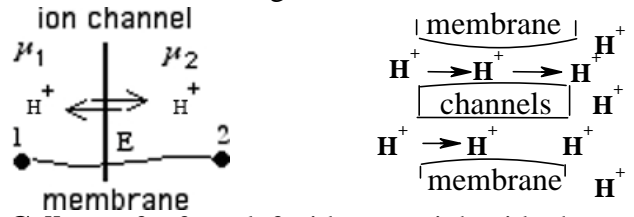


**HOMEOSTASIS Concentration gradient Membrane potentials** for ions  $H^+, Na^+, K^+, Ca^{2+}, Mg^{2+}, HCO_3^-, Cl^-$

$\Delta G = G_2 - G_1$       insideCell Left  $G_1$  Membrane  $G_2$  Right outsideCell

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One mol of the protons with charge  $n=+1$  from **inside Cell** transfer from left side  $\rightarrow$  to right side through membrane channels from left to **outsideCell** against concentration gradient of the protons is the non spontaneous free energy positive change  $\Delta G_r = W_{work}$  using exoergic metabolic reactions produced positive work  $W_{work}$ , applied with negative free energy exoergic change  $-\Delta G_{metabolic} = W_{wor}$  to form concentration outside  $K_{eq} > 1$  is greater  $[H^+]_{outsideCell} > [H^+]_{insideCell}$  if membrane  $K_{eq} = [H^+]_{outsideCell} / [H^+]_{insideCell}$  equilibrium constant. Than electric potential value  $E > 0$  is positive for one mole  $H^+$  positive charge ion  $n=+1$  by faradays number  $F=96485C$  respectively  $q = nF$ , and work calculated positive as  $W_{work} = qE = nFE = \Delta G_r = RT \ln K_{eq}$ .

Membrane equilibrium constant  $K_{eq} = \frac{[H^+]_{outsideCell}}{[H^+]_{insideCell}}$  give  $E_{membrane} = \frac{RT}{nF} \cdot \ln \left( \frac{[H^+]_{outsideCell}}{[H^+]_{insideCell}} \right)$  so

$E_{membrane} = 0$  and  $\Delta G_r = 0$  if  $\frac{[H^+]_{outsideCell}}{[H^+]_{insideCell}} = 1 = K_{eq}$  as well as  $\ln 1 = 0$ .

Nernst's equation in natural (number  $e=2.7$ ) logarithm  $\ln$  and decimal (number 10) logarithm  $\lg$  form  $\ln(a) = \ln(10) \cdot \lg(a) = 2.3 \dots \cdot \lg(a)$ . Temperature at standard conditions are  $T=298.15 K$  and  $R=8.3144 J/mol/K$ .

Converts natural logarithm to decimal  $\frac{\ln(10) \cdot R \cdot T}{F} = \frac{2.3 \cdot R \cdot T}{F} = 0,0591 V$ ;  $E = \frac{0.0591}{n} \cdot \lg \left( \frac{[H^+]_{outsideCell}}{[H^+]_{insideCell}} \right)$ ,

where  $n$  is the charge of ion (for proton  $H^+$   $n=+1$  as well hydroxonium  $H_3O^+$ , sodium cation  $Na^+$   $n=+1$ , for potassium cation  $K^+$   $n=+1$ , for chloride anion  $Cl^-$   $n=-1$  and for bicarbonate anion  $HCO_3^-$   $n=-1$ , so on others).

**Second (correct) approach to obtaining membrane potential expression.**

We are observing from inside Cell motion of one mole  $n$  charged ions with total molar charge  $q = nF$  thru the membrane channels and when equilibrium is established reactant and product chemical potential sum becomes equal across Cell membrane  $\mu_{H^+ insideCell} + nFE = \mu_{H^+ outsideCell}$

but each chemical compound chemical potential is:  $\mu = \Delta G^\circ + RT \ln(N_{H^+})$ , were  $N_{H^+}$  is substance  $H^+$  concentration in mol fraction units.  $\Delta G^\circ$  is given compound  $H^+$  standard potential of formation from elements. In chemical equilibrium given compounds sodium cation have  $\Delta G^\circ_{H^+ insideCell}$  and  $\Delta G^\circ_{H^+ outsideCell}$  are equal.

$\Delta G^\circ_{H^+} + RT \ln(N_{H^+ insideCell}) + nFE = \Delta G^\circ_{H^+} + RT \ln(N_{H^+ outsideCell})$

Expressing  $E$  from equilibrium conditions of the chemical potentials  $\mu$  :

$E_{membrane} = \frac{\Delta G^\circ_{H^+} - \Delta G^\circ_{H^+}}{nF} + \frac{RT}{nF} \cdot \ln \left( \frac{N_{H^+ outsideCell}}{N_{H^+ insideCell}} \right)$ , as  $\Delta G^\circ_{H^+} - \Delta G^\circ_{H^+} = 0$ .

