Transport System

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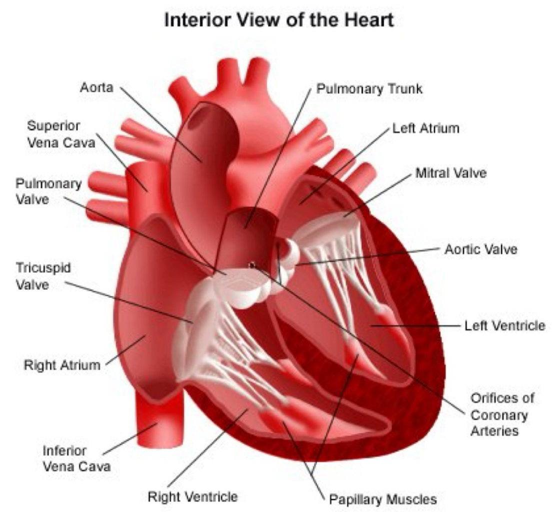
I. Circulatory system

1. Heart

* Heart anatomy

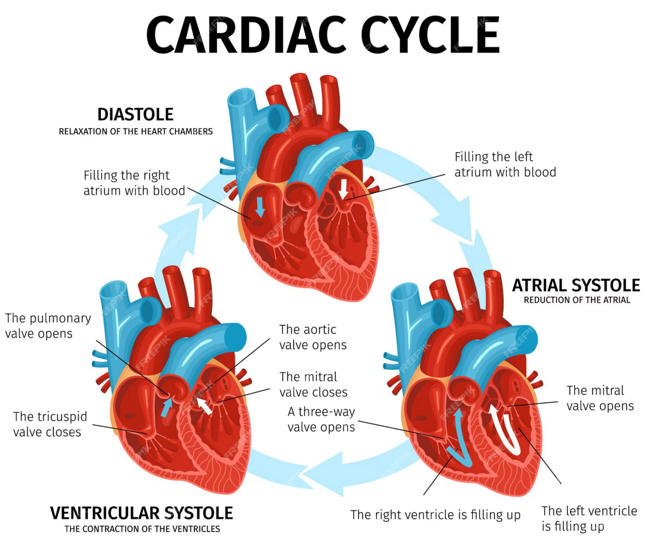


Right heart:
receives blood from the systemic system

Left heart:
receives blood from the pulmonary system

Atrium: low pressure chamber
Ventricle: high pressure chamber

* The cardiac cycle



The heart
- fills up and empties at constant pressure
- contracts at constant volume until the next valve opens
- relaxes at roughly a constant volume

* Simplified model of the cardiac cycle

End systolic volume:

$V_{ES} = V_{min} + C_s P_a$ — C_s: compliance of contracted tissue

End diastolic volume:

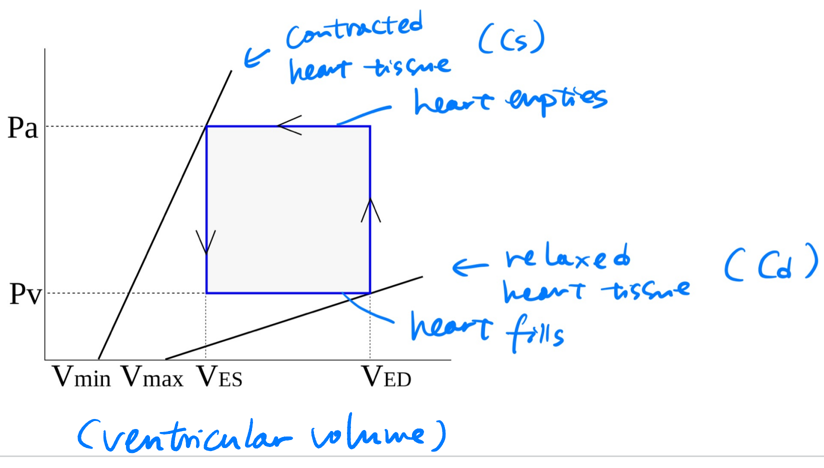
$V_{ED} = V_{max} + C_d P_v$ — C_d: compliance of relaxed tissue

