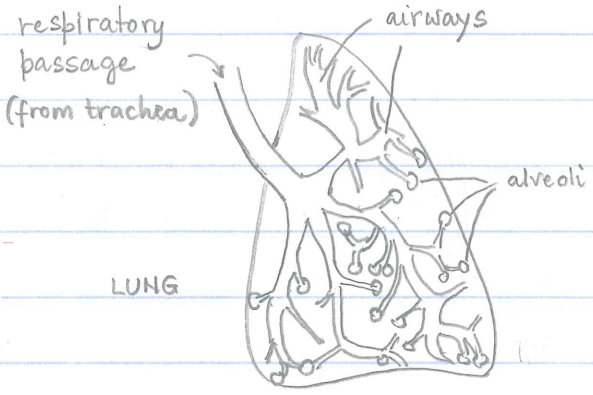
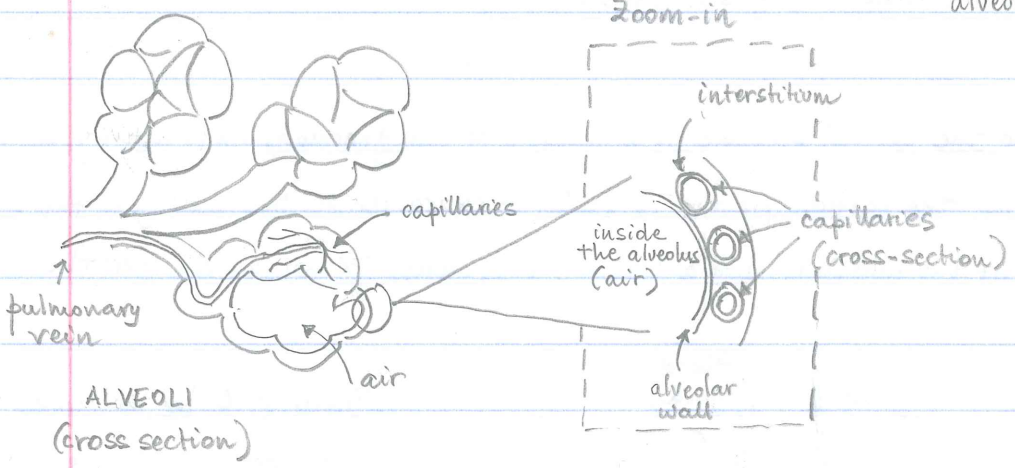
LECTURE 9

The lungs are the organs where the exchange of O_2 and CO_2 between the blood and the air takes place



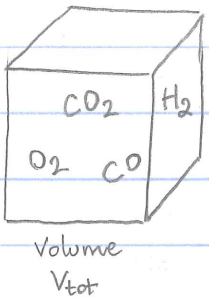
The lungs are part of the "respiratory system", which is the collection of organs (e.g., nose, mouth, trachea, larynx, etc.) and muscles that cooperate to perform the gas transfer between the tissues and the outside air

Anatomically, the gas transfer occurs within the alveoli, which are air sacs with a thin wall surrounded by capillaries ⇒ The gas transfer is at the interface alveolar wall-capillaries



Because the capillaries form a wide net of vessels around the alveolar wall, we can approximate the capillaries as a thin layer of blood surrounding the air sacs and directly model the gas exchange between blood and air. ⇒ We need to recall the laws in Physics that describe the interaction between a gas mixture and a liquid

* Partial pressure of a gas



Let us consider a volume V_{tot} occupied by a mixture of gasses $\Rightarrow$ The "partial pressure" of the gas X in the mixture is the (hypothetical) pressure that the gas would exert if it were occupying alone the entire volume V_{tot} at the same temperature