Standard potentials of pure protons one mol are equal and membrane potential is

$E_{membrane} = \frac{RT}{nF} \cdot \ln \left( \frac{N_{H^+ outsideCell}}{N_{H^+ insideCell}} \right)$ . as  $0 = \frac{\Delta G^\circ_{H^+} - \Delta G^\circ_{H^+}}{nF}$ .

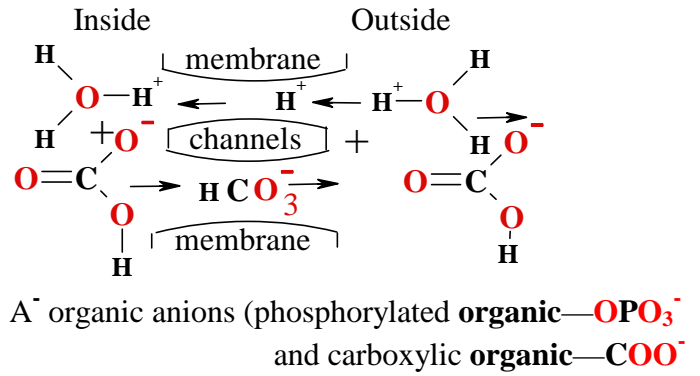
**conversion to molar concentrations** and decimal logarithm we obtain

$H^+_{insideCell} \xleftrightarrow{\text{membrane CHANNEL}} H^+_{outsideCell}$   $E_{membrane} = \frac{0.0591}{n} \cdot \lg \left( \frac{N_{H^+ outsideCell}}{N_{H^+ insideCell}} \right)$ .

For Physiological conditions  $T= 310.15 K$  and  $E_{membrane} = \frac{0.06154}{n} \cdot \lg \left( \frac{N_{H^+ outsideCell}}{N_{H^+ insideCell}} \right)$ .

**Table.** Concentration of some ions inside and outside mammalian spinal motor neurons.

Ion	Concentration (mmol/L of H <sub>2</sub> O)		Equilibrium Potential (mV)
	Inside Cell	Outside Cell	
Na <sup>+</sup>	15.0	150.0	+61.54
K <sup>+</sup>	150.0	5.5	-88.35
10 <sup>-7</sup> ·cH <sup>+</sup>	14.93	4.365	-32.87
Cl <sup>-</sup>	9.0	125.0	-70.32
<b>HCO<sub>3</sub><sup>-</sup></b>	27.0	8	+32.51
A <sup>-</sup>	122.49	43.79	+27.49



Total Resting membrane potential E = -70 mV.

Membrane potential for sodium cations Na<sup>+</sup> is calculated according membrane potential expression

$$\text{Membrane potential } E = \frac{0.06154}{+1} \cdot \lg\left(\frac{150}{15}\right) = +61.54 \text{ mV} ;$$

Membrane potential for potassium K<sup>+</sup> cations is calculated according membrane potential expression

$$\text{Membrane potential } E = \frac{0.06154}{+1} \cdot \lg\left(\frac{5.5}{150}\right) = -88.35 \text{ mV} ;$$

Membrane potential for hydrogen H<sup>+</sup> cations is calculated according membrane potential expression

$$\text{Membrane potential } E = \frac{0.06154}{+1} \cdot \lg\left(\frac{4.365}{14.93}\right) = -32.87 \text{ mV at outside Cell } \text{pH}=7.36 \text{ } c=4.365 \cdot 10^{-7} \text{ M} ;$$

inside mammalian spinal motor neurons. **pH<sub>inside</sub> = 6.826** ; C=14,93·10<sup>-7</sup> M

Membrane potential for chloride Cl<sup>-</sup> anions is calculated according membrane potential expression

$$\text{Membrane potential } E = \frac{0.06154}{-1} \cdot \lg\left(\frac{125}{9}\right) = -70.32 \text{ mV} ;$$

Membrane potential for bicarbonate **HCO<sub>3</sub><sup>-</sup>** anions is calculated according membrane potential expression

$$\text{Membrane potential } E = \frac{0.06154}{-1} \cdot \lg\left(\frac{8}{27}\right) = +32.51 \text{ mV} ;$$

Membrane potential for organic anions A<sup>-</sup> anions is calculated according membrane potential expression

$$\text{Membrane potential } E = \frac{0.06154}{-1} \cdot \lg\left(\frac{122.49}{43.79}\right) = +27.49 \text{ mV} .$$

**Table.** Steady-state membrane potential of mammalian skeletal muscle.<sup>1</sup>

Ion	Concentration c (mmol/L of H <sub>2</sub> O)		Equilibrium Potential (mV)
	Inside Cell	Outside Cell	
Na <sup>+</sup>	12.0	145.00	+66.60
K <sup>+</sup>	155.0	4.00	-97.74
10 <sup>-5</sup> ·c H <sup>+</sup>	13.0	3.80	-32.87
Cl <sup>-</sup>	3.8	120.00	-92.27
<b>HCO<sub>3</sub><sup>-</sup></b>	27.0	8.00	+32.51
A <sup>-</sup>	155.0	43.79	+33.78

Total Resting membrane potential E = -90 mV .

