

Attractors Ilya Prigogine Nobel Prize 1977 **Biochemical Thermodynamics**

Attractors Thermodynamics is the quantitative study of the energy **G** transductions that occur in living cells for the functions in nature of the **chemical processes** underlying these transductions which are drivers and destiny declared by Ilya Prigogine Nobel Prize 1977.

Living organisms are organic regulated complex systems dissipative structure containing, irreversible processes working, with certain **Attractors** driven Brownian molecular engines, evolution and surviving instruments of homeostasis.

<http://aris.gusc.lv/ChemFiles/Attractor/1977NobelPrize.pdf>

Atmospheric oxygen attractor **O₂** 20,95 % of Photosynthesis

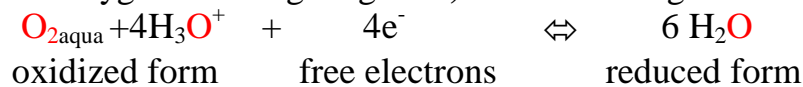
Green plants **CO₂** assimilation and **O₂ OSMOSIS** photosynthesis production attractors.

Experimental research of ability photosynthesis reach oxygen concentration 20,95 %. Preparation 2% oxygen air show retention during 24 hours the normal level, stopping the rate of photosynthesis at homeostasis concentration 20,95% of volume.

Attractor 20,95 % oxygen in atmosphere works locally for photosynthetic organisms and mesurments proof this attractor global influence of life.

Nernst's potential **O₂_{aqua}/H₂O** red-ox system physiologic mechanism of acidosis and oxidative stress. Destructive hazard for life! Oxidative stress causes chaos, contamination with **non enzymatic** oxidation in multiple chain reactions and parallel products so degrading and destroying the organism!

Water medium, blood plasma oxygen is strong reagent **1,229 V** referring to half reaction:



Concentration arterial [**O₂_{aqua}**] = $6 \cdot 10^{-5}$ M and pH=7,36 concentration [**H₃O⁺**] = $10^{-7,36}$ M.

$$E = 1,229 \text{ V} + 0,01478 \cdot \lg([\text{O}_{2\text{aqua}}] \cdot [\text{H}^+]^4) = 1,229 + 0,01478 \cdot \log(6 \cdot 10^{-5} \cdot 10^{-7,36 \cdot 4}) = \mathbf{0.70076 \text{ V}}$$

Water concentration 55,3 M decreases potential from **1,383 V** to standard **1,229 V**:

$$E_o = E^\circ + \frac{0.0591}{4} \cdot \lg\left(\frac{1}{[\text{H}_2\text{O}]^6}\right); [\text{H}_2\text{O}] = 55,3 \text{ M} = \frac{996 \text{ g/L}}{18 \text{ g/mol}}$$

$$E_o = E^\circ + \frac{0.0591}{4} \cdot \lg\left(\frac{1}{[\text{H}_2\text{O}]^6}\right) = 1,383 + 0,01478 \cdot \lg\left(\frac{1}{[55,3]^6}\right) = 1,383 - 0,01478 \cdot 10,456 = \mathbf{1,229 \text{ V}}$$

1) Water concentration decreases oxidative stress risk about **1,383-1,229 = 0.15449 V**.

If acid **H₃O⁺** concentration increases 10 times, than potential increases about + 0.2364 V :

ΔE increase as oxidative stress: 2) acidified medium $\Delta \text{pH}=1$ acidosis about $\Delta E = \mathbf{+0,236 \text{ V}}$.

Air 20.95% replaced with 100% oxygen [**O₂_{aqua}**] concentration increases 5 times and potential

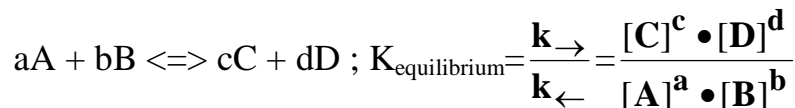
3) about $\Delta E = \mathbf{+0,01 \text{ V}}$ than oxidative stress risk increases about 5 times.

NASA Apollo Moon project closes 1972 because of oxidative stress and technical hazards risk.

Attractors two approaches for equilibrium

Living organisms thousands of Biochemical reactions have been studied as at equilibria.

Equilibrium Attractor is minimum of free energy change for mixture. The mixture equilibrium consist of Initial and product compounds expressed in constant equation calculations:



$$\Delta G_{\text{reaction}} = \Delta G_{\text{eq}} + R \cdot T \cdot \ln \left(\frac{[C]^c \cdot [D]^d}{[A]^a \cdot [B]^b} \right) = 0, \quad -\Delta G_{\text{eq}} = R \cdot T \cdot \ln \left(\frac{[C]^c \cdot [D]^d}{[A]^a \cdot [B]^b} \right),$$

where $\Delta G_{\text{reaction}} = \Delta H_{\text{reaction}} - T \cdot \Delta S_{\text{reaction}}$ or $\Delta G_{\text{reaction}} = \sum \Delta G_{\text{products}}^{\circ} - \sum \Delta G_{\text{init.compound}}^{\circ}$

For water ionisation reaction: $\text{H}_2\text{O} + \text{H}_2\text{O} + \text{Q} + \Delta G \rightleftharpoons \text{H}_3\text{O}^+ + \text{OH}^-$

$\Delta G_{\text{ionisation}} = \Delta H_{\text{ionisation}} - T \Delta S_{\text{ionisation}} = 101,9 \text{ kJ/mol}$. unfavored reaction .

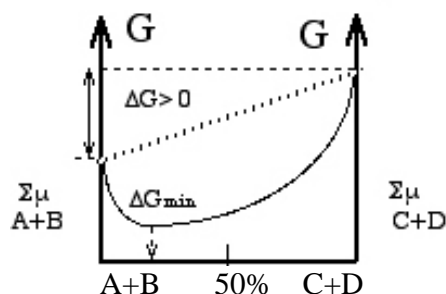
$$\Delta G_{\text{eq}} = -R \cdot T \cdot \ln \left(\frac{[\text{OH}^-] \cdot [\text{H}_3\text{O}^+]}{[\text{H}_2\text{O}] \cdot [\text{H}_2\text{O}]} \right) = 8,3144 \cdot 298,15 \cdot \ln(3,26 \cdot 10^{-18}) = 99,8 \text{ kJ/mol},$$

Endothermic and endoergic water ionisation reaction free energy

$\Delta G_{\text{ionisation}}$ increases and is $101,9 \text{ kJ/mol}$ as unfavored reaction, but

becomes smaller up to minimum $\Delta G_{\text{min}} = \Delta G_{\text{eq}} = 99,8 \text{ kJ/mol}$

reaching equilibrium $K_{\text{eq}} = \frac{[\text{OH}^-] \cdot [\text{H}_3\text{O}^+]}{[\text{H}_2\text{O}] \cdot [\text{H}_2\text{O}]} = 3,26 \cdot 10^{-18}$ with mixture $\text{H}_2\text{O} + \text{H}_2\text{O}$ initial compounds (A+B) and product compounds are $\text{H}_3\text{O}^+ + \text{OH}^-$ (C+D).



The small products amount $[\text{H}_3\text{O}^+] = [\text{OH}^-] = 10^{-7} \text{ M}$ and water concentration in power 2 two exponent for one liter : $[\text{H}_2\text{O}]^2 = \left(\frac{997 \text{ g/L}}{18 \text{ g/mol}} \right)^2 = 3065,96 \text{ M}^2$.

Equilibrium destiny is Prigogine attractor free energy change minimum ΔG_{min} .

