

Cardiac Muscle Physiology

Faisal Mohammed, MD, PhD

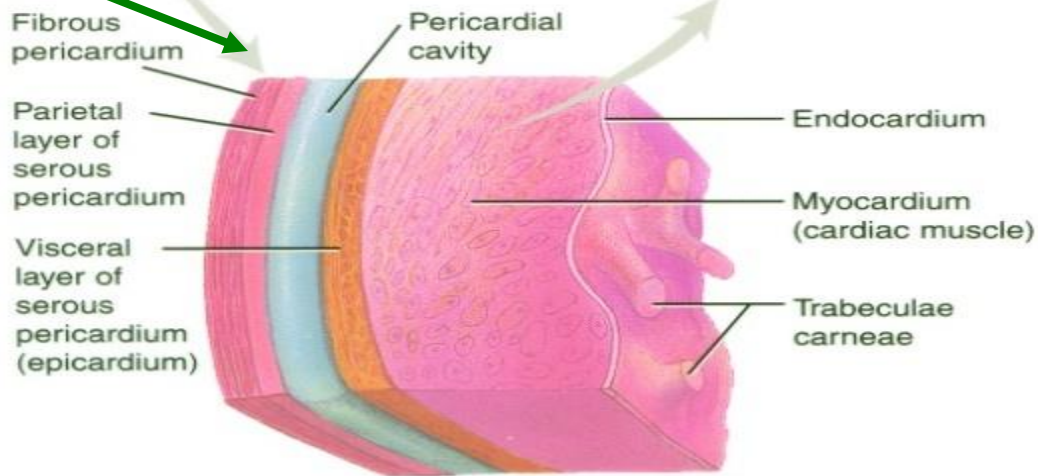
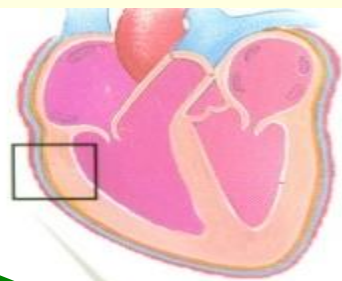
Alaa Bawaneh, MD.PhD

Objectives:

By The end of this lecture students should be able to:

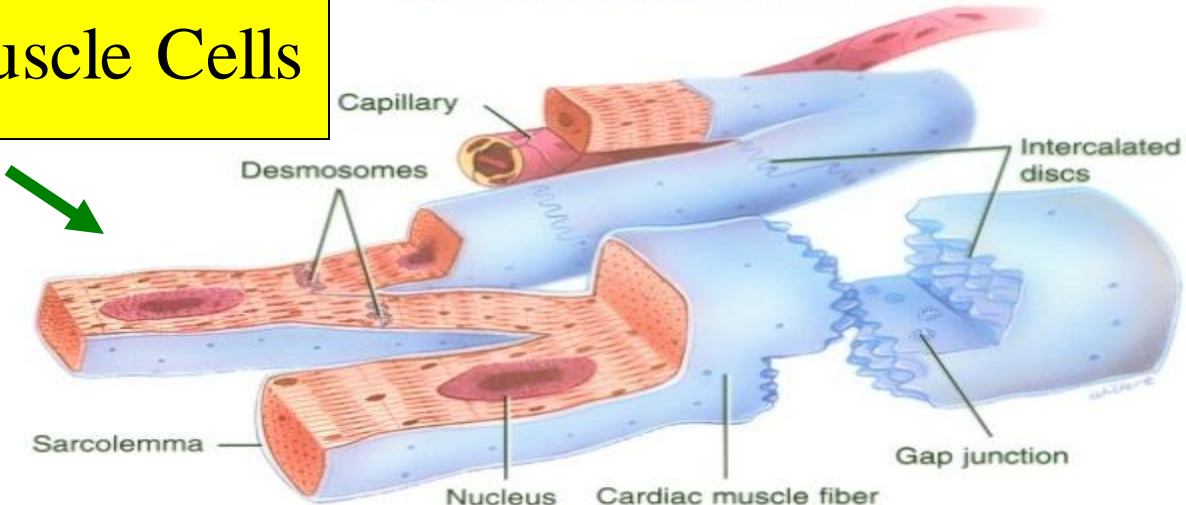
- Distinguish the cardiac muscle cell microstructure
- Describe cardiac muscle action potential
- Point out the functional importance of the action potential
- Outline the intracellular calcium homeostasis

