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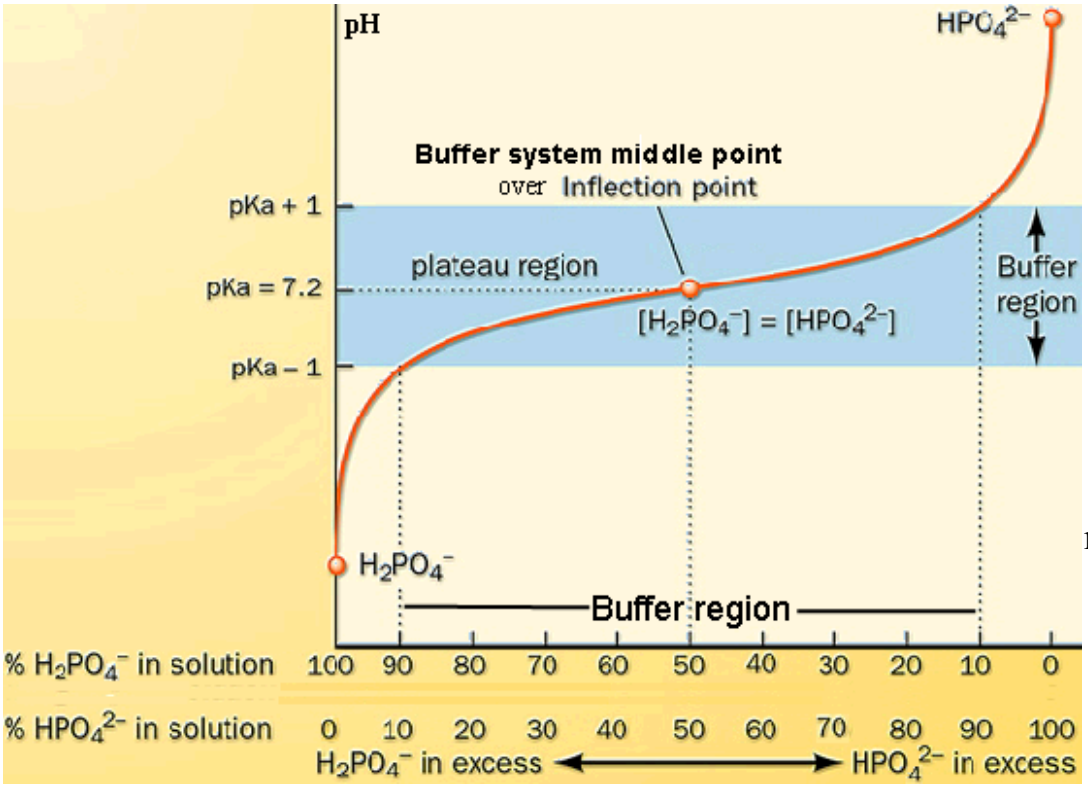
Three buffer systems in the homeostasis tend to Prigogine attractor **pH** value **7.36** formed of two dominate phosphate and bicarbonate buffer systems with **over inflection point** on the middle pK_a=7.199 and pK_a=7.0512. The create protonate amines **-NH_3^+** and deprotonate carboxylates **-COO^-** for functional activity of proteins and enzymes, amino acids, carbonic acids and amines with broadband silencing interval pH=6 ÷ 7.36.

1 . Phosphate $H_2PO_4^-+H_2O \Leftrightarrow HPO_4^{2-}+H_3O^+$ and 2 . Bicarbonate $CO_{2aqua}+2H_2O \xrightarrow{CA} H_3O^++HCO_3^-$ buffers at CRC data 2010 I=0.25 M are with classic K_a and thermodynamic K_{eq} acid constants expressed:

1. Dihydrogen phosphate *buffer system form phosphate, pyrophosphate, phosphate esters like ATP etc.* with *differing by one deprotonated* H^+ phosphate group *less* **$H_2PO_4^-$/ HPO_4^{2-}** , where



the weak acid contains greater number of hydrogen ions plays the role of proton donor

$H_2PO_4^-$

and deprotonated weak acid created base form contains one hydrogen atom less

HPO_4^{2-}.

Buffer region ±1=pH one unite wide band region from middle point pK_a, At over inflection middle point has maximum value:

$\beta_{max}=0.55*C_{buffer}$ on pH scale at pK_a .

$K_a=\frac{[HPO_4^{2-}]\cdot[H_3O^+]}{[H_2PO_4^-]}=10^{-7.199}$ and thermodynamic $K_{eq}=\frac{[HPO_4^{2-}]\cdot[H_3O^+]}{[H_2PO_4^-]\cdot[H_2O]}=K_a/[H_2O]=10^{-7.199}/55.3=1.143*10^{-9}$,

Henderson Haselbalh $pH=pK_a+\log\frac{[HPO_4^{2-}]_{base}}{[H_2PO_4^-]_{acid}}=7.36$ is with homeostasis ratio $\frac{[HPO_4^{2-}]}{[H_2PO_4^-]}=1.45$ expressed.

2. ENZYME Carbonic Anhydrase **CA** high rate protolysis equilibrium attractor in Biosphere *Buffer system:*

$Q+CO_{2aqua}+2H_2O \xrightarrow{CA} H_3O^++HCO_3^-$ endothermic equilibrium $K_a=10^{-7.0512}$ M=10^{-pKa};

Henderson Haselbalh equation $pH=pK_a+\log(n_{base}/n_{acid})=7.0512+\log(n_{HCO3-}/n_{CO2aqua})$.

3. Carbonic acids, fatty acids, amino acids (proteins), protonate amines at Physiologic conditions pH=7.36 :

3a. **$CH_3COOH+H_2O \Leftrightarrow H_3O^++CH_3COO^-$**; $K_a=\frac{[H^+]\cdot[CH_3COO^-]}{[CH_3COOH]_{nondis}}=10^{-4.76}$ $K_a=1.74*10^{-5}$ M =10^{-pKa}

3b. **AA-COOH+$H_2O \Leftrightarrow H_3O^+$+AA-$COO^-$**, $K_{aCOOH}=\frac{[AA\text{-}COO^-]\cdot[H^+]}{[AA\text{-}COOH]_{nondis}}=10^{-pKa}$ $2.0 < pK_{aAACOOH} < 4.9$;

3c. **AA-NH_3^++$H_2O \Leftrightarrow H_3O^+$+AA-$NH_2$** , $K_{aNH3+}=\frac{[AA\text{-}NH_2]\cdot[H^+]}{[AA\text{-}NH_3^+]_{protonate}}=10^{-pKa}$; $pK_{aAANH3+} > 8.8$;

3d. **NH_4^++$H_2O \Leftrightarrow H_3O^+$+$NH_{3\,aqua}$** ; $K_a=\frac{[H^+]\cdot[NH_3]_{aqua}}{[NH_4^+]}=10^{-pKa}=10^{-9.25}$ $K_a=\frac{10^{-14}}{1{,}78*10^{-5}}=10^{-9.25}$ M

Weak acid protolysis *Ostwald's* dilution law

The buffer system of weak acid protolytic equilibrium thermodynamic studies about pH value stability, if add water so dilute buffer solution and if add a strong acid or base.

1. CARBONIC ACID protolysis

Weak acid and classic dissociation form deprotonated conjugate base: $CH_3COOH \Leftrightarrow CH_3COO^- + H^+$.
Sodium acetate is the conjugate base strong electrolyte $\alpha = 1$: $CH_3COONa \Rightarrow CH_3COO^- + Na^+$.
As a great number of acetate ions salt do not let the dissociation of acetic acid as oppressed with acetate ions in products of dissociation equilibrium. According Le Chatelier's theorem acid dissociation is shifted to left. For this reason the dissociation degree of the acetic acid is close to zero $\alpha \Rightarrow 0$ but positive number.

If a strong acid is added to the buffer solution, the H_3O^+ ions react with base protonating CH_3COO^- acetate to form acetic acid : $H_3O^+ + CH_3COO^- \Leftrightarrow CH_3COOH + H_2O$

Now there are **2** reasons, why the **pH** remains constant:

1) the strong acid (H_3O^+ ion) is transformed to a weak acid CH_3COOH.

2) the concentration of acetic acid **C** increases, therefore for strong acid **pH** is more acidic. In fact, a weak acid acetic acid dissociation degree **α** decreases depending on **C** according ***Ostwald's* dilution law**: $\alpha = \sqrt{\frac{K}{C}}$

For this reason, when the concentration of acetic acid grows, its dissociation degree is adjusted to be smaller and therefore the concentration of H_3O^+ ions and **pH** remains constant.

Assuming it all in a shorter way, the strong acid is transformed into a weak one and the dissociation degree of the weak acid is adjusted to be smaller, therefore **pH** remains constant.

If a strong base is added to buffer, the OH^- ions from the strong base react with the weak acid (acetic acid) :

$$OH^- + CH_3COOH \Rightarrow CH_3COO^- + H_2O$$

Now the same two reasons for practically constant **pH** can be seen :

1) strong base OH^- ion deprotonates weak acid to form base form salt-acetate CH_3COO^- ion,
2) acetic acid was used, to do the concentration **C** of acetic acid decreases,
the dissociation degree **α** grows, hence, H_3O^+ concentration and **pH** remains constant. $\alpha = \sqrt{\frac{K}{C}}$

2. Protonate AMONIA weak acid NH_4^+ protolysis *Ostwald's* dilution law

Weak ammonium acid ions and deprotonated ammonia buffer solution: $NH_4^+ + H_2O \Leftrightarrow H_3O^+ + NH_{3aqua}$.

Ammonium chloride is a strong electrolyte $\alpha = 1$: : $NH_4Cl \Rightarrow NH_4^+ + Cl^-$

Base NH_{3aqua} protonation product NH_4^+ ions grate amount left side in buffer solution prevent protonation of ammonia as oppressed (as the presence of NH_4^+ shifts equilibrium to the right) and protonation degree for ammonia tends to zero but is asmall positive number $\alpha \Rightarrow 0$.

If a strong base is added to this solution OH^- ions react with weak acid NH_4^+ and form ammonia $NH_{3\ aqua}$:

$$OH^- + NH_4^+ \Rightarrow NH_{3\ aqua} + H_2O$$

Due to this reaction :

1) a very strong base OH^- ion is transformed into deprotonated weak acid form base $NH_{3\ aqua}$,

2) weak acid concentration **C** decreases deprotonation dissociation degree **α** is adjusted to be higher $\alpha = \sqrt{\frac{K}{C}}$.

Equilibrium : $NH_4^+ + H_2O \Leftrightarrow H_3O^+ + NH_{3\ aqua}$ shifts to right and H_3O^+ concentration **pH** remains constant.

When a strong acid is added, than H_3O^+ ions protonate ammonia $NH_{3\ aqua}$ and weak acid NH_4^+ concentration **C** increases but dissociation degree $\alpha = \sqrt{\frac{K}{C}}$ value decreases.

Strong base OH^- is transformed to buffer base $NH_{3\ aqua}$ but dissociation degree $\alpha = \sqrt{\frac{K}{C}}$ increases.

Henderson Haselbalh weak acid protolysis pH EQUATION

In discusion above we have prooved why **pH** of a buffer remains constant, but it is necessary to know, how particular value (**pK_a, n_{base} , n_{acid}**) will keep constant the **pH** by a given buffer solution.

