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Oxidation-Reduction Homeostasis

The **transfer** of **electron** in **oxidation-reduction RedOx** reactions is indispensible 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~hν=E$_{energy}$**. 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 $\Delta G_{eq}<0$ at equilibrium. Homeostasis contain a variety of molecular **energy transducers**, which convert the electron flow into work **W=ΔE•F•n** , where Δ **E** potential difference $\Delta E=E^{\circ}_{Red}-E^{\circ}_{Ox}$ 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**$^{\circ}$,

$$Ox^{n+}+ne^-<=>Red:$$

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

where **E**$^{\circ}$ standard potential of given **reduction** system measured at conditions for **E=E°** , as equal $[Ox^{n+}]=[Red]$ give log1=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**$^{\circ}$**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 ($[Ox^{n+}]/[Red]$) between **oxidized form** concentration factorial $[Ox^{n+}]$ over **reduced** form concentration [Red] factorial equilibrium state constant $K_{eq}=[Ox^{n+}]/[Red]$.

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 Δ**G** in terms of **reduction** reactions **electromotive force EMF**. Reduction - oxidation potential amplitude $E^{\circ}_{Red}-E^{\circ}_{Ox}$, expressed in volts **V** and **free-energy** change at equilibrium $\Delta G_{eq}=(E^{\circ}_{Red}-E^{\circ}_{Ox})\bullet F\bullet n$, expressed in joules over mol as Prigogine attractor free energy change minimum stay less $\Delta G_{eq}<\Delta G_{Hess}$ 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 $[H_2O]=55.3$ M, pH=7.36 concentration $[H_3O^+]=10^{-7.36}$ M activate functionally flow of electrons with producing positive work $W=-\Delta G_{eq}$ 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: $\Delta G_{homeostasis}=\Delta G_{eq}+R\bullet T\bullet\ln K_{Homeostasis}$;

$$\text{equilibrium } K_{eq}=\frac{X^{m}_{1Ox^{n+}}\bullet X^{n}_{2Red}}{X^{m}_{1Red}\bullet X^{n}_{2Ox^{n+}}}\ \text{ stop homeostasis to zero } 0=\Delta G_{eq}+R\bullet T\bullet\ln K_{eq}\ .$$

The reduced form supply negative **(-)Red$_1$-ne**$^-$**⇔Ox$_1$** electric charge **n** (n=2) number of electrons **ne**$^-$ flow to oxidized form with positive **(+)Ox$_2$+ne**$^-$**<=>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 $EMF=E^{\circ}_{Red}-E^{\circ}_{Ox}$ **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÷3.5 V**) can accomplish work **W=EMF•F•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 six oxygen molecules: O_{2aqua}**+4** H_3O^+**+4** e^-**=6** H_2O; inverse standard potential -**E°**$_{O2}$= -1.0868 V.

$C_6H_{12}O_6+42H_2O=24H_3O^++6H_3O^++6HCO_3^-+24\ e^-$; standard potential **E°**$_{C6H12O6}$=-0.1392 Volts. 6th page

$\Delta G_{eq}=(E°_{C6H12O6}-E°_{O2})\bullet F\bullet n=(-0.1392-1.0868)*96485*24=-1.226*96485*24=-2840\ ^{kJ}/_{mol}$:

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 in water $G_{O2aqua}=303.1\ ^{kJ}/_{mol}$ creating fire safe energy level $G_{O2Biochem}=78.08\ ^{kJ}/_{mol}$.

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 **ATP**$^{4-}$, **ADP**$^{3-}$, HPO_4^{2-} and H_3O^+ 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 **ATP**ase 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<=>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**$^{2+}$=> **Fe**$^{3+}$ **+ Cu**$^+$ describing with two **2** half-reactions (**Ox** ⇔**Red** systems) are used free electrons:

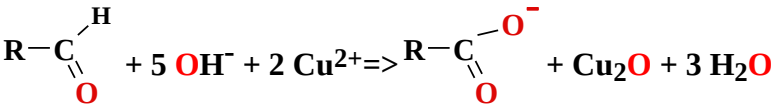
Red **Fe**$^{2+}$ **- e**$^-$<=> **Fe**$^{3+}$. The electron-donating- **e**$^-$ molecule is called Red the **reducing** agent or **reductant**;
Ox **Cu**$^{2+}$ **+ e**$^-$<=> **Cu**$^+$. The electron-accepting **+e**$^-$ molecule is the Ox **oxidising** agent or **oxidant.**

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

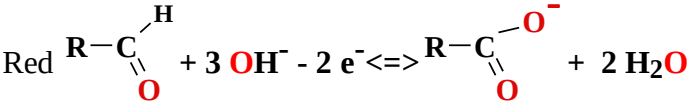
Reductant and oxidant free electrons are intermediates: electrons **donor**⇔**ne**$^-$+electrons **acceptor**.

Similar in Brensted protolysis with one proton, however in **RedOx** system free electron number **n** is integer equal or higher as one **n**≥**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:



Ox **2 Cu**$^{2+}$ **+ 2 e**$^-$ **+ 2 OH**$^-$ <=> **Cu**$_2$**O + H**$_2$**O**

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**$_2$**O**.

Dehydrogenation is Oxidation reaction

2.2<2.55<2.58<3.04<3.44
H < C ≈ S < N< O
ΔREN = X - **C** in order
-0.33<0.0<0.03<0.49<0.89

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.

In four valences make sum: for CH_4 is 4*-0.33=-1.32 **8** e^-; for H_3C-CH_3 is 3*-0.33+0=-0.99 **7** e^-;
for $H_2C=CH_2$ ΔREN=2*-0.33+2*0=-0.66 **6** e^-; for HC≡CH ΔREN=0.33+3*0=-0.33 **5** e^-;
for **H_3C=O** ΔREN=2*-0.33+0+2*0.89=-0.66+1.78=1.12 **4** e^-; for H_3C-**HC=O** ΔREN=-0.33+0+2*0.89=1.45 **3** e^-;
for H-**C=O-O-H** ΔREN=-0.33+3*0.89=-0.33+2.67=2.34 **2** e^-; for H_3C-**C=O-O-H** ΔREN=0+3*0.89=2.67 e^-;
for **O=C=O** ΔREN=4*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 ≡**C-C**≡ bond are shared equally, so each **:::C: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 ≡**C-:**, leaving **::·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 $CH_2=CH_2$** (**6** bound e^-) or to an **alkyne CH≡CH** (**5** bound e^-). This **oxidation** is loss of two hydrogen – **H** atoms from each of two adjacent carbon atoms: (2*7=**14**.2*6=**12**. 2*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 N_2** to ammonia **NH_3** :**6 H^+ + 6 e^- + °N_2=>2 $^{(-3)}NH_3$**, 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 **Fe^{2+} / Fe^{3+} Red Ox** pair can transfer an electron e^- to the **Cu^+ / Cu^{2+} RedOx** pair: **Fe^{2+} + Cu^{2+}=>Fe^{3+} + Cu^+**

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:**AH_2=>A+2e^-+2H^+**, where **AH_2** is **hydrogen** atoms **electrons donors**.

Note: Protolysis is proton jump H^+ in water medium only but not removal of a hydrogen atom. (H^+ + e^-).) **AH_2** and **A** together constitute a conjugate **Red Ox** pair (**A** / **AH_2**), in which **AH_2 reduce** another compound **B** (or **Red Ox** pair, **B** / **BH_2**) by transfer of hydrogen **H** atoms:

AH_2 + B =>A + BH_2

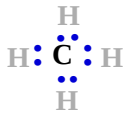
3. Transferred of hydride ion ($:H^-$), which has two **2** electrons e^-.

occurs with the B3 vitamin as **NADH<=>NAD^++$:H^-$** in **dehydrogenases**, enzymes, described below.

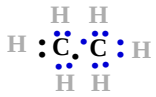
4. Through direct combination with **oxygen O_2**. In this case, oxygen O_2 combines with an **organic reductant** and is **covalently incorporated** in the product, as in the **oxidation** of a hydrocarbon to an alcohol by **transferred 1/2 O_2** presented as **O** squeezed between carbon and hydrogen atoms **≡C-H <=> ≡C-O-H**

R-H_2C-H+.:O:.=>R-H_2C-::O::-H

Methane **8 e**$^-$
ΔREN=-1,32



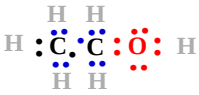
Ethane C**7 e**$^-$
ΔREN =-0.99



Ethene C**6 e**$^-$
ΔREN =-0.66

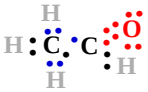
Acetylene **5 e**$^-$
ΔREN= -0.33

Ethanol C**5 e**$^-$
ΔREN =0.23
(alcohol)

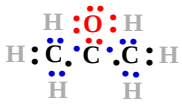


Formaldehyde **4 e**$^-$
ΔREN =1.12

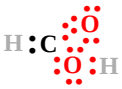
Acetaldehyde **3 e**$^-$
ΔREN =1.45



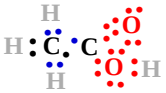
Acetone **2 e**$^-$
ΔREN=1.78



Formic acid **2 e**$^-$
ΔREN =2.34



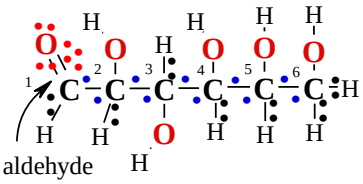
Acetic acid **e**$^-$
(carboxylic acid)
ΔREN=2.67



Carbon dioxide **0**
ΔREN =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 $FADH_2$ (vitamin B_2) or hydride ion **(:H**$^-$**)** with NADH (vitamin B_3) 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 2**e**$^-$ 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

7 C**:**-H, 5 C●-●C: 7*2+5*2=24 electrons

$C_6H_{12}O_6$+6**O_{2aqua}**+6**H_2O**=>6H_3O^++6HCO_3^-;

24H_3O^++6H_3O^++6HCO_3^-<=>**$C_6H_{12}O_6$**+42**H_2O**-24 e$^-$; **$E^\circ_{C6H12O6}$**=? V;

6*(**O_{2aqua}+4 H_3O^++ 4 e$^-$= 6 H_2O**) Suchotina **E°_{O2}**=1,0868 V;

-2840 $^{kJ}/_{mol}$=**$\Delta G_{eq}=\Delta E^\circ_{eq}\bullet F\bullet n=(E^\circ_{C6H12O6}-E^\circ_{O2})\bullet F\bullet n$** .

K_{eq}=exp(2840000/8.3144/298.15)=7.06*10^{90}=

-2840000/96485/24=**$\Delta G_{eq}/F/n=(E^\circ_{C6H12O6}-E^\circ_{O2})$**=-1.226 V;

$E^\circ_{C6H12O6}=\Delta E^\circ_{eq}+E^\circ_{O2}$=-1,226+1,0868=-0,1392 Volts. 6th page

24H_3O^++6H_3O^++6HCO_3^-=**$C_6H_{12}O_6$**+42**H_2O**-24 e$^-$;**$E^\circ_{C6H12O6}$**=-0.1392 V;

Hydrogen and Glucose standard reduction poyentials are:

$E^\circ_{H+/H}$=-0,2965V and **$E^\circ_{C6H12O6}$**=0.1392 V

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 CH_4 **8 e**$^-$ to carbon dioxide **CO_2 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=ΔREN to 3.56=ΔREN . 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**$^-$**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 CH_4 **8 e**$^-$ missing **n** is zero **n** =0 to carbon dioxide **CO_2 0** missing are eight **n**=8.

-2840000/96485/24=**$\Delta G_{eq}/F/n=(E^\circ_{C6H12O6}-E^\circ_{O2})=(E^\circ_{C6H12O6}$**--1,0868)=-1.226 Volts;

$E^\circ_{C6H12O6}=\Delta E^\circ_{eq}+E^\circ_{O2}$=-1,226+1,0868=-0,1392 Volts . 6th page

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

Attractor pH=7.36 staying at equilibrium have true p**O**H=6.64 value as pK_w=14= pH+p**O**H =7.36 +6.64**.**

Disaccount the water mass [$\mathbf{H_2O}$]=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:

$$\mathbf{\underline{H}(Pt)} <=> \mathbf{H^+ + e^-};\ \mathbf{E}_{classic}=E_{o\_classic}+0.0591\bullet\log \mathbf{K}°_{classic\mathbf{H}(Pt)}=0+0.0591\bullet\log[H^+]=0+0.0591\bullet\log(1\ M)=0\ Volts.$$

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

The ratio [H_3O^+]/[$\mathbf{H_2O}$]=1 M/52.5 M=$X_{\mathbf{H3O+}}/X_{\mathbf{H2O}}$ is mol fraction instead molarity [$\mathbf{H^+}$]=1 M at classic potential expression. The water account gave thermodynamic standard $E°_H$=0.10166 V on potential scale.

