidoreductase**; they are also commonly called **dehydrogenases**. For example, **alcohol dehydrogenase** catalyzes the first **1st** step in the **catabolism** of **ethanol**, in which **ethanol** is **oxidized** to **acet-aldehyde**:



Notice that one of the carbon atoms **-CH₂-OH** in **ethanol** has lost a hydrogen H^- atom as hydride and dissociates $-OH \Rightarrow H^+$ proton ;the compound has been **oxidized** from an **alcohol** to an **aldehyde** (Fig. 3a).

When **NAD⁺** or **NADP⁺** is **reduced** the hydride $:H^-$ ion tunneling of two sides the **nicotin-amide ring**: the front (**A** side) or the back (**B** side) as represented in Figure 3. Studies with isotopically labeled * **substrates** have shown that a given **enzyme** catalyzes tunneling either from **A** side or from **B** side transfer, but not both.

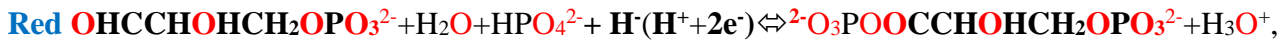
For example, **yeast alcohol dehydrogenase** and **lactate dehydrogenase** of vertebrate **heart** transfer a hydride $:H^-$ ion to (or remove a hydride $:H^-$ ion from) the **A** side of the **nicotin-amide ring**: they are classed as type **A dehydrogenases** to distinguish them from another group of **enzymes** that transfer a hydride $:H^-$ ion to (or remove a hydride $:H^-$ ion from) the **B** side of the **nicotin-amide ring** (Table 2).

The association between a **dehydrogenase** and **NAD** or **NADP** is relatively loose; the **coenzyme** readily drives directed from one **enzyme** to another, acting as a **water-soluble carrier** of electrons e^- from one **1 metabolite** to

next. For example, in the production of **alcohol** during **fermentation** of **glucose** by, **yeast** cells, a hydride **:H⁻** ion is removed from glycer-aldehyde 3-phosphate by, one 1 enzyme (glycer-aldehyde 3-phosphate dehydrogenase, a type **B enzyme**) and tunneling to **NAD⁺**. The **NADH** departure the **enzyme surface** and stick to **alcohol dehydrogenase**, a type **A enzyme**, which tunneling a hydride **:H⁻** ion to **acet-aldehyde**, producing **ethanol**:

Reduced (half reaction) at T=298.15 K glyceraldehyde3phosphate ⇌ 1,3-PhosphoGlycerate:

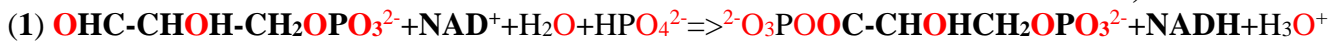
$$E^{\circ}_{H_2O} = -0.1314 + 0.00591/2 * \log([H_2O]) = -0.1314 + 0.02595 * \log(55,3333) = -0.1314 + 0.04523 = -0,08617 \text{ V}$$



(Ox) $NAD^+ + H^-(H^+ + 2e^-) \Leftrightarrow NADH$, $E^{\circ} = -0.113 \text{ V}$ (David Harris); Carnegie Mellon Univ;

$$\Delta G_{eq} = (-) * n * F = (-0,08617 + 0.113) = 0,02683 * 2 * 96485 = 5,1774 \text{ kJ/mol}$$

$$\Delta E^{\circ} = E^{\circ}_{H_2O} - E^{\circ} = -0,08617 + 0.113 = 0,02683 \text{ V};$$



(calculated) $\Delta G_{eq} = \Delta E^{\circ} * F * n = (-0.113 + 0,2415) * F * n = -0.3545 \text{ V} * 2 * 96485 = -68,408 \text{ kJ/mol}$

Notice: enzyme complex irreversibly net production and consumption of **coenzymes NAD⁺** or **NADH** like as molecular engine drive recycled repeatedly homeostasis concentration **C** of **[NAD⁺]+[NADH]**.

Figure 3. **NAD** and **(NADP)** $NAD^+ + H^-(2e^- + H^+) \Leftrightarrow NADH$; $E^{\circ} = -0.113 \text{ V}$ standard potential T=298,15 K (25° C)

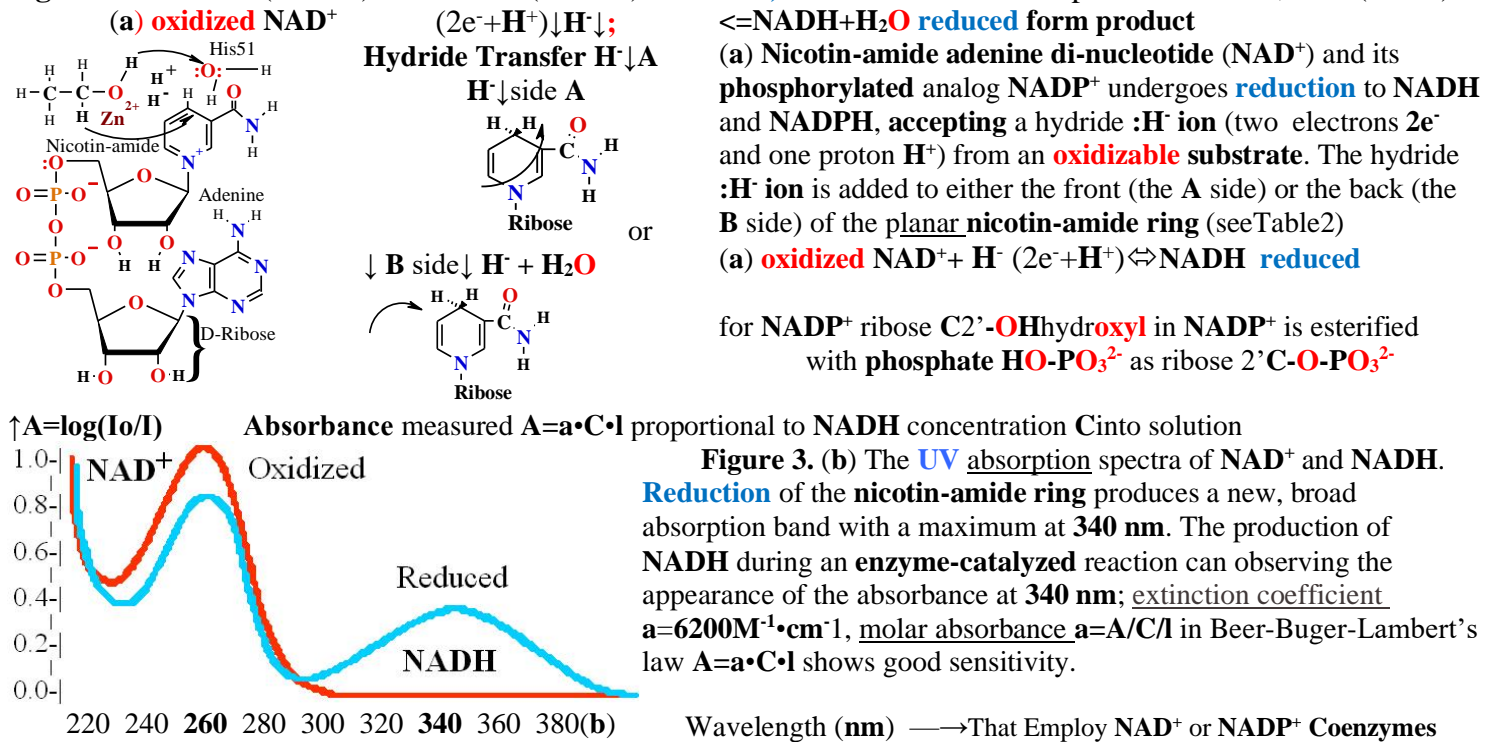


Table 2. Stereo specificity of Dehydrogenases

Enzyme Coenzyme Stereo chemical specificity nicotin-amide ring (A or B)

Iso-citrate dehydrogenase	NAD ⁺	A
α-Keto-glutarate dehydrogenase	NAD ⁺	B
Glucose 6-phosphate dehydrogenase	NADP ⁺	B
Malate dehydrogenase	NAD ⁺	A
Glutamate dehydrogenase	NAD ⁺ or NADP ⁺	B
Glyceraldehyde 3-phosphate dehydrogenase	NAD ⁺	B
Lactate dehydrogenase	NAD ⁺	A
Alcohol dehydrogenase	NAD ⁻	A

Table 3. Some Enzymes (Flavo-proteins) That Employ Flavin Nucleotide Coenzymes

Enzyme	Flavin	Nucleotide Enzyme
Fatty acyl-CoA dehydrogenase	FAD	
Di-hydro-lipoyl dehydrogenase	FAD	Glycerol 3-phosphate dehydrogenase
Succinate dehydrogenase	FAD	Thio-redoxin reductase
NADH dehydrogenase Complex I	FMN	Glycolate dehydrogenase

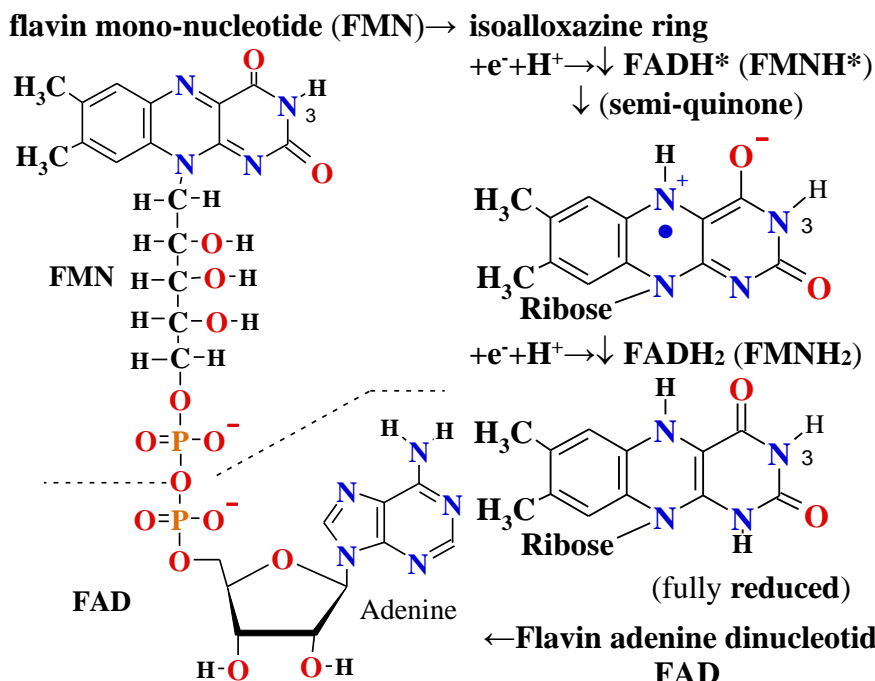


Figure 4. Structures of oxidized and reduced FAD and FMN. FMN consists of the structure above the dashed line shown on the oxidized (FAD) structure. The flavin nucleotides accept two hydrogen 2H atoms (two electrons 2e⁻ and two protons 2H⁺), both of which appear in the flavin ring system. When FAD or FMN accepts only one 1 hydrogen H atom, the semi-quinone, a stable free radical, forms.

