The <u>Water channels</u>, allow the <u>passive</u> but <u>selective</u> movement of <u>Water</u> and <u>O<sub>2</sub>,NO,CO</u> across cell wall and subcellular membranes like as <u>mitochondria</u>, <u>endoplasmic reticulum</u>, <u>peroxisomes</u>, <u>Golgi</u>, <u>lysosomes</u>..... Aquaporins have been classified into two sub-families:

I) strict Aquaporins that only allow the passage of Water,  $O_2$ , NO, CO and II) the <u>less</u> <u>selective</u> aquaglyceroporins that transport Water and other neutral solutes, such as Glycerol,  $CO_2$  or urea.

Recently, the identification and characterization of a number of archaeal and bacterial **Aquaporins** suggested the existence of a **third** sub-family; one that is neither a strict **Aquaporin** nor an **aquaglyceroporin**. The function and phylogeny of this **third** family is still a matter of debate.

## Water channels H<sub>2</sub>O common O<sub>2</sub>, NO, CO: an overview

AQP0	+ C <b></b> , <b>NO</b> <sup>3-</sup> eye-lens <u>cells</u> ; thin junctions between fiber <u>cells</u>
	AQP0 with a measured Water permeability <u>15-fold lower</u> than that of AQP1 at <u>pH 6.5</u> ;
	AQP0 is <u>reduced</u> a further <u>three fold at pH 7.5</u>
	AQP0 induce a gating effect <u>close</u> conformations of <u>extracellular loop A Met176, His40</u> AQP0 becomes more
	constrained near the conserved Ar/R constriction <u>site</u>
	+ Cl <sup>-</sup> , NO <sub>3</sub> <sup>-</sup> , <u>Aquaglyceroporins</u> : red blood cell (RBC),
AQP1-	apical & basolateral membranes of epithelial brain cell, rodent brain cell
	AQP1-null humans kidney proximal-tubule water reabsorption
	gastrointestinal tract Water absorption in the teleost intestine
	the ovary and in the oocyte ; salivary gland ;
AQP2	urinary bladder granular kidney <u>cells</u> & subcellular
	vasopressin regulated urine concentration (25% of the <b>blood</b> filtrate)
	trans located from the cytoplasmic pool to the apical plasma membrane
	of the granular cells of the pelvic patch and urinary bladder
	+Aqua glycero porins, urea: gastrointestinal tract Water absorption; rodent brain cell astrocyte end-feet
1002	Water enters in the principal cell through AQP2 and exits through located in the basolateral membranes
AQP3	trachea basal AOP3 & ciliated columnar AOP4 cells
AOP4	<b>Rodent</b> -brain; basolateral <b>membrane</b> of ciliated columnar cells alveolar epithelium; salivary gland
	stomach, duodenum, pancreas, airways, lungs, salivary gland, sweat glands, eyes, lacrimal glands, and the inner
AOP5	ear tears & pulmonary sub mucosal glands secretions apical membrane rodent brain cells
	+ $Cl^-$ , NO <sub>3</sub> <sup>-</sup> multi permeable channel: lens cells: may play a role in the body acid-base homeostasis
AOP6	in the intracellular vesicles of acid-secreting intercalated cells of the RCD colocalized with the $H^+$ -ATPase
	be $Hg^{2+}$ -inhibit able Water channel function is activated by $Hg^{2+}$ and low pH
AQP7	+ Aquaglyceroporing urea: kidney proximal tubule epithelium cell
	glycerol reabsorption : together with AOP1 in the brush border
	in the concentration of urine taking place in the proximal nephron
	75% of the <b>blood</b> filtrate which is 150–180 L per day
	$\mathbf{NH}_{4}^{+}$ : lens & kidney intracellular proximal tubule & small intestine absorptive: epithelium cell
AOP8	in the concentration of urine taking place in the proximal nephron also in mitochondria
	75% of the <b>blood</b> filtrate which is 150–180 L per day & <b>rodent brain cell</b>
	+Aquaglyceroporting urea purines pyrimidines & monocarboxylates argenite
AQP9	apical <b>membrane</b> of brain & small <b>intestine</b> absorptive epithelial & rodent <b>brain</b> & glial cells
AOP10	+ Aquaglyceroporting urea small intestine absorptive epithelial cells
AOP11	"super aquaporins" or sub cellular kidney cytoplasm of the proximal tubule & rodent brain cells
AOP12	"super aquaportins" or sub cellular $H_2O$ Channel is roughly 20-Å long and has a diameter 1.1 Å Water
<u></u>	the membrane share a shared protoing (WCDSs) are trans membrane protoing that have a specific
0=0	$\bigcup_{i=1}^{n} \bigcup_{j=0}^{n} \bigcup_{i=1}^{n} \bigcup_{j=1}^{n} \bigcup_{i$
, H	aquaporines H three-dimensional structure with a pore the SF radius 1.1 A is close average
o	$ -20\dot{A} $ to radius of water H–O–H longitudinal 1.4 A and 0.55 A bent size of dipole.
<b>`</b> \`	$\overset{\bullet}{\longrightarrow}$ It can be permeated by Water & O <sub>2</sub> , NO, CO molecules as solutes.
Н	H Aquaporins are large families (over <u>450 members</u> ) that are present <u>in all</u>
bilipid	<b>membrane</b> cross size <u>kingdoms of life</u> . Water permeability, allowing permeation of $3 \times 10^9$ water
55Å	molecules per <b>monomer</b> per second <b>AQP</b> 1 and other, which strictly prevents