If the mixture is made of ideal gasses $\Rightarrow$

$$\frac{pp_x}{p_{tot}} = \frac{V_x}{V_{tot}} = \frac{n_x}{n_{tot}}$$

$$p_{tot} = \sum_x pp_x$$ ↖ Dalton's Law

$n_x \triangleq$ moles of X

$pp_x \triangleq$ partial pressure of gas X

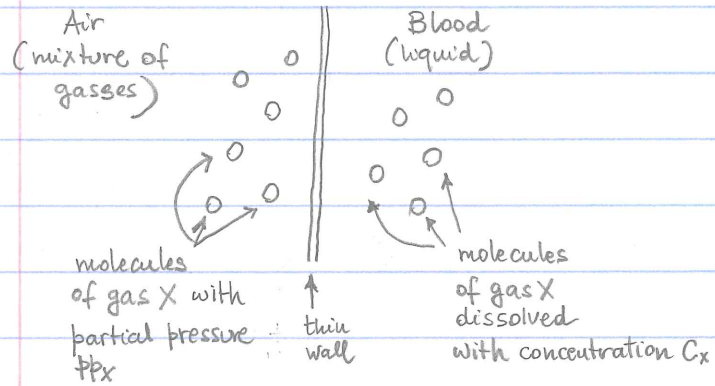
$\frac{n_x}{n_{tot}} \triangleq$ mole fraction

$p_{tot} \triangleq$ total pressure of the mixture

$n_{tot} \triangleq$ total number of moles in the mixture

$V_x \triangleq$ volume occupied by gas X in the mixture

Because the partial pressure is a measure of the thermodynamic activity of the gas' molecules, the partial pressure is useful to characterize the ability of the gas to diffuse at the interface with a liquid (e.g., blood) $\Rightarrow$ Let us consider the scenario:



There will be molecules of gas X that dissolve into the blood or leave the blood until equilibrium is reached (the opposing "drivers" of the transition are pp_x - from air to blood - and C_x - from blood to air -)

X = O_2, CO_2, CO, or else

At equilibrium, the ratio: $\frac{C_x}{pp_x} \triangleq \sigma_x$ is constant $\Rightarrow \sigma_x$ is called the "solubility" of gas X in the blood or "Henry's Law constant" and it is specific of the gas X.

If the gas X reaches the alveolar wall with a partial pressure $pp_x \neq \frac{C_x}{\sigma_x}$ then there will be an exchange of gas X with the blood

$$\Rightarrow \quad q = D_s \left(pp_x - \frac{C_x}{\sigma_x} \right) \qquad (1)$$

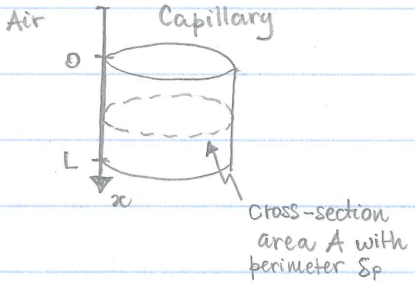
$q \triangleq$ net flux of gas X per unit area

$D_s \triangleq$ surface diffusion constant

* Transport of gas at the interface capillary - alveolar wall

Let us assume that the concentration of gas G along the interface is uniform across the cross-section area of the capillary, i.e.: $C_g = C_g(x,t)$. Let us call pp_g the partial pressure in the air mixture $\Rightarrow$ Then we have:

$$A \int_0^L C_g(x,t)\,dx \triangleq \text{total amount of G in the capillary at time } t$$



Because of mass conservation, we have:

$$\frac{d}{dt}\left(A \int_0^L C_g(x,t)\,dx \right) = \underbrace{v(0)\,A\,C_g(0,t)}_{\text{amount that goes into the capillary from the arterial vessel at time } t} - \underbrace{v(L)\,A\,C_g(L,t)}_{\text{amount that goes from the capillary into the venous vessel at time } t} + \underbrace{\delta_p \int_0^L q(x,t)\,dx}_{\text{amount that is exchanged with the air mixture at time } t \text{ along the perimeter}} \qquad (*)$$

