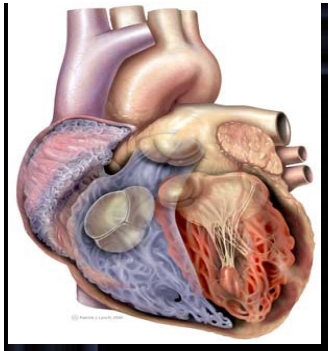
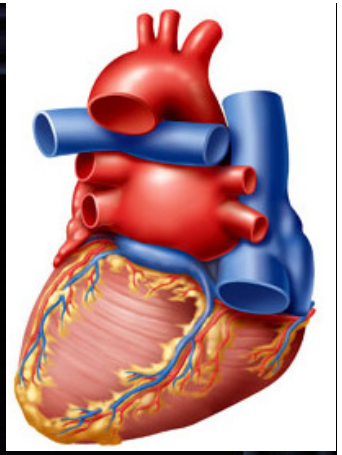
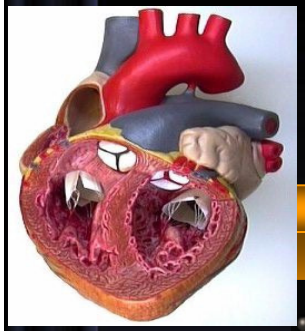
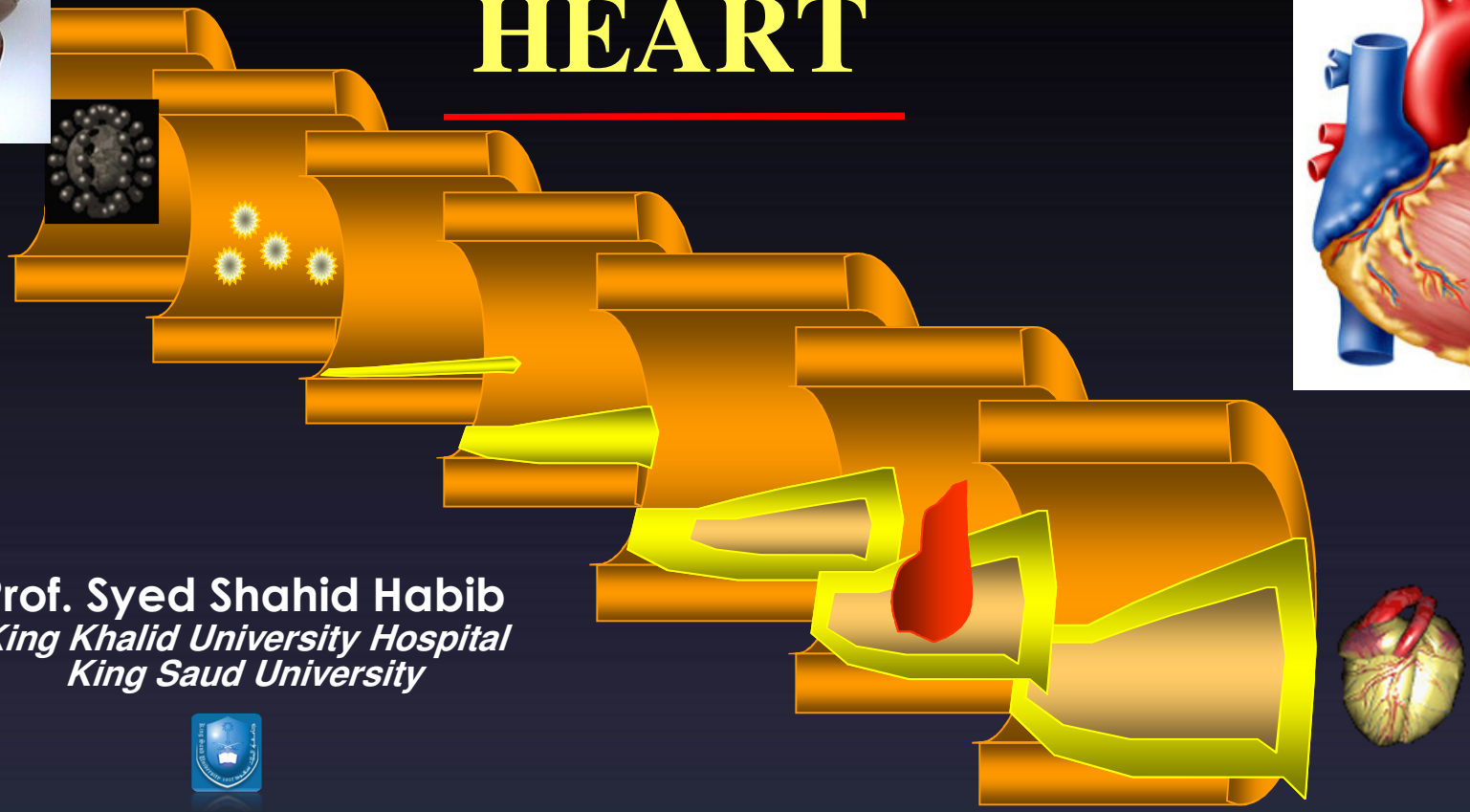


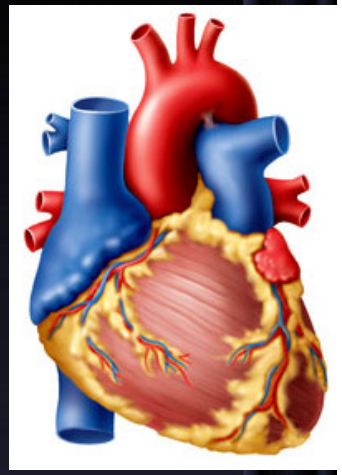




CARDIOVASCULAR SYSTEM

PROPERTIES OF HEART





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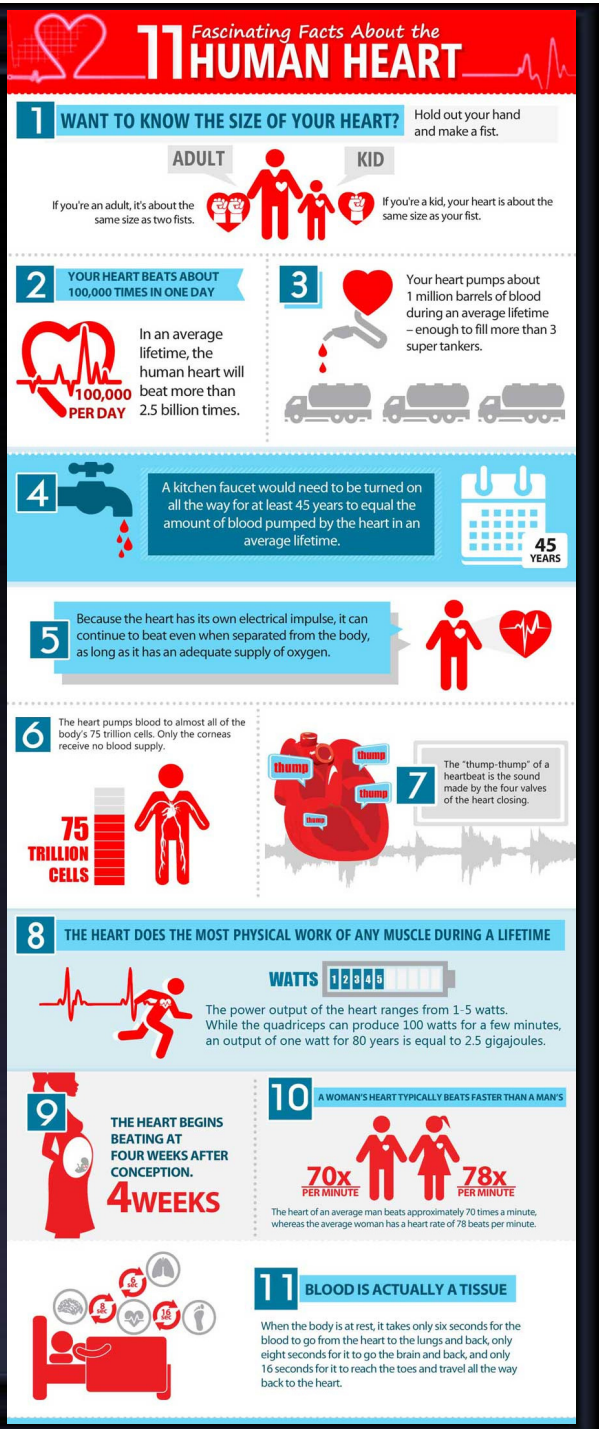
Points to Note

- ***The slides are for guidance and are not the replacement for your text book***
- ***Source of this lecture is Guyton 13th Ed and BRS 5th Ed.***
- ***Prerequisites for this lecture are that you should know about Membrane transport mechanisms, Ionic composition (ICF & ECF) , Syncytium and physiology of skeletal muscle contraction***

Facts About Our Heart

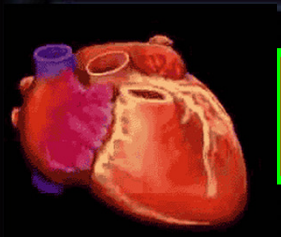
- **Size of a fist and weighing about 250 grams**
- **In lifetime 2,500 million times and pumps 110 million gallons of blood.**
- **Every day, your heart creates enough energy to drive a truck for 20 miles (32 km).**
- **In a lifetime, that is equivalent to driving to the moon and back**
- **Our heart has its own electrical impulse, it can continue to beat even when separated from the body, as long as it has an adequate supply of oxygen**



OBJECTIVES

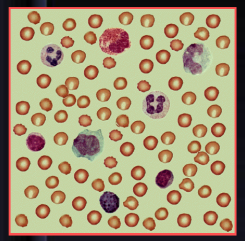
At the end of this lecture you should be able to

- Enumerate the properties of heart
- Explain cardiac muscle action potential and differentiate it from skeletal muscle action potential
- Describe characteristics of myocardial contraction
- List the components of conductive system of the heart
- Explain why SA node is the pacemaker of heart
- Elaborate effect of ANS, Ions and temperature on heart



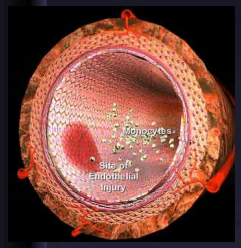
THE HEART

Serves as a pump to generate pressure



THE BLOOD

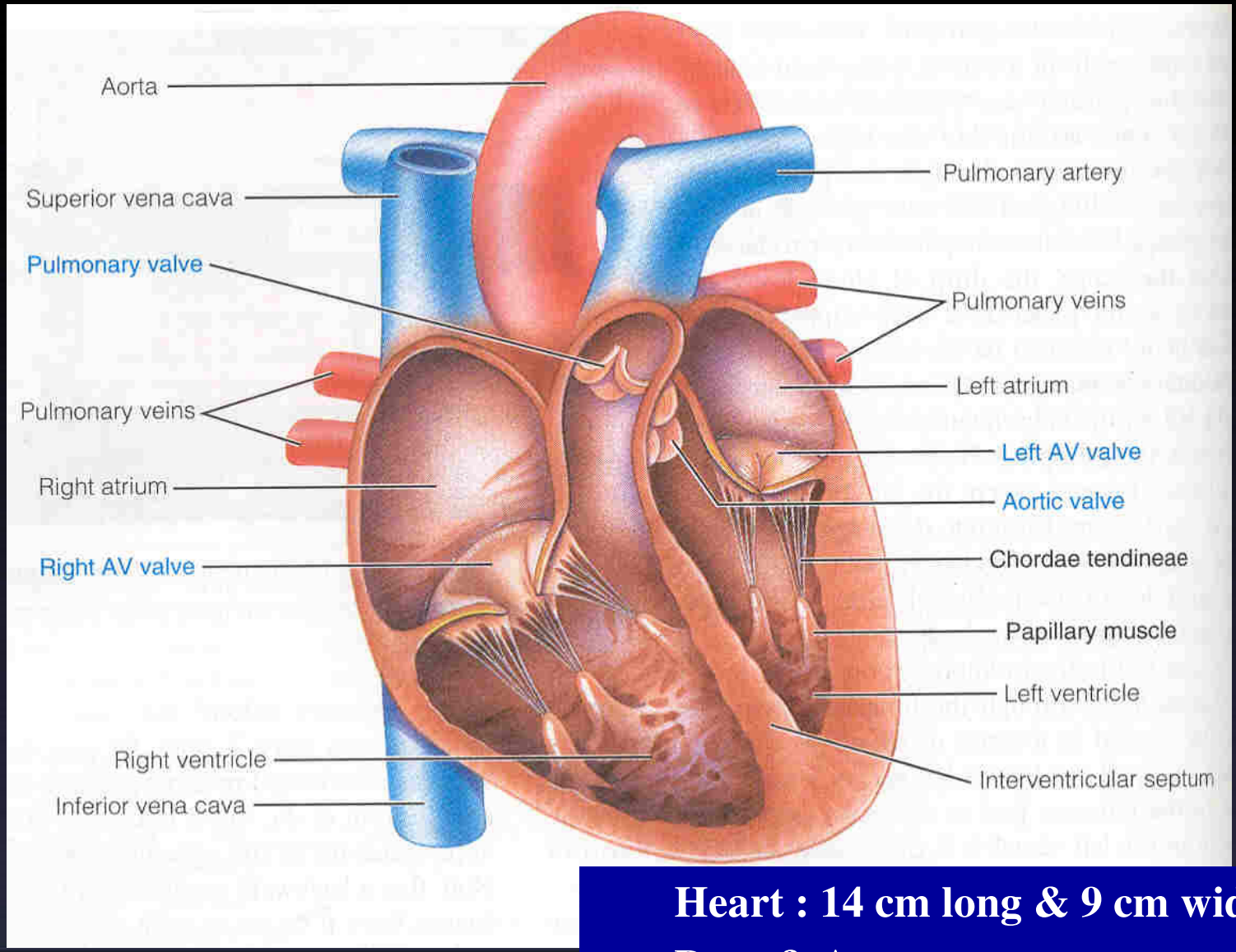
Serves as the transport medium



THE BLOOD VESSELS

Serve as the passageways for blood

Structure of the Heart



Heart : 14 cm long & 9 cm wide.