Wall of the heart



(a) Portion of pericardium and heart wall

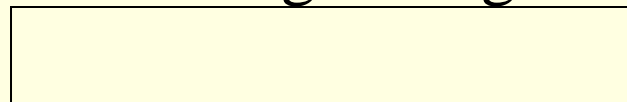
Cardiac Muscle Cells



(b) Cardiac muscle fibers

Layers of the Heart Wall

1. Epicardium (external layer)...prevent the heart from overstretching as we will see later when we discuss Frank-Starling law of the heart.
 - Visceral layer of serous pericardium
 - Smooth, slippery texture to outermost surface
2. Myocardium
 - 95% of heart is cardiac muscle
3. Endocardium (inner layer)
 - Smooth lining for chambers of heart, valves and continuous with lining of large blood vessels

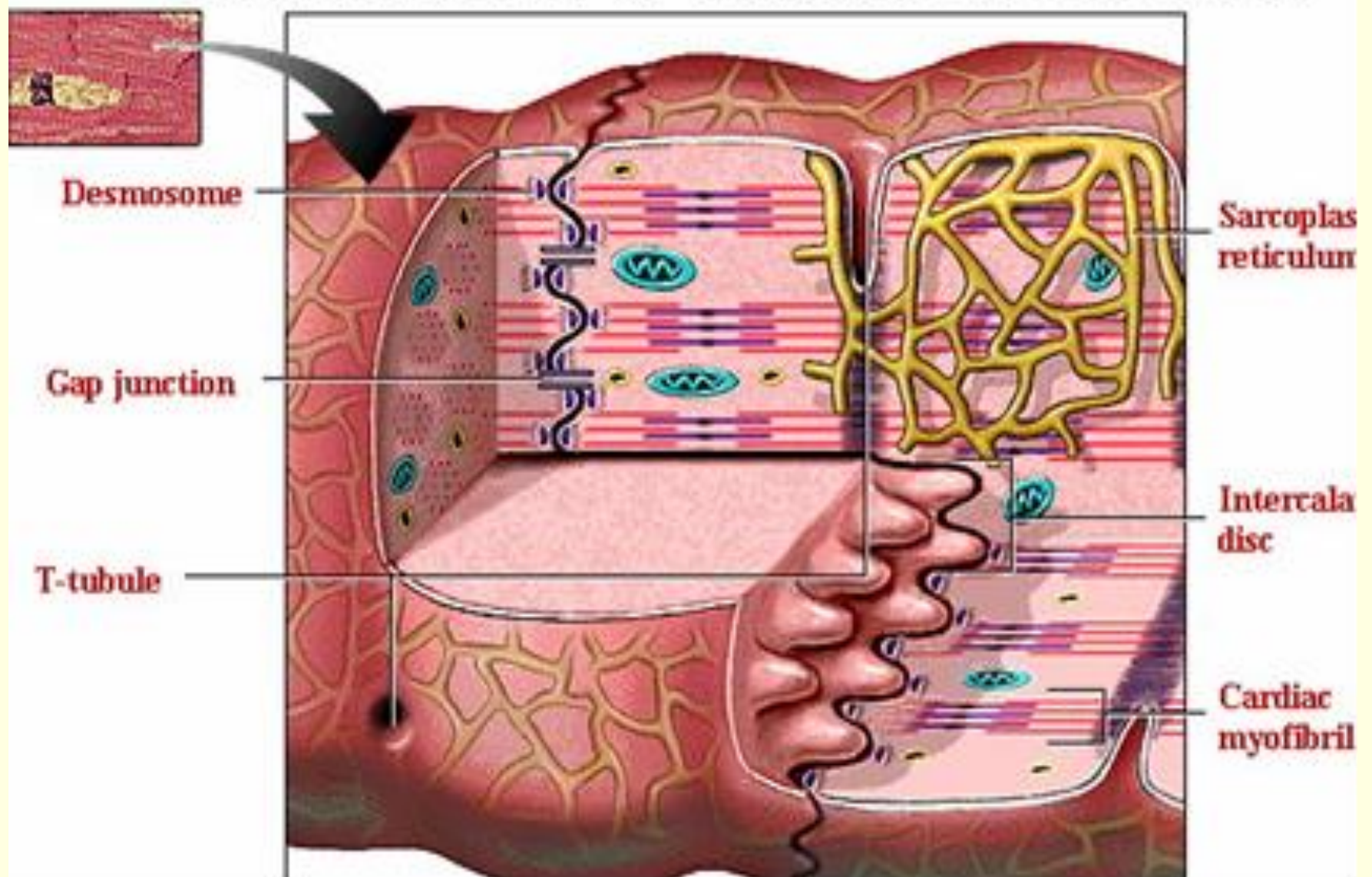


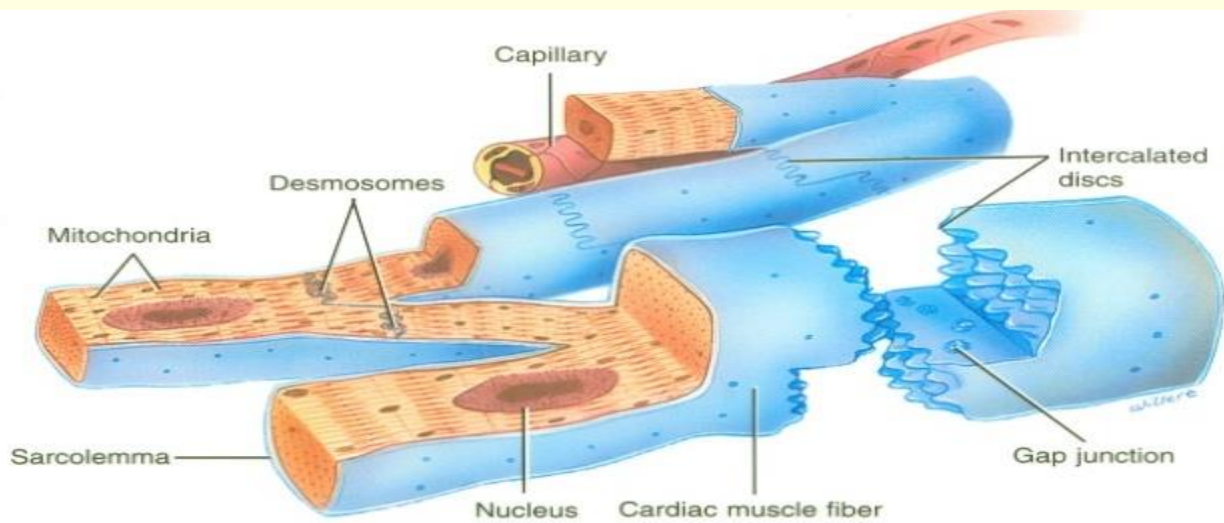
Cardiac Muscle Tissue and the Cardiac Conduction System

