Heart physiology (2)

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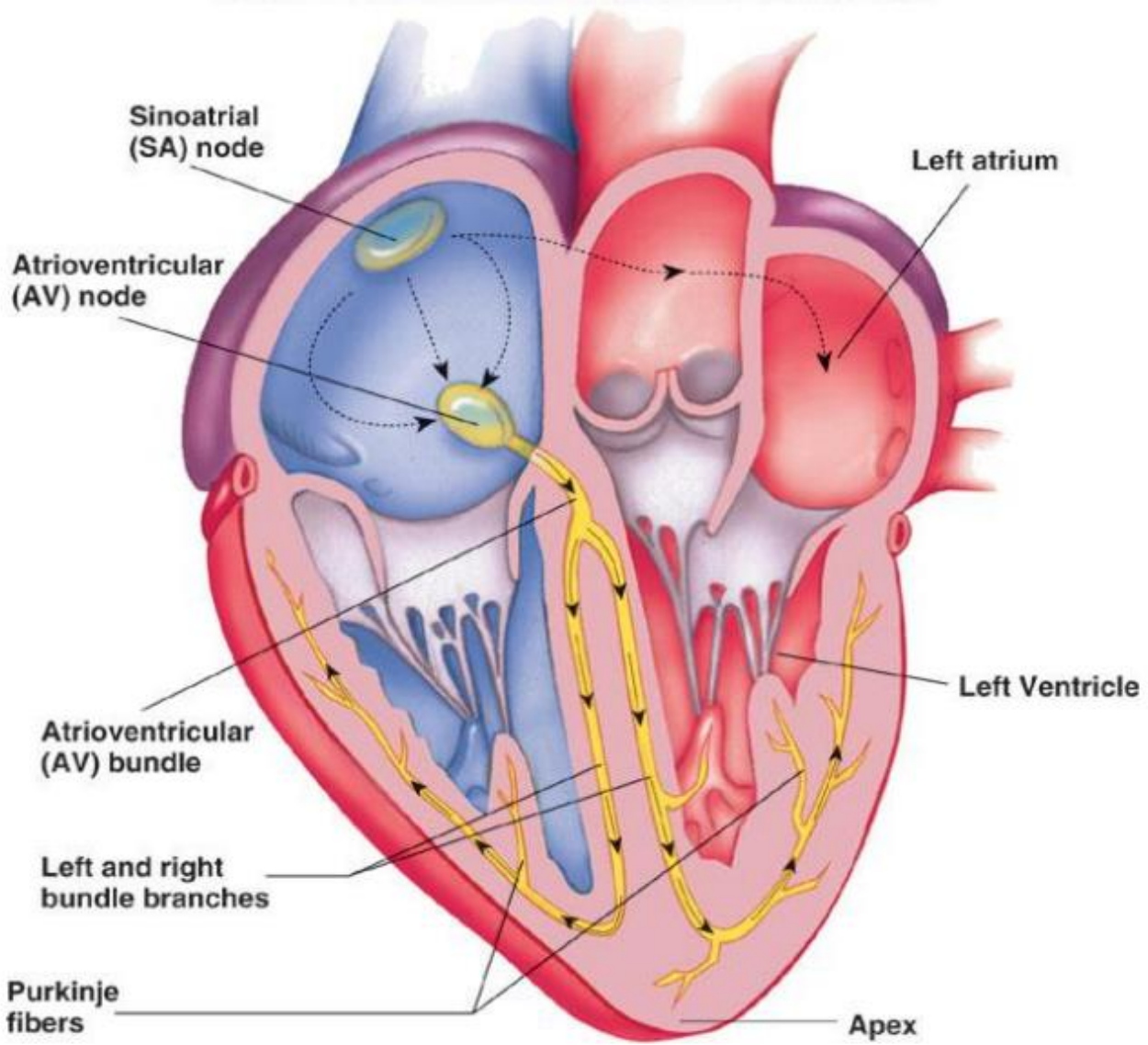