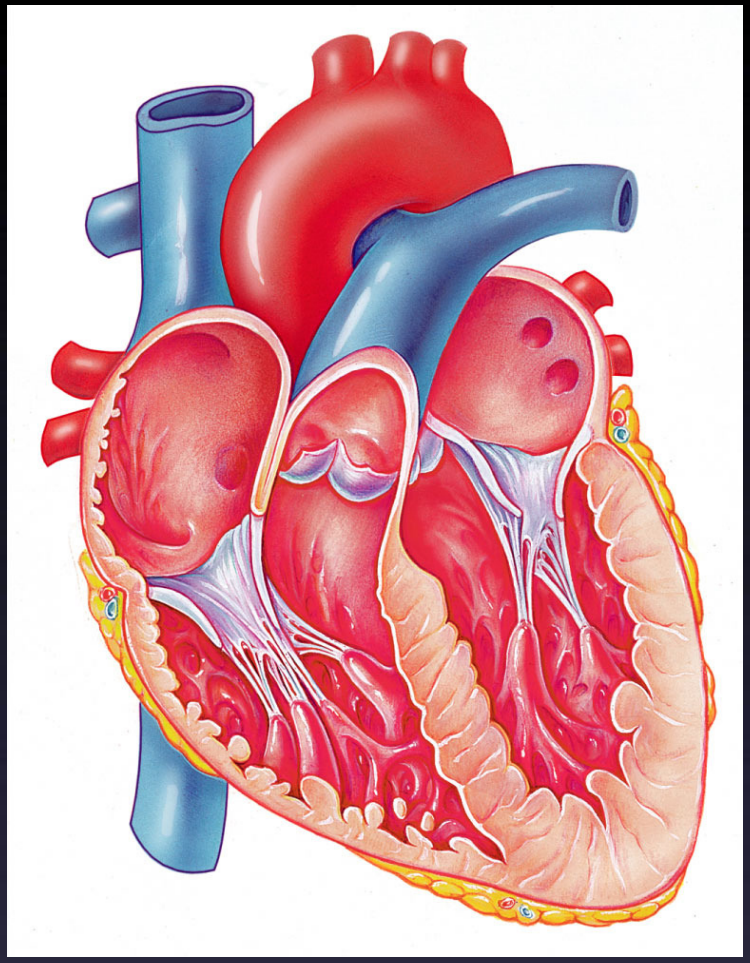
Base & Apex

HEART

- Between Atria and Ventricles there is layer of dense connective tissue known as fibrosis skeleton
- Atria attach to the upper margin of fibrous Skelton
- Ventricle attach to the lower margin of fibrous Skelton
- Therefore Myocardium of Atria and Ventricle are structurally and functionally separated from each other by fibrous skeleton
- Action potential from Atria to Ventricle travel via conductive tissue (It is specialized cardiac tissue)

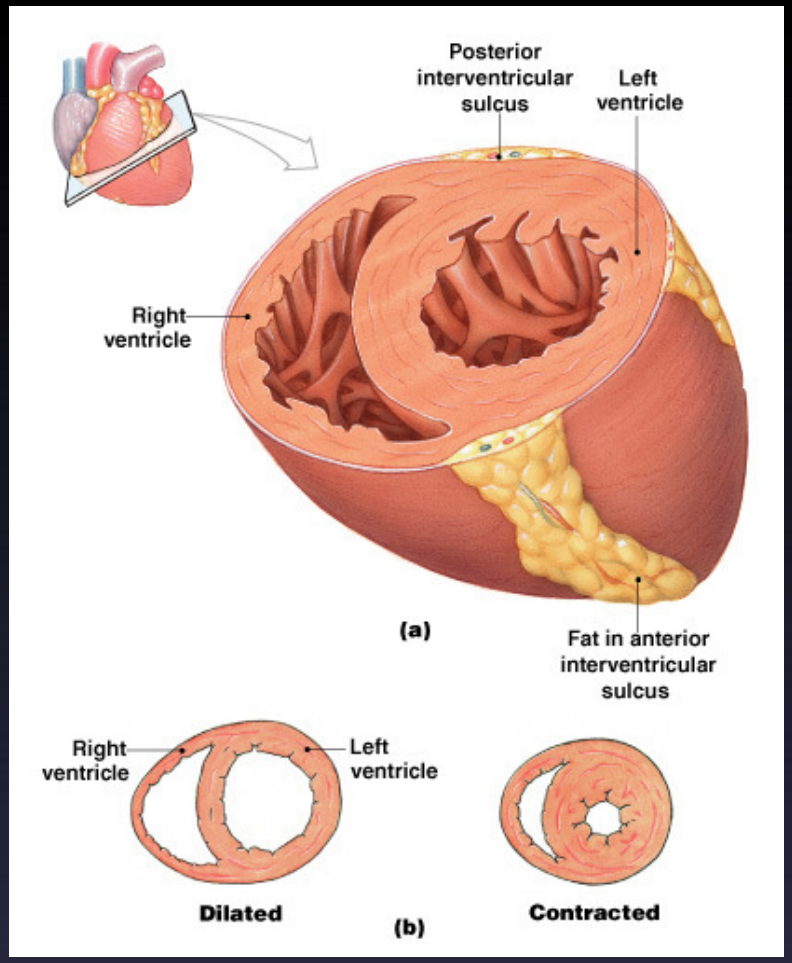
The Heart Chambers

- Atria
  - *Features*
    - small, thin-walled chambers
  - *Functions*
    - receiving chambers for blood returning to the heart from the circulation
    - push the blood into the adjacent ventricles.



The Heart Chambers

- Ventricles
  - Features
    - make up most of the mass of the heart
    - the walls of the left ventricle are 3X thicker than those of the right



HEART

- Rt. Atrium is separated from Left atrium by Interatrial septum
- Rt. Ventricle is separated from Left Ventricle by Interventricular septum
- Myocardial cells are joined together by Intercalated disc (cell membrane) which has Gap Junctions
- In the fibrous skeleton which separates Atria and Ventricle, there are four Valves

The Syncytial Interconnecting Nature of Cardiac Muscle

- The cell membranes fuse with one another in such a way that they form permeable "communicating" junctions (gap junctions) that allow almost totally free diffusion of ions.
- Ions move with ease in the intracellular fluid in cardiac muscle fibers, so that action potentials travel easily from one cardiac muscle cell to the next, past the intercalated discs.
- Therefore heart work as a **syncytium (as one unit)**

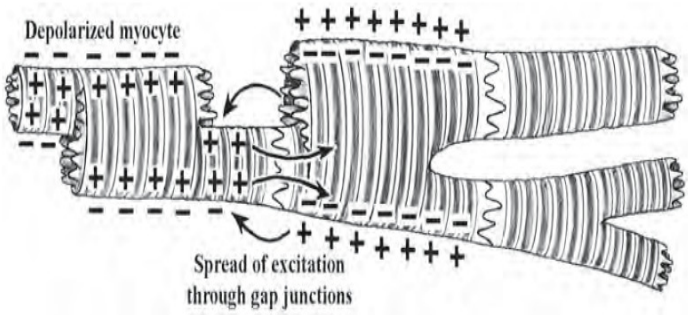
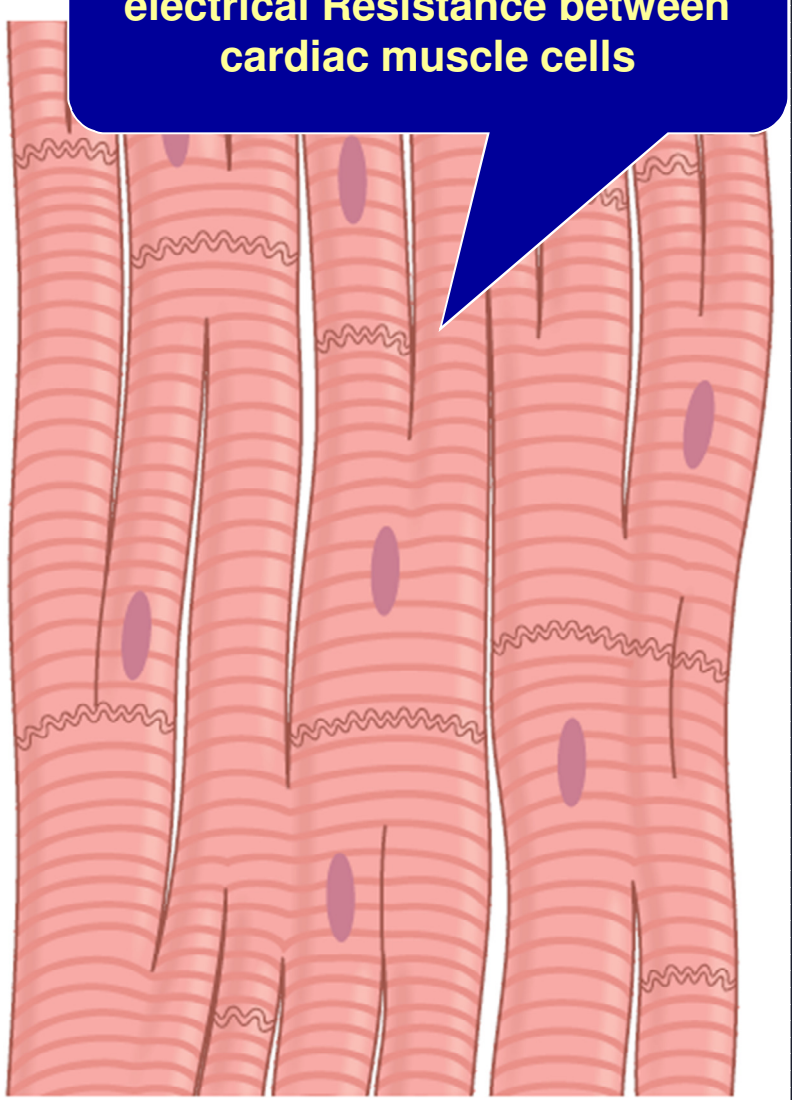


Fig. 11. Shown are several cardiac myocytes in different states of excitation. The depolarization that occurred in the cell on the left causes depolarization of the adjacent cell through cell-to-cell conduction via the gap junctions (nexus). Eventually, all adjoining cells will depolarize. An action potential initiated in any of these cells will be conducted from cell to cell in either direction.

Intercalated Discs Decrease electrical Resistance between cardiac muscle cells



PROPERTIES OF HEART

- Automaticity
- Rhythmicity
- Excitability
- Conductivity
- Contractility

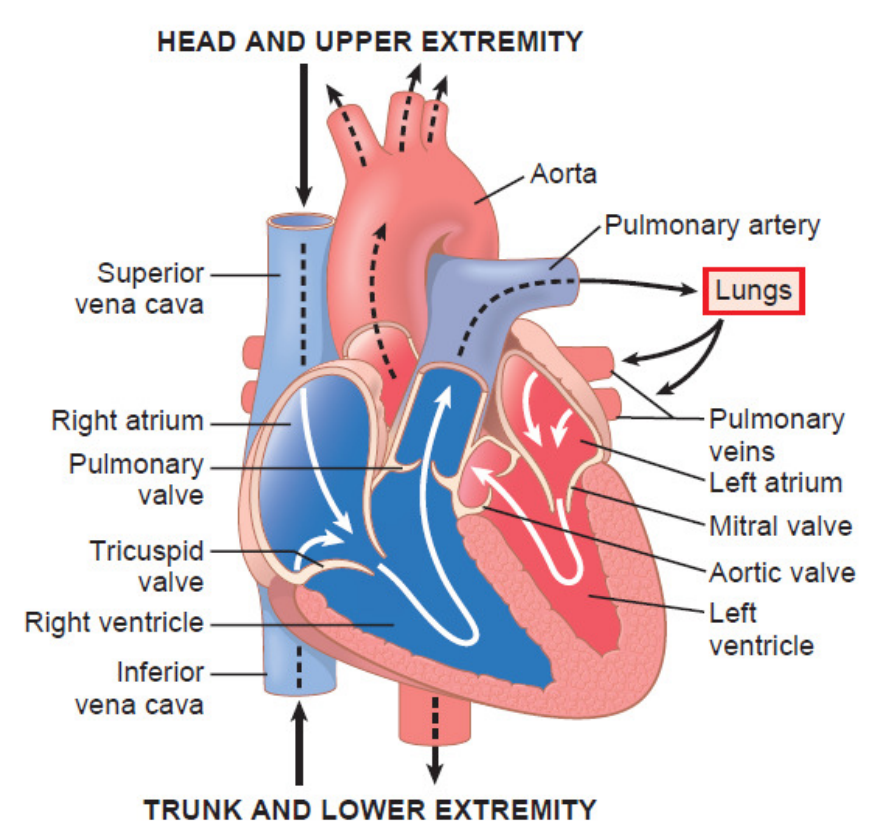


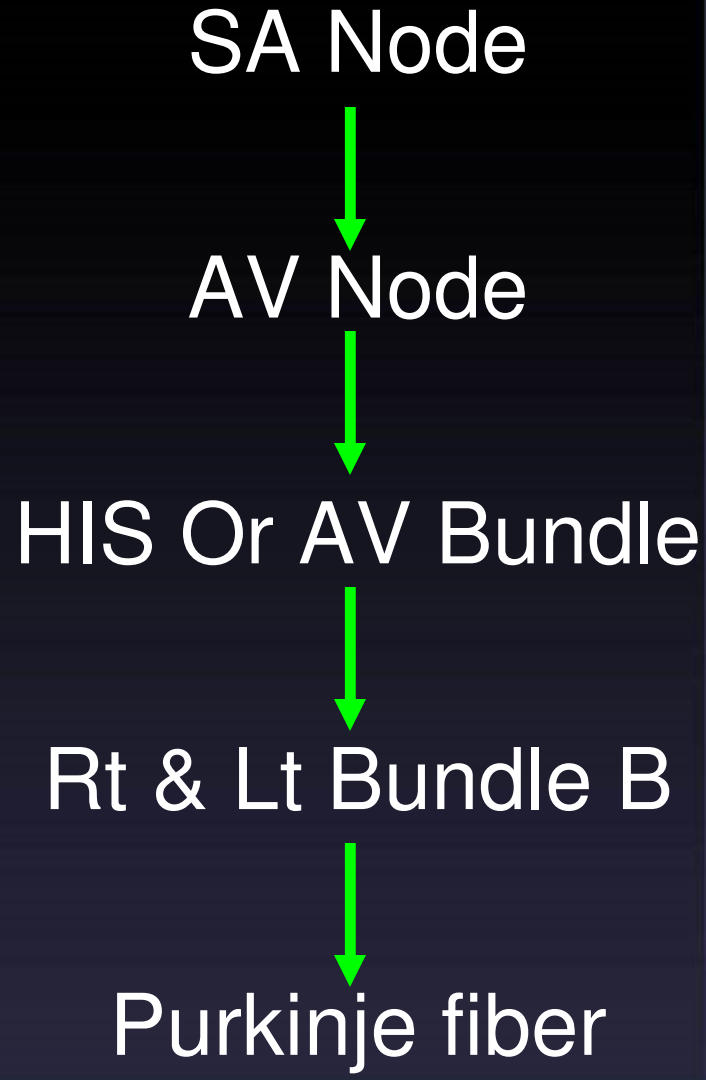
Figure 9-1. Structure of the heart and course of blood flow through the heart chambers and heart valves.

AUTOMATICITY & RHYTHMICITY

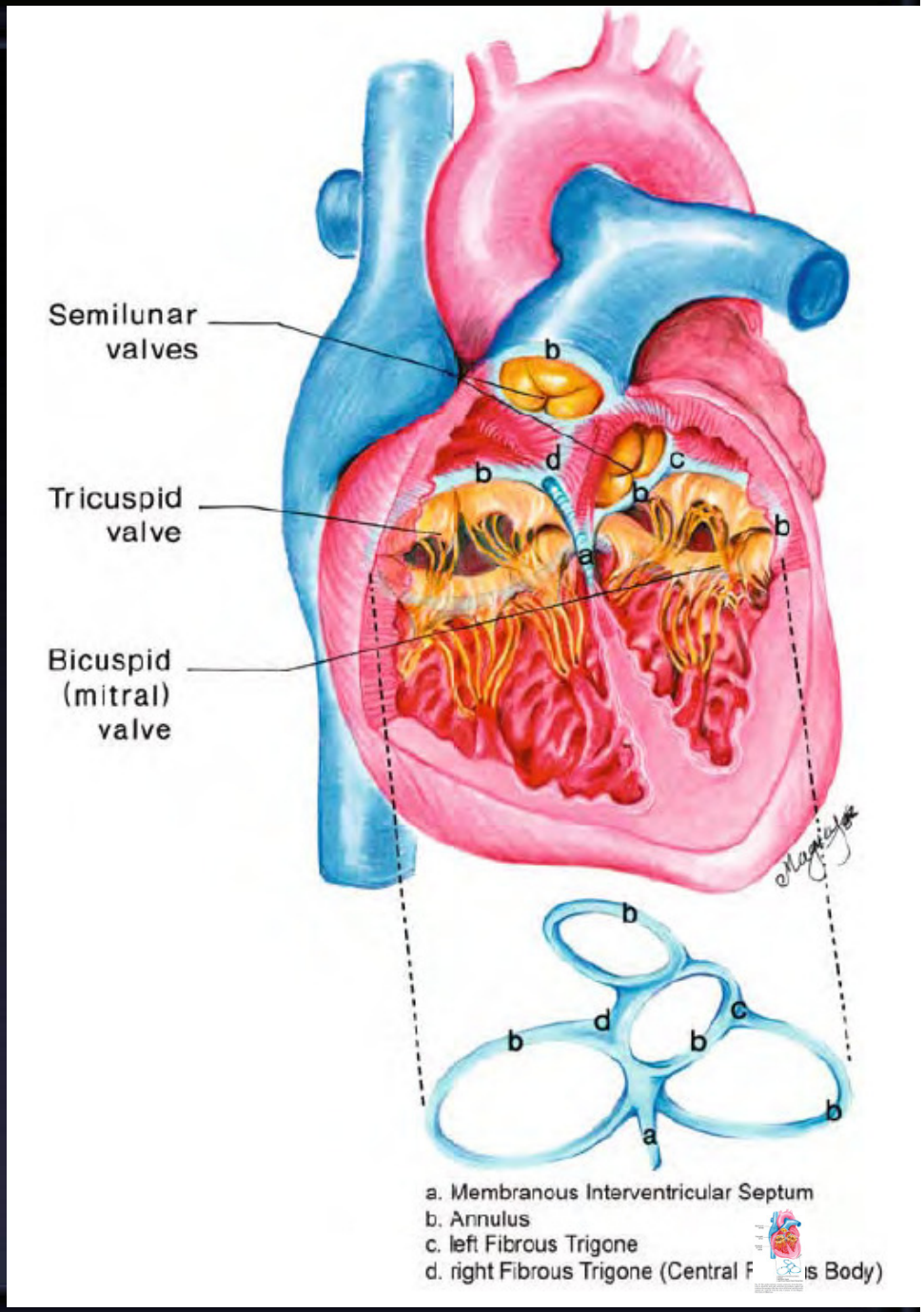
- The sinus node (also called sinoatrial node) is a small, flattened, ellipsoid strip of specialized cardiac muscle about 3 millimeters wide, 15 millimeters long, and 1 millimeter thick.
- The fibers of this node have almost no contractile muscle filaments and are each only 3 to 5 micrometers in diameter, in contrast to a diameter of 10 to 15 micrometers for the surrounding atrial muscle fibers.
- Sinus nodal fibers connect directly with the atrial muscle fibers