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

$$\mathbf{E}=E°_H+\frac{\ln(10)\bullet R\bullet T}{F\bullet 1}\bullet\log\frac{X_{H_3O^+}}{X_{H_2O}}=E_o+E°_H+0.0591*\log(1/52.5)=0.10166-0.10166=0\ V.$$

As ratio $\mathbf{1=K_{H(Pt)}}=X_{\mathbf{H3O+}}/X_{\mathbf{H2O}}$ is one than $E°_H$=0.10166 V is thermodynamic standard potential:

$$\mathbf{E}=E°_H+\frac{\ln(10)\bullet R\bullet T}{F\bullet 1}\bullet\log\frac{X_{H_3O^+}}{X_{H_2O}}=0.10166+0.0591*\log(1)=0.10166\ V.$$ Metal oxidation free energy change minimum is different endoergic $\Delta\mathbf{G_{eq}}=E°_H\bullet F\bullet 1\bullet 1=0.10166*96485*1=9.81\ ^{kJ}/_{mol}$ instead Alberty is exoergic .

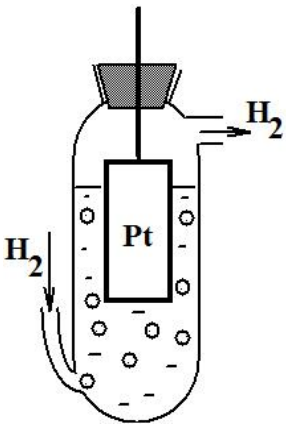
Alberty Hess value is exoergic; $\Delta\mathbf{G}_{Hess\_eq}=G_{H3O+}+G_{\underline{e}^-}-(G_{\mathbf{H}(Pt)}+G_{\mathbf{H2O}})=22,44+0-(\mathbf{51,05}+0)=\mathbf{-28,61}\ ^{kJ}/_{mol}$.

Free energy changes are determined on water and carbon dioxide gas zero $G_{\mathbf{H2O}}=G_{\mathbf{CO2}gas}=G_{\underline{e}^-}=0\ ^{kJ}/_{mol}$ reference scale. Iterative found on absolute scale hydrogen standard potential is: $E°_H$= -0,29654 V. Equilibrium free energy minimum is exoergic: $\Delta\mathbf{G_{eq}}=E°_H\bullet F\bullet 1\bullet 1=-0,29654*96485*1=\mathbf{-28,61}\ ^{kJ}/_{mol}$ coinciding with Alberty data. Absolute potential scale slips by ΔE=-0,29654-0,10166= -0,3982 Volts down. Nernst's hydrogen equilibrium constant is grater as one: $\mathbf{K_{H(Pt)\_Red}}=[H_3O^+]*[\mathbf{e}^-]/[\mathbf{H_2O}]/[H(Pt)]=EXP(-\Delta\mathbf{G}_{Alberty}/R/T)=EXP(\mathbf{28612}/8.3144/298.15)=102954$.

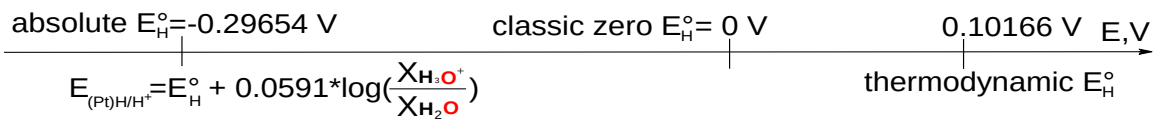
I type electrode Metal interface **H(Pt)** / on its cation H_3O^+ solution application.

High rate protolysis attractors [H_3O^+]=$10^{-7,36}$ M , pH=7.36 and water mass [$\mathbf{H_2O}$]=997/18=55.3 M account in liter shows metal hydrogen strong reducing potential: $\mathbf{E}_{pH=7,36}$=-0,29654+0,0591*log($10^{-7,36}$/55,3)= -0,8345 V and free energy change minimum $\Delta\mathbf{G_{eq}}_{pH\_7,36}=E°_H\bullet F\bullet 1=-0,8345*96485*1/1000=-80,5\ ^{kJ}/_{mol}$.

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



Platinum sheet immersed in hydroxonium ions [H^+]=[H_3O^+]=[H_2SO_4]=1 M sulfuric acid solutions $\mathbf{\underline{H}(Pt)} <=> \mathbf{H^+ + e^-}$: $\mathbf{E}=\mathbf{E}°+0.0591\bullet\log[H^+]=\mathbf{0.0}+0.0591\bullet\log(1\ M)=\mathbf{0}$ V is classic. Ratio [H_3O^+]/[$\mathbf{H_2O}$]=1/52.5=$X_{\mathbf{H3O+}}/X_{\mathbf{H2O}}$ give classic zero **0** insted thermodynamic standard potential: $E°_H$=0.10166 V and from Alberty data on absolute scale absolute standard potential is $E°_H$= -0,29654 Volts.



Absolute standard potential $E°_H$=-0,29654 V based on Alberty hydrogen data $G_{\mathbf{H2}gas}=\mathbf{85,64}\ ^{kJ}/_{mol}$ and $G_{\mathbf{H2}aq}=\mathbf{103,24}\ ^{kJ}/_{mol}$, which was detected on water and carbon dioxide gas zero scale $G_{\mathbf{H2O}}=G_{\mathbf{CO2}gas}=G_{\underline{e}^-}=0\ ^{kJ}/_{mol}$. reducing agent at pH=7,36 , [H_3O^+]=$10^{-7,36}$ M with potential **E**=-0,2965+0,0591*log($10^{\wedge(-7,36)}$/55,3)=-0,8345 V. is strong reductant. Free energy content in one mol metal hydrogen is: $G_{\mathbf{H}(Pt)}=\mathbf{51.05}\ ^{kJ}/_{mol}$.

Table 1. Nernst's half- / **inverse** reactions	Standard potentials E° Data from [1-24]	Classic water disaccount 0 V	Thermodynamic. scale 0.10166 V	Absolute -0.3982 V
OH^- = HO+ e^-	CRC	2.020	2.1217	1.7235
$4H_2O=H_2O_{2aqua}+2H_3O^++2\ e^-$	Suchotina	1.776	2.0837	1.6855
$H_2O_2+2H_2O=O^-_{2aqua}+2H_3O^++e^-$	David Harris	1.276	1.4811	1.0829
$6H_2O=O_{2aqua}+4H_3O^++4e^-$	Suchotina	1.229	1.4850	1.0868
$HNO_2+4H_2O=NO_3^-+3H_3O^++2e^-$	University Alberta	0.928	1.2352	0.8370
$NO_2^-+3H_2O=NO_3^-+2H_3O^++2e^-$	David Harris	0.835	1.0913	0.6931
Hydroquinone+$2H_2O$=p-quinone+$2H_3O^++2e^-$		0.699	0.9041	0.5059
$H_2O_{2aqua}+2H_2O=O_{2aqua}+2H_3O^++2e^-$	University Alberta	0.695	0.8477	0.4495
$H_2O_{2aqua}+H_2O=O_{2aqua}+H_3O^++H^-$	University Alberta	0.695	0.8477	0.4495
$Fe^{2+}=Fe^{3+}+e^-$	University Alberta	0.769	0.8707	0.4725
Ubiquinol+$2H_2O$=Ubiquinone+$2H_3O^++2e^-$		0.459	0.6638	0.2656
Succinate^{2-}+$2H_2O$=Fumarate^{2-}+$2H_3O^++2e^-$		0.4447	0.6494	0.2512
ButyrylCoA+$2H_2O$=CrotonylCoA+$2H_3O^++2e^-$		0.399	0.6038	0.2056
AscorbicAcid+$2H_2O=C_6H_6O_6+2H_3O^++2e^-$	DC.Harris	0.390	0.5947	0.1965
glycolate+$2H_2O$=Glyoxylate+$H^-+H_3O^+$	D.C.Harris	0.324	0.5287	0.1305
$HOO^-+H_2O=O_{2aqua}+H_3O^++2e^-$	Aris Kaksis	-	-	0.07587
Fe^{2+}=Cytochrome F $Fe^{3+}+e^-$	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
Malate^{2-}+$2H_2O$=Oxalo-acetate^{2-}+$2H_3O^++2e^-$		0.248	0.4528	0.0546
Fe^{2+}=Cytochrome a3 $Fe^{3+}+e^-$		0.350	0.4517	0.0535
Lactate$^-$ +H_2O=Pyruvate$^-$+H_3O^++H^-(H^++$2e^-$)$^-$		0.229	0.3823	-0.0159
$FADH_2+2H_2O$=FADfree+$2H_3O^++2e^-$;		0.195	0.3998	0.0016
$CH_3COO^-+2H_2O$=glycolate+$H^-+H_3O^+$;	D.C.Harris	0.161	0.3652	-0.0330
$C_6H_{12}O_6$+42H_2O=30H_3O^++6HCO_3^-+24 e^-; 6th page	Kaksis	0.0701	0.2590	-0.1392
H_2S_{aq}+$2H_2O$=$S_{rhombic}$+$2H_3O^+$+$2e^-$;	CRC 2010	0.142	0.3467	-0.0515
$CH_3CH_2OH+H_2O=CH_3CHO+H_3O^++H^-$;	KortlyShucha	0.190	0.3432	-0.0550
Fe^{2+}=Cytochrome a $Fe^{3+}+e^-$		0.2900	0.3917	-0.0065
2GlutathSH+$2H_2O$=GlutaS-Sthione+$2H_3O^++2e^-$		0.1841	0.3888	-0.0094
Fe^{2+}=Cytochrome c $Fe^{3+}+e^-$		0.2540	0.3557	-0.0425
LipSHSH+$2H_2O$=LipoicAcidS-S+$2H_3O^++2e^-$		0.1241	0.3288	-0.0694
Fe^{2+}=Cytochrome c1 $Fe^{3+}+e^-$		0.2200	0.3217	-0.0765
β-OH Butyrate$^-$+$2H_2O$=AcetoAcetate$^-$+$2H_3O^++2e^-$		0.0681	0.2728	-0.1254
isocitrate^{2-}+$2H_2O$=α-Ketoglutarate^{2-}+CO_2+$2H_3O^+$+2e-		0.0341	0.2388	-0.1594
Nernst's H_{2aq}+$2H_2O$=$2H_3O^+$+$2e^-$; Kaksis **ΔG_{Hess_H3O+}**=58,12 kJ/mol		on graphite electrode oxidation		0.3020
Inverse: $2H_3O^+$+$2e^-$=**H_{2aq}**+$2H_2O$; **ΔG_{Hess_H2aq}**=-58,12 kJ/mol		on graphite electrode reduction		-0.3020
H_{2aq}=2**H(Pt)**+**H_2O**; **$\Delta G_{Alberty\_sp\_H(Pt)}=2G_{H(Pt)}+G_{H2O}-(G_{H2aq})$=-1.14** kJ/mol		**$K_{sp\_H(Pt)}=[H(Pt)]^2*[H_2O]/[H_{2aq}]$**=1.584		
H(Pt)+H_2O=H_3O^++e^-; [H_3O^+]=1 M pH=0 classic zero		0; [H_2SO_4]=1 M	0.10166	**-0.2965**
Luciferin+OH^-=?luciferin+CO_2 aqua+OH^-+3H($3H^+$+$3e^-$)+e^-		0.0000	0.1017	-0.2965
Fe^{2+}=Cytochrome b $Fe^{3+}+e^-$		0.0770	0.1787	-0.2195
CH_3CHO+$3H_2O$=CH_3COOH+$2H_3O^++2e^-$	Suchotina	-0.1180	0.1382	-0.2600
Glycaldeh3-P^{2-}+H_2O+HPO_4^{2-}=**13PGlycerate^{4-}+H_3O^++H^-;**		-0.1314	0.0218	-0.3764
NADPH=$NADP^+$+H^-;		-0.1170	-0.0153	-0.4135
NADH=NAD^++H^-;	David Harris	-0.1130	-0.0113	-0.4095
O^-_{2aqua}=O_{2aqua}+e-	Suchotina	-0.2450	-0.1433	-0.5415
Ferredoxin Fe^{2+}=Ferredoxin $Fe^{3+}+e^-$		-0.4320	-0.3303	-0.7285
$C_6H_{12}O_6$+$4H_2O$=$2C_3H_4O_3$+$4H_3O^+$ + $4e^-$	Stryer	-0.5427	-0.3380	-0.7362
S^{2-}=$S_{rhombic}$+2 e^-;	CRC 2010	-0.4763	-0.3746	-0.7728
HS^-+OH^-=**$S_{rhombic}$**+H_2O+2e^-;	CRC 2010	-0.4780	-0.3248	-0.7230
H(Pt)+OH^-=H_2O+e^-	Suchotina	-0.8280	-0.6233	-1.0215
Ubiquinol6+$2H_2O$=Ubiquinone6+$2H_3O^++2e^-$	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+H_2O⇔H_3O^++e^- is **$\Delta G_{Alberty(Pt)H}=G_{H3O+}+G_{e-}-(G_{H2O}+G_{H(Pt)})$**=22,44+0-(0+**51**)=**-28,61** kJ/mol. Absolute scale

$E^{\circ}_{Habsolute} = \Delta G_{Alberty(Pt)H}/F/1 = \mathbf{-28610}/96485/1 = -0{,}29654$ V. High rate protolysis Attractor $[H_3O^+] = 10^{-7.36}$ M on zero scale $G_{H2O} = G_{CO2gas} = 0$ $^{kJ}/_{mol}$ activate metallic Hydrogen (Pt)H and Glucose $\mathbf{C_6H_{12}O_6}$ to strong reduction potential .