1. Henderson Haselbalh pH expressions

The Henderson Haselbalh expression derives from weak acid deprotonation constant **K_a** expression.

In human body exist four type weak acids protolysis with water equilibria .

1. Phosphate, 2. carboxylate, 3. Ammonium ions, 4. Amino acids **AA** (carboxilate, protonate amines, tyrozine, cysteine).

1. Phosphate: $H_2PO_4^- + H_2O \Leftrightarrow H_3O^+ + HPO_4^{2-}$; $K_a = \frac{[H^+]\cdot[HPO_4^{2-}]}{[H_2PO_4^-]} = 10^{-7.199}$ $10^{-7.199} = K_a = 6.3*10^{-8}$ M $= 10^{-pKa}$

2. $CH_3COOH + H_2O \Leftrightarrow H_3O^+ + CH_3COO^-$; $K_a = \frac{[H^+]\cdot[CH_3COO^-]}{[CH_3COOH]_{nondis}} = 10^{-4.76}$ $10^{-4.76} = K_a = 1.74*10^{-5}$ M $= 10^{-pKa}$

3. $NH_4^+ + H_2O \Leftrightarrow H_3O^+ + NH_{3\,aqua}$; $K_a = \frac{[H^+]\cdot[NH_3]_{aqua}}{[NH_4^+]} = 10^{-pKa} = 10^{-9.25}$ $K_a = \frac{10^{-14}}{1{,}78*10^{-5}} = 5.618*10^{-10}$ M

4a. $AA\text{-}COOH + H_2O \Leftrightarrow H_3O^+ + AA\text{-}COO^-$, $K_{aCOOH} = \frac{[AA\text{-}COO^-]\cdot[H^+]}{[AA\text{-}COOH]_{nondis}} = 10^{-pKa}$ $2.0 < pK_{aAACOOH} < 4.9$;

4b. $AA\text{-}NH_3^+ + H_2O \Leftrightarrow H_3O^+ + AA\text{-}NH_2$, $K_{aNH3+} = \frac{[AA\text{-}NH_2]\cdot[H^+]}{[AA\text{-}NH_3^+]_{protonate}} = 10^{-pKa}$; $pK_{aAANH3+} > 8.8$;

4c. Tyr-phenol-$OH + H_2O \Leftrightarrow H_3O^+ + Tyr\text{-}O^-$, $K_{aTyr} = \frac{[Tyr\,O^-]\cdot[H^+]}{[Tyr\,OH]_{nedis}} = 10^{-10.07}$; Tyrosine and cysteine at physiologic pH=7.36 are just not dissociate acids, which do not form buffer.

4d. $Cys\text{-}SH + H_2O \Leftrightarrow H_3O^+ + Cys\text{-}S^-$, $K_{aCys} = \frac{[Cys\,S^-]\cdot[H^+]}{[Cys\,SH]_{nedis}} = 10^{-8.18}$;

Ions origin in solution are two sources – weak acids and electrolytes. Deprotonated weak acid form base concentration in equilibrium constant **K_a** expression designated as **C_{base}**:

$[HPO_4^{2-}]$; $[CH_3COO^-]$; $[NH_{3\,aqua}]$; $[AA\text{-}COO^-]$; $[AA\text{-}NH_2]$; **C_{base}** (base).

Weak acid concentration in constant **K_a** expression is **C_{acid}**:

$[H_2PO_4^-]$; $[CH_3COOH]_{nedis}$; $[NH_4^+]$; $[AA\text{-}COOH]$; $[AA\text{-}NH_3^+]$; **C_{acid}** (weak acid)

Replacing in the equation of **K_a** the weak acid and deprotonated acid concentrations we have :

$K_a = \frac{[H^+]C_{base}}{C_{acid}}$. Calculate the $[H_3O^+] = \frac{K_a \bullet C_{acid}}{C_{base}}$. Taking a minus logarithm from both sides :

$\log[H^+] = -\log K_a - \log\frac{C_{acid}}{C_{base}}$ we got the Henderson Haselbalh equation $pH = -\log[H_3O^+] = pK_a + \log\frac{C_{base}}{C_{acid}}$

converting to **pH:** (note, logarithm mathematics rool **log a/b = -log b/a**)

Factors, *that affect the* ***pH*** *value of a buffer system* The **pH** value, that is kept **constant** by a buffer.

1) buffer system forming acid weakness pK_a exponent $K_a = 10^{-pKa}$;

2) deprotonated acid and weak acid ratio n_{base}/n_{acid} in buffer solution volume **V**;

3) not **pH** depends on dilution of buffer solution. Drinking the water leave safe the blood **pH=7.36** constant.

4)Fourth factor, that affects **pH** of a buffer system, is temperature - increases of temperature increase the value

of **K_a** and this shifts **pH** to lower values (as **pK_a = -log K_a**, the greater is acid **K_a**, the smaller is **pK_a**).

DIFFERENT FORMS OF pH Henderson Haselbalh EXPRESSION

Henderson Haselbalh buffer solution **pH** form weak acids and deprotonated acid form base.

$$pH=pK_a+\log\frac{C_{base}}{C_{acid}}$$

Components amount ratio logarithm forms **pH** value. **pH** expression of C_{base}/C_{acid} converting to number of moles ratio n_{base}/n_{acid} as buffer system volume **V** is common and can to scratch.

$$pH=pK_a+\log\frac{n_{base}}{n_{acid}} \qquad pH=pK_a+\log\frac{n_{base}/V}{n_{acid}/V}$$

It is very often necessary to express the **pH** of a buffer through the concentrations of the two initial solutions of weak acid and deprotonated acid base form. So practical mix together solutions.

If the buffer solution is prepared from two solutions than numbers of moles calculate **n = C'V'**, where **C'** and **V'** are the concentration and the volume of the initial solutions. Mixing total buffer solution volume is $V_{buf}=V'_{base}+V'_{acid}$. The **Henderson Haselbalh** equation is used for practical calculations for **pH** .

$$pH=pK_a+\log\frac{C'_{salt}\bullet V'_{salt}}{C'_{acid}\bullet V'_{acid}}$$

Δn_{ac} is a strong acid moles, for example **HCl**, added to buffer solution, which decreases Brensted base amount $n_{base}-\Delta n_{ac}$ and increases the buffer weak acid amount $n_{acid}+\Delta n_{ac}$, thus change the buffer system **pH** value about $\Delta pH= pH - pH_{ac}$ to decrease that. Adding the strong base, for example **NaOH**, change the buffer system **pH** value to increase that about $\Delta pH= pH_b - pH$.

$$pH_{ac}=pK_a+\log\frac{n_{salt}-\Delta n_{ac}}{n_{acid}+\Delta n_{ac}}$$

$$pH_b=pK_a+\log\frac{n_{salt}+\Delta n_b}{n_{acid}-\Delta n_b}$$

EXAMPLE OF BUFFER ACTION studies

Now, when the equation for buffer pH is derived, we can study the buffer action.

Let us imagine, that **0.01** mole of **HCl** is added to a buffer system, containing **0.5** moles of acetic acid and **0.5** moles of sodium acetate. **pH** values before and after addition of **HCl** ($pK_a = 4.74$ for acetic acid) can be calculated as follows: **pH** before addition of **HCl: pH = 4.74 + log(0.5/0.5) = 4.74 + log 1 = 4.74 + 0 = 4.74**

Strong acid addition of **HCl** causes a reaction : **$HCl + CH_3COONa \Rightarrow CH_3COOH + NaCl$**

As the number of moles of **HCl** is **0.01**, the number of moles of acetic acid will increase by **0.01** moles and n_{CH_3COONa} will decrease by **0.01** moles, therefore : **pH** after addition of **HCl**:

$$pH_2 = 4.74 + \log((0.5 - 0.01) / (0.5 + 0.01))= 4.74 + \log 0.996 = 4.74 - 0.002 = 4.738$$

and the **pH** change is $\Delta pH = pH_1 - pH_2 = 0.002$.

At the same time, if this amount of **HCl** was added to **1** liter of pure water (the initial **pH** = **7** in pure water), after addition of **HCl,** concentration of H^+ ions would be **0.01** mole/l (as **HCl** is added to **1** l of H_2O), making **pH** of solution: **pH = -log [H^+] = -log 0.01 = -(-2) = 2**. Thus, the **pH** change in this case is **ΔpH = 5 = 7 - 2**.

As one can see, the **pH** change, caused by **HCl** in a buffer solution is negligible when compared to the **pH** change, caused by the same amount of acid in pure water, where the change from **pH** = **7** to **pH** = **2** (from neutral to strongly acidic) is drastic for hydrogen ion **[H^+]** concentration $\frac{[H^+]_{HCl}}{[H^+]}=\frac{10^{-2}}{10^{-7}}=10^5$**=100000 times**.

BUFFER CAPACITY β

The **pH** value of the weak acid buffer system is **Henderson Haselbalh** equation:

$$\mathbf{pH=pK_a+\log\frac{n_{base}}{n_{acid}}}$$

where $\mathbf{n_{base}}$ and $\mathbf{n_{acid}}$ are the numbers of equivalents of salt and acid respectively.

If an acid is added to buffer solution, it will react with the base $\mathbf{n_{base}}$ and will decrease (at the same time, as more weak acid will be formed $\mathbf{n_{acid}}$ will increase).

This means, that the buffer system cannot stand against just any amount of added acid. If the number of equivalents of the added strong acid reaches the number of equivalents $\mathbf{n_{base}}$ of the base, present in buffer system, all base will be used up and the resistant **pH** constant buffer system doesn't exist anymore.

As well, if a strong base is added to the buffer system, it will use the weak acid of buffer system and the buffer system can stand against addition of base only until the number of equivalents of the added base is equal to the number of equivalents $\mathbf{n_{acid}}$ of weak acid.

From the discussion above one has to make a conclusion, that a value, that characterizes the ability of buffer system to stand against addition of strong acid or strong base, is necessary. Such a value is buffer capacity, which is expressed as $\mathbf{\beta = \frac{\Delta n}{\Delta pH \bullet V_{buffer}} = \left(\frac{mol}{Liter}\right)}$

where $\Delta\mathbf{n}$ is the number of equivalentmols of the strong acid or base, that is added to the buffer,

$\Delta\mathbf{pH}$ is the **pH** change, caused by the addition of strong acid $\Delta\mathbf{n_{ac}}$ or strong base $\Delta\mathbf{n_b}$,

$\mathbf{V_{buffer}}$ is the volume of the buffer solution, to which the strong acid or strong base is added.

Buffer capacity units are equivalent mol/Liter. The definition of buffer capacity in words is as follows :

*Buffer capacity **β** shows, what strong acid mol numbers $\Delta\boldsymbol{n_{ac}}$ or a strong base $\Delta\boldsymbol{n_b}$ can be added to **1** liter $\boldsymbol{V_{buffer}}$ of buffer solution to shift its **pH** value for **1 pH** unit.*

On middle point buffer capacity is affected by four reasons :

***1**.the total summary concentration of buffer solution* $\mathbf{C_{base}' + C_{acid}' = C'}$

Buffer capacity is proportional to summary total concentration $\mathbf{C' = C_{base}' + C_{acid}'}$.

