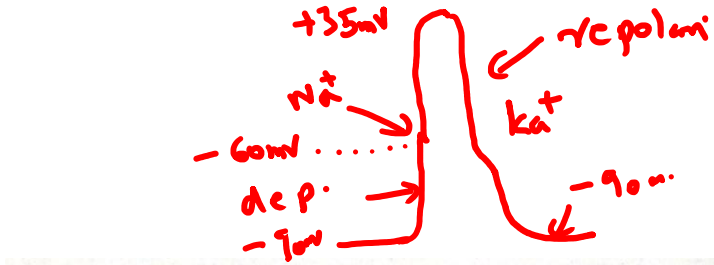
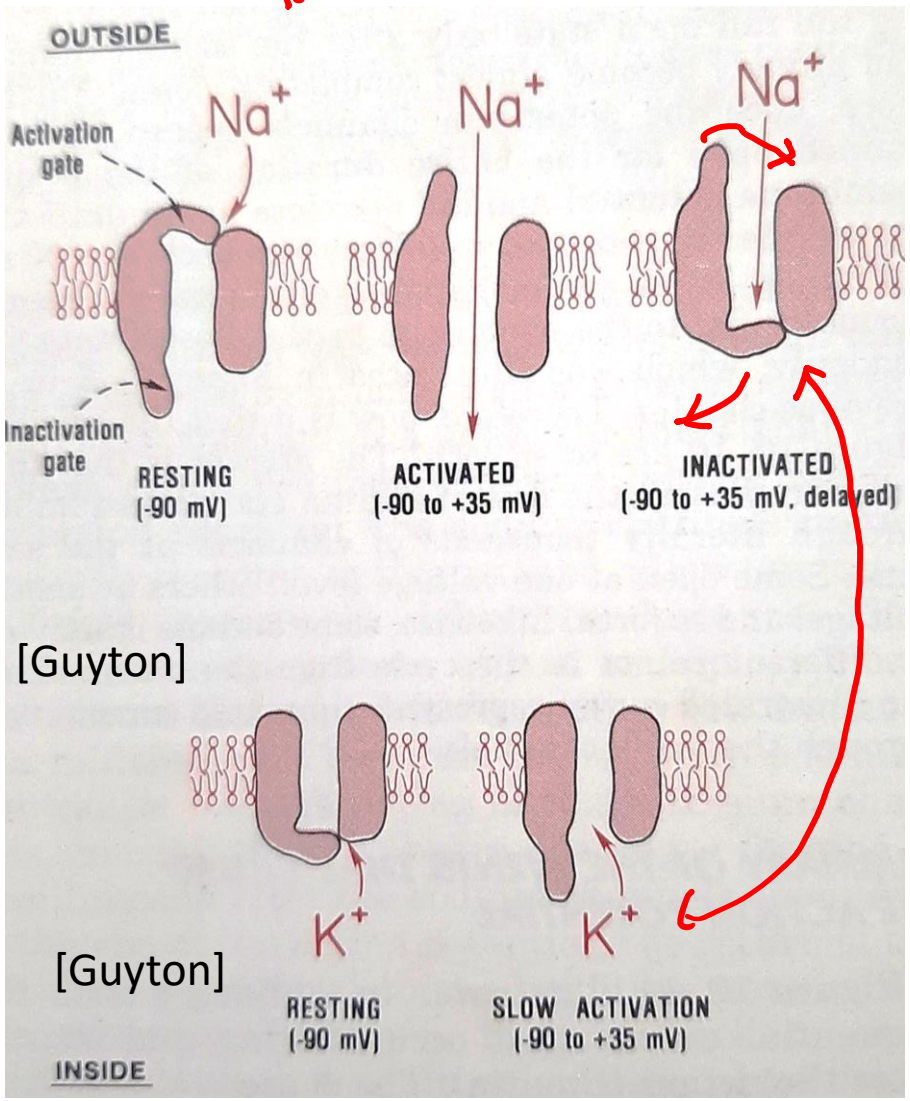
Neuron and the heart.

Hari Varma, BB101, IITB.



RECAP: Nerve action potential.



[Guyton]

[Guyton]

- Lets look at the voltage gated sodium and potassium channels that we have already discussed.
- In transport protein, in addition to the gate at outside there is also a gate opening to inside of cell. The outside gate is called activation gate and inside one is called the inactivation gate.
- When due to some external disturbance, the membrane potential moves from -90mV to say -70 to -50 mV (**this is called the threshold potential**). Then the sodium channel activation gate will open. At this time inactivation gate forced to close but with a delay . This causes NA to go inside and increasing the membrane potential abruptly to +35mV. This process is called "depolarization". Thus Na enters the cell within the time interval between activation gate opens and inactivation gate close.
- Then after a delay the "inactivation gate" is closed, causing the influx of the sodium to cease.
- When the sodium channel is activated, the potassium channel is also activated, but there is a delay in its gate to open and it will happen only when the sodium channel is deactivated (i.e., when sodium channel inactivation gate closes). This causes the potassium to go out , although after a delay of depolarization, thus reducing the membrane potential from +35mV to -90mV (that is back to resting potential). This process is called repolarization.
- Note: Inactivation gate in the sodium channel will now be open only when the membrane potential reaches the resting potential. That means this will happen only after repolarization and reaching to resting membrane potential.

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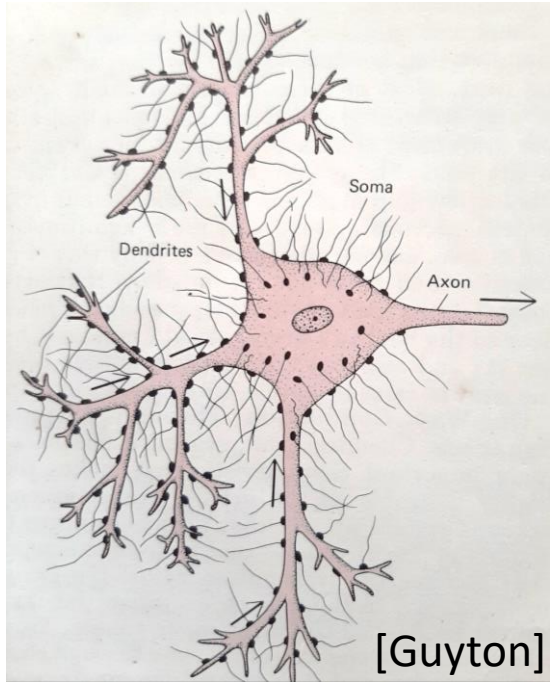
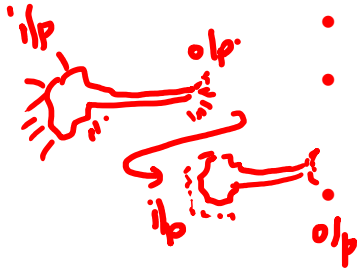
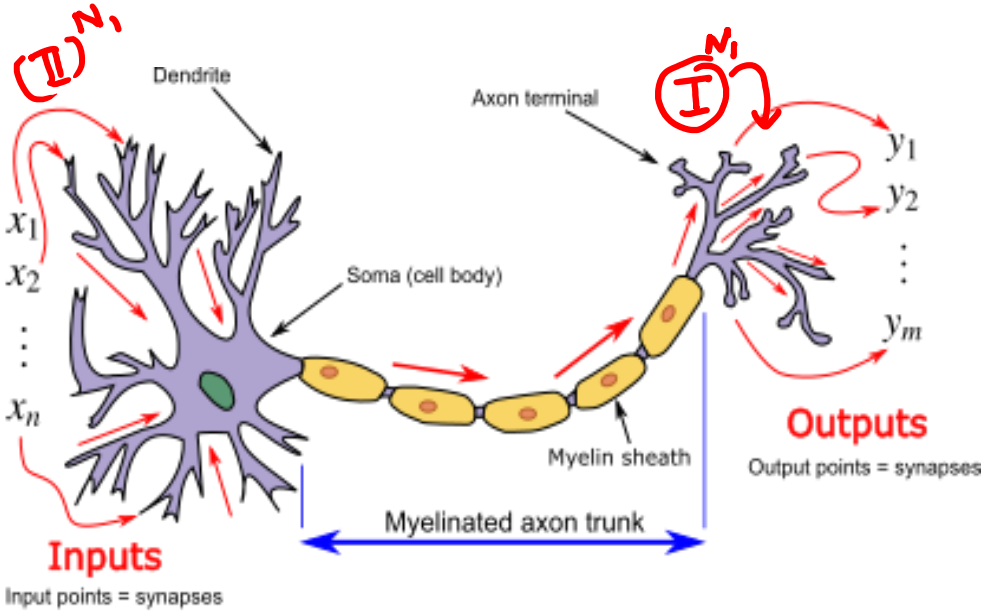
Neuron : structure and function brief.







https://commons.wikimedia.org/wiki/File:Neuron3.png

- Neuron or nerve cell : basic unit of the nervous system.
- It helps to interact or sense the environment: Sensory neurons receives signals from the environment while the motor neuron commands the muscle to move, breathe, speak, swallow etc..
- Soma : main body of the neuron. Motor neuron is shown in the figure.
- Single Axon: which extends from the soma into peripheral nerve
- Dendrites : the projections from soma that extends up to 1mm into surrounding areas.
- Presynaptic terminals : small knobs that lie on the surface of the dendrites and soma of the motor neuron. Roughly 6000 in number and 90% are on the dendrite. Here many neuron will have its nerve fibrils ending like a junction.
- **Role of presynaptic terminal**:

excitatory : secrete a substance that excites the post synaptic neuron

Inhibitory : secrete a substance that inhibits the neuron.

- Neurons are differentiated according to :

1. Size if the cell body
2. Length and size of dendrites
3. Length and size of axon
4. Number of presynaptic terminals.

Depending on above properties the function of neuron changes.