Free energy change minimum reaching stabilises equilibrium.

page 7th ÷ 8th <http://aris.gusc.lv/BioThermodynamics/H2ODissociation.pdf>

CH_3COOH protolysis reareaction with water: $\text{CH}_3\text{COOH} + \text{H}_2\text{O} + \Delta G \rightleftharpoons \text{H}_3\text{O}^+ + \text{CH}_3\text{COO}^- + \text{Q}$

$\Delta G_{\text{protolysis}} = \Delta H_{\text{protolysis}} - T \Delta S_{\text{protolysis}} = 42,36 \text{ kJ/mol}$ unfavored reaction.

Equilibrium reaches free energy minimum in mixture of compounds constantratio

$$K_a = \frac{[\text{H}^+] \cdot [\text{CH}_3\text{COO}^-]}{[\text{H}_2\text{O}] \cdot [\text{CH}_3\text{COOH}]_{\text{nedis}}} = 1,76 \cdot 10^{-5} / 55,3 = 10^{-6,497}$$

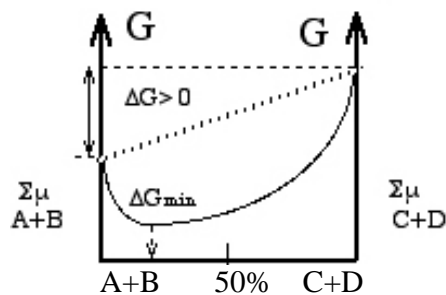
$$\Delta G_a = -R \cdot T \cdot \ln(K_a) = -8,3144 \cdot 298,15 \cdot \ln(10^{-6,497}) = 37,085 \text{ kJ/mol},$$

Endothermic and endoergic acetic acid protolysis reaction free energy is $\Delta G_{\text{protolysis}}$ positive $42,36 \text{ kJ/mol}$ as unfavored reaction,

but minimum $\Delta G_{\text{min}} = \Delta G_a = 37,085 \text{ kJ/mol}$ in mixture

reaching equilibrium $K_{\text{eq}} = \frac{[\text{H}^+] \cdot [\text{CH}_3\text{COO}^-]}{[\text{H}_2\text{O}] \cdot [\text{CH}_3\text{COOH}]_{\text{nedis}}} = 10^{-6,497}$

in mixture initial compounds $\text{CH}_3\text{COOH} + \text{H}_2\text{O}$ (A+B) and products are $\text{H}_3\text{O}^+ + \text{CH}_3\text{COO}^-$ (C+D).



Equilibrium destiny is Prigogine attractor free energy change minimum ΔG_{min} .

Free energy change minimum reaching stabilises equilibrium.

Ions from **crystalic** $\text{Na}^+\text{Cl}^- \rightleftharpoons \text{Na}^+ + \text{Cl}^-$ dissociation process as electrolyte solution (4.1)

$$\Delta G_{\text{dissociation}} = \Delta H_{\text{dissociation}} - T\Delta S_{\text{dissociation}} = -9,15 \text{ kJ/mol favored reaction.}$$

At equilibrium reached free energy change minimum according compounds mixture on expression:

$$K_{\text{eq}} = \frac{[\text{Na}^+]_{\text{aqua}} \cdot [\text{Cl}^-]_{\text{aqua}}}{[\text{Na}^+\text{Cl}^-]_{\text{solid}}} = 31,0365 = 10^{1,492},$$

$$\Delta G_{\text{eq}} = -R \cdot T \cdot \ln(K_{\text{eq}}) = -8,3144 \cdot 298,15 \cdot \ln(31,0365) = -8,51556 \text{ kJ/mol},$$

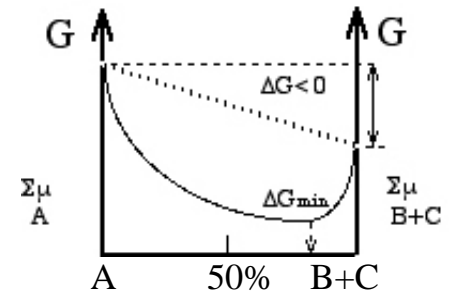
Endothermic and exoergic **crystals** Na^+Cl^-_s dissociations reaction

free energy $\Delta G_{\text{dissociation}}$ negative $-9,15 \text{ kJ/mol}$ as favored reaction,

but minimises up to $\Delta G_{\text{min}} = \Delta G_{\text{eq}} = -8,516 \text{ kJ/mol}$

$$\text{in mixture reaching equilibrium } K_{\text{eq}} = \frac{[\text{Na}^+]_{\text{aqua}} \cdot [\text{Cl}^-]_{\text{aqua}}}{[\text{Na}^+\text{Cl}^-]_{\text{solid}}} = 10^{1,492}.$$

Crystalic Na^+Cl^- mol fraction is one $[\text{Na}^+\text{Cl}^-]_{\text{solid}} = 1$ Na^+Cl^- (A) reactant and mixture in products $\text{Na}^+_{\text{aqua}} + \text{Cl}^-_{\text{aqua}}$ B+C



Equilibrium destiny is Prigogine attractor free energy change minimum ΔG_{min} .

Free energy change minimum reaching stabilises equilibrium mixture.

3rd ÷ 6th page: <http://aris.gusc.lv/BioThermodynamics/H2ODissociation.pdf>

Sodium acetate $\text{CH}_3\text{COONa}_s \rightleftharpoons \text{Na}^+_{\text{aqua}} + \text{CH}_3\text{COO}^-_{\text{aq}}$ electrolyte dissociations thermodynamics

$$\Delta G_{\text{dissociation}} = \Delta H_{\text{dissociation}} - T\Delta S_{\text{dissociation}} = 23,6 \text{ kJ/mol favored reaction.}$$

At equilibrium reached free energy minimum according compound mixture in expression:

$$K_{\text{eq}} = \frac{[\text{Na}^+][\text{CH}_3\text{COO}^-]}{[\text{CH}_3\text{COONa}]_{\text{solid}}} = 29,07539 = 10^{1,46}$$

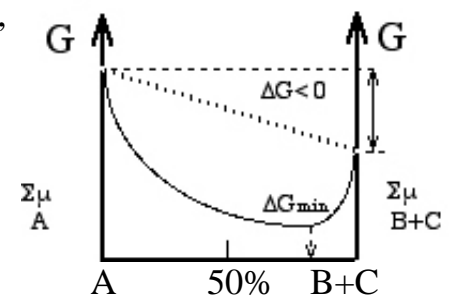
$$\Delta G_{\text{eq}} = -R \cdot T \cdot \ln(K_{\text{eq}}) = -8,3144 \cdot 298,15 \cdot \ln(29,07539) = -8,35375 \text{ kJ/mol},$$

Exothermic and exoergic $\text{CH}_3\text{COONa}_s$ dissociations reaction free

energy $\Delta G_{\text{dissociation}}$ negative $-23,65 \text{ kJ/mol}$ as favored reaction,

but minimises up to $\Delta G_{\text{min}} = \Delta G_{\text{eq}} = -8,35 \text{ kJ/mol}$

$$\text{in mixture reaching equilibrium } K_{\text{eq}} = \frac{[\text{Na}^+][\text{CH}_3\text{COO}^-]}{[\text{CH}_3\text{COONa}]_{\text{solid}}} = 10^{1,443}.$$



In mixture initial compound is crystalic $\text{CH}_3\text{COONa}_s$ (A) and products are $\text{Na}^+_{\text{aqua}} + \text{CH}_3\text{COO}^-_{\text{aqua}}$ (C+D).

Equilibrium destiny is Prigogine attractor free energy change minimum ΔG_{min} .

Free energy change minimum reaching stabilises equilibrium mixture.