$\uparrow$ variation of the amount of G in time

$v(x) \triangleq$ blood velocity at position x

Equation (*) can be written as:

$$\int_0^L A \frac{\partial C_g}{\partial t}(x,t)\,dx = -\int_0^L A \frac{\partial}{\partial x}\left(v(x)\,C_g(x,t)\right)dx + \int_0^L \delta_p\, q(x,t)\,dx$$

$$\Downarrow$$

At any position x along the longitudinal direction:

$$\frac{\partial C_g}{\partial t}(x,t) = -\frac{\partial}{\partial x}\left(v(x)\,C_g(x,t)\right) + \frac{\delta_p}{A}\,q(x,t) \qquad (2)$$

By assuming $v(x) = v$ - constant and replacing $q(\cdot)$ with (1) we obtain:

$$\frac{\partial C_g}{\partial t} = -v\frac{\partial C_g}{\partial x} + \frac{\delta_p D_s}{A}\left(pp_g - \frac{C_g}{\sigma_g}\right)$$

$\sigma_g \triangleq$ solubility of gas G in the blood

At steady-state we have: D_m

$$\frac{\partial C_g}{\partial t} = 0 \Rightarrow v\frac{\partial C_g}{\partial x} = \underbrace{\frac{\delta_p}{A}}_{\substack{\text{Surface-}\\ \text{to-volume}\\ \text{ratio } \chi}} \cdot \frac{D_s}{\sigma_g}\left(\sigma_g pp_g - C_g\right) \Rightarrow \frac{\partial C_g}{\partial x} = -\frac{D_m}{v}C_g + \frac{D_m \sigma_g pp_g}{v}$$

Hence, C_g increases with a rate that is inversely proportional to the blood velocity.

Assuming pp_g constant and calling $C_0 \triangleq C_g(x=0)$, at steady-state we have:

$$\frac{\partial C_g}{\partial x} = \frac{\partial}{\partial x}\left(C_g - \sigma_g pp_g\right) = -\frac{D_m}{v}\left(C_g - \sigma_g pp_g\right) \qquad (**)$$

$$\Rightarrow \ln\left(C_g - \sigma_g pp_g\right)\Big|_{x=0}^{x=L} = -\frac{D_m}{v}x\Big|_{x=0}^{x=L} \Rightarrow C_g(L) = \sigma_g pp_g + \left(C_0 - \sigma_g pp_g\right)e^{-D_m L/v}$$

↑ integration by parts

From this, we can determine the total flux Q of gas G across the wall at steady-state:

- By definition: $Q \triangleq \int_0^L \delta_p q(x)\,dx = \frac{Dm}{A}\int_0^L (\sigma_g pp_g - C_g(x))\,dx$

Note that we have dropped the dependence on t because at steady-state

- From (2), at steady-state: $-v\frac{\partial C_g}{\partial x} + \frac{\delta_p}{A} q(x) = 0$

$$\Downarrow$$

$$Q = \int_0^L \delta_p q(x)\,dx = \int_0^L Av\frac{\partial C_g}{\partial x}\,dx = Av\,C_g\Big|_{x=0}^{x=L} = Av\left(C_g(L) - C_0\right)$$

$$\Rightarrow Q = Av\left(\sigma_g pp_g - C_0\right)\left(1 - e^{-Dm L/v}\right)$$

Note: $pp_0 \triangleq \frac{C_0}{\sigma_g} \Rightarrow Q = A\sigma_g v\left(pp_g - pp_0\right)\left(1 - e^{-Dm L/v}\right) \Rightarrow$ As $L \to \infty$, $Q \to A\sigma_g v \Delta pp$

where $\Delta pp \triangleq pp_g - pp_0$, i.e., the quantity of gas exchanged has a finite flux even if the length of the capillary is infinite. Also, note that, from the formula of $C_g(L)$ it follows that the partial pressure of G at the interface with the capillary varies according to the formula:

$$C_g(x) = \sigma_g pp_g + \left(C_0 - \sigma_g pp_g\right)e^{-Dm x/v} \Rightarrow pp(x) = pp_g + \left(pp_0 - pp_g\right)e^{-Dm x/v}$$