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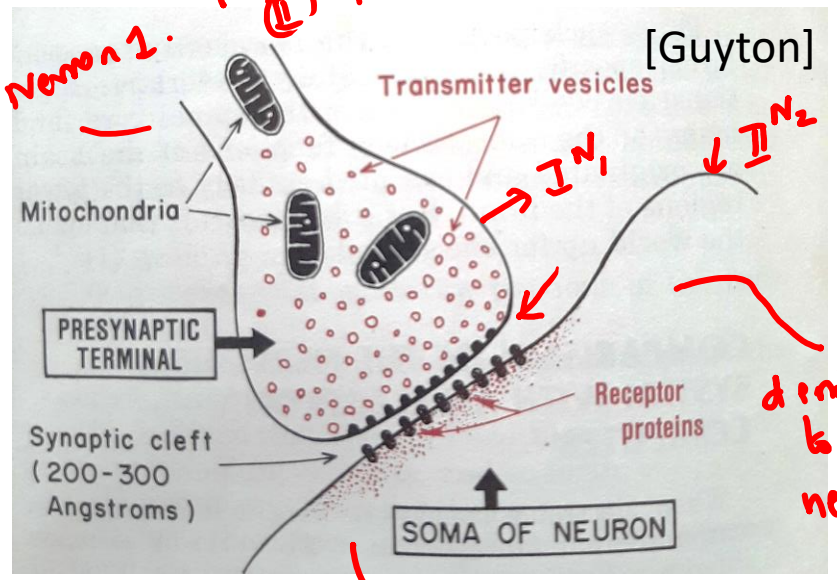
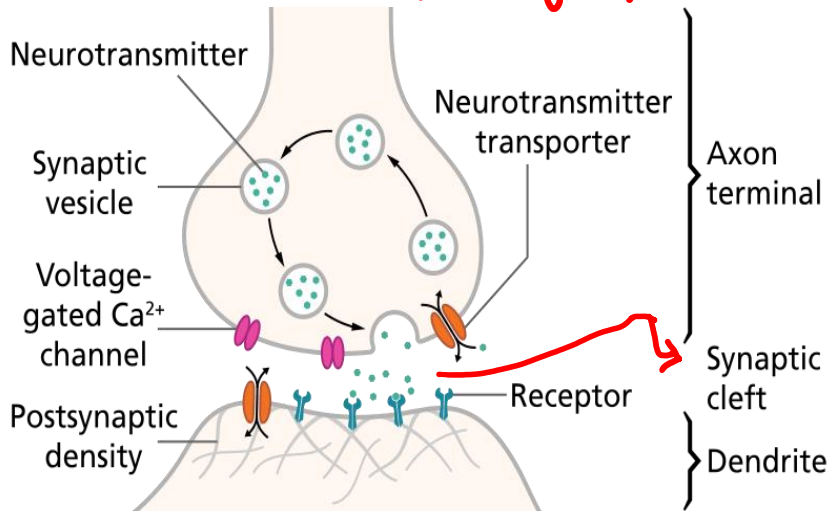
Presynaptic terminal





https://commons.wikimedia.org/wiki/File:SynapseSchematic_en.svg#file

- Two important structures: synaptic vesicles and mitochondria.
- Vesicles means "small bladder filled with fluid"
- Vesicles has lipid bilayer which separates it content from the cytoplasm.
- Synaptic vesicle has a transmitter substance which when released to the synaptic cleft will either inhibits or excites the neuron.
- Excitation happens when the neuron contains excitatory receptors
- Inhibition happens if it contains inhibitory receptors
- Mitochondria : generates energy (ATP to ADP) needed for synthesis of neurotransmitters. The transmitter amount in vesicle is small and it has to be released so frequently that it has to be synthesized rapidly and frequently.

- Action : when the action potential from the cell body reaches the terminal via the axon, large number of calcium and sodium ion are generate in the terminal. The calcium ion cause the vesicle to release the neurotransmitter to synaptic cleft.

Cell - Cell Communication.

Two ways.

① Via neurotransmitter } This is ligand initiated gate opening.

② Current flow across the Synaptic cleft and initiating voltage-gated channels.

Both creates Post Synaptic potential.

we look at ligand initiated channel opening

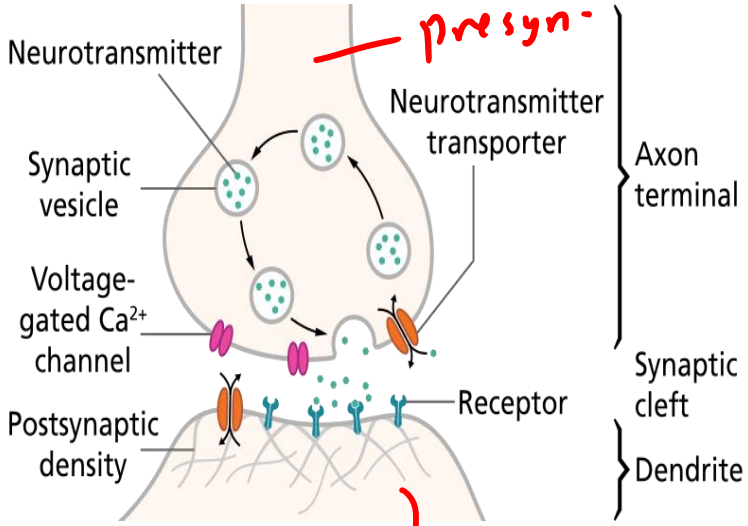
Post synaptic potential

Excitatory post Synaptic potential :EPSP

Depolarization of post synaptic terminal happens.

Post synaptic membrane potential is pushed above threshold so that action potential can happen.

Excitatory neurotransmitter : Glutamate. opens up Na ion channels resulting in depolarization.



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inhibitory post Synaptic potential :IPSP

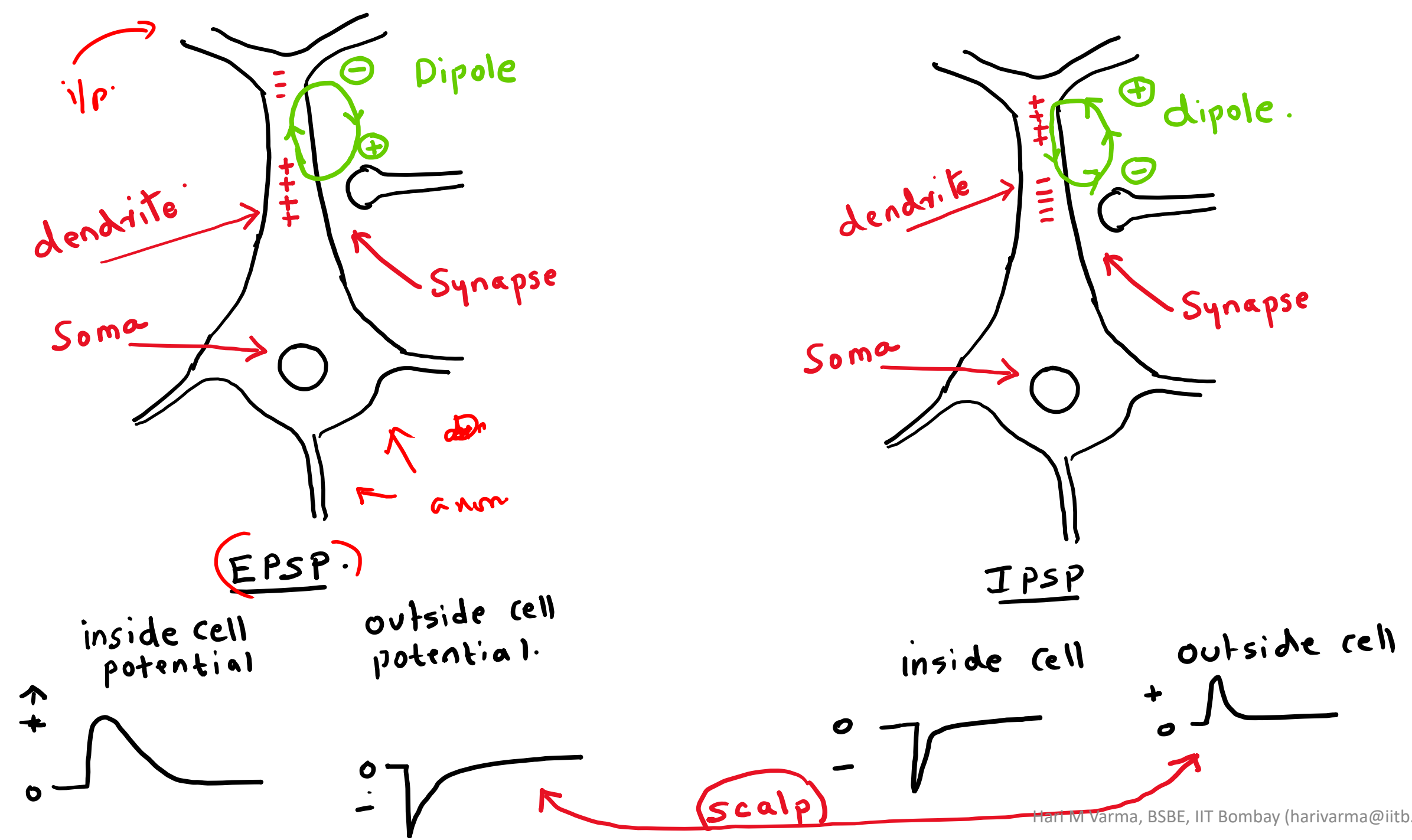
Hyperpolarization of post synaptic terminal happens.

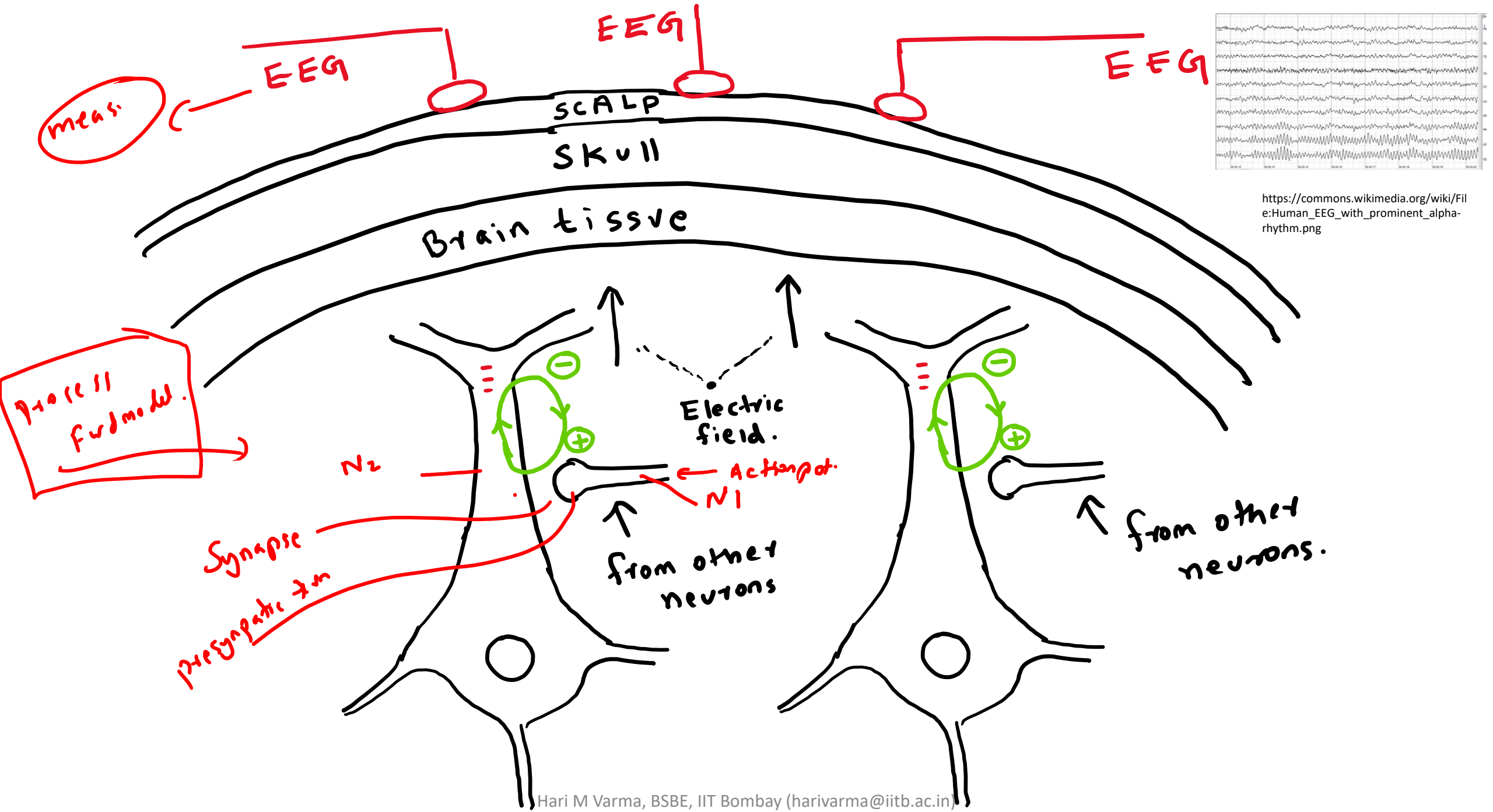
Post synaptic membrane potential is pushed much below the resting membrane potential so that action potential cannot happen.