***2**. the ratio between buffer components* on **middle point** is $\frac{\mathbf{n_{base}}}{\mathbf{n_{acid}}}=1$ with reaching

2. <u>maximal value</u> $\mathbf{\beta_{acid}=\beta_{base}=0.55\cdot C'}$. **Henderson Haselbalh** buffer equation on middle point $\mathbf{pH=pK_a+\log\frac{n_{base}}{n_{acid}}}$ is equal to weak acid constant $\mathbf{pH=pK_a}$ value. because $\mathbf{\log\frac{n_{baze}}{n_{skab}}=\log1=0}$.

3. deviated from the ratio one $\mathbf{n_{base}/n_{acid}=1}$ „middle point" both buffer capacities against strong acid $\mathbf{\beta_{ac}}$ and buffer capacity against strong base $\mathbf{\beta_b}$ fast becomes smaller.

Single weak acid buffer system action broad $\mathbf{pH=pK_a\pm1}$ is in two units of **pH**.

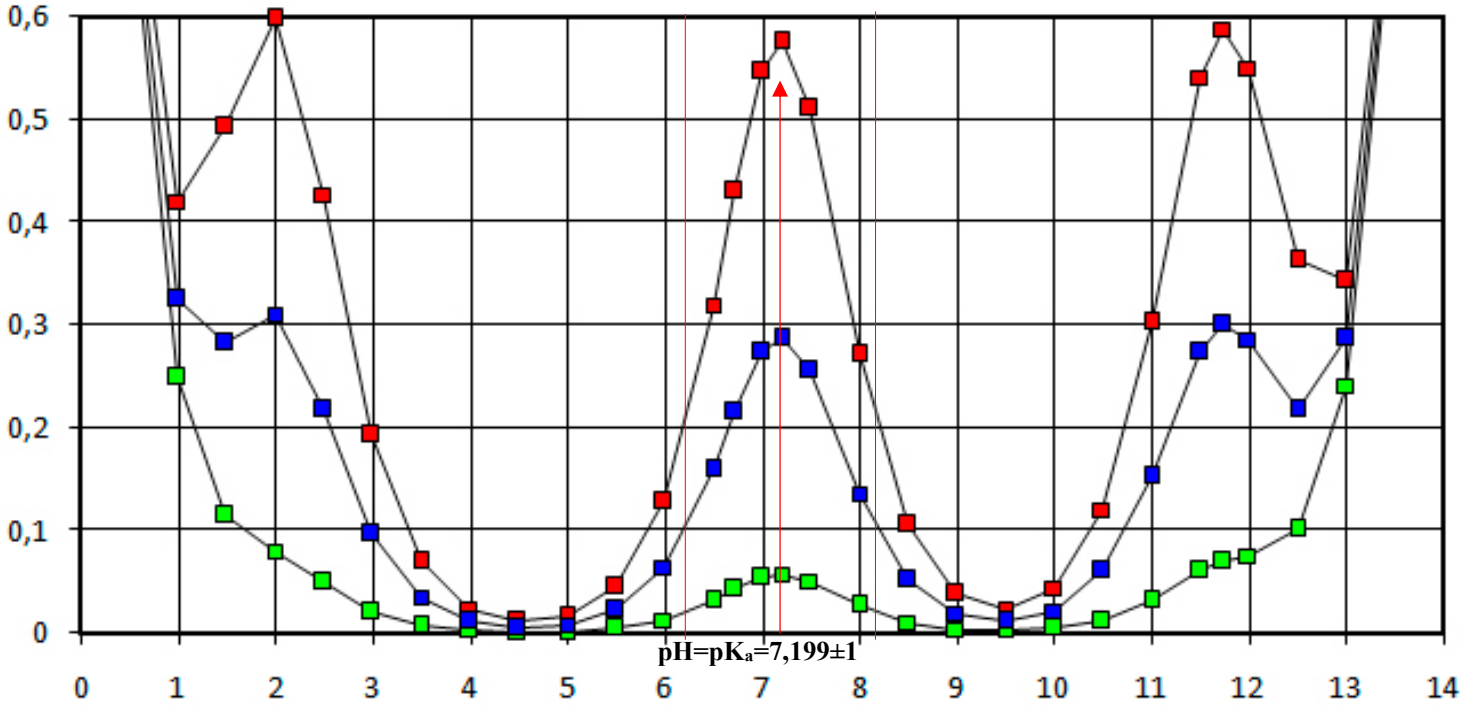
4. Buffer capacities on „middle point" are *symmetrically* equal $\mathbf{\beta_{ac}=\beta_b}$. Added strong acid pH decreases about $\Delta\mathbf{pH=-1}$, but added strong base pH increases about $\Delta\mathbf{pH=+1}$.

5. Amino acids and proteins using 47 pK_a constants create broadband buffer systems with inactive buffer capacity silencing zone pH 6 to 7.36. On this zone dominate phosphate pK_a=7.199 and bicarbonate pK_a=7.0512 buffer systems maintaining 7.36 pH.

Phosphate buffer system $H_2PO_4^-/HPO_4^{2-}$; $pH=pK_a+\log\frac{[HPO_4^{2-}]}{[H_2PO_4^-]}=7.199+\log\frac{1.45}{1}=7.36$

Buffer capacity strong acid Δn_{ac} or strong base Δn_b equivalent mole/ into one Liter buffer solution $\Delta pH=\pm 1$

β , eq.mol/L **$pK_a=7.199$, $H_2PO_4^-/HPO_4^{2-}$**



Buffer system **middle point** $pH=pK_a=7.199$ over inflection point maximum of buffer capacity β=0.55

pH

Concentration of Buffer solution C_{buffer}= 1 M — red

Concentration of Buffer solution C_{buffer}=0.5 M — blue

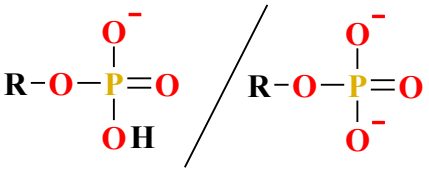
Concentration of Buffer solution C_{buffer}=0.1 M — green

$H_2PO_4^-$ weak acid, contains one number hydrogen more and $H_2PO_4^-$ is weak acid.

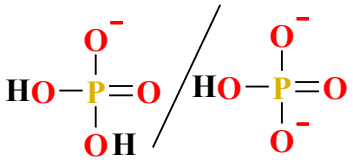
HPO_4^{2-} deprotonated weak acid form of base, contains one hydrogen les and HPO_4^{2-} is protolytic base

1) Biological important phosphate buffer system $H_2PO_4^-$ / HPO_4^{2-} with pK=7.199 value.

1a) Biological ubiquities exist phosphate buffer system of the organic esters of phosphoric acid so as ATP (adenosine tri phosphate), ADP (adenosine diphosphate), CTP, CDP, GTP, GDP, TTP, TDP, UTP, UDP, NADH B_3 vitamin, $FADH_2$ B_2 vitamin, phospho proteins, glucose phosphate, fructose:



phosphate, etc. If there are any difficulties to understand the structure 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.



Total concentration 0.155 M=[$H_2PO_4^-$]+[HPO_4^{2-}] in muscle cells cytosole.

2) Inactive silencing interval ΔpH from 6 to 7.36 indispensible serve for proteins, amino acids, carbonic acids, amines, phosphates charged negative **R–COO⁻** , **HPO_4^{2-}/R-PO_4^{2-}**, positive **R–NH_3^+** functional groups activation. Like to hemoglobin proteins as long chain polypeptides and free amino acids with four type weak acid groups constitute 47 values of weak acid constants: $pK_{a\text{-}COOH}$, $pK_{a\text{-}NH3+}$, $pK_{aRgroup}$.

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

R-COO⁻ deprotonated carboxyl negative anion salt groups, protonated positive charged ammonium groups **R-NH_3^+**, neutral phenolic acid Tyr–**OH** and Cys-**SH** neutral sulfhydryl groups.

In physiologic medium pH=7.36 ±0.01

Carbonic acid groups deprotonated negative charged **R-COO⁻** and amino groups **R-NH_3^+** protonated positive charged.

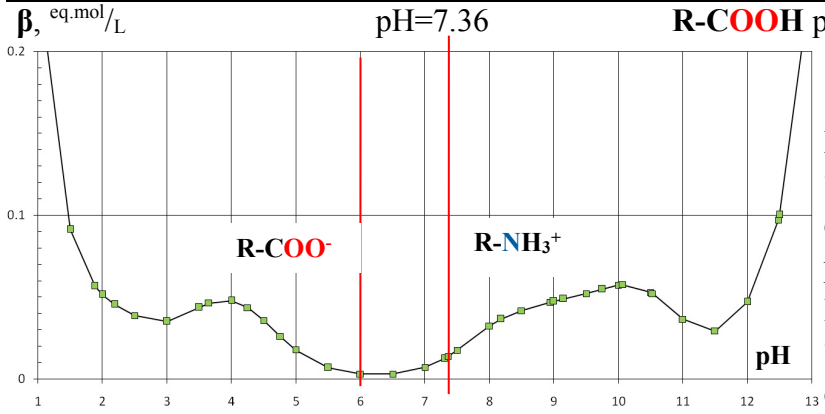
Table given maximal $pK_{a\text{-}COOH}^-$ value smaller about 7.36: $pK_{a\text{-}COOH}^-$=4.25<4.9 (fatty acids) <7.36 and given smallest $pK_{a\text{-}NH3+}$ value grater about 7.36 < 9.04 = $pK_{a\text{-}NH3+}$

20 amino acids have four protolytic pK_a equilibria in 47 groups:

1. **R-COOH** ⇔**R-COO⁻** +**H⁺**, 22 groups of 47
2. **R-NH_3^+** ⇔**R-NH_2** + **H⁺** 22+1 group of 47
3. **Tyrosine**-phenol-**OH**⇔**Tyrosine**-phenolate-**O⁻** +**H⁺** one group,
4. **Cysteine-SH** ⇔**Cysteine-S⁻** + **H⁺** one group .

NpK_a number of parallel protolytic equilibria average pK_{a_mean} value is calculated as $pK_{a\_mean}=(\Sigma pK_{a\ R\ group}+\Sigma pK_{a\text{-}NH3+}+\Sigma pK_{a\text{-}COOH})/NpK_a$

In *Ostwald's dilution law* calculates one the pH of solution at concentration C logarithm: $pH=\frac{pK_{a\_mean}-\log C}{2}=$.....



R-COOH pK_a values are on interval from 2 to 4.9 and **R–NH_3^+** pK_a values are on interval from 8 to 10 .

Proteins buffer have silence region from **pH=6** to 7.36 . Albumin total buffer solution concentration C_{buffer}=1 mM . Buffer capacity at physiologic pH=7.36 is **β** =12,5 mM.

Indispensible silencing interval ΔpH from 6 to 7.36 providing attractor pH=7.36 with two dominate buffer systems Bicarbonate and Phosphates .

