Imperial College London

Medical Science 1
Cardiovascular and Respiratory Systems

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based on the lectures from Prof. Peter D Weinberg in Autumn, 2019

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Preface

These notes were initially compiled align to the module BIOE40010 Medical and Biological Science 1, Part 1: Cardiovascular and Respiratory Systems, lectured by Professor P D Weinberg in Autumn 2019. Later typesetting works were carried out in Auguet 2021, March 2023, and most recently May 2024. Due to the incompleteness of the original work, the author could not guarantee the following notes reflect the actual syllabus for teaching in the current and future academic years.

Please note that the following notes were not proof read by anyone – read with discretion. Please report any typos, inconsistencies, and errors to binghuan.li19@imperial.ac.uk.

To my undergraduate years.

May 2024

London

Table of Contents

Part I – Cardiovascular System

i. Introduction to the circulation

a. Why do we need the circulation?

Circulation supplies the cells. Small animals use *diffusion* for mass transport, diffusion depends on thermal motion of particles.

How fast is the diffusion?

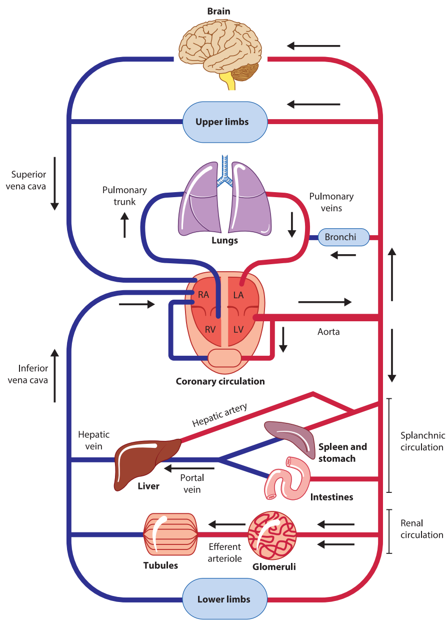
$$t = \frac{x^2}{2D}$$

where D is the diffusion coefficient, sometimes the denominator can be $4D$, $6D$ …
Determinants of D: size of particles, temperature, viscosity of medium.

> Example: O_2 in tissue, $D = 2.4 \times 10^{-5}\ \mathrm{cm^2/s}$
>
> At $x_1 = 5\,\mu\mathrm{m}$, this would result $t_1 \approx 5\ \mathrm{ms}$
>
> At $x_2 = 1\ \mathrm{m}$, this would result $t_2 \approx 7$ years

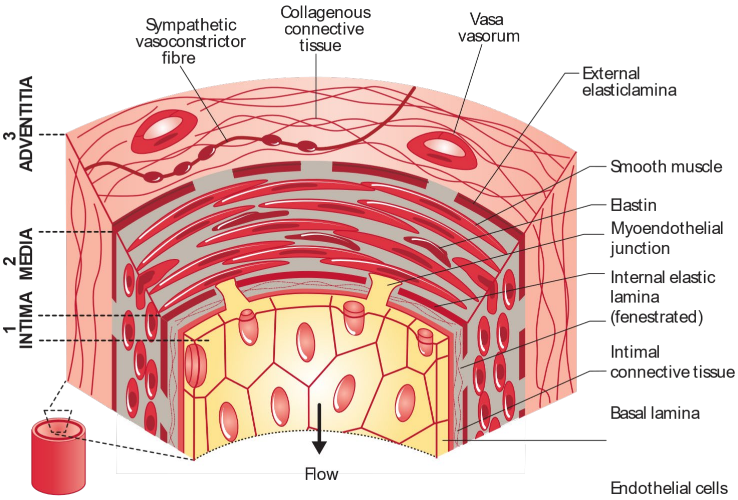
- In fact, we use diffusion only over micrometre distance. Instead, we use bulk flow to supply our cells (advection/convection).

b. Components of the Circulation



- *Systemic* and *pulmonary* circulations are *in series*. Within the systemic circulation, different organs are *in parallel*.
- However, there are two exceptions:
  - Blood first goes to gut then to liver;
  - Blood first goes to glomerulus then to tubules.

  This is due to:
  - Special needs: liver tends to clean poisons from gut before spreading out.
  - Disadvantage: liver gets a second-hand blood.
- Structure of vessels:
  - **Intimal**: endothelial cells, internal elastic lamina (elastin)
  - **Medial**: smooth muscle cells, constrict or dilate
  - **Adventitial**: blood vessels to supply cells, nerves



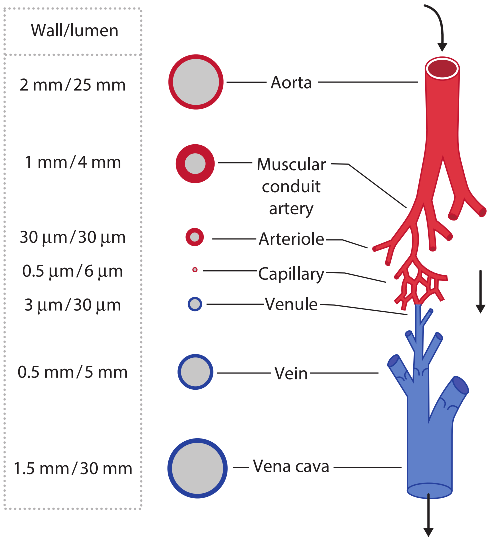
- Vessels' properties:

  - **Elastic arteries (*e.g.,* aorta)**: does not give a constant pressure
  - **Muscular arteries**: stop bleeding, can spasm
  - **Arterioles**: control, has very thick walls
  - **Capillaries**: intimal only, has very thin walls.
  - **Venules, veins (*e.g.,* vena cava)**: storage, give capacitance of vessel.

- Law of Laplace:

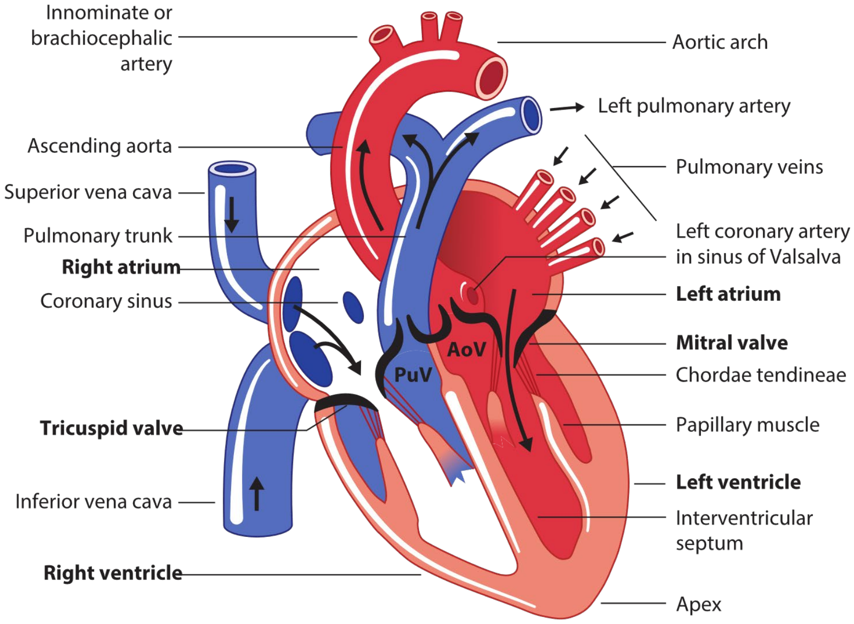
$$\text{tension} = \text{pressure} \times \text{radius}$$

Specifically for arteries: wall thickness is proportional to radius.