Inhibitory neurotransmitter : GABA.
push more K+ ions out of cell or push more cl- ions inside: in both case intercellular potential becomes more negative.

EEG and the Post synaptic potential

- EEG is created by special neuron with pyramidal structure arranged in the cortex (outer layer of cerebrum).
- It has multiple dendrites and a single axon but both of them with several branches.
- These long apical dendrites are stacked parallelly in the cortex and perpendicular to the cortical surface, skull and scalp.
- Post synaptic potential created in these dendrites creates dipoles. Electric field from several such dipoles of several neurons add ups and is available at the scalp to be measured as EEG.


i/p
Dipole
dendrite
Synapse
Soma
EPSP
dipole.
dendrite
Synapse
Soma
IPSP
inside cell potential
outside cell potential.
inside cell
outside cell
scalp



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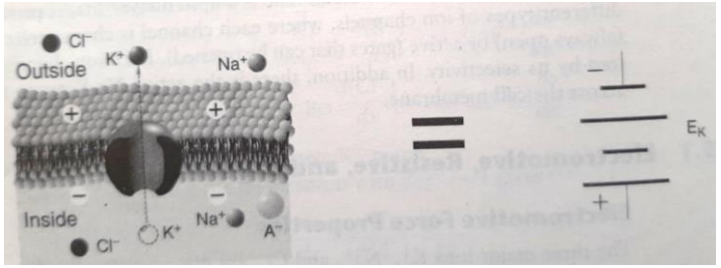
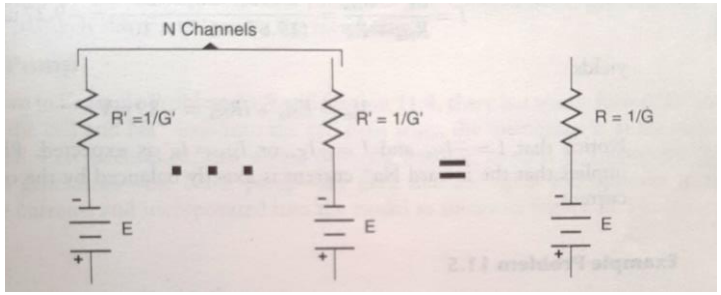
Neuron modelling using passive components.

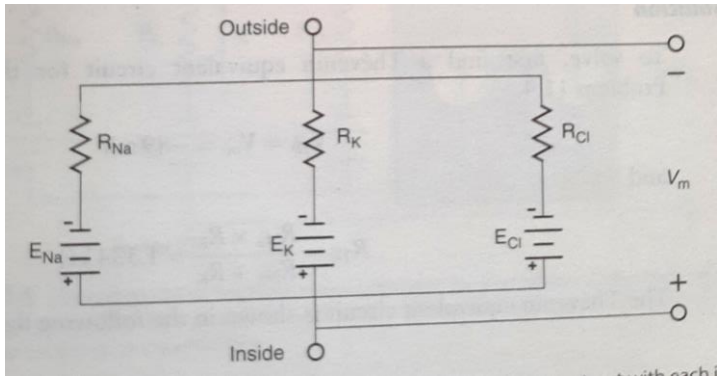


- The Nernst potential as a battery across the terminal cell membrane

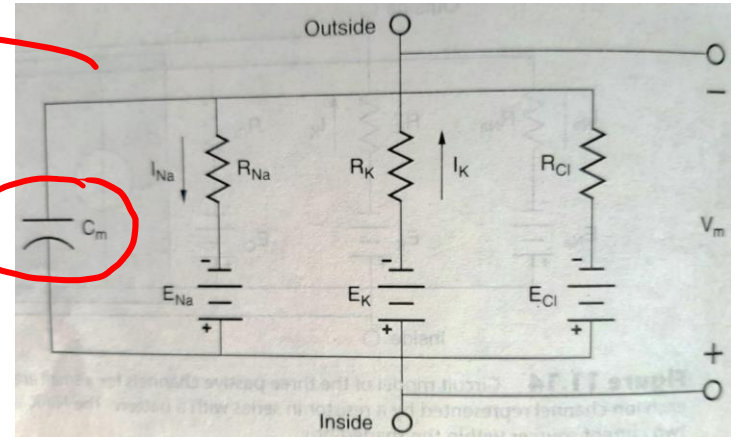


- There are resistance to the movement of ions through the channels.

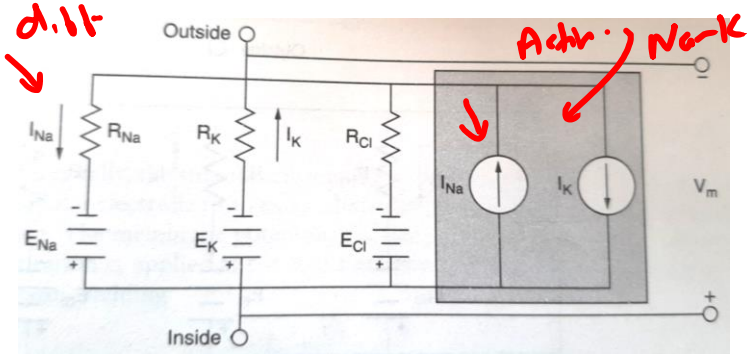
KCL
ICVL



- Several channel form parallel circuit



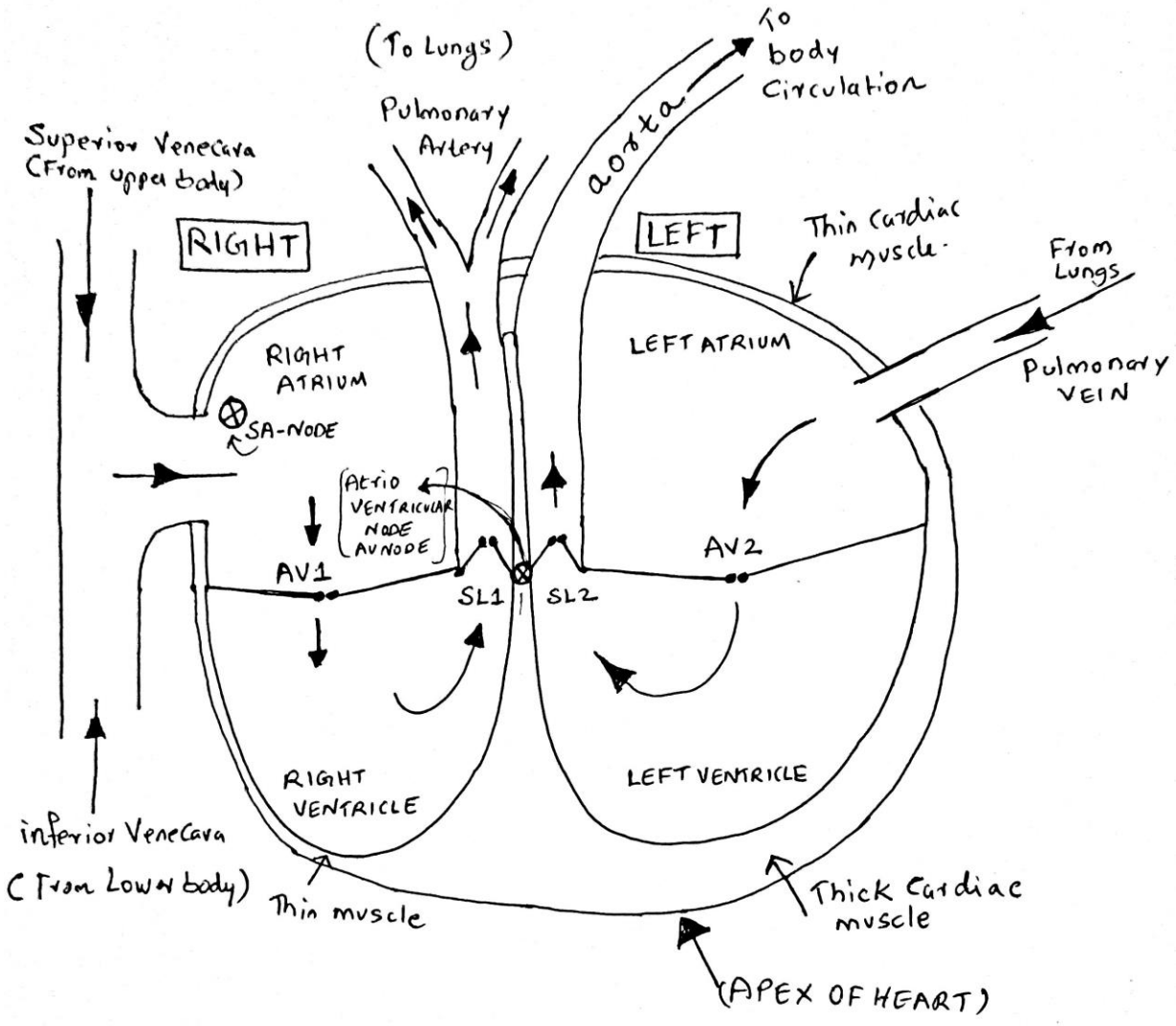
With capacitance of the membrane.



- Sodium potassium pump inject current in opposite direction to the voltage gated channel.

All pictures taken from Reference [Enderle].

Heart : its working and ECG.



- Heart has four chambers : Left and right atria (upper chambers) and Left and right ventricles (lower chambers)
- The left and the right is as if you look the person in the screen.
- The right half : right atrium receives the less oxygenated blood from the body and pumps to the right the ventricle. Right ventricles pumps it to the lungs for oxygenation.
- The left half: left atrium receives the oxygenated blood from the lungs and pumps it to the left ventricle. Left ventricle pumps it to the body circulation.
- Veins : carried blood towards the heart . Here Superior and inferior venecava carries deoxygenated blood from the circulation to the heart (to right atrium). The pulmonary veins carries oxygenated blood from the lungs ('pulmonary' – related to lungs) to the heart (to the left atrium).
- Arteries : carried blood away from the heart. Here pulmonary artery from the right ventricle take de-oxygenated blood from the heart to the lungs. The aorta (largest artery in human body) takes the oxygenated blood from the left ventricle to the body circulation.
- Most often the veins carries the deoxygenated blood while arteries carried oxygenated ones : exception : pulmonary vein and pulmonary artery .