CONDUCTIVE SYSTEM OF THE HEART

- **Action Potential that originates in SA node spread to both Atria through intercalated disc and gap junction**
- **From atria it can not pass to ventricle due to fibrous Skelton of heart which separates atria and ventricles**
- **Therefore specialized conducting tissue is required (it is composed of modified Myocardial cells)**



HEART SKELETON



Conductive System Of Heart

Velocity of Signal Conduction in Cardiac Muscle

***Atrial and ventricular muscle fibers* is 0.3 to 0.5 m/sec**

***Purkinje fibers*—is as great as 4 m/sec**

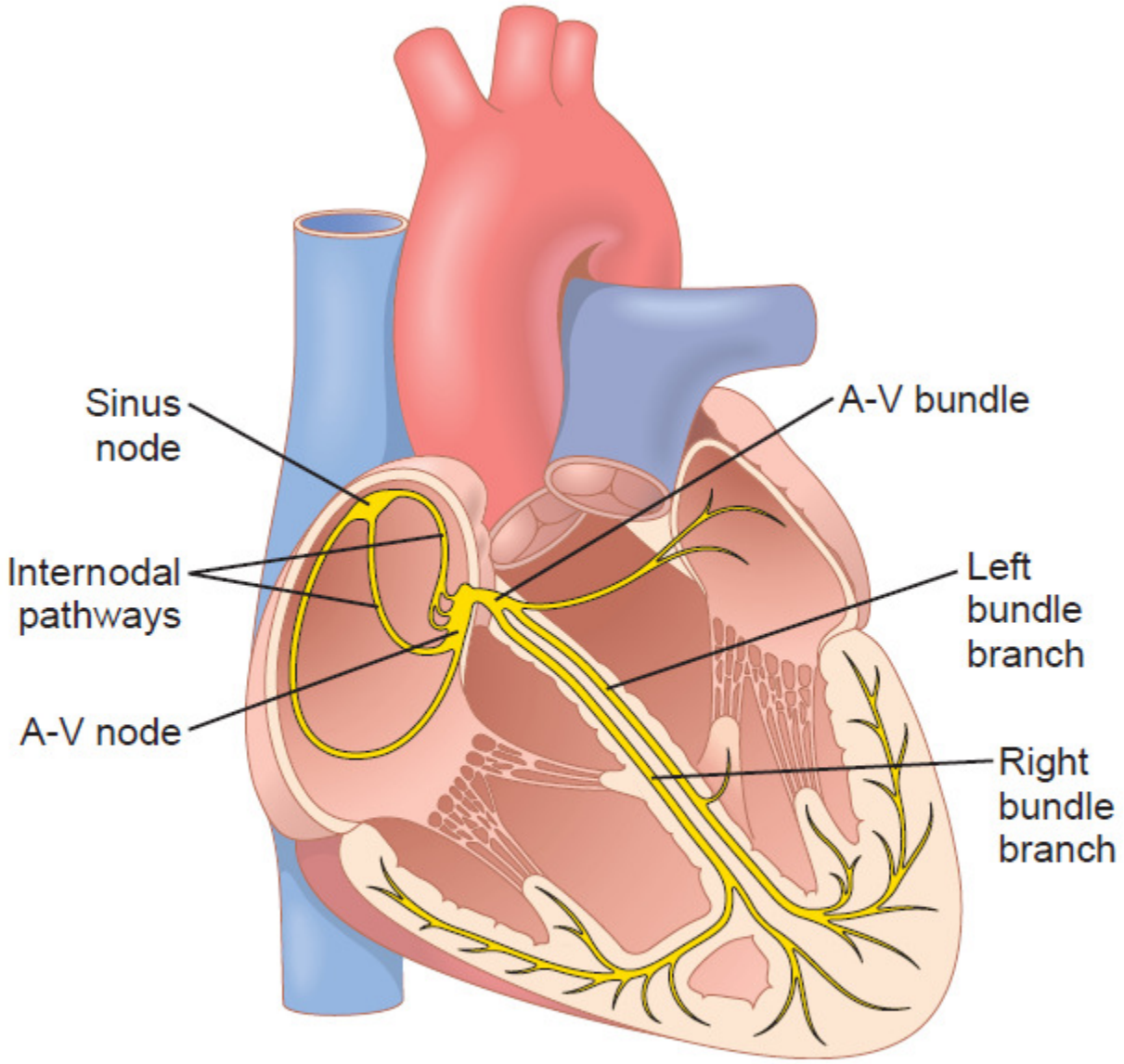
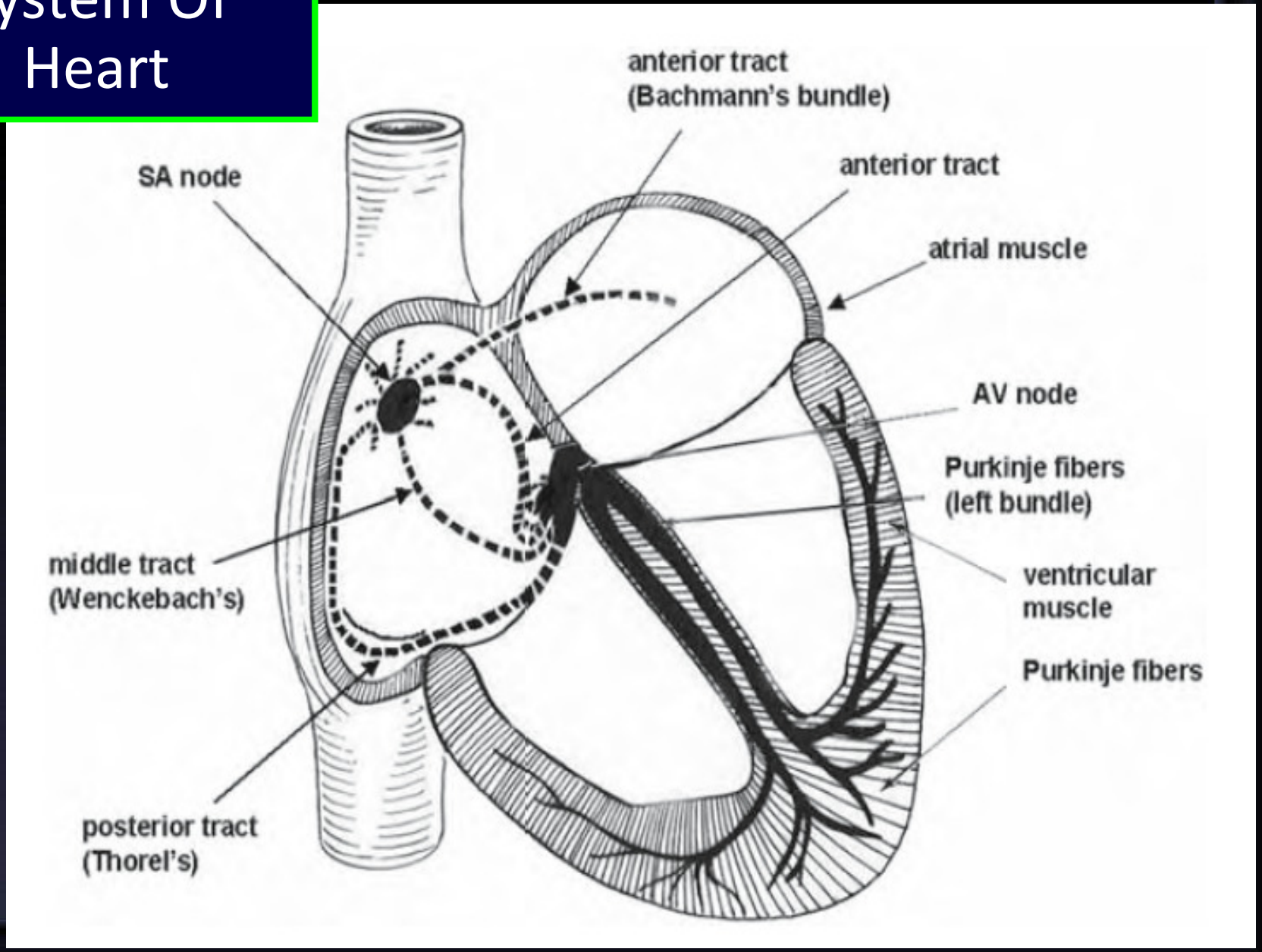


Figure 10-1. Sinus node and the Purkinje system of the heart, showing also the atrioventricular *(A-V)* node, atrial internodal pathways, and ventricular bundle branches.

Conductive System Of Heart



Time lags of Transmission of cardiac impulse through Conductive System Of Heart

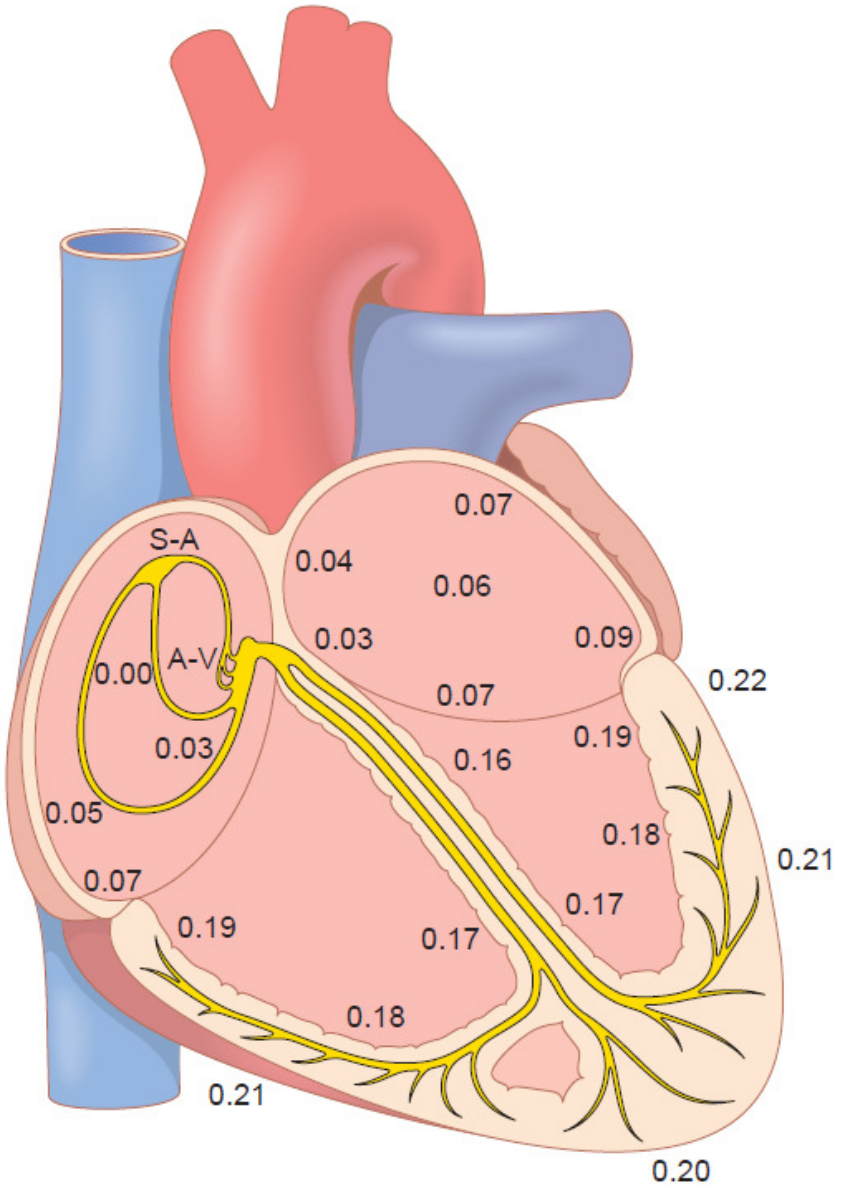
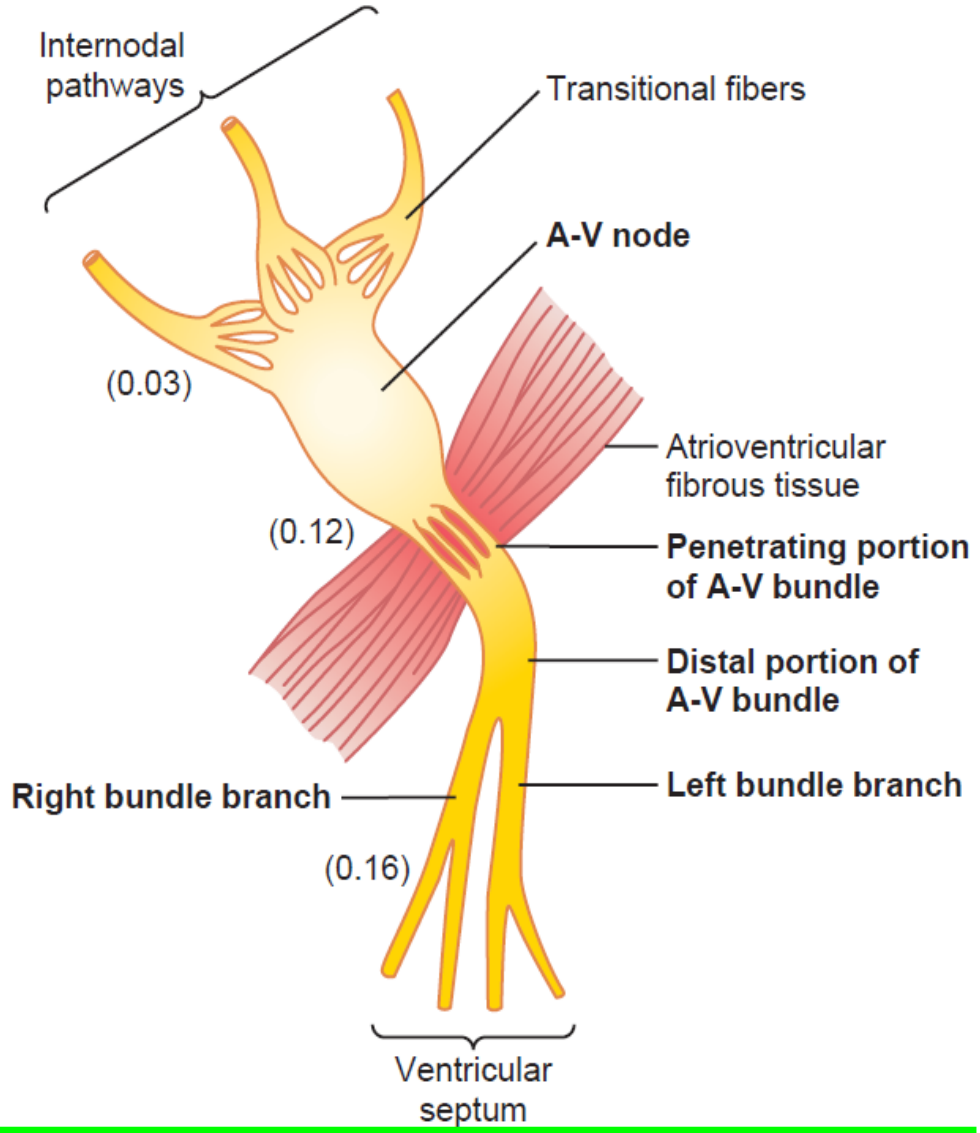


Figure 10-4. Transmission of the cardiac impulse through the heart, showing the time of appearance (in fractions of a second after initial appearance at the sinoatrial node) in different parts of the heart. A-V, atrioventricular; S-A, sinoatrial.