7th page <http://aris.gusc.lv/BioThermodynamics/CO2O2Thermodynamic15A.pdf>

Ammonium chloride $\text{NH}_4\text{Cl}_{(s)} \Rightarrow \text{NH}_4^+_{(aq)} + \text{Cl}^-_{\text{aqua}}$ electrolyte dissociations process

$$\Delta G_{\text{dissociation}} = \Delta H_{\text{dissociation}} - T\Delta S_{\text{dissociation}} = -7,75 \text{ kJ/mol favored reaction.}$$

At equilibrium reached free energy minimum according compound mixture in expression:

$$K_{\text{eq}} = \frac{[\text{NH}_4^+]_{\text{aqua}} \cdot [\text{Cl}^-]_{\text{aqua}}}{[\text{NH}_4\text{Cl}]_{\text{aqua}}} = 10,7142 = 10^{1,03}$$

$$\Delta G_{\text{eq}} = -R \cdot T \cdot \ln(K_{\text{eq}}) = -8,3144 \cdot 298,15 \cdot \ln(10,7142) = -5,879 \text{ kJ/mol},$$

Endothermic and exoergic $\text{NH}_4\text{Cl}_{(s)}$ dissociations reaction free energy $\Delta G_{\text{dissociation}}$ negative $-7,75 \text{ kJ/mol}$ as favored reaction,

but minimises up to $\Delta G_{\text{min}} = \Delta G_{\text{eq}} = -5,879 \text{ kJ/mol}$

$$\text{in mixture reaching equilibrium } K_{\text{eq}} = \frac{[\text{NH}_4^+]_{\text{aqua}} \cdot [\text{Cl}^-]_{\text{aqua}}}{[\text{NH}_4\text{Cl}]_{\text{aqua}}} = 10^{1,03}.$$

Mixture initial compound is crystalline ammonium chloride $\text{NH}_4\text{Cl}_{\text{aqua}}$ (A) and products

are $\text{NH}_4^+_{\text{aq}} + \text{Cl}^-_{\text{aqua}}$ (C+D).

Equilibrium destiny is Prigogine attractor free energy change minimum ΔG_{min} .

Free energy change minimum reaching stabilises equilibrium mixture.

8th page <http://aris.gusc.lv/BioThermodynamics/CO2O2Thermodynamic15A.pdf>

Ammonium water $\text{NH}_4^+_{\text{aq}} + \text{H}_2\text{O} + \Delta G + Q \Rightarrow \text{NH}_3_{\text{aq}} + \text{H}_3\text{O}^+$ protolysis - dissociations thermodynamics

$$\Delta G_{\text{protolysis}} = \Delta H_{\text{protolysis}} - T\Delta S_{\text{protolysis}} = 138,8 \text{ kJ/mol unfavored reaction.}$$

At equilibrium reached free energy minimum according compound mixture in expression:

$$\frac{[\text{NH}_3]_{\text{aqua}} \cdot [\text{H}_3\text{O}^+]}{[\text{NH}_4^+]_{\text{aqua}} \cdot [\text{H}_2\text{O}]} = K_a = [\text{H}_2\text{O}] \frac{3,26 \cdot 10^{-18}}{1,78 \cdot 10^{-5}} = 55,3 \cdot 1,832 \cdot 10^{-13} = 1,013 \cdot 10^{-11}$$

$$\Delta G_{\text{eq}} = -R \cdot T \cdot \ln(K_{\text{eq}}) = -8,3144 \cdot 298,15 \cdot \ln(5,6025 \cdot 10^{-10}) = 62,76 \text{ kJ/mol},$$

Endothermic and endoergic $\text{NH}_4^+_{(aq)}$ protolysis reaction free energy

$\Delta G_{\text{protolysis}}$ positive $138,8 \text{ kJ/mol}$ as unfavored reaction,

but minimises up to $\Delta G_{\text{min}} = \Delta G_{\text{eq}} = 62,76 \text{ kJ/mol}$

$$\text{in mixture reaching equilibrium } K_{a\text{eq}} = \frac{[\text{NH}_3]_{\text{aqua}} \cdot [\text{H}_3\text{O}^+]}{[\text{NH}_4^+]_{\text{aqua}} \cdot [\text{H}_2\text{O}]} = 1,013 \cdot 10^{-11}.$$

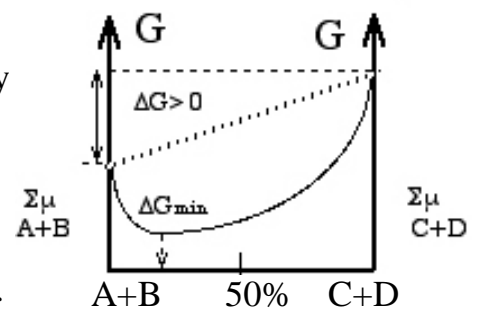
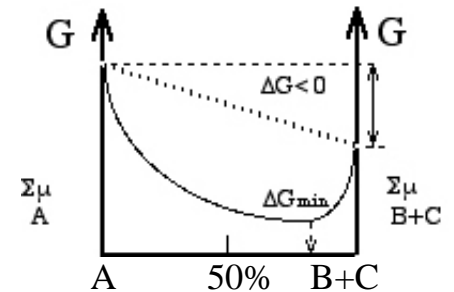
Mixture initial compounds are $\text{NH}_4^+_{(aq)} + \text{H}_2\text{O}$ (A) and

products are $\text{NH}_3_{(aq)} + \text{H}_3\text{O}^+$ (C+D).

Equilibrium destiny is Prigogine attractor free energy change minimum ΔG_{min} .

Free energy change minimum reaching stabilises equilibrium mixture.

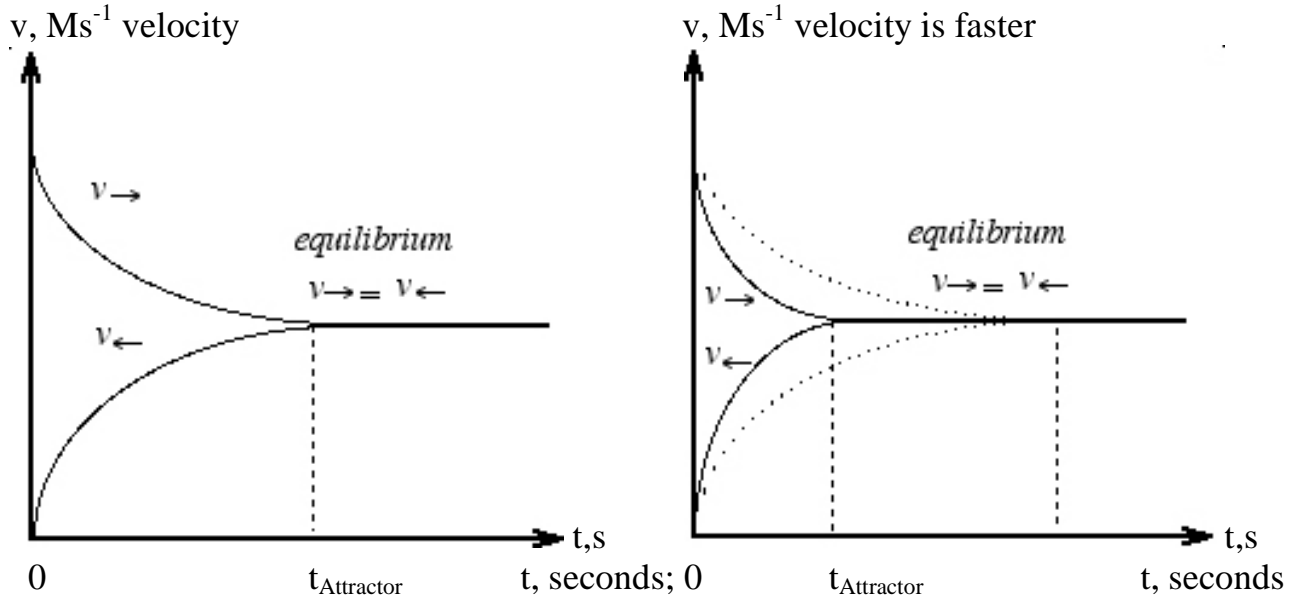
11th page <http://aris.gusc.lv/BioThermodynamics/CO2O2Thermodynamic15A.pdf>



Living organisms thousands of Biochemical reactions have been studied as at equilibria. Following equilibrium Attractor is velocity of reaction state constant value because forwards direct reaction of Initial compounds is equal to reverse reaction of products $v = v_{\rightarrow} = v_{\leftarrow}$:

Direct reaction forwards $\Rightarrow aA + bB \rightleftharpoons cC + dD \leftarrow$ reverse reaction.