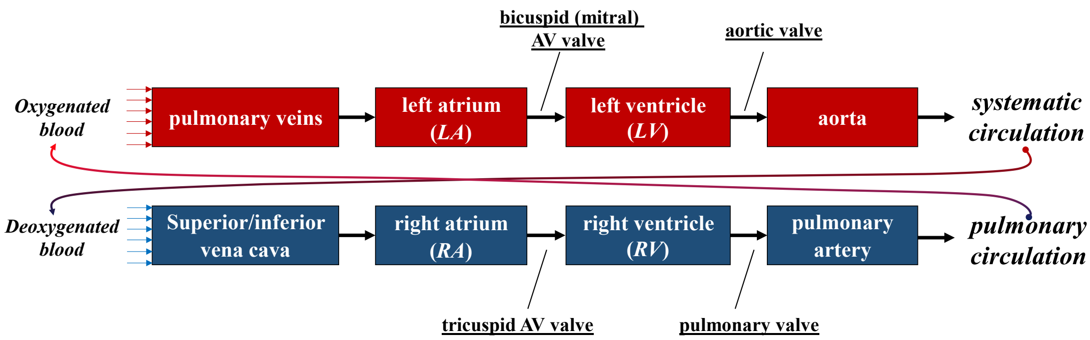
i. The Heart: Structure and Mechanisms of Cardiac Cycle

a. The Heart



- ***Atrium***: reservoir; ***Ventricle***: pump.
- ***Valves***: <u>all valves are passive!</u>
- ***Fibrotendinous ring***: all 4 valves lie in a single plane massive fibre around valves to join them together. They are electrical insulators.

A *simplified* structure of the heart with the circulation pathways in a human body can be drawn as



b. Pressure and Volumes During the Cardiac Cycle

Systole and **diastole** refer to two cardiac events in one cardiac cycle:

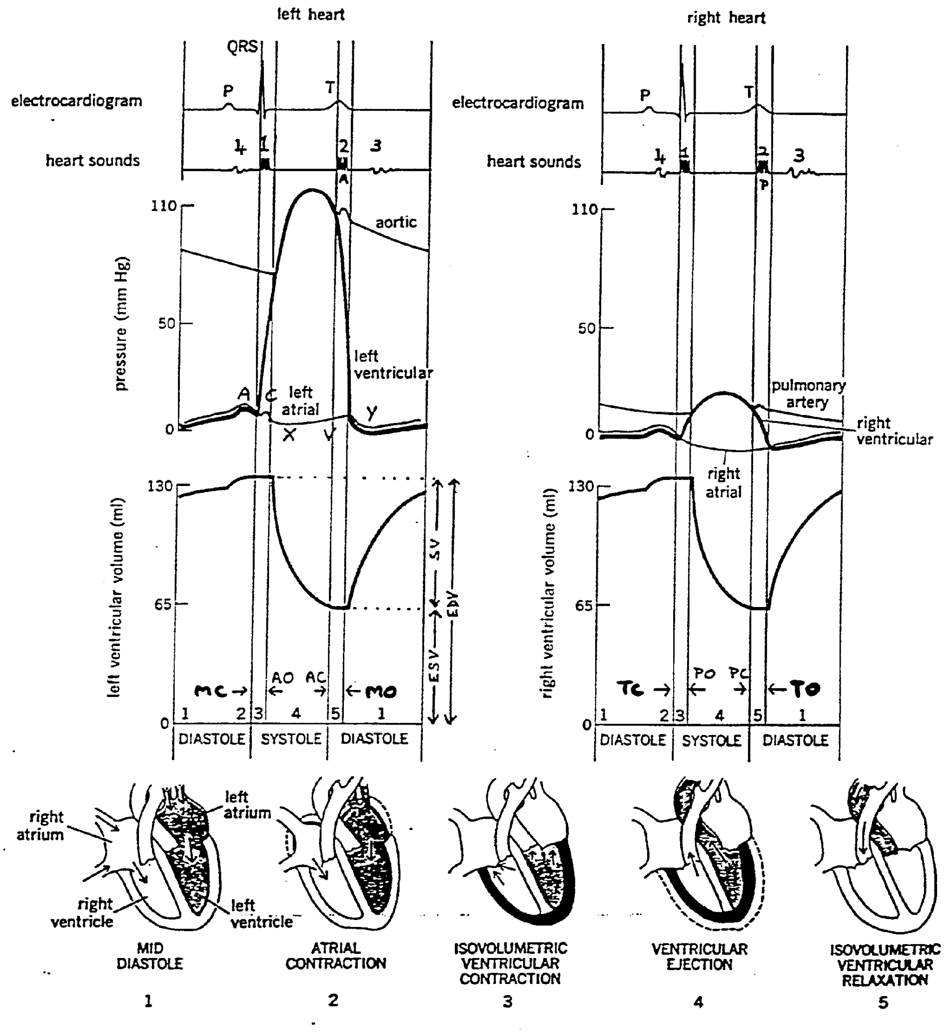
- Diastole: ventricle relaxation, AV valve opens, aortic valve closes, blood fills in the ventricle
- Systole: ventricle contraction, AV valve closes, aortic valve opens, blood is ejected to the body

Arterial pressure is *pulsatile* because the heart ejects blood intermittently (systole), with rests in-between (diastole).

- Systolic blood pressure: typically at 120 mmHg ("millimetres of mercury")
- Diastolic blood pressure: typically at 80 mmHg

There are two **heart sounds** in one cardiac cycle:

- First heart sound: "*lub*", from the close of the AV valve.
- Second heart sound: "*dub*", from the close of the aortic valve.



Stroke volume and **cardiac output**:

- Stroke volume (*SV*) is the difference between the end-diastolic volume (*EDV*) and the end-systolic volume (*ESV*)

$$SV = EDV - ESV$$

- Cardiac output (*CO*) is the stroke volume multiplied by the heart rate (*HR*)

$$CO = SV \times HR$$

Example:

For an adult man, the SV is about 70 mL per heartbeat, the HR is about 70 beats per minute, therefore, the cardiac output is calculated as:

$$CO = 70\,[\text{ml/b}] \times 70\,[\text{bpm}] \approx 5\,[\text{L/min}]$$

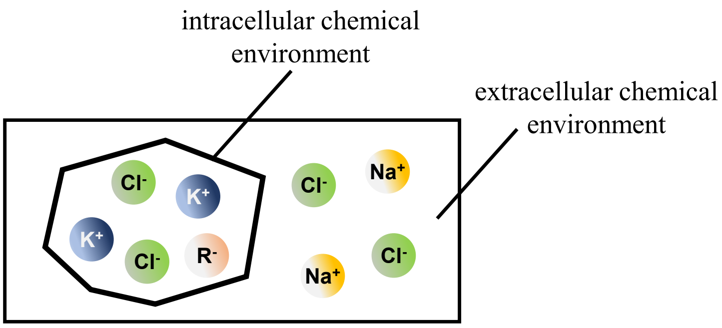
Pressure-volume (P-V) loop is used to illustrate the relation between the pressure and volume in a heart ventricle in one cardiac cycle. Four phases can be identified in a P-V loop, namely

Phase a	Ventricular filling (diastole)
Phase b	isovolumetric contraction (systole)
Phase c	Ejection (systole)
Phase d	Isovolumetric relaxation (diastole)

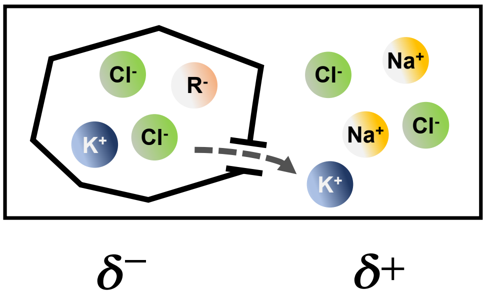
ii. The Heart: Electrics of Cardia Cycle

a. Resting Potential

- Cells in the heart are called "excitable cells". There is a potential difference between the membranes.
- **At rest:**

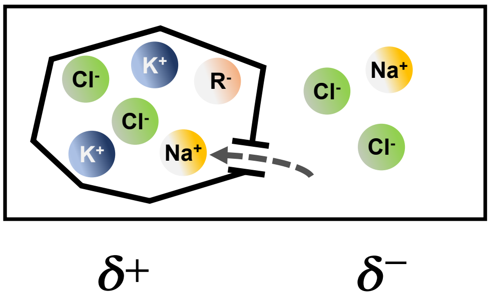


If chemical gradient = electrical gradient, reaches the Donnan Equilibrium, which is the equilibrium potential of K^+.