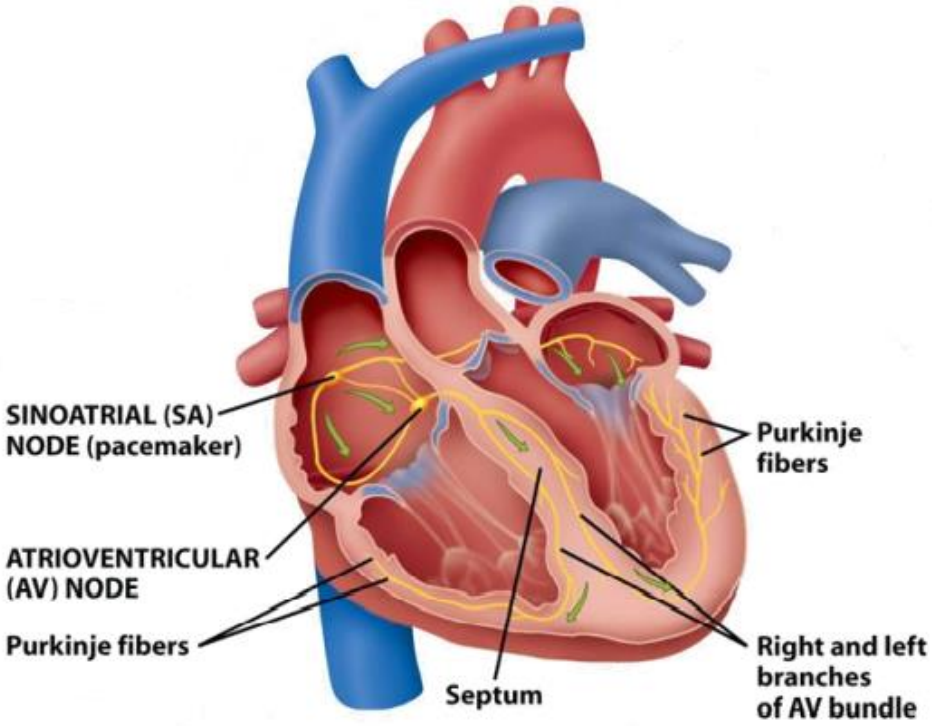
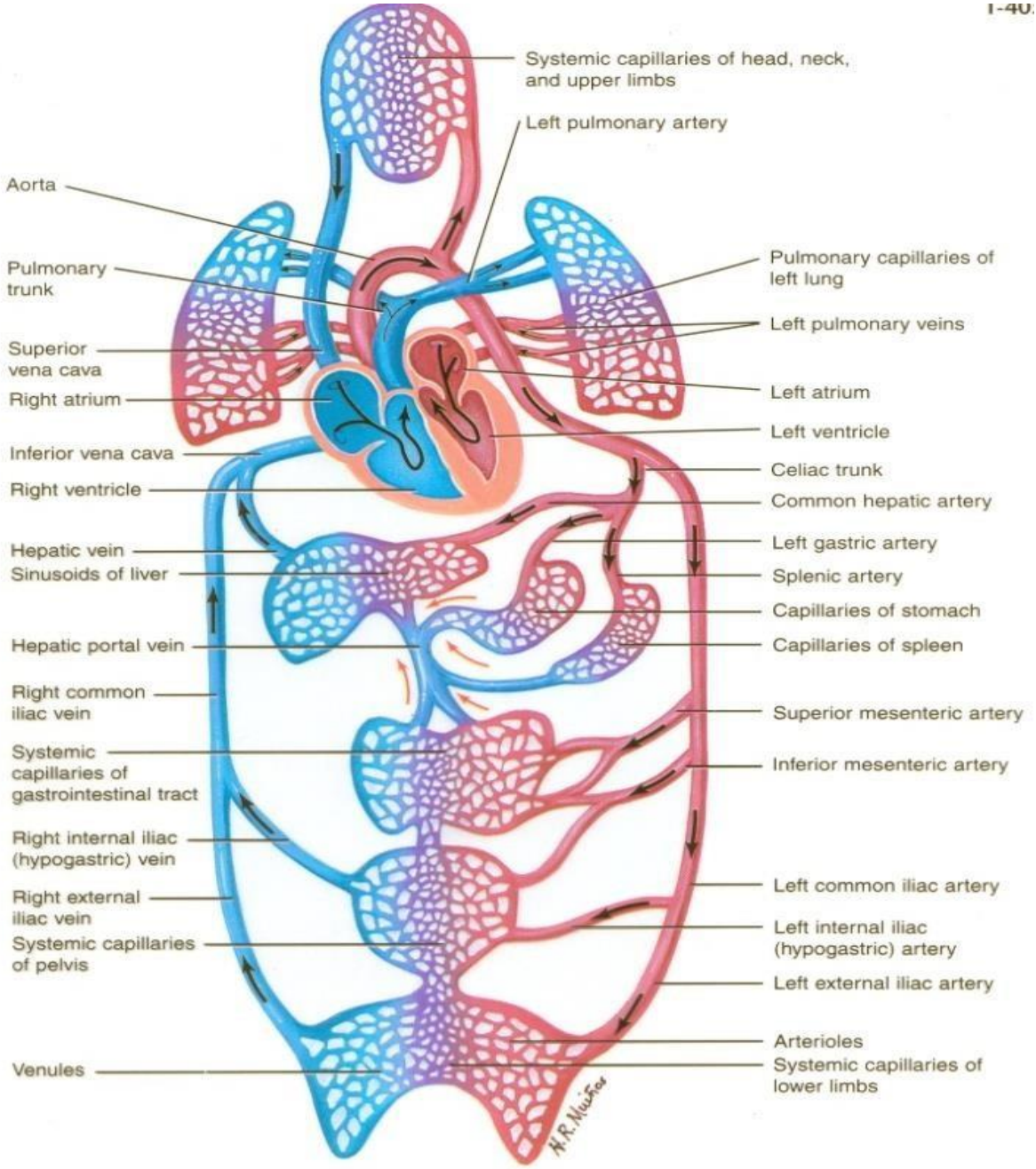
Topics of the lecture

