Heart is part of the excitable tissue in the human body

Human cells:

1. Excitable, performs its function only upon excitation

For example: Heart, smooth muscles, skeletal muscles, nervous system cells which can't perform their function unless excitation occurs.

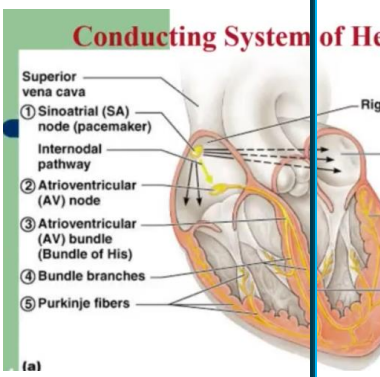
2. Non excitable, performs its function without any need of excitation like endocrine cells that can secrete hormones without excitation.

### What is excitation?

Reversal of membrane potential which means turning the negative potential inside cells into positive potential (ex. Turning the inner potential from -70 mV to 10mV)

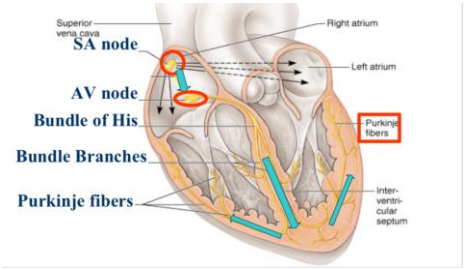
How does it occur? By introducing positive charges to the interior of the cells like Na+ or Ca++or both.

## Excitation in the heart:



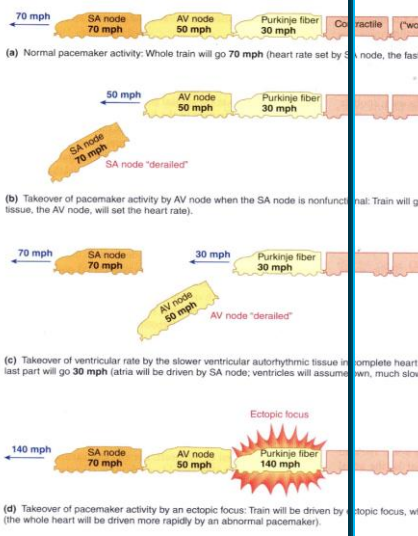

1. excitation begins in the SA nodal cells
2. Excitation then travels to the atrioventricular (AV) node by conductive pathways.
3. Then to the atrioventricular (AV) bundle (bundle of His) (function of AV bundles is conduction not contraction even though they are a part of the heart (about 1%) this is because they lack actin and myosin)
4. Then to the left and right bundle branch followed by purkinje fibers
5. Lastly to the myochardium it self (the heart muscle)

This is the sequence of events produced by electrical behavior of the heart.




** approximately 1% of cardiac muscle cells are autorhythmic rather than contractile.

- If SA node was the pace maker of the heart (decides it's rythme) heart rate would be between 70-80 beat per minute.
- If AV node was the pace maker the speed rate would be 40-60 beat/min.
- Purkinje fibers : 15-40 beat/min.
- Normal heart rate is between 60-100 beat/min. Bellow 60 bpm is bradycardia and above 100 bpm is tachycardia




SA nodal cells is the fastest in reaching threshold therefore it is the pacemaker, but in some conditions it doesn't function properly because of damage, inflammation or if the node is ischemic (dead). In this case AV nod becomes the pace maker as a result heart rate decreases and becomes 40-60 beat/min and people are still able to live normally.

If we stop communication between the atrium and ventricle purkenji fibers become the pacemakers with a heart rate of 15-40 which is not enough for people to live therefore an artificial pacemaker is needed which gives impulse every 0.8 seconds which results in 75 beat per minute.

An example of damaged AS node is SSS (sick sinus syndrome)

**Note* SSS is a disease in which the heart's natural pacemaker located in the upper right heart chamber (right atrium) becomes damaged and is no longer able to generate normal heartbeats at the normal rate.