**Mitochondria** have active value of **pH = 7.36** inside and **pH = 5** in extra mitochondrial space.

**Bicarbonate** concentration in cytosol-blood  $[\text{HCO}_3^-] + [\text{CO}_2] = 0.023\text{M}$  and  $[\text{HCO}_3^-] = 0.015\text{M}$  and using Henderson Haselbalh equation calculated concentration  $\text{CO}_2$   $[\text{CO}_2]$  we can express:

$\text{pH} = \text{pK} + \lg([\text{HCO}_3^-]_{\text{cytosol}}/[\text{CO}_2])$ ;  $7.36 = 7.0512 + \lg([\text{HCO}_3^-]_{\text{cytosol}}/[\text{CO}_2])$  and anti logarithming  $10^{7.36-7.0512} = [\text{HCO}_3^-]_{\text{cytosol}}/[\text{CO}_2] = 2.036 = 0.0154\text{M}/[\text{CO}_2]$  where  $[\text{CO}_2] = 0.0154\text{M}/2.036 = 0.0076\text{M}$  is calculated concentration of carbon dioxide in blood, cytosol, but in mitochondria **pH = 7.36**  $[\text{HCO}_3^-] + [\text{CO}_2] = 0.023\text{M} + 0.02527\text{M} = 0.05054\text{M}$  and

$$[\text{HCO}_3^-] = 0.033892\text{M}; [\text{CO}_2] = 0.05054 - 0.033892 = 0.01665\text{M}$$

$10^{7.36-7.0512} = [\text{HCO}_3^-]_{\text{Mitohon}}/[\text{CO}_2] = 2.36 = [\text{HCO}_3^-]_{\text{Mitohon}}/0.01665\text{M}$  and inside **Mitochondria** bicarbonate concentration is  $2.2 = [\text{HCO}_3^-]_{\text{Mitohon}}/[\text{HCO}_3^-] = 0.0338919\text{M}/0.0154\text{M} = 2.2$  times higher .

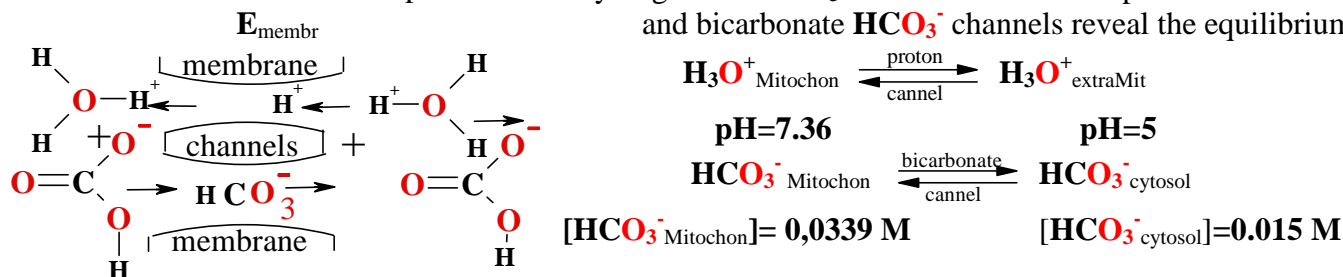
Human body temperature  $t = 37^\circ\text{C}$ ;  $T = 310.15^\circ\text{K}$ .  $0.02754\text{M} + 0.023\text{M} = 0.05054 = [\text{HCO}_3^-] + [\text{CO}_2]$ . Calculate

$10^{7.36-7.0512} = [\text{HCO}_3^-]_{\text{Mitochon}}/[\text{CO}_2] = 2.036 = [\text{HCO}_3^-]_{\text{Mitochon}} = x/(0.05054-x)$ ; as  $\text{pH} = 7.36$  so

$x = 2.036 \cdot (0.05054 - x) = 2.036 \cdot 0.05054 - 2.036 \cdot x = x$ ;  $x(1 + 2.036) = 2.036 \cdot 0.05054$ ; so  $x = [\text{HCO}_3^-]_{\text{Mitochon}}$

$[\text{HCO}_3^-]_{\text{Mitochon}} = x = 2.036 \cdot 0.05054 / (1 + 2.036) = 0.10289944 / 3.036 = 0.0338919\text{M} = [\text{HCO}_3^-]_{\text{Mitochon}} = x$