the conduction of protons H<sup>+</sup>. Serine, Tyrosine, Threonine mbrane trafficking of AQP1, AQP2, AQP5, and AQP8, and the gating of AQP4.

Phosphorylation to trigger the me

**Cation conduct**ance has been <u>induced</u> in **AQP**1 by activation of <u>cyclic **GMP**-dependent</u> pathways and was <u>blocked</u> by  $Hg^{2+}$ 

Red blood cells against colligative osmomolar concentration in water solutions

Water and oxygen osmosis against osmo molar concentration gradient crosses cell membranes

**Osmosis** is organised for  $H_2O$  and  $O_2$  movement against concentration gradients-difference of colligative properties  $\Delta C_{osm} = i\Delta C_M$  through an Aquaporins across cell membranes to form the osmotic pressure:  $\pi = i\Delta C_M RT (kPa)$ ,

where  $R=8,3144 \text{ J/(mol}\cdot\text{K})$  universal gas constant, T temperature in Kelvin's degree (K)  $T=t^{+}273.15$  (if  $t=37^{\circ}$  than  $T=37^{\circ}+273.15=310.15$  K).

Note: Transfer water and oxygen molecules through membrane aquaporin tunnel in erythrocytes with rate  $3 \cdot 10^9$  sec<sup>-1</sup> in both directions transfer 3000 oxygen molecules in one second.

Mechanism of osmosis through membrane aquaporins drive colligative concentration gradient

 $Na^+Cl^- => Na^+ + Cl^- m = 2$  electrolyte dissociation  $\alpha = 1$  the concentration gradient doubled as i is 2  $i=1+\alpha(m-1)=1+1(2-1)=2$ ;  $i\Delta C_M = 2\Delta C_M = \Delta C_{osm}$  and pressure on membrane is  $\pi = 2\Delta C_M RT = \Delta C_{osm} RT$ .

 $Press \Rightarrow on membrane to right.$ 

Water  $H_2O_1O_2$  oxygen flow left side against the concentration gradient from 0 to C<sub>osm</sub>=0.305 M because Na<sup>+</sup>Cl<sup>-</sup> ions make osmo molar concentration left side  $C_{left}$ - $C_{right}$ = $C_{osm}$ -0= $C_{osm}$ = $iC_M$ and <u>close</u>  $H_2O$ ,  $O_2$  flow to right side.



 $C_{blood} = C_{osm} = i_1C_1 + i_2C_2 + i_3C_3 + \dots = \Sigma i_kC_k = 0,305 \text{ M}$ 

Human erythrocytes red blood cells with osmo molar concentration 0.305 M of all solutes sum  $\Sigma i_k C_k$ :  $C_{blood}$  glucose, salts, hydroxonium  $H_3O^+$ , hydroxyl  $OH^-$  ions, amino acids, proteins, bicarbonate etc.



Isotonic medium  $C_{blood} = 0.305 \text{ M}$ 



Hypotonic medium distilled water 0 M or at least



Hypertonic solution  $C_{\text{Hyperton}} \ge 0.4 \text{ M}$ . Hypertonic salt solutions to

apply foe purulent wounds, because pumps water toxic compounds out and stimulates blood circulation.

Osmosis  $H_2O$  and  $O_2$  against concentration gradient through alveolar epithelial membrane

A) Oxygens  $O_2$  from AIR 20.95%  $O_2$  gas assimilation reaction dissolution in water to form  $O_{2aqua}$ 

exothermic  $\Delta H_r$ =-55,7 kJ/mol and exoergic  $\Delta G_r$ = -27,7 kJ/mol as water soluble oxygen :

Hypotonic water medium the flow is greater towards the cell against the

concentration gradient-difference 0.305 - 0.2=0,105 M and the cell puffs up

until its membrane is broken but content leak in plasma.