Shuttle hemoglobin-based bicarbonate 4HCO_3^-, proton H^+ to oxygen O_{2aqua}. Actual shown concentrations of arterial and venous components at arterial oxygen fresh saturated blood state and venous states: [6,14]

$O_2+(H^+BPG^{5-})Hb_T$…salt bridge...$(HCO_3^-)+H_2O\leftrightarrow Hb_R(O_2)+H_3O^++HCO_3^-+BPG^{5-}$;

$K=[Hb_R(O_2)]*[BPG^{5-}]*[H_3O^+]*[HCO_3^-]/[(H^+BPG^{5-})Hb_T..\text{salt bridge}(HCO_3^-)]/[H_2O]/[O_{2aqua}]=2.43*10^{-8}$;

arterial $K=0.96*$ **0.005*** $10^{-7.36}*$ 0.0154/ 0.04/ 55.3/ $6/10^{-5}=2.43*10^{-8}$;

venous $K=0.63*$ **0.005*** $10^{-7.36}*$ 0.0154/ 0.37/ $55.3/0.426/10^{-5}=2.43*10^{-8}$;

high land venous $K=0.48*$**0.008***$10^{-7.36}*$ 0.0154/ 0.52/ $55.3/0.3692/10^{-5}=2.43*10^{-8}$;

See level air oxygen $[O_2]$=20.95% have in erythrocytes $[BPG^{5-}]$=**5 mM**, but high land (see Oxygen in blood [6]) of low air $[O_2]$ erythrocytes have content of $[BPG^{5-}]$=**8 mM** and keep equilibrium at $K=2.43*10^{-8}$.

Stabilized multi functional Attractor pH=7.36 sustain $[HCO_3^-]$=0.0154 M, $[CO_{2aqua}]$=0.0076 M despite blood circulation cycle generate amounts of $[H^+]=459*6\cdot10^{-5}$ M, 0.0275 M=$[HCO_3^-]$. Arterial concentrations $[O_2]=6\cdot10^{-5}$ M, $[Hb_R(O_2)]$=0.96, $[(H^+)Hb_T..\text{salt bridge}..(HCO_3^-)]$=0.04 and venous homeostasis concentrations are $[O_2]=0.426\cdot10^{-5}$ M, $[Hb_R(O_2)]$=0.66, $[(H^+)Hb_T..\text{salt bridge}..(HCO_3^-)]$=0.33. [6,14]

In blood *plasma* dominate enzyme **CA** bicarbonate **pH=7.36** and phosphate buffer solutions - protein silence.

In sweat, urine and digestive apparatus dominates bicarbonate system and phosphate system is too present.

Besides the normal "chemical" mechanisms of buffer action in maintaining constant **pH=7.36**±0.01, with deoxy hemoglobin $(H^+His63,58)_4Hb_T$ (Tense state), oxy hemoglobin $(O_2His63,58)_4Hb_R$ (**Relax** state) and with carbonic anhydrase **CA** driven bicarbonate buffer systems a joint physiological mechanism of action carries out the inhaled O_2 and exhaled CO_2 between AIR in ***lungs*** and tissues on interface human body / environment**.**

3) Bicarbonate buffer system in Biosphere create protolysis of oxidation products H_3O^++HCO_3^-.

Protolysis attractors **pH**=7.36, **CA**, oxygen 20.95% functional activate homeostasis

CA dominate buffer system using hemoglobin **shuttle** stabilizes pH=7.36 and arterial level $[O_{2aqua}]$ =$6\cdot10^{-5}$ M:

deoxy **hemoglobin**(H^+His63,58)$_4Hb_T$(Tense state)<=>**oxy hemoglobin**(O_2His63,58)$_4Hb_R$(**Relax** state)+**4**H^+

Carbonic Anhydrase **CA** indispensible Biosphere attractor, that generate concentration gradients H_3O^++HCO_3^-.

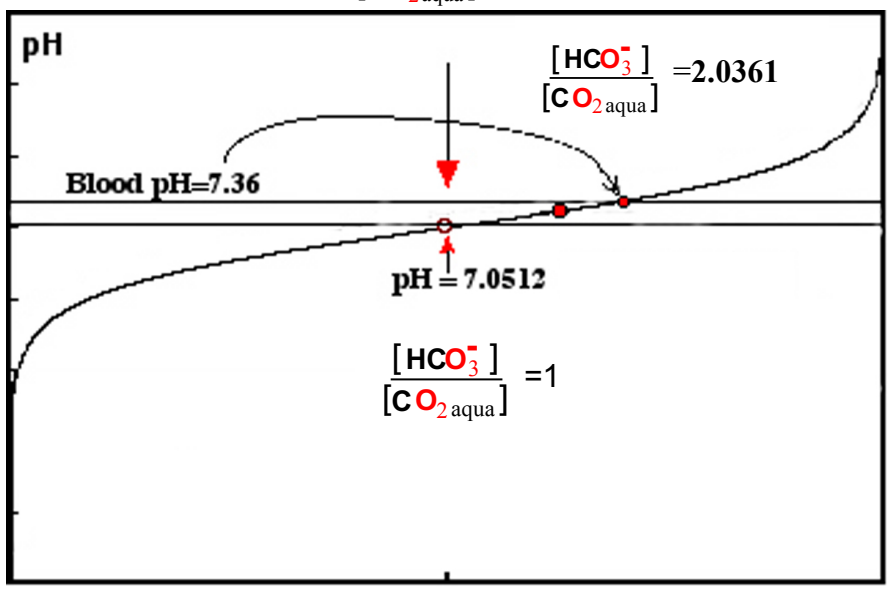
Organism store oxidation products H^+ , HCO_3^- in hemoglobin capturing proton in distal histidine and salt bridge linked HCO_3^-…$H_3{}^+N$- bicarbonate, that transport out of organism to ***lungs***. Oxygen adsorption on deoxy hemoglobin **shuttle**: **4**O_{2aqua}+(H^+His63,58)$_4Hb_T$<=>(O_2His63,58)$_4Hb_R$+**4**H^+ release through proton channels H^+ and through bicarbonate channels HCO_3^- across membranes breathing out $CO_2\uparrow_{gas}$, that stabilize blood pH=7.36 and restore arterial concentration $[O_{2aqua}]$ =$6\cdot10^{-5}$ M:

Biosphere attractor Carbonic anhydrase **CA** protolysis valueless water $2H_2O$ and CO_{2aqua} activate functional to H_3O^++HCO_3^- . Activate products accumulate free energy value $G_{H3O+HCO3-}$=68.5 $^{kJ}/_{mol}$ maintaining endothermic dominate buffer system $Q+CO_{2aqua}+2H_2O \xrightarrow{CA} H_3O^+ + HCO_3^-$ and high rate protolysis equilibrium biosphere attractor value pH=7.36. At absence of **CA** CO_2 slow react OH^- ions: $CO_{2aqua}+OH^-=>HCO_3^-$ with velocity constant k_{1OH}=1.5*10^2 $M^{-2}s^{-1}$, concentrations $[OH^-]$=10^(-6.64) M, $[CO_{2aqua}]$=0.0007512 M. Velocity of reaction is negligible small: $v=k_{1OH}*[CO_{2aqua}]*[OH^-]$=1.5*10^2*0.0007512*10^(-6.64)= 2.58*10^{-8} Ms^{-1}.

High rate protolysis equilibrium attractors in Biosphere pH=7.36 concentration $[H_3O^+]$=$10^{-7.36}$ M, water concentration $[H_2O]$=55.3 M, carbonic anhydrase CA and air oxygen 20.95% since 500 million Years are buffer solutions with **Henderson-Haselbalh** equation:

$$7.36=pH=pK+\log\frac{[HCO_3^-]}{[CO_{2\,aqua}]}=7.0512+\log\frac{[HCO_3^-]}{[CO_{2\,aqua}]};$$

$$\frac{[HCO_3^-]}{[CO_{2\,aqua}]}=10^{(pH-pK)}=10^{(7.36-7.0512)}=10^{0.3088}=\frac{2.0361}{1}.$$



Buffer middle point region, overinflection point in graph ○ and buffer capacity maximum:

β_{max}=0.55·C, if sum C=$[HCO_3^-]$+$[CO_2]$=0.023 M

β_{max}=0.55*0.023=0.01265 $^{eq.mol}/_L$.

Attractor value 7.36=pH

7.36=pK_a+log($[HCO_3^-]/[CO_2]$)=

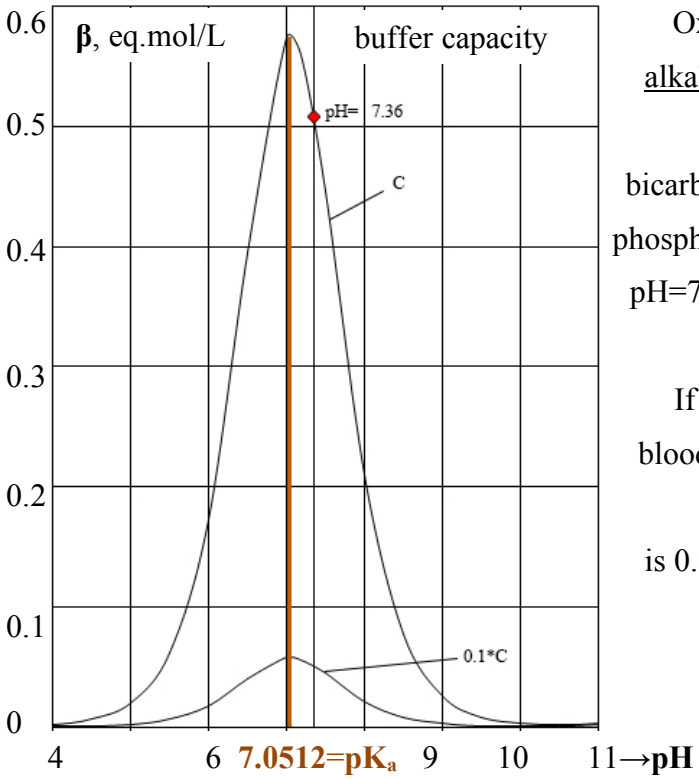
=**7.0512**+**log(2.0361)**=7.36.

Alkaline reserve ratio $[HCO_3^-]/[CO_{2aqua}]$ is **2.0361/1**.

HCO_3^-0% **50%** 100% **salt** – buffer system **base**

CO_2+ $2H_2O$ 100% **50%** 0% **weak acid** buffer component

Carbon dioxide CO_{2aqua} reaction velocity with OH^- slower $10^{16.54}$ times about neutralization: $H_3O^+ + HCO_3^- => CO_{2aqua} + 2H_2O + \Delta G + Q$, because neutralization velocity constant is $k_2 = 5.17 * 10^{18}\ M^{-1}s^{-1}$. Just carbon dioxide CO_{2aqua}, bicarbonate HCO_3^- and hydroxonium ions H_3O^+ concentration in water H_2O are included in high rate protolysis equilibrium attractors **pH** Henderson Haselbalh equation, because any generate concentration gradient ratio are at equilibrium. Therefore multi functional biosphere attractors pH=7.36 are at equilibrium , while homeostasis continues , because is non-equilibrium state. Deviation from attractors: pH=7.36 concentration $[H_3O^+]=10^{-7.36}$ M, water concentration $[H_2O]$=55.3 M, synthesis of carbonic anhydrase CA and global oxygen 20.95% on air since 500 million Years stop homeostasis and it extinct from Biosphere. Buffer capacity $\beta_{max}=0.55 \cdot C$ analyzing with one molar concentration C=1M= $[HCO_3^-]+[CO_{2aqua}]$ and carbonic anhydrase acid dissociation constant value pK_a=7.0512 is friendly to blood **pH**=7.36.