$pp(x) \triangleq C_g(x)/\sigma_g$

$\Rightarrow$ The partial pressure varies exponentially from pp_0 to pp_g. This behavior captures the actual release of CO_2 in the alveoli but it does not match the intake of O_2 from the air (i.e., the partial pressure of O_2 along the capillary does not vary in an exponential way from the value p_0 at the entrance of blood to the value p_g in the air)

Furthermore, $\sigma_{g_{O_2}} \cong \frac{1}{20}\sigma_{g_{CO_2}} \Rightarrow$ In order to have balance between intake of O_2 and release of CO_2 at steady-state, we should have: $|pp_0 - pp_g|_{O_2} \cong 20|pp_0 - pp_g|_{CO_2} \Rightarrow$

This does not happen in reality ($|pp_O - pp_g|_{O_2} \cong 12\,|pp_O - pp_g|_{CO_2}$) $\Rightarrow$ The model is not accurate when it comes about O_2 $\Rightarrow$ We are missing the important fact that O_2 and CO_2 are involved in chemical reactions while dissolved in the blood $\Rightarrow$ These reactions have an impact on the gas exchange

* A more accurate model of CO_2 removal

While in blood, part of the CO_2 molecules react with H_2O according to the formula:

$$CO_2 + H_2O \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} HCO_3^- + H^+$$

By applying the law of mass action we can write:

$g_1 \triangleq [CO_2]$ $g_2 \triangleq [HCO_3^-]$ $h \triangleq [H^+]$ $w \triangleq [H_2O]$

$$\left.\begin{aligned} \frac{\partial g_1}{\partial t} &= -k_1 g_1 w + k_{-1} g_2 h \\ \frac{\partial g_2}{\partial t} &= -k_{-1} g_2 h + k_1 g_1 w \end{aligned}\right\} \Rightarrow$$

These equations must be combined with the equation (2) for the transport of CO_2 and HCO_3^- across the capillary wall:

$$CO_2)\quad \frac{\partial g_1}{\partial t} = \underbrace{-k_1 g_1 w + k_{-1} g_2 h}_{\text{LoMA}} \underbrace{- v\frac{\partial g_1}{\partial x} + Dm_{CO_2}\left(\sigma_{CO_2} pp_{CO_2} - g_1\right)}_{\text{gas exchange}}$$

$$HCO_3^-)\quad \frac{\partial g_2}{\partial t} = \underbrace{-k_{-1} g_2 h + k_1 g_1 w}_{\text{LoMA}} \underbrace{- v\frac{\partial g_2}{\partial x} + Dm_{HCO_3^-}\left(\sigma_{HCO_3^-} pp_{HCO_3^-} - g_2\right)}_{\text{gas exchange}}$$

$pp_x \triangleq$ partial pressure of gas $X = CO_2, HCO_3^-$

$\sigma_x \triangleq$ solubility of gas $X = CO_2, HCO_3^-$

$Dm_x \triangleq$ rate constant for gas $X = CO_2, HCO_3^-$

At steady-state, noticing that $\omega \cong 1$, we have:

$$v \frac{\partial g_1}{\partial x} = -k_1 g_1 + k_{-1} g_2 h + Dm_{CO_2} (\sigma_{CO_2} pp_{CO_2} - g_1)$$

$$v \frac{\partial g_2}{\partial x} = k_1 g_1 - k_{-1} g_2 h + Dm_{HCO_3^-} (\sigma_{HCO_3^-} pp_{HCO_3^-} - g_2)$$