1)  $O_{2AIR}+H_2O \Leftrightarrow H_2O+O_{2aqua}+Q+\Delta G$ . Penetrate in Human body through aquaporins by concentration gradient from  $[O_2]=9,768 \cdot 10^{-5}$  M to venous blood  $[O_{2aqua}]=0,426 \cdot 10^{-5}$  M.

2)  $\Delta GO_2 = RTln([O_{2Blood}]/[O_{2aqua}]) = -4,29 \text{ kJ/mol}$  exoergic entrance human organism;

**3)**  $O_{2aqua} + H_2 O \xrightarrow{Aquaporins} H_2 O + O_{2aqua} + \Delta G$  against concentration gradient 0,305 M / 0,2 M:

 $\Delta GH_2O = RTln([H_2O]_{right}/[H_2O]_{left}) = -8,3144*310,15*ln(0,305/0,2) = -1.088 \text{ kJ}/_{mol}$ 

exoergic  $\Delta G O_{2+} = -5,379^{kJ}/mol.$  Deoxy hemoglobin Hb<sub>T</sub> adsorbs 4  $O_{2aqua}$  from blood plasma of inspired fresh AIR releases four protons  $4H^+$  and  $4 HCO_3^-$  stabilizing arterial  $[O_2]=6 \cdot 10^{-5}$  M concentration  $4O_{2aqua} +$  $(\mathbf{H}^{+}\mathrm{His}63,58)_{4}\mathbf{Hb}_{T} \Leftrightarrow \mathbf{Hb}_{R}(\mathbf{O}_{2})_{4}+4\mathbf{H}^{+}$ .

Total exothermic  $\Delta H_r = -55.7 \text{ kJ}_{mol}$  and exoergic  $\Delta GO_2 = -27.7 + -4.29 + -1.088 = -33.078 \text{ kJ}_{mol}$ 

Osmosis is **water** and oxygen flow left side against gradient of concentration 0.2 M to  $C_{osm}$ =0.305 M because water and oxygen flow to right side closed by made left side osmo molar  $C_{left}$ - $C_{right}$ = $C_{osm}$ - $C_{osm\_right}$ = $\Delta C_{osm}$ concentration as difference  $\Delta C_{osm}$ =0.105 M.  $C_{osm}$ = $i_1C_1$  +  $i_2C_2$  +  $i_3C_3$ +...= $\Sigma$   $i_kC_k$ =0,305 M;  $C_{osm\_right}$ =0,2 M;  $\Delta C_{osm}$ =0.305–0.2=0.105 M

B)



Breath out  $H_2O$ ,  $CO_2$  in endothermic but excergic reactions on alveolar epithelial surface

 $\mathbf{Q}_{aqua} + \mathbf{CO}_{2aqua} + 2\mathbf{H}_{2}\mathbf{O} \xleftarrow{\mathbf{CA}} \mathbf{H}_{3}\mathbf{O}^{+} + \mathbf{HCO}_{3} \xleftarrow{\mathbf{Membrane}} \mathbf{H}_{3}\mathbf{O}^{+} + \mathbf{HCO}_{3} \Leftrightarrow \mathbf{H}_{2}\mathbf{O} + \mathbf{H}_{2}\mathbf{CO}_{3} + \mathbf{Q}_{gas} \leftrightarrow \mathbf{H}_{2}\mathbf{O} + \mathbf{CO}_{2}\uparrow_{gas} + \mathbf{H}_{2}\mathbf{O}.$ endothermic  $\Delta \mathbf{H}_{r} = 9.75 \text{ kJ}_{mol}$ ; athermic  $\Delta \mathbf{H}_{r} = 0 \text{ kJ}_{mol}$ ; exothermic  $\Delta \mathbf{H}_{r} = -9.76 \text{ kJ}_{mol}$ ; endothermic  $\Delta \mathbf{H}_{r} = 20.3 \text{ kJ}_{mol}$ ; endoergic  $\Delta \mathbf{G}_{r} = 58.4 \text{ kJ}_{mol}$ ; exoergic  $\Delta \mathbf{G}_{r} = -22.5 - 1.96 \text{ kJ}_{mol}$ ; exoergic  $\Delta \mathbf{G}_{r} = -58.2 \text{ kJ}_{mol}$ ; exoergic  $\Delta \mathbf{G}_{r} = -8.54 \text{ kJ}_{mol}$ ;