Table 1. Standard Electrodes Potentials classic, Thermodynamic, absolute in Volts

Atom	Reduced form = Oxidized form	H_2O disaccount classic zero E_o	Thermodynamic. scale 0.10166 V	Absolute scale -0.3982 V
H	$\underline{\mathbf{H}(Pt)} + H_2O = H_3O^+ + (Pt) + \mathbf{e^-}$	classic zero **0**	**0.10166**	-0.2965
	$\underline{\mathbf{H}(Pt)} + OH^- = H_2O + (Pt) + \mathbf{e^-}$	-0.828	-0.8294	-1.2272
	$\mathbf{H_{2aq} + 2H_2O = 2H_3O^+ + 2e^-}$ **; graphite Kaksis**	-	-	0.302
O	$6H_2O = O_2^{(g)} + 4\,H_3O^+ + \mathbf{4e^-}$	1.2288	+1.48466	1.0865
	$H_2O_2 + 2H_2O = O^-_{2aqua} + 2H_3O^+ + \mathbf{e^-}$	1.2764	+1.58416	1.0829
	$4H_2O = H_2O_2 + 2\,H_3O^+ + \mathbf{2e^-}$	1.776	+2.08366	1.6855
	$\mathbf{H_2O_{2aqua} + 2H_2O = O_{2aqua} + 2H_3O^+ + 2e^-}$ University Alberta	0.6945	0.8477	0.4495
	$\mathbf{HOO^- + H_2O = O_{2aqua} + H_3O^+ + 2e^-}$; Kaksis	-	-	0.07587
N	$NO_2^- + 2OH^- = NO_3^- + H_2O + \mathbf{2e^-}$; Suchotina	0.01	0.06016	-0.3380
	$H\,NO_2 + 4H_2O = NO_3^- + 3H_3O^+ + \mathbf{2e^-}$; Kortly, Shucha	1.63	1.93765	1.5395
	$NO^{(g)} + 6H_2O = NO_3^- + 4H_3O^+ + \mathbf{3e^-}$; Kortly, Shucha	0.96	1.26765	0.8695
	$NH_4^+ + 13H_2O = NO_3^- + 10H_3O^+ + \mathbf{8e^-}$; Suchotina	0.87	1.13903	0.74083
Br	$2Br^- = Br_2(aq) + \mathbf{2e^-}$; CRC	1.0873	1.18896	0.79076
Bi	$Bi\,O^+ + 6H_2O = BiO_3^- + 4H_3O^+ + \mathbf{2e^-}$; Suchotina	1.80	2.210645	1.81245
Mn H^+	$Mn^{2+} + 12H_2O = MnO_4^- + 8H_3O^+ + \mathbf{5e^-}$; Kortly, Shucha	1.51	1.85885	1.46065
$\mathbf{H_2O}$	$\underline{MnO_2}\downarrow + 4OH^- = MnO_4^- + 2H_2O + \mathbf{3e^-}$; Suchotina	0.603	0.63600	0.23780
$\mathbf{OH^-}$	$MnO_4^{2-} = MnO_4^- + \mathbf{e^-}$; Suchotina	0.558	0.65966	0.26146
Pb	$Pb^{2+} + 6H_2O = \underline{PbO_2}(s) + 4H_3O^+ + \mathbf{2e^-}$; Kortly, Shucha	1.455	1.865645	1.46745
S	$H_3SO_3 + 3H_2O = SO_4^{2-} + 2H_3O^+ + \mathbf{2e^-}$; Suchotina	0.172	0.42815	0.029953
	$SO_3^{2-} + 2OH^- = SO_4^{2-} + H_2O + \mathbf{2e^-}$; Suchotina	-0.93	-0.87984	-1.27804
	$S^{2-} = \underline{S}(s) + \mathbf{2e^-}$; Kortly, Shucha	-0.48	-0.37834	-0.77654
	$H_2S + 2H_2O = \underline{S}(s) + 2H_3O^+ + \mathbf{2e^-}$; Kortly, Shucha	0.141	0.34566	-0.05254
	$2S_2O_3^{2-} = S_4O_6^{2-} + \mathbf{2e^-}$; Suchotina	0.08	0.18166	-0.2165
Fe	$Fe^{2+} = Fe^{3+} + \mathbf{e^-}$	0.769	0.8707	0.4725
Ag	$Ag(s) = Ag^+ + \mathbf{e^-}$; Kortly, Shucha	0.799	0.90066	0.5025
I	$2Ag(s) + 2OH^- = \mathbf{Ag_2O}(s) + H_2O + \mathbf{2e^-}$; Suchotina	0.345	0.39516	-0.00304
Cu	$3I^- = I_3^- + \mathbf{2e^-}$; Kortly, Shucha	0.6276	0.72926	0.33106
F	$Cu(Hg) = Cu^{2+} + (Hg) + \mathbf{2e^-}$; Kortly, Shucha	0.3435	0.44516	0.04696
Cl	$2F^- = F_2(g) + \mathbf{2e^-}$; Kortly, Shucha	2.87	2.97166	2.5735
	$2Cl^- = Cl_2(g) + \mathbf{2e^-}$; Kortly, Shucha	1.358	1.45966	1.06146
Cr	$Cl_2(g) + 4H_2O = 2HOCl + 2H_3O^+ + \mathbf{2e^-}$; Kortly, Shucha	1.63	1.93765	1.53945
	$2Cr^{3+} + 21H_2O = Cr_2O_7^{2-} + 14H_3O^+ + \mathbf{6e^-}$; Kortly, Shucha	1.33	1.7921	1.3939
C	$Cr^{3+} + 11H_2O = HCrO_4^- + 7H_3O^+ + \mathbf{3e^-}$; Kortly, Shucha	1.20	1.6793	1.2811
Cr	$H_2C_2O_4 + 2H_2O = 2CO_2 + 2H_3O^+ + \mathbf{2e^-}$; Suchotina	-0.49	-0.2853	-0.6835
Zn	$Cr = Cr^{3+} + \mathbf{3e^-}$; Suchotina	-0.744	-0.6423	-1.0405
Al	$Zn = Zn^{2+} + \mathbf{2e^-}$; Kortly, Shucha	-0.7628	-0.6611	-1.0593
H. C	$Ubiquinol + 2H_2O = Ubiquinone + 2H_3O^+ + \mathbf{2e^-}$	0.459	0.664	0.2656
	$Succinate^{2-} + 2H_2O = Fumarate^{2-} + 2H_3O^+ + \mathbf{2e^-}$	0.445	0.650	0.2516
	$AscorbicAcid + 2H_2O = C_6H_6O_6 + 2H_3O^+ + \mathbf{2e^-}$	0.390	0.595	0.1965
	$glycolate + 2H_2O = Glyoxylate + 2H_3O^+ + \mathbf{2e^-}$	0.324	0.529	0.1305
	$CH_3CH_2OH + H_2O = CH_3CHO + H_3O^+ + H^-$	0.190	0.343	-0.0550
	$C_6H_{12}O_6 + 42H_2O = 30H_3O^+ + 6HCO_3^- + \mathbf{24e^-}$ **; Kaksis**	0.0701	0.2590	-0.1392

Ox: $O_{2aqua}+4H_3O^+ + 4e^- \Leftrightarrow 6H_2O$; E°_{O2}=**1.0868** Volti; Red: $\underline{4(Pt)H}+4H_2O \Leftrightarrow 4H_3O^+ + 4e^-$; E°_H=**-0.2965** V

$O_{2aqua}+\underline{4(Pt)H} => 2H_2O$; $\Delta G_{eq2H2O}=(E^\circ_H - E^\circ_{O2})\bullet F\bullet 1\bullet 4=(\mathbf{-0.2965-1.0868})*96485*4=2*-266.94$ $^{kJ}/_{mol}$;

$\Delta G_{eq2H2O}=2G_{H2O}-4G_{H(Pt)}-G_{O2aqua}=2*0-(4*G_{H(Pt)}+\mathbf{330})=-533.9=2*-267$ $^{kJ}/_{mol}$;

$G_{H(Pt)}=(2G_{H2O}-\Delta G_{eq2H2O}-G_{O2aqua})/4=(2*0+533.886-\mathbf{330})/4=\mathbf{51.05}$ $^{kJ}/_{mol}$; $G_{(Pt)H}=\mathbf{51.05}$ $^{kJ}/_{mol}$;

If homeostasis zero are $G_{H2O}=G_{CO2gas}=0$ $^{kJ}/_{mol}$.

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

$$\mathbf{E=E^\circ+\frac{0{,}0591}{n}\bullet\log(K_{eq})};\ \mathbf{E=E^\circ+\frac{0.0615V}{n}\bullet\log(K_{eq})};\ \mathbf{K_{eq}}=\left(\frac{[Ox^{n+}]}{[Red]}\right);$$

Half-reactions involve high rate protolysis equilibrium attractors pH=7.36 concentration $[\mathbf{H_3O^+}]=10^{-7.36}$ M and water concentration $[\mathbf{H_2O}]$=55.3 M. Water protonation $\mathbf{H^+}$ form **hydroxonium** ions $\mathbf{H_3O^+}$ and rule the homeostasis reactions promotion. Thermodynamic calculations demand use in expressions the **standard reduction potential** $\mathbf{E^\circ_{H2O}}$ and $\mathbf{K_{eq}}$. Therefore the **standard reduction potentials** $\mathbf{E^\circ_{H2O}}$ given in Table 1 are indispensible used throughout this book: classic standard **E°** and thermodynamic $\mathbf{E^\circ_{H2O}}$ or **E°37;** .

Notice: For complete calculations at standard temperature are used standard potential $\mathbf{E^\circ_{H2O}}$ **(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** $\mathbf{E_{Red}}$ and $\mathbf{E_{Ox}}$ for two **2** half-cells reactions. Therefore $\mathbf{EMF=E_{Red}-E_{Ox}}$ values are difference reductants minus oxidants. Electrons will flow to side half-cell with more positive $\mathbf{E^\circ_{Ox2}}$ and the trend strength is proportional to negative $\mathbf{\Delta E^\circ<0}$ value because always $\mathbf{E^\circ_{Red1}<E^\circ_{Ox2}}$: $\mathbf{\Delta E^\circ=E^\circ_{Red1}-E^\circ_{Ox2}}$.

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

-W is proportional ~ to **ΔE°**. **Oxidized** form $\mathbf{Ox^{n+}}$ formed with lost electrons $\mathbf{ne^-}$ flows. In this process **RedOx** system are accomplished the chemical work **W= -ΔE°•F•n** by spending given **RedOx** system **free energy** in conversion of **reduced** form **Red1** and $\mathbf{Ox2^{n+}}$ to **oxidized** form $\mathbf{Ox1^{n+}}$and **Red2** :

$\mathbf{Red1 - ne^- \Leftrightarrow Ox1^{n+}}$; $\mathbf{Ox2^{n+} + ne^- \Leftrightarrow Red2}$; $\mathbf{W = -\Delta E^\circ\bullet F\bullet n = -(E^\circ_{Red1} - E^\circ_{Ox2})\bullet F\bullet n =- \Delta G_{eq}= -(G_{Red1}-G_{Ox2})}$ (4)

Here **n** represents the number of electrons $\mathbf{ne^-}$ 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** $\mathbf{\Delta G_A}$ 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 $\mathbf{\Delta G^\circ_A}$ has the pure compound **A** itself per **1 mol** amount, no mixture of compounds, the **chemical potential** $\mathbf{\mu_A}$ of compound **A** if amount with in mixture others for molar number is $\mathbf{\Delta n_A = 1\ mol}$

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

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

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

Conflict in consideration pure compound $\mathbf{\Delta G^\circ_A}$ greater as mixture amount for one mole $|\mathbf{\mu_A}|<|\mathbf{\Delta G^\circ_A}|$.