Because the transport of HCO_3^- across the capillar wall is $\cong 0$, i.e., $Dm_{HCO_3^-} \cong 0$, we have that the total variation along the length of the capillary is:

$$v \frac{d}{dx} (g_1 + g_2) = Dm_{CO_2} (\sigma_{CO_2} pp_{CO_2} - g_1) \quad (3)$$

Also, let us assume that $h \triangleq [H^+]$ - constant (this is reasonable given the relative abundance of H^+ in the blood) and that, at any position $0 < x < L$, the concentration g_2 reaches equilibrium much earlier than g_1 and much faster than the variation along the x-axis, i.e.:

$$HCO_3^-) \quad \frac{\partial g_2}{\partial t} = -k_{-1} g_2 h + k_1 g_1 - \underbrace{v \frac{\partial g_2}{\partial x}}_{\cong 0} + \underbrace{Dm_{HCO_3^-} (\sigma_{HCO_3^-} pp_{HCO_3^-} - g_2)}_{\cong 0}$$

$$\text{QSS approximation} \Downarrow$$

$$g_2 = \underbrace{\frac{k_1}{k_{-1} h}}_{k_c} g_1$$

By replacing g_2 in (3) we have:

$$v (1 + k_c) \frac{dg_1}{dx} = Dm_{CO_2} (\sigma_{CO_2} pp_{CO_2} - g_1) \Rightarrow \text{Beside factor } (1+k_c), \text{ this equation}$$

is exactly as (**) $\Rightarrow g_1(x) = \sigma_{CO_2}(1+k_c) \left[pp_{CO_2} + (pp_0 - pp_{CO_2}) e^{-Dm_{CO_2} x / v(1+k_c)} \right]$

where $pp_0 \triangleq \frac{g_1(0)}{\sigma_{CO_2}}$

The total flux Q of CO_2 exchanged between blood and air is then:

$$Q = \int_0^L Av(1+k_c)\frac{\partial g_1}{\partial x}dx = Av(1+k_c)\left(g_1(L) - g_1(0)\right) =$$

$$= Av(1+k_c)\sigma_{co_2}\left(pp_{co_2} - p_0\right)\left(1 - e^{-Dmco_2 L/v(1+k_c)}\right)$$

As a result, the value of Q as $L \to \infty$ is: $Q_\infty = Av(1+k_c)\sigma_{co_2}\left(pp_{co_2} - p_0\right)$

$\Rightarrow$ The flux is increased by a factor $1+k_c > 1$. For typical values of k_1, k_{-1}, and $[H^+]$, it can be obtained: $k_c \cong 20$.

NOTE: It is usually $k_{-1} \gg k_1 \Rightarrow$ The flux increases because the continuous conversion of HCO_3^- into CO_2 replenishes the CO_2 lost to the air

* A more accurate model of O_2 uptake

While in blood, part of the O_2 molecules react with Hb (hemoglobin). We saw (Lecture 3) that it is an example of cooperative reaction. However, for sake of simplicity here, let us neglect the variation in reaction rates for each new O_2 molecule bound to one Hb molecule and let us assume:

$$Hb + 4O_2 \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} Hb(O_2)_4$$

By following the same argument as for CO_2 we have:

$g_1 \triangleq [O_2]$ $\quad g_2 \triangleq [Hb(O_2)_4]$ $\quad e \triangleq [Hb]$ $\quad e + g_2 = e_0 - \text{const}$

$$\frac{\partial g_1}{\partial t} = \underbrace{-4k_2(e_0 - g_2)g_1^4 + 4k_{-2}g_2}_{\text{LoMA}} \underbrace{- v\frac{\partial g_1}{\partial x} + Dm_{O_2}\left(\sigma_{O_2} pp_{O_2} - g_1\right)}_{\text{gas exchange}}$$

$$\frac{\partial g_2}{\partial t} = k_2 (e_0 - g_2) g_1^4 - k_{-2} g_2 - v \frac{\partial g_2}{\partial x} + D_{m_{HL_8}} \left(\sigma_{HL_8} pp_{HL_8} - g_2 \right)$$