Oxidation products CO_{2aqua} are acids, which compensate with alkaline reserve. Alkaline reserve in homeostasis form high rate protolysis equilibrium attractors as concentration gradients bicarbonate $[HCO_3^-]/[CO_{2aqua}]$=**2/1** and $[HPO_4^{2-}]/[H_2PO_4^-]$=**1.45** phosphate ratio with **pH** 7.36 in blood. ***Alkaline reserve*** of blood pH=7.36 analyze adding to **100** mL blood sample sulfuric acid H_2SO_4 , that react and CO_2 is released.

If **56.23** mL (**50-60** mL) of gas CO_2 evolved from **100** mL blood sample, ***alkaline reserve*** of homeostasis is **normal** and total ***alkaline reserve*** amount concentrations sum is 0.023M = $[HCO_3^-]+[CO_{2aqua}]$ constitute of concentrations $[HCO_3^-]$ = 0.0154 M und $[CO_{2aqua}]$=0.0076 M.

Alkalosis and ***acidosis***

Two types of **diseases** occur deviation from attractor valur pH=7.36..

1) *Respiratory alkalosis* occurs, if **lungs** are hyperventilated, for example, during anesthesia. If CO_{2aqua} concentration decreases **pH>7.36 alkalosis** due to hyperventilation, the blood vessels are broadened and their tonus is lowered as a result of it, therefore O_2 supply to brain is shortened.

For this reason it is necessary to use AIR mixtures of O_2 and CO_2 during anesthesia instead of pure oxygen. If respiratory alkalosis occurs for other reasons than hyperventilation of **lungs**, the ratio **2/1** of the buffer components can be re-established in a longer period of breathing normal, CO_2-containing AIR 400 ppm.

2) *Respiratory acidosis* occurs in the cases, when the concentration of CO_2 in the AIR is increased. The result of this is that the action of breathing muscles becomes more difficult. Again, this can be canceled, if the patient starts breathing normal AIR. Hoverer, if increased CO_2 content in the AIR lasts long, metabolic acidosis occurs **pH**<7.36.

Metabolic acidosis hemoglobin reserves depleted oxygen concentration below venous $[O_2]=0.486 \cdot 10^{-5}$ M.

Carbonic Anhydrase **CA** and **shuttle** hemoglobin

I) $O_{2AIR}+H_2O \overset{membrane}{\rightleftharpoons} H_2O+O_{2aqua}$; $4O_{2aqua}+deoxy(H^+His63,58)_4Hb_T => oxyHb_R(O_2)_4+4H^+$, $[O_2]=6\cdot10^{-5}$ M;

$C_6H_{12}O_6+6O_{2aqua}+6H_2O \rightarrow 6H_3O^++6HCO_3^-$ oxidation products transport down the concentration gradient.

II) $Qaqua+CO_{2aqua}+2H_2O \overset{CA}{=>} H_3O^++HCO_3^- \overset{membrane}{\rightleftharpoons} H_2O+CO_2\uparrow_{gas}+H_2O$. 4th, 45th, 46th pages .

II) Activate products accumulate free energy value $G_{H3O+HCO3-}$=68.5 kJ/mol maintaining endothermic $Q+CO_{2aqua}+2H_2O \overset{CA}{\rightarrow} H_3O^++HCO_3^-$ ΔH_{Hess} =9.7576 kJ/mol; dominate buffer system and high rate protolysis equilibrium biosphere attractor value pH=7.36 since 500 million Years.

Prigogine attractors equilibrium K_{eq} , classic acid K_a constant and free energy change minimum ΔG_{eq}:

$$\frac{[HCO_3^-]_{aqua}\cdot[H_3O^+]}{[CO_2]_{aqua}\cdot[H_2O]^2} = K_{eq}=K_a/[H_2O]^2=10^{-7.0512}/55.3457339^2=2.906*10^{-11}=10^{-10.54}$$;

minimum ΔG_{eq}=-RTln(K_{eq})=-8.3144•298.15•ln($10^{-10.224}$)= 60.145 kJ/mol .

$K_{Homeostasis}=[H_3O^+]*[HCO_3^-]/[H_2O]^2/[CO_{2aqua}]=10^{\wedge(-7.36)}*0.0154/55.3457339^{\wedge2}/0.0076=2.89*10^{-11}$.

High rate protolysis stai at equilibrium, while homeostasis continues $K_{Homeostasis}=2.89*10^{-11}<2.906*10^{-11}=K_{eq}$;

Membrane concentration gradients and electrochemical potentials drive ions HCO_3^- , H^+ gradients on transport:

1. H^+ gradient potential $E_H=P\bullet lg([10^{-pH}{}_{extraMit}/10^{-pH}{}_{Mitochon})=0.06154*lg(10\wedge2.36)=0.14523$ V;
2. Gradient $E_{HCO3-}=-P\bullet log([HCO_3^-{}_{cytosole}]/[HCO_3^-{}_{Mitochon}])=-0.06154*log(0.0154/0.0338919)=0.0210821$ V;

$E_{sum}=0.14523+0.0210821=0.1663168$ V=$E_{membrane}$; $\Delta G_F=nFE=-1*96485*0.1663168=-16.0471$ kJ/mol;

3. $\Delta G_{HCO3-}=RTln([HCO_{3cytosol}]/[HCO_{3Mitoch}])=8.3144*310.15*log(0.0154/0.0338919)=-2.0341094$ kJ/mol;
4. $\Delta G_{H+}=-RTln([H_3O^+]_{extraMit}/[H_3O^+]_{Mitochon})=-RTln(10^{-7.36}/10^{-5})=-8.3144*310.15*ln(10\wedge^{2.36})=-23.3943$ kJ/mol ;

$\Delta G_{total}=\Delta G_F+(\Delta G_{HCO3-}+\Delta G_{H+})=-16.0471+(-2.0341094)+(-23.3943)=-41.4755$ kJ/mol exoergic drive ions.

Neutralization: $H_3O^++HCO_3^- \rightarrow 2H_2O+CO_{2aqua}+Q=7.1928$ kJ/mol exothermic+$\Delta G=-60.15$ kJ/mol exoergic.

Neutralization velocity; $v_2=k_2\bullet[H_3O^+][HCO_3^-]=1.6958*10\wedge^{15}*10\wedge^{(-5)}*0.0154=261153200$ Ms^{-1};

Evaporation from solution $[CO_{2aqua\_air}]=K_{sp}*[CO_{2air}]*[H_2O]=0.034045*0.0004*55.3=0.000751$ M;

Equilibrium K= $\frac{[CO_2 gas]\cdot[H_2O]}{[CO_2\ aqua\_air]}$ =29.4; $K_{CA\_aqua\_air}=[CO_{2aqua}+HCO_3^-]/[CO_{2aqua\_air}]=0.023/0.000751=30.6$ times.

In lungs exhale 30.6 times more $CO_2\uparrow_{gas}$. Lungs epithelia surface do not have CA enzymes.

Evaporation absent Carbonic Anhydrase CA $CO_{2aqua}+Q$(20.3 kJ/mol) endothermic <=>$CO_2\uparrow_{gas}+\Delta G$(-8.379 kJ/mol);

Substance	$\Delta H°_{Hess}$, kJ/mol	$\Delta S°_{Hess}$, J/mol/K	$\Delta G°_{Hess}$, kJ/mol
H_3O^+	-285.81	-3.854	-213.274599
$-OH^-$	-230.015	-10.9	-157.2
HCO_3^-	-689.93	98.324	-586.93988
HCO_3^-	**-692.4948**	**-494.768**	**-544.9688**
H_2O	-285.85	69.9565	-237.191
H_2O	**-286.65**	**-453.188**	**-151.549**
CO_{2aqua}	-413.7976	117.5704	-385.98
$CO_2\uparrow_{gas}$	-393.509	213.74	-394.359

Evaporation $\Delta H_{Hess}=\Delta H°_{CO2gas}-\Delta H°_{CO2aq}=20.3$ kJ/mol =-393.509+413.7976=20.3 kJ/mol; **endothermic**.....

Evaporation $\Delta G_{Hess}=\Delta G°_{CO2gas}-\Delta G°_{CO2aq}=-8.379$ kJ/mol =-394.359+385.98= -8.379 kJ/mol **exoergic**.....

Solubility $\Delta G_{Hess}=\Delta G°_{CO2aq}-\Delta G°_{CO2gas}=8.379$ kJ/mol

$K_{sp}=K_{eq}=EXP(-\Delta G_{eq}/R/T)=0.034045=1/29.375$

$$\frac{[CO_2\ aqua]}{[CO_2\ gas]\cdot[H_2O]} = K_{sp}=0.03405=1/29.4$$

$[CO_2\uparrow_{gas}]=29.4*[CO_{2aqua}]/[H_2O]=29.4*0.0076/55.3=0.00403$ mol fraction; pH=7.36 .

$[HCO_3^-]=0.0154$ M and $[CO_{2aqua}]=0.0076$ M if pH=7.36; At pH=5=7.0512+log(0.001/$[CO_{2aqua}]$);

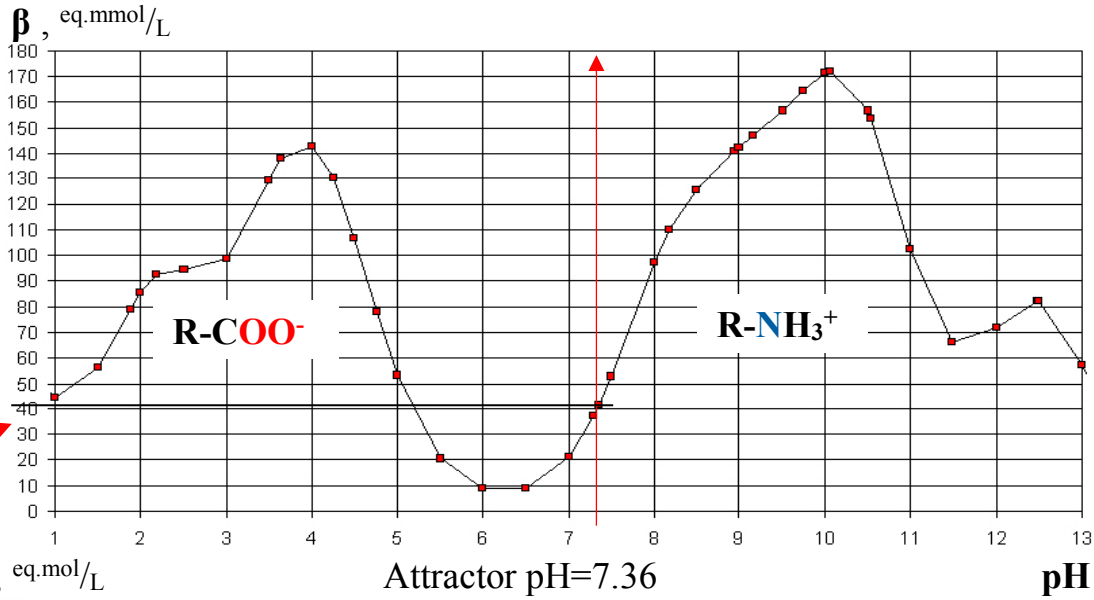
10^(5-7.0512)= 0.001/$[CO_{2aqua}]$; $[CO_{2aqua}]=0.001/10\wedge(5-7.0512)=0.1125$; pH=5 ;

$[CO_2\uparrow_{gas}]=29.4*[CO_{2aqua}]/[H_2O]=29.4*0.1125/55.3=0.0597$ mol daļas Atmospheric 0.0004.