Stroke volume:

$V_{stroke} = V_{ED} - V_{ES}$

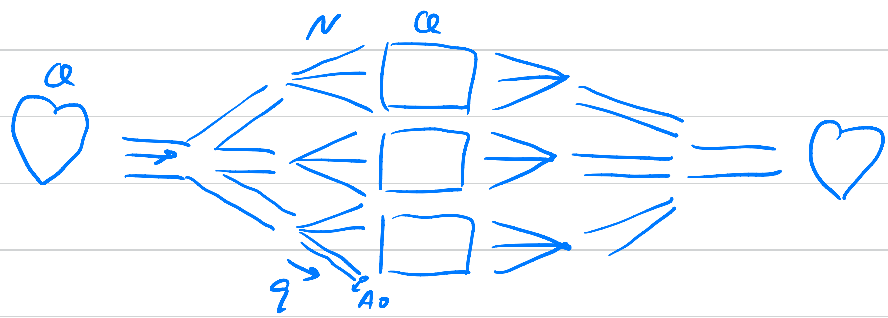
Cardiac output:

$Q = F V_{stroke}$ — F: beat rate



2. Blood flow in vessels

* Systemic circulation



* Assume blood is Newtonian

flux: $q = -\frac{A_0^2}{8\pi\mu}\frac{\partial P}{\partial x}$

total flux: $Q = Nq$

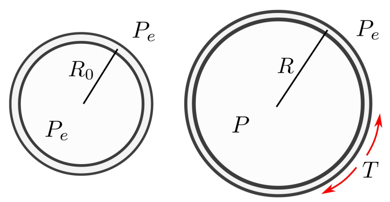
$$= \frac{NA_0^2}{8\pi\mu}\left(-\frac{dP}{dx}\right)$$

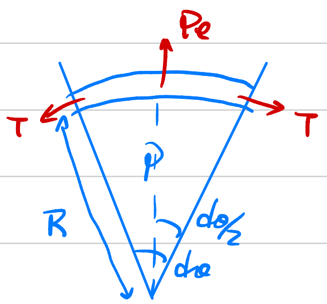
$$= \frac{AA_0}{8\pi\mu}\left(-\frac{dP}{dx}\right) \quad \text{with } A = NA_0$$

pressure drop: $\frac{\partial P}{\partial x} L_v \propto \frac{L_v}{AA_0}$

* Arterial wall elasticity

Local compliance of a vessel





$$(P-P_e)R\,d\theta = T\cancel{\sin\left(\frac{d\theta}{2}\right)}\times 2 \quad \approx \frac{d\theta}{2}$$

$$\Delta P = P - P_e = T/R$$

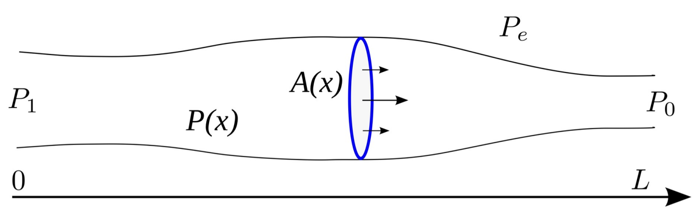
where $\underset{\text{tension}}{T} \approx \underset{\text{tissue stiffness}}{E}\,\frac{\overbrace{R-R_0}^{\Delta R}}{R_0}\,\underset{\text{tissue thickness}}{\delta}$

$$\Delta A = C\cdot\Delta P \quad \text{with } C = \frac{2\pi R_0^3}{E\delta}$$

(since $\Delta A = 2\pi R_0 \Delta R$)