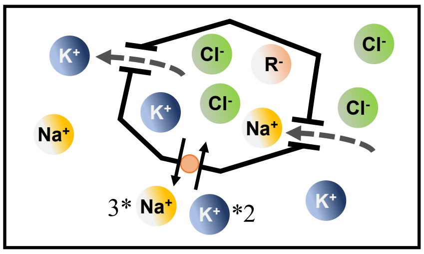
From the right figure: there is an electrical gradient because of the chemical gradient which drives the outflow of K^+.

- Open Na^+ channels:



Also creates an electrical gradient.
There is also an equilibrium potential for Na^+.

- Open both K^+, Na^+ channels:



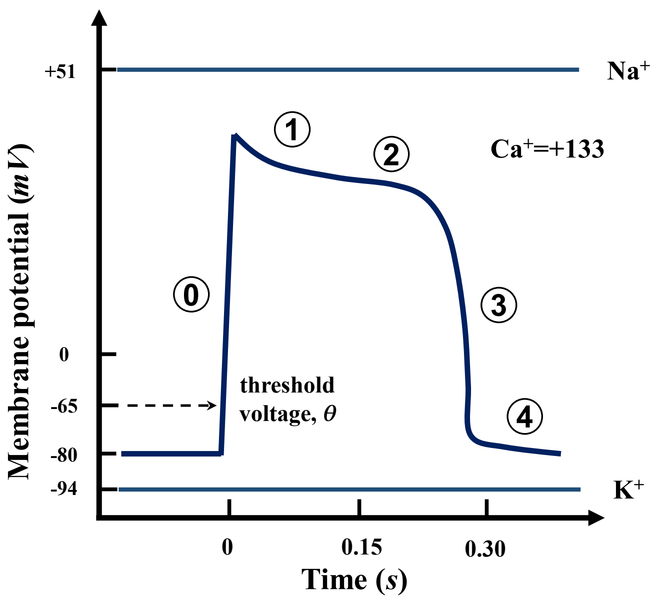
There is also a pump which will transport K^+, Na^+ ions, known as the <u>sodium–potassium pump</u>, to maintain the equilibrium potential.

- Normally, reasting potentials is at -80 mV (membrane inside relative to the membrane outside). This is because the number of K^+ channels is greater than that of Na^+ channels.

b. Action Potential

- At the resting potential, cells are *<u>polarised</u>*.
  - *<u>Depolarisation</u>*: zero potential difference across the membrane
  - *<u>Repolarisation</u>*: the potential difference across the membrane reverts to the resting potential

- Polarisation, depolarisation, and repolarisation are achieved by *controlling the open and close of ion channels*.
  - *<u>Na^+ (sodium) channel</u>*: opens rapidly due to depolarization of the membrane ("*voltage-gated*"), allowing for a rapid flow of sodium into the cell, resulting in further depolarization. They are *fast channels*.
  - *<u>Ca^{2+} (calcium) channel</u>*: "voltage gated", second inward current, Ca^{2+} channels are *slow channels*, they are also "voltage gated" and cause depolarization.
  - *<u>K^+ (potassium) channels</u>*



Phase 0: when the membrane potential reaches ~-65mV, the fast Na^+ channel opens. The inward Na^+ ions cause the occurrence of depolarisation.

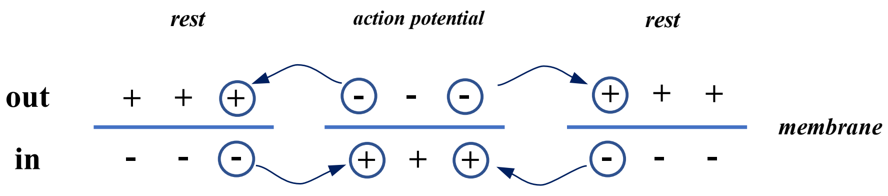
Phase 1 & 2: plateau behaviour. Phase 1 is caused by a rapid but incomplete repolarisation due to open of the K^+ channel. Phase 2 is due to the slow but long-lasting inflow of the Ca^+ ions. There is also a Na^+-Ca^+ exchange that maintains the late stage of the plateau.

Phase 3: slow K^+ channel opens causes the repolarisation.

Phase 4: resting potential

- In heart, there is no tenancy because of after the action potential, there is known as the *refractory period*.
  - *Absolute refractory period*: the myocyte is electrically inexcitable throughout its prolonged depolarization.
  - *Relative refractory period*: by the time repolarization reaches -50 mV, many but not all the fast Na^+ channels have reset from the inactivated state to a closed-but-activatable state.

c. Spreading of Action Potentials: local currents



d. Excitation-contraction Coupling: How does action potential cause muscle contraction?

Ca^{2+} stores in sarcoplasmic reticulum. The release of Ca^{2+} would cause muscle contraction. There are two ways would cause the release of Ca^{2+}:

- action potential
- second inward current of Ca^{2+}.

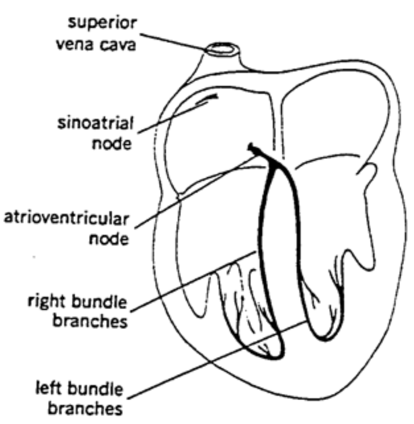
e. Initiation and Coordination of Action Potential

The action potential is initiated from the **pacemaker cells** – they are the cells have their spontaneous action potential. Pacemaker cells have *slow channels* only.

How can the pacemaker cells depolarise spontaneously? Two theories would explain:

- K^+ channels close so that Na^+ channels dominate.
- "funny current": Na^+ channels opens when depolarising.

Fastest depolarised cells will set the heart rate, which are known as dominance.

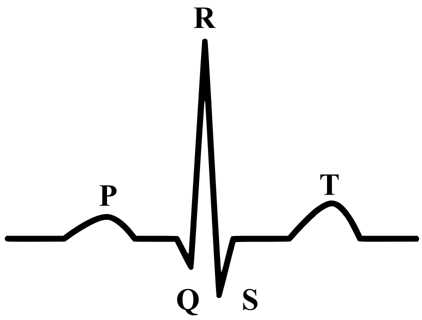


Conduction of action potential:

SA node(pacemaker cells) ⇒ AV node ⇒ Left/right bundle branches

f. Electrocardiogram (ECG)

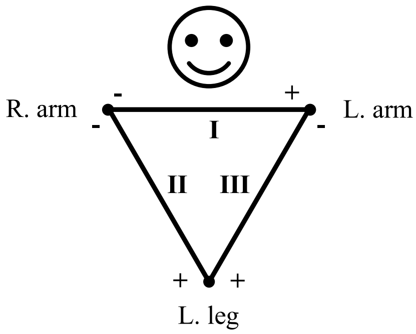
Action potential activity within the heart can be recorded to produce an electrocardiogram (ECG). A typical ECG wave is shown as



P wave	atrial depolarisation
QRS complex	ventricular depolarisation
T wave	repolarisation

There is no wave correspondent to the atrial repolarization due to such wave is too small to be detected.