B)  $Q_{aqua}+CO_{2aqua}+2H_2O \leftarrow CA \rightarrow H_3O^++HCO_3^- +Q \leftarrow Membrane \rightarrow H_2O+CO_2\uparrow_{gas}+H_2O\uparrow_{gas}$ . endothermic $\Delta H_r=9.75 \text{ kJ}/_{mol}$ ; endothermic  $\Delta H_r=54,5 \text{ kJ}/_{mol}$ ; summary endothermic  $\Delta H_r=64,25 \text{ kJ}/_{mol}$ ; endoergic  $\Delta G_r=58.4 \text{ kJ}/_{mol}$ ; exoergic  $\Delta G_r=-82,1 \text{ kJ}/_{mol}$ ; summary exoergic  $\Delta G_r=-23,7 \text{ kJ}/_{mol}$ ;

Venous **deoxy Hb<sub>T</sub> shuttle** adsorbs four **oxygen**  $4O_{2Hb}$  molecules, create  $4H^+$ , promoting  $CO_2$  breathe out as increase production of  $H^+$ ,  $HCO_3^- 473*6\cdot10^{-5}$  M=0,0284 M=[ $HCO_3^-$ ]=[ $H^+$ ] amounts shifts equilibrium to right  $H^+ + HCO_3^- + Q \leftrightarrow H_2O + CO_2\uparrow_{gas}$  via membrane channels. So pH=7,36 remains constant, as bicarbonate ion and hydrogen ion produce  $CO_2$  right side.

The epithelial cell surface of *lungs* has the specific building. S=950 nm x 950 nm= 0.9  $\mu$ m<sup>2</sup> is surface area with super thin 0.6 nm water layer volume: 0.5415•10<sup>-3</sup>  $\mu$ m<sup>3</sup> = 0.5415•10<sup>-18</sup> L. Created acidity in thin water layer volume increases up to pH=5.5 if one proton H<sup>+</sup> crosses the membrane channels reaching the surface. Hydrogen ion concentration is: [H<sub>3</sub>O<sup>+</sup>]=10<sup>-pH</sup>=10<sup>-5.5</sup> M. Respiration in *lungs* Hemoglobin released protons H<sup>+</sup> during oxygen adsorbtion for total amount concentration:

 $[\mathbf{O}_{2Hb}] = [\mathbf{H}_3\mathbf{O}^+] = 473*6 \cdot 10^{-5} \text{ M} = 0,0284 \text{ M}$  forms hydrogen ion concentration gradient:

 $[\mathbf{H_3O^+}]_{right}/[\mathbf{H_3O^+}]_{left}=10^{-5.5}/0,0284$ , which drives excergic  $\Delta \mathbf{G} = -22,5 \text{ kJ/mol}$  proton movement through epithelial cell membrane proton channels:  $\mathbf{H_3O^+}_{left} \leftarrow \underline{\text{proton channel}} \rightarrow \mathbf{H_3O^+}_{right} + \Delta \mathbf{G}$ . General process  $\mathbf{H_2O+CO_2}\uparrow_{gas}+\mathbf{H_2O}\uparrow_{gas}$  require heat supply endothermic  $\Delta H=54,5 \text{ kJ/mol}$  to drive spontaneous

 $\Delta G$ = -82,0679 kJ/mol products evaporation  $CO_2\uparrow_{gas}$  and  $H_2O\uparrow_{gas}$  keeping moisture  $H_2O$  on surface of membrane. Hydrogen ions water acidity shift endothermic  $\Delta H_r$ = +54,5 <sup>kJ</sup>/<sub>mol</sub> and exoergic  $\Delta G_r$ = -82,1 <sup>kJ</sup>/<sub>mol</sub> decomposition  $H_3O^+$ +HCO<sub>3</sub><sup>-</sup> breath out to AIR CO<sub>2</sub>↑<sub>gas</sub> with  $H_2O\uparrow_{gas}$ :

 $H_{3}O^{+}+HCO_{3}^{-}+Q \leftarrow \xrightarrow{\text{Membrane}} H_{2}O + CO_{2}\uparrow_{\text{gas}} + H_{2}O\uparrow_{\text{gas}} + \Delta G_{r} = -82,1 \text{ kJ/mol. excergic}.$ 

Aquaporins are wide class of membrane crossing channel proteins, which are integrated in all living organisms: animals, plants, bacteria. On <u>Cell membranes</u> effecting Physiology, Biochemistry and Health. Aquaporins are large families (over <u>450 members</u>) that are present <u>in all kingdoms of life</u>.