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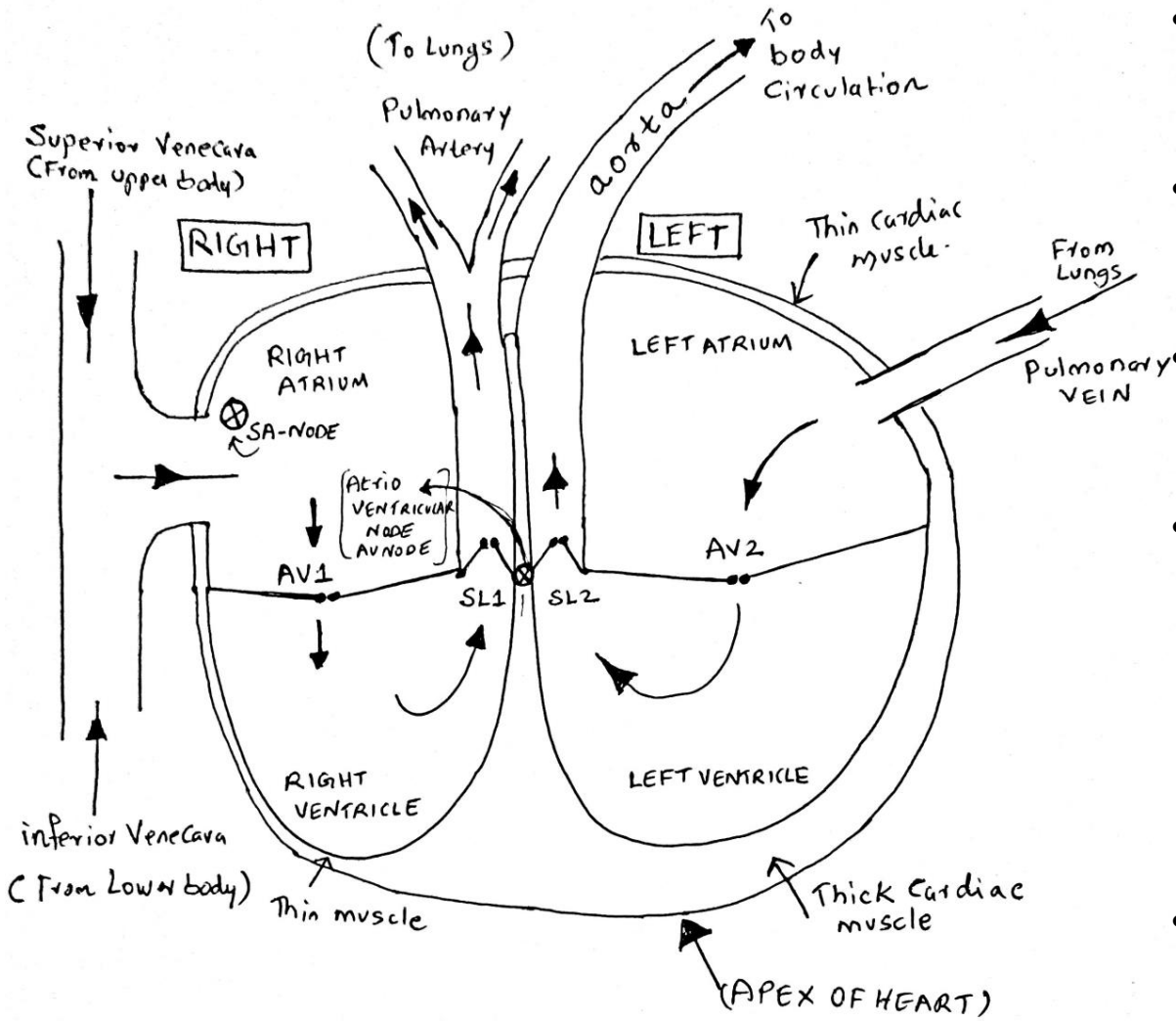
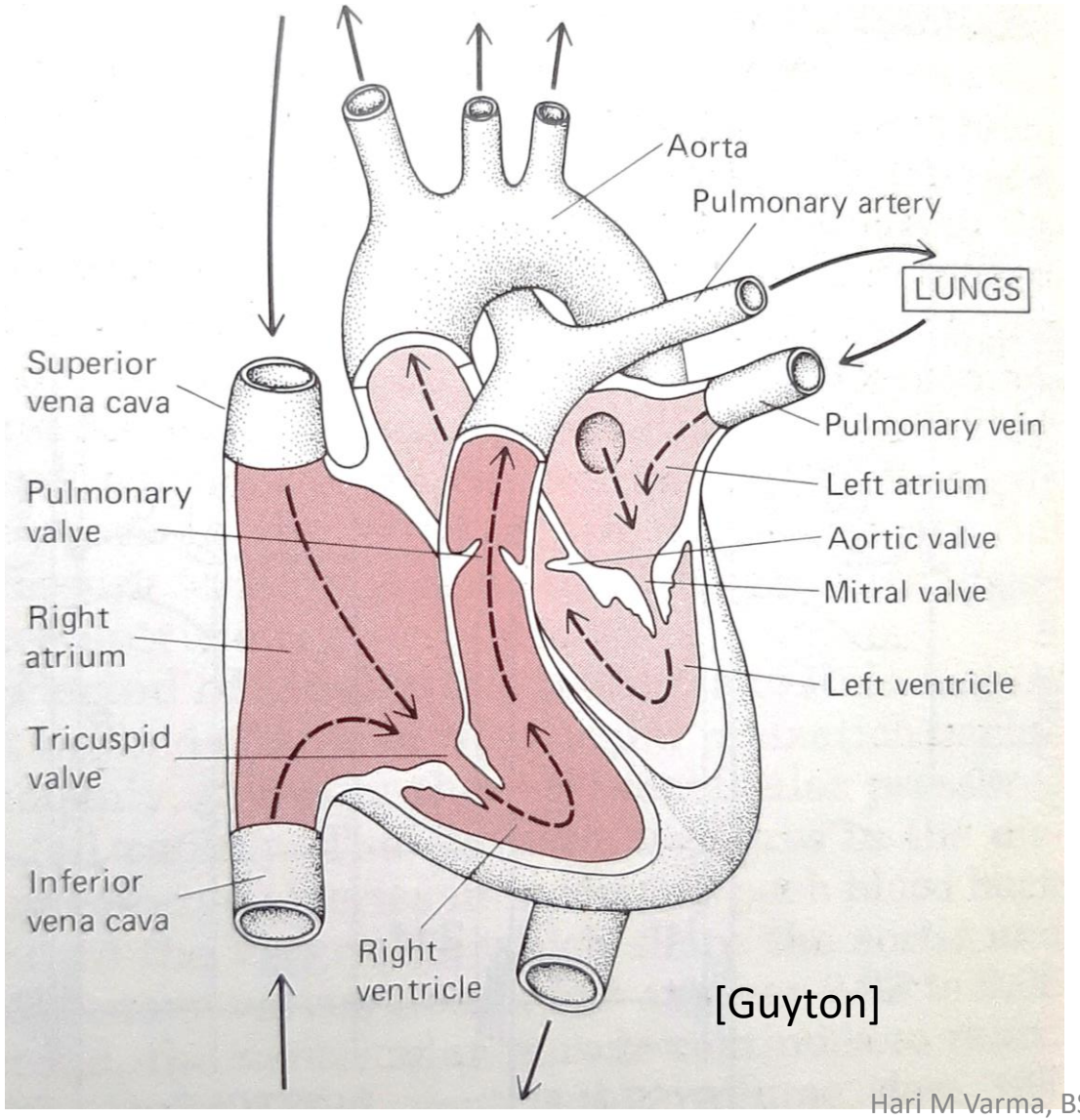
This picture (re-drawn) is based on a very popular lecture video : Cardiovascular System 1, Heart, Structure and Function – YouTube By Dr. John Campbell



Action potentials initiates **contraction** to muscles. Contraction can be lengthening or shortening or muscle or simply changing the muscle tension without changing the length (eg: holding weight)

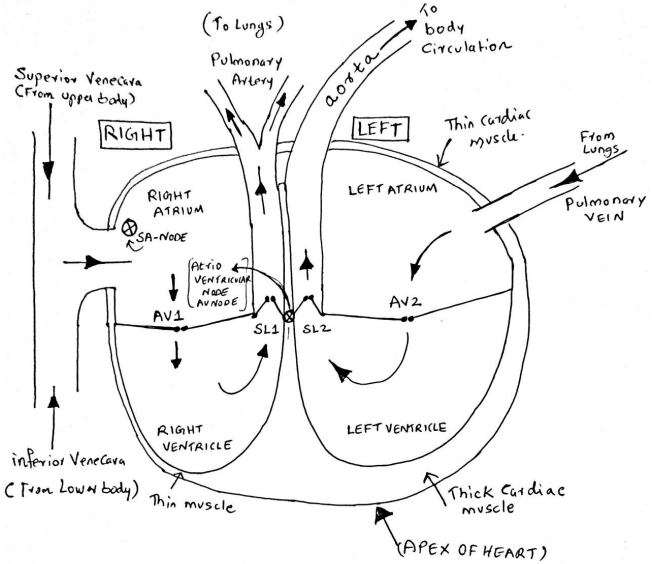
- The left ventricle myocardium is thicker than the left one, as it has to pump the blood to whole body via aorta.
- Right ventricle need to pump the blood to lungs which is nearby and hence do not require much pressure to do so.
- Cells all over the body utilize the oxygen from the blood and hence partially oxygenated blood reaches to the right atria via venecavas.
- The left ventricle push the blood through aorta to whole body which requires high pressure. This is accomplished by the contraction of cardiac muscles i.e., push it to inwards leading to reduced left ventricular volume and hence high pressure. It also do a twisting give more push. (inwards + upwards + twisting movement)
- There is a layer smooth endothelium cells in the inner chambers to give a smooth flow of blood. This is called endocardium.
- Similarly there is a fibrous sack surrounding the heart giving physical protection and also to avoid over expansion. This is called pericardium.