Mass action Law for Direct $v_{\rightarrow} = k_{\rightarrow} \cdot C_A^a \cdot C_B^b \leftarrow$ reverse reaction $v_{\leftarrow} = k_{\leftarrow} \cdot C_C^c \cdot C_D^d$.



Velocity of reaction for Direct reaction decreases and for Reverse reaction increases.

Attractor equilibrium state reaching time $t_{\text{Attractor}}$ depends on Direct reaction velocity. Hydrogen peroxide conversion to life resources is slow $k_{\rightarrow} = 1.191 \cdot 10^{-8} \text{ Ms}^{-1}$, but CATALASE peroxide consume thirty million times $30 \cdot 10^6$ faster. Irreversible CATALASE reactivity for peroxide consuming is Prigogine attractor, that indispensable for Krebs cycle driving to fumarate 100% efficiency erasing $\text{H}_2\text{O}_{2\text{aqua}}$ molecules. <http://aris.gusc.lv/BioThermodynamics/CATALASE.pdf>

Carbon dioxide not react with water but small amount disolute in water:

$\text{CO}_2 \uparrow_{\text{gas}} + \Delta G_{\text{aqua}} \rightleftharpoons \text{Q} + \text{CO}_{2\text{aqua}}$ forming ratio $K_{\text{eq}} = [\text{CO}_{2\text{aqua}}] / [\text{CO}_2 \uparrow_{\text{gas}}] = 10^{-1.4846} = 0,032764 = 1/30,52$.

Enzyme CA (Carbonic Anhydrase) perform irreversible in water disolute carbon dioxide reaction with two water molecules: $\text{CO}_{2\text{aqua}} + 2\text{H}_2\text{O} + \text{Q} \xrightarrow{\text{CA}} \text{H}_3\text{O}^+ + \text{HCO}_3^-$, so improveing ratio 42,31 time up to ratio $K_{\text{eq}} = [\text{CO}_{2\text{aqua}} + \text{HCO}_3^-] / [\text{CO}_2 \uparrow_{\text{gas}}] = 1,3864$:

<http://aris.gusc.lv/BioThermodynamics/BufferSolutionLat.pdf>

Irreversible enzyme reactivity for products reaching in living organism are Ilya Prigogine declared attractors for organism complex reaction five types, which inactive compounds convert to following favored irreversible process, that works as Brownian molecular engine so drive organism to evolution, homeostasis, survival.

Attractors driven **HOMEOSTASIS** in four **ENZYME COMPLEX** reactions
 Human five 5 complex equilibria types versus non enzymatic chaos in reactions
HOMEOSTASIS attractors reaching instruments

1. gradual-sequential reactions,
2. ENZYMES **specificity** 100% efficiency of product **singularity**; PARALLEL reactions proceeding in Chemistry
3. joint-tandem reactions,
4. competitive-regulatory metabolites depending enzyme equilibria complexes;
- 5.(1. Catalase radical reactivity;) 5. Pollutions and environment Chemistry: radical chain reactions

5 complex Enzyme reactions

Versus non Enzymatic reactions

Enzyme governed complex reactions drive the LIFE in 5 ways

chaos and contamination

1. GRADUAL-CONSECUTIVE organized

7th page: <http://aris.gusc.lv/BioThermodynamics/Kinetics.pdf>

favored reaction sequence of **ENZYME** complexes for
 Glycolysis, Krebs cycle; Polycondensation: Replication,
 Polymerisation, Proteins Translation Synthesis

1. Chaotic

2. ENZYMES specificity 100% efficiency of product singularity

2. PARALLEL reaction preceeding in chemistry as side products

3. JOINT-TANDEM SYNTHESIS

Ribosomes for polypeptides, proteins
 Photosynthesis glucose and oxygen

Thermodynamic forbidden impossible reaction
 unfavored is positive free energy change $\Delta G = \Delta H - \Delta S \cdot T > 0$

1st to 5th page: <http://aris.gusc.lv/BioThermodynamics/74LidzsvarsDabaEngl.pdf>

4. COMPETITIVE regulation as inhibition and allostery

sensitive to concentration $O_{2(aqua)}$, HCO_3^- , H^+ (Le Chatelier principle)

His63,58 as for hemoglobin, His64 as for myoglobin as regulated back response

prevent (hypo amount) deficiency and (hyper amount) overproduction

so stabilises Physiologic pH=7.36, venouse $[O_{2(aqua)}] = 1.8 \cdot 10^{-5}$ M and arterial $[O_{2(aqua)}] = 6 \cdot 10^{-5}$ M.

Photosynthesis global stabilises oxygene concentration $[O_{2(AIR)}] = 20,95\%$ in Earth Atmosphere.

4. Chaotic

5. CATALASE radical reactivity drive the maintainance of life process

5. Pollution and environment chemistry the chaotic radical chain reactions

page 6th <http://aris.gusc.lv/BioThermodynamics/74LidzsvarsDabaEngl.pdf>

Prigogine attractors: enzymes reactivity in reaching equilibrium from chaos create organic regulated order of life maintenance. With enzyme specification as selectivity attractors organise: gradual-consecutive, joint-tandem, competitive regulation (allostery and inhibition), enzyme radical restricted reactions.

The Living organisms are organic regulated complex systems dissipative structure containing, irreversible processes working, with certain **Attractors** driven Brownian molecular engines, evolution and surviving instruments of homeostasis.

Certain aspects of **Attractor** pH=7,36 hydrogen ions concentration $[H^+]=10^{-7,36}$ M

Brønsted CA $CO_{2,aqua} + H_2O$, hemoglobin **shuttle** of O_2 and $HCO_3^- + H^+$ enzymes complexes
8. ÷ 10. Page: <http://aris.gusc.lv/BioThermodynamics/BufferSolution.pdf>

Enzyme **Carbonic anhydrase (CA)** made acid/base equilibrium $H_2O-CA-CO_2/HCO_3^- + H_3O^+$

There are **shuttle** buffer systems, that act in the human organism and allow **pH** of the organism to be stabilized constant in narrow interval to prevent changes ($pH = 7.36_{-0,01}^{+0,02}$) despite the fact, that organism produces great amount of metabolic $[CO_{2,aqua}]+[HCO_3^-]=0,0275$ M in homeostasis.