- 0- Introduction
- 1- Conductive system of the heart
- 2- Action potential of cardiac cells
- 3- Pacemaker
- 4- Comparation between SA node & ventricle action potential
- 5- Comparation between cardiac muscle and skeletal muscle
- 6- Effect of autonomic nervous system on heart

0- Introduction



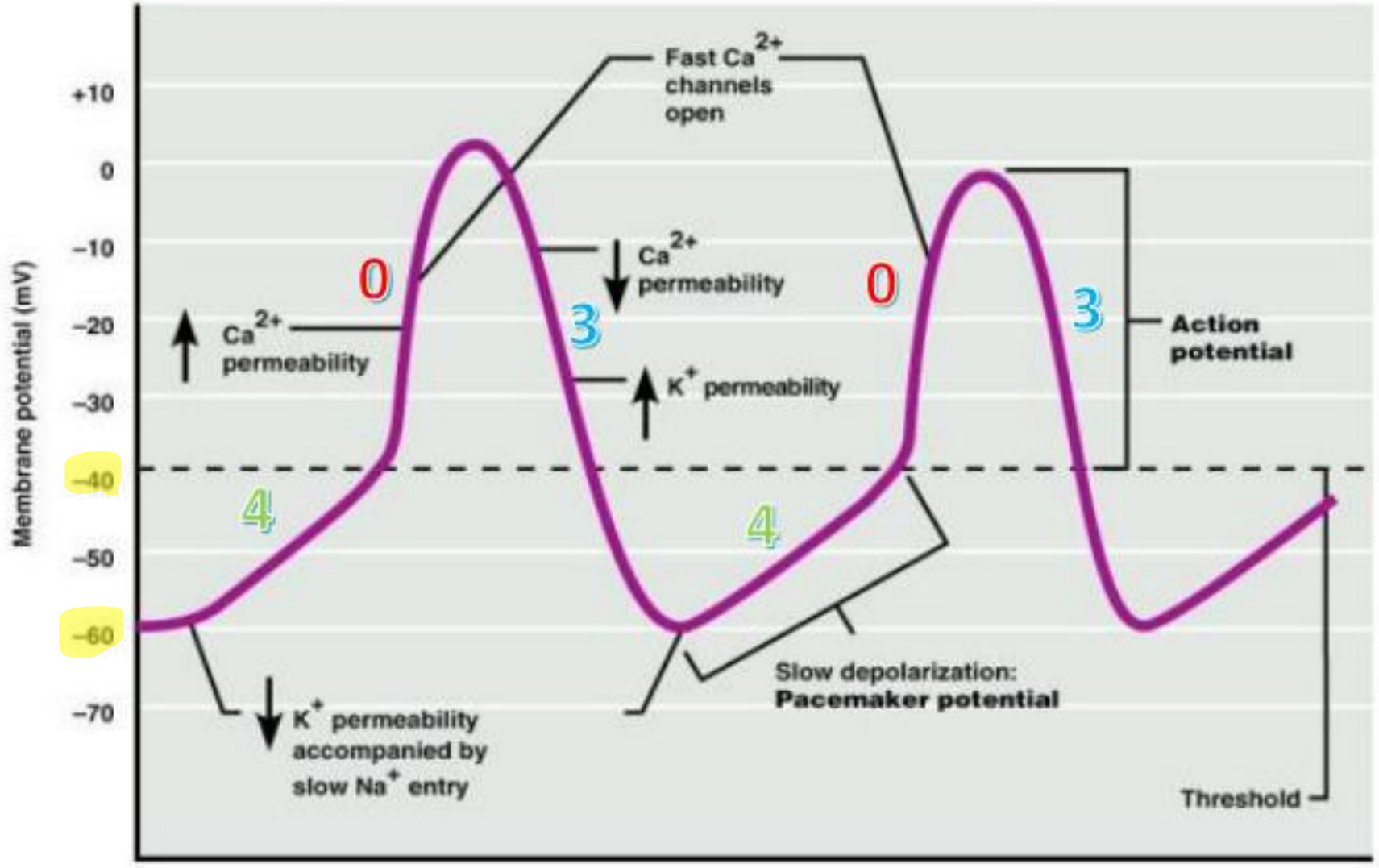




General plan of circulation

1- Conductive system of the heart

➢ THE SINOATRIAL (SA) NODE POTENTIAL:



→ Phase 4: 650 ms
→ Phase 0+3: 150 ms

→ Total time = 0.8 s

→ heart rate = 60/0.8 = 75 BPM

1- Conductive system of the heart

→ In the second half of this phase, Ca++ channels start to open

I. **Phase 4:**
- Is slow depolarization.
- Accounts for the pacemaker activity of the SA node (automaticity).
- Is caused by an increase in Na^+ conductance, which results in an inward Na^+ current. (Slope increase upon sympathetic stimulation = increase HB)

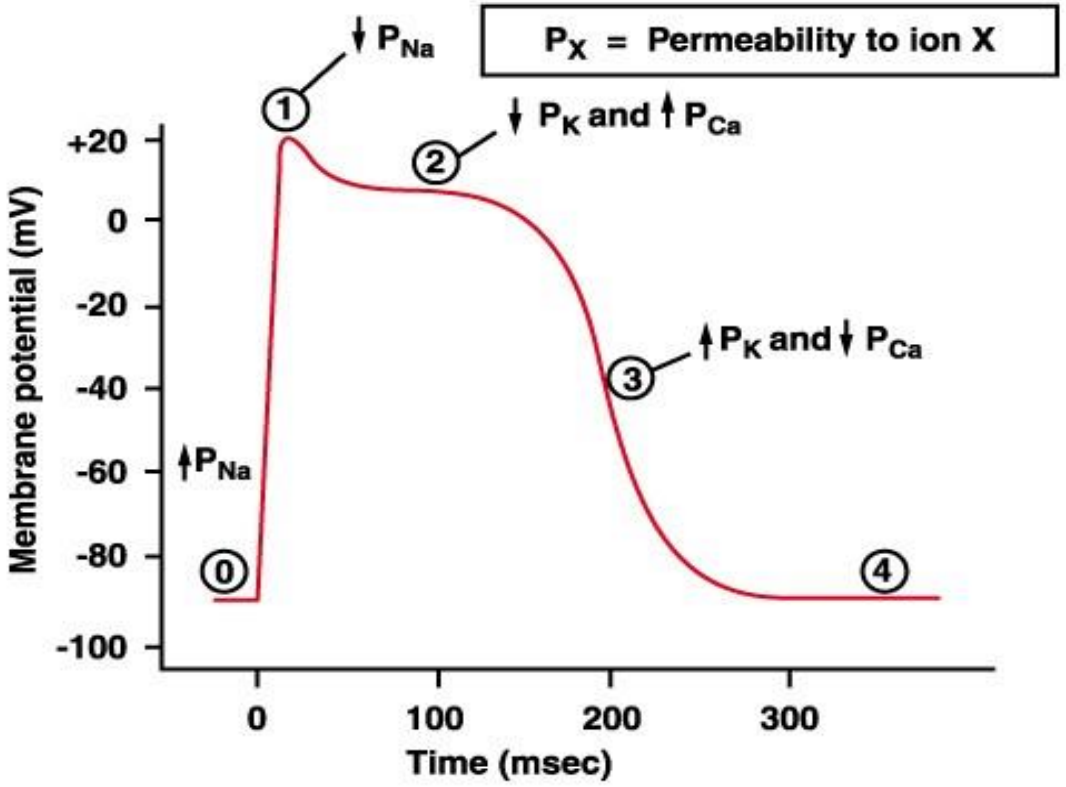
II. **Phase 0:**
- Is the upstroke of the action potential.
- Is caused by an increase in Ca^{2+} conductance. This increase causes an inward Ca^{2+} current that drives the membrane potential toward the Ca^{2+} equilibrium potential. (Increase activation of L-type Ca++ channels)

III. **Phase 3:**
- Is repolarization.
- Is caused by an increase in K^+ conductance, which results in an outward K^+ current that causes repolarization of the membrane potential.