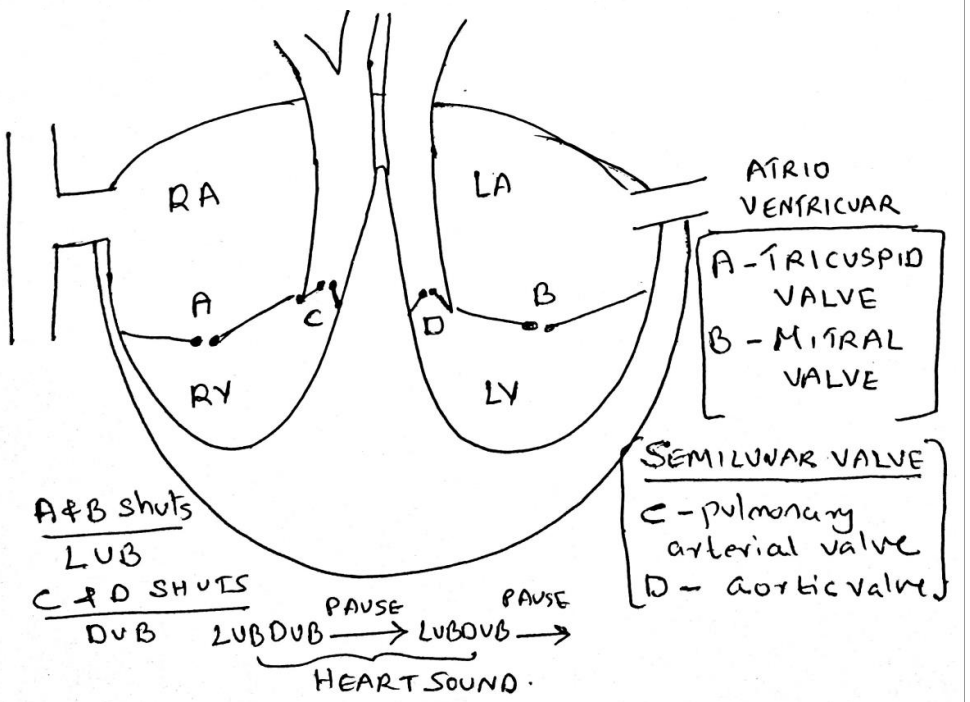
Pumping of blood



[Guyton]

- Pumping action is achieved in the heart by exciting the cardiac muscle with electric potentials (action potentials) generated with in the heart.
- When the signals passes, cardiac muscles contracts which reduces volume of chamber, and thus increasing pressure resulting in a pumping action.
- The flow of blood is controlled by the atrio ventricular and semilunar valves.
- Systole : is a period of contraction of myocardium which initiates a pumping action. Hence this is associated with high pressure.
- Diastole : a period of relaxation of cardiac muscles after the pumping.





- In short : Left and right atrium contract simultaneously (atrial systole). Similarly , LV and RV contracts simultaneously.

In left atria: oxygenated blood from the lungs fills the LA and due to high pressure valve B opens down to the LV and fills it.

In right atria : deoxygenated blood from the circulation fills the RA and due to high pressure, the vale A open and blood fills the RV.

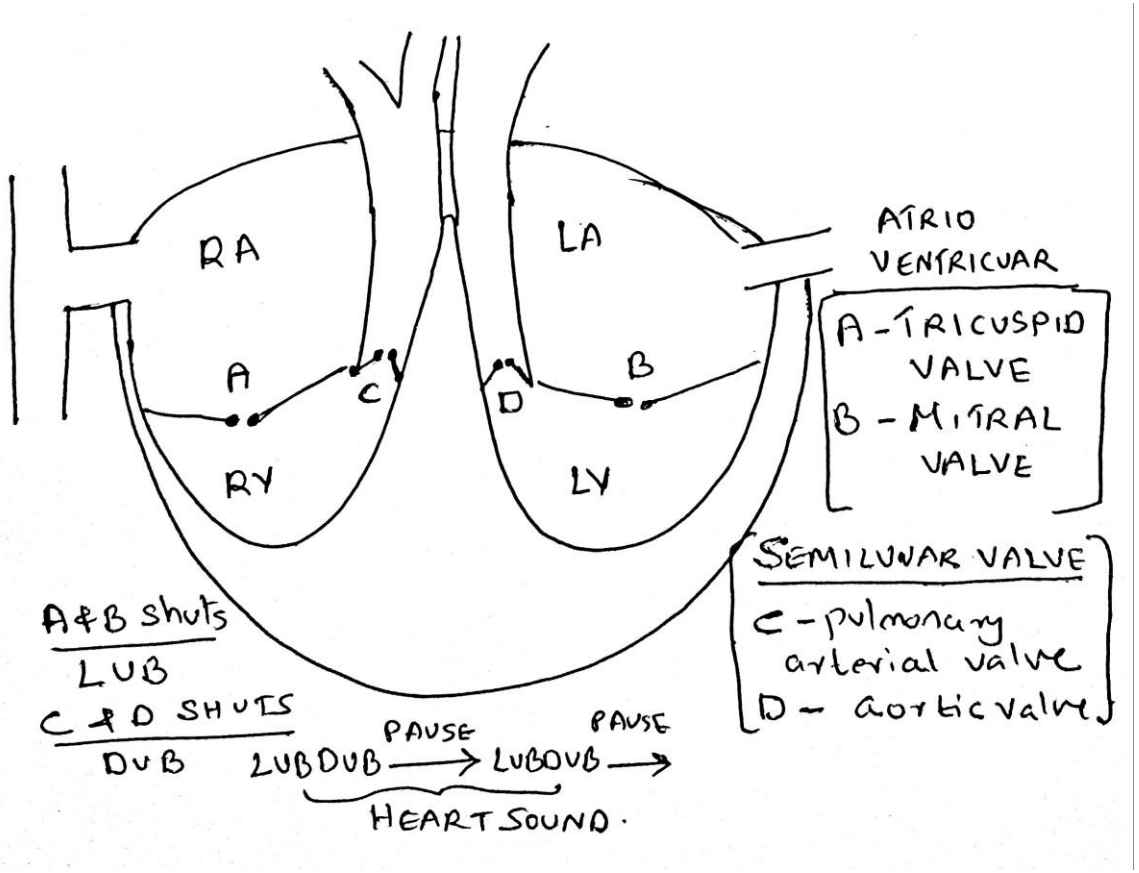
- Ventricular systole : some time after the arterial systole, ventricular systole happens where :

In left ventricle: blood is pushed to aorta for circulation via the valve D

In right Ventricle : blood is pushed from the RV to pulmonary artery for lungs via the valve C.

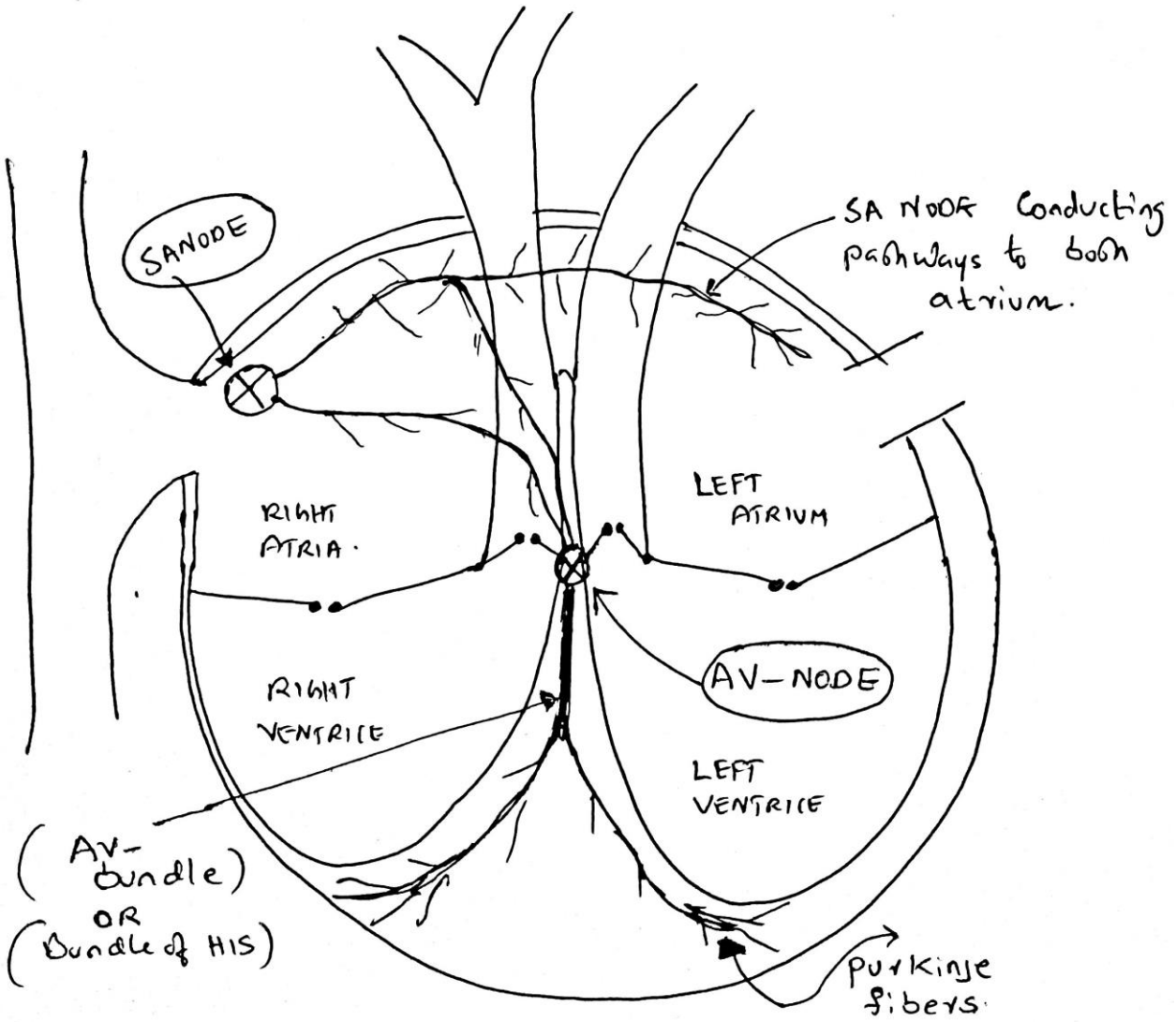
- There is a chance that the due to high pressure during ventricular contraction, blood can push open the valves A and B. This is avoided by tendinous cords attached to these valves which holds them in closed position (of course this is how it acts as valve – one direction) . Tendinous cords are connected to the heart muscles.
- Nutshell : left side of the heart pumps blood to body and hence called “body pump” and right side of heart pumps blood to lungs and hence called to “lung pump”.
- Most of the blood from the atrium flows down the gravity and high pressure. But atrial contraction also give additional push which increase the efficiency.
- When ventricular pressure drops, C and D closes and hence blood will not come back. All these valves opens and closes based on blood pressure difference in the chambers.