Proteins buffer have silence region from **pH=6** to 7.36 . 23 thousand protein total buffer solution concentration is C_{buffer}=3 mM. Muscle cytosol proteins the Buffer capacity at physiologic pH=7.36 is

β =40 mM

30.3 %=40/132*100%

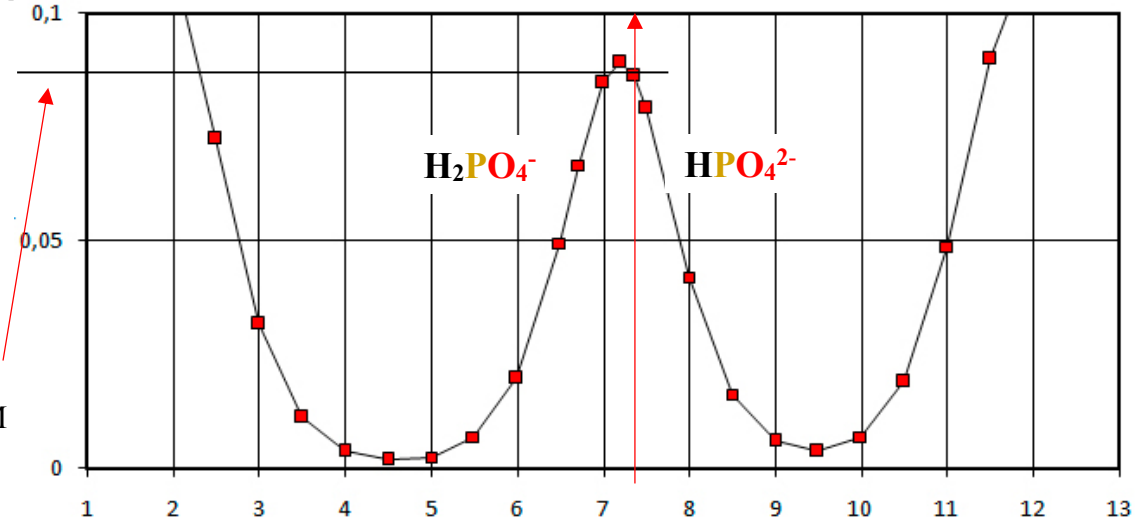


Total phosphate buffer systems concentration $[H_2PO_4^-]+[HPO_4^{2-}]$ in muscle cells cytosol is C_{buffer}=0.155 M

The Buffer capacity at physiologic pH=7.36 is

β =80 mM

66.6 %=80/132*100%



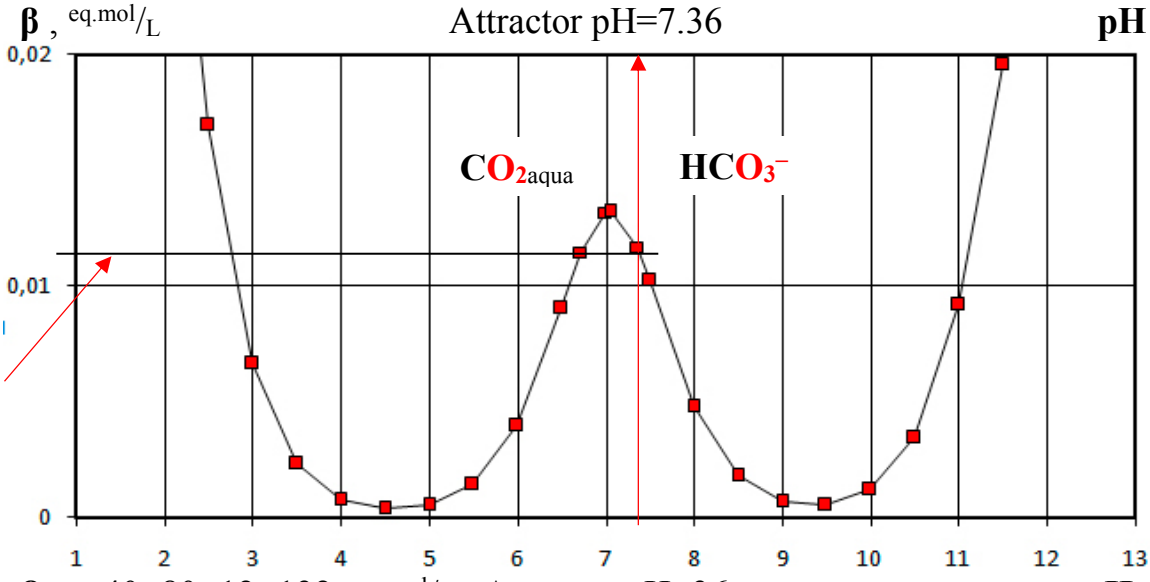
Total bicarbonate buffer system concentration $[CO_{2aqua}]+[HCO_3^-]$ is

C_{buffer}=0.023 M.

The Buffer capacity at physiologic pH=7.36 is

β =12 mM

9.1 %=12/132*100%



Total Buffer capacity β_{sum}=40+80+12=132 $^{eq.mmol}/_{L}$; Attractor pH=36 **pH**

Figure 3. Cytosol muscle cells. Buffer capacities versus pH values from 1 to 13. Actual buffer capacity at Attractor pH=7.36 for two dominate phosphates , bicarbonate and total protein made buffer capacity sum.

proteins + phosphates + bicarbonate ,

at pH=7.36: proteins +($[H_2PO_4^-]+[HPO_4^{2-}]$)+($[CO_{2aqua}]+[HCO_3^-]$),

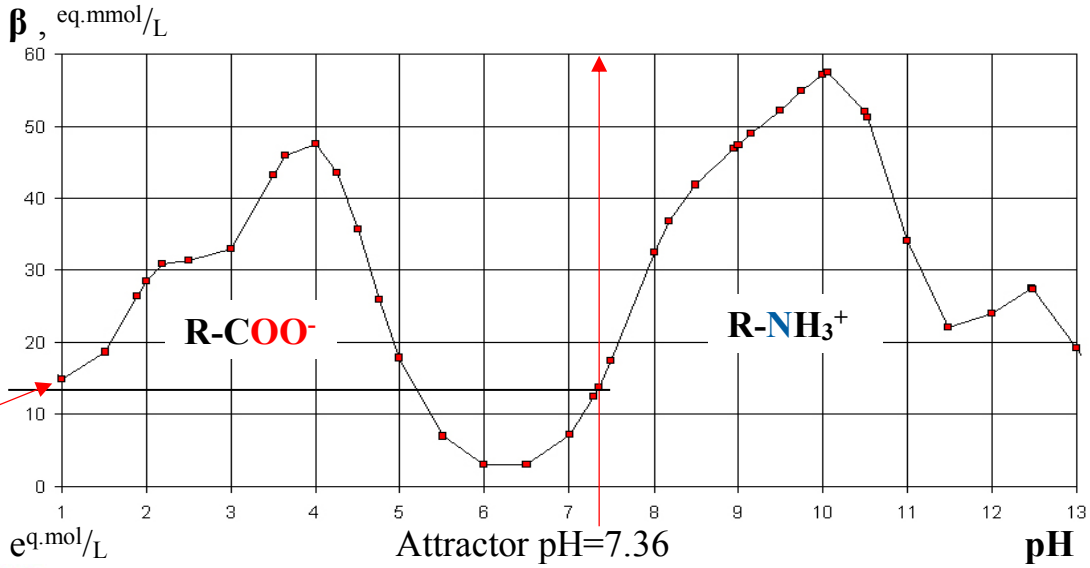
total buffer capacity: 100% = **30.3 %** + **66.6 %** + **9.1** %;

Buffer capacity is acid Δn_{ac} or base Δn_b equivalent_mols / in one Liter changing pH per one unit **ΔpH**=±1.

Three buffer systems in human organism by total sum as stabile attractor pH=7.36 create in Cytosol muscle cells functional activity as charged groups. **R-COO-**, **R-NH_3^+**, **HPO_4^{2-}**, **R-PO_4^{2-}**, **HCO_3^-**.

Proteins buffer have silence region from **pH=6** to 7.36 . Protein total buffer solution concentration C_{buffer}=1 mM for albumin.
The Buffer capacity at physiologic pH=7.36 is

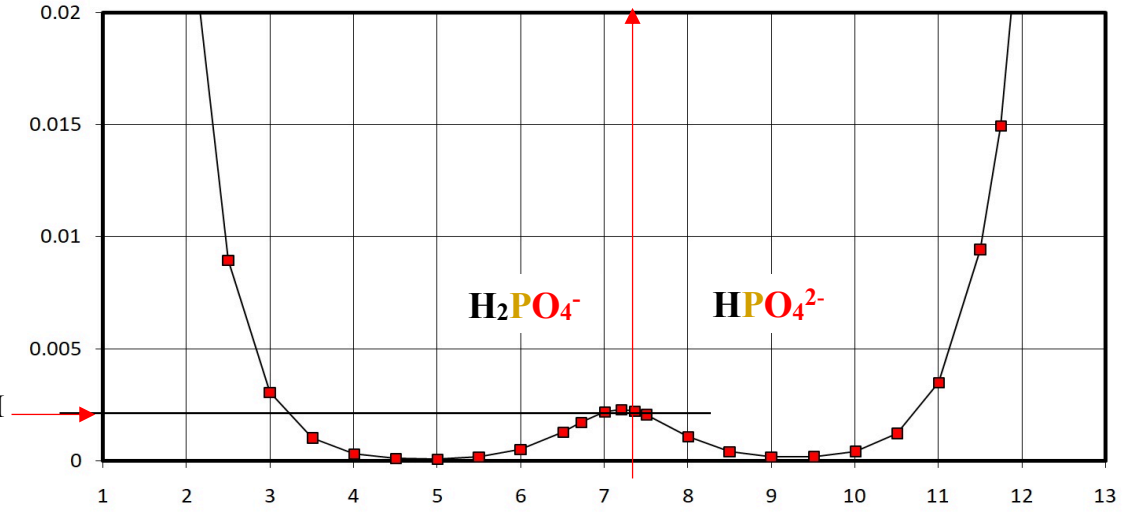
β =12 mM
46.15%=12/26*100%



Total phosphate buffer systems concentration $[H_2PO_4^-]+[HPO_4^{2-}]$ in blood plasma C_{buffer}=0.004 M.