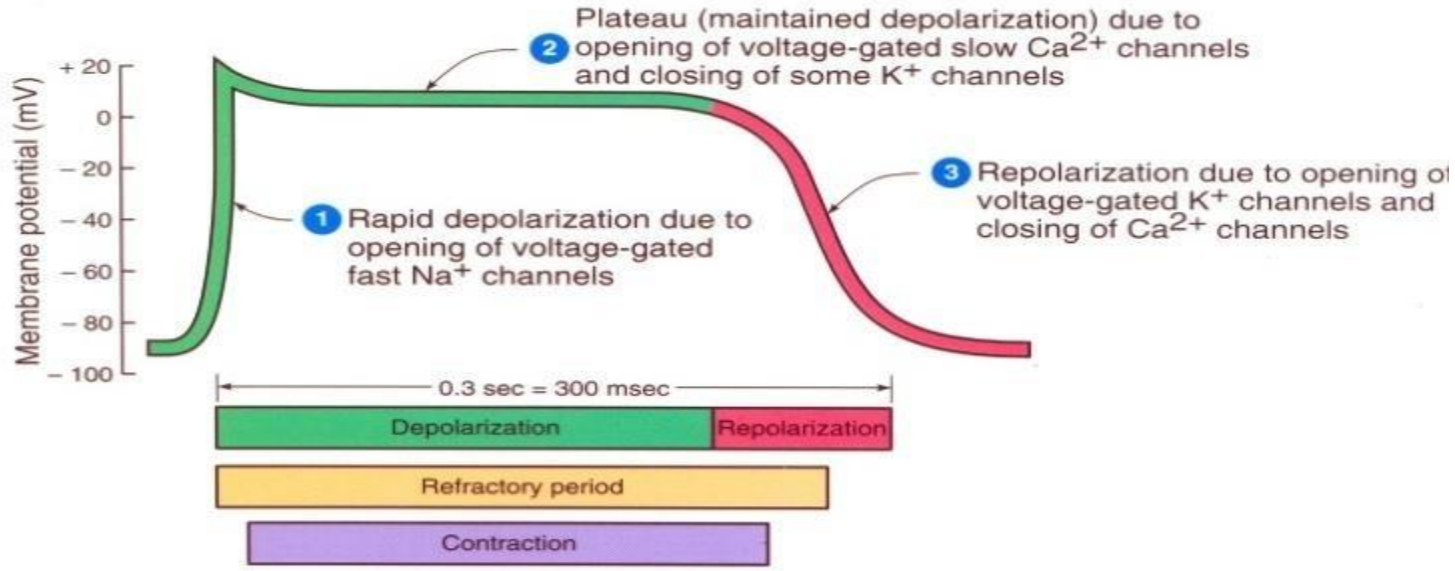
Some notes:
- The resting membrane potential will never reach -90mV due to the leakage of Na^+ in phase 4.
- Since they leak Na^+ in a slow manner, the membrane potential will slowly reach the threshold due to slow depolarization. So when reaching the threshold, the inactivation gate of Na^+ channels had enough time to close and no Na^+ can enter the cell, luckily there are Ca^{2+} slow gated channels (slower than Na^+ channels) which allow the Ca^{2+} influx.

- what Cause the movement of sodium ions at phase 4?
  Answer:
  Regarding ohm's law
  - Current (I) = Driving force X conductance (G)
  - Driving force = (Em-Ex) or (resting membrane potential – ion’s equilibrium potential)
  → electrochemical gradient (the driving force) is high but conductance is very low, that’s why sodium moves slowly

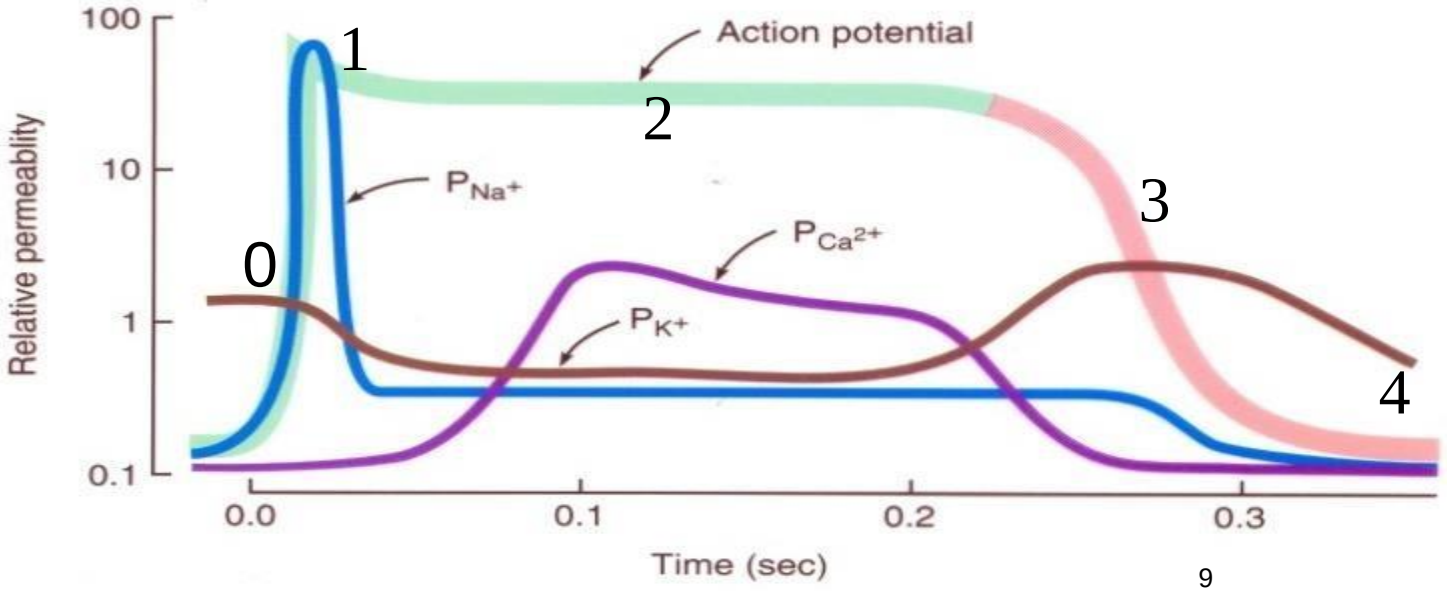
2- Action potential of cardiac cells



Phase	Membrane channels
0	Na^+ channels open
1	Na^+ channels close
2	Ca^{2+} channels open; fast K^+ channels close
3	Ca^{2+} channels close; slow K^+ channels open
4	Resting potential