$$= k_2 (e_0 - g_2) g_1^4 - k_{-2} g_2 - v \frac{\partial g_2}{\partial x}$$

$D_{m_{HL_8}} = 0$ since no bound $HL(O_2)_4$ is exchanged

At steady-state we have:

$$v \frac{\partial g_1}{\partial x} = -4 k_2 (e_0 - g_2) g_1^4 + 4 k_{-2} g_2 + D_{m_{O_2}} \left(\sigma_{O_2} pp_{O_2} - g_1 \right)$$

$$v \frac{\partial g_2}{\partial x} = k_2 (e_0 - g_2) g_1^4 - k_{-2} g_2$$

$$\Downarrow$$

$$v \frac{d}{dx} (g_1 + 4 g_2) = D_{m_{O_2}} \left(\sigma_{O_2} pp_{O_2} - g_1 \right) \qquad (***)$$

As before, we expect that the variation of g_2 with x is slow if compared with the variation of g_2 with t, and that g_2 reaches equilibrium much faster than g_1

$$\Downarrow$$

QSS approximation: $\frac{\partial g_2}{\partial t} = 0 \iff k_2 (e_0 - g_2) g_1^4 = k_{-2} g_2$

It results: $g_2 = \frac{k_2 e_0 g_1^4}{k_{-2} + k_2 g_1^4} = \frac{e_0 g_1^4}{k_{O_2}^4 + g_1^4}$ $\qquad k_{O_2}^4 \triangleq k_{-2} / k_2$

Hence we have in $(***)$:

$$v \frac{d}{dx} \left(g_1 + \frac{4 e_0 g_1^4}{k_{O_2}^4 + g_1^4} \right) = D_{m_{O_2}} \left(\sigma_{O_2} pp_{O_2} - g_1 \right)$$

To determine the total flux Q we can write:

$$Q = A D_{mo_2} \int_0^L (\sigma_{o_2} pp_{o_2} - g_1)\, dx = A v \int_0^L \frac{d}{dx}\left(g_1 + 4 e_o \frac{g_1^4}{k_{o_2}^4 + g_1^4} \right) dx$$

(because of the previous eq.)

$$\Rightarrow Q = A v \left(g_1(x) + 4 e_o \frac{g_1^4(x)}{k_{o_2}^4 + g_1^4(x)} \right)\Bigg|_{x=0}^{x=L} =$$

$$= A v \left[g_{1L} - g_{10} + 4 e_o \left(\frac{g_{1L}^4}{k_{o_2}^4 + g_{1L}^4} - \frac{g_{10}^4}{k_{o_2}^4 + g_{10}^4} \right) \right] \qquad g_{10} \triangleq g_1(0), \quad g_{1L} \triangleq g_1(L)$$

If we compare this model to the original model without chemical reactions $Q = A v (\sigma_{o_2} pp_{o_2} - g_{10})(1 - e^{-D_{mo_2} L / v})$, we note:

- The model is not exponential and the partial pressure g_1/σ_{o_2} will vary along x-axis with a slope much steeper than before $\Rightarrow$ It is in good agreement with experimental data

- If one solves for $g_1(x)$, the ODE to consider is:

$$\underbrace{v \frac{d}{dx}\left(g_1 + 4 e_o \frac{g_1^4}{k_{o_2}^4 + g_1^4} \right)}_{\Updownarrow} = D_{mo_2} (\sigma_{o_2} pp_{o_2} - g_1)$$

$$v \frac{d}{dg_1}\left(g_1 + 4 e_o \underbrace{\frac{g_1^4}{k_{o_2}^4 + g_1^4}}_{f(g_1)} \right) \frac{dg_1}{dx} = v \left(1 + f'(g_1) \right) \frac{dg_1}{dx} \qquad f' \triangleq \frac{df}{dx}$$

Hence the exchange rate is amplified by the factor $(1 + f'(g_1)) > 1$. Although this is a variable factor, it can be estimated that the enhancement is by ~ 40 times on average.