Flavin Nucleotides Bound in proteins

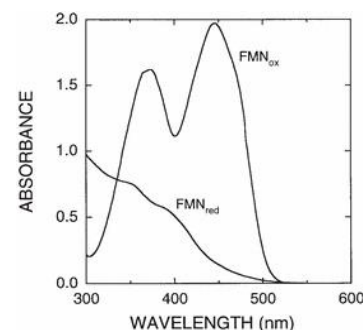
Flavo-proteins (Table 3) are enzymes that catalyze oxidation-reduction reactions using either flavin mono-nucleotide (FMN) or flavin adenine dinucleotide (FAD) as coenzyme (Fig. 4). These coenzymes are derived from the vitamin riboflavin. The fused ring structure of flavin nucleotides

(the isoalloxazine ring) undergoes reversible reduction, accepting either one 1 or two 2 electrons e⁻ in the form of one 1 or two 2 hydrogen 2H atoms (each atom an electron e⁻ plus a proton H⁺) from a reduced substrate. The fully reduced forms are abbreviated FADH₂ and FMNH₂. When a fully oxidized flavin nucleotide accepts only one 1 electron e⁻ (one hydrogen H atom), the semi-quinone form of the isoalloxazine ring is produced, abbreviated FADH* and FMNH*. Because flavo-proteins can participate in either one-1 or two electron 2e⁻ transfers, this class of proteins is involved in a greater diversity of reactions than the pyridine nucleotide-linked dehydrogenases.

Like the nicotin-amide coenzymes, the flavin nucleotides undergo a shift in a major absorption band on reduction. Oxidized FMN have an absorption maximum $a = 15499 \text{ M}^{-1}\text{cm}^{-1}$ (3) and at $\lambda = 445 \text{ nm}$. In some cases the proteins lower the pKa for the N(3)-H (in 10,3 for free flavin) promoting dissociation of proton and lower molar absorption coefficient $a = 9200 \text{ M}^{-1}\text{cm}^{-1}$.

The flavin nucleotide in most flavo-proteins are bound tightly to the protein, and in some enzymes, such as succinate dehydrogenase, it is bound covalently. Protein bound groups including coenzymes are called prosthetic groups. They work together with enzyme. Flavo-protein hold electrons e⁻ while it catalyzes electron e⁻ transfer from a reduced substrate to an electron e⁻ acceptor. Important feature of the flavo-proteins is the variability in the standard reduction potential (E°) and absorption specter of the bound flavin nucleotide.

Flavin ring a reduction potential E typical of particular flavo-protein, sometimes quite different from that of the free flavin nucleotide. FAD bound to succinate dehydrogenase, for example, has a positive potential compared with E°_{H2O} = -0.29815 V in Table 1 for free FAD. Flavo-proteins are often very complicated enzyme complex members: some have, in addition to a flavin nucleotide, tightly bound inorganic ions (iron Feⁿ⁺ or molybdenum Moⁿ⁺, for example) capable of participating in electron e⁻ transfer.



Summary

Hess law thermodynamic pure products over pure reactants ratio constants K_{Hess} and change of free energy, enthalpy and entropy as pure products minus pure reactants difference ΔG_{Hess} , ΔH_{Hess} , ΔS_{Hess} . Equilibrium state is attractor for non equilibrium state. To attractor irreversibly trend homeostasis, but never reach free energy change absolute minimum $\Delta G_{\text{eq}} = -R \cdot T \cdot \ln(K_{\text{eq}})$, because is non equilibrium state. At equilibrium state constant expression K_{eq} is for mixture of products over reactants concentration ratio. Homeostasis non-equilibrium mixture constant expression $K_{\text{Homeostasis}}$ is products factorial of concentration over reactants factorial ratio of concentration. The homeostasis non-equilibrium state has smaller than equilibria state constant $K_{\text{Homeostasis}} < K_{\text{eq}}$, that keep homeostasis irreversible duration continues for evolution and surviving.

High rate protolysis attractors stay at equilibria while homeostasis perfect order continues irreversibly.

High rate protolysis equilibria drive life processes with molecules functional activating attractor : air 20.95% [O₂] oxygen since 500 million Years, osmolar concentration 0,305 M, ionic strength 0,25 M, pH=7,36

concentration $[\text{H}_3\text{O}^+] = 10^{-7.36}$ M, generate concentration gradients like $[\text{NAD}^+]/[\text{NADH}]$ and molekulu funkcionālās aktivitātes atraktoru vērtībām: $[\text{ATP}^4]/[\text{ADP}^3]$, 310,15 K degree.

Organisms are dissipative structure containing and compartmented five type complex reactions clusters in the mixture of compounds. High rate protolysis attractors activate molecules for irreversible reactivity to trend reaching free energy change minimum, so perform the homeostasis work **W**. **Attractors** self-accumulate energy with high rate protolysis so stay at equilibrium state while homeostasis continues as non-equilibrium state. The homeostasis is driven with attractors activation as Brownian molecular engines working instruments for evolution and surviving: for performed **movement**, for the generation of **electric currents**, for the production of **light**.

Energy E transformations in compartmented 10^{12} cells in human organism trend to Prigogine attractors by complex reactions clusters of five types. The total source of net driving force in reactions are : the free-energy **G** decrease from $G_{\text{reactants}}$ to G_{products} . Cells driven by free energy **G** change perform the work **W**.

The equilibrium attractor free-energy change minimum $\Delta G_{\text{eq}} = \Delta G_{\text{min}}$ is a physical **constant** for **reaction** derived from the **equilibrium constant** K_{eq} for the reaction: $\Delta G_{\text{eq}} = -R \cdot T \cdot \ln(K_{\text{eq}})$. Homeostasis free-energy change $\Delta G_{\text{Homeostasis}}$ and constant $K_{\text{Homeostasis}} < K_{\text{eq}}$ has smaller absolute value, because depends on concentrations **C** of **reactants** and **products**: $\Delta G_{\text{Homeostasis}} = \Delta G_{\text{eq}} + R \cdot T \cdot \ln([\text{products}]/[\text{reactants}])$, but totally always negative change for irreversibility. When $\Delta G_{\text{Homeostasis}}$ is negative, the reaction irreversibly to go in the forward direction, when it is positive, the reaction tends to go in the reverse direction; but when reached zero $\Delta G_{\text{Homeostasis}} = 0$ is established **equilibrium**. The free-energy change ΔG for a reaction is independent on the **pathway** by which the reaction occurs only on **reactants** and **products** concentrations **C**. Free-energy changes ΔG are additive in the net chemical reactions that results from the successive occurrence of reactions sharing a common **intermediate** has an overall free-energy change ΔG that is the sum of the $\Delta G = \Delta G_1 + \Delta G_2$ values for the individual reactions **1** and **2**.

ATP⁴⁻ production and consumption is the chemical procession-bridge between catabolism and anabolism. Its build the energy portions as bricks in to the cell and organisms. **Exoergic** coupling to a **endoergic** reactions add to products bricks of energy by conversion to **ADP³⁻** and **HPO₄²⁻** or to **AMP²⁻** and **HO₃P-O-PO₃³⁻**. **ATP⁴⁻ hydrolysis** transfer the **phosphoryl**, **pyro-phosphoryl**, or **adenylyl** group from **ATP⁴⁻** to a **substrate** or **enzyme** molecule that couples the energy of **exoergic hydrolyse** to **endoergic** transformations of **substrates**. **ATP⁴⁻** provides the energy bricks for anabolic reactions, including the **synthesis** of informational molecules, and for the **transport** of molecules and ions across membranes down and osmosis against concentration gradients but down electrical potential ΔE gradients. Muscle contraction is one of several exceptions to this generalization; the initiate conformational changes for muscle contraction are driven by **ATP⁴⁻** hydrolysis directly.

Cells contain **metabolites** with large, negative $\Delta G < 0$, free energies of **hydrolysis**, including **phospho-enol-pyruvate**, **1,3-bis-phospho-glycerate**, and **phospho-creatine**. These high-energy compounds, like **ATP**, have a high **phosphoryl group transfer potential**; they are good **donors** of the **phosphoryl** group. **Thio-esters** also have high free energies **G** of **hydrolysis**.