Conductive System Of Heart

AV Nodal Delay

There is a delay of another 0.09 second in the A-V node itself before the impulse enters the penetrating portion of the A-V bundle, where it passes into the ventricles. A final delay of another 0.04 second occurs mainly in this penetrating A-V bundle, is caused mainly by diminished numbers of gap junctions between successive cells in the conducting pathways



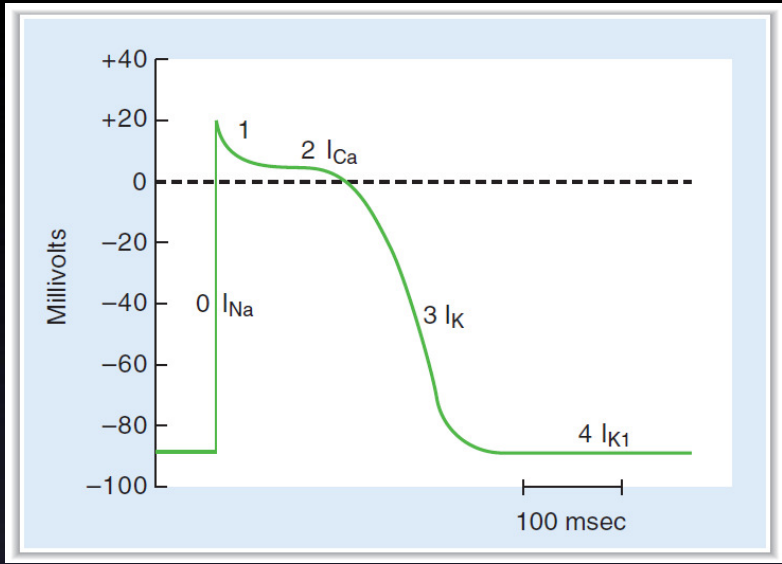
Significance

The delay in AV node causes atrial contraction before ventricular contraction to ensure ventricular filling

TABLE 29–1 Conduction speeds in cardiac tissue.

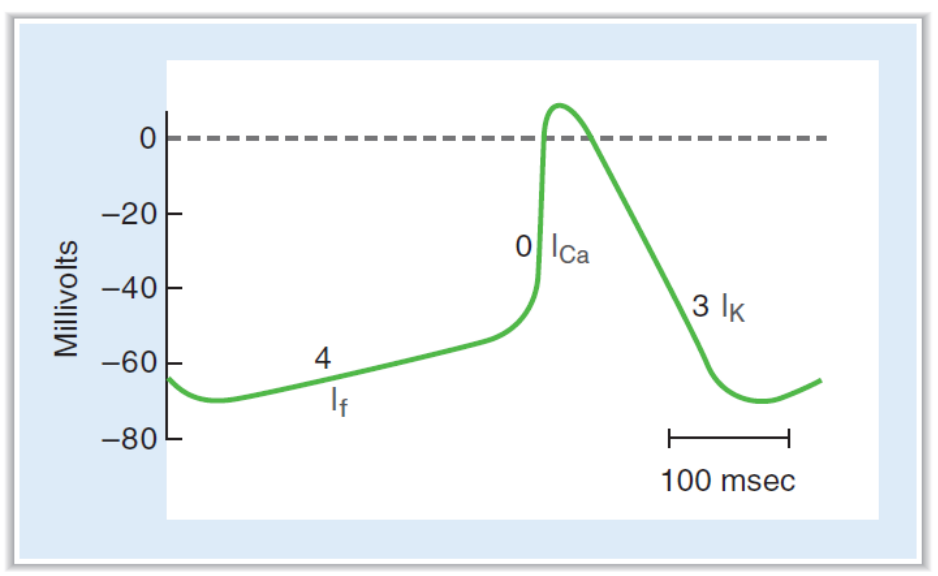
Tissue	Conduction Rate (m/s)
SA node	0.05
Atrial pathways	1
AV node	0.05
Bundle of His	1
Purkinje system	4
Ventricular muscle	1

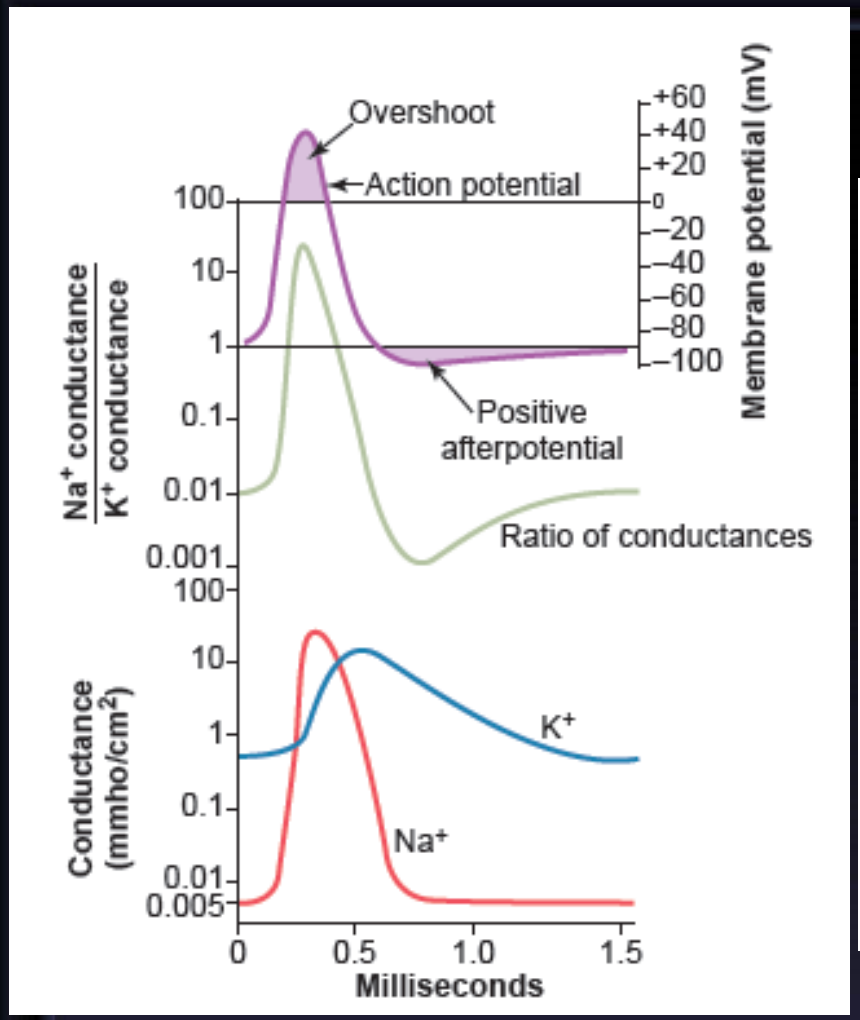
Myocardial AP & Pacemaker Potential

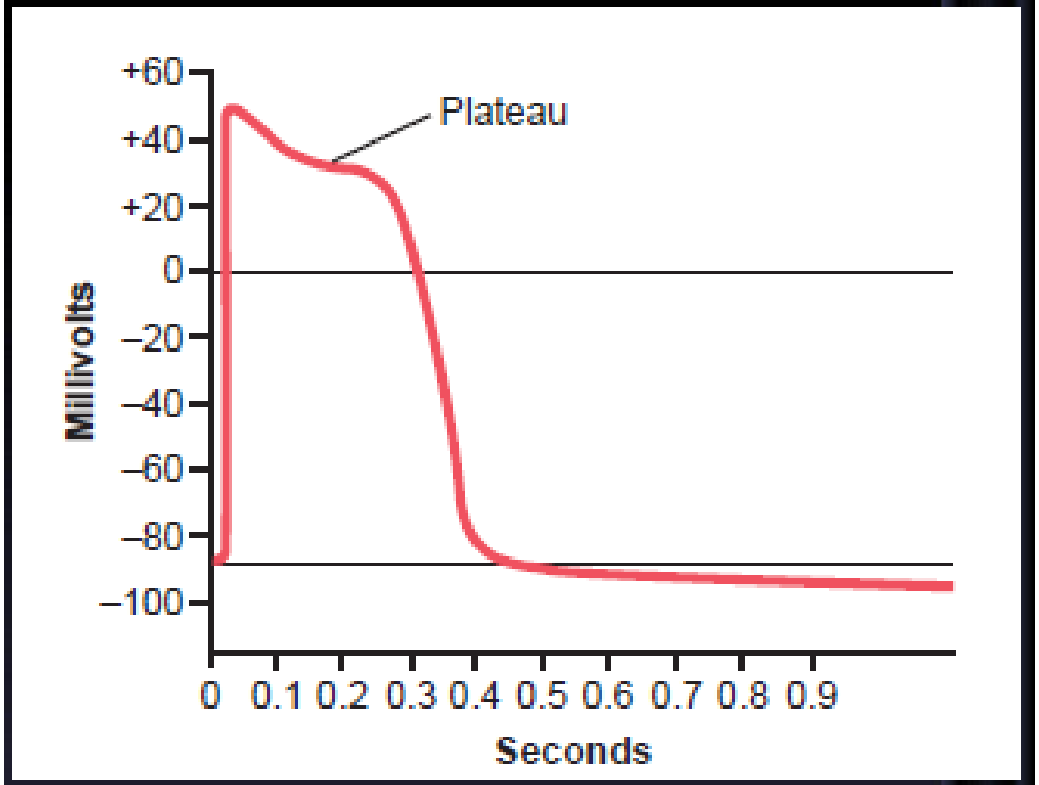


Myocardial AP

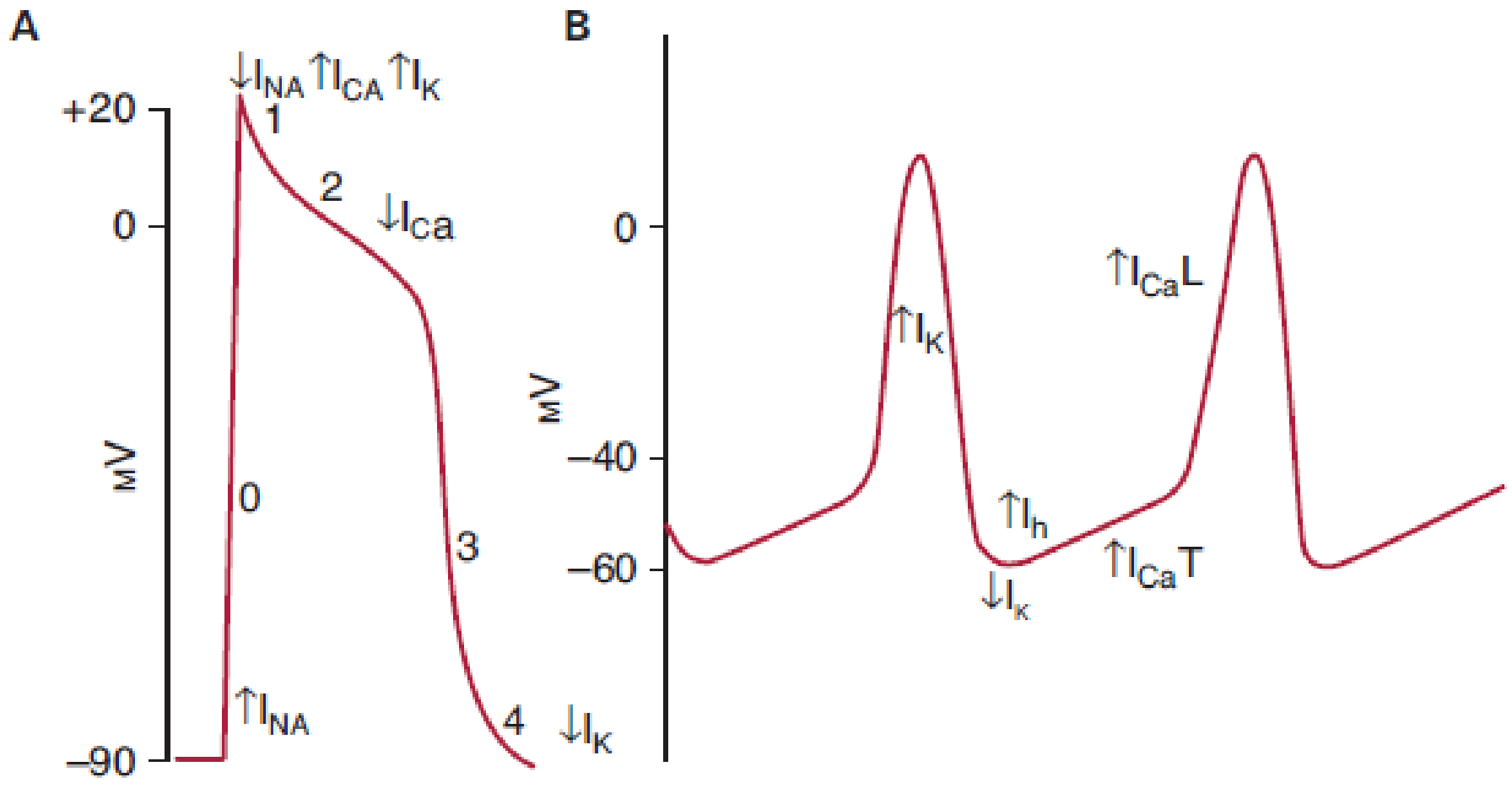
Pacemaker Potential




Overshoot
Action potential
Positive afterpotential
Ratio of conductances
Membrane potential (mV)
+60
+40
+20
0
–20
–40
–60
–80
–100
Na+ conductance / K+ conductance
100
10
1
0.1
0.01
0.001
Conductance (mmho/cm2)
K+
Na+
0.005
0
0.5
1.0
1.5
Milliseconds


Plateau
Millivolts
+60
+40
+20
0
–20
–40
–60
–80
–100
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
Seconds

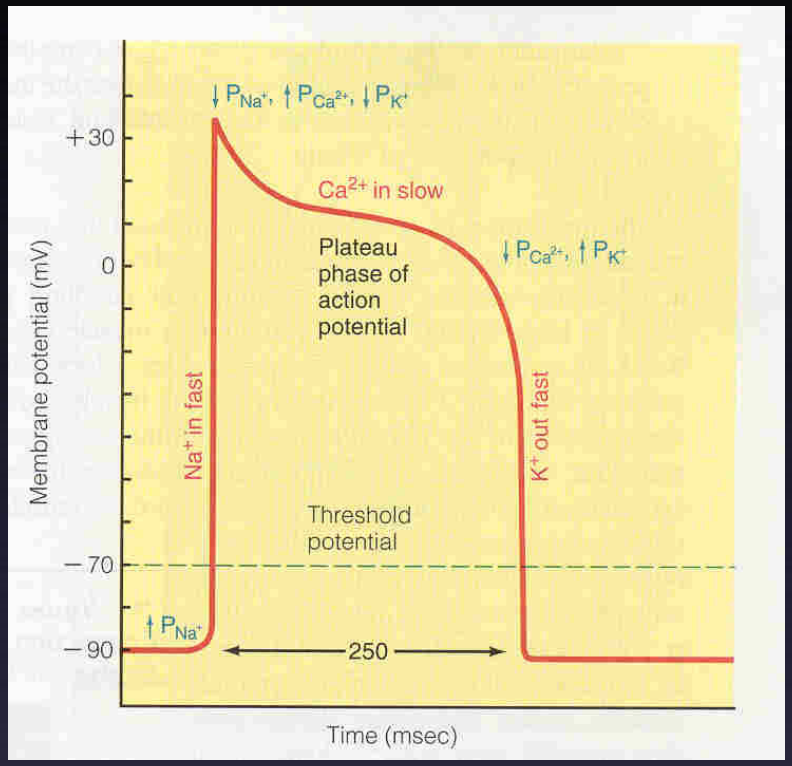
Comparison of Myocardial AP & Pacemaker Potential