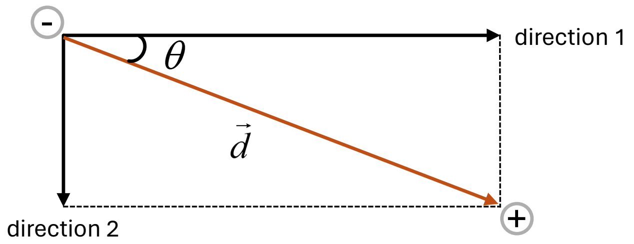
Einthoven's Triangle: there are three bipolar limb leads: *left arm*, *right arm*, and *left leg*. When they are connected with the configuration shown below, a sensing tringle is formed, with each lead serving as a view of the heart – producing the ECG in the simplest way.



Lead I	Left arm (+) to right arm (-)	Angle of view 0°
Lead II	Left leg (+) to right arm (-)	Angle of view +60°
Lead III	Left leg (+) to left arm (-)	Angle of view +120°

(in addition to the such three bipolar limbs leads, there are three unipolar limbs leads and six unipolar precordinal leads, which forms the standard 12-lead ECG set up)

Dipoles: Electrical dipoles are raised due the presence of positive and negative potential fields. Dipoles are *vectors* (with both the magnitude and direction) used to describe the gradient of the charge.



Hence, one can decompose a dipole into two orthogonal directions. These two directions are often chosen to be the directions of two perpendicular ECG leads.

If an ECG lead is…	**This would result in…**
parallel to the dipole	maximum signal
perpendicular to the dipole	no signal could be measured

Also, the strength of the dipole relates to the strength of the measured ECG signal: small dipoles give small signal; large dipoles give large signal.

iii. Cardiac Output and its Regulation

By $CO = SV \times HR$, controlling of the cardiac output can be achieved by controlling the heart rate or the stroke volume.

a. Control of Heart Rate

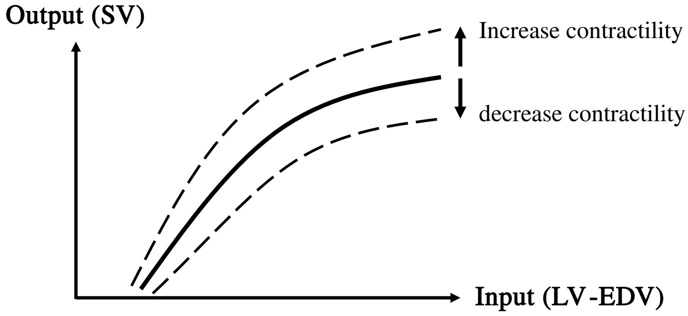
HR is controlled by both nerves and hormones. Suppose the absence of any effects from nerves or hormones, HR would be reach 100 bpm.

- Nerves: automatic nervous system
    - **Sympathetic:** release noradrenaline (NorAdr), opens Na^+ and Ca^{2+} channels which will increase heart HR.
    - **Parasympathetic:** release acetylcholine (Ach), opens K^+ channels which will slows down HR.
- Hormones: **Adrenaline, Noradrenaline**, hormones from adrenal glands which will increase HR.

b. Control of Stroke Volume

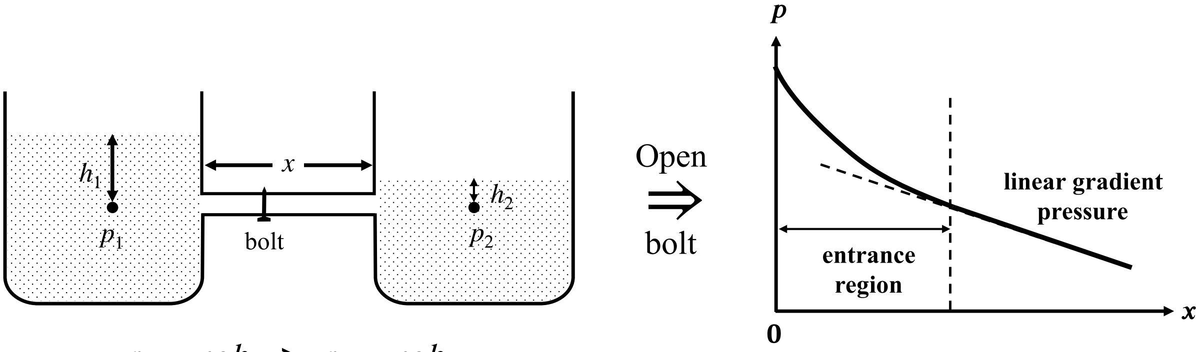
Controlling of SV is achieved by **Starling's Law of the heart** (Frank–Starling Mechanism): how SV changes under a given EDV. Such a mechanism auto-balancesmthe input and output of the opposite two ventricles –more received, more will be pumped out.

The heart's contractility is increase by Adr and Nor-Adr, hence, the heart will contract stronger (inotropic).



iv. Introduction to Haemodynamics

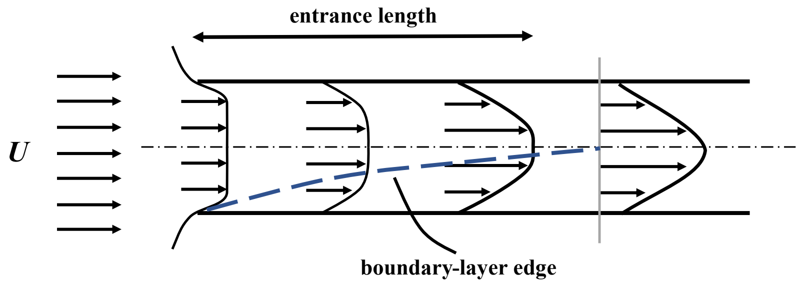
a. Flow in Pipes



$$p_1 = \rho g h_1 > p_2 = \rho g h_2$$

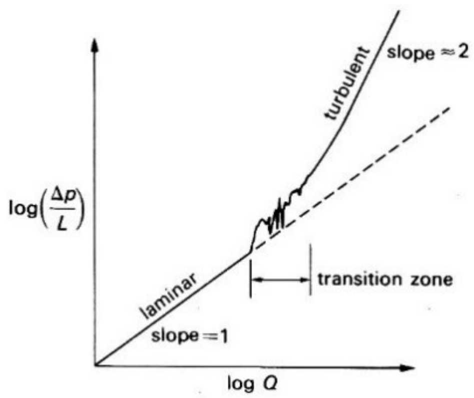
There are two reasons that explains why the pressure decreased with the length: (1) the liquid is accelerating, gain in kinetic energy is corresponding to the loss of potential energy; (2) due to the existence of viscosity, the fluid needs to overcome the (vascular) wall friction.

A (roughly) sketched fluid velocity profile:



There are 3 sections in the sketch above, from left to right:

1. Non-slip condition
2. Near-wall flow deaccelerated due to the friction.
3. Fully developed (velocity independent from the location) Poiseuille flow with a parabolic profile



Darcy's Law:

$$\Delta P = Q \times R$$

where the resistance R is the difference in mean pressure needed to drive one unit of flow in the steady state.

Poiseuille's Law:

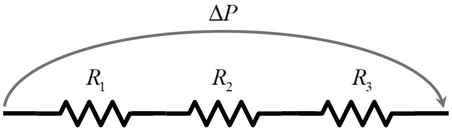
$$R = \frac{128}{\pi} \cdot \frac{\mu L}{d^4}$$

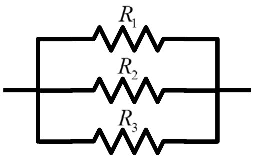
where μ is viscosity, L is the length of the pipe and d is the diameter of the pipe.