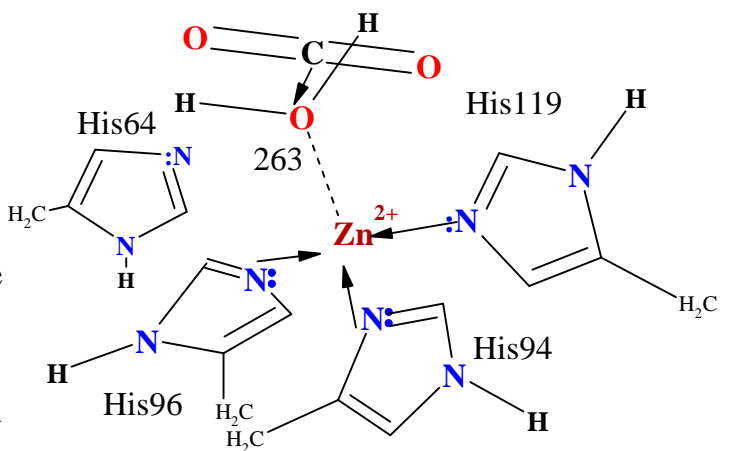
The **CA** made amount of acidic products is $[H_3O^+]=[HCO_3^-]=0,0275$ M compensated by **shuttle** hemoglobin, myoglobin and buffer solution of **CA**. **CA** buffer of blood are connected to **shuttle** hemoglobin captured proton H^+ and HCO_3^- by oxygen $O_{2,aqua}$ desorbition, due to consumed oxygen, are formed metabolic oxidation products in target cells of *tissues*:

Hydrogen carbonate buffer system carbonic anhydrase equilibrium keeps weak acid $CO_{2,aqua}$ and bicarbonate ions at normal levels $[HCO_3^-]=0.0154$ M, $[CO_{2,aqua}]=0.0076$ M, referring to 56,23 released volume CO_2 from 100 mL blood as *alkaline reserve* 2,036 / 1 in clinic evaluation. Carbon dioxide forms by oxidation of carbohydrates, of fats and of proteins.

Bicarbonate is created as hydration product by CA enzyme active coordination center of ion Zn^{2+} . It's location in enzyme carbonic anhydrase coordination pocket drive the hydration process:

$CO_{2,aqua} + 2H_2O \rightleftharpoons CA(Zn^{2+}) \rightleftharpoons H_3O^+ + HCO_3^-$ and

more details as: $(CAZn^{2+})H_2O(263) + H_2O + CO_{2,aqua} \rightleftharpoons (CAZn^{2+} \leftarrow OH^- + H^+ + H_2O) \rightleftharpoons HCO_3^- + H_3O^+$



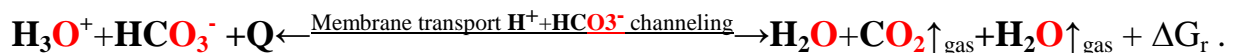
Shuttle of O_2 , $(HCO_3^- + H^+)$ enzymes Hemoglobin, Myoglobin

$Hb_R(O_2)_4 + 4H^+ + 4HCO_3^- \rightleftharpoons 4O_{2,aqua} + (H^+His63,58)_4Hb_T$...salt bridges... $4HCO_3^-$ stabilizing blood arterial concentration $[O_{2,aqua}]=6 \cdot 10^{-5}$ M and minimum venous $[O_{2,aqua}]=1.85 \cdot 10^{-5}$ M.

Deoxy hemoglobin $(H^+His63,58)_4Hb_T$ capture four protons $4H^+$ at histidine residues and $4HCO_3^-$ in venous hemoglobin form of erythrocytes **deoxy** $(H^+His63,58)_4Hb_T$ (**Tense** state). In **lungs shuttle** absorbs oxygen make arterial **oxy** hemoglobin $(O_2His63,58)_4Hb_R$ (**Relax** state) releasing $4H^+$ and $4HCO_3^-$.

1) First of four human buffer systems is enzyme **CA** made Brønsted Acid/Base endothermic process: $\text{Q} + \text{CO}_{2\text{aq}} + 2\text{H}_2\text{O} \xleftarrow{\text{CA}} \text{H}_3\text{O}^+ + \text{HCO}_3^-$ which consume heat **Q** of exothermic oxidation reactions. Its shift to right support low stabilized $\text{pH} = 7,36 \pm 0,01$ of hydrogen ions H_3O^+ concentration $[\text{H}_3\text{O}^+] = 10^{-7,36}$ M in products and drive high water $2\text{H}_2\text{O}$ concentration in square exponent $[\text{H}_2\text{O}]^2 = (993,36/18,0153)^2 = 55,139^2 = 3040,4$. Oxidation product $\text{CO}_{2\text{aq}}$ as bicarbonate salt bridge linked $\text{HCO}_3^- \dots \text{H}_3^+ \text{N-}$ and equal produced protons $[\text{H}^+] = [\text{CO}_{2\text{aq}}] = 0,0275 = [\text{HCO}_3^-]$ captures **deoxy** $(\text{H}^+ \text{His}63,58)_4 \text{Hb}_T \dots$ salt bridges $\dots 4\text{HCO}_3^-$ **shuttle** and brings to **lungs**.

Lungs evaporates $\text{CO}_2 \uparrow_{\text{gas}} + \text{H}_2\text{O} \uparrow_{\text{gas}}$ endothermic $\Delta H_r = +54,5 \text{ kJ/mol}$, but exoergic $\Delta G_r = -82,1 \text{ kJ/mol}$:



Symbol $(\text{H}^+ \text{His}63,58)_4 \text{Hb}_T$ to a **Shuttle** molecule of hemoglobin is convenient to write instead the complicated structure of hemoglobin. **Deoxy** hemoglobin is capturing $4\text{O}_{2\text{aq}}$ and **oxy** hemoglobin completely deprotonated 4H^+ and desorbed 4HCO_3^- . Equilibrium is oxygen concentration $[\text{O}_{2\text{aq}}] = 6 \cdot 10^{-5}$ M sensitive:



Lungs venous blood hemoglobin saturation with oxygen 459 times restore circulated arterial blood $[\text{O}_{2\text{aq}}] = 6 \cdot 10^{-5}$ M amount in one liter [O2Solutions.doc](#) Adsorbed four $4\text{O}_{2\text{aq}}$ $(\text{O}_2 \text{His}63,58)_4 \text{Hb}_R + 4\text{H}^+ + 4\text{HCO}_3^-$ in products release four protons 4H^+ and bicarbonate ions 4HCO_3^- , promoting evaporation $\text{CO}_2 \uparrow_{\text{gas}} + \text{H}_2\text{O} \uparrow_{\text{gas}}$ on **lungs** epithelia surface, and removing out of organism $[\text{H}^+] = 459 \cdot 6 \cdot 10^{-5} = 0,0275$ M amount $\text{H}^+ + \text{H}_2\text{O} \Rightarrow \text{H}_3\text{O}^+$, that is equal to total by respiration evaporated $[\text{CO}_2 \uparrow_{\text{gas}}] = 0,0275$ M amount on one liter of blood volume.

Shift to the left $(\text{O}_2 \text{His}63,58)_4 \text{Hb}_R + 4\text{H}^+ + 4\text{HCO}_3^-$ from **deoxy** captured **shuttle** $(\text{H}^+ \text{His}63,58)_4 \text{Hb}_T \dots$ salt bridges $\dots 4\text{HCO}_3^-$ oxygen depending concentration $[\text{O}_{2\text{aq}}] = 6 \cdot 10^{-5}$ M adsorbtion-desorbtion equilibrium explain pH stabilization at 7.36.