Note: Phases 1 and 2 n are not present in the SA node action potential

Myocardial Action Potential

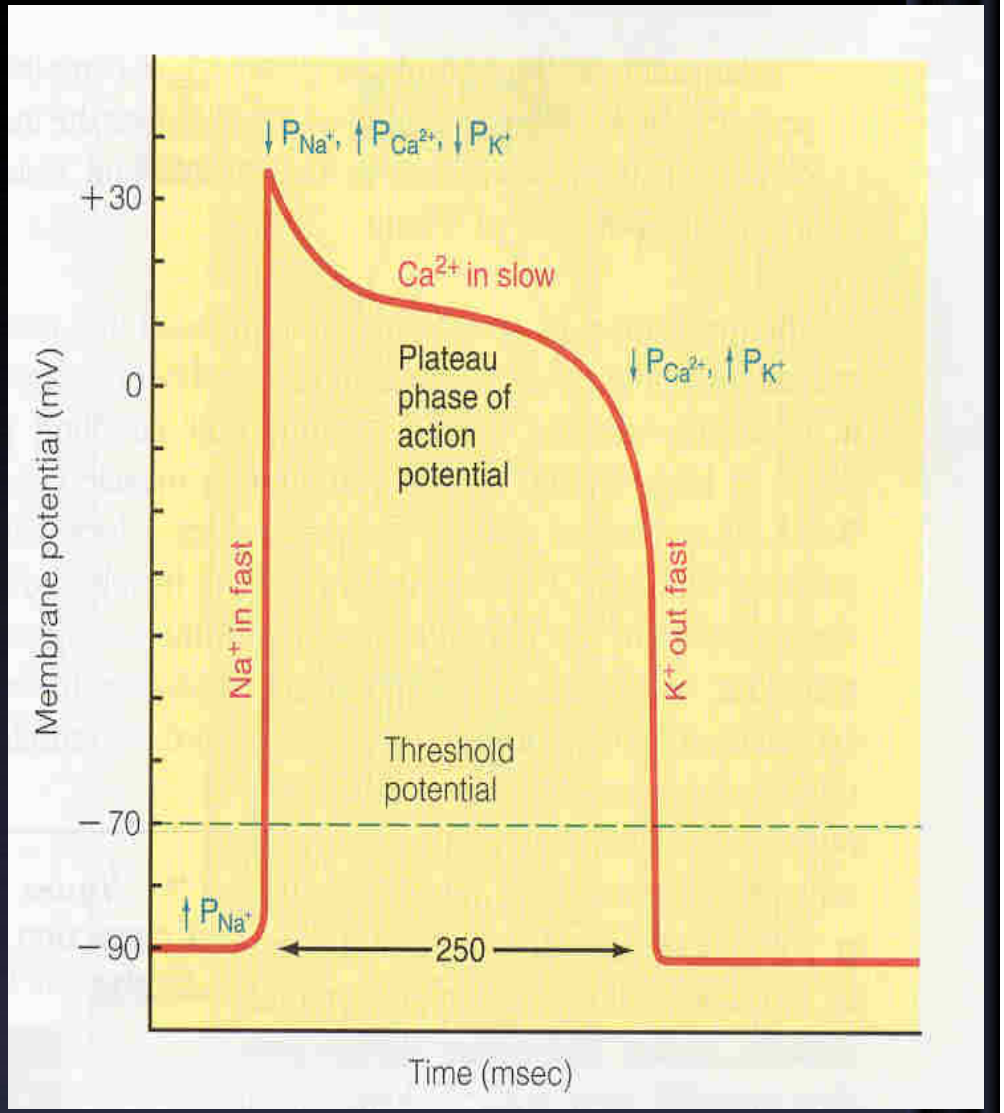
Once myocardial cells are stimulated by action potential originating in SA node, it produces its own action potential



Action Potential From Ventricular Muscle Fiber

Myocardial Action Potential

- **RMP** is about -90mv (**Phase 4**)
- Rapid depolarization (**Phase 0**) due to Na+ influx
- **Initial Rapid repolarization** (**Phase 1**) Due to closure of Na+ channels
- **Plateau** (**Phase 2**) is maintained for 200 – 300 ms due to Ca++ influx
- **Repolarization** (**Phase 3**) due to K+ efflux



Myocardial AP

- RMP is about -90mv (Phase 4)
- Rapid depolarization (Phase 0) due to Na+ influx
- Initial Rapid repolarization (Phase 1) Due to closure of Na+ channels
- Plateau (Phase 2) - is maintained for 200 – 300 ms due to Ca++ influx
- Repolarization (Phase 3) – due to K+ efflux

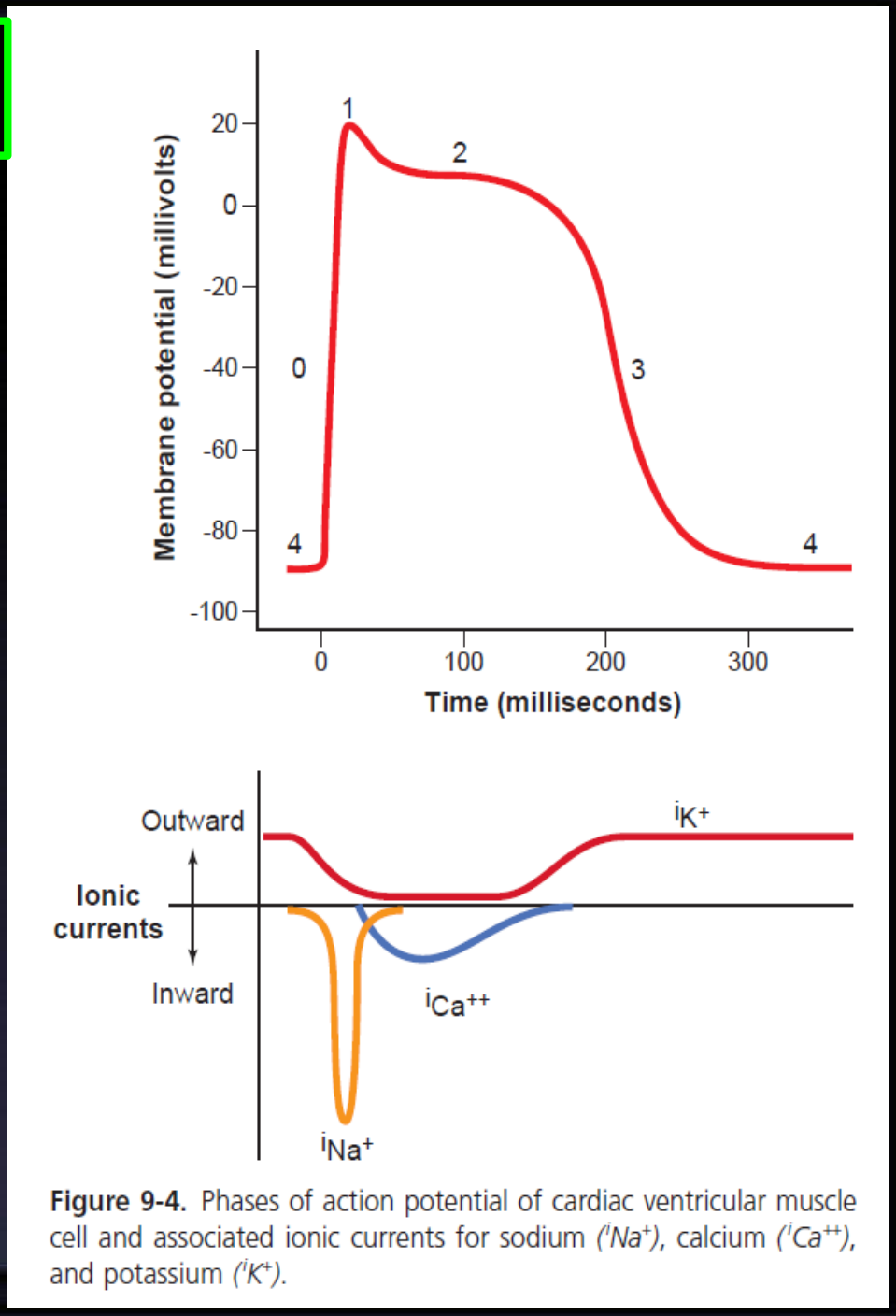


Figure 9-4. Phases of action potential of cardiac ventricular muscle cell and associated ionic currents for sodium ($^{i}Na^{+}$), calcium ($^{i}Ca^{++}$), and potassium ($^{i}K^{+}$).

Refractory Period of Cardiac Muscle

- **During which a normal cardiac impulse cannot re-excite an already excited area of cardiac muscle. The normal refractory period of the ventricle is 0.25 to 0.30 second**
- **Relative refractory period is 0.05 sec; more difficult than normal to excite but nevertheless can be excited by a very strong excitatory signal, as demonstrated by the early "premature" contraction**
- **Atrial RF is much shorter than ventricular muscle 0.15 vs 0.25-0.30 sec**

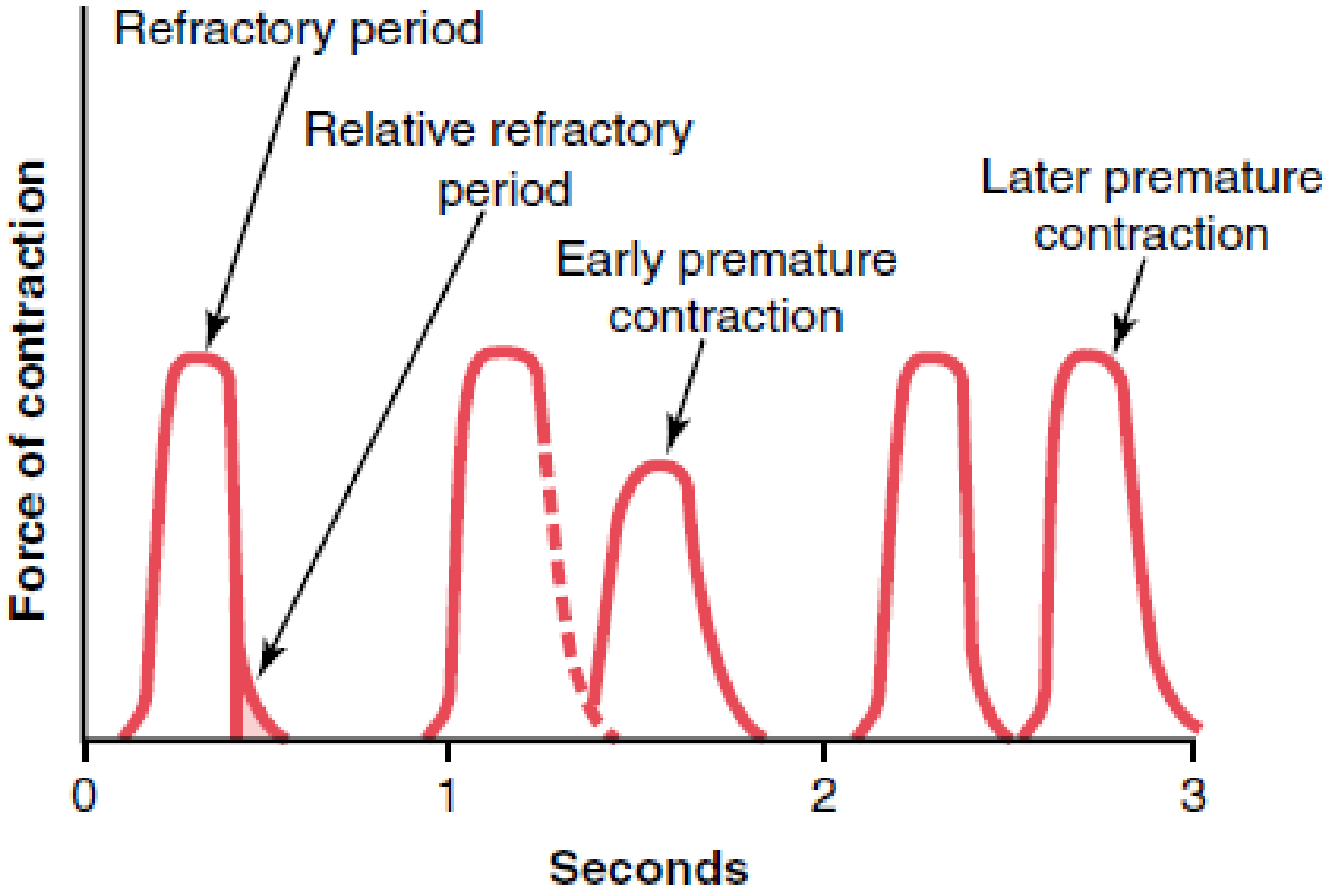


Figure 9-4 Force of ventricular heart muscle contraction, showing also duration of the refractory period and relative refractory period, plus the effect of premature contraction. Note that premature contractions do not cause wave summation, as occurs in skeletal muscle.

Changes in excitability over the course of the action potential…… refractory periods

1. Absolute refractory period (ARP) 0.25 to 0.30 Sec

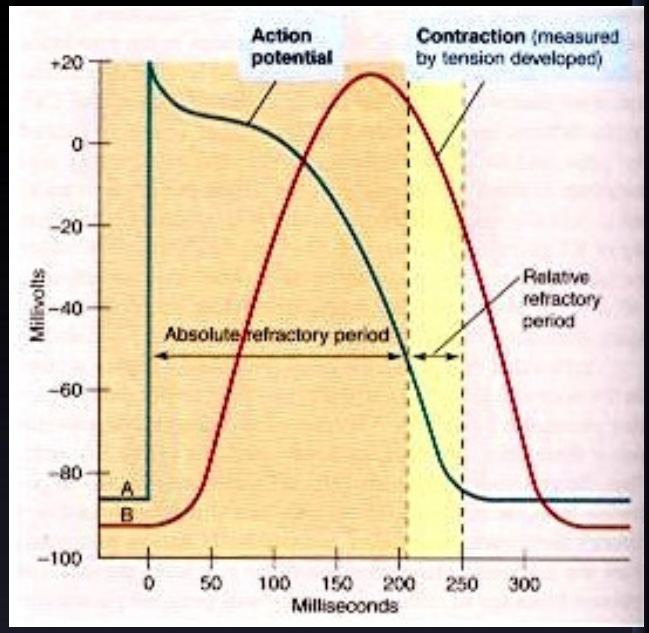
- begins with the upstroke of the action potential and ends after the plateau.
- No action potential can be initiated, regardless of how much inward current is supplied.

2. Effective refractory period (ERP)

- is slightly longer than the ARP.
- is the period during which a conducted action potential cannot be elicited.

3. Relative refractory period (RRP) 0.05 sec

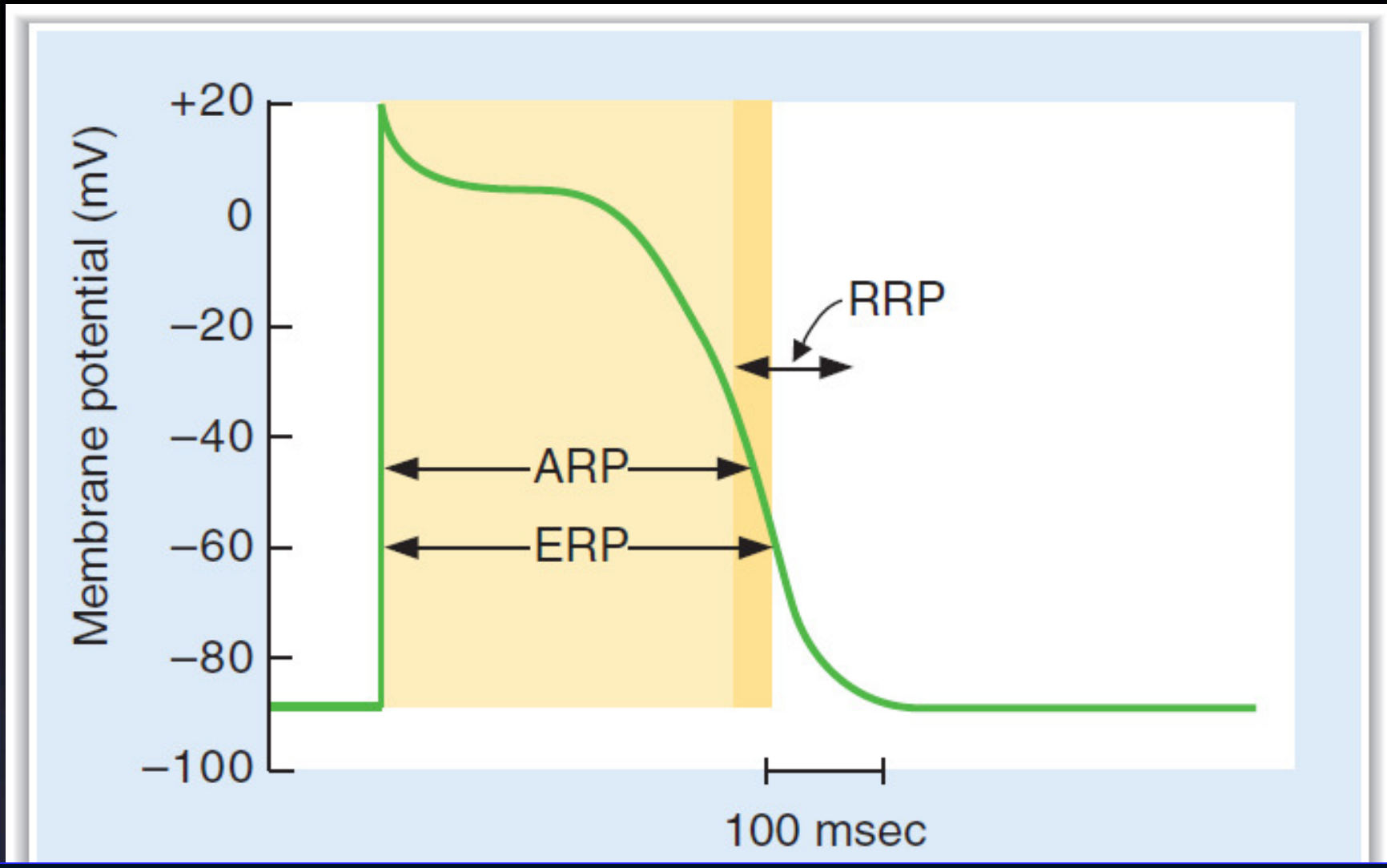
- is the period immediately after the ARP when repolarization is almost complete.
- is the period during which an action potential can be elicited, but more than the usual inward current is required.