(a) Action potential, refractory period, and contraction



(b) Membrane permeability (P) changes

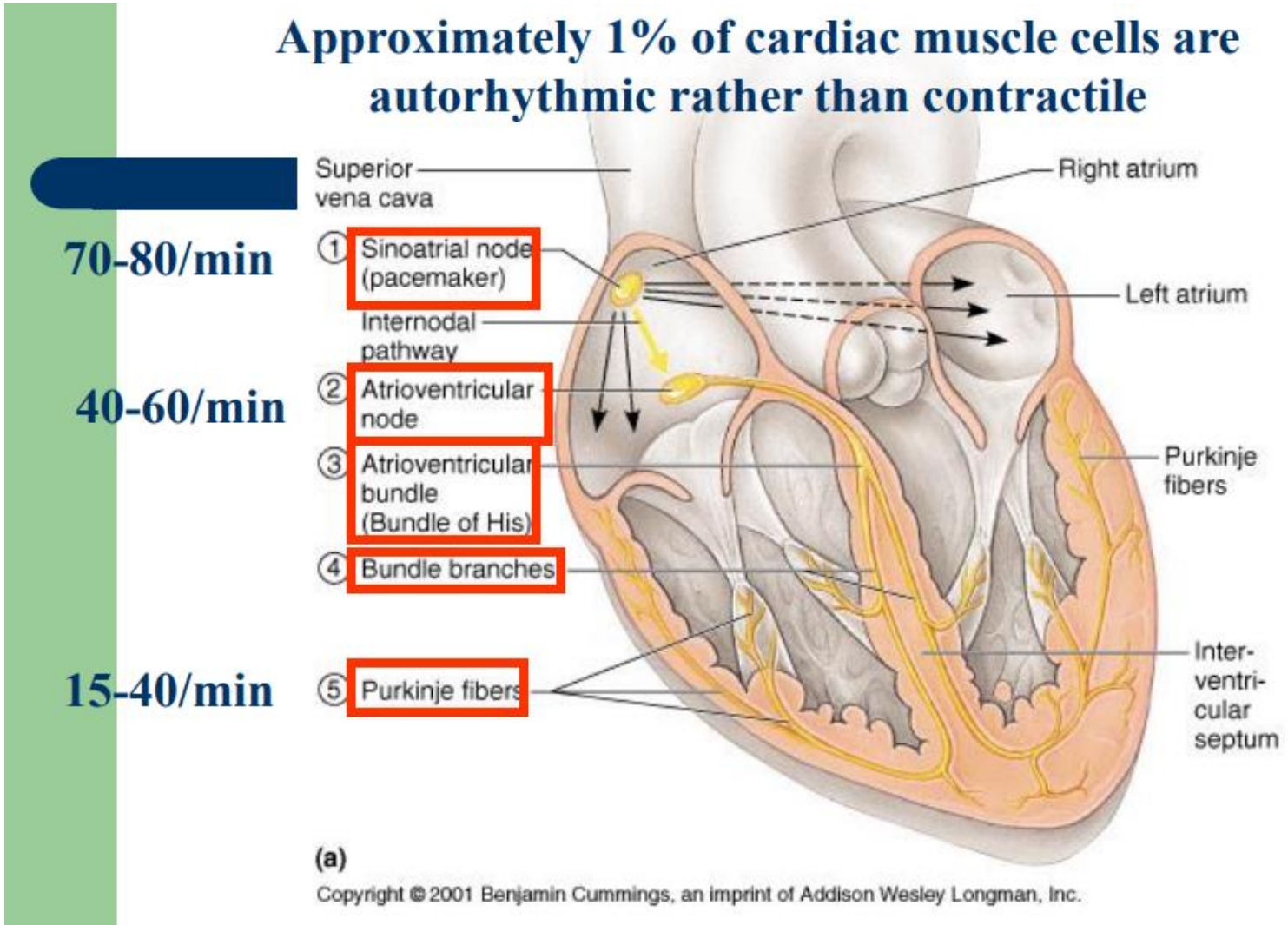
phase 0 can proceed quickly (almost in no time) in ventricles due to the presence of the fast Na+ channels, which Cause fast depolarizing of the membrane ,another important factor is the presence of gap junctions between ventricles, these two factors cause fast stimulation for ventricular cells which allow them to work as a one unit ,and contract at the same time (Syncytium)

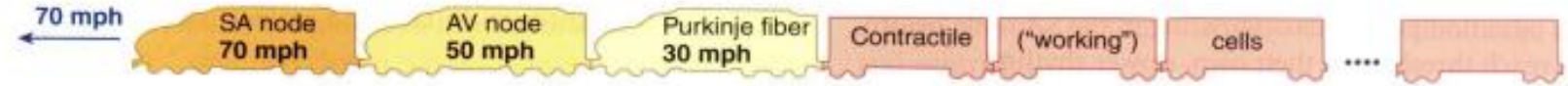
2- Action potential of cardiac cells

- As for cardiac muscle, the resting membrane potential is more negative, around -90 mV. The action potential has 5 phases:
- Phase 0 (depolarization): fast Na+ channels open. When the cardiac muscle cell is stimulated, voltage gated sodium channels (fast sodium channels) open and permit sodium to rapidly flow into the cell depolarizing it.
- Phase 1 (initial repolarization): cell begins to repolarize, due to K+ leaving cells through open K+ channels & maybe the action of some chloride channels.
- Phase 2 (plateau): slow voltage gated Ca+2 channels open so the calcium moves according to its electrochemical gradient from outside to inside (extracellular fluid calcium =10-3 M, while intracellular fluid calcium = 10-7 M) [this calcium is very important for contraction] and some K+ channels close (decreased permeability).
- Phase 3 (rapid repolarization): voltage gated Ca+2 channels close and K+ channels open and K+ goes out of the cell
- Phase 4 (resting membrane potential): averages about -90 mV (and here we're back to the resting state)