That explain, why pH is not changed, despite acid $\text{CO}_{2\text{aq}}$ product which involved in **CA** equilibrium. Henderson-Haselbalh homeostasis pH value expression leave the ratio $[\text{HCO}_3^-]/[\text{CO}_{2\text{aq}}] = 2,0263$ practically unchanged as intact both concentrations bicarbonate $[\text{HCO}_3^-]$ and carbon dioxide $[\text{CO}_{2\text{aq}}]$:

$7.36 = \text{pH} = \text{pK} + \log([\text{HCO}_3^-]/[\text{CO}_{2\text{aq}}]) = 7.0512 + \log([\text{HCO}_3^-]/[\text{CO}_2])$ anti logarithm is being alkaline reserve $[\text{HCO}_3^-]/[\text{CO}_{2\text{aq}}] = 10^{(\text{pH}-\text{pK})} = 10^{(7,36-7,0512)} = 10^{0,3088} = 2,0361/1$. **Lungs** when in venous blood erythrocytes **deoxy** $(\text{H}^+ \text{His}63,58)_4 \text{Hb}_T \dots$ salt bridges $\dots 4\text{HCO}_3^-$ **Shuttle** enzymes by oxygen $\text{O}_{2\text{aq}}$ adsorbtion release of protons H^+ and HCO_3^- so in **Lungs** evaporates carbon dioxide $\text{CO}_2 \uparrow_{\text{gas}}$ as breathed out in AIR. In such a way two equilibria stabilize arterial oxygen concentration $[\text{O}_{2\text{aq}}] = 6 \cdot 10^{-5}$ M with **shuttle** enzymes by oxygen adsorbtion-desorbtion and **CA** buffer system made value $\text{pH} = 7,36$ with oxidation driven the exchange metabolism of O_2 and CO_2 respiration to interface human body / environment.

2) Second buffer system, that support pH=7,36 in organisms, is the protein buffer system. This one has to be explained as 47 parallel multiple equilibria of protolytic acid groups of amino acids (shown in Table) are present on identical combinations repeating on each protein molecule.

At physiologic pH=7, 36 ±0.01 carboxylic groups **R-COO⁻** negative charged and amino groups **R-NH₃⁺** positive charged. For example, glutamic acid pK_a reference to physiologic pH value smaller as pK_{aR-COO⁻}=4.25<7.36. So for all **R-COO⁻** groups negative charge at pH=7.36. For protonated amines pK_a are greater for pH 7.36. For example glutamic acid protonated amine have greater pK_{a-NH₃⁺}= 8.8 > 7.36 . So for all **R-NH₃⁺** groups positive charge at pH=7.36.

Table show 47 constants pK_a for 20 amino acids of four type protolytic equilibria:

- | | | | |
|--|-----------------------------------|-------------------|--|
| acid | = base | +H ⁺ ; | Average constant pK_{a_mean} value for parallel protolytic |
| 1. R-COOH | = R-COO⁻ | +H ⁺ ; | equilibria sum is divided by number NpK _a of equilibria: |
| 2. R-NH₃⁺ | = R-NH₂ | +H ⁺ ; | pK_{a_mean} = (Σ pK _{a R group} + pK _{a-NH₃⁺} + pK _{a-COOH})/NpK _a |
| 3. Tyr-phenol- OH | =Tyr-phenol- O⁻ | +H ⁺ ; | In <i>Ostwald's dilution law</i> Attractor pH=7.36 of solution |
| 4. Cys- SH | =Cys- S⁻ | +H ⁺ | relates to physiologic concentration C logarithm: |

$$\text{Attractor pH} = \frac{\text{pK}_{a_mean} - \log C}{2} = 7.36 \text{ physiologic condition in living organisms}$$

Amino acid and protein at isoelectric point value pH=IEP sum of total overall **ion** charge is zero

0 — acidic charge (+) ————— zero „0” charge IEP ————— in basic medium charge minus (-) ————— pH scale
-COOH & **-NH₃⁺** positive charge **-COO⁻** & **-NH₃⁺** charge is negative **-COO⁻** & **-NH₂**

<http://aris.gusc.lv/ChemFiles/Albumin/1E7GpI.doc>; IgG1.pdb

<http://aris.gusc.lv/ChemFiles/ChromoHem/MyoGlobOxDeoxCoBiliverdin/1MBOaaLin153.doc>;

Amino Acid	pK _{aCOOH}	pK _{aNH3+}	pK _{aRgroup}
Isoleucine	2.36	9.68	
Valine	2.32	9.62	
Leucine	2.36	9.60	
Phenylalanine	1.83	9.13	
Cysteine	1.96	10.28	8.18
Methionine	2.28	9.21	
Alanine	2.34	9.69	
Proline	1.99	10.96	
Glycine	2.34	9.60	
Threonine	2.11	9.62	
Serine	2.21	9.15	
Tryptophan	2.38	9.39	
Tyrosine	2.20	9.11	10.07
Histidine	1.82	9.17	6.00
Aspartate	1.88	9.60	3.65
Glutamate	2.19	9.67	4.25
Asparagine	2.02	8.80	
Glutamine	2.17	9.13	
Lysine	2.18	8.95	10.53
Arginine	2.17	9.04	12.48

Attractor pH=7,36 ±0.01 at physiologic conditions

Table given maximal pK_{a-COOH⁻} value smaller about 7,36:

pK_{a-COOH⁻}=4.25<7,36 and given

smallest pK_{a-NH₃⁺} value grater about 7,36<8,80=pK_{a-NH₃⁺}

Table5.3 Reginald H. Garrett, Charles M. Grishman,
Biochemistry, University of Virginia 1995

Myoglobin pK_{a_mean} =7,3641 attractor concentration **C** =10^{-7.3559} M

Albumin molecule E7G.pdb 7,32=IEP 7 fatty acids small (-) charge and 7,40=IEP absent faaty acids small (+) positive at physiologic pH=7.36, but

gamma *Globulin* IgG1.pdb molecule has positive (+) charge,

as is greater pK_{a_mean} =IEP=7.91 at physiologic pH=7.36.

Attractor pH=7.36 physiologic concentration is **C**=10^{-6.80838} M

Human genome encoded 31078 are identified 23371 and unknown 7707 proteins. Attractor 7,36 pH concentration ranges from 10^{-6.2} M to 10^{-7.4002} M and average mean 10⁻⁷ M. Refer to 20000 proteins in summary concentration is 2*10⁻³ = 0,002 M. For bicarbonates summary [CO_{2aqua}]+[HCO₃⁻]=0,023 M determines pH=7,36 as well 20 alpha L-amino acids providing Attractor pH=7,36 concentration for all proteins in organisms. For example 18 proteins:

$$\begin{aligned} \text{pH} &= \frac{\text{pK}_a - \log C}{2} = \frac{7,3198 - \log 10^{-7,4002}}{2} = \mathbf{14,720/2=7,36} \text{ albumin Attractor concentration is } C=10^{-7,4002} \text{ M.} \\ \text{pH} &= \frac{\text{pK}_a - \log C}{2} = \frac{7,3641 - \log 10^{-7,3559}}{2} = \mathbf{14,720/2=7,36} \text{ mioglobin Attractor concentration is } C=10^{-7,3559} \text{ M} \\ \text{pH} &= \frac{\text{pK}_a - \log C}{2} = \frac{7,91162 - \log 10^{-6,80838}}{2} = \mathbf{14,720/2=7,36} \text{ } \gamma\text{-globulin Attractor concentration } C=10^{-6,80838} \text{ M} \\ \text{pH} &= \frac{\text{pK}_a - \log C}{2} = \frac{8,5228261 - \log 10^{-6,2}}{2} = \mathbf{14,720/2=7,36} \text{ AQP-0 Attractor concentration } C=10^{-6,2} \text{ M} \\ \text{pH} &= \frac{\text{pK}_a - \log C}{2} = \frac{7,637963 - \log 10^{-7,082}}{2} = \mathbf{14,720/2=7,36} \text{ AQP-1 Attractor concentration } C=10^{-7,082} \text{ M} \\ \text{pH} &= \frac{\text{pK}_a - \log C}{2} = \frac{7,36988 - \log 10^{-7,3502}}{2} = \mathbf{14,720/2=7,36} \text{ CA-2 Attractor concentration } C=10^{-7,3502} \text{ M} \\ \text{pH} &= \frac{\text{pK}_a - \log C}{2} = \frac{7,48983 - \log 10^{-7,23017}}{2} = \mathbf{14,720/2=7,36} \text{ CATALASE Attractor conc. } C=10^{-7,23017} \text{ M} \\ \text{pH} &= \frac{\text{pK}_a - \log C}{2} = \frac{7,9782 - \log 10^{-6,7418}}{2} = \mathbf{14,720/2=7,36} \text{ PCTP Attractor conc. } C=10^{-6,7418} \text{ M} \\ \text{pH} &= \frac{\text{pK}_a - \log C}{2} = \frac{7,3515556 - \log 10^{-7,368444}}{2} = \mathbf{14,720/2=7,36} \text{ CERT Attractor conc. } C=10^{-7,3684} \text{ M} \\ \text{pH} &= \frac{\text{pK}_a - \log C}{2} = \frac{7,8124638 - \log 10^{-6,9075362}}{2} = \mathbf{14,720/2=7,36} \text{ CPTP Attractor conc. } C=10^{-6,9075} \text{ M} \\ \text{pH} &= \frac{\text{pK}_a - \log C}{2} = \frac{7,6758065 - \log 10^{-7,0441935}}{2} = \mathbf{14,720/2=7,36} \text{ ACD11 Attractor conc. } C=10^{-7,04419} \text{ M} \\ \text{pH} &= \frac{\text{pK}_a - \log C}{2} = \frac{7,5906111 - \log 10^{-7,1293889}}{2} = \mathbf{14,720/2=7,36} \text{ GAP ASAP1 Attractor conc. } C=10^{-7,1293889} \text{ M} \\ \text{pH} &= \frac{\text{pK}_a - \log C}{2} = \frac{7,6496 - \log 10^{-7,0704}}{2} = \mathbf{14,720/2=7,36} \text{ mouse STARD4 Attractor conc. } C=10^{-7,0704} \text{ M} \\ \text{pH} &= \frac{\text{pK}_a - \log C}{2} = \frac{8,0456818 - \log 10^{-6,6743182}}{2} = \mathbf{14,720/2=7,36} \text{ human STARD1 Attractor conc. } C=10^{-6,6753} \text{ M} \\ \text{pH} &= \frac{\text{pK}_a - \log C}{2} = \frac{7,4338926 - \log 10^{-7,2861074}}{2} = \mathbf{14,720/2=7,36} \text{ KES1_YEAST Attractor conc. } C=10^{-7,286} \text{ M} \\ \text{pH} &= \frac{\text{pK}_a - \log C}{2} = \frac{8,1354167 - \log 10^{-6,5845833}}{2} = \mathbf{14,720/2=7,36} \text{ NLTP1_WHEAT Attractor conc. } C=10^{-6,58458} \text{ M} \\ \text{pH} &= \frac{\text{pK}_a - \log C}{2} = \frac{7,8727 - \log 10^{-6,8473}}{2} = \mathbf{14,720/2=7,36} \text{ COX-2 human 1DIY.pdb Attractor conc. } C=10^{-6,8473} \text{ M} \\ \text{pH} &= \frac{\text{pK}_a - \log C}{2} = \frac{7,6666087 - \log 10^{-7,0533913}}{2} = \mathbf{14,720/2=7,36} \text{ ADH IV human Attractor conc. } C=10^{-7,0533913} \text{ M} \\ \text{pH} &= \frac{\text{pK}_a - \log C}{2} = \frac{7,7505286 - \log 10^{-6,96947}}{2} = \mathbf{14,720/2=7,36} \text{ human AR TES Attractor conc. } C=10^{-6,96947} \text{ M} \end{aligned}$$

3) Biochemical important phosphate buffer system Henderson Haselbalh studies on **system** middle point $[\text{Na}_2\text{HPO}_4]=[\text{NaH}_2\text{PO}_4]$ pH is equal to constant value $\text{pH}=\text{pK}_a=7,199$.

$$7.199 = \text{pK}_a + \log \frac{[\text{HPO}_4^{2-}]}{[\text{H}_2\text{PO}_4^-]} ; \text{ as } \log \frac{[\text{HPO}_4^{2-}]}{[\text{H}_2\text{PO}_4^-]} = \log 1 = 0$$

Calculate the ratio $[\text{HPO}_4^{2-}] / [\text{H}_2\text{PO}_4^-]$ of solution having **Attractor pH** = 7,36 value !

$$\text{Attractor } 7.36 = \text{pK}_a + \log \frac{[\text{HPO}_4^{2-}]}{[\text{H}_2\text{PO}_4^-]} ; \text{ ratio } \frac{[\text{HPO}_4^{2-}]}{[\text{H}_2\text{PO}_4^-]} = 10^{7.36-7.199} = 10^{0.161} = 1.45 \text{ the ratio}$$

Salt $[\text{HPO}_4^{2-}]$ prevails over weak acid form $[\text{H}_2\text{PO}_4^-]$ times 1.45 as ratio .

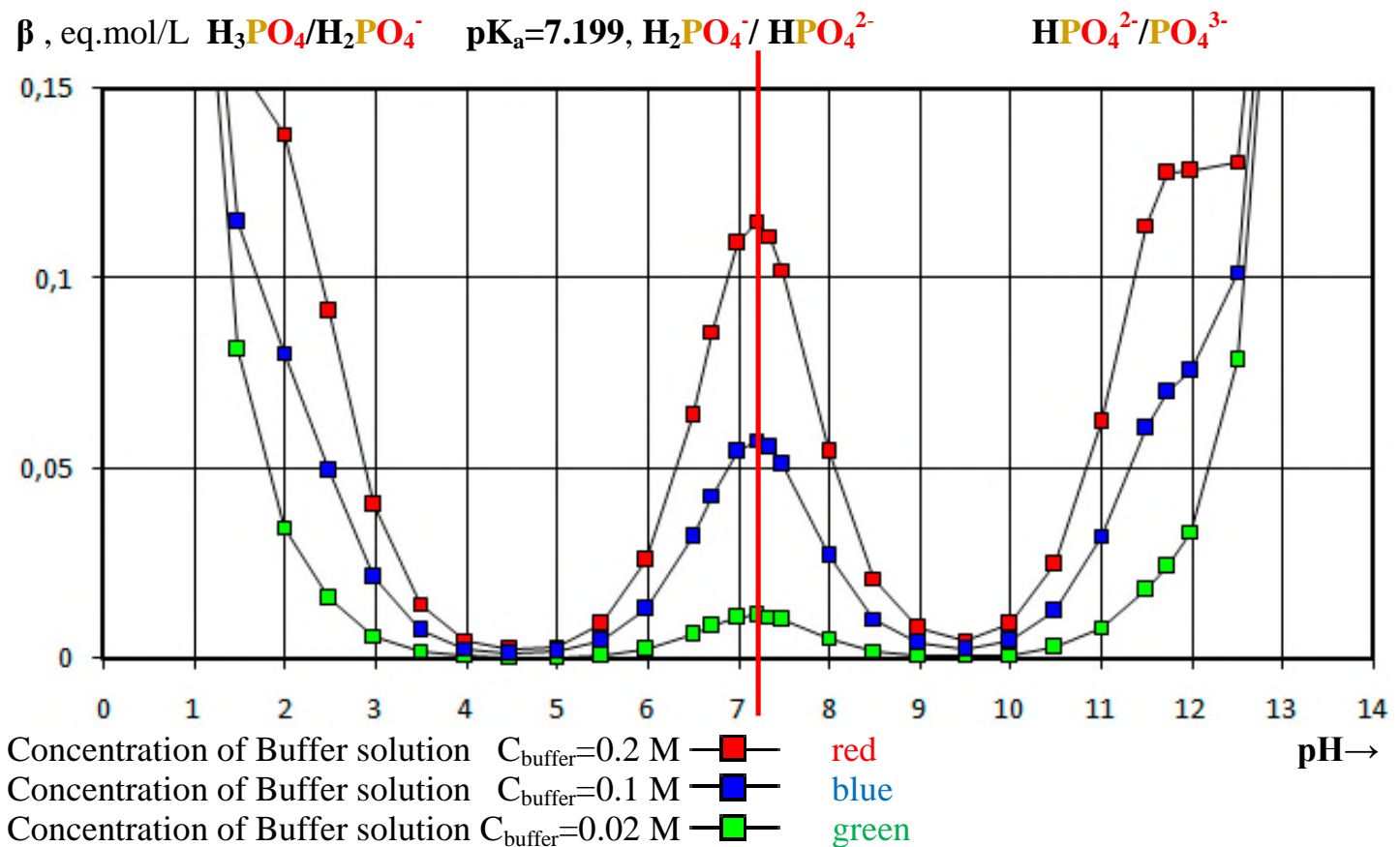
Buffer capacity β on buffer system middle point is friendly to Attractor 7.36.