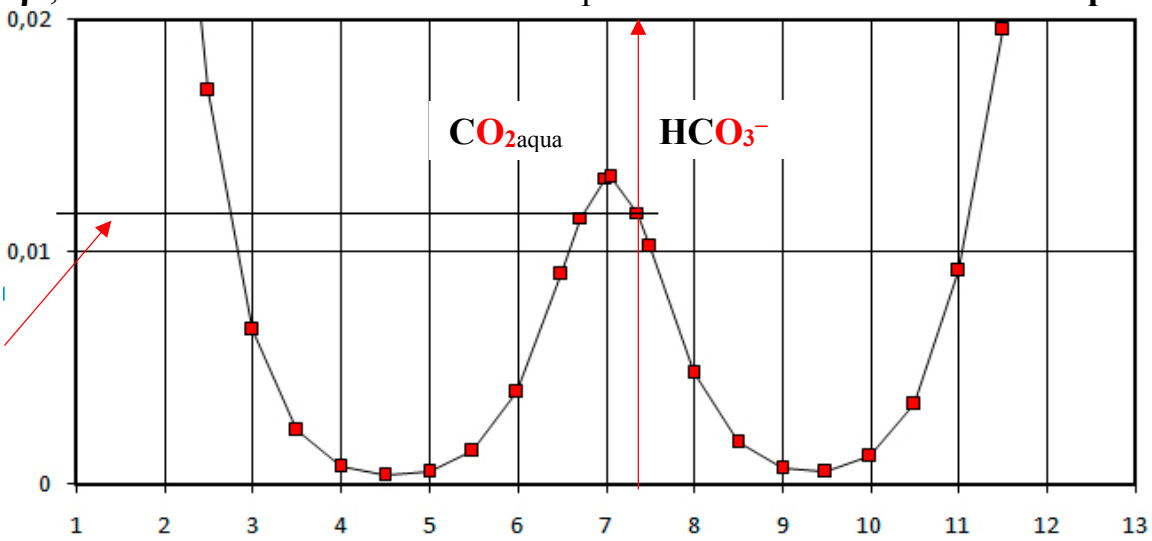
The Buffer capacity at physiologic pH=7.36 is

β =2 mM
7.7 %==2/26*100%



Total bicarbonate buffer system concentration $[CO_{2aqua}]+[HCO_3^-]$ in blood plasma is C_{buffer}=0.023 M.
The Buffer capacity at physiologic pH=7.36 is

β =12 mM
46.15%=12/26*100%



Total Buffer capacity β_{sum}=12+2+12=26 $^{eq.mmol}/_{L}$ Attractor pH=7.36 **pH**

Figure 4. Extra Cellular space Blood plasma. Buffer capacities versus pH values from 1 to 13. Actual buffer capacity at Attractor pH=7.36 for two dominate phosphates , bicarbonate and total protein made buffer capacity sum.

proteins + phosphates + bicarbonate ,
at pH=7.36: proteins +([$H_2PO_4^-$]+[HPO_4^{2-}])+([CO_{2aqua}]+[HCO_3^-]),
total buffer capacity: 100% = **46.15%** + **7.7%** + **46.15%**;
Buffer capacity is acid Δn_{ac} or base Δn_b equivalent_mols / in one Liter changing pH per one unit **ΔpH**=±1.

Three buffer systems in human organism by total sum as stabile multipurpose Attractor pH=7.36 create in Extra Cellular space, Blood plasma functional activity with charged groups **R-COO**$^-$, **R-NH**$_3^+$, HPO_4^{2-}, **R-**PO_4^{2-}, HCO_3^-linked in proteins, nucleic acids, carbohydrates, vitamins, coenzymes as **R** molecules.

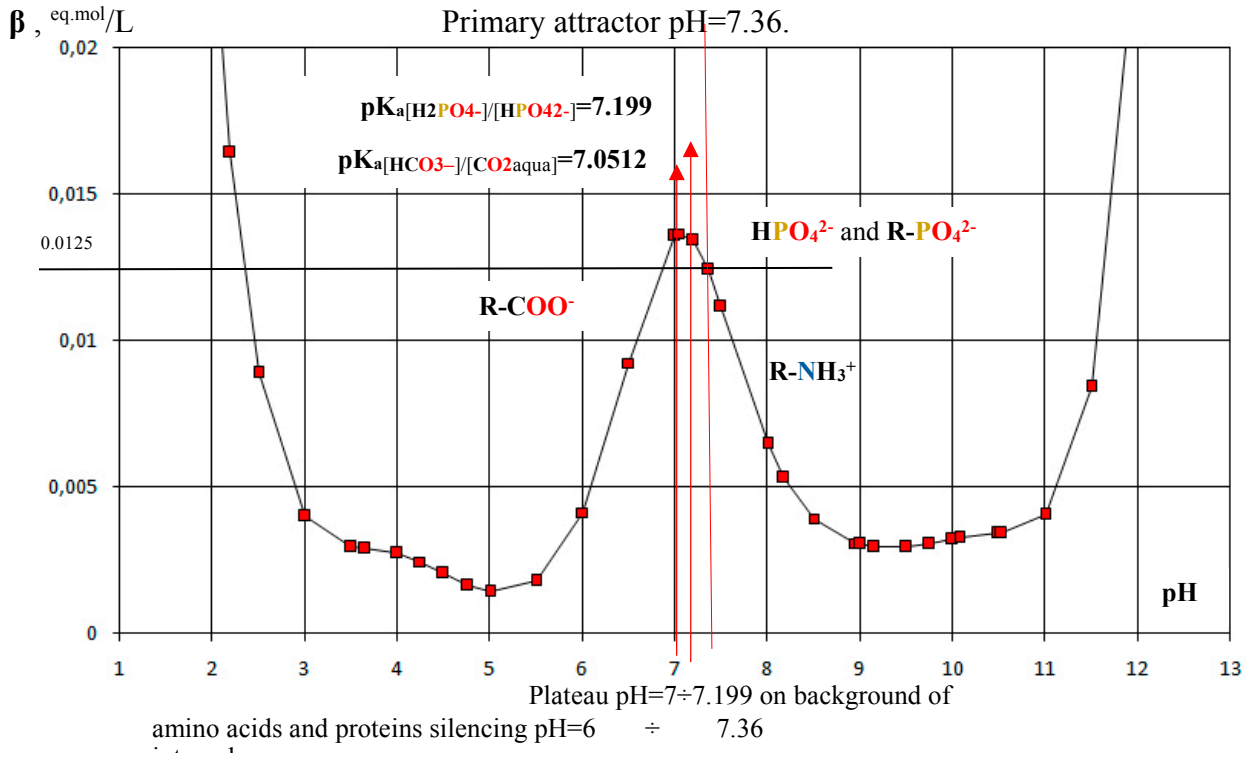


Figure. Attractor equilibrium state pH=7.36 create two classic acid constants buffers maximums:

1. first CA Carbonic Anhydrase pKa=7.0512 at pH=7.36 created bicarbonate 2/1=$[HCO_3^-]/[CO_{2aqua}]$ alkaline reserve keep generate concentrations $[HCO_3^-]$=0.0154 M, $[CO_{2aqua}]$=0.0076 M as perfect order homeostasis reactions products ratio 0.0154/0.0076=2.03:

$$\mathbf{7.36=pH=pKa+\log\frac{[HCO_3^-]}{[CO_{2\,aqua}]}=7.0512+\log\frac{[HCO_3^-]}{[CO_{2\,aqua}]}\;;\;\frac{[HCO_3^-]}{[CO_{2\,aqua}]}=10^{(pH-pKa)}=10^{(7.36-7.0512)}=0^{0.3088}=\frac{2.0361}{1}}$$ and

2. second phosphates maximum classic constant value pK_a=7.199 at pH=7.36 keep generate alkaline reserve ratio $[H_2PO_4^-]/[HPO_4^{2-}]$=1.45/1 in Henderson Haselbalh expression:

$$\mathbf{pH=pK_a+\log\frac{[HPO_4^{2-}]}{[H_2PO_4^-]}=7.199+\log\frac{1.45}{1}=7.36}.$$

Dominate buffers two maximums - positions **pKa=7.0512** and **pK_a=7.199** are located on background of proteins silencing interval from pH=6 to pH=7.36. The buffer capacity sum within three buffer systems create broad band capacity maximum plateau on interval from pH=7 to pH=7.199. [14]

In blood *plasma* dominate two buffers: the enzyme **CA** Carbonic Anhydrase bicarbonate and phosphate buffer capacity maximums plateau interval pH 7÷7.199. Alkaline reserve 2 and 1.45 at Attractor **pH=7.36** value is created on the protein buffer capacity silencing interval at pH=6 to pH=7.36 background. [14]

In sweat, urine and digestive apparatus dominate bicarbonate and phosphates together.

High rate protolysis Attractors **pH**=7.36, CA, H_2O functionally activate arterial and venous oxygen concentrations by driving Shuttle of bicarbonate HCO_3^- , of proton H^+, of oxygen O_2. Those work on interface to environment through homeostasis irreversibly exchange in ***lungs*** from AIR inhaling O_2 and exhaling CO_2. High rate protolysis equilibrium Attractors activate in perfect order Brownian molecular engines for irreversible homeostasis the biosphere evolution and survival.

Protolysis attractors **CA** and hemoglobin **shuttle** enzymes of $O_2 \Leftrightarrow HCO_3^- + H^+$ mechanism

High rate protolysis attractors carbonic anhydrase CA activate zero valueless $CO_{2\ qua} + 2H_2O$ substances accumulate free energy content $HCO_3^- + H_3O^+$ $G_{H3O+HCO3-}$=68.5 $^{kJ}/_{mol}$ for homeostasis use. Attractors pH=7.36 concentration $[H_3O^+]=10^{-7.36}$ M, water concentration $[H_2O]$=55.3 M, carbonic anhydrase CA synthesis and global oxygen 20.95% in air since 500 millions Years stabilize arterial concentration $[O_2]=6\bullet10^{-5}$ M by **shuttle**:

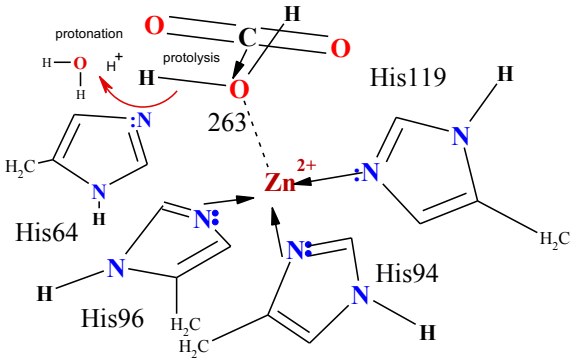
$$\mathbf{4O_{2aqua} + (H^+His63,58)_4Hb_T \cdots salt \cdots bridges(HCO_3^-)_4 \Leftrightarrow Hb_R(O_2)_4 + 4H^+ + 4\ HCO_3^-}.$$

Lungs by oxygene saturate hemoglobin in circulation restor 459 times arterial up to venous $[O_2]=0.426\bullet10^{-5}$ M amount of one liter O2SolutionsL.pdf. Adsorption of four $4O_{2aqua}$, release in products four protons 4 H^+ and bicarbonate ions 4 HCO_3^- , that endothermic ΔH_{Hess}=54.5 $^{kJ}/_{mol}$, but exoergic ΔG_{Hess}=-82.1 $^{kJ}/_{mol}$ evaporate $CO_2\uparrow_{gas} + H_2O\uparrow_{gas}$ on surface tin water layer of lungs epithelia, and evolved amount in one blood circulation from liter of blood is: $[H_3O^+]=459*6*10^{-5}=0.0275$ M=$[CO_2\uparrow_{gas}]$.

In tisues oxygen desorbs: $\mathbf{Hb_R(O_2)_4 + 4H^+ + 4\ HCO_3^- \Leftrightarrow 4O_{2aqua} + (H^+His63,58)_4Hb_T \cdots salt \cdots bridges(HCO_3^-)_4}$.