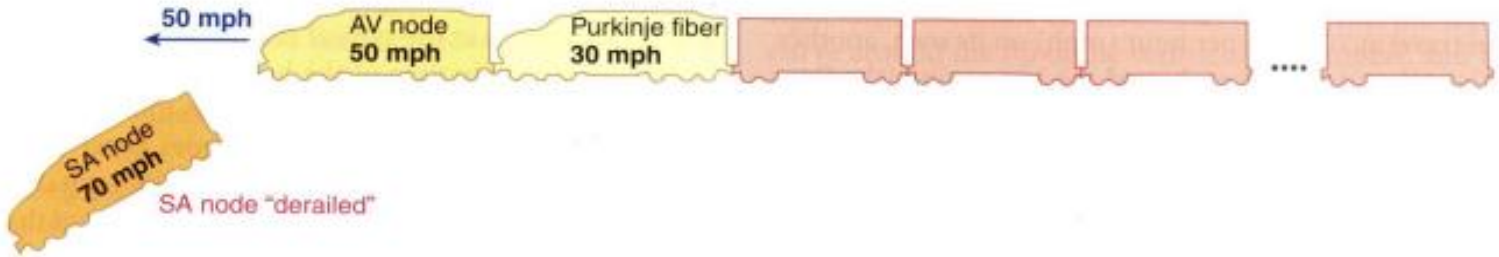
3- Pacemaker

- Here is an exam question , what is so special about the SA node (which allow it to produce action potential)?
- because it is the most leaky to Sodium



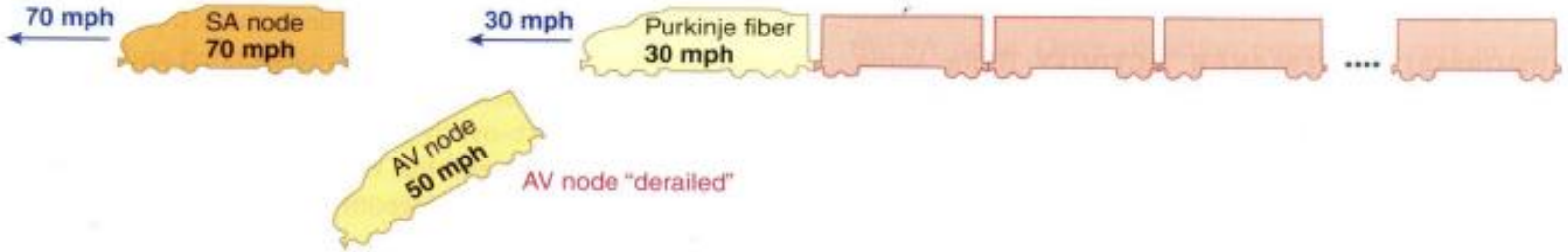


(a) Normal pacemaker activity: Whole train will go **70 mph** (heart rate set by SA node, the fastest autorhythmic tissue).



(b) Takeover of pacemaker activity by AV node when the SA node is nonfunctional: Train will go **50 mph** (the next fastest autorhythmic tissue, the AV node, will set the heart rate).

the AV node is suppressed and driven by the SA node (overdrive suppression)



(c) Takeover of ventricular rate by the slower ventricular autorhythmic tissue in complete heart block: First part of train will go **70 mph**; last part will go **30 mph** (atria will be driven by SA node; ventricles will assume own, much slower rhythm).

(d) Takeover of pacemaker activity by an ectopic focus: Train will be driven by ectopic focus, which is now going faster than the SA node (the whole heart will be driven more rapidly by an abnormal pacemaker).

4- Comparation between SA node & ventricle action potential

For phase 4

	SA node	ventricle
RMP	-65mv	**-90mv**
Relationship with EK^+	Close but notvery much	**very close to K^+ potential equilibrium**
Driving force of Na^+	lower	**higher**
Threshold	-45mV (almost)	**- 70 mv**
D V / Dt	>0 (not stable) does not need a stimulation	**= 0 (Stable) needs a stimulation**
Fast Na^+ channels	closed and inactive so depolarizing will be slower	**closed and ready to open so when we reach the threshold they will open by positive feedback à will Cause depolarizing in a very short time (phase 0),this is very important because cardiac muscle cells must work as one unit(syncytium),and what really enable these cells to do that is the gap Junctions**