Pressure drop / flux in a compliant vessel

☆ Assumption: steady state $\longrightarrow$ Poiseuille flow



$$\frac{\partial P}{\partial x} A^2(P) = -8\pi\mu Q \quad \text{(from Poiseuille)}$$

$$\int_0^x \frac{\partial P}{\partial x} A^2(P(x'))\,dx' = \int_{P(0)}^{P(x)} A^2 P\,dP = -8\pi\mu Q x$$

Using a simple linear relationship: $A = A_0 + C(P - P_e)$ (with $P_e = 0$)

$$\Rightarrow \boxed{Q = \frac{A_0^2}{8\pi\mu}\frac{P_1 - P_0}{L}\left(1 + \gamma(P_0 + P_1) + \gamma^2 \frac{P_0^2 + P_0 P_1 + P_1^2}{3}\right)} \quad \gamma = \frac{C}{A_0}$$

☆ internal pressure increases diameter

$\rightarrow$ lower flow resistance

(veins are more compliant that arteries $\rightarrow$ smaller ΔP)

* Pulsatile blood flow

Pulsatile flow profile

$$\rho\frac{\partial u_x}{\partial t} = -\frac{\partial P}{\partial x} + \frac{\mu}{r}\frac{\partial}{\partial r}\left(r\frac{\partial u_x}{\partial r}\right)$$

with $\dfrac{\partial P}{\partial x} = \dfrac{\Delta P}{L}\cos(\omega t) = \mathrm{Re}(A e^{i\omega t})$

try $u_x(r,t) = u(r)e^{i\omega t} \rightarrow i\rho\omega u e^{i\omega t} = -Ae^{i\omega t} + \dfrac{\mu}{r}\dfrac{\partial}{\partial r}\left(r\dfrac{\partial u}{\partial r}\right)e^{i\omega t}$

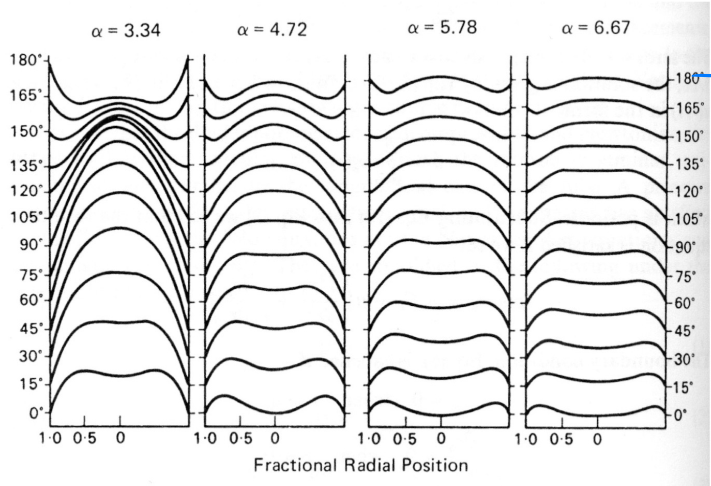
$$\frac{d^2u}{dr^2} + \frac{1}{r}\frac{du}{dr} - \frac{i\omega\rho}{\mu}u = \frac{A}{\mu} \xrightarrow[\tilde{r} = r/R]{\text{dimensionless form}} \underbrace{\frac{d^2u}{d\tilde{r}^2} + \frac{1}{\tilde{r}}\frac{du}{d\tilde{r}}}_{\text{viscosity term}} - \underbrace{i\,\underbrace{\frac{R^2\omega\rho}{\mu}}_{\alpha^2}u}_{\text{inertial term}} = \frac{R^2 A}{\mu}$$

$$\boxed{\text{Womersley number: } \alpha = \sqrt{\frac{R^2\omega\rho}{\mu}}}$$

Solution: $u_x(r,t) = \dfrac{A}{i\omega\rho}\left(1 - \dfrac{J_0(i^{3/2}\alpha r/R)}{J_0(i^{3/2}\alpha)}\right)e^{i\omega t}$