* Balance between ventilation and perfusion

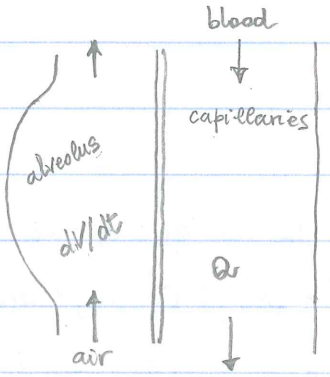
The models developed thus far for the gas exchange in the alveoli are based on the condition that (i) there is air in the alveolar volume and (ii) there is blood in the capillaries ⇒ An effective gas exchange depends on having:

- a good VENTILATION (i.e., movement of air between alveoli and the environment)
- a good PERFUSION (i.e., passage of blood through the capillaries)

⇓

A way to quantify the ability of the alveoli to complete a good gas exchange is by introducing the "ventilation-perfusion" ratio $\mathcal{R}$:

$$\mathcal{R} \triangleq \frac{dV/dt}{Q}$$



$\frac{dV}{dt} \triangleq$ volume flow rate of air reaching to the alveoli

$Q \triangleq$ volume flow rate of blood in and out the alveolar capillaries

To estimate $\mathcal{R}$, though, we do not need to measure Q and dV/dt. Let us observe:

- For a gas G ($G = CO_2, O_2$, etc.) the amount of gas exchanged through the alveolar-capillar wall per unit of time is: $\Delta G = Q(g_v - g_a)$

  where: $g_v \triangleq [G]$ at the entrance into the capillaries from the veins

  $g_a \triangleq [G]$ at the exit from the capillaries into the arteries

- The same amount ΔG must be carried outside (if CO_2) or inside (if O_2) the alveolus through ventilation:

$$\Delta G = \frac{dV}{dt}\left(\begin{array}{c}\text{concentration of G}\\ \text{in alveolar air}\end{array} - \begin{array}{c}\text{concentration of G}\\ \text{in inspired air}\end{array}\right)$$

Notice this:

$$\text{concentration of G in the air} = \frac{\#\text{ of moles of G}}{\text{total volume}} = \frac{n_g}{V_{tot}} = \frac{n_{tot}}{p_{tot} V_{tot}} pp_g \qquad \text{where } \frac{n_{tot}}{p_{tot} V_{tot}} \cong \text{const.}$$

Dalton's Law: $n_g = \frac{n_{tot}}{p_{tot}} pp_g$

We cannot use the solubility here because we are considering the air, not the blood

Hence, denoted with:

$pp_{g,a} \triangleq$ partial pressure of G in the alveolar air

$pp_{g,i} \triangleq$ partial pressure of G in the inspired air

$RT \triangleq \frac{p_{tot} \cdot V_{tot}}{n_{tot}}$

We have: $$\Delta G = \frac{dV}{dt} \cdot \frac{pp_{g,a} - pp_{g,i}}{RT} = Q(g_v - g_a)$$

$$\Rightarrow \mathcal{R} = \frac{dV/dt}{Q} = RT \frac{g_v - g_a}{pp_{g,a} - pp_{g,i}}$$

If the gas of interest is $G = CO_2$, then note:

- $pp_{g,i} \cong 0$, i.e., there is usually very little CO_2 in freshly inspired air
- $g_v = g(0) = \sigma_{CO_2}(1 + k_C) pp_{v,CO_2}$ (in the model we determined earlier in this lecture (pag. 7))

pp_{v,CO_2} is the partial pressure of CO_2 at the entrance of the capillary and was denoted with "pp_0" at the end of pag. 7