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.

$\mathbf{Red <=> Ox^{n+} + ne^-}$; $\mathbf{W = - E\bullet F\bullet n = G_{Red}}$; $\mathbf{\Sigma\mu_{Red} + E\bullet F\bullet n = \Sigma\mu_{Oxn+} + n\ \mu_{e-}}$ (6)

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

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

$\mathbf{G_{Red}} = (\Sigma\boldsymbol{\mu}_{Oxn+} + \mathbf{n}\ \mu_{e-}) - \Sigma\mu_{Red} = \mathbf{E{\bullet}F{\bullet}n}$, and **equilibrium** establishes when electric work is compensated by free energy change $\mathbf{-W = G_{Red} = E{\bullet}F{\bullet}n}$ and on electrode absolute **potential E** formes which remains unknown.

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

$$\mathbf{G_{Red} + R{\bullet}T{\bullet}\ln(X_{Red}) + E{\bullet}F{\bullet}n = G_{Oxn+} + R{\bullet}T{\bullet}\ln(X_{Oxn+}) + n\ G_{e-} + n{\bullet}R{\bullet}T{\bullet}\ln(X_{e-})} \quad (7)$$

$$\mathbf{\Delta G_{eq} = E{\bullet}F{\bullet}n = G_{Oxn+} + n\ G_{e-} - G_{Red} + R{\bullet}T{\bullet}\ln(\ X_{Oxn+} / X_{Red}\ )}$$

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

$$\mathbf{|\ G_{HessRed}\ | = |\ \Delta G°_{Oxn+} + n\Delta G°_{e} - \Delta G°_{Red}\ | > |\ E°_{Red}{\bullet}F{\bullet}n\ | = |\ G_{Red}\ |} \quad \text{and} \quad (8)$$

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

nor reductant: $\mathbf{G_{RedHomeostasis} = E_{Red}{\bullet}F{\bullet}n = E°_{Red}{\bullet}F{\bullet}n + R{\bullet}T{\bullet}\ln(X_{Oxn+}/X_{Red})}$,

nor oxidant: $\mathbf{G_{OxHomeostasis} = -E_{Ox}{\bullet}F{\bullet}n = -E°_{Ox}{\bullet}F{\bullet}n - R{\bullet}T{\bullet}\ln(X_{Oxn+}/X_{Red})}$ (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 $|+\mathbf{m'{\bullet}ne^-}| = |-\mathbf{n'{\bullet}me^-}|$ we have balanced **oxidation-redaction** reaction and can get the summary reaction of both half-reactions : **(-)** $\mathbf{Red_1 \Leftrightarrow Ox_1^{n+} + ne^-|{\bullet}m'}$; **(+)** $\mathbf{Ox_2^{m+} + me^- \Leftrightarrow Red_2|{\bullet}n'}$

$\mathbf{m'{\bullet}Red_1 + n'{\bullet}Ox_2^{m+} => m'{\bullet}Ox_1^{n+} + n'{\bullet}Red_2}$ **; reactants** forming **products** direction of reaction.

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

$\mathbf{\Delta G_{eq} = m'{\bullet}G_{Red1} - n'{\bullet}G_{2Oxn+} = m'{\bullet}E°_{Red1}{\bullet}F{\bullet}n - n'{\bullet}E°_{2Oxn+}{\bullet}F{\bullet}m = (E°_{Red1} - E°_{2Oxn+}){\bullet}F{\bullet}(m'n = n'm)}$, where $\mathbf{n'/N\ m'/N = nm}$ is equivalent - common number of electrons **e$^-$** involved in **RedOx** reaction $\mathbf{n'm' \le n{\bullet}m}$. can be less by number **N** of common devider $\mathbf{Red_1}$ or $\mathbf{Ox_2^{m+}}$. The **free-energy** content **G** according (9) at known concentrations $\mathbf{X_{Red}}$ and $\mathbf{X_{Oxn+}}$ of the each species ($\mathbf{G_{red}}$ and $\mathbf{G_{Oxn+}}$) participating in the reaction.

$$\mathbf{\Delta G_{eq} = m'{\bullet}G_{Red1} + n'{\bullet}G_{2Oxn+} = m'{\bullet}E_{Red1}{\bullet}F{\bullet}n - n'{\bullet}E_{2Oxn+}{\bullet}F{\bullet}m = (E_{Red1} - E_{2Oxn+}){\bullet}F{\bullet}(m'n = n'm) =}$$

$$\mathbf{= (E°_{Red1} - E°_{2Oxn+}){\bullet}F{\bullet}(m'n = n'm) + R{\bullet}T{\bullet}\ln((X_{1Oxn+}{\bullet}\ X_{2Red})/(X_{1Red}{\bullet}\ X_{2Oxn+}))}, \quad \text{where} \quad (10)$$

$\mathbf{K_{homeostasis}} = \dfrac{\mathbf{X^m_{1Ox^{n+}}} \bullet \mathbf{X^n_{2Red}}}{\mathbf{X^m_{1Red}} \bullet \mathbf{X^n_{2Ox^{n+}}}}$ is homeostasis ratio as a multiple **products** over **reactants** concentrations. Equilibrium free energy change $\mathbf{\Delta G_{eq} = \Delta G_{min}}$ is Prigogine attractor constant $\mathbf{K_{eq}}$ calculation $\mathbf{\Delta G_{eq} = (E°_{Red1} - E°_{2Oxn+}){\bullet}F{\bullet}(m'n = n'm)}$; $\mathbf{K_{eq} = \exp(-\Delta G_{eq}/R/T)}$

Acetaldehyde reduced by **NADH** hydride **H⁻(2e⁻)** tunneling and protolysis.

$H_3C\text{-}CH{=}O + NADH + H_3O^+ \Leftrightarrow H_3C\text{-}CH_2\text{-}OH + NAD^+ + H_2O$ (11)

$\Delta G_{Hess}=\Delta G°_{CH3CH2OH}+\Delta G°_{H2O}+\Delta G°_{NAD+}-\Delta G°_{H3O}-\Delta G°_{CH3CHO}-\Delta G°_{NADH}$= -159 $^{kJ}/_{mol}$ 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:

Red NADH <=> **$NAD^+ + H^-(2e^-)$** ; **$E°^1 = -0{,}113$ V** ;

Ox $CH_3CHO+H_3O^+ + H^-(2e^-)$ <=>**$CH_3CH_2OH+H_2O$** ; **$E°^2_{H2O} = 0{,}190$**+0,0591/2*log([H_2O])=**0,2415 V**;

By convention (10) balanced **n = 2 = m** number of electrons **$2e^-\Delta E°$** is expressed as **$E°^1$** of the electron **donor** minus **$E°^2_{H2O}$** of the electron **acceptor**. **Acetaldehyde** is **accepting** hydride **H^-** from NADH in tunneling, **n** is **2**: **$\Delta E°=E°^2_{H2O}-E°^1=0.2415–(-0.113)= 0.3545$ V.** Equilibrium free energy change is favored Homeostasis joined $\Delta G_{AnaerobicRed}=\Delta E°\bullet F\bullet n=0{,}3545*2*$96485 $^{C}/_{mol}=-R\bullet T\bullet\ln(K_{eq})=-68{,}4$ $^{kJ}/_{mol}$. Oxidation reduction free-energy change at equilibrium is zero **$\Delta G=0$** oposit for Homeostazis $\Delta G_{Homeostasis}\neq 0$ negative for anaerobic :

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

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 **$\Delta G=-0.2$** $^{J}/_{mol}$ but anaerobic with NAD^+/NADH=1/10 **$\Delta G=-27{,}8$** $^{J}/_{mol}$**=-68,4** +40,5 produces ethanol ten times over acetaldehyde 10% practical efficiency and reaction shifted toward ethanol negative **-27,9** $^{kJ}/_{mol}$. Anaerobic shifted to **ethanol** negative:

$$[CH_3CHO]/[CH_3CH_2OH]=1/10;\ \Delta G_{AnaerobicRed}=(E°_{Red1}-E°_{2Oxn+})\bullet F\bullet(m'n=n'm)+R\bullet T\bullet\ln\frac{X^m_{1Ox^{n+}}\bullet X^n_{2Red}}{X^m_{1Red}\bullet X^n_{2Ox^{n+}}}=$$ page 8;

$$=-68{,}4+8{,}3144*298.15*\ln\frac{[NAD^+]\cdot[CH_3CH_2OH]\cdot[H_2O]}{[NADH]\cdot[CH_3CHO]\cdot[H_3O^+]}=(\frac{1}{10}\bullet\frac{1}{10}\bullet\frac{55.3}{10^{-7.36}})=-68.35+40.5=-27.9\ ^{kJ}/_{mol};$$

Oxidation of ethanol: $\Delta G_{AnaerobicRed}=-68{,}4+8{,}3144*298.15*\ln(\frac{700}{1}\bullet\frac{1}{10}\bullet\frac{55.3}{10^{-7.36}})=(8{,}875*10^{10})=-0{,}2$ $^{kJ}/_{mol}$;

$\Delta G_{AnaerobicRed}=-68{,}4+=8{,}3144*298{,}15*\ln(700/1*1/1*55{,}3457/10\text{^}(^{-7{,}36}))/1000=-68{,}4+68{,}2=-0.2$ $^{kJ}/_{mol}$ negative.

$\Delta G_{AerobicOx}=68{,}4+8{,}3144*298{,}15*\ln(1/700*1/10*10\text{^}(^{-7{,}36})/55{,}3457)/1000=68{,}4-73.91=-5{,}51$ $^{kJ}/_{mol}$.

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**: **$C_6H_{12}O_6+ 6O_{2aqua}+6H_2O=>6HCO_3^-+6H_3O^++\Delta G+Q$** is exoergic ΔG_{Hess}= **-3049,55** $^{kJ}/_{mol}$. This is a much larger release of free energy than is required for **ATP** synthesis erythrocyte mitochondria at **pH = 7.36** use **-55,16** $^{kJ}/_{mol}$ 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 **$FADH_2$** with transfer two hydrogen atoms **2H** (**$2H^++2e^-$**) (vitamins B_3 and B_2).

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** ⇔ **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 ⇔**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 ⇔**reduction** of the **nicotinamide ring** (Fig. 3).As a **substrate** molecule undergoes **oxidation** (**dehydridation**), 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 molecul **H_2O** converts to hydronium ion **H_3O^+**. The half-reactions for each type of **nucleotide** are similar:

(1) NADH ⇔ **$NAD^+ + H^-(H^+ + 2e^-)$** **$E^{\circ 1} = -0.113$ V** (David Harris)
(2) NADPH ⇔ **$NADP^+ + H^-(H^+ + 2e^-)$** **$E^{\circ 2} = -0.117$ V** (CRC)

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 □ 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 AH_2**, 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**⇔H_3C-**CH=O** + NAD**H** + **H_3O^+** (11)
where **AH_2**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**:

Red substrate **$AH_2 + NAD^+ + H^-(H^+ + 2e^-)$⇔ A + NADH** **$E^{\circ 1} = -0.113$ V** (David Harris) (11)
Ox substrate **A + NADPH ⇔ $AH_2 + NADP^+ + H^-(H^+ + 2e^-)$** **$E^{\circ 2} = -0.117$ V** (CRC) (11)

Notice that one of the carbon atoms **-CH_2-OH** in **ethanol** has lost a hydrogen **H**$^-$ atom as hydride and dissociates **–OH=>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** saide 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°^{2}$_{H2O}$ = -0.1314+0,00591/2*log([H_2O])= **-0.1314**+0,02595*log(55,3333)= **-0.1314**+0.04523= **-0,08617 V**

Red OHCCHOHCH$_2$OPO$_3^{2-}$+H_2O+HPO_4^{2-}**+ H$^-$(H$^+$+2e$^-$)**⇔$^{2-}O_3$POOCCHOHCH$_2$OPO$_3^{2-}$+H_3O^+,
(Ox) NAD$^+$+ H$^-$(H$^+$+2e$^-$) ⇔ **NADH, E°^{2}=-0.113 V** (David Harris); Carnegie Mellon Univ;
ΔG$_{eq}$=()*n*F=(-0,08617+0.113)= 0,02683*2*96485=5,1774 kJ/mol

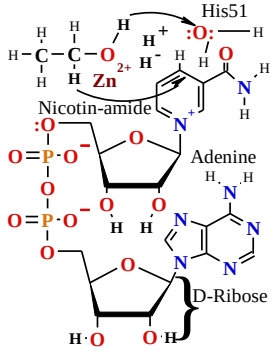
ΔE°= E^1$_{H2O}$ - E°^{1}=-0,08617+0.113=0,02683 V ;