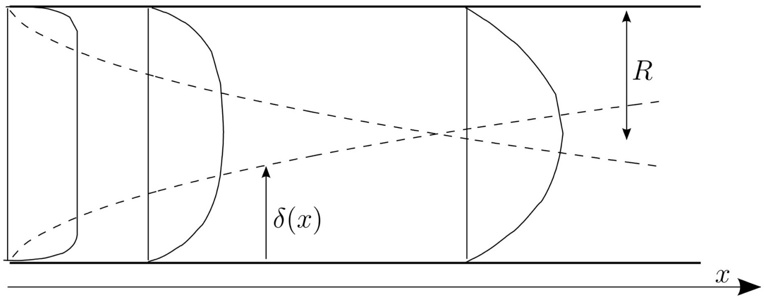
J_0: Bessel function of order 0

Poiseuille flow ←
(boundary layer forms quickly)



→ plug flow
(boundary layer does not have enough time to grow)

Boundary layer



Boundary layer grows along the pipe

$$\delta(x) = \sqrt{\mu x / \rho u}$$

The flow becomes Poiseuille flow when the boundary layer spans the whole cross-section (all region affected by viscous forces)

$$\delta(\Delta L) = R$$

$$\Delta L = \frac{R^2 \rho u}{\mu}$$

↓ the distance needed to reach the steady state profile

Transient flow: $u \Delta t = \Delta L$

$$\Delta t = \frac{\rho R^2}{\mu}$$

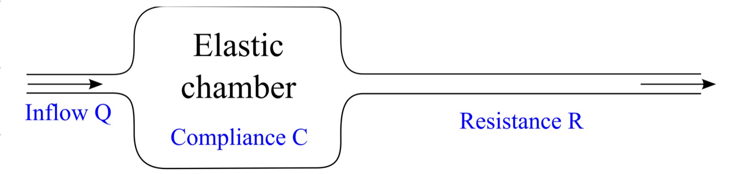
↓ time needed to reach the steady state

☆ Recall that $\alpha = R\sqrt{\omega\rho/\mu} \propto \Delta t$

- large α → flow oscillates too rapidly for boundary layer to grow
- small α → boundary layer have enough time to grow

* Intermittent flow in a compliant vessel

Windkessel model



Volume variation:

$$dV = \text{flow in} - \text{flow out} = Q\,dt - (\underbrace{P}_{\text{chamber pressure}}/R)\,dt$$

vessel elasticity:

$$dV = C\,dP$$

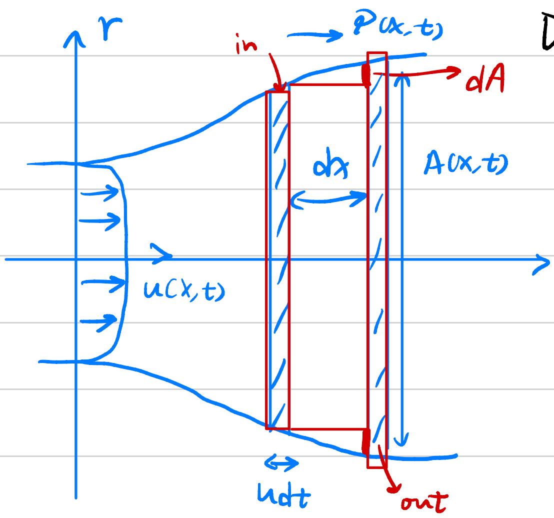
$$\Rightarrow \boxed{Q = C\frac{dP}{dt} + P/R}$$

If $Q = Q_0$ — constant, flow out $= Q_0$

If Q is a step function:

$$\text{flow out} = P/R = Q_0\left(1 - e^{-t/RC}\right)$$

Pressure wave



During time dt, by conservation of mass (volume)

$$dV = \underbrace{dA\,dx}_{\text{change in volume}} = \underbrace{(Au)(x)\,dt}_{\text{volume in}} - \underbrace{(Au)(x+dx)\,dt}_{\text{volume out}}$$

$$\boxed{\frac{\partial A}{\partial t} = -\frac{\partial (Au)}{\partial x}}$$

with $A(P) = A_0 + cP$

$$\boxed{c\left(\frac{\partial P}{\partial t} + u\frac{\partial P}{\partial x}\right) + A\frac{\partial u}{\partial x} = 0}$$