Ventricle contraction occurs during absolute refractory period therefore two contraction cannot be summated therefore heart muscle can not be Tetanized

Eg: early "premature" contraction

Changes over the course of the action potential. These changes in excitability are described by refractory periods



Absolute (ARP), effective (ERP), and relative refractory periods (RRP) in the ventricle.

SA Nodal AP

- 1-At the peak of each impulse, I_K begins and brings about repolarization. **[PHASE 3]**

- 2-I_K then declines, and a channel permeable to both Na^+ and K^+ is activated **["h" channel or funny "f " channel]** . As I_h increases, the membrane begins to depolarize, forming the first part of the prepotential

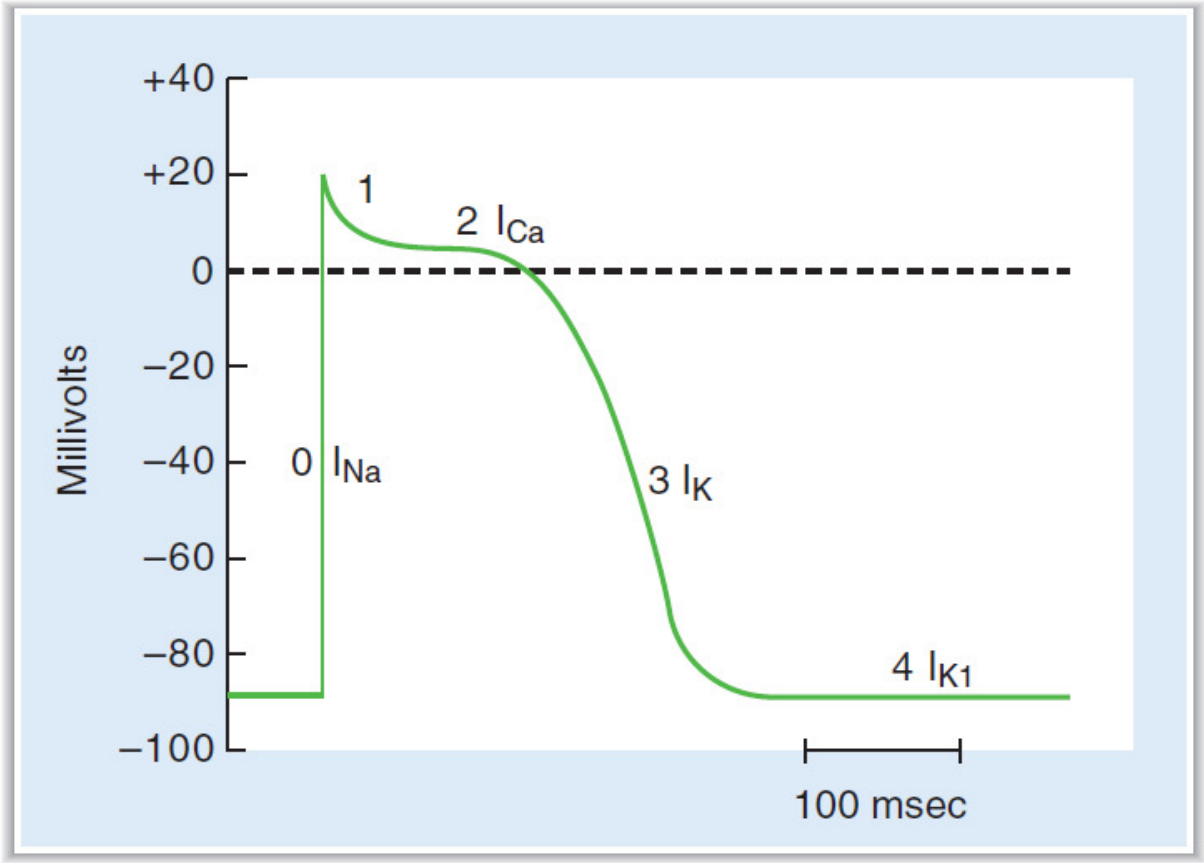
Phases 1 and 2 are not present in the SA node action potential

SA Nodal AP

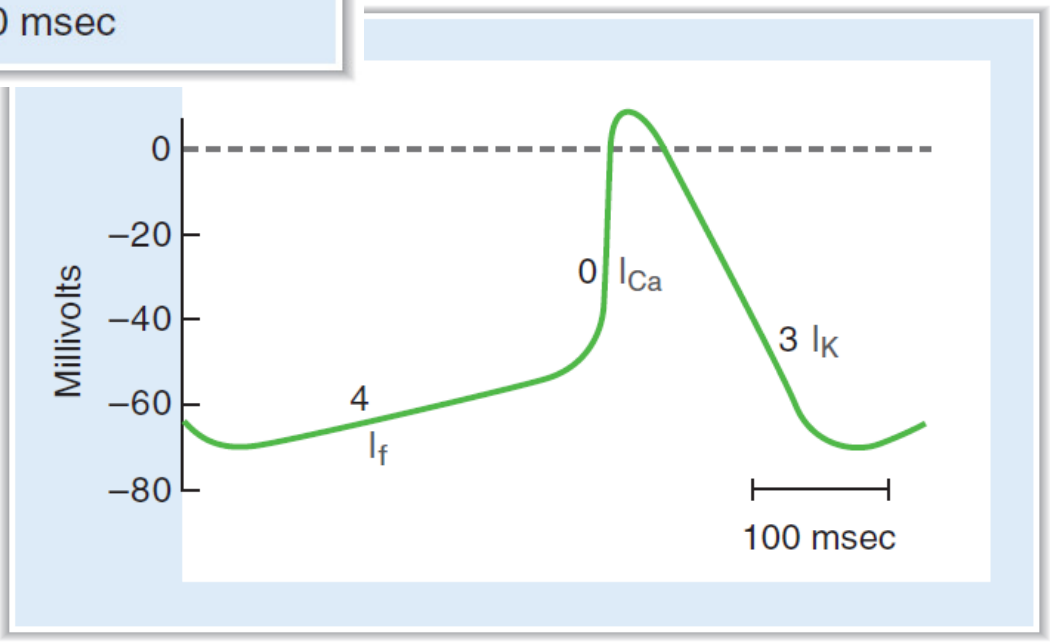
•3-Ca 2+ channels then open. two types in the heart, the T (for transient) channels and the L (for long-lasting) channels. . The calcium current (I_{Ca}) due to opening of T channels completes the prepotential, **[PHASE 4]**

•4-and I_{Ca} due to opening of L channels produces the impulse. **[PHASE 0]** Also local Ca^{2+} release from the sarcoplasmic reticulum (Ca^{2+} sparks) occurs during the prepotential.

Phases 1 and 2 are not present in the SA node action potential



Membrane potential begins at -60mv and slowly depolarizes to -40mv, which is threshold for producing Action Potential



Comaring Myocardial AP & Pacemaker Potential

Myocardial AP

- Resting Membrane Potential is about -90mv
- It is stable
- Needs stimulus
- No Prepotential
- Phases 0,1,2,3 & 4
- Rapid depolarization due to Na^{+} influx

Pacemaker Potential

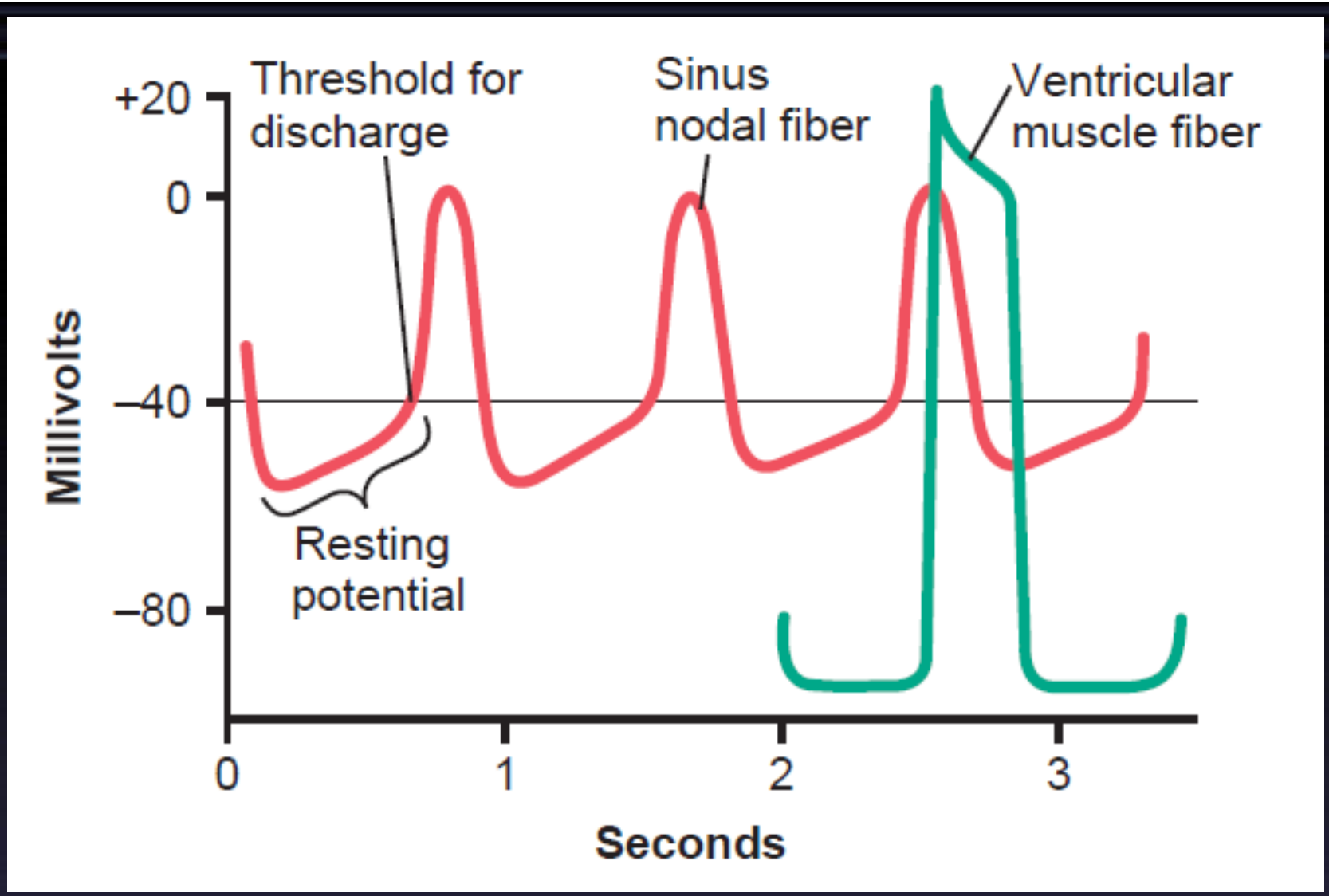
- Membrane Potential is about -60mv
- It is unstable
- Automatic
- Prepotential
- Phase 0,3 ,4.(no phase 1 & 2)
- slow depolarization due to Ca^{++}influx

Latent Excitability in Conductive System

- The AV node and the His-Purkinje systems are LATENT PACEMAKERS that may exhibit automaticity and override the SA node if it is suppressed [Ectopic Pacemaker].
- The intrinsic rate of phase 4 depolarization (and heart rate) is fastest in the SA node and slowest in the His-Purkinje system:

TABLE 4–3. Firing Rate of Sinoatrial Node and Latent Pacemakers in the Heart

Location	Intrinsic Firing Rate (impulses/min)
Sinoatrial node	70–80
Atrioventricular node	40–60
Bundle of His-Purkinje fibers	15–40



- Rhythmical Discharge of Sinus nodal Fiber.
- SA Node Action Potential compared with Ventricular Muscle Fiber

TABLE 4–2. Comparison of Action Potentials in Cardiac Tissues

Cardiac Tissue	Action Potential Duration (msec)	Upstroke	Plateau	Phase 4 Depolarization
Sinoatrial node	150	Inward Ca^{2+} current T-type Ca^{2+} channels	None	Inward Na^+ current (I_f) Normal pacemaker
Atrium	150	Inward Na^+ current	Inward Ca^{2+} current (slow inward current) L-type Ca^{2+} channels	None
Ventricle	250	Inward Na^+ current	Inward Ca^{2+} current (slow inward current) L-type Ca^{2+} channels	None
Purkinje fibers	300	Inward Na^+ current	Inward Ca^{2+} current (slow inward current) L-type Ca^{2+} channels	Latent pacemaker

table 3-1 Autonomic Effects on the Heart and Blood Vessels

	Sympathetic		Parasympathetic	
	Effect	*Receptor*	*Effect*	*Receptor*
Heart rate	↑	β_1	↓	Muscarinic
Conduction velocity (AV node)	↑	β_1	↓	Muscarinic
Contractility	↑	β_1	↓ (atria only)	Muscarinic
Vascular smooth muscle				
Skin, splanchnic	Constriction	α_1		
Skeletal muscle	Constriction	α_1		
	Relaxation	β_2		

AV = atrioventricular.

TABLE 4-4. Effects of Autonomic Nervous System on the Heart and Blood Vessels

Autonomic Division	Heart Rate (Chronotropic)	Conduction Velocity (AV Node)	Contractility (Inotropic)	Vascular Smooth Muscle	
				Skin and Splanchnic	Skeletal Muscle
Sympathetic	↑ β_1 Receptors	↑ β_1 Receptors	↑ β_1 Receptors	Constriction α_1 Receptors	Dilation β_2 Receptors Dilation Muscarinic receptors
Parasympathetic	↓ Muscarinic receptors	↓ Muscarinic receptors	↓ (atria only) Muscarinic receptors	Dilation (EDRF released from endothelium)	Dilation (EDRF released from endothelium)

AV, atrioventricular; EDRF, endothelial-derived relaxing factor.

MYOCARDIAL CONTRACTILITY

Characteristics

- T tubules of cardiac muscle have a diameter 5 times as great as that of the skeletal muscle tubules
- Calcium "pulse" in the cardiac muscle lasts for 1/3 of a sec while in skeletal muscle fiber lasts about 1/20
- Cardiac contractility depends on both extracellular and Sarcoplasmic Ca while in muscle it depends only on sarcoplasmic reticulum Ca
- Source of Ca for heart Ms is 80% from SR and 20% from ECF
- Cardiac Ms cannot be tetanized
- Cardiac Ms does not fatigue
- Act as Syncytium
- Long refractory period

Excitation–contraction coupling

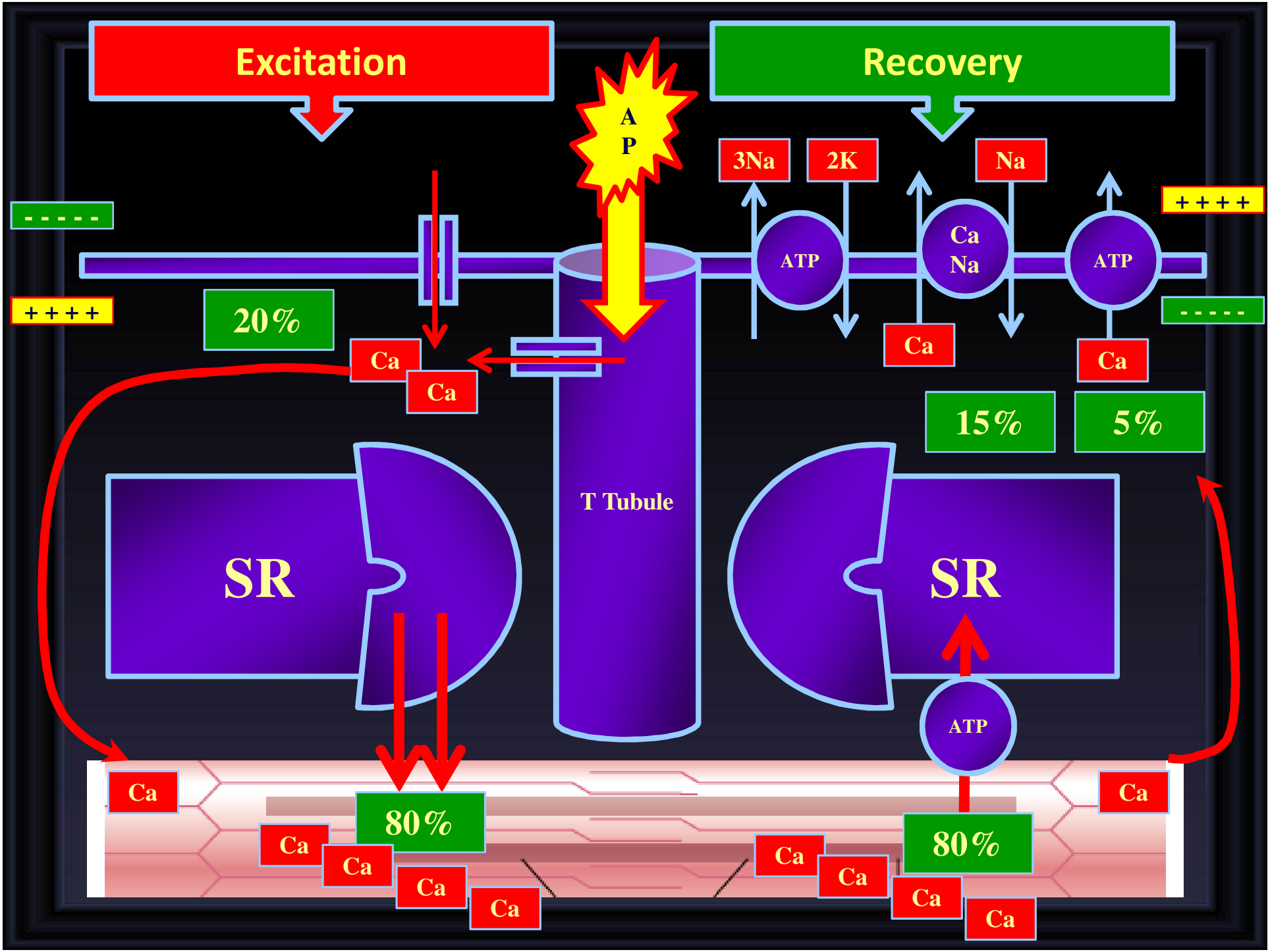
1. The AP spreads from the cell membrane into the T tubules.