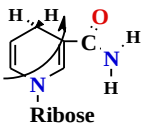
(1) OHC-CHOH-CH$_2$OPO$_3^{2-}$+NAD$^+$+H_2O+HPO_4^{2-}=>$^{2-}O_3$POOC-CHOHCH$_2$OPO$_3^{2-}$**+NADH**+H_3O^+
(2) H$_3$C-CH=O+NADH+H$_3$O$^+$⇔H$_3$C-CH$_2$-OH+NAD$^+$+H$_2$O ΔG$_{eq}$= -68,408 kJ/mol

(calculated) **ΔG$_{eq}$ = ΔE°•F•n=(-0.113+0,2415)•F•n= -0.3545 V•2•96485= -68,408** kJ/mol
Notice: enzyme complexe irreversible 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$^+$**)⇔NADH**; Eo=-0.113V** standard potential T=298,15 K (25° C)

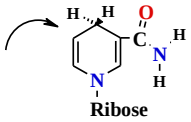
(**a**) **oxidized NAD$^+$** (2e$^-$+**H$^+$**)↓**H$^-$**↓**;**
Hydride Transfer H$^-$↓A
H$^-$↓side **A**





or

↓ **B** side↓ **H$^-$ + H$_2$O**



<=**NADH+H$_2$O reduced form product**
(**a**) **Nicotin-amide adenine di-nucleotide** (**NAD$^+$**) and its **phosphorylated** analog **NADP$^+$** undergoes **reduction** to **NADH** and **NADPH**, **accepting** a hydride **:H$^-$ ion** (two electrons **2e$^-$** and one proton **H$^+$**) from an **oxidizable substrate**. The hydride **:H$^-$ ion** is added to either the front (the **A** side) or the back (the **B** side) of the planar **nicotin-amide ring** (seeTable2)
(**a**) **oxidized NAD$^+$+ H$^-$** (2e$^-$+**H$^+$**)⇔**NADH reduced**

for **NADP$^+$** ribose **C**2'-**OH**hydr**oxyl** in **NADP$^+$** is esterified with **phosphate HO-PO$_3^{2-}$** as ribose 2'**C-O-PO$_3^{2-}$**

↑**A=log(Io/I)** **Absorbance** measured **A=a•C•l** proportional to **NADH** concentration **C**into solution

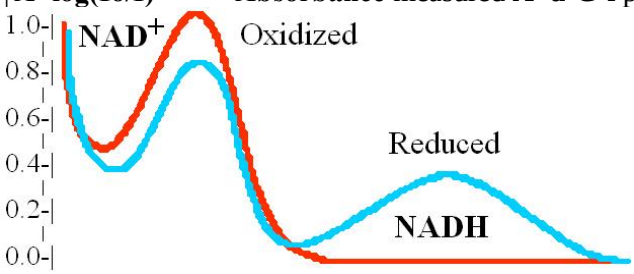


Figure 3. (**b**) The **UV** absorption spectra of **NAD$^+$** and **NADH**. **Reduction** of the **nicotin-amide ring** produces a new, broad absorption band with a maximum at **340 nm**. The production of **NADH** during an **enzyme-catalyzed** reaction can observing the appearance of the absorbance at **340 nm**; extinction coefficient **a=6200M^{-1}•cm^{-1}**, molar absorbance **a=A/C/l** in Beer-Buger-Lambert's law **A=a•C•l** shows good sensitivity.

Wavelength (**nm**) ⟶That Employ **NAD$^+$** or **NADP$^+$ Coenzymes**

Table 2. Stereo specificity of **Dehydrogenases**

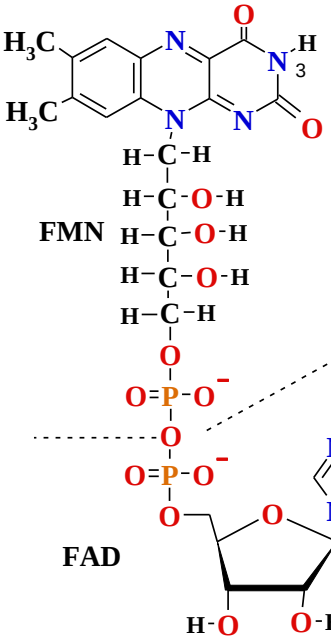
Enzyme **Coenzyme Stereo chemical** specificity **nicotin-amide ring** (**A** or **B**)

Iso-citrate dehydrogenase	**NAD$^+$**			**A**	
a-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

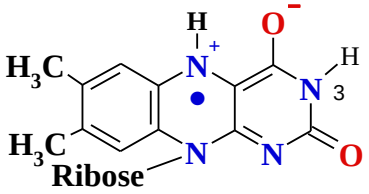
Enzyme	Flavin	Nucleotide Enzyme
Fatty acyl-CoA dehydrogenase	**FAD**	
Di-hydro-lipoyl dehydrogenase	**FAD**	Glycerol 3-phosphate dehydrogenase
Succinate dehydrogenase	**FAD**	Thio-redoxin reductase
NADH dehydrogenase Complex1	**FMN**	Glycolate dehydrogenase

flavin mono-nucleotide (**FMN**)→ **isoalloxazine ring**

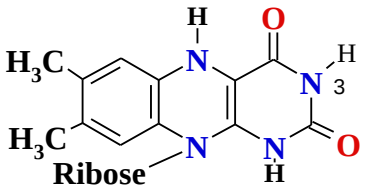


+e⁻+H⁺→↓ FADH* (FMNH*)

↓ (semi-quinone)



+e⁻+H⁺→↓ FADH₂ (FMNH₂)



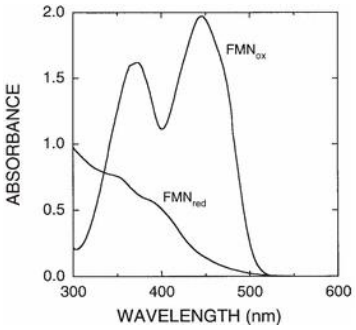
(fully **reduced**)

←**Flavin adenine dinucleotide FAD**

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 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 $M^{-1}cm^{-1}$ (3) and at λ=445 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 $M^{-1}cm^{-1}$.

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 an positive potential compared with $\mathbf{E°_{H2O}}$**=-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 $\mathbf{Fe^{n+}}$ or molybdenum $\mathbf{Mo^{n+}}$, for example) capable of participating in electron **e⁻** transfer.

Summary

Hess law thermodynamic pure products over pure reactants ratio constants $\mathbf{K}_{Hess}$ and change of free energy, enthalpy and entropy as pure products minus pure reactants difference $\Delta\mathbf{G}_{Hess}$, $\Delta\mathbf{H}_{Hess}$, $\Delta\mathbf{S}_{Hess}$. Equilibrium state is attractor for non equilibrium state. To attractor irreversibly trend homeostasis, but never reach free energy change absolute minimum $\Delta\mathbf{G_{eq}=-R\bullet T\bullet ln(K_{eq})}$, because is non equilibrium state. At equilibrium state constant expression $\mathbf{K}_{eq}$ is for mixture of products over reactants concentration ratio. Homeostasis non-equilibrium mixture constant expression $\mathbf{K}_{Homeostasis}$ is products factorial of concentration over reactants factorial ratio of concentration. The homeostasis non-equilibrium state has smaller than equilibria state constant $\mathbf{K}_{Homeostasis} < \mathbf{K}_{eq}$, 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% [O_2] oxygen since 500 million Years, osmolar concentration 0,305 M, ionic strength 0,25 M, pH=7,36

concentration [H_3O^+]=$10^{-7,36}$ M, generate concentration gradients like [NAD^+]/[NADH] and molekulu funkcionālās aktivitātes atraktoru vērtībām: [ATP^{4-}]/[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 $G_{reactants}$ to $G_{products}$. Cells driven by free energy **G** change perform the work **W**.

The equilibrium attractor free-energy change minimum $\Delta G_{eq}=\Delta G_{min}$ is a physical **constant** for **reaction** derived from the **equilibrium constant** K_{eq} for the reaction: $\Delta G_{eq}=-R\bullet T\bullet \ln(K_{eq})$. Homeostasis free-energy change $\Delta G_{Homeostasis}$ and constant $K_{Homeostasis}<K_{eq}$ has smaller absolute value, because depends on concentrations **C** of **reactants** and **products**: $\Delta G_{Homeostasis}=\Delta G_{eq}+R\bullet T\bullet \ln([products]/[reactants])$, but totally always negative change for irreversibility. When $\Delta G_{Homeostasis}$ 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 $\Delta G_{Homeostasis}=0$ 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**.

ATP^{4-} 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 ADP^{3-} and HPO_4^{2-} or to AMP^{2-} and $HO_3P\text{-}O\text{-}PO_3^{3-}$. ATP^{4-} **hydrolysis** transfer the **phosphoryl**, **pyro-phosphoryl**, or **adenylyl** group from ATP^{4-} to a **substrate** or **enzyme** molecule that couples the energy of **exoergic** hydrolise to **endoergic** transformations of **substrates**. ATP^{4-} 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 iniciate conformational changes for muscle contraction are driven by ATP^{4-} 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,** $E°_{H2O}$ 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 $\Delta E°=(E°_{Red1} - E°_{2Oxn+})$ of the two half-cells:

$$\Delta G_{eq} = F\bullet n\bullet \Delta E° = -R\bullet T\bullet \ln(K_{eq}).$$

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 ATP^{4-} and electrons 24 e^- transfer to six 6 O_{2aqua} in half-cell expressions:

$$O_{2aqua}+4\ H_3O^+ + 4\ e^- = 6\ H_2O;\ E°_{H2O} = 1.383 \text{ Volts.}$$

$$24\ H_3O^+ + 6\ H_3O^+ + 6\ HCO_3^- + 24\ e^- = C_6H_{12}O_6 + 42 H_2O;\ E°_{H2O} = 0.157 \text{ Volts.}$$ 6th page

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Further Reading

Bio-energetic and Thermodynamics

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Phosphoryl Group Transfers and ATP

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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.

Problems1. 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**) $\Delta G_{eq} = - R \cdot T \cdot \ln(K_{eq}) = -8.3144*298.15 \cdot \ln(6.8) = -2479.0215*1.916923 = -4752.093331 = -4.752$ **kJ/mol**

Glutamate + oxalo-acetate⇔aspartate amino-transferase⇔ aspartate + α-keto-glutarate $K_{eq}= 6.8$

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

Di-hydroxy-acetone phosphate⇔triose phosphate isomerase⇔ glyceraldehyde 3-phosphate $K_{eq}= 0.0475$

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

Fructose 6-phosphate^{-} + ATP^{4-}⇔phospho-fructo-kinase⇔fructose 1,6-bisphosphate^{2-} + ADP^{3-} $K_{eq}= 254$

$\Delta G_{eq} = -R \cdot T \cdot \ln(K_{eq})$; 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** = 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

$$H_2PO_4^-{}_{aq} + H_2O + \Delta G + Q \Rightarrow HPO_4^{2-}{}_{aq} + H_3O^+ \; ; \; K_{eq} = \frac{[HPO_4^{2-}]_{aqua} \cdot [H_3O^+]}{[H_2PO_4^-]_{aqua} \cdot [H_2O]} = 1.1436 \cdot 10^{-9}$$ (Kortly Shucha);

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

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

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

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

(**a**) Glucose 6-phosphate^{2-} + H_2O <=>glucose+ HPO_4^{2-} ; $^{-}$; **K=261.573**; ΔG°_{eq}**=-13.8** kJ/mol pH=7,36

Equilibrium for Glucose 6-phosphate at pH=7,36: $Glc6P^{2-} + H_2O <=> Glc + HPO_4^{2-}$;

$\Delta G_{Lehniger} = -13,8$; $K_{Lehniger} = EXP(--13.8*1000/8.3144/298.15) = EXP(5.5669) = K_{eq} \cdot [H_2O] = 261.62$;

Prigogine attractor $\Delta G_{min} = \Delta G_{eq}$ equilibrium $\frac{[Glc] \cdot [HPO_4^{2-}]}{[Glc6P^{2-}] \cdot [H_2O]} = K_{eq} = K_{Lehniger}/[H_2O] = 261.62/55,3 = 4,728$

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

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

$\Delta G_r = \Delta G^\circ_{Glc} + \Delta G^\circ_{HPO42-} - \Delta G^\circ_{H2O} - \Delta G^\circ_{Glc6P} = -402,05-1057,143-(-151,549-1296,262) = -1459,193+1447,811 = -11,382$ kJ/mol

(**b**) Lactose + H_2O <=> glucose + galactose $K_{Lehniger} = K_{eq}[H_2O] = 610.221*55.3457 = 33773.1084$