The total resistance, R_{total} , follows the rules below:

$$R_{\text{total}} = R_1 + R_2 + \ldots + R_n, \quad \text{for } R \text{ connected in series}$$

$$1/R_{\text{total}} = 1/R_1 + 1/R_2 + \ldots + 1/R_n, \quad \text{for } R \text{ connected in parallel}$$





b. Flow in the Body

Flow in the body is more complicated than the flow in a long, straight pipe.

1. Entrance length is long: ~1 m
2. Pulsatile flow: steady + oscillatory
3. Blood is the suspension of cells, not simply a fluid

Note that: maximum R happens in arterioles, not in capillaries, this is because: (1) capillaries are very short: 0.5 ~ 1 mm; and (2) large amount capillaries are in parallel.

v. Control of Arteriolar Tone

- **vasodilation** refers to the increase of the diameter of blood vessel
- **vasoconstriction** refers to the decrease of the diameter of blood vessel

a. Roles of Resistance Vessels

Total peripheral resistance, *TPR*:

- Whole body – change pressure, P
- One organ – change flow, Q

Two ways to change *TPR*:

- Intrinsic control: change *TPR* in one specific organ
- Extrinsic control: change *TPR* in the whole body by hormones and nerves

b. Local (intrinsic) Control of Arteriolar Tone

Extrinsic control of arteriolar tone changes R in one organ.

i) Active hyperaemia:
   - metabolites cause vasodilation
   - CO_2, H^+, O_2, some ATP breakdown products: ADP, AMP, PO_4^{3-}, adenosine

ii) Pressure autoregulation

iii) Relative hyperaemia: combination of (i) and (ii) above.

iv) Local temperature:

v) Response to injury:

- Constriction: release of 5HT, haemostasis
- Dilation: inflammation, histamine

vi) Endothelium release chemicals

- Dilation: endothelium derived relaxing factor: Ach ADP, histamine, blood flow, bradykinin. Release of NO.
- Constriction: endothelin

c. Extrinsic Control of Arteriolar Tone

Extrinsic control of arteriolar tone changes R in the whole body.

i) Sympathetic system:

- In most arterioles
- Release NorAdr at α -receptors, which causes vessel constriction

ii) Parasympathetic system

- Only in some vessels, it is rare
- Release Ach, which causes dilation

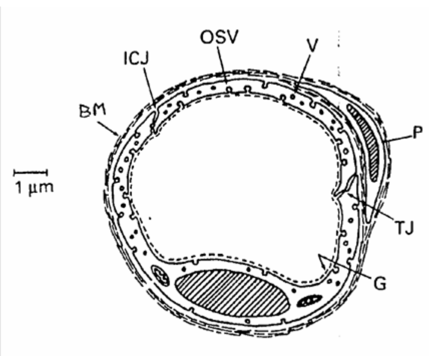
iii) Hormones

- Adr + NorAdr bind to α-receptors, which cause vessel constriction
- Adr binds to β -receptors, which causes dilation
- 3 exception organs: heart, skeletal muscles, liver. They have more β -receptors than α -receptors, so Adr will domain the effect, which causes dilation.
- Other organs have more α -receptors, so Adr causes constriction.

vi. Capillary, Interstitium and Lymph: Solute Exchange and Fluid Balance

a. Structures of Capillaries

- Capillary module: groups of capillaries supplied by one same arteriole.
  - Small diameter: 5-8 μm
  - No smooth muscle, gives a thin wall
  - Distribution density: lung > brain / heart > muscles.
- Cross-section of continuous capillaries:



P	pericyte
ICJ	intercellular junction – a gap between two endothelial cells (15~20 nm)
TJ	tight junction
V	vesicle – diameter around 60 nm
OSV	open-surface vesicle
G	glycocalyx
BM	basement membrane = based lamina

b. Methods for Solute Exchange

Two methods for solute exchange: diffusion and convection

1. Lipid-soluble molecules: dissolve in membrane
2. Small lipid-insoluble molecules: diffusive transport
3. Large lipid-insoluble molecules: large proteins

How do large lipid-insoluble molecules transport? There are three possible theories:

4. Ferry-boat of vesicles
5. Vesicles fuse together to form a temporary tube
6. Transport through ICJs. But ICJs will not open when: cell division, death, inflammation.

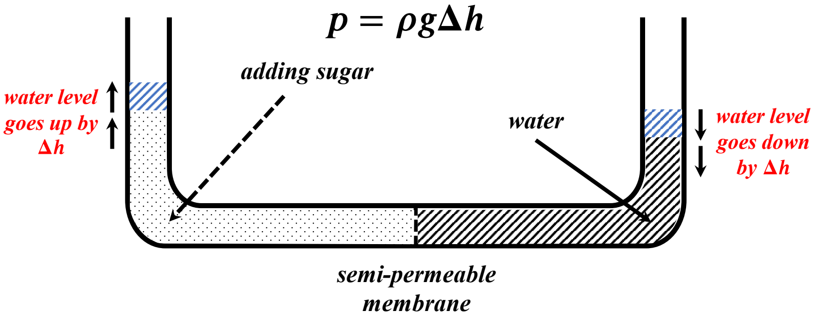
However, there are three exceptions:

1. Blood-brain barrier: TJs form a continuous seal, fewer vesicles
2. Fenestrated capillaries: where need the increase of exchange of water and small lipid-insoluble molecules. *e.g.*, glands, kidney
3. Discontinuous capillaries: large gaps between endothelial cells.

c. Modification of Solute Exchange

- Increase the concentration gradient from metabolism → increase the diffusion
- Capillary recruitment: Krogh Cylinders
- Increase of flow in each capillary: keeps some solutes(rapid transport), not others(slow transport across the capillary wall).

d. Movement of Water: Water transport across the capillary walls



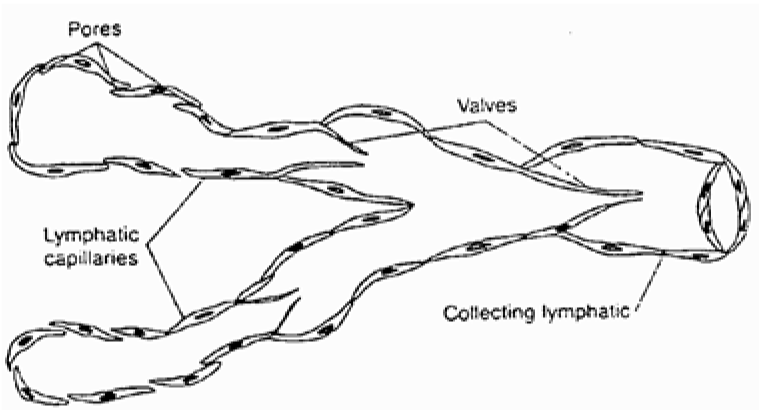
$$J_v = L_p S[(P_c - P_i) - \sigma(\pi_p - \pi_i)]$$

- J_v : flux (volume), vol/L
- L_p : hydraulic conductivity
- S : surface area
- P_c : pressure in capillary
  - 30-40 mmHg in the arterial ends
  - 25 mmHg in the middle of capillaries
  - 10-15 mmHg in the venous ends
- P_i : pressure in intersititium

- Negatively charged GAGs can attract positively charged ions, which will produce an oncotic pressure.