2. During the plateau of the action potential, Ca2+ conductance is increased and Ca2+ enters the cell from the extracellular fluid L-type Ca2+ channels [20%]

3. This Ca2+ entry triggers the release of even more Ca2+ from the SR (Ca2+-induced Ca2+ release) [80%] through Ca2+ channels and intracellular [Ca2+] increases.

5. Ca2+ binds to troponin C, and tropomyosin is moved out of the way, removing the inhibition of actin and myosin binding, which slide and cell contracts. The magnitude of the tension that develops is proportional to the intracellular [Ca2+].

7. Relaxation occurs when Ca2+ is reaccumulated by the SR by an active Ca2+-ATPase pump.


Excitation
Recovery
A
P
3Na
2K
Na
ATP
Ca
Na
ATP
+ + + +
- - - - -
+ + + +
- - - - -
20%
Ca
Ca
Ca
Ca
15%
5%
T Tubule
SR
SR
ATP
Ca
Ca
Ca
Ca
80%
Ca
Ca
Ca
Ca
80%
Ca
Ca
Ca
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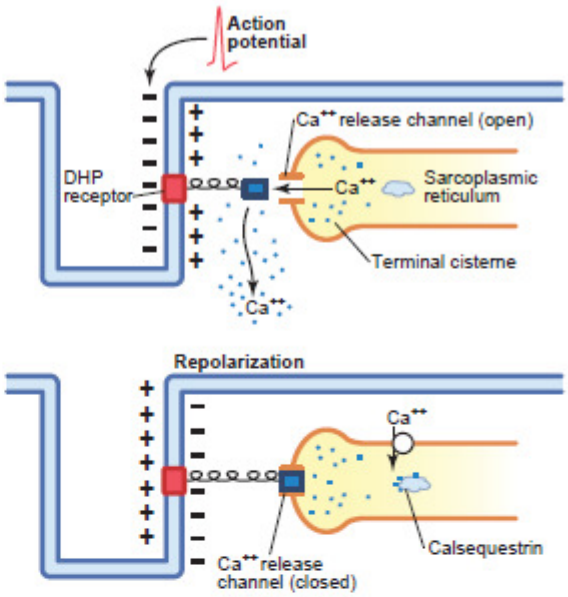


Figure 7-6. Excitation-contraction coupling in skeletal muscle. The *top panel* shows an action potential in the transverse tubule that causes a conformational change in the voltage-sensing dihydropyridine *(DHP)* receptors, opening the Ca^{++} release channels in the terminal cisternae of the sarcoplasmic reticulum and permitting Ca^{++} to rapidly diffuse into the sarcoplasm and initiate muscle contraction. During repolarization *(bottom panel)*, the conformational change in the DHP receptor closes the Ca^{++} release channels and Ca^{++} is transported from the sarcoplasm into the sarcoplasmic reticulum by an adenosine triphosphate–dependent calcium pump.

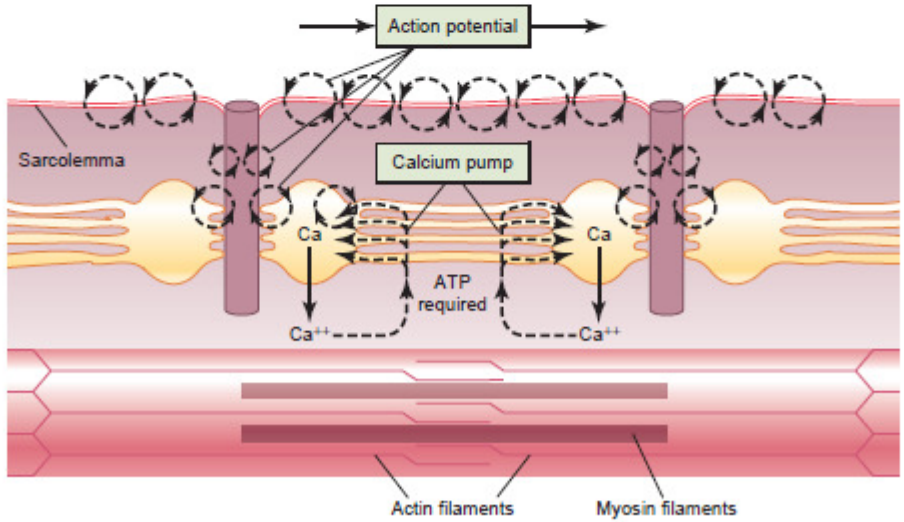


Figure 7-7. Excitation-contraction coupling in the muscle, showing (1) an action potential that causes release of calcium ions from the sarcoplasmic reticulum and then (2) re-uptake of the calcium ions by a calcium pump. ATP, adenosine triphosphate.

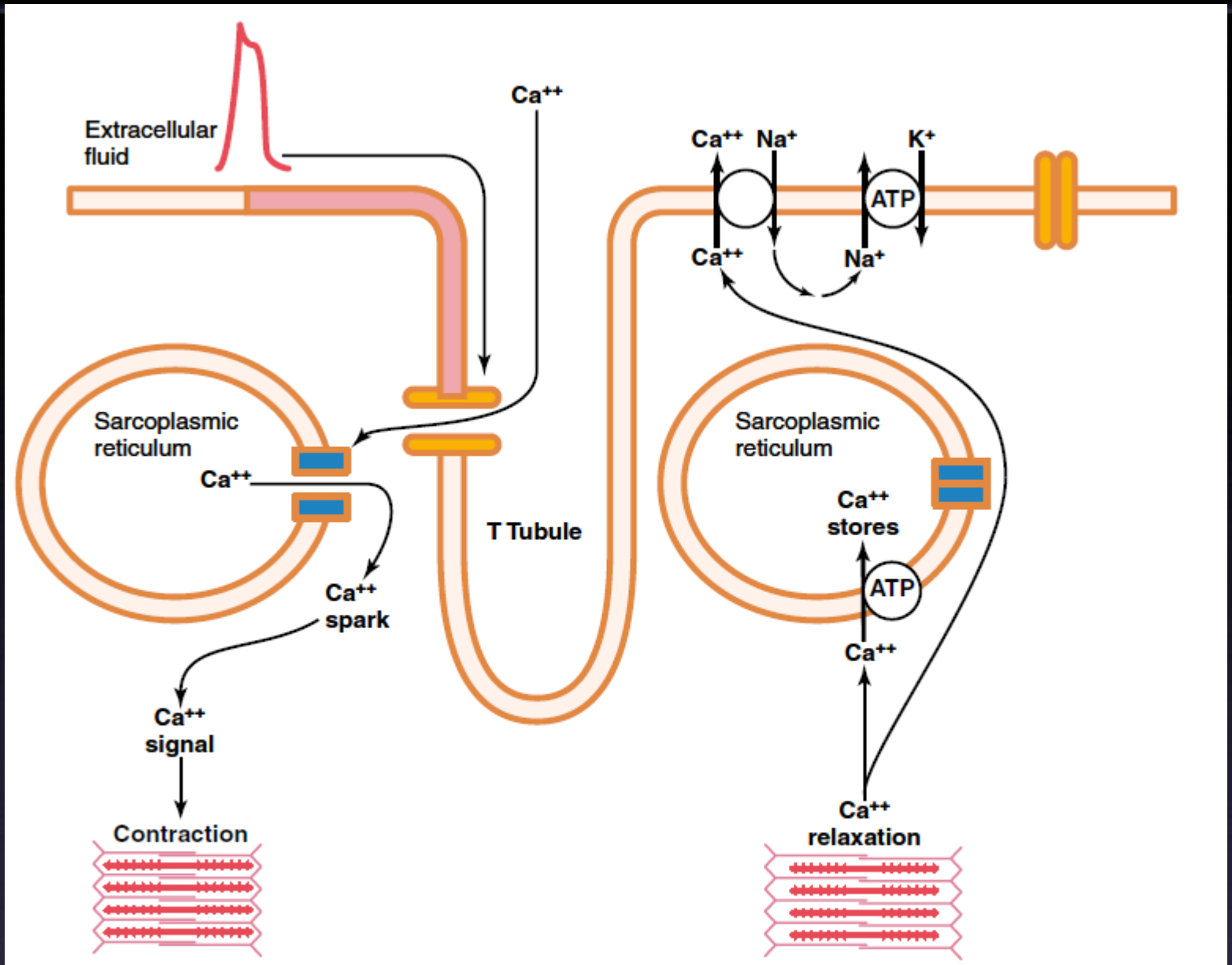
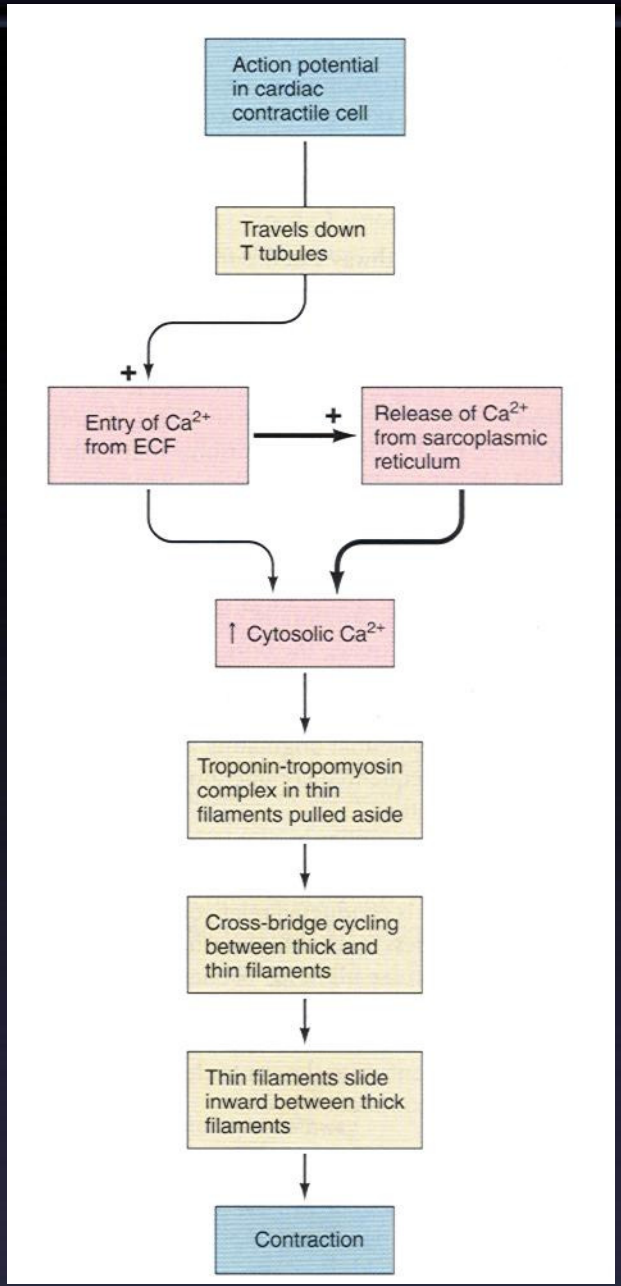


Figure 9-5 Mechanisms of excitation-contraction coupling and relaxation in cardiac muscle.



Steps in Cardiac muscle contraction

Effect of Sympathetic & Parasympathetic Nerves

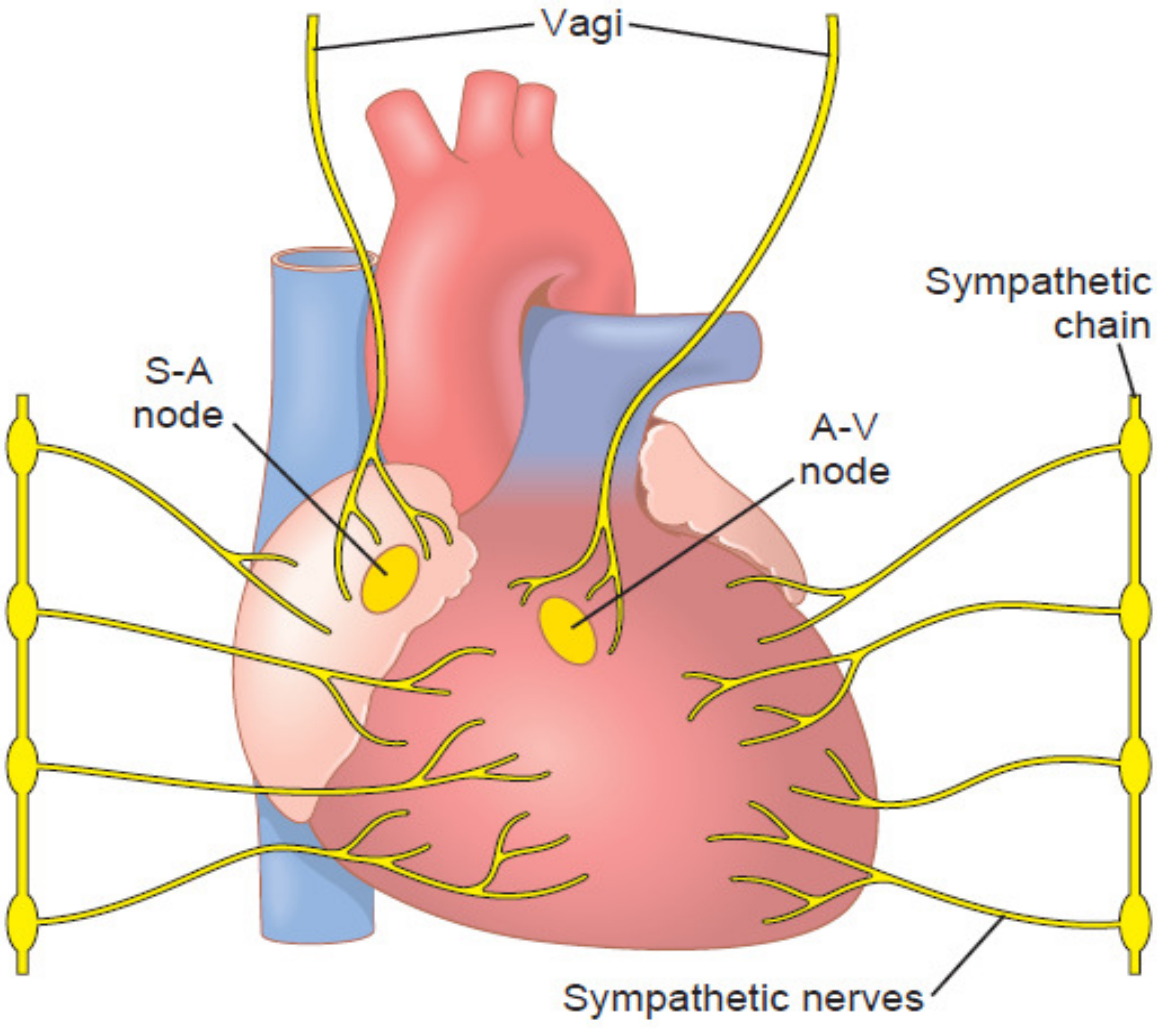


Figure 9-13. Cardiac *sympathetic* and *parasympathetic* nerves. (The

The SA node, atria, and AV node have parasympathetic vagal innervation, but the ventricles do not. The neurotransmitter is acetylcholine (ACh), which acts at muscarinic receptors.