- $g_a = g(L) = \sigma_{CO_2}(1 + k_C)\left[pp_{a,CO_2} + (pp_{v,CO_2} - pp_{a,CO_2}) e^{-D_{m CO_2} L / v (1+k_C)}\right] \cong$ ($L \to \infty$)

$$\sigma_{CO_2}(1 + k_C) pp_{a,CO_2}$$

pp_{a,CO_2} was "pp_{CO_2}" on pag. 7 and is equal to $pp_{CO_2,a}$ (i.e., partial pressure of CO_2 in the alveolus)

Hence we have:

$$\mathcal{R} = RT \sigma_{CO_2}(1 + k_C) \frac{pp_{v,CO_2} - pp_{a,CO_2}}{pp_{a,CO_2}}$$

$\Rightarrow$ Because $pp_{v,CO_2} \cong 45$ mmHg - constant, we can plot pp_{a,CO_2} as a function of $\mathcal{R}$

We can repeat the same argument in case $G = O_2$. In this case, we must remember:

- The total concentration of $[O_2]$ (either bound to Hb or free) is:

$$[O_2]_t = g_1 + 4\,e_0 \underbrace{\frac{g_1^4}{k_{O_2}^4 + g_1^4}}_{f(g_1)} \qquad \text{(see eq. on pag. 9)}$$

- $pp_{g,i} \neq 0 \quad pp_{g,a} \neq 0 \quad$ with $g = O_2$

Hence we have:

$$\mathcal{R} = \frac{RT}{pp_{O_2,a} - pp_{O_2,i}} \left[g_{1,v} - g_{1,a} + 4\,e_0 \left(f(g_{1,v}) - f(g_{1,a}) \right) \right]$$

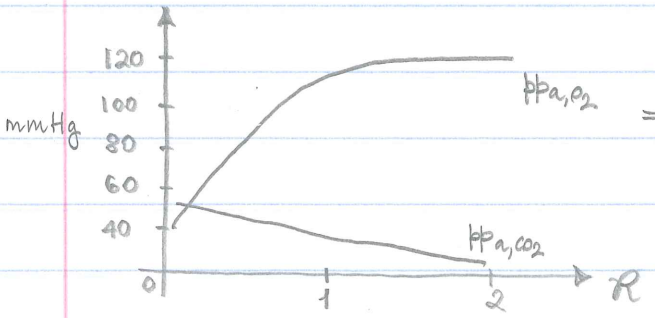
In the blood (liquid) we can use the notion of solubility and write:

$$g_{1,v} = \sigma_{O_2}\, pp_{v,O_2} \qquad g_{1,a} = \sigma_{O_2}\, pp_{a,O_2} \qquad pp_{a,O_2} = pp_{O_2,a}$$

$$\Downarrow$$

$$\mathcal{R} = \frac{RT\sigma_{O_2}}{pp_{a,O_2} - pp_{O_2,i}} \left[pp_{v,O_2} - pp_{a,O_2} + \frac{4\,e_0}{\sigma_{O_2}} \left(f(\sigma_{O_2} pp_{v,O_2}) - f(\sigma_{O_2} pp_{a,O_2}) \right) \right]$$

Because $pp_{O_2,i} \cong 150$ mmHg and $pp_{v,O_2} \cong 40$ mmHg are typically constant, it is possible to plot pp_{a,O_2} as a function of $\mathcal{R}$



$\Rightarrow$ The two partial pressures have opposite behavior as $\mathcal{R}$ increases $\Rightarrow$ Increments in $\mathcal{R}$ correspond to improvements in ventilation efficiency

HYPERVENTILATION $\triangleq$ Increment of $\mathcal{R}$ above the normal value $\mathcal{R}_{normal} = 1$

HYPOVENTILATION $\triangleq$ Decrement of $\mathcal{R}$ below the normal value $\mathcal{R}_{normal} = 1$

REFERENCE :

Textbook (volume 2) : chapter 14, sec. 14.1.1; 14.1.2; 14.1.3; 14.1.4; 14.2; 14.2.1