Conservation of momentum

$$F = ma = \frac{dp}{dt},\quad dp = F\,dt,\quad p = \rho A\,dx\,u$$

$$dp = \rho\,d(Au)\,dx \rightarrow \text{change in momentum in CV}$$

$$\rho\,d(Au)\,dx = \Big(\underbrace{(PA)(x,t) - (PA)(x+dx,t) + P\,dA}_{\text{pressure force}}\Big)dt + \underbrace{\rho(Au^2)(x,t)\,dt - \rho(Au^2)(x+dx,t)\,dt}_{\text{flux term}}$$

Divide by $\rho\,dx\,dt$

$$\frac{\partial (Au)}{\partial t} + \frac{\partial (Au^2)}{\partial x} = -\frac{1}{\rho}A\frac{\partial P}{\partial x}$$

$$\frac{\partial (Au)}{\partial t} + \frac{\partial (Au^2)}{\partial x} = u\frac{\partial A}{\partial t} + A\frac{\partial u}{\partial t} + u\frac{\partial (Au)}{\partial x} + Au\frac{\partial u}{\partial x}$$

$$= \cancel{-u\frac{\partial (Au)}{\partial x}} + \cancel{u\frac{\partial (Au)}{\partial x}} + A\frac{\partial u}{\partial t} + Au\frac{\partial u}{\partial x}$$

$$A\frac{\partial u}{\partial t} + Au\frac{\partial u}{\partial x} = -\frac{1}{\rho}A\frac{\partial P}{\partial x}$$

$$\Rightarrow \quad \rho\left(\frac{\partial u}{\partial t} + u\frac{\partial u}{\partial x}\right) = -\frac{\partial P}{\partial x}$$

$$\boxed{\rho\frac{Du}{Dt} = -\frac{\partial P}{\partial x}}$$

Wave equation

Removing second order terms in u or P:

$$\rho\frac{\partial u}{\partial t} + \frac{\partial P}{\partial x} = 0$$

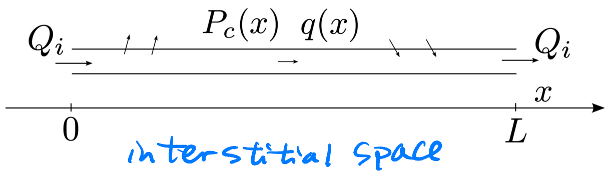
$$c\frac{\partial P}{\partial t} + A_0\frac{\partial u}{\partial x} = 0$$

$$\Rightarrow \quad \boxed{\frac{\partial^2 P}{\partial t^2} = \frac{A_0}{c\rho}\frac{\partial^2 P}{\partial x^2}}$$

wave speed $V_w = \sqrt{\frac{A_0}{c\rho}}$

3. Micro Circulation

* Blood filtration in capillaries



$q(x)$: blood flow rate along the capillary

$P_c(x)$: hydrostatic pressure along the capillary

Assumption : recover the <u>same amount of blood</u> at the end Q_i

The flow into the capillary is :

osmotic pressure in tissue

$$\frac{dq}{dx} = \phi_p(x) = K_f(P_i - \pi_i - P_c + \pi_c)$$

interstitial pressure / blood pressure / blood osmotic pressure

Denoting the capillary resistance by ρ :