Oxidation-reduction reactions solutions give two half-reactions (called **RedOx** systems), each with a characteristic **standard reduction potential**, $E^\circ_{\text{H}_2\text{O}}$ for **Reductant** and **Oxidant**. When two **2** electro-chemical half-cells connected, in closed circuit, electrons e^- tend to flow to the half-cell with the higher **reduction potential** **E**. The equilibrium free-energy change ΔG_{eq} for an **oxidation-reduction** reaction is directly proportional to the difference in **standard reduction potentials** difference $\Delta E^\circ = (E^\circ_{\text{Red1}} - E^\circ_{\text{2Oxn+}})$ of the two half-cells:

$$\Delta G_{\text{eq}} = F \cdot n \cdot \Delta E^\circ = -R \cdot T \cdot \ln(K_{\text{eq}}).$$

Many **oxidation** reactions are **dehydrogenation** in which one **1** or two **2** hydrogen **H** atoms (electron e^- and proton H^+) are transferred from a **substrate** to a hydrogen **H** **acceptor**. **Oxidation-reduction** reactions involve specialized electron e^- **carriers**. **NADH** and **NADPH** **coenzymes**, which are charged ions P_2^{2-} P_3^{4-} of many **dehydrogenases**. Both **NAD⁺** and **NADP⁺** **accept** two **2** electrons e^- and one **1** proton as H^+ . **FAD** and **FMN**, the **flavin nucleotides**, serve as tightly bound **prosthetic** groups of flavo-proteins. They can **accept** either one **1** or two **2** electrons e^- . The **stepwise oxidation** of **glucose**, in which produce 36 molecules **ATP⁴⁻** and electrons 24 e^- transfer to six **6** $\text{O}_{2\text{aqua}}$ in half-cell expressions:



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8. **Westheimer, F.H.** (1987) Why nature chose phosphates. *Science* 235, 1173-1178. A chemist's description of the unique suitability of phosphate esters and anhydrides for metabolic transformations.

Biochemical Oxidation- Reduction Reactions

- Dolphin, D., Avramovic, O., & Poulson, R.** (eds) (1987) *Pyridine Nucleotide Coenzymes: Chemical, Biochemical, and Medical Aspects*, John Wiley & Sons, Inc., New York.
An excellent two-volume collection of authoritative reviews. Among the most useful are the problems by Kaplan, Westheimer, Veech, and Ohno and Ushio.

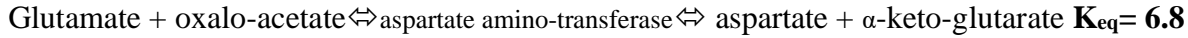
Problems 1. Entropy Changes during Egg Development

Consider a system consisting of an egg in an incubator. The white and yolk of the egg contain proteins, carbohydrates, and lipids. If fertilized, the egg is transformed from a single meiotic cell to a complex mitotic cells in organism. Discuss this irreversible process in terms of the entropy changes ΔS in the system, surroundings, and universe. Be sure that you first clearly define the system and surroundings-environment.

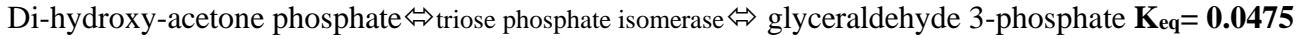
2. Calculation of Prigogine attractor free energy change minimum ΔG_{eq} from **Equilibrium Constants K_{eq}**

Calculate the standard free-energy changes ΔG_{eq} the following metabolically important enzyme-catalyzed reactions at **25°C** and **pH 7.36** from the equilibrium constants K_{eq} given.

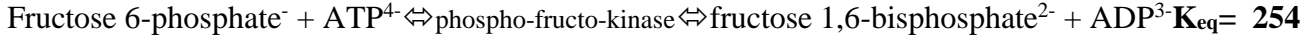
(a) $\Delta G_{eq} = -R \cdot T \cdot \ln(K_{eq}) = -8.3144 \cdot 298.15 \cdot \ln(6.8) = -2479.0215 \cdot 1.916923 = -4752.093331 = -4.752 \text{ kJ/mol}$



(b) $\Delta G_{eq} = -R \cdot T \cdot \ln(K_{eq}) = -8.3144 \cdot 298.15 \cdot \ln(0.0475) = -2479.0215 \cdot -3.04703 = 7553.65288 = 7.553 \text{ kJ/mol}$



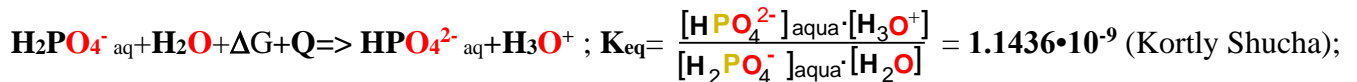
(c) $\Delta G_{eq} = -R \cdot T \cdot \ln(K_{eq}) = -8.3144 \cdot 298.15 \cdot \ln(254) = -2479.0215 \cdot 5.537334 = -13727.170039 = -13.727 \text{ kJ/mol}$



$\Delta G_{eq} = -R \cdot T \cdot \ln(K_{eq})$; for equilibrium is zero $\Delta G = 0 = \Delta G_{eq} + R \cdot T \cdot \ln(K_{eq})$

3. Hess law calculation $\Delta G_r = G_{products} - G_{reactants}$ products minus reactants Constant $K = \text{EXP}(-\Delta G_r / (R \cdot T))$

Hess law constants K for each ΔG_r on page 15: <http://aris.gusc.lv/BioThermodynamics/BioThermodynamics.pdf>

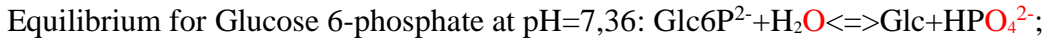


Hess law calculation order products sum minus reactants sum shows unfavored free energy change positive:

$$\Delta G_r = \Delta H_r - T \cdot \Delta S_r = 10,5 - 298,15 \cdot -0,199784 = 70,0 \text{ kJ/mol;}$$

Calculation Prigogine attractor free energy change minimum ΔG_{min} :

$$\Delta G_{min} = \Delta G_{eq} = -R \cdot T \cdot \ln(K_{eq}) = -8,3144 \cdot 298,15 \cdot \ln(1,1436 \cdot 10^{-9}) = 51,0 \text{ kJ/mol,}$$



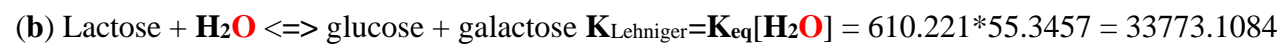
$$\Delta G_{Lehniger} = -13,8; K_{Lehniger} = \text{EXP}(-13,8 \cdot 1000 / 8.3144 / 298.15) = \text{EXP}(5.5669) = K_{eq} \cdot [\text{H}_2\text{O}] = 261.62;$$

$$\text{Prigogine attractor } \Delta G_{min} = \Delta G_{eq} \text{ equilibrium } \frac{[\text{Glc}] \cdot [\text{HPO}_4^{2-}]}{[\text{Glc6P}^{2-}] \cdot [\text{H}_2\text{O}]} = K_{eq} = K_{Lehniger} / [\text{H}_2\text{O}] = 261.62 / 55,3 = 4,728$$

$$\text{pH}=7,36; \Delta G_{min} = \Delta G_{eq} = -R \cdot T \cdot \ln(K_{eq}) = -R \cdot T \cdot \ln(4,7281) = -8,3144 \cdot 298,15 \cdot 1,55334 = -3,851 \text{ kJ/mol ;}$$

Hess law calculation order products sum minus reactants sum shows favored free energy change negative:

$$\Delta G_r = \Delta G^\circ_{\text{Glc}} + \Delta G^\circ_{\text{HPO}_4^{2-}} - \Delta G^\circ_{\text{H}_2\text{O}} - \Delta G^\circ_{\text{Glc6P}} = -402,05 - 1057,143 - (-151,549 - 1296,262) = -1459,193 + 1447,811 = -11,382 \text{ kJ/mol}$$



$$\Delta G_{min} = \Delta G_{eq} = \Delta G_{Lehniger} = -15,9 \text{ kJ/mol; Lehninger 2000;}$$

$$K_{Lehniger} = \frac{[\text{Glc}] \cdot [\text{Gal}]}{[\text{Lactose}] \cdot [\text{H}_2\text{O}]} = K_{eq} = \text{EXP}(-15,9 \cdot 1000 / 8.3144 / 298.15) = \text{EXP}(6,414) = 610,35;$$

Hess law calculation order products sum minus reactants sum shows favored free energy change negative:

$$\Delta G_r = \Delta H_r - T \cdot \Delta S_r = 1,52 - 298,15 \cdot 0,073298 = -20,334 \text{ kJ/mol exoergic}$$

$$\text{pH}=7,36; \Delta G_{min} = \Delta G_{eq} = -R \cdot T \cdot \ln(K_{eq}) = -R \cdot T \cdot \ln(610,35) = -8,3144 \cdot 298,15 \cdot 6,414 = -15,9 \text{ kJ/mol ;}$$



$$\Delta G_{Lehniger} = -15,9; Lehninger 2000;$$

$$K_{Lehniger} = \frac{[\text{Glc}] \cdot [\text{Gal}]}{[\text{Lactose}]} = K_{eq} \cdot [\text{H}_2\text{O}] = \text{EXP}(-15,9 \cdot 1000 / 8.3144 / 298.15) = \text{EXP}(6,414) = 610,35;$$

Hess law calculation order products sum minus reactants sum shows favored free energy change negative:

$$\Delta G_r = \Delta H_r - T \cdot \Delta S_r = 1,52 - 298,15 \cdot 0,073298 = -20,334 \text{ kJ/mol exoergic}$$

$$\text{Prigogine attractor } \Delta G_{min} = \Delta G_{eq} \text{ equilibrium } K_{eq} = \frac{[\text{Glc}] \cdot [\text{Gal}]}{[\text{Lactose}] \cdot [\text{H}_2\text{O}]} = 610.35 / 55,3(3) = K_{Lehniger} [\text{H}_2\text{O}] = 11,03;$$

$$\text{pH}=7,36; \Delta G_{min} = \Delta G_{eq} = -R \cdot T \cdot \ln(K_{eq}) = -R \cdot T \cdot \ln(11,03) = -8,3144 \cdot 298,15 \cdot 2,4006 = -5,951 \text{ kJ/mol ;}$$

$$K_{eq \text{H}_2\text{O}} = 0.004615 = 3.1 \cdot 1000 / 8.314400 / 298.15 = \text{EXP}(-1.2505) = 0.28636 = [\text{fumarate}] \cdot [\text{H}_2\text{O}] / ([\text{Malate}]) = K_{eq} / [\text{H}_2\text{O}] =$$

$$= 0.255400 / 55.3457 = 0.004615 = K_{eq}^\circ; K_{eq}^\circ = \frac{[\text{Fumarate}] \cdot [\text{H}_2\text{O}]}{[\text{Malate}]} = 0.28636 ; \Delta G^\circ = 3.1 \text{ kJ/mol}$$

4. Experimental Determination of K_{eq}° and ΔG°

If a **0.1 M** solution of **glucose 1-phosphate** is incubated with a catalytic amount of **phospho-gluco-mutase**, the **glucose 1-phosphate** is transformed to **glucose 6-phosphate**. At equilibrium, the concentrations of the reaction components are:

Glucose 1-phosphate \leftrightarrow phospho-gluco-mutase \leftrightarrow glucose 6-phosphate⁻

$$[\text{Glc1P}^-] = 4.5 \cdot 10^{-3} \text{ M} \quad 9.6 \cdot 10^{-2} \text{ M} = [\text{Glc6P}^-]$$

$$= 0.096/0.0045 = 21.3333 = K_{\text{eq}}^{\circ} \Delta G^{\circ} = -R \cdot T \cdot \ln(21.3333) = -8.3144 \cdot 298.15 \cdot 3.06027/1000 = -7.58648$$

Calculate $K_{\text{eq}}^{\circ} = [\text{Glc6P}^-]/[\text{Glc1P}^-] = 21.3$ and $\Delta G^{\circ} = -R \cdot T \cdot \ln(21.33) = -7.586 \text{ kJ/mol}$ for this reaction at **25°C**.