The diagram

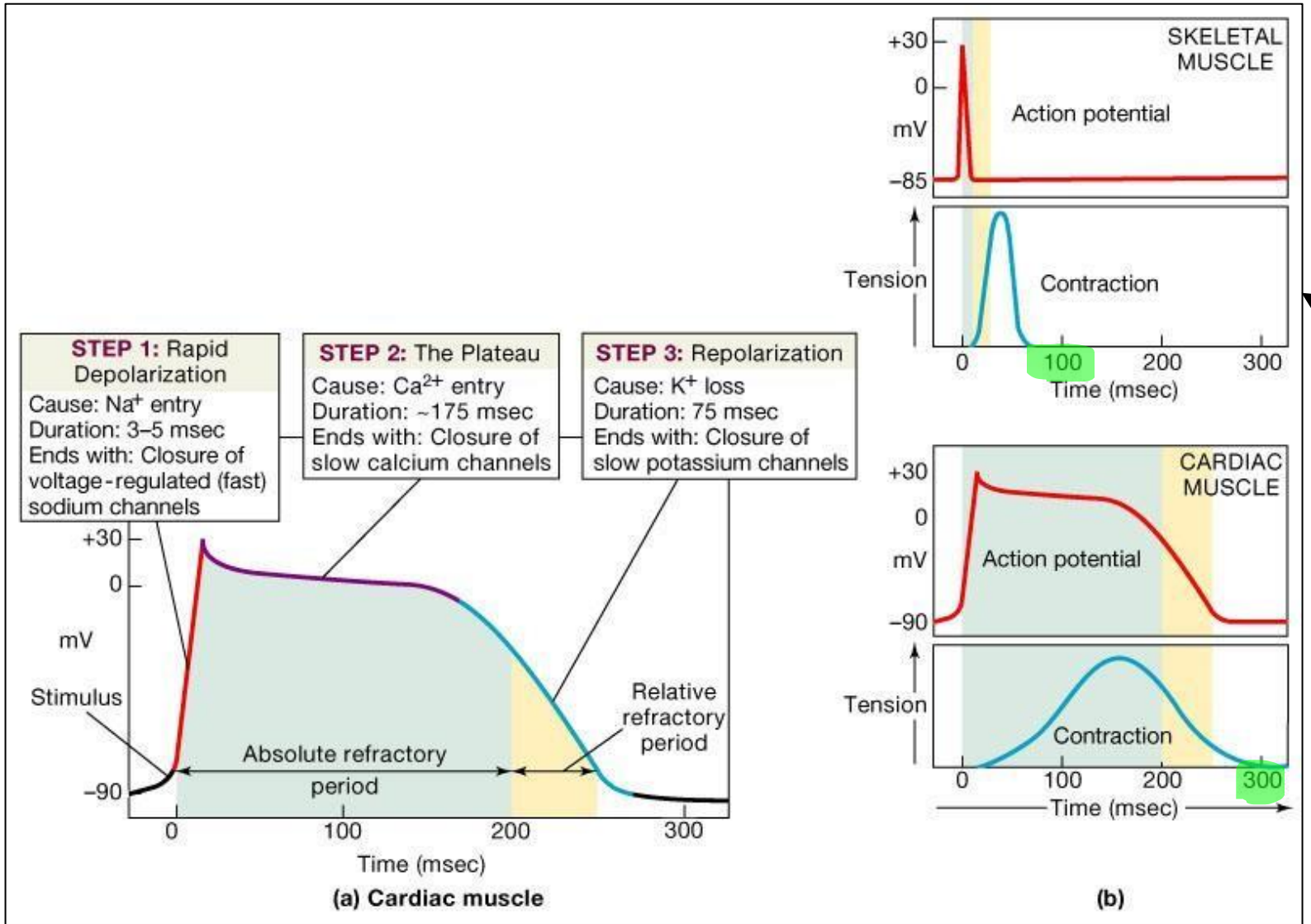
On slide 4 and 7

4- Comparation between SA node & ventricle action potential

For phase 0

	SA NODE	ventricle
Dv/Dt (the slope)	lower	very high(almost ∞
The extend	+10 mv	+30mv(more Na_+ and Ca^{2+} channels are open)
The difference between the Peak and the RMP	-75mv	-120m v
Phase1 (initial repolarizing)	no phase 1	there is phase 1 after phase 0
phase 2 (Plateau)	No plateau	there is a plateau after phase 1
The diagram	Refer to slide 4 & 7	

5- Comparation between cardiac muscle and skeletal muscle



Notice that the action potential of skeletal muscles is very short and all this action potential occurs during the latent period [before the muscle contracts] this means, you can have a lot of AP adding up until this muscle can be tetanized.

5- Comparation between cardiac muscle and skeletal muscle

- The length of this action potential is around 300msec. The absolute refractory extends through the AP to around-half of the repolarization, that time gives space for the muscle to contract AND relax [by repolarization] so, when the next AP comes the muscle would be relaxed and ready to contract again in a way that will never produce tetanus [the muscle doesn't receive signals to contract again, while it's already contracting, rather when it is relaxed]. i.e. the cardiac muscle won't be tetanized because of this long absolute refractory period unlike skeletal muscles. (Note: absolute refractory period is when we can't establish new action potential because we have already established one)
- another difference in the action potential between cardiac and skeletal muscles is that at the end of phase 0 and through phases 1&2 there is a decrease in the permeability of k+ by the closing of fast K+ channels until the efflux plateaus at phase 2, as we know the resting state permeability of k+ is much higher than that of Na+ , it is about 100 times more. This K + permeability during phase 0 decreases and stays low until the end of phase 2 then it starts to increase before phase 3, this is very important as it maintains the plateau phase
- Note :relaxation (filling the heart with blood) is more important than contraction(emptying the heart) , it takes about 0, 5 s while contraction takes 0, 3 s.
  Contraction (systole) →0,3 s
  Relaxation(diastole) → 0, 5 s
  systole + diastole → 0, 8 s=the cardiac cycle

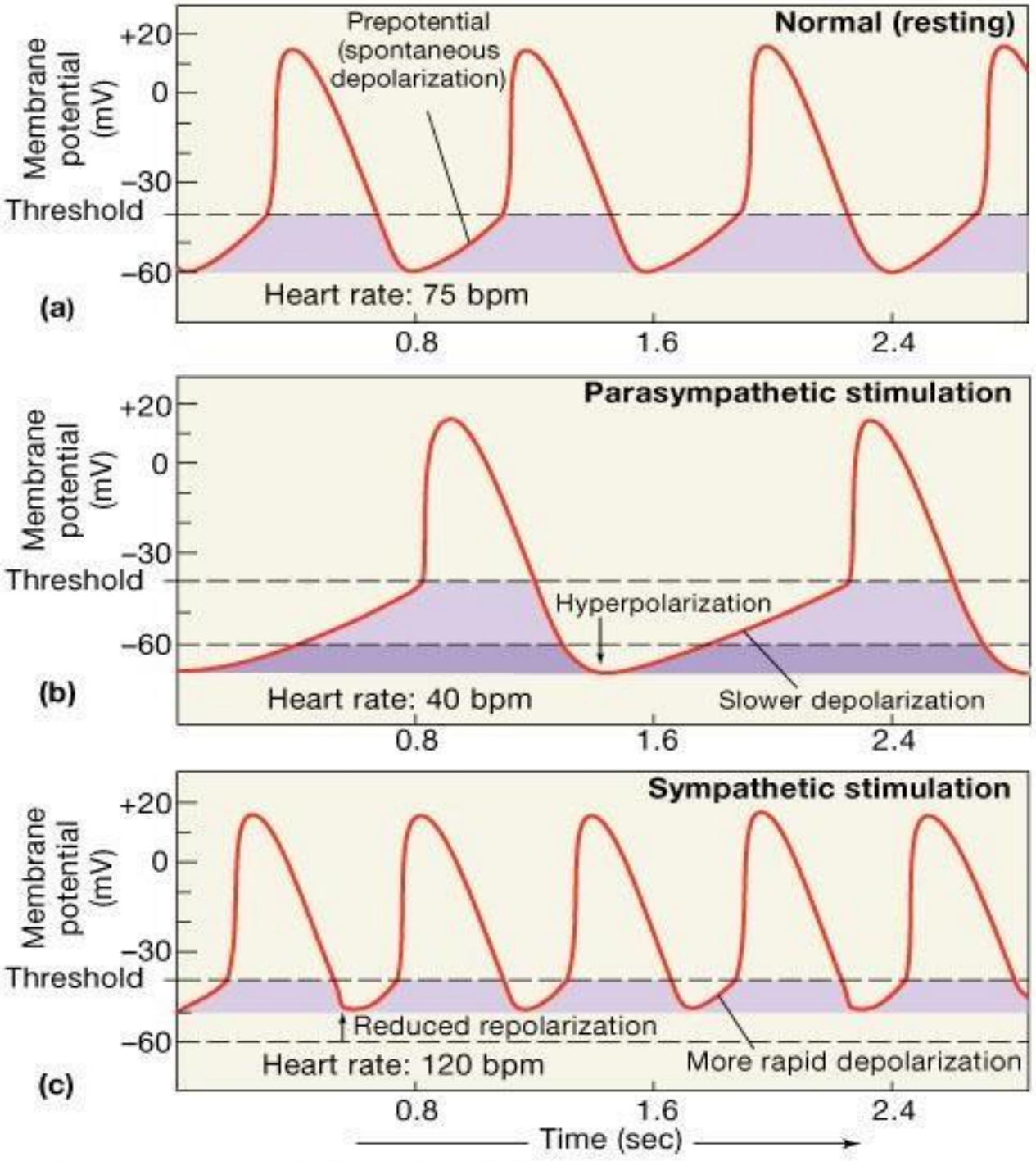
6- Effect of autonomic nervous system on heart