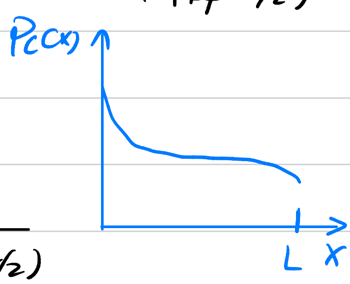
$$\frac{dP_c}{dx} = -\rho q(x)$$

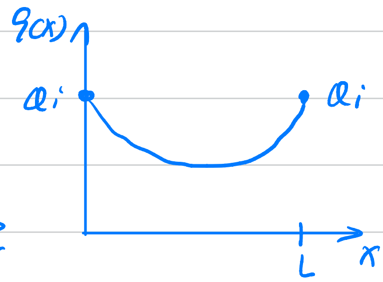
$$\Rightarrow \frac{d^2P_c}{dx^2} - \rho K_f P_c = -\rho K_f (P_i - \pi_i + \pi_c)$$

Solution :

$$P_c(x) = P_i + \pi_c - \pi_i - \frac{P_c(0) - P_c(L)}{2}\,\frac{\sinh(\sqrt{\rho K_f}(x - L/2))}{\sinh(\sqrt{\rho K_f}\, L/2)}$$

$$q(x) = Q_i\,\frac{\cosh(\sqrt{\rho K_f}(x - L/2))}{\cosh(\sqrt{\rho K_f}\, L/2)}$$





$$\Rightarrow Q_i = \frac{1}{\rho}\,\frac{P_c(0) - P_c(L)}{L}\,\frac{\sqrt{\rho K_f}\, L/2}{\tanh(\sqrt{\rho K_f}\, L/2)}$$

Filtration rate : maximal flow rate in the interstitial space

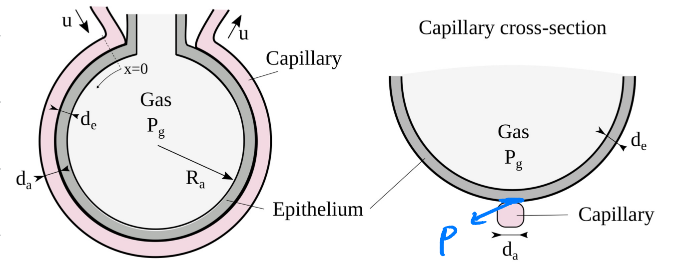
$$Q_f = Q_i - q(L/2)$$

$$\boxed{\frac{Q_f}{Q_i} = 1 - \operatorname{sech}\sqrt{\rho K_f}\, L/2}$$

II. Respiration

1. Gas exchange in the lungs

* Capillary - alveolar gas exchange model



Diffusion through the epithelium

$$D_e \frac{\partial^2 C_e}{\partial y^2} = \frac{\partial C_e}{\partial t}$$

diffusion const. (D_e) — gas conc. in the epithelium (C_e)

Assuming steady state:

$$C_e(y) = C_b + \frac{\sigma P_g - C_b}{d_e} y$$

(C_b: gas conc. in the capillary)

The flux through the epithelium is:

$$J = -\frac{\partial C_e}{\partial y} = -\frac{D_e}{d_e}(\sigma P_g - C_b)$$

Mass Conservation

$$u A C_b(x) = u A C_b(x+dx) + J p\, dx$$

(p: Section of the vessel perimeter in contact with the epithelium $p \approx d_a$)

$$\rightarrow \quad u \frac{dC_b}{dx} = -\frac{p}{A} J = \frac{p D_e}{A d_e}(\sigma P_g - C_b)$$

$$= \frac{\sigma P_g - C_b}{\tau} \quad \text{with} \quad \tau = \frac{A d_e}{p D_e}$$

Solution

$$\boxed{\begin{aligned} C_b(x) &= C_b(0) + (\sigma P_g - C_b(0))(1 - e^{-x/\lambda}) \quad \text{with} \quad \lambda = u\tau \\ C_b(t) &= C_b(0) + (\sigma P_g - C_b(0))(1 - e^{-t/\tau}) \end{aligned}}$$

Consider a blood lump

* Carbon dioxide removal

$$CO_2 + H_2O \underset{k_-}{\overset{k_+}{\rightleftharpoons}} \underset{h}{H^+} + \underset{C_d}{HCO_3^-}$$