Deoxy hemoglobin $\mathbf{(H^+His63,58)_4Hb_T}$ captures four protons 4 $\mathbf{H^+}$ at histidine residue and 4 $\mathbf{HCO_3^-}$ salt bridges $\mathbf{HCO_3^- \ldots H_3^+N-}$ at protonate amines and transport to **lungs**.

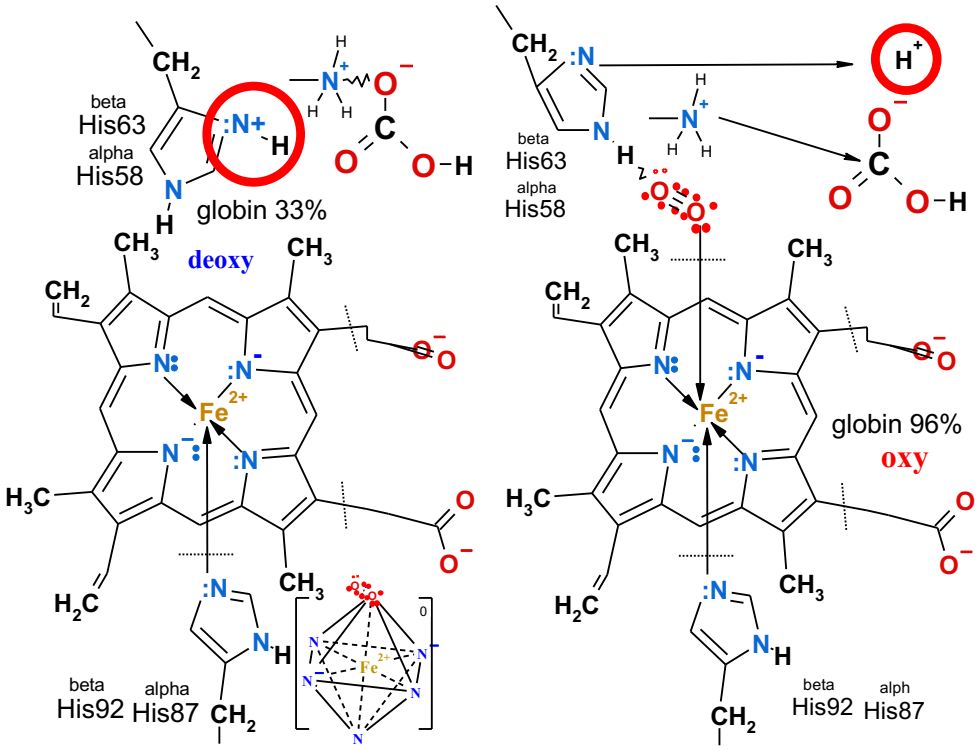
Human hemoglobin **shuttle** and carbonic anhydrase CA bufer systems stabilize attractor to what trend **pH=7.36** homeostasis. Hydrogen carbonate ions norma $[HCO_3^-]$=0.0154 M, $[CO_{2aqua}]$=0.0076 M corresponds to 56.23 mL (50-60 mL) released volume CO_2 of 100 mL blood as *alkaline reserve* 2.036 . Valueless zero carbon dioxide and water activates CA high rate protolysis reaction invest energy $G_{H3O+HCO3-}$=68.5 $^{kJ}/_{mol}$ in hydrogen carbonate and hydroxonium ions. Carbonic anhydrase CA enzyme $\mathbf{Zn^{2+}}$ ion coordinative pocket active site protolytic collisions products are:



$$CO_{2aqua} + 2H_2O <=> CA(\mathbf{Zn^{2+}}) <=> H_3O^+ + HCO_3^-;$$

$$CA\text{-}\mathbf{Zn^{2+}}\text{-}263H_2O + CO_{2aqua} + H_2O => CA\text{-}\mathbf{Zn^{2+}} < (\text{-}OH^- + CO_{2aqua}) + H^+_{His64} + H_2O => HCO_3^- + H_3O^+ + CA\text{-}\mathbf{Zn^{2+}}$$

$CA\text{-}\mathbf{Zn^{2+}}\text{-}263H_2O$ moiety ordered next water molecules $318H_2O$ and $292H_2O$.



O2Solutions.pdf. Oxygen adsorbs donor-acceptor coordination bond in center on iron(II) $\mathbf{Fe^{2+}}$ hem and release protons $\mathbf{H^+}$ $\mathbf{Hb_RO_2}$. Protonate water molecule turns to hydroxonium $\mathbf{H_3O^+}$ ion. *In **tissues*** desorbed oxygen restore $[\mathbf{O_2}]=6\cdot10^{-5}$ M concentration in blood plasma 459 times and deoxy hemoglobin capture four protons $\mathbf{H^+}$ so continues maintain constant pH=7.36.

Oxygen turns to oxidation product $\mathbf{CO_2}$. High rate protolysis with carbonic anhydrase **CA** produce $\mathbf{HCO_3^-}$ and $\mathbf{H_3O^+}$.

Self-organization attractors :

pH=7.36 $[\mathbf{H_3O^+}]=10^{-7.36}$ M , water concentration $[H_2O]$=55.3 M, carbonic anhydrase CA synthesis and oxygen 20.95% in air 500 millions Years stabilizes arterial concentration $[O_2]=6\cdot10^{-5}$ M with **shuttle** hemoglobin.

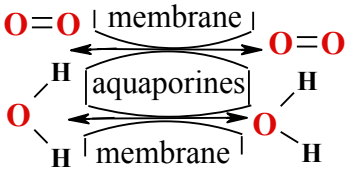
Shuttle hemoglobin-CA oxidation driven O_2 transport and CO_2 exhalation mechanism

Arterial **shuttle oxy** hemoglobin, **carbonic anhydrase CA**, venous **deoxy** hemoglobin **shuttle**:

$$\text{oxy } Hb_R(O_2)_4 + 4H^+ + 4\,HCO_3^- \Leftrightarrow 4O_{2aqua} + \text{deoxy } (H^+His63,58)_4Hb_T\cdots\text{salt}\cdots\text{bridges}(HCO_3^-)_4 ,$$

which **oxy** $Hb_R(O_2)_4$ saturate 0.96%, but **deoxy** Hb_T is protonate 4 H^+ and salt bridges four 4 HCO_3^- bound.

Solubility: $O_{2AIR} + H_2O \overset{\text{akvaporins}}{\rightleftarrows} H_2O + O_{2aqua}$ increase free energy content $G_{O2šķ}$=26.58 $^{kJ}/_{mol}$. In ***lungth***:



In erytrocite membrane aquaporins water H_2O with oxygen O_{2aqua} move by velocity 10^9 sec^{-1} and O_{2aqua} concentration in blood remarkable increases from **venous** $[O_2]$=0.426•10^{-5} M to arterial concentration $[O_2]$=6·10^{-5} M.

$G_{O2arterial} = G_{O2aqua} + \Delta G_{arterial} + G_{O2sp}$=237.19-251.6+26.58=12.2 $^{kJ}/_{mol}$. [14]

Oxigen O_{2aqua} decreases free energy content from water G_{O2aqua}=237.2 $^{kJ}/_{mol}$ to $G_{O2Biochem}$=12.2 $^{kJ}/_{mol}$.

$\Delta E_{H2O} = E^{\circ} - E_o$=1.383-0.731=-0.652 Volts; $\Delta G_{arterial} = \Delta E_{H2O} * F * n$=-0.652*96485*4/1000=-251.6 $^{kJ}/_{mol}$.

Bisphospho glycerate BPG^{5-} drive hemoglobin O_2 concentration sensitive adsorption⇔desorption equilibrium. Hemoglobin saturation 0.96% 459 times restore to venous saturation 0.63% **shuttle deoxy** hemoglobin releasing total amount $[H^+]=[HCO_3^-]=[O_2]$=495*6·10^{-5} M =0.0275 M.

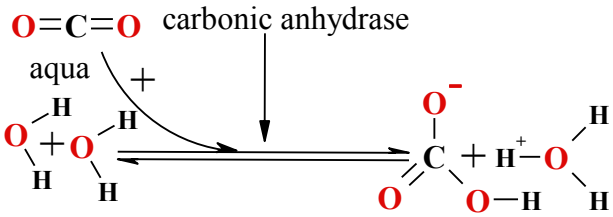
$$4O_2 + (H^+His63,58)_4Arg^+His^+BPG^{5-}betaVal1(NH_4^+)_2Hb_T \leftrightarrow (His63,58)_4Arg^+His^+betaVal1(NH_4^+)_2Hb_R(O_2)_4 + 4H^+ + BPG^{5-}$$

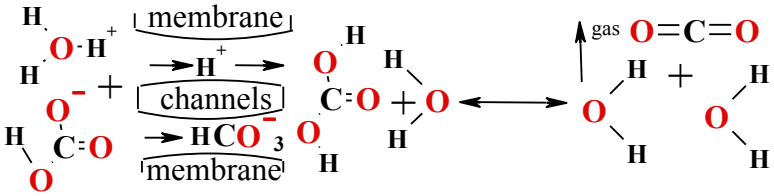
Each adsorbed molecule O_{2aqua} release proton H^+ and HCO_3^-, which increases acidity on epithelia cell surface of ***lungth***. ***E***pithelia surface has specific building: supper tin 0.6 nm water S=950 nm*950 nm=0.9 μm^2 layer square area with small volume 0.5415•10^{-3} μm^3=0.5415•10^{-18} L liters increase acidity to pH=5.5, if one proton crossing membrane channel reach surface. It cause fast neutralization $H_3O^+ + HCO_3^-$. Fast exhales $CO_2\uparrow$ gas in air at absence of carbonic anhydrase CA.

Oxidation with O_{2aqua} produce CO_{2aqua} in ***tissue*** cells which is transported to destiny the lungth:

$$Q_{aqua} + CO_{2aqua} + 2H_2O \xrightarrow{CA} H_3O^+ + HCO_3^- \xrightarrow{membrane} H_2O + CO_2\uparrow_{gas} + H_2O .$$

Enzyme carbonic anhydrase **CA** shift to right high rate protolysis equilibrium mixture by endothermic ΔH_{Hess}=9.76 $^{kJ}/_{mol}$ reaction: $Q + 2H_2O + CO_{2aqua} + \Delta G_{CO2aqua} \xrightarrow{CA} H_3O^+ + HCO_3^-$ accumulate free energy $\Delta G_{CO2aqua}$=60.14 $^{kJ}/_{mol}$:





Exothermic neutralization $H_3O^+ + HCO_3^- \xrightarrow{membrane} H_2O + CO_{2aqua} + H_2O$ (4^{th}, 45^{th}, 46^{th} pages) evaporate endothermic ΔH_{Hess}=20.3 $^{kJ}/_{mol}$ CO_{2aqua} +Q <=> $CO_2\uparrow_{gas} + H_2O$ but exoergic ΔG_{O2aqua}=-8.379 $^{kJ}/_{mol}$:

Protons H^+ and bicarbonate HCO_3^- through channels drive homeostasis high rate protolysis generate concentration gradients: $[H_3O^+]_{labā}/[H_3O^+]_{kreisā}=10^{-7.36}/0.0339$ and for bicarbonate ions: $[HCO_3^-]_{labā}/[HCO_3^-]_{kreisā}$=0.0154 $M_{labā}$/0.0339 $M_{kreisā}$ exhaled from organism to air carbon dioxide gas $CO_2\uparrow_{gas}$.

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