5. Experimental Determination of ΔG° for ATP Hydrolysis

A direct measurement of the standard free-energy change ΔG° 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 ΔG° can be calculated indirectly, however, from the equilibrium constants of two **2** other **enzymatic** reactions having less favorable equilibrium constants:

$$\Delta G^{\circ}_1 = \Delta G^{\circ}_o + G^{\circ}_{\text{HPO}_4} + G^{\circ}_{\text{H}_3\text{O}^+} - G^{\circ}_{\text{H}_2\text{PO}_4} - G^{\circ}_{\text{H}_2\text{O}} = -13.8 + (-1282) + (-284.7) - (-1323) - (-306.7) = 49.306 \text{ kJ/mol}$$

$$270 \cdot 1.1469 \cdot 10^{-9} = 3.096630 \cdot 10^{-7} = K_{\text{eq}}^{\circ} = K_{\text{H}_2\text{PO}_4} \cdot K_{\text{eq}}; \Delta G^{\circ} = -R \cdot T \cdot \ln(270) = -13879 \text{ kJ/mol}$$

$$\text{H}_2\text{PO}_4^- + \text{H}_2\text{O} \leftrightarrow \text{HPO}_4^{2-} + \text{H}_3\text{O}^+; K_{\text{H}_2\text{PO}_4}^{\circ} = 1.1469 \cdot 10^{-9} \text{ (KortlyShucha)}$$

$$\text{Glucose-6-phosphate}^- + \text{H}_2\text{O} \Rightarrow \text{glucose} + \text{H}_2\text{PO}_4^-; K_{\text{eq}} = 270; \Delta G^{\circ}_{\text{eq}} = -13.879 \text{ kJ/mol}$$

$$\text{Glucose 6-phosphate}^- + \text{H}_2\text{O} \leftrightarrow \text{glucose} + \text{H}_2\text{PO}_4^-; K_{\text{o}}^{\circ} = 261.573; \Delta G^{\circ}_o = -13.8 \text{ kJ/mol}$$

$$K_{\text{eq}}^{\circ} \cdot K_{\text{H}_2\text{PO}_4}^{\circ} = K_{\text{eq1}}^{\circ} = \frac{[\text{Glc}] \cdot [\text{HPO}_4^{2-}] \cdot [\text{H}_3\text{O}^+]}{[\text{Glc} - 6\text{P}^-] \cdot [\text{H}_2\text{O}]^2} = 3.1 \cdot 10^{-7};$$

$$= 4.7262 \cdot 10^{-7} = 1.1469 \cdot 261.573 \cdot 10^{-9} = \Delta G^{\circ}_{\text{eq1}} = 37.16 \text{ kJ/mol}$$

$$(1) \text{Glucose-6-phosphate}^- + 2 \text{H}_2\text{O} \Rightarrow \text{glucose} + \text{HPO}_4^{2-} + \text{H}_3\text{O}^+; K_{\text{eq1}}^{\circ} = 3.097 \cdot 10^{-7}; \Delta G^{\circ}_1 = 49.3 \text{ kJ/mol}$$

$$(2) \text{ATP}^{4-} + \text{glucose} \Rightarrow \text{ADP}^{3-} + \text{glucose 6-phosphate}^-; K_{\text{eq2}} = 890$$

$$K_{\text{eq2}}^{\circ} = \frac{[\text{ADP}^{3-}] \cdot [\text{Glc} - 6\text{P}^-]}{[\text{Glc}] \cdot [\text{ATP}^{4-}]} = 890; \Delta G^{\circ}_{\text{eq2}} = -16.836 \text{ kJ/mol}$$

Using this information, calculate the standard free energy ΔG° of hydrolysis of **ATP** at **25°C**.

$$K_{\text{eq3}}^{\circ} = \frac{[\text{ADP}^{3-}] \cdot [\text{HPO}_4^{2-}] \cdot [\text{H}_3\text{O}^+]}{[\text{ATP}^{4-}] \cdot [\text{H}_2\text{O}]^2} = K_{\text{eq1}}^{\circ} \cdot K_{\text{eq2}}^{\circ} = \frac{[\text{Glc}] \cdot [\text{HPO}_4^{2-}] \cdot [\text{H}_3\text{O}^+]}{[\text{Glc6P}^-] \cdot [\text{H}_2\text{O}]^2} \cdot \frac{[\text{ADP}^{3-}] \cdot [\text{Glc6P}^-]}{[\text{Glc}] \cdot [\text{ATP}^{4-}]}$$

$$3.09663 \cdot 890 \cdot 10^{-7} = 2.7560 \cdot 10^{-4} = K_{\text{eq3}}^{\circ}; \Delta G^{\circ}_1 + \Delta G^{\circ}_{\text{eq2}} = -16.836 + 49.3 = 32.464 = \Delta G^{\circ}_3$$

$$-R \cdot T \cdot \ln(K_{\text{eq3}}^{\circ}) = -8.1344 \cdot 298.15 \cdot \ln(0.0002756) = 20.3194 \text{ kJ/mol} = \Delta G^{\circ}_{\text{eq3}}$$

$$\Delta G^{\circ}_3 = \Delta G^{\circ}_o + G^{\circ}_{\text{HPO}_4} + G^{\circ}_{\text{H}_3\text{O}^+} - G^{\circ}_{\text{H}_2\text{PO}_4} - G^{\circ}_{\text{H}_2\text{O}} = -30.5 + (-1282) + (-284.7) - (-1323) - (-306.7) = 32.606 \text{ kJ/mol}$$

$$(3) \text{ATP}^{4-} + 2\text{H}_2\text{O} \Rightarrow \text{ADP}^{3-} + \text{HPO}_4^{2-} + \text{H}_3\text{O}^+; K_{\text{eq3}}^{\circ} = 0.0002756; \Delta G^{\circ}_{\text{eq3}} = 20.32 \text{ kJ/mol}; \Delta G^{\circ}_{123} = 32.464 \text{ kJ/mol}$$

$$K_{\text{eq}^{\circ}} = 0.0002756/1.146910^{-9} = 240300; -28981 = \Delta G_{\text{eq}^{\circ}} = -R \cdot T \cdot \ln(K_{\text{o}}^{\circ}) = -8.3144 \cdot 298.15 \cdot \ln(240300) =$$

$$= -30714; K_{\text{o}}^{\circ} = \text{EXP}(-\Delta G^{\circ}/R/T) = \text{EXP}(-30500/8.3144/298.15) =$$

$$K_{\text{eq}^{\circ}} = \frac{[\text{ADP}^{3-}] \cdot [\text{H}_2\text{PO}_4^-]}{[\text{ATP}^{4-}] \cdot [\text{H}_2\text{O}]^2} = K_{\text{eq3}}^{\circ}/K_{\text{H}_2\text{PO}_4}^{\circ} = 240300; \Delta G_{\text{eq}^{\circ}} = -30.714 \text{ kJ/mol}$$

$$(3) \text{ATP}^{4-} + \text{H}_2\text{O} \Rightarrow \text{ADP}^{3-} + \text{H}_2\text{PO}_4^{2-}; K_{\text{o}}^{\circ} = 220409; \Delta G^{\circ}_o = -30.500 \text{ kJ/mol}$$

6. Difference between ΔG° and ΔG Consider the following inter conversion, which occurs in **glycolysis** :

Fructose 6-phosphate⁻ \leftrightarrow glucose 6-phosphate⁻; $K_{\text{eq}}^{\circ} = 1.97$

$$K_{\text{eq}}^{\circ} = \frac{[\text{Glc6P}^-]}{[\text{Fruc6P}^-]} = 1.97 = 531 \text{ 331}; \Delta G^{\circ} = -R \cdot T \cdot \ln(K_{\text{eq}}^{\circ}) = -1.5399 \text{ kJ/mol}$$

$$= 0.5/1.5 = 0.3 = K_{\text{eq}}^{\circ} \Delta G^{\circ} = -R \cdot T \cdot \ln(1.97) = -8.3144 \cdot 298.15 \cdot 3.06027/1000 = -1539.9$$

(a) What is ΔG° for the reaction (assuming that the temperature is **25°C**)?