Intrinsic Conduction System's Function: initiate & distribute impulses so heart depolarizes & contracts in orderly manner from atria to ventricles.

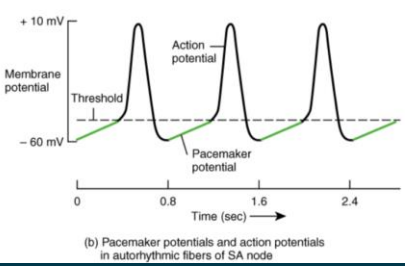
## SA node:

Also known as Sinus Node (Sinoatrial node):

- Specialized cardiac muscle connected to atrial muscle.
- Acts as pacemaker because membrane leaks Na and membrane potential is -55 to -60mV
- When membrane potential reaches -40 mV, slow Ca channels open causing action potential.
- After 100-150 msec Ca channels close and K channels open more thus returning membrane potential to -55mV.

Has Na leaky channels which produces the impulse for action potential (depolarization )(impuls is born in the node) therefor the SA node doesn't need external stimulus from niether the nervous nor the hormonal system.
SA nodal cells' Membrane potential increases to the threshold on its own then complete depolarization and reploarization. This means that SA nodal cells excite themselves by themselves which is called **autorythmic**, this means that the cell has the ability to bring the membrane potential towards threshold by itself… intrinsic ability to stimulate itself and generate action potential.
Intrinsic Automaticity: The ability to initiate its own beat.
Intrinsic Rhythmicity: The regulatory of such pacemaking activity.

Remember: Threshold is the level which when reached certain channels are opened wildly to allow positive ions to



(b) Pacemaker potentials and action potentials in autorhythmic fibers of SA node

enter cells (normally leaky channels open wildly Na+, Ca++ or both).

We already know that excitation is through the entry of positive charges to the cell like Na+ current or Ca++ current, then it moves to the neighboring cell and to next cells by gap junctions which transmit action potential between neighboring cells (**syncytium**) syn means together while cytium means cells, this means once a cell is stimulated neighboring cells all are stimulated (think of domino pieces) , there is also low electrical resistance between cells which in turn leads to excitation easily transferring between cells.

In short, once a cell in the heart is excited the entire heart is excited . Not entire heart but entire atria or entire ventricles This is important for the heart to contract as one cell to have an effective contraction. Unlike skeletal muscles where force of contraction is great, for example if you are holding something in your hand the number of muscles used is different depending on what you are holding. In skeletal, in weak contraction, few fibers are contracted, others are relaxed. Contraction is graded not as syncytium.

This is called graded contraction in skeletal muscle and is possible due to the absence of syncytium (no gap junctions) each cell is on its own.

Na concentration outside the cell is 140 inside 14 moves by simple diffusion in the cell bringing positive charges inside. If the channels stay open Na will keep entering until the electrical force inside the cell starts repelling Na.
When chemical force of Na = the electrical force but opposite to each other then Na moving inside= Na moving outside.

*Movement never reachs zero only the net is zero.

Ion channels for the same ion on the cell membrane have different behaviors Voltage ligand …

How positive does the cell potential need to become in order to stop Na entry to the cell? (How much electrical force do we need?)

$$E_{ion} = \frac{RT}{zF} \ln\left(\frac{[ion]_o}{[ion]_i}\right)$$

=-61log (in/out)

-61log (14/140) = -61 * -1=61 mV

This is the potential that when reached stops sodium entry.

If the resting membrane potentail= -60

In depolarization membrane potential becomes 10

How much sodium enters the cell ?

A very small amount that is not measurable.

What is the sodium concentration outside and inside the cell at the end of depolarization ? The **same** as before.

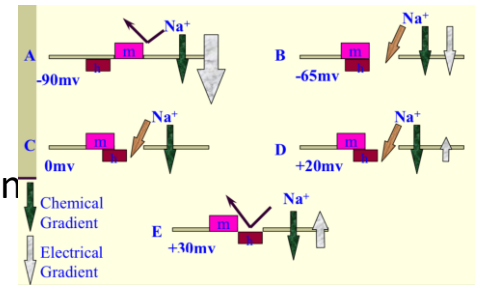
If you want equal concentration on both sides you will need 500000 depolarization, 1 action potential doesn't change the concentration, and still the increase in Na inside is sent back outside by the Na k pump to maintain the same gradient.