Heart sounds

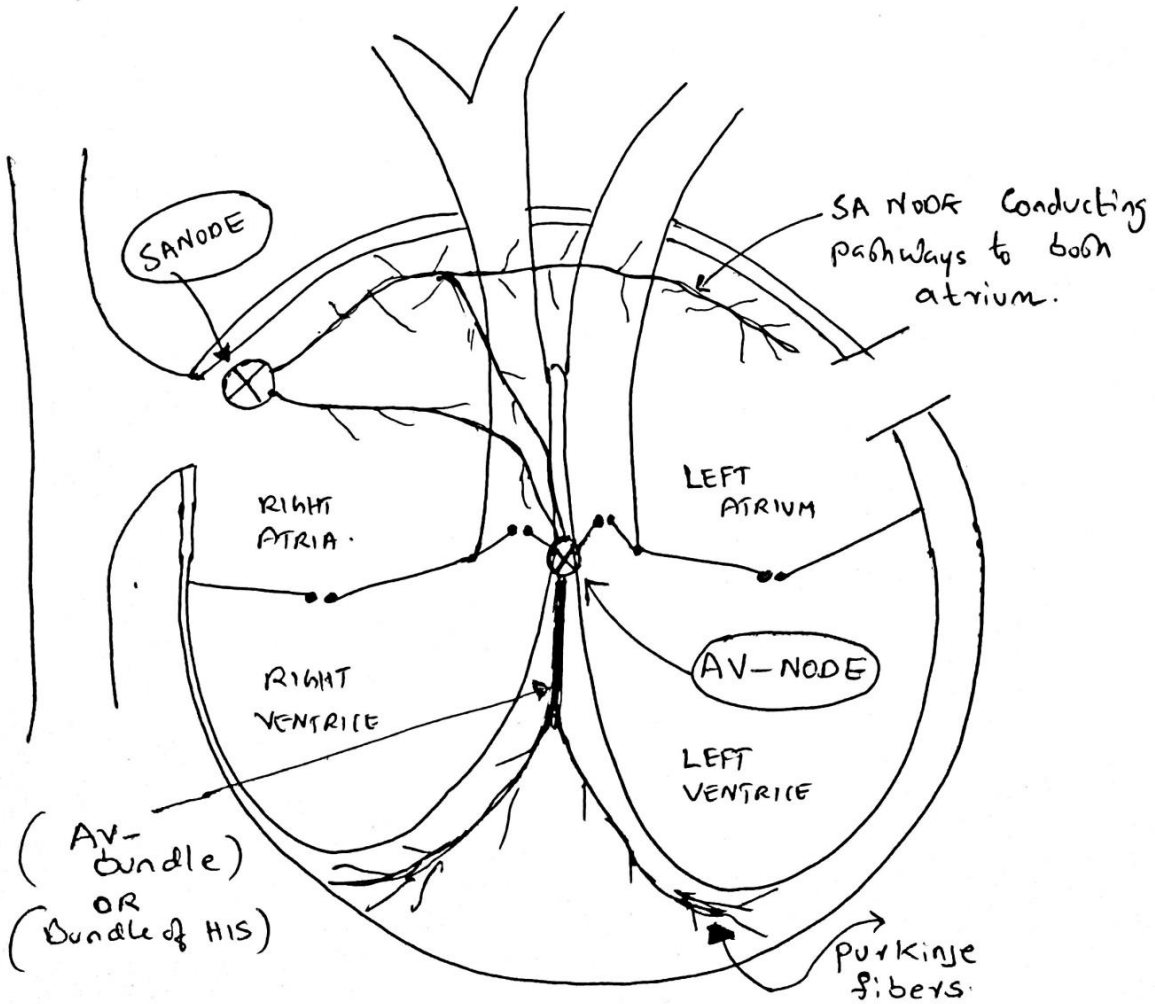


- When the ventricle contracts, it will shut the tricuspid (A) and mitral (B) valves. While these valves closes, it makes a sound called “LUB”.
- When the blood pumped to pulmonary artery and aorta tries to come back to LV and RV, the C and D closes which creates another sound termed as “DUB”
- Heart sound is thus
  LUB DUB –pause--- LUB DUB---pause ---LUBDUB

Electrical system : signal causing the contraction of heart muscles.

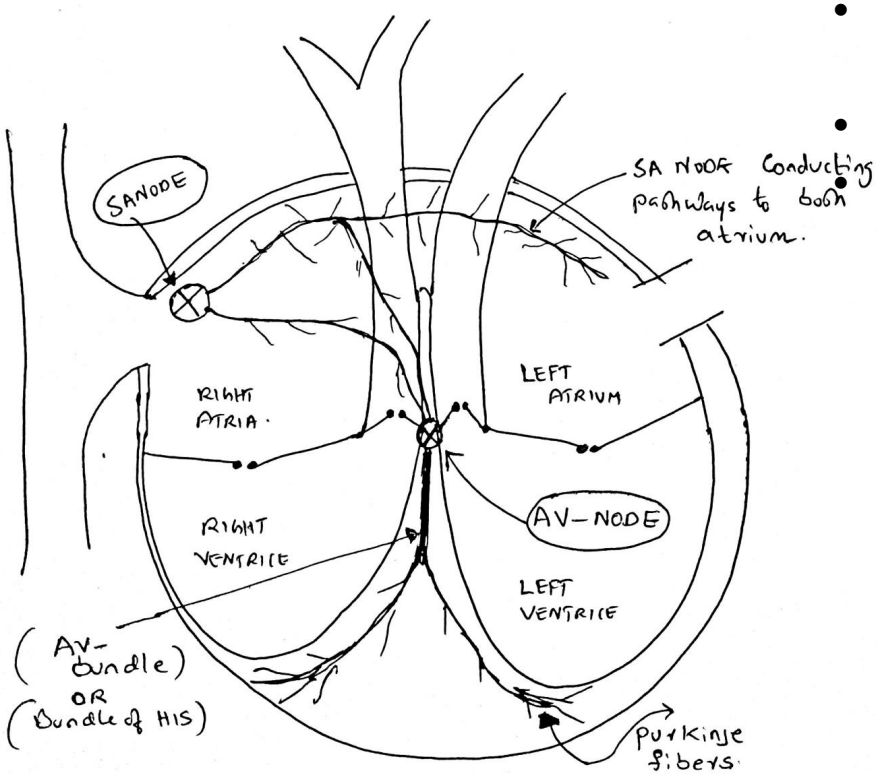


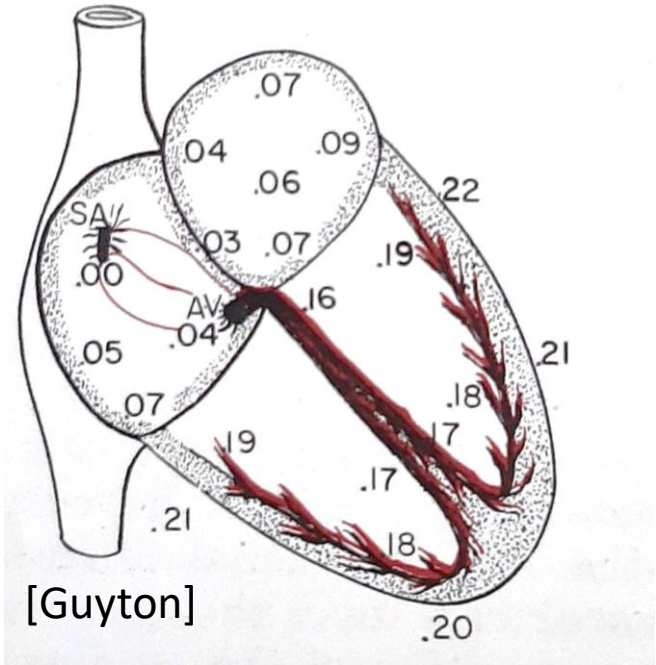
- Sino atrial node (SA Node) : sinus rhythm of the heart is made by this specialized myocardial tissue
- Located near to superior venerate.
- It is not a nerve tissue but specialized myocardial tissue capable of generating action potential.
- SA node depolarizes "WITH OUT" any disturbance i.e., intrinsically generating a rhythmic signal 60-100 times a minute.
- There is another electrically active muscles called atrio ventricular node (AV-Node) which sits in the lower back section of intraarterial septum ("which separates").
- AV node like SA node can generate intrinsic signals. But its depolarization rate is lower compared to that of SA node and hence SA node dominates and dictates the rhythm of the heart.



- Instead AV node acts as a relay of the electric signals from the SA node (sitting in atria) to be passed to the ventricular muscles.
- SA node generates the sinus rhythm and pass it to the LA, septum and the RA via specialized conductive pathways. These pathways will take the signals to the atrial myocardium and contracts it for the pumping action.
- One branch ot this conductive fiber terminates in the AV node.
- AV node will pass this signals from the atrium to the ventricular chambers.
- There is a membrane (atrio ventricular ring) which is an electrical insulator which separates the atrium from the ventricles. Hence the signals from SA node which is spread n the atrium cannot directly reach the ventricle. It has to come through the AV node.
- **Important point** : AV node delays the signals by approx. 40ms while it passed through it.
- This delay will ensure that atrial contraction will happen and fills the ventricles with blood before the signal reaches the ventricle and contracts it (which means it pumps)

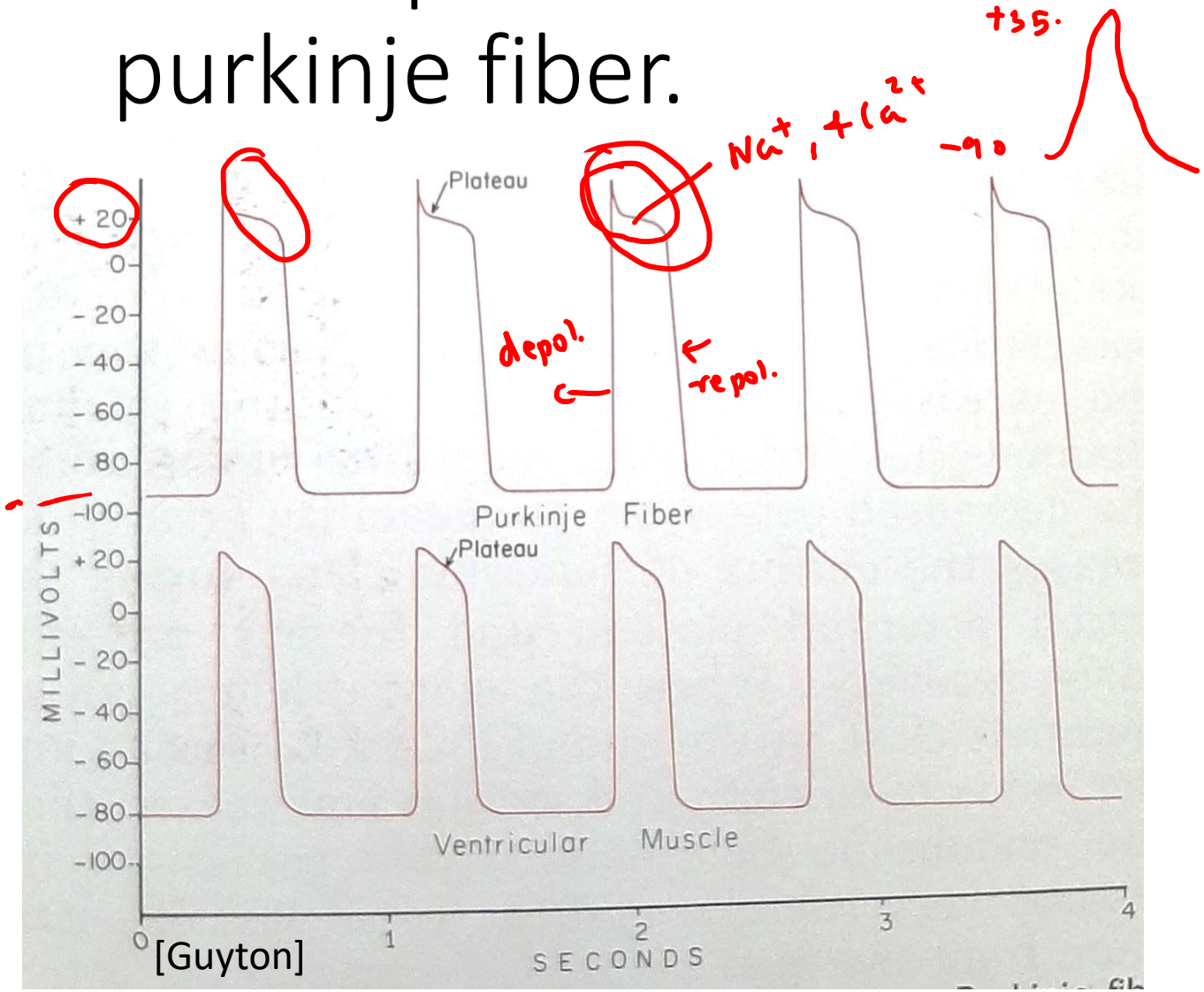
- Delayed electric signals from the AV node is taken to the ventricular myocardium via the AV bundle or bundle of HIS. This fiber branches out to both ventricles and has small branches called purkinje fibers. This will pass the signals to the myocardium which contracts upon receiving the signal, which in turn results in pumping.
- Although the SA node generates signals intrinsically, its beats are controlled by the parasympathetic nerves (we will not worry abut these here.).
- SA node rhythm is 90 beats per minute. But heart rate is 60-100 beats per minute.
- The resting potential of the normal cardiac muscle is -85mV to -95mV
For purkinje fiber resting potential is -90mV to -100mV





[Guyton]

Action potentials in ventricular muscles and purkinje fiber.