1 Buffer solution dilution dose no change value pH is constant as $n_{\text{salt}}/n_{\text{acid}} = \text{constant}$.
the same for ten times diluted buffer $n_{\text{salt}}/n_{\text{acid}} = \text{const}$. amount ratio logarithm is $\log(1)=0$!

1.a Water drinking in human organism $\text{pH}=7,36$ value do not change and not intact!

2. Buffer capacity is proportional to concentration $\beta \sim C$!

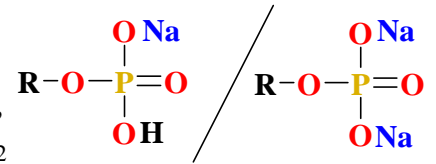
3. Buffer solution **Middle point** $\text{pH}=\text{pK}_a$. Buffer capacity has the maximal value β_{max} !
Mark on graph maximum !



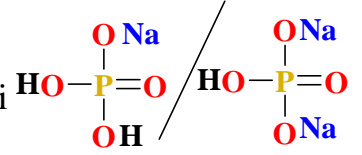
4. Buffer capacity at **middle point** is $\beta_{\text{max}} = 0.55 \cdot C$ as $\beta = 0.55 \cdot 0.2 = 0.11 \text{ eq.mol/L}$ and
 $\beta' = 0.55 \cdot 0.02 = 0.011 \text{ eq.mol/L}$!

5. Buffer solution **middle point** Buffer capacity against the acid and the base
 is symmetrically equal $\beta_{\text{ac}} = 0.11 \text{ eq.mol/L} = \beta_{\text{b}}$, $\beta'_{\text{ac}} = 0.011 \text{ eq.mol/L} = \beta'_{\text{b}}$!

4) Biological ubiquities exist besides the inorganic phosphate buffer system, buffer systems of the organic esters of phosphoric acid so as ATP (adenosine tri phosphate), ADP (adenosine di phosphate), CTP, CDP, GTP, GDP, TTP, TDP, UTP, UDP, NADH B₃ vitamin, FADH₂ B₂ vitamin, phospho proteins, glucose phosphate, fructose phosphate, etc. :If there are any difficulties to understand the structure of last two groups of compounds ,



remember, that phosphoric acid can be shown in structure as in the ester of phosphoric acid one of the hydrogen atoms is replaced by an organic radical. Practically the buffer system consists of a mono substituted and bi substituted salts of the ester. Likely as for phosphates .

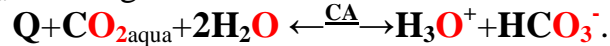


Not all of these 4 buffer systems act in the same organism body water solutions.

In *erythrocytes* main are bicarbonate buffer with **shuttle** hemoglobin-based proton oxygen O_{2aqua} sensitive exchange:



Krebs cycle product CO_{2aqua} exchanged to bicarbonate buffer solution:



In blood *plasma* enzyme CA bicarbonate pH=7.36±0,01, protein and phosphate buffer solutions.

In organisms dominate bicarbonate 0,023 M and phosphate buffer systems 0.155 M in muscles.

Besides the normal “chemical” mechanisms of buffer action in maintaining constant

pH=7.36±0,01, with

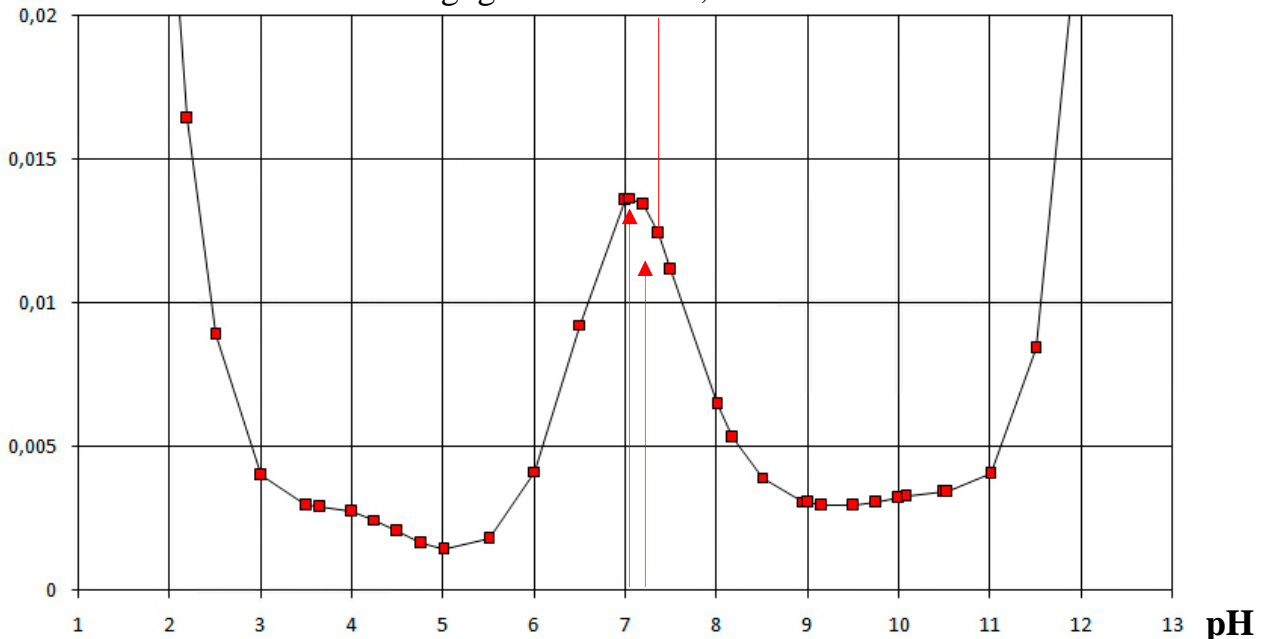
deoxy hemoglobin (H⁺His63,58)₄Hb_T...salt bridges...4HCO₃⁻ (Tense state),

oxy hemoglobin (O₂His63,58)₄Hb_R (Relax state)

and with carbonic anhydrase CA driven bicarbonate buffer systems are a joint physiological mechanism of action. Attractors as irreversible engines carries out the exchange of breathed in O₂ and breathed out CO₂ between AIR in *lungs* on interface human body / environment driven with and to certain Attractors. 12th Page: <http://aris.gusc.lv/BioThermodynamics/BufferSolution.pdf>

β , eq.mol/L

Prigogine attractor 7,36 value



Three buffer systems sum in living organisms forms broadband capacity maximum at bicarbonate protolytic constant value pK_a=7,0512 in range from pH=5 to pH=9.

Biochemistry Thermodynamics Attractors of life, evolution and survival.