Sodium channels have 3 different states, normally closed by m gate (closed active) , open, closed by h gate (closed inactive).

Resting membrane potential =-90mV for example in skeletal muscle cells it has **m gate** in this channels that closes it but opens upon stimulation (activation gate) fast channels need 0.2ms to open upon proper stimulation, another gate **h gate** (inactivation gate) closes after this fast

stimulatin happens because it is voltage

gated channel that works after depolarization




- H gate is slow in closing, takes 1 ms to allow sodium ions to enter and make depolarization.

- H gates won't reopen unless membrane potential returns to resting -90 mV.
- M gates open easily by stimulus unlike h channels which are harder to open.

A fourth state for na channels is found in SA nodal cells :

Partially open (leaking Na+ in) takes much longer to reach threshold but does it on its own autorythmic, Ca++ channels also help in depolarization.

This is not found in skeletal muscles.

Na keeps entering the cell trying to achieve $E_{Na}$ to reach equilibrium where no forces would be affecting sodium ions or pushing it in any direction.

Chemical forces = electrical forces only in quantity but have opposite directions

$E_{Na}$ = change in concentration (10x) (remember 140 out and 14in)

Calcium concentration inside cell is 10^-7 and outside the cell is 10^-3

Outside is 10000 more times than in the cell

$E_{ca}$ (calcium equilibrium potential which is equal to the chemical gradient and opposite to it) =

-61/2 log (10^-7/10^-3) = -30.5 *-4 =~ +120

K+ in is 150 outside 4

Ek=-61log (150/4) =-90 mV

Each ion tries to get the membrane potential close to its own equilibrium potential.

The movement or flow of each ion inwards or outwards is called a current and is represented by the letter I.

I = DF / R  The unit is flow/time

DF=driving force

R=resistance

Flow is directly proportional to DF and inversely proportional to the resistance.

Flow means anything happening or moving per unit time.

Resistance tells you about the difficulty of the process, but it is a vague expression so to make it easy to calculate we take the permeability instead

I=DF * K where K is the permeability.

Permeability tells you how easy the process will be and is used for non charged molecules like aminoacides and glucose.

For the charged ions it is called conductance (g), g could be 0 when channels are completely closed ,1 where channel are complete open or any number between 0 and 1

I= DF * g

The driving force might be 10000 but the current would be zero because the conductance is zero.

What is the driving force?

The equilibrium potential for an ion from the membrane = Em-Ex

Em is the membrane potential

Ex is the resting membrane potential for the certain molecule. (Ex: is the equilibrium potential for that specific ion)

Ex. $I_k$ = (-90-(-90)) *g k+= 0 the net movement is zero

So to generate a current we need both a driving force and conductance.

I Ca++= (-90-120) *0= 0

## Resting membrane potential

What is common between excitable and non excitable cells?
Both have resting membrane potential

- RBCs have rmp of -7
- Sa node -60
- Smooth muscle cells -30
- AV nodal cells -65
- Neurons -70
- Cardiac cells -90

Even though all of these cells are surrounded by the same concentration of ions they have different resting membrane potential, why?

The ion conductance is different and the ion with the highest conductance (highest current) determines the resting membrane potential.

For example, when the resting membrane potential is -90, we can tell that potassium has the highest conductance and is very low for Ca and Na ions.

While in RBCs conductances for both Na and K are very similar.

In SA nodal cells, potassium has the highest conductance, but it is also affected by sodium conductance.

1. In SA nodes $I_{Na}$ is called funny $I_f$ because it only opens till the potential reaches -50.
2. There are also transient calcium channels which open when the potential is -50 and close when it reaches -45.
3. Finally, long lasting calcium channels open and depolarization occurs, and action potential continues.