- σ : reflection coefficient, ranges from 0~1, which describes how good the membrane is at holding back large molecules (*e.g.*, proteins).
  - 0 – poor at holding proteins
  - 1 – good at holding proteins
- π_p : osmotic pressure in plasma
  - Osmotic pressure is defined as $\pi = \frac{n}{V} RT$, which is also known as Van't Hoff's Law ("ideal solutes").
  - Typically range from 21-29 mmHg (which is higher than the ideal solutes), mainly due to albumin (75%).
- π_i : osmotic pressure in interstitium
  - By definition, osmotic pressure in interstitium is due to plasma proteins that have leaked into interstitium.
  - Typical value: ~8 mmHg under 40% concentration of plasma.

e. Lymphatic System



Two types of pumps in lymphatic systems:

- Intrinsic: smooth muscle
- Extrinsic: peristalsis and exercise
  - Can generate 25-50 mmHg pressure, flow will increase 10-30 times during exercise.

f. Starling Balance

By $J_v = L_p S[(P_c - P_i) - \sigma(\pi_p - \pi_i)]$, there are two ways that can potentially change the Starling balance:

- **Physiological change**:
  - Posture change:

stand up, $P_c \uparrow$

⇓

Arterioles contracts, $R \uparrow$

⇓

$\Delta P \downarrow$

⇓

Prevent the increase of R

- Exercise:

Dilate arterioles

⇓

$R \downarrow$

⇓

$\Delta P \downarrow$

⇓

$P_c \uparrow$

- **Pathological change** due to tissues swell too much, *e.g.*, odema

g. Odema

- Reasons for odema:
  1. Increase of P_c : venous thrombosis
  2. Decrease of π_p : lack of proteins (albumin), e.g.,
     - Malnutrition
     - Poor protein absorption in the gut
     - Protein loss due to kidney damage
     - Liver damage
  3. Increase of L_p : inflammation
  4. Damage to the lymphatic system, e.g.,
     - Parasites
     - Developmental diseases
     - Surgical procedures
- Fetal oedema:
  - Pulmonary oedema
  - Cerebral oedema: water accumulates in the brain

vii. Return of Water and Solutes to the Heart

The return of water and solutes back to the heart depends on the functions of two systems:

- Lyphatic system
- Venous system:
  - Venules $\Rightarrow$ veins $\Rightarrow$ vena cava: $2/3$ of the blood is storing in the veneous system. Veins have very high compliance.
  - Controlled by smooth muscle and nervous system

- Veins have valves: they only have *extrinsic* pumping but no intrinsic pumping.

viii. Control of Blood Pressure

By $\Delta P = Q \times R$, the pressure difference ΔP is defined as

ΔP = *presssure of blood leave the heart – pressure of blood back to the heart*

and mathematically,

$$BP = CO \times TPR$$

Also given that $CO = HR \times SV$, to combine,

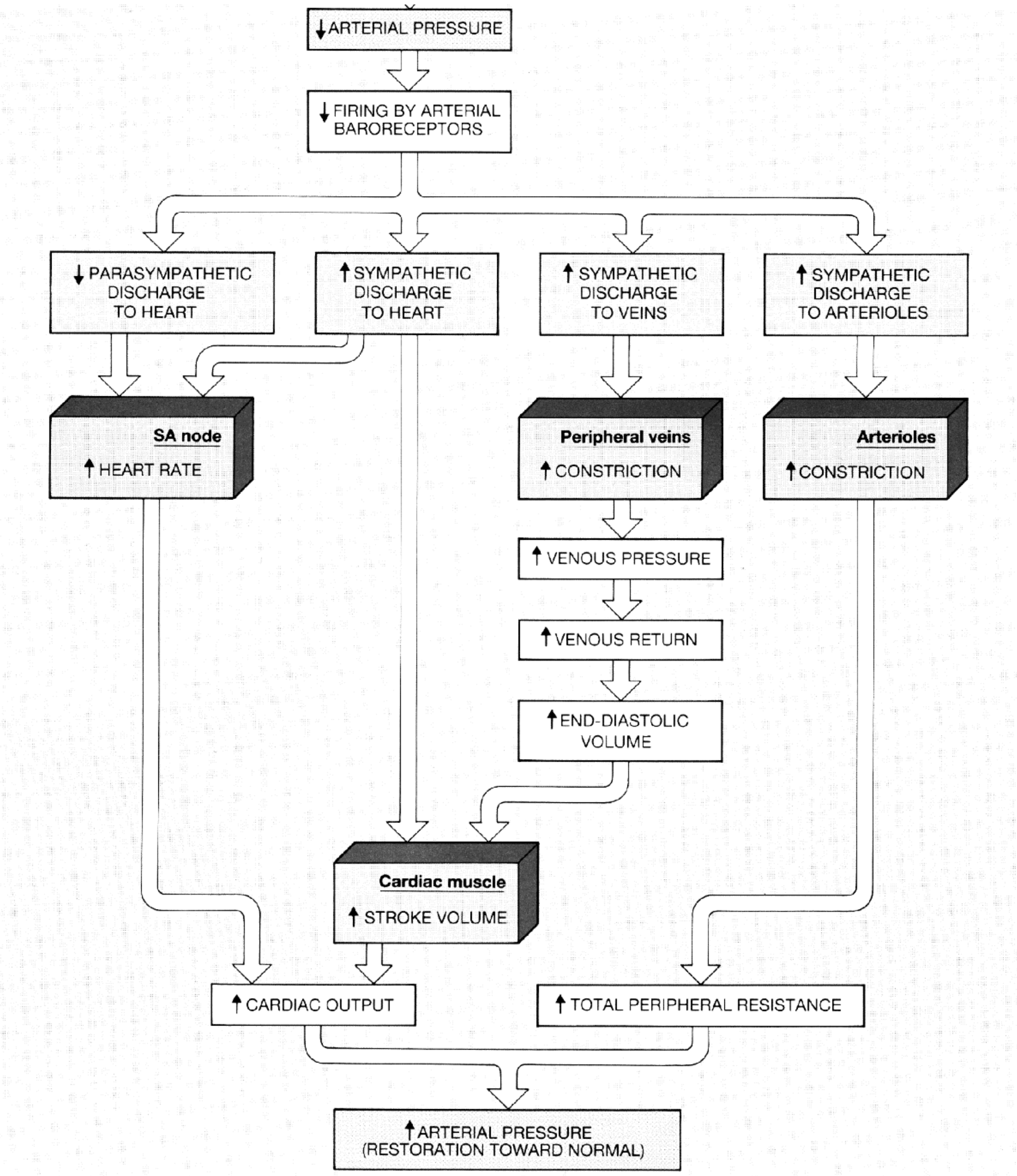
$$BP = HR \times SV \times TPR$$

This states the control of BP can be achieved by controlling *HR*, *SV*, and *TPR*.

short-term (only) control: barorecrptors

- Locates in carotic sinus and aotric arch
- Detects pressure change (vessal stratch), including palse pressure and average pressure
- It will send AP to medulla, which will change sympathetic and parasympathetic system activities, to change *HR*/*SV*/*TPR*
- The mechanism provides negative feedback

Long-term control of BP: control the blood (fluid) volume. Patients can adapt the diuretics by producing more urine to control the volume of blood.