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

$K_{Lehniger} = \frac{[Glc] \cdot [Gal]}{[Lactose] \cdot [H_2O]} = K_{eq} = EXP(--15,9*1000/8.3144/298.15) = EXP(6,414) = 610,35$;

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

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

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

(**c**) Malate^{2-} <=fumarase=>fumarate^{2-} + H_2O ;

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

$K_{Lehniger} = \frac{[Glc] \cdot [Gal]}{[Lactose]} = K_{eq} \cdot [H_2O] = EXP(--15,9*1000/8.3144/298.15) = EXP(6,414) = 610,35$;

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

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

Prigogine attractor $\Delta G_{min} = \Delta G_{eq}$ equilibrium $K_{eq} = \frac{[Glc] \cdot [Gal]}{[Lactose] \cdot [H_2O]} = 610.35/55,3(3) = K_{Lehniger}[H_2O]) = 11,03$;

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

$K_{eqH2O} = 0.004615 = 3.1*1000/8.314400/298.15 = EXP(-1.2505) = 0.28636 = [fumarate] \cdot [H_2O]/([Malate]) = K_{eq}/[H_2O] =$

$= 0.255400/55.3457 = 0.004615 = K^\circ_{eq}$; $K^\circ_{eq} = \frac{[Fumarate] \bullet [H_2O]}{[Malate]} =$ **0.28636 ; ΔG° = 3.1 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⇔phospho-gluco-mutase⇔glucose 6-phosphate$^-$

[**Glc1P**$^-$] = **4.5•10^{-3} M 9.6•10^{-2} M** = [**Glc6P**$^-$]

= **0.096/0.0045 = 21.3333** = **K°$_{eq}$ΔG°= -R•T•ln(21.3333) = -8.3144*298.15*3.06027/1000 = -7.58648**

Calculate **K°$_{eq}$=[Glc6P$^-$]/[Glc1P$^-$]=21.3** and **ΔG°=-R•T•ln(21.33)=-7.586 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:

ΔG°$_1$=ΔG°$_o$+G°$_{HPO4}$+G°$_{H3O+}$-G°$_{H2PO4}$-G°$_{H2O}$= -13.8 + (-1282)+(-284.7)-(-1323)-(-306.7) = 49.306 kJ/mol

270*1.1469•10^{-9} = 3.096630•10^{-7} =K°$_{eq}$= K$_{H2PO4}$•K$_{eq}$; ΔG°= -R•T•ln(270)= -13879 kJ/mol

$H_2PO_4^-$ + H_2O⇔HPO_4^{2-} + H_3O^+ ; **K°$_{H2PO4}$ = 1.1469•10^{-9}** (KortlyShucha)

Glucose-6-phosphate$^-$ + H_2O => glucose + $H_2PO_4^-$; **K$_{eq}$= 270 ; ΔG°$_{eq}$= -13.879 kJ/mol**

Glucose 6-phosphate$^-$ + H_2O⇔glucose + $H_2PO_4^-$; **K°$_o$ = 261.573 ; ΔG°$_o$= -13.8 kJ/mol**

K°$_{eq}$•K°$_{H2PO4}$=K°$_{eq1}$= $\frac{[Glc]\bullet[HPO_4^{2-}]\bullet[H_3O^+]}{[Glc-6P^-]\bullet[H_2O]^2}$ **=3.1•10^{-7};**

=4.7262•10^{-7}=1.1469*261.573•10^{-9} =ΔG°$_{eq1}$=37.16 kJ/mol

(**1**) Glucose-6-phosphate$^-$ + 2 H_2O => glucose + HPO_4^{2-} + H_3O^+ ; **K°$_{eq1}$= 3.097•10^{-7};ΔG°$_1$= 49.3 kJ/mol**

(**2**) ATP^{4-} + glucose => ADP^{3-} + glucose 6-phosphate$^-$; **K$_{eq2}$= 890**

K°$_{eq2}$ = $\frac{[ADP^{3-}]\bullet[Glc-6P^-]}{[Glc]\bullet[ATP^{4-}]}$ **= 890 ;ΔG°$_{eq2}$= -16.836 kJ/mol**

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

K°$_{eq3}$= $\frac{[ADP^{3-}]\bullet[HPO_4^{2-}]\bullet[H_3O^+]}{[ATP^{4-}]\bullet[H_2O]^2}$ **=K°$_{eq1}$•K°$_{eq2}$ =** $\frac{[Glc]\bullet[HPO_4^{2-}]\bullet[H_3O^+]}{[Glc6P^-]\bullet[H_2O]^2}\bullet\frac{[ADP^{3-}]\bullet[Glc6P^-]}{[Glc]\bullet[ATP^{4-}]}$

3.09663*890•10^{-7} = 2.7560•10^{-4} =K°$_{eq3}$;ΔG°$_1$+ΔG°$_{eq2}$ = -16.836+49.3= 32.464 = **ΔG°$_3$**

-R•T•ln(K°$_{eq3}$) = -8.1344*298.15*ln(0.0002756) = **20.3194 kJ/mol** = **ΔG°$_{eq3}$**

ΔG°$_3$=ΔG°$_o$+G°$_{HPO4}$+G°$_{H3O+}$-G°$_{H2PO4}$-G°$_{H2O}$= -30.5 + (-1282) + (-284.7) - (-1323) - (-306.7) = 32.606 kJ/mol

(**3**)ATP^{4-}+2H_2O=>ADP^{3-}+HPO_4^{2-}+H_3O^+; **K°$_{eq3}$=0.0002756;ΔG°$_{eq3}$=20.32 kJ/mol;ΔG°$_{123}$=32.464 kJ/mol**

K$_{eq}$°$_o$ =0.0002756/1.146910^{-9} = 240300 ;-28981= **ΔG$_{eq}$°$_o$= -R•T•ln(K°$_o$)** = **-8.3144*298.15*ln(240300) =**

= -30714 ;K°$_o$= EXP(-ΔG°/R/T)= EXP(-30500/8.3144/298.15) =

K$_{eq}$°$_o$= $\frac{[ADP^{3-}]\bullet[H_2PO_4^-]}{[ATP^{4-}]\bullet[H_2O]^2}$ **=K°$_{eq3}$/K°$_{H2PO4}$= 240300** ; **ΔG$_{eq}$°$_o$ = -30.714 kJ/mol**

(**3**) ATP^{4-} + H_2O =>ADP^{3-} + $H_2PO_4^{2-}$; **K°$_o$= 220409 ; ΔG°$_o$ = -30.500 kJ/mol**

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

Fructose 6-phosphate$^-$⇔ glucose 6-phosphate$^-$; **K°$_{eq}$= 1.97**

K°$_{eq}$= $\frac{[Glc6P^-]}{[Fruc6P^-]}$ **= 1.97 = 531 331** ; **ΔG°= -R•T•ln(K°$_{eq}$) = -1.5399 kJ/mol**

= **0.5/1.5 = 0.3** =**K°$_{eq}$ΔG°= -R•T•ln(1.97) = -8.3144*298.15*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

[Glc6P$^-$] is adjusted to **0.5 M**, what is ΔG? **-1539.9+R•T•ln(0.3) =**

(**c**) Why are $\Delta G°$ and ΔG different? $\Delta G = \Delta G° + R•T•\ln(\frac{[Glc6P^-]}{[Fruc6P^-]})$ **= -1539.9+-2723.54 =-4.263.4 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 $\Delta G°_o$**=-30.5 kJ/mol**. If **ATP** is **hydrolyzed** under standard conditions but at **pH=5.0**, is more or less free energy released? Why?

$K°_{eq3}=\frac{[ADP^{3-}]\bullet[HPO_4^{2-}]\bullet[H_3O^+]}{[ATP^{4-}]\bullet[H_2O]^2}$ **=1.94•10^{-6};$K°_{eq3}/K°_{H2PO4}=K°_o=\frac{[ADP^{3-}]\bullet[H_2PO_4^-]}{[ATP^{4-}]\bullet[H_2O]^2}$ =220409**

EXP(-32606/8.3144/298.15)=EXP(-13.1528)=1.94•10^{-6}=$K°_{eq}$;$K°_{eq3}$ = 1.94•10^{-6}=
=$\Delta G°$; $K°_{eq3}$=EXP(--30.5*1000/8.3144/298.15)=EXP(12.3032)=220409;
$\Delta G°_3=\Delta G°_o+G°_{HPO4}+G°_{H3O+}-G°_{H2PO4}-G°_{H2O}$= -30.5 + (-1282) + (-284.7) - (-1323) - (-306.7) = 32.606 kJ/mol

$\Delta G=\Delta G°+R•T•\ln\frac{[ADP^{3-}]\bullet[HPO_4^{2-}]\bullet[H_3O^+]}{[ATP^{4-}]\bullet[H_2O]^2}$**=32606+R•T•ln(**0.0001/0.01/aoHOH/aoHOH*0.01**•10^{-pH})=19397.7-7981.3= -10.11 kJ/mol (pH=0)**; at **T=298 K** (**25 °C**)
-38.65 kJ/mol (**pH=5**); **-50.06 kJ/mol** (**pH=7**); **-52.12 kJ/mol** (**pH=7.36**); **-57.88 kJ/mol** (**pH=8.37**)
-11.83 kJ/mol (**pH=0**); at **T = 310 K** (**37 °C**) in mitochondria
-41.52 kJ/mol (**pH=5**); **-53.39 kJ/mol** (**pH=7**); **-55.53 kJ/mol** (**pH=7.36**); **-61.53 kJ/mol** (**pH=8.37**)

8. The $\Delta G°$ for Coupled Reactions

Glccose 1-phosphate$^-$ is converted into fructose 6-phosphate$^-$ in two **2** successive reactions:
Glucose 1-phosphate$^-$=> glucose 6-phosphate$^-$; **$\Delta G°_1$ = -7.3 kJ/mol**

Glucose 6-phosphate$^-$=>.fructose 6-phosphate$^-$**$\Delta G°_2$ = +1.7 kJ/mol**

Using the $\Delta G°$ values in Table 1.1, calculate the equilibrium constant,

$\Delta G°=\Delta G°_1+\Delta G°_2$ = -7.3+1.7 = -5.6 kJ/mol for the sum of the two **2** reactions at **25°C**:

Glucose 1-phosphate$^-$=>fructose 6-phosphate$^-$; **$K°_{eq}=K_{eq1}\bullet K_{eq2}$ = EXP(5600/8.314400/298.15) =**

EXP(2.258956) = 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 **$H_2PO_4^-$** and **HPO_4^{2-}** is described by the equation at **T = 310.15 K**:

(**a**)Glucose + **$H_2PO_4^-$**=>. glucose 6-phosphate$^-$ + H_2O, **$\Delta G_o°$ =13.8 kJ/mol**

$K°_a=\frac{[Glc6P^-]\bullet[H_2O]}{[Glc]\bullet[H_2PO_4^-]}$; $K°_{a2}\bullet K°_{H2PO4}=\frac{[Glc6P^-]\bullet[H_2O]^2}{[Glc]\bullet[HPO_4^{2-}]\bullet[H_3O^+]}\bullet\frac{[HPO_4^{2-}]\bullet[H_3O^+]}{[H_2PO_4^-]\bullet[H_2O]}$

EXP(49306/RF/T)= 2.01195544•10^{+8} = $K°_{eq3}$; $\Delta G°_1+\Delta G°_{eq2}$ = -16.836+49.3= 32.464 = **$\Delta G°_3$**

-R•T•ln($K°_{eq3}$) = -8.1344*298.15*ln(0.0002756) = **20.3194 kJ/mol** = **$\Delta G°_{eq3}$ 0.0000105738**

(**a2**) Glucose + **HPO_4^{2-}** + H_3O^+=>.glucose 6-phosphate$^-$ + 2 H_2O, **$\Delta G°$ = -49.306 kJ/mol**

$K°_{a2}=\frac{[Glc6P^-]\bullet[H_2O]^2}{[Glc]\bullet[HPO_4^{2-}]\bullet[H_3O^+]}=\frac{[Glc6P^-]\bullet\left(1+\frac{[H_3O^+]}{K_{H2PO4}\bullet[H_2O]}\right)\bullet[H_2O]^2}{[Glc]\bullet 4.8\bullet[H_3O^+]}$ **= 2.0119•10^{+8}**

$\Delta G°=\Delta G_o°+G°_{H2O}-G°_{H3O+}$=13.8+(-284.7)-(-306.7)=-8.231= 30.83876 ;

$K°_{H2PO4}=\frac{[HPO_4^{2-}]\bullet[H_3O^+]}{[H_2PO_4^-]\bullet[H_2O]}$; **$P_i$ = 4.8 mM = [$H_2PO_4^-$]+[HPO_4^{2-}]** ; **[HPO_4^{2-}] = 4.8 -** $\frac{[HPO_4^{2-}]\bullet[H_3O^+]}{K_{H2PO4}\bullet[H_2O]}=$