$CO_2 \to C_b$

$$\frac{dC_b}{dt} = \frac{pD_e}{Ad_e}(\sigma P_g - C_b) + k_- h C_d - k_+ C_b$$

$$\frac{dC_d}{dt} = k_+ C_b - k_- h C_d$$

Assume equilibrium with the bicarbonate ion is very fast — quasi-steady equilibrium

Also, pH assumed to be constant

$$C_d = \frac{k_+}{hk_-} C_b = K C_b$$

$$\frac{d}{dt}(C_d + C_b) = \frac{pD_e}{Ad_e}(\sigma P_g - C_b)$$

$$(1+K)\frac{dC_b}{dt} = \frac{pD_e}{Ad_e}(\sigma P_g - C_b)$$

Since $\frac{dC_b}{dt} = u\frac{dC_b}{dx}$ ($dx = u\,dt$), in vessel frame

$$u(1+K)\frac{dC_b}{dx} = \frac{pD_e}{Ad_e}(\sigma P_g - C_b)$$

Distance necessary to equilibriate CO_2:

$$\lambda_{CO_2} = (1+K)u\tau$$

* Oxygen uptake

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

$$\frac{dC_b}{dt} = \frac{pD_e}{Ad_e}(\sigma P_g - C_b) - 4k_+[Hb]C_b^4 + 4k_-[Hb(O_2)_4]$$

$$\frac{d[Hb(O_2)_4]}{dt} = k_+[Hb]C_b^4 - k_-[Hb(O_2)_4]$$

$$\frac{d[Hb]}{dt} = k_{-1}[Hb(O_2)_4] - k_+[Hb]C_b^4$$

Assume that the haemoglobin association / dissociation is much faster than the gas transport through the epithelium — quasi-steady equi.

$$[Hb(O_2)_4] = \underset{\text{total amount of haemoglobin}}{Hb_0}\frac{C_b^4}{K^{-1}+C_b^4} \quad \text{with } K = \frac{k_+}{k_-}$$

$$\frac{dC_b}{dt} + 4\frac{d[Hb(O_2)_4]}{dt} = \frac{d}{dt}\left(C_b + 4Hb_0\frac{C_b^4}{K^{-1}+C_b^4}\right) = \frac{pD_e}{Ad_e}(\sigma P_g - C_b)$$

In vessel frame:

$$u\frac{d}{dx}\left(C_b + 4Hb_0\frac{C_b^4}{K^{-1}+C_b^4}\right) = \frac{pD_e}{Ad_e}(\sigma P_g - C_b)$$

$$\Rightarrow \quad u\frac{dC_b}{dx} = \frac{pD_e}{Ad_e}\frac{\sigma P_g - C_b}{1+4Hb_0Y'(C_b)}$$

where $Y'(C_b) = \frac{1}{C_b}\frac{C_b^4}{K^{-1}+C_b^4}$ → $Y(C_b)$, the haemoglobin saturation curve

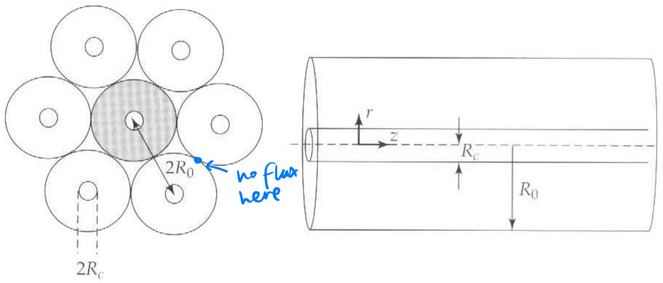
☆ When oxygen concentration (C_b) increases,