(b) If the concentration of [Fruc6P⁻] is adjusted to **1.5 M** and that of

$$[\text{Glc6P}^-] \text{ is adjusted to } \mathbf{0.5 M}, \text{ what is } \Delta G? \mathbf{-1539.9 + R \cdot T \cdot \ln(0.3) =}$$

(c) Why are ΔG° and ΔG different? $\Delta G = \Delta G^\circ + R \cdot T \cdot \ln\left(\frac{[\text{Glc6P}^-]}{[\text{Fruc6P}^-]}\right) = \mathbf{-1539.9 + -2723.54 = -4.263.4 \text{ kJ/mol}}$

7. Dependence of ΔG on pH. The free energy ΔG released by the **hydrolysis** of **ATP** under standard conditions at **pH=7** is $\Delta G^\circ = -30.5 \text{ kJ/mol}$. If **ATP** is **hydrolyzed** under standard conditions but at **pH=5.0**, is more or less free energy released? Why?

$$K_{\text{eq3}}^\circ = \frac{[\text{ADP}^{3-}] \cdot [\text{HPO}_4^{2-}] \cdot [\text{H}_3\text{O}^+]}{[\text{ATP}^{4-}] \cdot [\text{H}_2\text{O}]^2} = \mathbf{1.94 \cdot 10^{-6}}; K_{\text{eq3}}^\circ / K_{\text{H}_2\text{PO}_4}^\circ = K_{\text{eq3}}^\circ = \frac{[\text{ADP}^{3-}] \cdot [\text{H}_2\text{PO}_4^-]}{[\text{ATP}^{4-}] \cdot [\text{H}_2\text{O}]^2} = \mathbf{220409}$$

$$\text{EXP}(-32606/8.3144/298.15) = \text{EXP}(-13.1528) = \mathbf{1.94 \cdot 10^{-6}} = K_{\text{eq3}}^\circ; K_{\text{eq3}}^\circ = \mathbf{1.94 \cdot 10^{-6}} =$$

$$= \Delta G^\circ; K_{\text{eq3}}^\circ = \text{EXP}(-30.5 \cdot 1000/8.3144/298.15) = \text{EXP}(12.3032) = \mathbf{220409};$$

$$\Delta G^\circ_3 = \Delta G^\circ_0 + G^\circ_{\text{HPO}_4} + G^\circ_{\text{H}_3\text{O}^+} - G^\circ_{\text{H}_2\text{PO}_4} - G^\circ_{\text{H}_2\text{O}} = \mathbf{-30.5 + (-1282) + (-284.7) - (-1323) - (-306.7) = 32.606 \text{ kJ/mol}}$$

$$\Delta G = \Delta G^\circ + R \cdot T \cdot \ln \frac{[\text{ADP}^{3-}] \cdot [\text{HPO}_4^{2-}] \cdot [\text{H}_3\text{O}^+]}{[\text{ATP}^{4-}] \cdot [\text{H}_2\text{O}]^2} = \mathbf{32606 + R \cdot T \cdot \ln(0.0001/0.01/\text{aoHOH}/\text{aoHOH} \cdot 0.01 \cdot 10^{\text{pH}})}$$

$$\text{pH}) = \mathbf{19397.7 - 7981.3 = -10.11 \text{ kJ/mol (pH=0)}; \text{ at } T = \mathbf{298 \text{ K (25 }^\circ\text{C)}}$$

$$\mathbf{-38.65 \text{ kJ/mol (pH=5)}; -50.06 \text{ kJ/mol (pH=7)}; -52.12 \text{ kJ/mol (pH=7.36)}; -57.88 \text{ kJ/mol (pH=8.37)}$$

$$\mathbf{-11.83 \text{ kJ/mol (pH=0)}; \text{ at } T = \mathbf{310 \text{ K (37 }^\circ\text{C) in mitochondria}}$$

$$\mathbf{-41.52 \text{ kJ/mol (pH=5)}; -53.39 \text{ kJ/mol (pH=7)}; -55.53 \text{ kJ/mol (pH=7.36)}; -61.53 \text{ kJ/mol (pH=8.37)}$$

8. The ΔG° for Coupled Reactions

Glucose 1-phosphate⁻ is converted into fructose 6-phosphate⁻ in two **2** successive reactions:

Glucose 1-phosphate⁻ \Rightarrow glucose 6-phosphate⁻; $\Delta G^\circ_1 = \mathbf{-7.3 \text{ kJ/mol}}$

Glucose 6-phosphate⁻ \Rightarrow fructose 6-phosphate⁻; $\Delta G^\circ_2 = \mathbf{+1.7 \text{ kJ/mol}}$

Using the ΔG° values in Table 1.1, calculate the equilibrium constant,

$$\Delta G^\circ = \Delta G^\circ_1 + \Delta G^\circ_2 = \mathbf{-7.3 + 1.7 = -5.6 \text{ kJ/mol}}$$
 for the sum of the two **2** reactions at **25°C**:

$$\text{Glucose 1-phosphate}^- \Rightarrow \text{fructose 6-phosphate}^-; K_{\text{eq}}^\circ = K_{\text{eq1}} \cdot K_{\text{eq2}} = \text{EXP}(5600/8.314400/298.15) =$$

$$\text{EXP}(2.258956) = \mathbf{9.57309}$$

9. Strategy for Overcoming an Unfavorable Reaction: 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 **H₂PO₄⁻** and **HPO₄²⁻** is described by the equation at **T = 310.15 K**:

(a) Glucose + **H₂PO₄⁻** \Rightarrow glucose 6-phosphate⁻ + H₂O, $\Delta G^\circ = \mathbf{13.8 \text{ kJ/mol}}$

$$K_{\text{eqa}}^\circ = \frac{[\text{Glc6P}^-] \cdot [\text{H}_2\text{O}]}{[\text{Glc}] \cdot [\text{H}_2\text{PO}_4^-]}; K_{\text{eqa}2}^\circ \cdot K_{\text{H}_2\text{PO}_4}^\circ = \frac{[\text{Glc6P}^-] \cdot [\text{H}_2\text{O}]^2}{[\text{Glc}] \cdot [\text{HPO}_4^{2-}] \cdot [\text{H}_3\text{O}^+]} \cdot \frac{[\text{HPO}_4^{2-}] \cdot [\text{H}_3\text{O}^+]}{[\text{H}_2\text{PO}_4^-] \cdot [\text{H}_2\text{O}]}$$

$$\text{EXP}(49306/RF/T) = \mathbf{2.01195544 \cdot 10^{+8}} = K_{\text{eq3}}^\circ; \Delta G^\circ_1 + \Delta G^\circ_{\text{eq2}} = \mathbf{-16.836 + 49.3 = 32.464 = \Delta G^\circ_3}$$

$$\mathbf{-R \cdot T \cdot \ln(K_{\text{eq3}}^\circ) = -8.1344 \cdot 298.15 \cdot \ln(0.0002756) = 20.3194 \text{ kJ/mol} = \Delta G^\circ_{\text{eq3}} \mathbf{0.0000105738}}$$

(a2) Glucose + **HPO₄²⁻** + H₃O⁺ \Rightarrow glucose 6-phosphate⁻ + 2 H₂O, $\Delta G^\circ = \mathbf{-49.306 \text{ kJ/mol}}$

$$K_{\text{eqa}2}^\circ = \frac{[\text{Glc6P}^-] \cdot [\text{H}_2\text{O}]^2}{[\text{Glc}] \cdot [\text{HPO}_4^{2-}] \cdot [\text{H}_3\text{O}^+]} = \frac{[\text{Glc6P}^-] \cdot \left(1 + \frac{[\text{H}_3\text{O}^+]}{K_{\text{H}_2\text{PO}_4} \cdot [\text{H}_2\text{O}]}\right) \cdot [\text{H}_2\text{O}]^2}{[\text{Glc}] \cdot 4.8 \cdot [\text{H}_3\text{O}^+]} = \mathbf{2.0119 \cdot 10^{+8}}$$

$$\Delta G^\circ = \Delta G^\circ_0 + G^\circ_{\text{H}_2\text{O}} - G^\circ_{\text{H}_3\text{O}^+} = \mathbf{13.8 + (-284.7) - (-306.7) = -8.231 = 30.83876};$$

$$K_{\text{H}_2\text{PO}_4}^\circ = \frac{[\text{HPO}_4^{2-}] \cdot [\text{H}_3\text{O}^+]}{[\text{H}_2\text{PO}_4^-] \cdot [\text{H}_2\text{O}]}; P_i = \mathbf{4.8 \text{ mM}} = [\text{H}_2\text{PO}_4^-] + [\text{HPO}_4^{2-}]; [\text{HPO}_4^{2-}] = \mathbf{4.8} \cdot \frac{[\text{HPO}_4^{2-}] \cdot [\text{H}_3\text{O}^+]}{K_{\text{H}_2\text{PO}_4} \cdot [\text{H}_2\text{O}]}$$

$$[\text{HPO}_4^{2-}] + [\text{HPO}_4^{2-}] \cdot \frac{[\text{H}_3\text{O}^+]}{K_{\text{H}_2\text{PO}_4} \cdot [\text{H}_2\text{O}]} = \mathbf{4.8} = [\text{HPO}_4^{2-}] \cdot \left(1 + \frac{[\text{H}_3\text{O}^+]}{K_{\text{H}_2\text{PO}_4} \cdot [\text{H}_2\text{O}]}\right);$$

$$[\text{HPO}_4^{2-}] = \frac{4.8}{\left(1 + \frac{[\text{H}_3\text{O}^+]}{K_{\text{H}_2\text{PO}_4} \cdot [\text{H}_2\text{O}]}\right)}; [\text{Glc6P}^-] = \frac{2.012 \cdot [\text{Glc}] \cdot 4.8 \cdot [\text{H}_3\text{O}^+]}{\left(1 + \frac{[\text{H}_3\text{O}^+]}{K_{\text{H}_2\text{PO}_4} \cdot [\text{H}_2\text{O}]}\right) \cdot [\text{H}_2\text{O}]^2} = 1.0574 \cdot 10^{-5} \text{M}$$

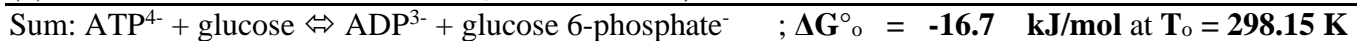
(a) Calculate the equilibrium constant K°_a for the above reaction. In the rat **hepatocyte** **pH=7.36** and at **pH=7** the physiological concentrations of **glucose** and $[\text{H}_2\text{PO}_4^-] + [\text{HPO}_4^{2-}]$ are maintained at approximately **4.8 mM**. What is the equilibrium concentration of glucose 6-phosphate⁻ obtained by the direct **phosphorylation** of **glucose** by $\text{H}_2\text{PO}_4^- + \text{HPO}_4^{2-}$? Respectively $[\text{Glc6P}^-] = 8.5 \cdot 10^{-8} \text{M}$ and $1.275 \cdot 10^{-7} \text{M}$ (**pH 7.36** and **7**)

Does this reaction represent a reasonable metabolic step 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 $\text{H}_2\text{PO}_4^- + \text{HPO}_4^{2-}$. Assuming a fixed concentration of $\text{H}_2\text{PO}_4^- + \text{HPO}_4^{2-}$ at **4.8 mM**, how high would the intracellular concentration of **glucose** have to be to give an equilibrium concentration of glucose 6-phosphate⁻ of $[\text{Glc6P}^-] = 250 \mu\text{M}$ (normal physiological concentration)? Would this route be physiologically reasonable, given that the maximum solubility of **glucose** is less than **1 M**?