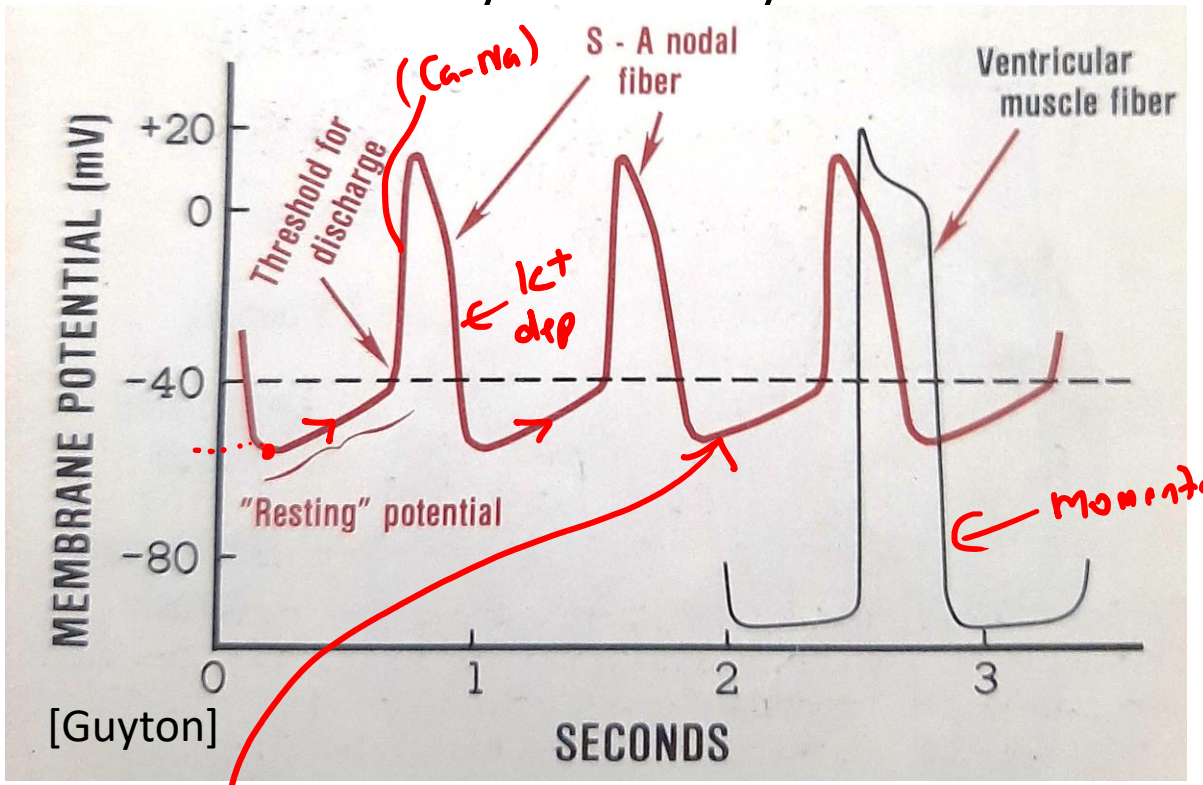


[Guyton]

- Depolarization time which includes the plateau for (a) atrial muscle is 0.2 s and for ventricular muscle is 0.3 s.
- The plateau causes more time of depolarization which implies more contraction of muscles which in turn implies better pumping action. This is in contrast with other skeletal muscles which repolarize faster (that is depolarization time is less.)
- In nutshell the cardiac muscle is designed specifically for better contraction and high pumping action.

Na+ , K+ Ca+

Automatic rhythmicity of SA node



[Guyton]

Mechanism in ventricular muscle

- Resting potential of ventricular muscle is -85mV to -90mV.
- A depolarization occur due to usual fast sodium gated channel resulting in fast transition to +20mV.
- Then a slow (it means it take some time to open channels upon the increase in potential inside relative to sodium channel) calcium-sodium channel opens causing more calcium and sodium to enter inside the cell and thus maintaining the depolarization for more time resulting in a plateau (unlike in skeletal muscles.).
- At the end of sodium channel, the potassium channel has to open. But due to presence of calcium, this will happen bit delayed and hence repolarization happens after the plateau.

Mechanism in SA node

- Resting potential of SA node is -65 to -60 mV and is dynamic.

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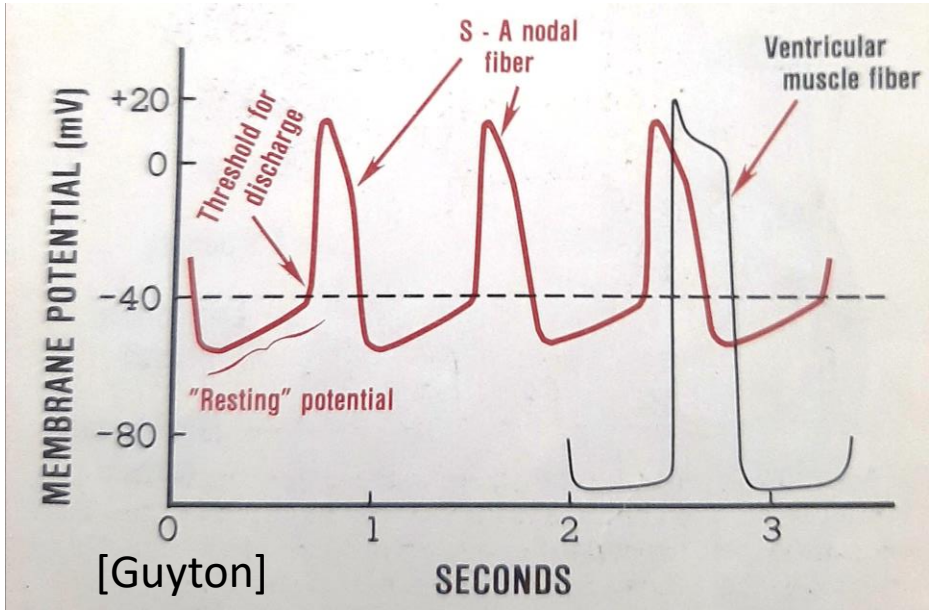
Automatic rhythmicity of SA node



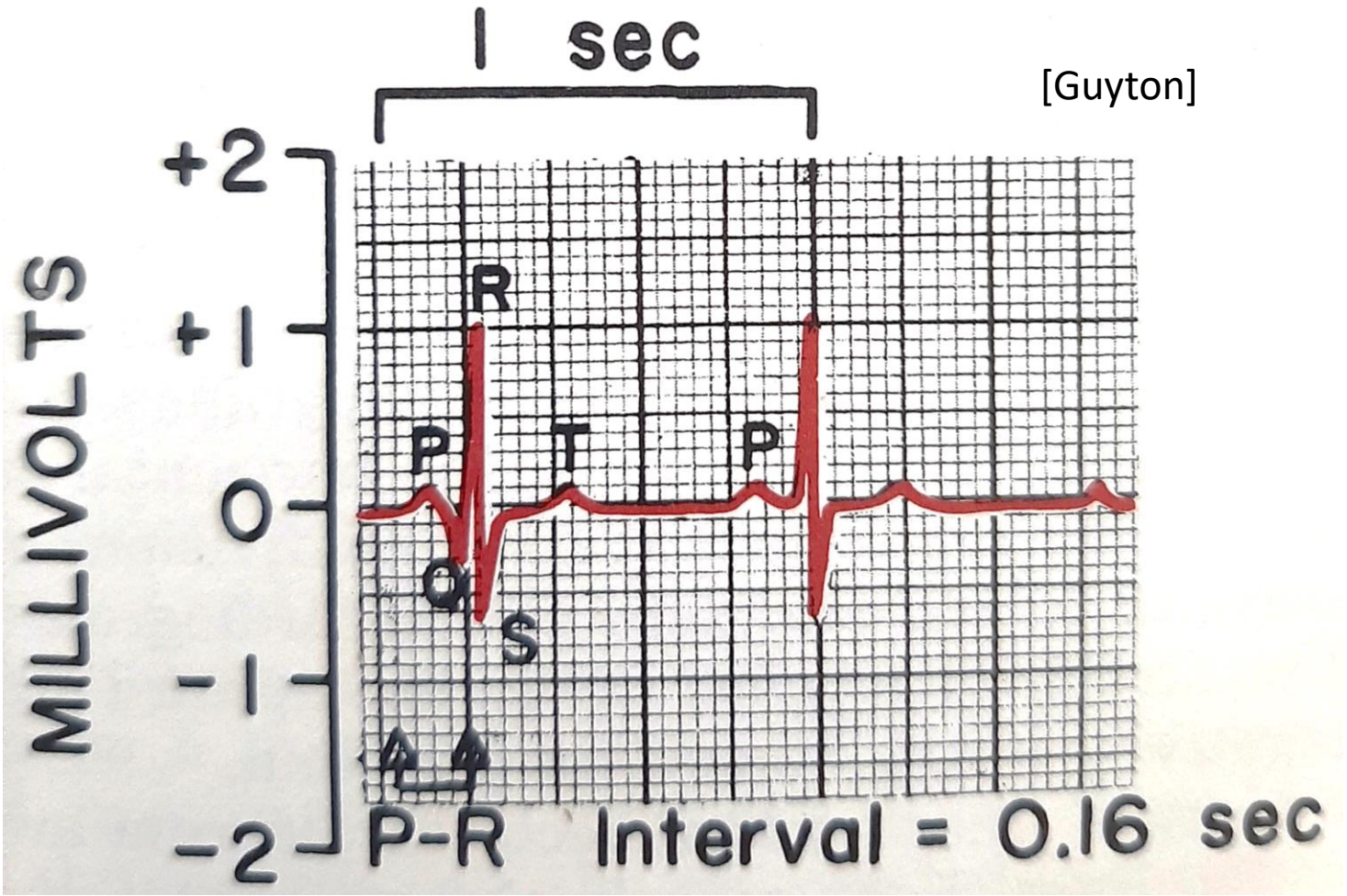
[Guyton]

- As we discussed , action potentials are associated with a positive feedback Hodgkin cycle.
- Positive feedback is synonym with oscillators.
- Action potentials in nerve fibbers are not rhythmic. Because the repolarization pushes it to rest.
- In heart, the leaky channels makes it repeat. In true sense, it's a oscillator.