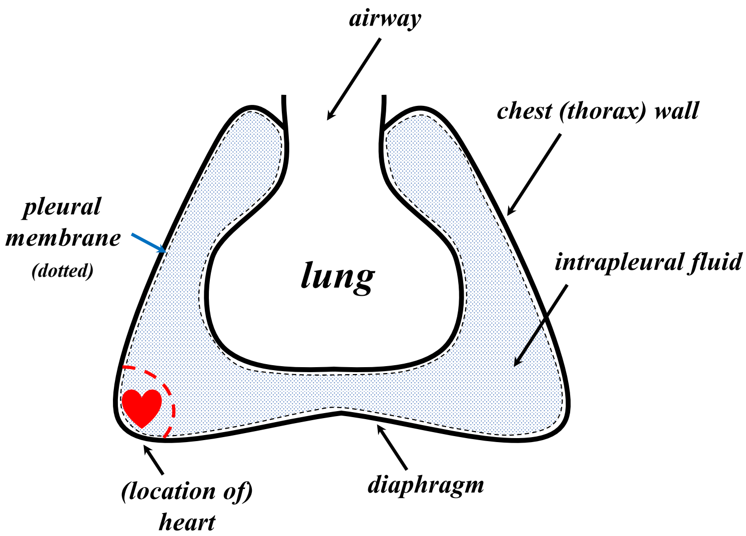
↓ARTERIAL PRESSURE
↓FIRING BY ARTERIAL BARORECEPTORS
↓PARASYMPATHETIC DISCHARGE TO HEART
↑SYMPATHETIC DISCHARGE TO HEART
↑SYMPATHETIC DISCHARGE TO VEINS
↑SYMPATHETIC DISCHARGE TO ARTERIOLES
SA node
↑HEART RATE
Peripheral veins
↑CONSTRICTION
Arterioles
↑CONSTRICTION
↑VENOUS PRESSURE
↑VENOUS RETURN
↑END-DIASTOLIC VOLUME
Cardiac muscle
↑STROKE VOLUME
↑CARDIAC OUTPUT
↑TOTAL PERIPHERAL RESISTANCE
↑ARTERIAL PRESSURE (RESTORATION TOWARD NORMAL)

Part II – Respiratory System

1. Lung Mechanics and Structure

a) Thoracic Arrangement

A rough sketch of the lung structure is shown below: both lung and chest wall have an elastic structure. A negative 4mmHg pressure relative to atmosphere enables the normal breathing. Gas in intrapleural fluid, volume change, chest wall being pushed out



b) Ventilation: Breathing

- Inspiration (breathing in): $P_{\text{atomsphere}} > P_{\text{lung}}$

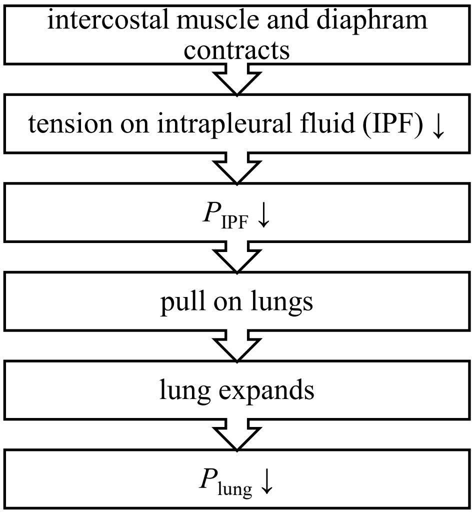
  Expiration (breathing out): $P_{\text{atomsphere}} < P_{\text{lung}}$

- Darcy's Law:

$$Q = \Delta P / R = \frac{P_{\text{atomsphere}} - P_{\text{lung}}}{R_{\text{airway}}}$$

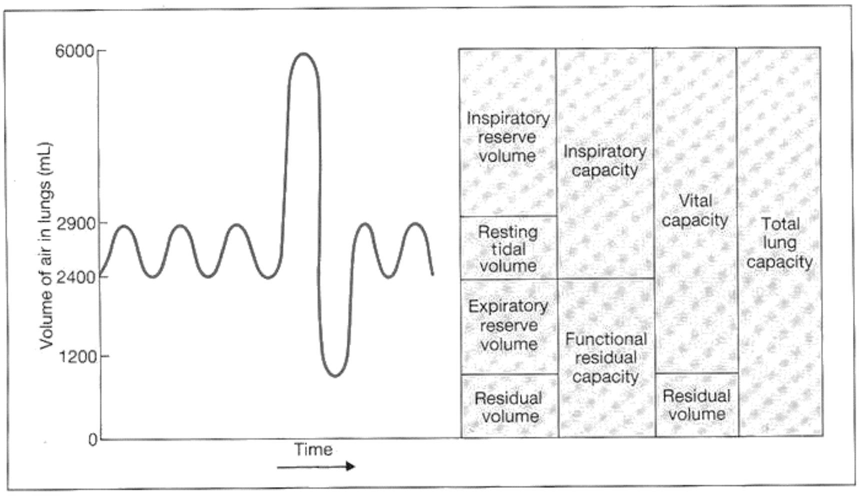
  - Q: flow rate
  - $\Delta P = P_{\text{atomsphere}} - P_{\text{lung}}$: difference between the atmospheric pressure and lung pressure
  - R_{airway}: resistance of airway

- During inspiration:



Therefore, according to the Darcy's law, during inspiration, as $P_{lung}\downarrow$, the flow rate Q increases.

- Rate of ventilation: 5000 mL/min $\approx$ tidal volume $\times$ respiratory rate (10 times per minute)
- Dead space: a constant volume where no gas change during respiration, $\approx$ 150 mL.



c) Resistance

In the respiratory system, resistance is usually low, this is due to:
- Air has a low viscosity
- Airway is short and wide

Pathological increase in the resistance would cause asthma.

d) Compliance

- Compliance: how stiff the airway is. Mathematically, the compliance C is described as the ratio of the change in volume to the change of pressure.

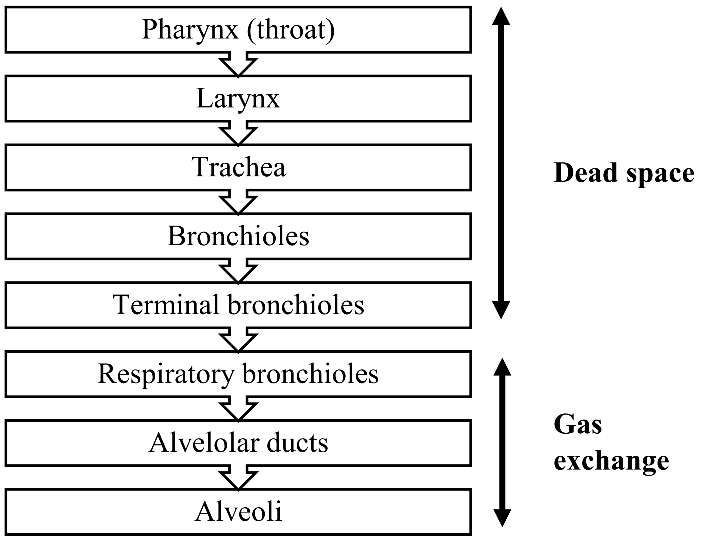
$$C = \Delta V / \Delta P$$

- The compliance is determined by the surface tension of the fluid lining on the membrane. The surface tension always has a tendency to minimize the surface area. In lungs, the surface area is about 75 m^2.

- Such surface tension in lung can be reduced by adding a phospholipid surfactant (produced by Type II cells).