Inotropic Chronotropic & Dromotropic

CONTRACTILITY

Positive inotropic agents produce an increase in contractility.

Negative inotropic agents produce a decrease in contractility

HEART RATE

Positive chronotropic effect

Negative chronotropic effect

CONDUCTION VELOCITY

Positive dromotropic effect

Negative dromotropic effect

Parasympathetic effects on heart

Negative chronotropic effect:

- decreases heart rate by decreasing the rate of phase 4 depolarization.
- Fewer action potentials occur per unit time because the threshold potential is reached more slowly .
- The mechanism is decreased If, the inward Na+ current that is responsible for phase 4 depolarization in the SA node.

Negative dromotropic effect

- decreases conduction velocity through the AV node.
- Action potentials are conducted more slowly from the atria to the ventricles. increases the PR interval.
- The mechanism is decreased inward Ca2+ current and increased outward K+ current.

Negative inotropism

- ACh via muscarinic receptors decreases the force of contraction in the atria by decreasing the inward Ca2+ current during the plateau of the cardiac action potential.

Sympathetic effects on heart

Positive chronotropic effect

- increases heart rate by increasing the rate of phase 4 depolarization.
- More action potentials occur per unit time because the threshold potential is reached more quickly .
- The mechanism is increased If, the inward Na+ current that is responsible for phase 4 depolarization in the SA node.

Positive dromotropic effect

- Increases conduction velocity through the AV node.
- Action potentials are conducted more rapidly from the atria to the ventricles, and ventricular filling may be compromised. decreases the PR interval.
- The mechanism of the positive dromotropic effect is increased inward Ca2+ current.

Positive Inotropism

- Increases the force of contraction by two mechanisms:

(1) It increases the inward Ca2+ current during the plateau of each cardiac action potential.

(2) It increases the activity of the Ca2+ pump of the SR (by phosphorylation of phospholamban); as a result, more Ca2+ is accumulated by the SR and thus more Ca2+ is available for release in subsequent beats.

NE Alpha1 receptors.

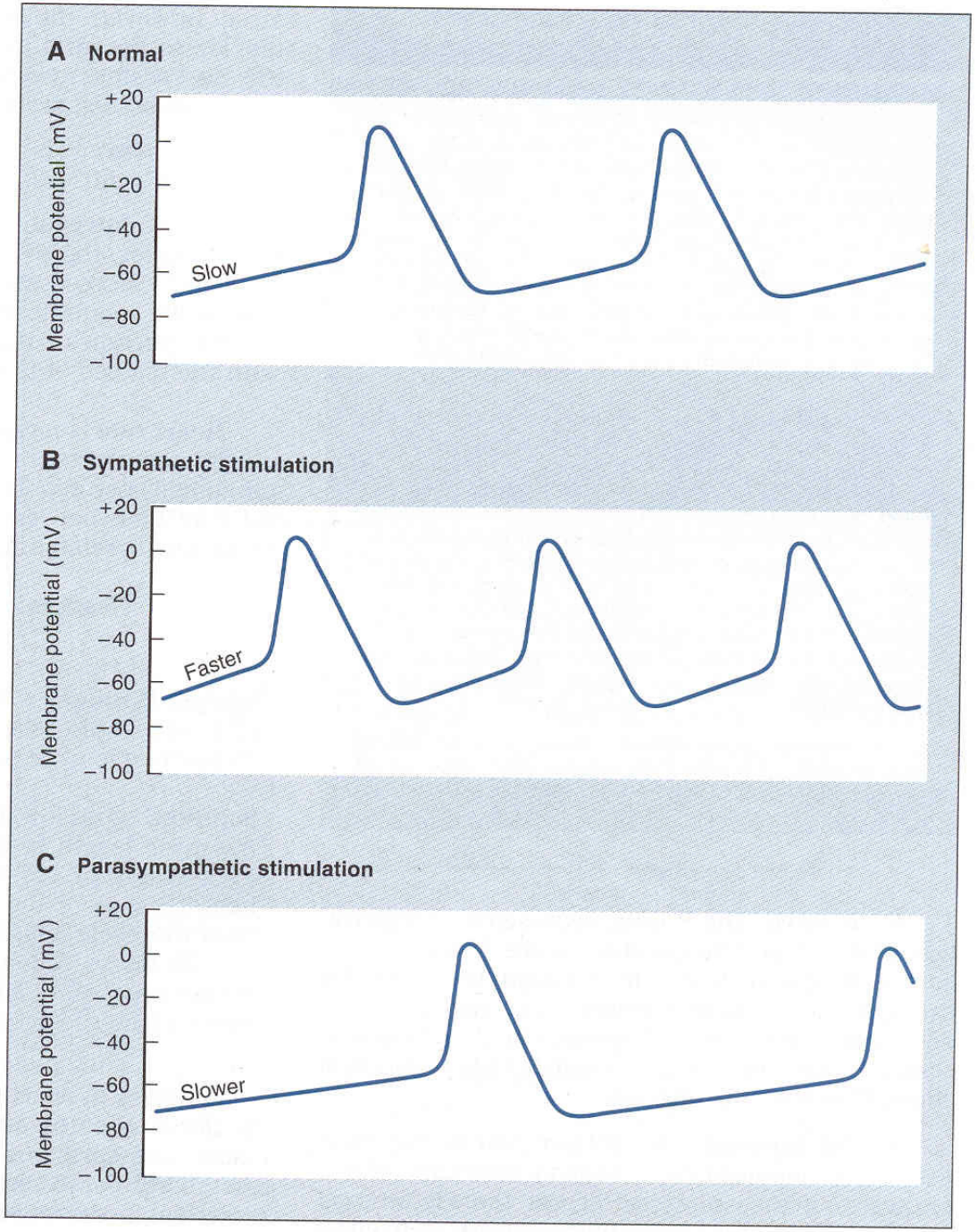


FIGURE 4–15. Effect of sympathetic and parasympathetic stimulation on the SA node action potential. **A**, Normal; **B**, sympathetic stimulation increases the rate of phase 4 depolarization and increases the frequency of action potentials; **C**, parasympathetic stimulation decreases the rate of phase 4 depolarization and decreases the frequency of action potentials.

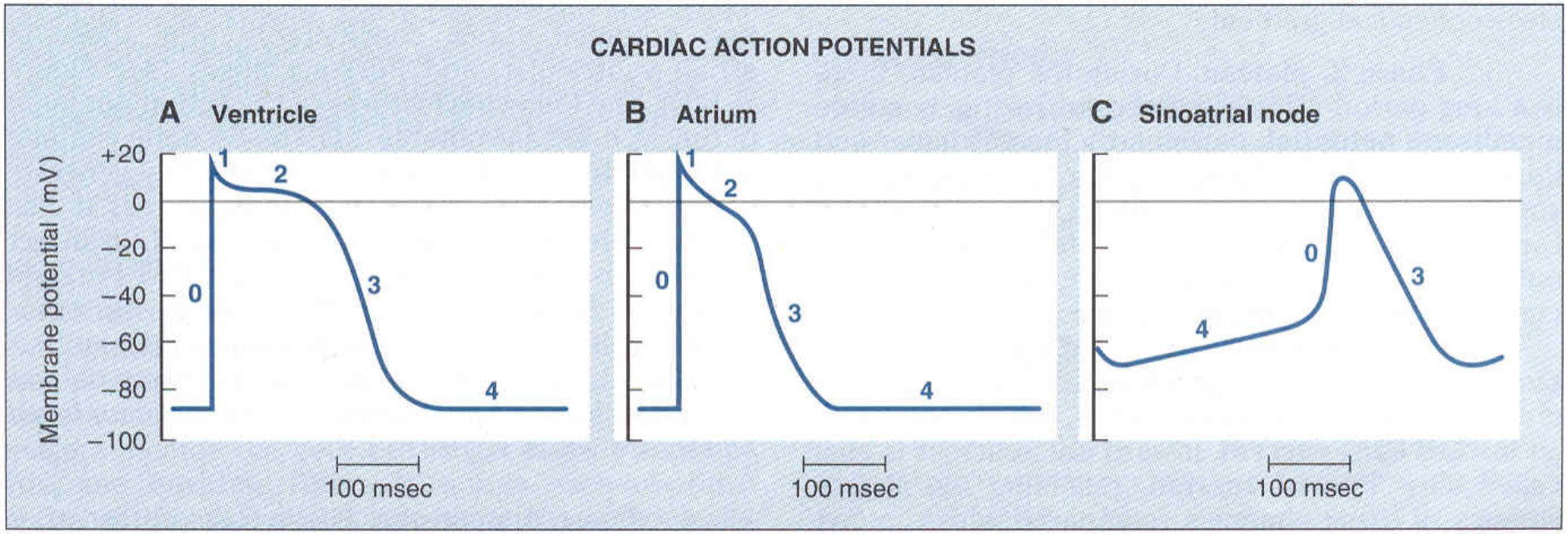


FIGURE 4–12. Cardiac action potentials in the ventricle, atrium, and sinoatrial node. The numbers correspond to the phases of the action potentials.

Effect of Ions and Temp

- ↑K…. in the extracellular fluids causes the heart to become dilated and flaccid and also slows the heart rate… ↑K decreases the resting membrane potential in the cardiac muscle fibers… the intensity of the action potential also decreases, which makes contraction of the heart progressively weaker

- ↑Ca causes spastic contraction. This is caused by a direct effect of calcium ions to initiate the cardiac contractile process. ↓ Ca causes flaccidity.

- ↑ Temp… causes a greatly increased heart rate, sometimes to as fast as double normal [↑ permeability to ions that self-excitation]. Decreased temperature causes a greatly decreased heart rate, falling to as low as a few beats per minute

FACTORS AFFECTING CONTRACTILITY

- **Positive ionotropic effect. (FORCE OF CONTRACTION)**
  - ✓ Sympathetic stimulation
  - ✓ Adrenaline & Noradrenaline
  - ✓ Calcium ion
  - ✓ Caffine
  - ✓ Drugs e.g. Digitalis (Digoxin)
- **Negative ionotropic effect:**
  - ✓ Parasympathetic stimulation
  - ✓ Acetyl choline
  - ✓ Potassium ion
  - ✓ Hypoxia (Decrease oxygen)
  - ✓ Acidosis
  - ✓ Bacterial toxin
  - ✓ Drugs e.g.. Calcium channel blockers, β- Blockers

FRANK – STARLING'S LAW

Within physiologic limits, the heart pumps all the blood that returns to it by the way of the veins.

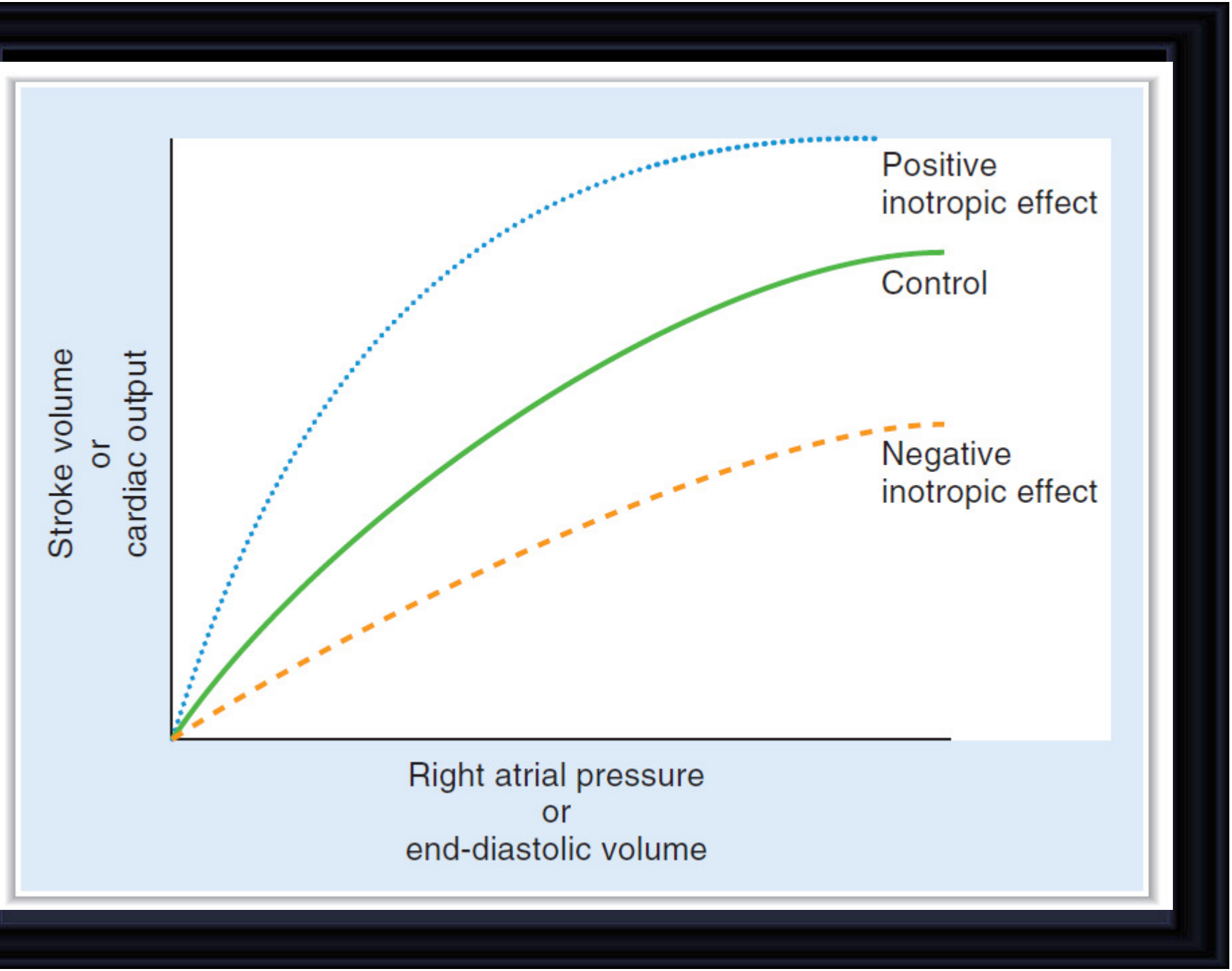
OR

The greater the stretch of the cardiac muscle the greater would be the force of contraction.

OR

"The energy of contraction is proportional to the initial length of the cardiac muscle fibers" and for the muscle is proportional to the End Diastolic Volume.

Because Actin & Myosin filaments are brought to more optimal degree of sliding therefore increase force of contraction.


Positive
inotropic effect
Control
Negative
inotropic effect
Stroke volume
or
cardiac output
Right atrial pressure
or
end-diastolic volume

Comparison of Skeletal and Cardiac Muscle

Characteristic	Skeletal Muscle	Cardiac Muscle
Function	Movement of body in relation to External environment	Pump blood out of heart
Mechanism of contraction	Sliding filament mechanism	Sliding filament mechanism
Innervation	Somatic nerve system (alpha motor neuron)	Autonomic nervous system
Level of control	Under voluntary control; also subject to subconscious regulation	Under involuntary control
Initiation of contraction	Neurogenic	Myogenic (pacemaker activity)
Presence of thick myosin and thin actin filament	Yes	Yes
Striated due to orderly arrangement of filament	Yes	Yes
Presence of T tubules	Yes	Yes
Level of development of sarcoplasmic reticulum	Well developed	Moderately developed
Source of increased cytosolic Ca++	Sarcoplasmic reticulum	Extra cellular fluid and sarcoplasm reticulum
Presence of gap junctions Intercalated Disc	No	Yes, therefore works as Syncytium
Obeys All or Non Law	No	Yes
Action Potential duration	2 ms	250 – 300 ms
ARP (absolute Refractory Period)	Depolarization + 1/3rd Repolarization	Depolarization + Plateau + ½ Repolarization
Can be tetanized	Yes	No


THANKS