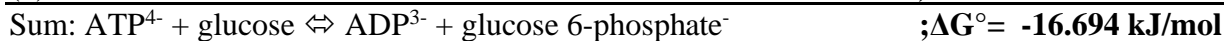
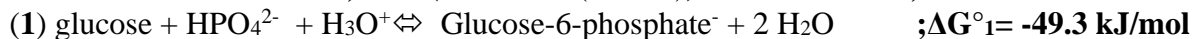
$$[\text{Glc}] = \frac{[\text{Glc6P}^-] \cdot \left(1 + \frac{[\text{H}_3\text{O}^+]}{K_{\text{H}_2\text{PO}_4} \cdot [\text{H}_2\text{O}]}\right) \cdot [\text{H}_2\text{O}]}{K_{a2} \cdot 4.8 / 1000 \cdot [\text{H}_3\text{O}^+]} = 23.64 \text{M at pH} = 7.36 \quad 23.64259868$$

(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 **endoergonic phosphorylation** of **glucose** at **T = 310.15 K**:



$$K^{\circ}_o = 842.63 \leftarrow \text{EXP}(-\Delta G^{\circ}/R/T) = \underline{649.3 = K^{\circ}}; K^{\circ}_{\text{eqo}} = \frac{[\text{ADP}^{3-}] \cdot [\text{Glc6P}^-]}{[\text{ATP}^{4-}] \cdot [\text{Glc}]} = 890 ; \Delta G^{\circ}_{\text{eqo}} = -16.836 \text{ kJ/mol}$$

$$\Delta G^{\circ}_o = 13.8 + (-30.5) = -16.7 ; \text{EXP}(-16.7/R/F/(T_o+25)) = 842.631 = K^{\circ}_o; K^{\circ} = 649.2998 = \text{EXP}(-16700/R/F/T)$$



$$\Delta G^{\circ}_2 = \Delta G^{\circ}_{o2} + G^{\circ}_{\text{HPO}_4} + G^{\circ}_{\text{H}_3\text{O}^+} - G^{\circ}_{\text{H}_2\text{PO}_4} - G^{\circ}_{\text{H}_2\text{O}} = -30.5 + (-1282) + (-284.7) - (-1323) - (-306.7) = 32.606 \text{ kJ/mol}$$

$$[\text{Glc}] = \frac{[\text{ADP}^{3-}] \cdot [\text{Glc6P}^-]}{K^{\circ} \cdot [\text{ATP}^{4-}]} = \frac{1.32 \cdot 0.25 / 1000}{649.2998 \cdot 3.38} = 1.504 \cdot 10^{-7} \text{M not depend on concentration } [\text{H}_3\text{O}^+]$$

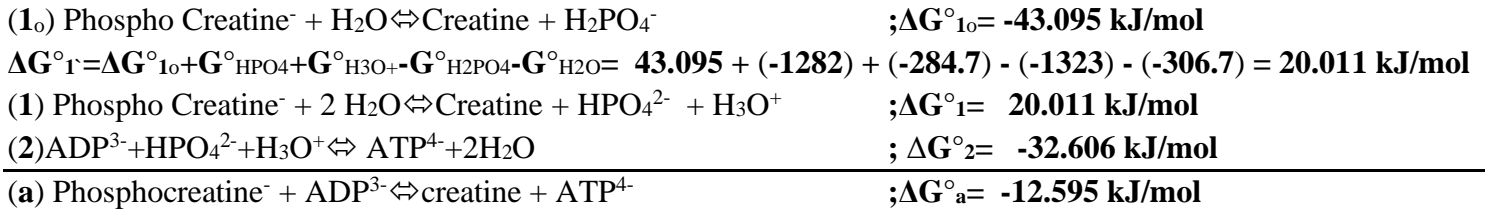
$$[\text{Glc}] = 1.32 \cdot 0.25 / 1000 / 649.2998 / 3.38 = 1.50366804509526 \text{E-07}$$

Calculate **K** for the overall reaction. For the **ATP-dependent phosphorylation** of **glucose**, what concentration of **glucose** is needed to achieve a **250 μM** intracellular concentration of glucose 6-phosphate when the concentrations of **ATP** and **ADP** are **3.38** and **1.32 mM**, respectively? Does this coupling process provide a feasible route, at least in principle, for the **phosphorylation** of **glucose** in the cell? Explain.

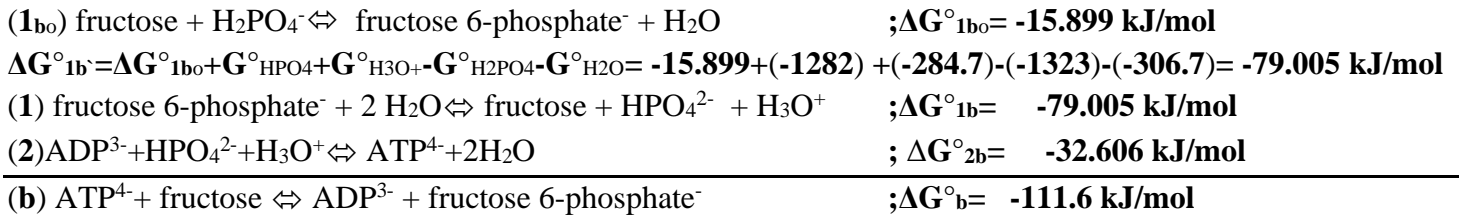
(d) Although coupling **ATP hydrolysis** to **glucose phosphorylation** makes thermodynamic sense, how this coupling is to take place has not been specified. Given that coupling requires a common intermediate, one conceivable route is to use **ATP hydrolysis** to raise the intracellular concentration of $\text{H}_2\text{PO}_4^- + \text{HPO}_4^{2-}$ and thus drive the unfavorable phosphorylation of glucose by $\text{H}_2\text{PO}_4^- + \text{HPO}_4^{2-}$. Is this ~i reasonable route? (Think about the solubility products of metabolic intermediates.)

(e) The **ATP-coupled phosphorylation** of **glucose** is catalyzed in **hepatocytes** by the enzyme **gluco kinase**. This enzyme binds **ATP** and **glucose** to form a **glucose-ATP-enzyme** complex, and the **phosphoryl** group is transferred directly from **ATP** to **glucose**. Explain the advantages of this route.

10. Calculations of ΔG° for ATP-Coupled Reactions From data in Table 1-2 calculate the ΔG° value for the reactions: $\Delta G^\circ = 20.011 + (-32.606) = -12.595$; $-10.3 \cdot 4.184 = -43.095$;



$\Delta G^\circ = -79.005 + (-32.606) = -111.611$; $3.8 \cdot 4.184 = 15.899$;



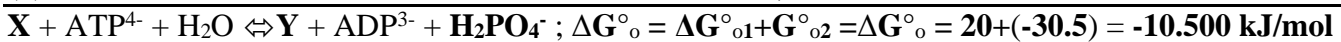
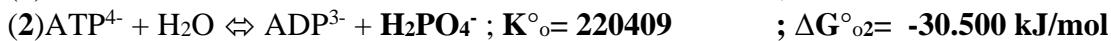
11. Coupling ATP Cleavage to an Unfavorable Reaction.

To explore the consequences of coupling **ATP hydrolysis** under physiological conditions to a thermodynamically unfavorable biochemical reaction, consider the hypothetical transformation **X** ⇌ **Y**, for which $\Delta G^\circ = 20$ kJ/mol.

(a) What is the ratio $[Y]/[X]$ at equilibrium? $K^\circ = 3.135 \cdot 10^{-4}$

$$K_{eq} = [Y]/[X] = \text{EXP}(-\Delta G^\circ_{o1}/R/T) = \text{EXP}(-20000/R/T) = 0.0003135;$$

(b) Suppose **X** and **Y** participate in a sequence of reactions during which **ATP⁴⁻** is **hydrolyzed** to **ADP³⁻** and **H₂PO₄⁻**, The overall reaction is :



$$K^\circ_{eqo} = \frac{[ADP^{3-}] \cdot [H_2PO_4^-] \cdot [Y]}{[ATP^{4-}] \cdot [H_2O] \cdot [X]} = 69.1 ; K^\circ_{eqo} \cdot [H_2O] = \frac{[Y]}{[X]} = 3810$$

$$\frac{[Y]}{[X]} = \frac{[ATP^{4-}] \cdot [H_2O] \cdot K^\circ_{eqo} \cdot \left(1 + \frac{K_{H_2PO_4} \cdot [H_2O]}{[H_3O^+]}\right)}{8.05/1000 \cdot [ADP^{3-}]} = 1.994 \cdot 10^6 ; [H_2PO_4^-] = \frac{8.05/1000}{1 + \frac{K_{H_2PO_4} \cdot [H_2O]}{[H_3O^+]}}$$

$$P_i = 8.05 \text{ mM} = [H_2PO_4^-] + [HPO_4^{2-}] ; [H_2PO_4^-] = 8.05/1000 \cdot \frac{[H_2PO_4^-] K_{H_2PO_4} \cdot [H_2O]}{[H_3O^+]}$$

$$K^\circ_o = \text{EXP}(-\Delta G^\circ_{o1}/R/T) = \text{EXP}(-10500/R/T) = 69.0991 ; a_{HOH} \cdot 69.1 / 8.05 \cdot 1000 \cdot (1 + 2.543489E-9 \cdot a_{HOH} / 10^{-7.36})$$

$$[Y]/[X] = a_{HOH} \cdot 8.05 \cdot 69.0991 / 0.93 / 8.05 \cdot 1000 = 1994007.686579$$

Calculate $[Y]/[X]$ for this reaction at equilibrium. Assume that the concentrations of **[ATP⁴⁻]**, **[ADP³⁻]**, and **([H₂PO₄⁻] + [HPO₄²⁻])** are all **1 M** when the reaction is at equilibrium **T = 310.15 K**.