The heart is supplied with both sympathetic and parasympathetic nerves. The parasympathetic nerves are distributed mainly to the SA and AV nodes, and, to a lesser extent, to the muscle of the two atria, and slightly directly to the ventricular muscle. The sympathetic nerves, conversely, are distributed to all parts of the heart, with strong representation to the ventricular muscle, as well as to all the other areas.

-**Parasympathetic fibers:** Vagus (X) nerve → supply only the atria, SA & AV node.
-**Sympathetic fibers:** sympathetic ganglia (cervical ganglia & superior thoracic ganglia T1-T4). → supply all parts of the heart.

-To understand the effect of sympathetic and parasympathetic on the heart, you should be familiar with these terms:

1- **Chronotropic effect**: produce changes in heart rate.
2- **Dromotropic effect**: produce changes in conduction velocity.
3- **Inotropic effect**: intrinsic ability of cardiac muscle to develop force at a given muscle length (contractility).



- **Sympathetic** – increases heart rate by ↑ Ca^{+2} & I_f channel (net Na^+) flow, and decreases K +
- **Parasympathetic** – decreases rate by ↑ K^+ efflux & ↓ Ca^{+2} influx (opposite to before)

6- Effect of autonomic nervous system on heart

PARASYMPATHETIC INNERVATION TO THE HEART:

Increase the permeability of the cardiac cells to K^+ and decrease its permeability to Na^+ and Ca^{2+} in response to ACH, which causes hyperpolarization (mainly because of increased K+ permeability). This causes decreased transmission of impulses, maybe temporarily, stopping the heart rate.

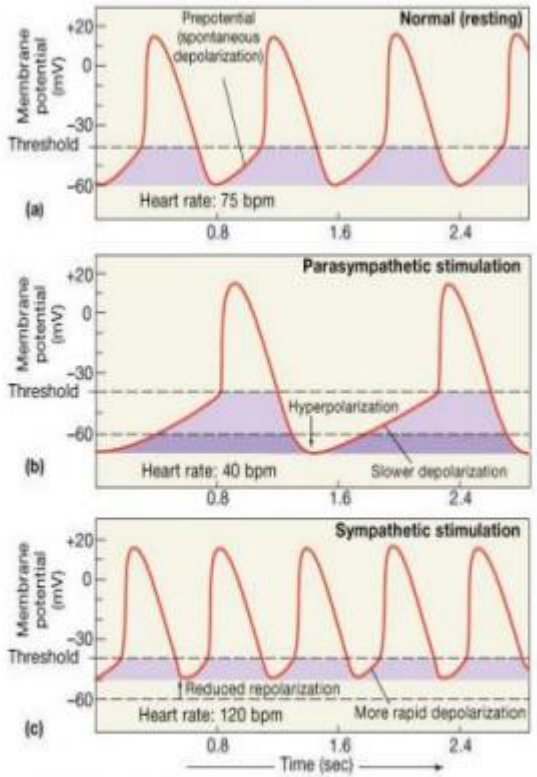
Parasympathetic effects:

- ✓ **Decreases the heart rate** (negative chronotropic effect): Due to increasing the permeability for potassium (efflux) and decreasing it for sodium and calcium, the resting membrane potential becomes more negative→the slow depolarization occurs slower (decreasing the slope of phase 4) →takes more time to reach threshold→ the heart rate decreases.
- ✓ **Negative inotropic and dromotropic** effects on the *atria* only.
- ✓ **Has no effect on the contractility of ventricles**. As vagus nerve does not supply ventricles only atria, so only atrial contractility is affected.

6- Effect of autonomic nervous system on heart

SYMPATHETIC INNERVATION TO THE HEART:

Increase the permeability of the cardiac cells to Na^+ and Ca^{2+}, mediated by epinephrine and norepinephrine results in:



- ✓ Increase the heart rate **(positive chronotropic effect)**: Due to increasing the permeability to sodium (influx) and calcium, the resting membrane potential become less negative→the slow depolarization occurs faster (increasing the slope of phase 4) →reaching threshold faster→ the heart rate increases.
- ✓ Increase the strength of contraction **(positive inotropic effect)**: Increasing the permeability to calcium. (note: calcium is not important for conduction system but it is important for contractile cells (ex. ventricular cells)). Force of contraction increases in atria and ventricles.
- ✓ Increase the rate of conduction of impulse **(positive dromotropic effect)**.

Effect of autonomic nerve activity on the heart

Region affected	Sympathetic Nerve	Parasympathetic Nerve
SA node	Increased rate of diastole depolarization ; increased cardiac rate	Decreased rate of diastole depolarization ; Decreased cardiac rate
AV node	Increase conduction rate	Decreased conduction rate
Atrial muscle	Increase strength of contraction	Decreased strength of contraction
Ventricular muscle	Increased strength of contraction	No significant effect