- Lack of such surfactant may lead to respiratory distress syndrome due to the high stiffness of the lung.

e) Airway Structure



2. Gas Transport and Exchange

a) Gas Exchange

- Typically, at rest, rate of gas exchange of O_2 is 250 mL/min, of CO_2 is 200 mL/min. Therefore, we could define the respiratory quotient, R_Q as

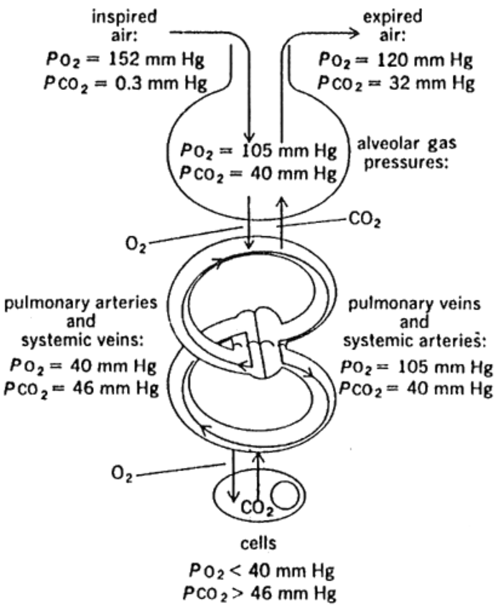
$$R_Q = \frac{\mathrm{CO_2(out)}}{\mathrm{CO_2(in)}} \approx 0.8$$

  However, R_Q changes with human diet:
  - For the diet with purely carbohydrate: $R_Q \approx 1$
  - For the diet with purely fat: $R_Q \approx 0.7$
  - For the diet with purely protein: $R_Q \approx 0.8$

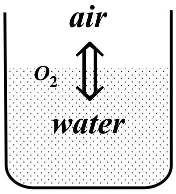
- **Partial pressure**: how much of the total pressure, P, is exerted by each individual (compartments/components) in the gas. Partial pressure describes the proportional of a gas mixture.

$$P_{\mathrm{gas}} = \text{mole fraction of a particular gas } \times P$$

> Example:
>
> partial pressure of O_2: $P_{O_2} = 0.21 \times 760\,[\mathrm{mmHg}] \approx 160\,[\mathrm{mmHg}]$



- When the gas dissolve in liquid, the gradient of partial pressure drives the occurrence of diffusion.



At equilibrium state:

P_{O_2} in air = P_{O_2} in water

- Concentration of the gas dissolved in a liquid = partial pressure $\times$ the solubility of the gas

    - Hyperventilation (hyporea): decrease of ventilation because of decrease of metabolism.
    - Hypoventilation: increase of ventilation because of increase of metabolism.

b) Oxygen Transport in Blood

- The concentration of O_2 in blood: 200 mL/L. However, for every 200 mL of blood, only about 3 mL of oxygen is dissolved. A strong oxygen carrier is required. The hemoglobin carries the rest of the oxygen in blood.
- The hemoglobin (Hb): 1 molecule has 4 Fe atoms $\Rightarrow$ carries 4 O_2.

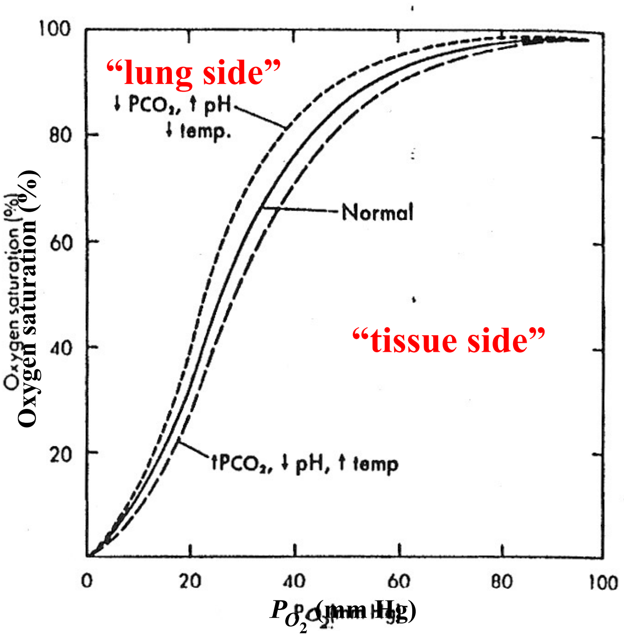
$$\mathrm{Hb} + \mathrm{O_2} \rightleftharpoons \mathrm{HbO_2}$$

- Percentage saturation are used to describe the amount of O_2 carried by Hb:

$$\%\text{ saturation} = \frac{\text{amount of } \mathrm{O_2} \text{ carried by Hb}}{\text{maximum amount of } \mathrm{O_2} \text{ that Hb can carry}} \times 100\%$$

What are the determinants of the % saturation?

- The main determinant is $P_{\mathrm{O_2}}$
- Other determinants include $P_{\mathrm{CO_2}}$, pH of the blood, and the body temperature ("tissue side", "lung side")



c) Carbon Dioxide Transport in Blood

- The concentration of CO_2 in blood: 520 mL/L. Breakdown:
  - 10% is dissolved in plasma
  - 30% combined with amino groups within the protein (hemoglobin)
  - 60% as carbonate ions: hydrogen carbonate

$$H_2O + CO_2 \underset{①}{\rightleftharpoons} H_2CO_3 \underset{②}{\rightleftharpoons} HCO_3^- + H^+$$

①: catalyzed by the enzyme carbonate arlychase in the red blood cells, producing unstable carbonate acid

②: the unstable carbonate acid further breaks down into bicarbonate and hydrogen ions. A portion of hydrogen ions bind to proteins, *e.g.*, Hb.

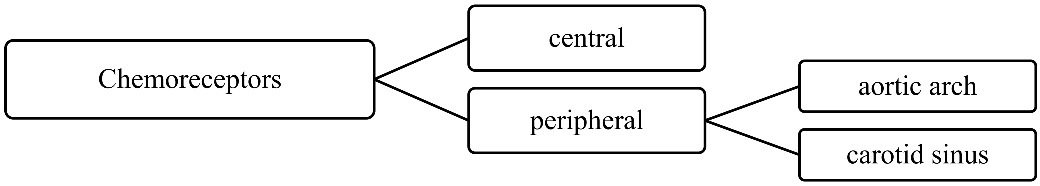
3. Control of Ventilation and Perfusion

a) Rule of Medulla

- The skeletal muscles require nerve impulses to control their contractions.
  - skeletal muscles: diaphragm and intercostal muscles
- Such nerve impulses are originated from a specific region in the brain – **medullary inspiratory neurons.**

b) Control of Frequency

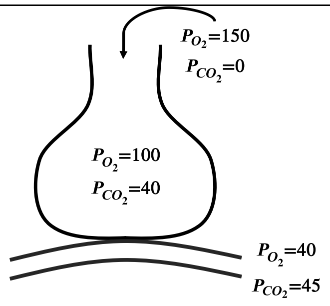
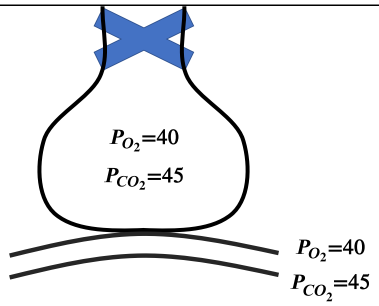
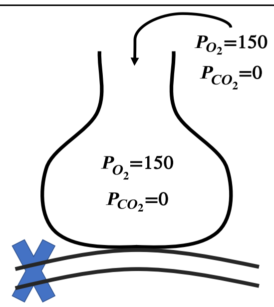
- Frequency of ventilation is controlled by P_{CO_2} , P_{O_2} , and $[H^+]$ in the plasma of large arteries.
- Chemoreceptors (*not* baroreceptors!) provides negative feedback to control the frequency.



- Once P_{O_2} falls below <u>60 mmHg</u>, ventilation frequency will increase.
- Once P_{CO_2} increases above <u>40 ~ 50 mmHg</u>, ventilation frequency will increase by 3 times.

- The chemoreceptors are more sensitive to the partial fraction of CO_2 than O_2 – low P_{CO_2} triggers lose of ventilation, thus leading to hyperventilation.

c) Control of Ventilation-Perfusion Ratio

Case 1: normal condition	**Case 2: ventilation blockage** *"a peanut in the airway"*	**Case 3: perfusion blockage** *"an embolism in the vessel"*
		
Note: all numbers are labelled in unit *mmHg*		

- Therefore, to plot P_{CO_2} against P_{O_2} in lung (the V-Q plot),
  - To reverse low P_{O_2} – constrict vessels
  - To reserve low P_{CO_2} – constrict airway