$(\sigma P_g - C_b)\downarrow$ and $Y'(C_b)\downarrow$

→ $\frac{dC_b}{dx}$ roughly constant

2. Oxygen delivery to tissues

* The Krogh cylinder model



$$\frac{\partial c}{\partial t} - D\nabla^2 c = -\rho$$

$\left(\frac{\partial c}{\partial t} = 0\right)$

In steady state and cylindrical geometry:

$$\frac{D}{r}\frac{d}{dr}\left(r\frac{dc}{dr}\right) = \rho$$

Solution:

$$c(r) = \frac{\rho}{4D}r^2 + A\ln(r) + B$$

Boundary conditions : $c(R_c) = c_c$ and $\frac{dc}{dr}(R_0) = 0$

$$\Rightarrow \frac{c(r)}{c_c} = 1 + \frac{\rho R_0^2}{4c_c D}\left(\frac{r^2}{R_0^2} - \frac{R_c^2}{R_0^2} - 2\ln(r/R_c)\right)$$

$$\frac{c(r)}{c_c} = 1 + \Phi\left(r^{*2} - R^{*2} - 2\ln(r^*/R^*)\right)$$

For tissue to be properly oxygenated: $c(r = R_0) > 0$

$$\Rightarrow \boxed{\Phi\left(R^{*2} - 2\ln(R^*) - 1\right) < 1}$$

where $\Phi = \frac{\rho R_0^2}{4c_c D}$ — dimensionless reaction rate

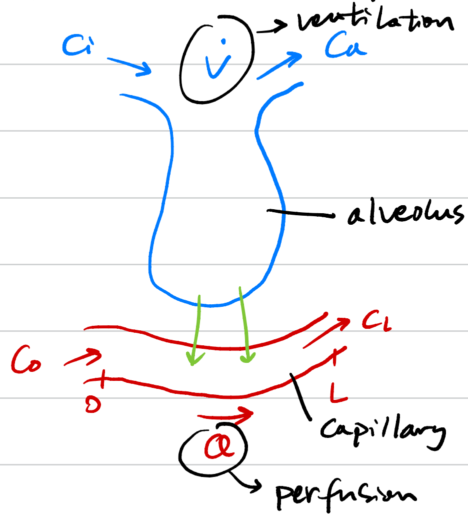
$r^* = r/R_0$

$R^* = R_c/R_0$

☆ If ρ increases, decrease R_0 or increase R_c

3. Ventilation and perfusion

* Ventilation – perfusion ratio



Rate of gas transfer from the air:

$$\dot{V}(C_i - C_a) \qquad \left(\begin{array}{l} P_i = RTC_i \\ P_a = RTC_a \end{array} \right)$$

Rate of gas transfer to the blood:

$$\dot{Q}(C_L - C_o)$$

Mass conservation:

$$\dot{V}(C_i - C_a) = \dot{Q}(C_L - C_o)$$

Ventilation-perfusion ratio:

$$\frac{\dot{V}}{\dot{Q}} = \frac{C_L - C_o}{C_i - C_a}$$

* Case of carbon dioxide

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

At equilibrium

$$[HCO_3^-] = \frac{k_+}{[H^+]k_-}[CO_2] = K[CO_2]$$

$$\frac{\dot{V}}{\dot{Q}} = \underset{\text{Solubility}}{\sigma} RT(1+K)\frac{P_L - P_o}{P_i - P_a}$$

Gas exchange is complete when the blood leaves the capillary $\rightarrow$ Assume $P_L = P_a$

Assume CO_2 from the atmosphere is low $\rightarrow P_i = 0$

$$\rightarrow \frac{\dot{V}}{\dot{Q}} = \sigma RT(1+K)\frac{P_o - P_a}{P_a}$$

* Case of oxygen

total quantity of oxygen = $C_{O_2} + \underbrace{4Hb_{tot}Y(C_{O_2})}_{\text{bounded oxygen}}$

$$\rightarrow \frac{\dot{V}}{\dot{Q}} = RT\frac{C_{O_2}^{(a)} + 4Hb_{tot}Y(C_{O_2}^{(a)}) - C_{O_2}^{(o)} - 4Hb_{tot}Y(C_{O_2}^{(o)})}{P_i - P_a}$$

4. Fetal respiration

- Placenta provides oxygen, nutrients and waste removal
- fetal haemoglobin saturates in oxygen at lower partial pressure