Mechanism in SA node

- Resting potential of SA node is -65 to -60 mV and is dynamic.
- Main point : the sodium channel in SA node is leaky. This causes the resting potential of the SA node to be at -55mV.
- But we have seen that if the membrane potential is at >-60mV for a prolonged period, then sodium channel will not get activated (it will wait till repolarization complete and the membrane potential reaches the resting potential. Like a "dead time" of sensors.)
- Sodium keeps flowing inside by leaking and when the membrane potential reaches -40mV the sodium-calcium channels opens.
- The only channel that can be activated at this membrane potential is sodium-calcium channels and hence it opens to create the action potential.
- Finally the potassium channel open and it flow out causing repolarization and the membrane potential reaches to the resting one i.e., -55mV. The potassium channel now closes. But leaky sodium channel is always operating and this causes the resting potential not to "rest" anymore and it starts rising again and the process continues till one dies.

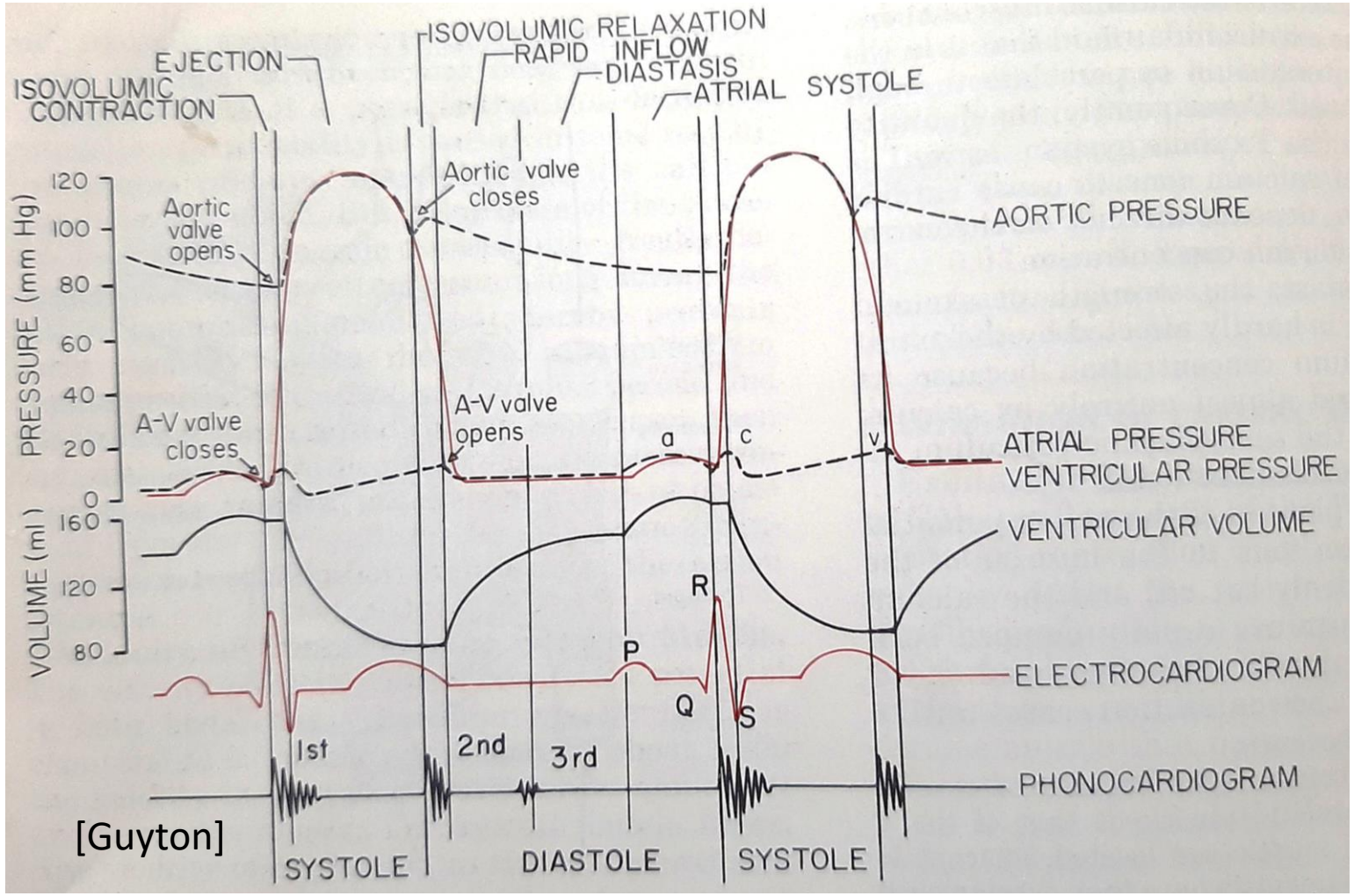
Electro cardiogram (ECG)



[Guyton]

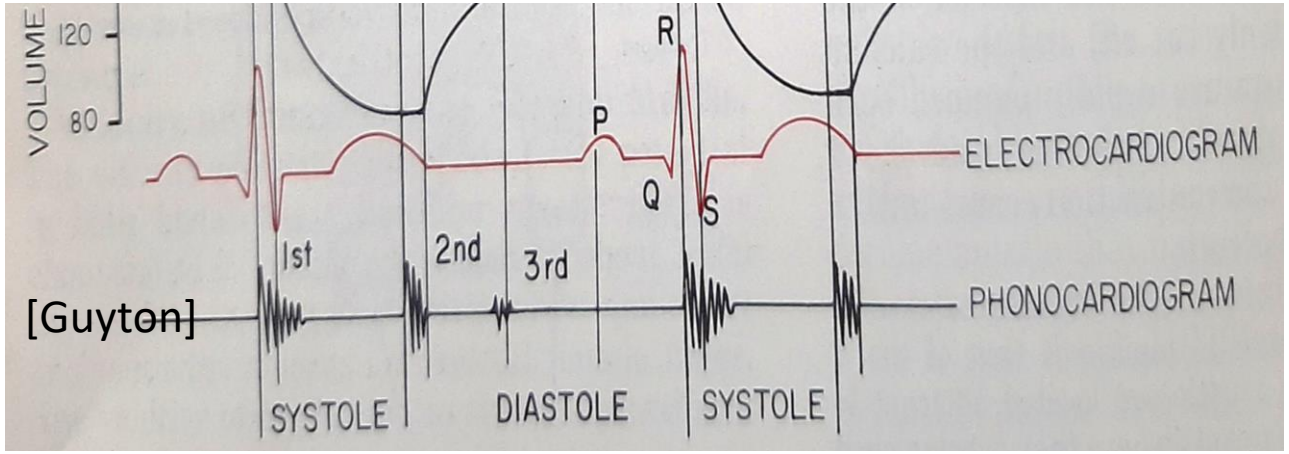
- P : spread of the depolarization through the atria during atrial contraction. The arterial pressure will increase immediately after P-wave.
- QRS : is caused by the depolarization of the ventricles. After this the ventricle contracts which decrease its volume and increase the pressure. (pumping)). Thus this happens just before ventricular systole.
- T : repolarization of the ventricles during the relaxation. Immediately after this the ventricular volume increases and its pressure come down.
- There is another wave which is due to the atrial repolarization. But this is a low signal and almost coincided with the QRS and QRS dominates.
- The magnitude and polarity of the PQRST complex will depend on the relative position of the electrodes.

Cardiac cycle

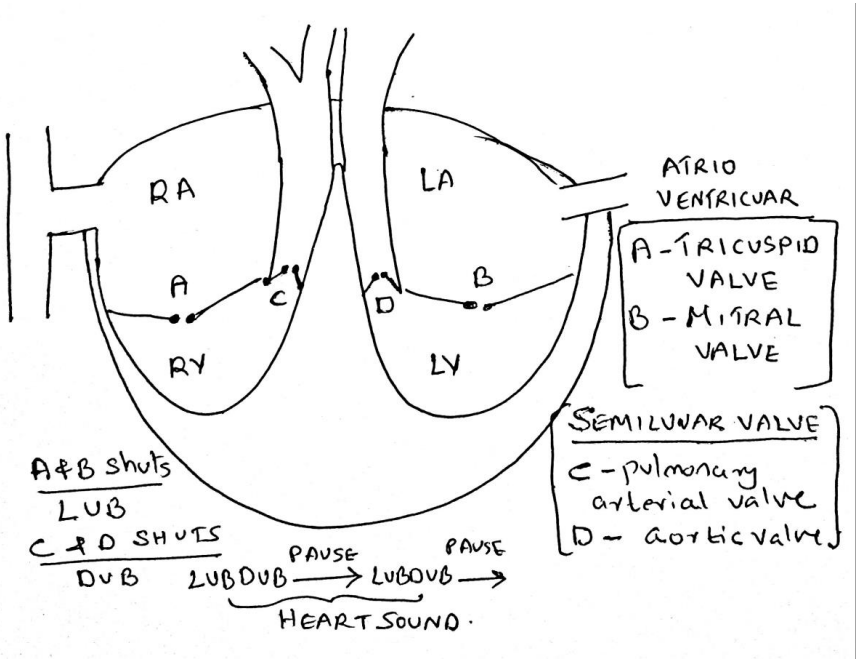


- The period from the end of one heart contraction to the end of the next is called cardiac cycle.
- Each cycle is initiated by the action potential generated at the SA-node
- Systole :period of contraction and diastole : period relaxation.
- immediately after atrial contraction (P-Wave) , atrial pressure slightly increases and eventually leads to AV valve to open.
- Once its open, blood fills ventricle, its contracts (QRS) and thus ventricular pressure rises, along with that aortic pressure increases. This is pumping. The ventricle shrinks, repolarization happens (T) and simultaneously the aortic pressure also come down.

Heart sounds.



[Guyton]



- Opening of the valves is a slow process and hence not much noisy to be heard
- Closing of the valves is noisy and it creates the LUB-DUB as have already seen.
- This mainly because of the sudden pressure difference while valve is suddenly closes causing turbulence and sound is propagated in all directions in the chest.
- I st heard sound : is due to the AV valves (A and B). When ventricles contract the AV valves closes creating a sound which is of low pitch and lasting long. (LUB)
- 2 nd sound : due to the closing of the aortic and pulmonary valves (C and D) which is of shorter duration. (DUB)
- 3rd sound : is often by the rumbling motion in the ventricles.
- There is also another some sound generating while blood moves from atria to ventricle. Measuring this sound and the third sound requires special instruments.
- Systole :ideally period between the closing and opening of AV valves. But now way to find the Opening time. Therefore, since the semilunar valves closes almost same time a the AV vales opens, we define systolic time as time between the AV valve closes and aortic valve closes. Diastolic is time between aortic valve closes an closure of AV valve.