(c) We know that **[ATP⁴⁻]**, **[ADP³⁻]**, and **[H₂PO₄⁻]** are not **1 M** under physiological conditions. Calculate $[Y]/[X]$ for the **ATP-coupled** reaction when the values of **[ATP⁴⁻]**, **[ADP³⁻]**, and **[H₂PO₄⁻]** are those found in rat myocytes (Table 1-3).

12. Calculations of ΔG at Physiological Concentrations.

Calculate the physiological ΔG (not ΔG°) for the reaction : at **T=310.15 K**



$$\Delta G = \Delta G^\circ + R \cdot T \cdot \ln \frac{[\text{ATP}^{4-}] \cdot [\text{Cr}]}{[\text{ADP}^{3-}] \cdot [\text{PCr}^-]} = -12500 + R \cdot T \cdot \ln(2.6 \cdot 1 / 0.73 / 4.7) = -13215.2 = -13.215 \text{ kJ/mol}$$

at **37 °C** as it occurs in the **cytosol** of **neurons**, in which **phospho creatine**⁻ is present at **[PCr⁻] = 4.7 mM**, creatine at **[Cr] = 1.0 mM**, **ADP³⁻** at **0.73 mM**, and **ATP⁴⁻** at **2.6 mM**.

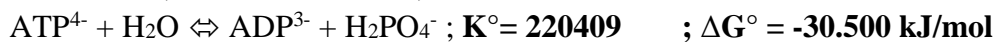
13. Free Energy Required for ATP Synthesis under Physiological Conditions.

In the **cytosol** of **rat hepatocytes**, the **mass-action ratio** is :

$$R_o = \frac{[\text{ATP}^{4-}]}{[\text{ADP}^{3-}] \cdot ([\text{HPO}_4^{2-}] + [\text{H}_2\text{PO}_4^-])} = 5.33 \cdot 10^{-2} \text{ M}^{-1} \quad ; \text{ at } 37^\circ\text{C } T = 310.15 \text{ K}$$

$$P_i = [\text{H}_2\text{PO}_4^-] + [\text{HPO}_4^{2-}] ; [\text{H}_2\text{PO}_4^-] = \frac{[\text{ATP}^{4-}]}{[\text{ADP}^{3-}] \cdot R_o} - \frac{[\text{H}_2\text{PO}_4^-] \cdot K_{\text{H}_2\text{PO}_4} \cdot [\text{H}_2\text{O}]}{[\text{H}_3\text{O}^+]}$$

$$[\text{H}_2\text{PO}_4^-] = \frac{\frac{[\text{ATP}^{4-}]}{[\text{ADP}^{3-}] \cdot R_o}}{\left(1 + \frac{K_{\text{H}_2\text{PO}_4} \cdot [\text{H}_2\text{O}]}{[\text{H}_3\text{O}^+]}\right)} ; \Delta G = \Delta G^\circ + R \cdot T \cdot \ln(R_o \cdot \left\{ \text{H}_2\text{O} \right\} \left(1 + \frac{K_{\text{H}_2\text{PO}_4} \cdot [\text{H}_2\text{O}]}{[\text{H}_3\text{O}^+]}\right)) = 36.99 \text{ kJ/mol}$$



$$+30500 + R \cdot T \cdot \ln(0.0533 \cdot a_{\text{HOH}} \cdot (1 + 2.543489 \cdot 10^{-9} \cdot a_{\text{HOH}} / 10^{(-7.36)})) = 36988.76$$

Calculate the free energy ΔG required to synthesize ATP^{4-} in a **rat hepatocyte**.

14. Daily ATP Utilization by Human Adults.

(a) A total of **30.5 kJ/mol** of free energy ΔG is needed to synthesize ATP^{4-} from ADP^{3-} and H_2PO_4^- when the **reactants** and **products** are at **1 M** concentration (standard state). Because the actual **physiological** concentrations of ATP^{4-} , ADP^{3-} , and H_2PO_4^- are not **1 M**, the free energy ΔG required to synthesize ATP^{4-} under physiological conditions is different from ΔG° . Calculate the free energy ΔG required to synthesize ATP^{4-} in the **human hepatocyte** when the physiological concentrations of ATP^{4-} , ADP^{3-} , ($\text{H}_2\text{PO}_4^- + \text{HPO}_4^{2-}$) are **3.5, 1.50, 5.0 mM** and **pH=7.36**, respectively, at **37°C**.

$$K_{\text{H}_2\text{PO}_4}^\circ = \frac{[\text{HPO}_4^{2-}] \cdot [\text{H}_3\text{O}^+]}{[\text{H}_2\text{PO}_4^-] \cdot [\text{H}_2\text{O}]} ; P_i = 5 \text{ mM} = [\text{H}_2\text{PO}_4^-] + [\text{HPO}_4^{2-}] ; [\text{H}_2\text{PO}_4^-] = 5 - \frac{[\text{H}_2\text{PO}_4^-] \cdot K_{\text{H}_2\text{PO}_4} \cdot [\text{H}_2\text{O}]}{[\text{H}_3\text{O}^+]}$$

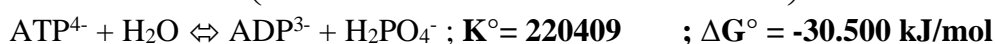
$$K_{\text{H}_2\text{PO}_4}^\circ = 1.1469 \cdot 10^{-9} ; \Delta G^\circ = -R \cdot T \cdot \ln(K_{\text{H}_2\text{PO}_4}^\circ) = 51.034 \text{ kJ/mol at } T = 298.15 \text{ K}$$

$$\Delta G^\circ = -R \cdot T \cdot \ln(1.1469 \cdot 10^{-9}) = 51033.6 ;$$

$$K_{\text{H}_2\text{PO}_4}^\circ = \text{EXP}(-51033.6 / T / R) = 2.543489 \cdot 10^{-9} \text{ at } T = 310.15 \text{ K}$$

$$[\text{H}_2\text{PO}_4^-] = \frac{5 / 1000}{\left(1 + \frac{K_{\text{H}_2\text{PO}_4} \cdot [\text{H}_2\text{O}]}{[\text{H}_3\text{O}^+]}\right)} ; \Delta G^\circ = -R \cdot T \cdot \ln \frac{[\text{ATP}^{4-}] \cdot [\text{H}_2\text{O}]}{[\text{ADP}^{3-}] \cdot [\text{H}_2\text{PO}_4^-]} \text{ at } T = 310.15 \text{ K}$$

$$\Delta G = \Delta G^\circ + R \cdot T \cdot \ln \left(\frac{[\text{ATP}^{4-}] \cdot [\text{H}_2\text{O}] \cdot \left(1 + \frac{K_{\text{H}_2\text{PO}_4} \cdot [\text{H}_2\text{O}]}{[\text{H}_3\text{O}^+]}\right)}{[\text{ADP}^{3-}] \cdot 5 / 1000} \right) = 60.3976 \text{ kJ/mol at } T = 310.15 \text{ K}$$



$$+30500 + R \cdot T \cdot \ln(3.5 / 1.5 \cdot a_{\text{HOH}} / 5 \cdot 1000 \cdot (1 + 2.543489 \cdot 10^{-9} \cdot a_{\text{HOH}} / 10^{(-7.36)})) = 60397.598 = 58998.4$$

(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 ΔG is used to synthesize ATP^{4-} , which then provides energy ΔG for the body's daily **chemical** and **mechanical work** $W = -\Delta G$. Assuming that the efficiency of converting food energy **E** into ATP^{4-} is **50%**, calculate the weight m_{ATP} of ATP^{4-} used by a **human** adult in **24 h**. What percentage of the body weight does this represent?

$$n_{\text{ATP}} = 8360/60.397598/2 = 69.208 \text{ mol} ; m_{\text{ATP}} = n_{\text{ATP}} \cdot M_{\text{ATP}} = 69.208050 \cdot 506.91 = 35082 \text{ g}$$

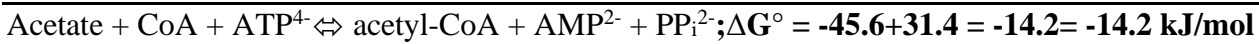
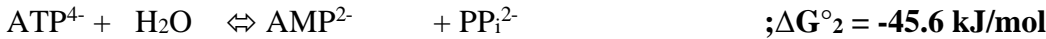
(c) Although adults synthesize large amounts of ATP⁴⁻ daily, their body weight, structure, and composition do not change significantly during this period. Explain this apparent contradiction.

15. Rates of Turnover of α and γ Phosphates of ATP⁴⁻ A-O-OPO-O-OPO-O-OPO-O⁻ (A- α - β - γ -O⁻).

If a small amount of ATP⁴⁻ labeled with radioactive phosphorus in the terminal position, [γ -³²P] ATP⁴⁻, is added to a yeast extract, about half 1/2 of the ³²P activity is found in H₂PO₄⁻ within a few minutes, but the concentration of [ATP⁴⁻]= const remains unchanged. Explain. If the same experiment is carried out using ATP⁴⁻ labeled with ³²P in the central position, [β -³²P] ATP⁴⁻, the ³²P does not appear in H₂PO₄⁻ within such a short time. Why?

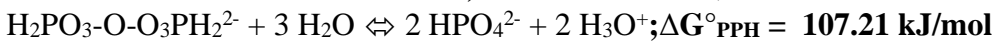
16. Cleavage of ATP to AMP and PP_i during Metabolism

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 -31.4 kJ/mol and that for hydrolysis of ATP⁴⁻ to AMP²⁻ and PP_i²⁻ is -45.6 kJ/mol. Calculate ΔG° for the ATP-dependent synthesis of acetyl-CoA.