Actual membrane potential for hydrogen cations  $\text{H}_3\text{O}^+$  via the membrane proton  $\text{H}^+$  channels and bicarbonate  $\text{HCO}_3^-$  channels reveal the equilibrium



$$\text{membran } E_{\text{H}^+} = P \cdot \lg(10^{-\text{pH}_{\text{extraMit}}}/10^{-\text{pH}_{\text{Mitochon}}}) = P \cdot \lg(10^{-5}/10^{-7.36}) = 0.06154 \cdot \lg(10^{2.36}) = 0.14523\text{V} .$$

Actual membrane potential for bicarbonate anions equilibrium  $\text{HCO}_3^-_{\text{Mitochon}} \rightleftharpoons \text{HCO}_3^-_{\text{cytosol}}$  is

$$E_{\text{HCO}_3^-_{\text{Mitochon}}} = -P \cdot \lg([\text{HCO}_3^-]_{\text{cytosol}}/[\text{HCO}_3^-]_{\text{Mitochon}}) = -0.06154 \cdot \lg(0.0154/0.0338919) = 0.0210821\text{V} ,$$

where  $P = \frac{\ln(10) \cdot R \cdot T}{F} = \frac{2.3 \cdot 8.3144(\text{J/mol/K}) \cdot 310.15^\circ\text{K}}{96485\text{C}} = 0.06154\text{V}$ , at Human body  $t = 37^\circ\text{C}$ ;  $T = 310.15^\circ\text{K}$ .

Hydrogen and bicarbonate total membrane potential is sum of  $0.14523\text{V} + 0.0210821\text{V} = E_{\text{membr}} = 0.1663\text{V}$ .

Electric free energy change for  $\text{H}^+$   $\Delta G_E = -E_{\text{membr}} \cdot F \cdot n_{(\text{ion charge} +1)} = -0.1663 \cdot 96485 \cdot (+1) = -16,045\text{ kJ/mol}$

$$\Delta G_{\text{H}^+} = RT \ln([\text{H}_3\text{O}^+]_{\text{extraMit}}/[\text{H}_3\text{O}^+]_{\text{Mitochon}}) = RT \ln(10^{-5}/10^{-7.36}) = 8,3144 \cdot 310,15 \cdot \ln(10^{2.36}) = -14,013\text{ kJ/mol}$$

free energy change for concentration gradient driven through proton  $\text{H}^+$  channels crossing lipid bilayer membranes.  $\Delta G_{\text{membr}} = \Delta G_E + \Delta G_{\text{H}^+} = -16,0454\text{ kJ/mol} - 14,013\text{ kJ/mol} = -30,05846\text{ kJ/mol}$  per one mole of proton  $\text{H}^+$  drive ATPase to make work is 19 times per  $\text{H}_3\text{O}^+$  effective as one mol mass **one gram** of proton  $\text{H}^+$  in direction from extra membrane space ( $\text{H}_3\text{O}^+_{\text{extraMit}}$ ) to mitochondrial matrix space ( $\text{H}_3\text{O}^+_{\text{Mitochon}}$ ).

The proton  $\text{H}^+$  concentration gradient  $\Delta G = \Delta G_{\text{membr}} + \Delta G_{\text{channel}} = -30,058\text{ kJ/mol}$  sum with electrochemical free energy change drive ATPase nano engine to synthesizing ATP molecules.

Both free energy negative changes sum per one ATP mole is  $4 \cdot -30,058\text{ kJ/mol} = -120,232\text{ kJ/mol}$ , consuming four protons  $4\text{H}^+$ , drive ATPase nano engine rotation to synthesizing one ATP molecule. One mole 503 grams ATP production have been used 4 grams as four moles of protons. Free energy negative change is  $\Delta G = -120\text{ kJ/mol}$ . Macro ergic ATP phosphate anhydride bond in hydrolyze releases free energy  $\Delta G = -53.47\text{ kJ/mol}$  for human erythrocyte (<http://aris.gusc.lv/BioThermodynamics/BioThermodynamics.pdf> page13). ATP accumulated chemical free energy efficiency is 44,6% ( $-53.47\text{ kJ/mol}$ ) of theoretically efficiency 100% ( $-120\text{ kJ/mol}$ ). Oxidative phosphorylation 55,4% of used four proton chemo osmose energy consumes the friction of ATPase rotor to heat production and ATP movement in cytosol water medium forming the concentration gradients across lipid bilayer membranes as transportation free energy source to drive ATP molecules.

Evidently any other charged cation molecule, for example,  $\text{Na}^+$  cation 23 times heavier or potassium cation  $\text{K}^+$  39 times heavier and its relatively less efficiency per one gram of mass are transferred 23 times or 39 times less energy for ATP synthesis comparing with charged proton  $\text{H}^+$  transfer through membrane channels.

Life choose the best **small by size, by mass and bearing whole one unit positive charge** proton  $\text{H}^+$ .