[HPO_4^{2-}]+[HPO_4^{2-}]$\frac{[H_3O^+]}{K_{H2PO4}\bullet[H_2O]}$ **= 4.8 = [HPO_4^{2-}]•(1+**$\frac{[H_3O^+]}{K_{H2PO4}\bullet[H_2O]}$**);**

$[\mathbf{HPO_4^{2-}}]= \dfrac{4.8}{\left(1+\dfrac{[H_3O^+]}{K_{H2PO4}\bullet[H_2O]}\right)}$; $[\mathbf{Glc6P^-}] = \dfrac{2.012\bullet[Glc]\bullet 4.8\bullet[H_3O^+]}{\left(1+\dfrac{[H_3O^+]}{K_{H2PO4}\bullet[H_2O]}\right)\bullet[H_2O]^2} = \mathbf{1.0574\bullet10^{-5}M}$

(**a**) Calculate the equilibrium constant $\mathbf{K°_a}$ for the above reaction. In the rat **hepatocyte pH=7.36** and at **pH=7** the physiological concentrations of **glucose** and $[\mathbf{H_2PO_4^-}]+[\mathbf{HPO_4^{2-}}]$ are maintained at approximately **4.8 mM**. What is the equilibrium concentration of glucose 6-phosphate$^-$ obtained by the direct **phosphorylation** of **glucose** by $\mathbf{H_2PO_4^-} + \mathbf{HPO_4^{2-}}$? Respectively $[\mathbf{Glc6P^-}] = \mathbf{8.5\bullet10^{-8}M}$ and $\mathbf{1.275\bullet10^{-7}M}$ (**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 $\mathbf{H_2PO_4^-} + \mathbf{HPO_4^{2}}$. Assuming a fixed concentration of $\mathbf{H_2PO_4^-} + \mathbf{HPO_4^{2-}}$ 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 $[\mathbf{Glc6P^-}]$=**250 µM** (normal physiological concentration)'? Would this route be physiologically reasonable, given that the maximum solubility of **glucose** is less than **1 M**?

$[\mathbf{Glc}] = \dfrac{[Glc6P^-]\bullet\left(1+\dfrac{[H_3O^+]}{K_{H2PO4}\bullet[H_2O]}\right)\bullet[H_2O]}{K_{a2}\bullet 4.8/1000\bullet[H_3O^+]} = \mathbf{23.64M}$ at **pH = 7.36 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**:

(**1**) Glucose + $\mathbf{H_2PO_4^-}$ ⇔. glucose 6-phosphate$^-$ + H_2O **;$\Delta G°_{o1}$ =13.8 kJ/mol**
(**2**)$ATP^{4-} + H_2O \Leftrightarrow ADP^{3-} + H_2PO_4^-$; **$K°_o$= 220409 ; $\Delta G°_{o2}$= -30.500 kJ/mol**
Sum: ATP^{4-} + glucose ⇔ ADP^{3-} + glucose 6-phosphate$^-$; **$\Delta G°_o$ = -16.7 kJ/mol** at **T_o = 298.15 K**

$K°_o$= 842.63 <= EXP(-ΔG°/R/T) = 649.3 = K°; $K°_{eqo}$= $\dfrac{[ADP^{3-}]\bullet[Glc6P^-]}{[ATP^{4-}]\bullet[Glc]}$ **=890 ; $\Delta G°_{eqo}$= -16.836 kJ/mol**

$\Delta G°_o$ =13.8+-30.5= -16.7 ; EXP(--16.7/RF/(To+25))= 842.631 = $K°_o$;K° = 649.2998 = EXP(--16700/RF/T)
(**1**) glucose + HPO_4^{2-} + H_3O^+⇔ Glucose-6-phosphate$^-$ + 2 H_2O **;$\Delta G°_1$= -49.3 kJ/mol**
(**2**)$ATP^{4-}+2H_2O \Leftrightarrow ADP^{3-}+HPO_4^{2-}+H_3O^+$ **; $\Delta G°_2$= 32.606 kJ/mol**
Sum: ATP^{4-} + glucose ⇔ ADP^{3-} + glucose 6-phosphate$^-$ **;ΔG°= -16.694 kJ/mol**

$\Delta G°_2=\Delta G°_{o2}+G°_{HPO4}+G°_{H3O+}-G°_{H2PO4}-G°_{H2O}$= -30.5 + (-1282) + (-284.7) - (-1323) - (-306.7) = 32.606 kJ/mol

$[\mathbf{Glc}] = \dfrac{[ADP^{3-}]\bullet[Glc6P^-]}{K^o\bullet[ATP^{4-}]} = \dfrac{1.32\bullet0.25/1000}{649.2998\bullet3.38} = \mathbf{1.504\bullet10^{-7}M}$ not depend on concentration $[\mathbf{H_3O^+}]$

[Glc]=1.32*0.25/1000/649.2998/3.38= 1.50366804509526E-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 $\mathbf{H_2PO_4^-} + \mathbf{HPO_4^{2-}}$ and thus drive the unfavorable phosphorylation of glucose by $\mathbf{H_2PO_4^-} + \mathbf{HPO_4^{2-}}$. 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: $\Delta G°_o$ **=20.011+-32.606= -12.595 ; -10.3*4.184** = **-43.095;**

(1_o) Phospho Creatine$^-$ + H_2O⇔Creatine + $H_2PO_4^-$ **;ΔG°$_{1o}$= -43.095 kJ/mol**

ΔG°$_{1'}$=ΔG°$_{1o}$+G°$_{HPO4}$+G°$_{H3O+}$-G°$_{H2PO4}$-G°$_{H2O}$= 43.095 + (-1282) + (-284.7) - (-1323) - (-306.7) = 20.011 kJ/mol

(**1**) Phospho Creatine$^-$ + 2 H_2O⇔Creatine + HPO_4^{2-} + H_3O^+ **;ΔG°$_1$= 20.011 kJ/mol**

(**2**)ADP^{3-}+HPO_4^{2-}+H_3O^+⇔ ATP^{4-}+2H_2O **; ΔG°$_2$= -32.606 kJ/mol**

(**a**) Phosphocreatine$^-$ + ADP^{3-}⇔creatine + ATP^{4-} **;ΔG°$_a$= -12.595 kJ/mol**

ΔG°$_o$ =-79.005+-32.606= -111.611 ; 3.8*4.184 = **15.899;**

(1_{bo}) fructose + $H_2PO_4^-$⇔ fructose 6-phosphate$^-$ + H_2O **;ΔG°$_{1bo}$= -15.899 kJ/mol**

ΔG°$_{1b'}$=ΔG°$_{1bo}$+G°$_{HPO4}$+G°$_{H3O+}$-G°$_{H2PO4}$-G°$_{H2O}$= -15.899+(-1282) +(-284.7)-(-1323)-(-306.7)= -79.005 kJ/mol

(**1**) fructose 6-phosphate$^-$ + 2 H_2O⇔ fructose + HPO_4^{2-} + H_3O^+ **;ΔG°$_{1b}$= -79.005 kJ/mol**

(**2**)ADP^{3-}+HPO_4^{2-}+H_3O^+⇔ ATP^{4-}+2H_2O **; ΔG°$_{2b}$= -32.606 kJ/mol**

(**b**) ATP^{4-}+ fructose ⇔ ADP^{3-} + fructose 6-phosphate$^-$ **;ΔG°$_b$= -111.6 kJ/mol**

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 **ΔG° 20 kJ/mol**.

(**a**) What is the ratio [**Y**]/[**X**I at equilibrium? **K°$_o$= 3.135•10^{-4}**

K$_{eq}$= [Y]/[X] =EXP(-ΔG°$_{o1}$/R/T)= EXP(-20000/R/T)= 0.0003135;

(**b**) Suppose **X** and **Y** participate in a sequence of reactions during which **ATP**$^{4-}$ is **hydrolyzed** to **ADP**$^{3-}$ and **$H_2PO_4^-$**, The overall reaction is :

(**1**) **X** ⇔**Y** ; **ΔG°$_{o1}$ = 20 kJ/mol**

(**2**)ATP^{4-} + H_2O ⇔ ADP^{3-} + **$H_2PO_4^-$** ; **K°$_o$= 220409 ; ΔG°$_{o2}$= -30.500 kJ/mol**

X + ATP^{4-} + H_2O ⇔**Y** + ADP^{3-} + **$H_2PO_4^-$** ; **ΔG°$_o$ = ΔG°$_{o1}$+G°$_{o2}$ =ΔG°$_o$ = 20+(-30.5)** = **-10.500 kJ/mol**

$$\mathbf{K°_{eqo}}= \frac{[ADP^{3-}]\bullet[H_2PO_4^-]\bullet[Y]}{[ATP^{4-}]\bullet[H_2O]\bullet[X]} = \mathbf{69.1} \;;\mathbf{K°_{eqo}\bullet[}H_2O\mathbf{]} = \frac{[Y]}{[X]} = \mathbf{3810}$$

$$\frac{[Y]}{[X]} = \frac{[ATP^{4-}]\bullet[H_2O]\bullet K^{o}_{eqo}\bullet\left(1+\frac{K_{H2PO4}\bullet[H_2O]}{[H_3O^+]}\right)}{8.05/1000\bullet[ADP^{3-}]} = \mathbf{1.994\bullet10^6} \;;[\mathbf{H_2PO_4^-}] = \frac{8.05/1000}{1+\frac{K_{H2PO4}\bullet[H_2O]}{[H_3O^+]}}$$

$$\mathbf{P_i = 8.05\ mM} = [\mathbf{H_2PO_4^-}]+[\mathbf{HPO_4^{2-}}] \;;\; [\mathbf{H_2PO_4^-}] = \mathbf{8.05/1000} - \frac{[H_2PO_4^-]K_{H2PO4}\bullet[H_2O]}{[H_3O^+]} \;;$$

K°$_o$=EXP(-ΔG°$_{o1}$/R/T)=EXP(-10500/R/T) = **69.0991;** aHOH*69.1/8.05*1000*(1+2.543489E-9*aHOH/$10^{-7.36}$)

[**Y**]/[**X**] = **aoHOH*8.05*69.0991/0.93/8.05*1000 = 1994007.686579**

Calculate [**Y**]/[**X**] for this reaction at equilibrium. Assume that the concentrations of [**ATP**$^{4-}$], [**ADP**$^{3-}$], and ([**$H_2PO_4^-$**]+ [**HPO_4^{2-}**])are all **1 M** when the reaction is at equilibrium **T = 310.15 K**.

(**c**) We know that [ATP^{4-}], [ADP^{3-}], and [**$H_2PO_4^-$**l are not **1 M** under physiological conditions. Calculate [**Y**]/[**X**] for the **ATP-coupled** reaction when the values of [ATP^{4-}], [ADP^{3-}], and [**$H_2PO_4^-$**l 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**

Phospho creatine$^-$ + ADP^{3-}⇔creatine + ATP^{4-} **;ΔG°= -12.5 kJ/mol -43+30.5**

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

at **37 °C** as it occurs in the **cytosol** of <u>neurons</u>, in which **phospho creatine**$^{-}$ is present at [**PCr**$^{-}$] **= 4.7 mM**, creatine at [**Cr**] **= 1.0 mM**, ADP^{3-} at **0.73 mM**, and ATP^{4-} 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 :

$R°_o=\frac{[ATP^{4-}]}{[ADP^{3-}]•([HPO_4^{2-}]+[H_2PO_4^{-}])}$ **=5.33•10^{-2} M^{-1}** ; at **37 °C T = 310.15 K**

P_i = [$H_2PO_4^-$]+[HPO_4^{2-}] ; **[$H_2PO_4^-$]** $=\frac{[ATP^{4-}]}{[ADP^{3-}]•R_o^o}-\frac{[H_2PO_4^{-}]•K_{H2PO4}•[H_2O]}{[H_3O^+]}$;

[$H_2PO_4^-$]$=\frac{\frac{[ATP^{4-}]}{[ADP^{3-}]•R_o^o}}{\left(1+\frac{K_{H2PO4}•[H_2O]}{[H_3O^+]}\right)}$ **;ΔG=ΔG°+R•T•ln(R°$_o$•{H_2O]** $\left(1+\frac{K_{H2PO4}•[H_2O]}{[H_3O^+]}\right)$**)=36.99 kJ/mol**

$ATP^{4-} + H_2O \Leftrightarrow ADP^{3-} + H_2PO_4^-$; **K°= 220409 ; ΔG° = -30.500 kJ/mol**

+30500+RF*T*ln(0.0533*aHOH*(1+2.543489E-9*aHOH/10^(-7.36))**)= 36988.76**
Calculate the free energy Δ**G** required to synthesize ATP^{4-} in a <u>rat</u> **hepatocyte**.