(b) Almost all cells contain the enzyme inorganic pyro-phosphates, which catalyzes the hydrolysis of PP_i²⁻ to H₂PO₄⁻. What effect does the presence of this enzyme have on the synthesis of acetyl-CoA? Explain!



17. Energy for H₃O⁺ Pumping The parietal cells of the stomach lining contain membrane "pumps" that transport hydrogen ions H₃O⁺ from the cytosol of these cells (pH_{plasma} 7.36) into the stomach, contributing to the acidity of gastric juice (pH_{stomach} 1.2). Calculate the free energy required to transport 1 mol of hydrogen H₃O⁺ ions through these pumps. (Hint: See Oxidative Phosphorylation.)

Assume a temperature of 37 °C or T = 310.15 K. 1445440



$$\Delta G^\circ = -R \cdot T \cdot \ln(K_{\text{eq}}) = -36577 = -36.577 \text{ kJ/mol}$$

18. Standard Reduction Potentials The standard reduction potential, E°, of any RedOx pair is defined for the half-cell reaction in equilibrium of each RedOx system:



The E° values for the NAD⁺/NADH and pyruvate/lactate conjugate RedOx pairs are -0.113 and 0.2291 V, respectively but E°₃₇: -0.059 and 0.3193 V.

(a) Which conjugate pair has the greater tendency to lose electrons? Explain.

(b) Which is the stronger oxidizing agent? Explain.

(c) Beginning with 1 M concentrations of each reactant and product at pH 7.36, in which direction will the following reaction proceed?



$$\Delta G = \Delta G^\circ + R \cdot T \cdot \ln \left(\frac{[\text{lactate}^-] \cdot [\text{NAD}^+] \cdot [\text{H}_2\text{O}]}{[\text{pyruvate}^-] \cdot [\text{NADH}] \cdot [\text{H}_3\text{O}^+]} \right) = -18.957 \text{ kJ/mol favorable direction of reaction}$$

$$\Delta G^\circ_o = 96485 \cdot 2 \cdot (-0.059 - 0.3193) = -73000.5510 ;$$

$$\Delta G = -73000.5510 + R \cdot T \cdot \ln(1/1 \cdot 1/1 \cdot a_{\text{OH}}/10^{(-7.36)}) = -18957.02$$

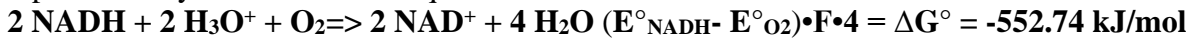
(d) What is the standard free-energy change (ΔG°) at 37 °C for the conversion of pyruvate to lactate

(e) What is the equilibrium constant (K_{eq}) for this reaction?

$$K_{\text{eq}} = \frac{[\text{lactate}^-] \cdot [\text{NAD}^+] \cdot [\text{H}_2\text{O}]}{[\text{pyruvate}^-] \cdot [\text{NADH}] \cdot [\text{H}_3\text{O}^+]} = 6.149 \cdot 10^{12}; [\text{H}_3\text{O}^+] \cdot K_{\text{eq}} = \frac{[\text{lactate}^-] \cdot [\text{NAD}^+] \cdot [\text{H}_2\text{O}]}{[\text{pyruvate}^-] \cdot [\text{NADH}]} = 268417$$

$$\text{EXP}(-73000.5510/R/T) = 6149086393492.1 \cdot 10^{(-7.36)} = 268417.356457188 = K^\circ_o;$$

19. Energy Span of the Respiratory Chain Electron e^- transfer in the mitochondrial respiratory chain may be represented by the net reaction equation



$$\Delta G^\circ = 96485 \cdot 4 \cdot (-0.059 - 1.3732) = -552743.2680/52000 = 10.6297$$

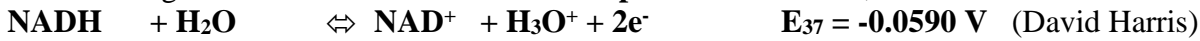
(a) Calculate the value of ΔE° for the net reaction of mitochondrial electron e^- transfer at 37°C .

(b) Calculate ΔG° for this reaction. $\Delta E^\circ = E^\circ_{\text{NADH}} - E^\circ_{\text{O}_2} = -0.059 - 1.3732 = -1.4322 \text{ V}$

(c) How many **nATP** molecules can theoretically be generated by this reaction if the free energy of **ATP** synthesis under cellular conditions is **52 kJ/mol**? **n = 10.63**

20. Dependence of Electromotive Force on Concentrations

Calculate the electromotive force **EMF** (in volts **V**) registered by an electrode immersed in a solution containing the following mixtures of **NAD⁺** and **NADH** at **pH 7.36** and **37 °C**, with reference to a half-cell of **E° 0.00 V**.



$$E = -0.059 + R \cdot T / F \cdot 2 \cdot \ln(1 \cdot 10^{(-7.36)} / 10 / a_{\text{HOH}}) = -0.36983 \text{ V}$$

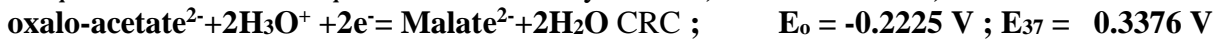
$$\text{EMF} = E = E_{37} + R \cdot T / F \cdot 2 \cdot \ln \left(\frac{[\text{NAD}^+] \cdot [\text{H}_2\text{O}]}{[\text{NADH}] \cdot [\text{H}_3\text{O}^+]} \right) = -0.36983 \text{ V}$$

(a) **1.00 mM NAD⁺** and **10.0 mM NADH**; **E = -0.36983 V**

(b) **1.00 mM NAD⁺** and **1.00 mM NADH**; **E = -0.33906 V**

(c) **10.0 mM NAD⁺** and **1.00 mM NADH**; **E = -0.30829 V**

21. Electron Affinity of Compounds List the following substances in order of increasing \square tendency to accept electrons e^- at **pH = 7.36** by **RedOx potential E_o** values:



(a) α -keto-glutarate + CO_2 (yielding iso-citrate);

(b) oxalo-acetate;

(c) O_2 ;

(d) NADP^+ .

22. Direction of Oxidation-Reduction Reactions

Which of the following reactions would you expect to proceed in the direction shown under **standard conditions pH = 7.36** and **37°C**, assuming that the appropriate **enzymes** are present to catalyze them?

$$(E^\circ_{\text{Red}} - E^\circ_{\text{Ox}}) \cdot F \cdot n = \Delta G^\circ \text{ kJ/mol ;}$$

$$\Delta G^\circ = 96485 \cdot 2 \cdot (0.33757 - 0.059) = 53755.65290 = 10.6297$$

$$\Delta G = \Delta G^\circ + R \cdot T \cdot \ln \left(\frac{[\text{oxaloacetate}^{2-}] \cdot [\text{NADH}] \cdot [\text{H}_3\text{O}^+]}{[\text{malate}^{2-}] \cdot [\text{NAD}^+] \cdot [\text{H}_2\text{O}]} \right) = 10.053 \text{ kJ/mol unfavorable direction} \Rightarrow \text{for (a)}$$

$$\Delta G = 53755.65290 + R \cdot T \cdot \ln(10^{(-7.36)}) = 10052.76$$

(a) $\text{Malate}^{2-} + \text{NAD}^+ + \text{H}_2\text{O} \Rightarrow \text{oxalo-acetate}^{2-} + \text{NADH} + \text{H}_3\text{O}^+$; $(E^\circ_{\text{malate}} - E^\circ_{\text{NAD}^+}) \cdot F \cdot 2 = \Delta G^\circ = 53.756 \text{ kJ/mol}$

$$\Delta G^\circ = 96485 \cdot 2 \cdot (-0.059 - 0.16453) = -43134.58410$$

$$\Delta G = -43134.58410 - R \cdot T \cdot \ln(10^{(-7.36)}) = -568.3108$$

$\Delta G = \Delta G^\circ - R \cdot T \cdot \ln(10^{-7.36}) = 0.568 \text{ kJ/mol} \leq$ direction favorable to left for (b)

(b) $\text{aceto-acetate}^- + \text{NADH} + \text{H}_3\text{O}^+ \Rightarrow \beta\text{-hydroxy-butyrate}^- + \text{NAD}^+ + \text{H}_2\text{O}$; $\Delta G^\circ = -43.135 \text{ kJ/mol}$

$$\Delta G^\circ = 96485 \cdot 2 \cdot (-0.059 - 0.3193) = -73000.5510$$

$$\Delta G = -73000.5510 - R \cdot T \cdot \ln(10^{(-7.36)}) = -29297.7$$

$\Delta G = \Delta G^\circ - R \cdot T \cdot \ln(10^{-7.36}) = -29.298 \text{ kJ/mol} \Rightarrow$ direction favorable to right

(c) $\text{Pyruvate}^- + \text{NADH} + \text{H}_3\text{O}^+ \Rightarrow \text{lactate}^- + \text{NAD}^+ + \text{H}_2\text{O}$; $\Delta G^\circ = -73.001 \text{ kJ/mol} \Rightarrow$ direction

$$\Delta G^\circ = 96485 \cdot 2 \cdot (0.16453 - 0.3193) = -29865.96690$$

(d) $\text{Pyruvate}^- + \beta\text{-hydroxy-butyrate}^- \Rightarrow \text{lactate}^- + \text{aceto-acetate}^-$; $\Delta G^\circ = -29.866 \text{ kJ/mol} \Rightarrow$ direction

$$\Delta G^\circ = 96485 \cdot 2 \cdot (0.33757 - 0.3193) = 3525.56190$$

(e) $\text{Malate}^- + \text{pyruvate}^- \Rightarrow \text{oxalo-acetate}^- + \text{lactate}^-$; $\Delta G^\circ = 3.526 \text{ kJ/mol} \leq$ direction

$$\Delta G^\circ = 96485 \cdot 2 \cdot (0.52695 - 0.286255) = 46446.914150$$

(f) $\text{Acetaldehyde} + \text{succinate}^{2-} \Rightarrow \text{ethanol} + \text{fumarate}^{2-}$; $\Delta G^\circ = 46.447 \text{ kJ/mol} \leq$ direction