14. **Daily ATP Utilization by Human Adults**.

(**a**) A total of **30.5 kJ/mol** of free energy Δ**G** 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 Δ**G** required to synthesize ATP^{4-} under physiological conditions is different from Δ**G°**. Calculate the free energy Δ**G** required to synthesize ATP^{4-} m the <u>human</u> **hepatocyte** when the physiological concentrations of
ATP^{4-}, ADP^{3-}, ($H_2PO_4^-$+ HPO_4^{2-}) are **3.5,1.50**, **5.0 mM** and **pH=7.36**, respectively, at **37°C**.

K°$_{H2PO4}$ $=\frac{[HPO_4^{2-}]•[H_3O^+]}{[H_2PO_4^{-}]•[H_2O]}$; **$P_i$ = 5 mM=[$H_2PO_4^-$]+[HPO_4^{2-}]**; **[$H_2PO_4^-$]=5 -** $\frac{[H_2PO_4^{-}]•K_{H2PO4}•[H_2O]}{[H_3O^+]}$

K°$_{H2PO4}^{25}$= 1.1469•10^{-9}; ΔG° = -R•T•ln(K°$_{H2PO4}$) = 51.034 kJ/mol at **T = 298.15 K**
ΔG° = -RF*(To+25)*ln(1.1469E-9) = 51033.6 ;
K°$_{H2PO4}^{37}$= EXP(-51033.6/T/RF) = 2.543489•10^{-9} at **T = 310.15 K**

[$H_2PO_4^-$] $=\frac{5/1000}{\left(1+\frac{K_{H2PO4}•[H_2O]}{[H_3O^+]}\right)}$ **; ΔG° = -R•T•ln** $\frac{[ATP^{4-}]•[H_2O]}{[ADP^{3-}]•[H_2PO_4^{-}]}$ at **T = 310.15 K**

ΔG=ΔG°+R•T•ln $\left(\frac{[ATP^{4-}]•[H_2O]•\left(1+\frac{K_{H2PO4}•[H_2O]}{[H_3O^+]}\right)}{[ADP^{3-}]•5/1000}\right)$ **=60.3976 kJ/mol** at **T=310.15 K**

$ATP^{4-} + H_2O \Leftrightarrow ADP^{3-} + H_2PO_4^-$; **K°= 220409 ; ΔG° = -30.500 kJ/mol**

+30500+RF*T*ln(3.5/1.5*aHOH/5*1000*(1+2.543489E-9*aHOH/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 <u>metabolized</u> and the free energy Δ**G** is used to synthesize ATP^{4-}, which then provides energy Δ**G** for the body's daily <u>chemical</u> and <u>mechanical</u> **work W=-ΔG**. 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 <u>human</u> adult in **24 h**. What percentage of the body weight does this represent?

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

(**c**) Although adults synthesize large amounts of ATP^{4-} daily, their body weight, structure, and composition do not change significantly during this period. Explain this apparent contradiction.

15. **Rates of Turnover of □and □ Phosphates of ATP^{4-} A-O-OPO^--O-OPO^--O-OPO^--O^-** (**A**-α-β-γ-$\mathbf{O^-}$).

If a small amount of ATP^{4-} labeled with radioactive phosphorus in the terminal position, [γ-^{32}**P**] ATP^{4-}, is added to a yeast extract, about half **½** of the ^{32}**P** activity is found in $H_2PO_4^-$ within a few minutes, but the concentration of [ATP^{4-}]= const remains unchanged. Explain. If the same experiment is carried out using ATP^{4-} labeled with ^{32}**P** in the central position, [γ-^{32}**P**] ATP^{4-}, the ^{32}**P** does not appear in $H_2PO_4^-$ 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:

$Acetate + CoA^{4-} \Leftrightarrow$ acetyl-$CoA^{4-} + H_2O$ **; $\Delta G°_1$= 31.4 kJ/mol**

$ATP^{4-} + H_2O \Leftrightarrow AMP^{2-} + PP_i^{2-}$ **;$\Delta G°_2$ = -45.6 kJ/mol**

$Acetate + CoA + ATP^{4-} \Leftrightarrow$ acetyl-CoA + $AMP^{2-} + PP_i^{2-}$ **;$\Delta G°$ = -45.6+31.4 = -14.2= -14.2 kJ/mol**

(**a**) The **$\Delta G°$** for the **hydrolysis** of **acetyl-CoA** to **acetate** and **CoA** is **-31.4 kJ/mol** and that for **hydrolysis** of ATP^{4-} to AMP^{2-} and PP_i^{2-} is **-45.6 kJ/mol**. Calculate **$\Delta G°$** for the **ATP-dependent** synthesis of **acetyl-CoA**.

(**b**) Almost all cells contain the enzyme inorganic **pyro-phosphates**, which catalyzes the **hydrolysis** of PP_i^{2-} to $H_2PO_4^-$. What effect does the presence of this enzyme have on the synthesis of **acetyl-CoA**? Explain!

H_2PO_3-O-$O_3PH_2^{2-}$+$H_2O \Leftrightarrow 2\ H_2PO_4^-$**;$\Delta G°_{PP}$=-19kJ/mol;$\Delta G°_{total}$=$\Delta G°$+$\Delta G°_{PP}$=-45.6+31.4=-14.2-19=-33.2kJ/mol**

H_2PO_3-O-$O_3PH_2^{2-} + 3\ H_2O \Leftrightarrow 2\ HPO_4^{2-} + 2\ H_3O^+$**;$\Delta G°_{PPH}$ = 107.21 kJ/mol**

17. **Energy for H_3O^+ Pumping** The parietal cells of the stomach lining contain membrane "pumps" that transport hydrogen ions **H_3O^+** 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 **H_3O^+** ions through these pumps. (Hint: See Oxidative Phosphorylation.)

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

$H_3O^+_{plasma} \Leftrightarrow\ H_3O^+_{stomach}$**;$K_{eq}$** = $[H_3O^+_{stomach}]/[H_3O^+_{plasma}] = 10^{-pHplasma}/10^{-pHstomach}$ **= $1.445 \bullet 10^6$**

$\Delta G° = -R \bullet T \bullet \ln(K_{eq}) = -36577 = -36.577$ 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**:

Oxidizing agent^{n+} + $n_{\underline{electrons}}^-$ $\Leftrightarrow$ reducing agent

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?

Pyruvate$^-$+ H_3O^+ + NADH => lactate$^-$+ NAD^+ + H_2O ;($E°_{NADH}$- $E°_{pyruvate}$)•F•2 = $\Delta G°$ = -73.000 kJ/mol

ΔG= **$\Delta G°$ + R•T•ln**$\left(\frac{[\text{lactate}^-]\bullet[NAD^+]\bullet[H_2O]}{[\text{pyruvate}^-]\bullet[NADH]\bullet[H_3O^+]}\right)$ = **-18.957 kJ/mol** favorable direction of reaction

$\Delta G°_o$ = 96485*2*(-0.059-0.3193)= -73000.5510 ;

ΔG = -73000.5510 + R•T•ln(1/1*1/1*aoHOH/10^(-7.36)) = **-18957.02**

(**d**) What is the standard free-energy change (**$\Delta G°$**) at **37 °C** for the conversion of **pyruvate** to **lactate**

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

K_{eq}=$\frac{[\text{lactate}^-]\bullet[NAD^+]\bullet[H_2O]}{[\text{pyruvate}^-]\bullet[NADH]\bullet[H_3O^+]}$ **=$6.149 \bullet 10^{12}$; [H_3O^+] •K_{eq}=**$\frac{[\text{lactate}^-]\bullet[NAD^+]\bullet[H_2O]}{[\text{pyruvate}^-]\bullet[NADH]}$ **=268417**

EXP(--73000.5510/R/T)= 6149086393492.1•10^(-7.36) = **268417.356457188** = **$K°_o$;**

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

2 NADH + 2 H_3O^+ + O_2=> 2 NAD^+ + 4 H_2O ($E°_{NADH}$- $E°_{O2}$)•F•4 = ΔG° = -552.74 kJ/mol

ΔG°$_o$ = 96485*4*(-0.059-1.3732)= -552743.2680/52000 = 10.6297

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

(**b**) Calculate Δ**G**° for this reaction. **ΔE° = $E°_{NADH}$- $E°_{O2}$ = -0.059-1.3732 = -1.4322 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**.

NADH + H_2O ⇔ NAD^+ + H_3O^+ + 2e$^-$ E_{37} = -0.0590 V (David Harris)

E = -0.059 + RF*T/F/2*ln(1*10^(-7.36)/10/aHOH) = **-0.36983 V**

$$\mathbf{EMF = E} = E_{37} + \mathbf{R•T/F/2•ln}\left(\frac{[NAD^+]\bullet[H_2O]}{[NADH]\bullet[H_3O^+]}\right) = \mathbf{-0.36983\ V}$$

(**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 tendency to accept electrons **e**$^-$ at **pH = 7.36** by **RedOx potential E_o** values:

O_{2g}+4 H_3O^++ 4 e$^-$= 6 H_2O Suchotina**;** **E_o = 0.8130 V ; E_{37} = 1.3732 V**

O_{2aq}+2H_3O^++2e$^-$=H_2O_{2aqua}+2H_2O University Alberta**; E_o = 0.2336 V ; E_{37} = 0.7937 V**

oxalo-acetate^{2-}+2H_3O^+ +2e$^-$= Malate^{2-}+2H_2O CRC **; E_o = -0.2225 V ; E_{37} = 0.3376 V**

O_{2g}+ e$^-$ = O^-_{2aq}Suchotina**; E_o = -0.2355 V ; E_{37} = -0.2355 V**

$NADP^+$+H_3O^+ +2e$^-$= NADPH + H_2O CRC **; E_o = -0.3429 V ; E_{37} = -0.0629 V**

α-Ketoglutarate+CO_2+2H_3O^++2e$^-$= isocitrate+2H_2O ; E_o = -0.4283 V ; E_{37} = 0.13185 V

(**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?

($E°_{Red}$-$E°_{Ox}$)•F•n = ΔG° kJ/mol ;

ΔG°$_o$ = 96485*2*(0.33757-0.059)= 53755.65290 = 10.6297

$$\mathbf{\Delta G} = \Delta G° + \mathbf{R•T•ln}\left(\frac{[oxaloacetate^{2-}]\bullet[NADH]\bullet[H_3O^+]}{[malate^{2-}]\bullet[NAD^+]\bullet[H_2O]}\right) = \mathbf{10.053\ kJ/mol}$$ unfavorable direction => for (**a**)

ΔG = 53755.65290 + RF*T*ln(10^(-7.36)) = **10052.76**

(**a**) Malate^{2-}+ NAD^++ H_2O => oxalo-acetate^{2-}+NADH+H_3O^+;**($E°_{malate}$-$E°_{NAD+}$)•F•2 = ΔG°= 53.756 kJ/mol**

ΔG°$_o$ = 96485*2*(-0.059-0.16453)= -43134.58410

ΔG = -43134.58410-RF*T*ln(10^(-7.36))=568.3108

ΔG=**ΔG°-R•T•ln($10^{-7.36}$)=0.568 kJ/mol**<=direction favorable to left for (**b**)

(**b**) aceto-acetate$^-$ + NADH + H_3O^+=>β-hydroxy-butyrate$^-$ + NAD^+ + H_2O; **ΔG°= -43.135 kJ/mol**

ΔG°$_o$ = 96485*2*(-0.059-0.3193)= -73000.5510

ΔG = -73000.5510-RF*T*ln(10^(-7.36)) = **-29297.7**

ΔG= **ΔG° - R•T•ln($10^{-7.36}$) = -29.298 kJ/mol** => direction favorable to right

(**c**) Pyruvate$^-$ + NADH + H_3O^+=> lactate$^-$ + NAD^+ + H_2O ; **ΔG°= -73.001 kJ/mol** =>direction

ΔG°$_o$ = 96485*2*(0.16453-0.3193)= -29865.96690

(**d**) Pyruvate$^-$ + β-hydroxy-butyrate$^-$=> lactate$^-$ + aceto-acetate$^-$; **ΔG°= -29.866 kJ/mol** => direction

ΔG°$_o$ = 96485*2*(0.33757-0.3193)= 3525.56190

(**e**) Malate$^-$ + pyruvate$^-$=>oxalo-acetate$^-$ + lactate$^-$; **ΔG°= 3.526 kJ/mol** <= direction

ΔG°$_o$ = 96485*2*(0.52695-0.286255)= 46446.914150

(**f**) Acetaldehyde + succinate^{2-}=> ethanol + fumarate^{2-} ; **ΔG°= 46.447 kJ/mol** <= direction