■ Histology

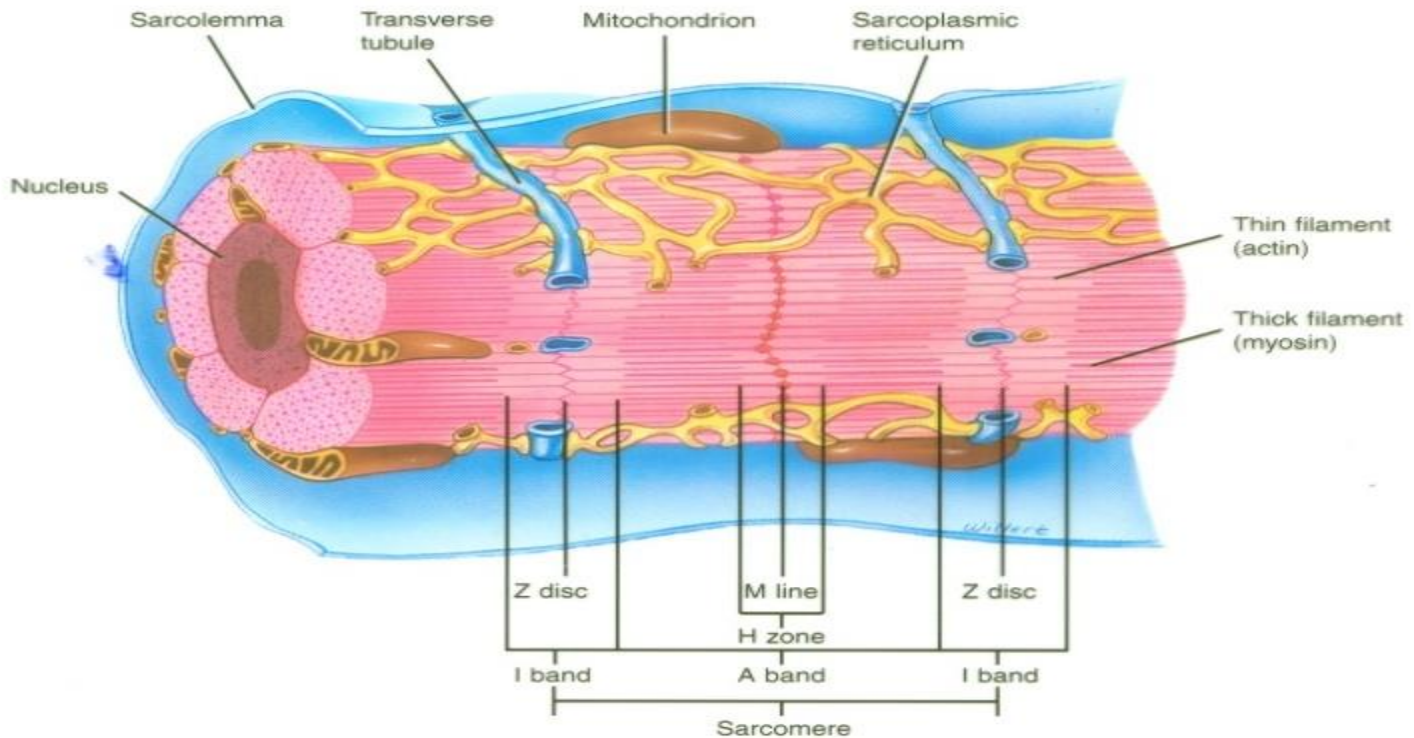
- Shorter and less circular than skeletal muscle fibers
- Branching gives “stair-step” appearance
- Usually, one centrally located nucleus
- Ends of fibers connected by intercalated discs
- Discs contain desmosomes (hold fibers together) and gap junctions (allow action potential conduction from one fiber to the next) → **syncytium**
- Mitochondria are larger and more numerous than skeletal muscle
- Same arrangement of actin and myosin

MAGNIFIED VIEW OF CARDIAC MUSCLE CELLS



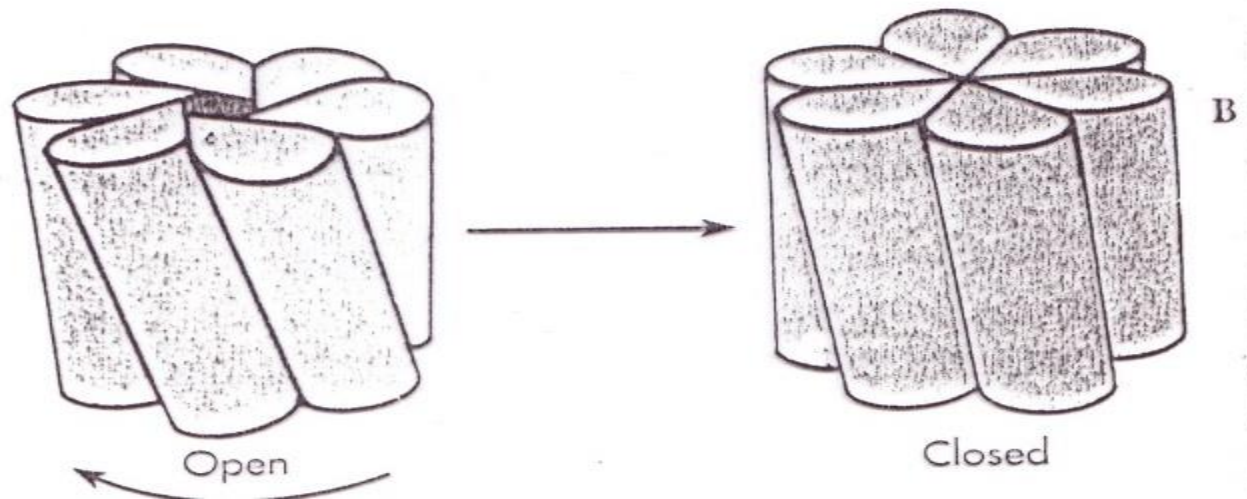
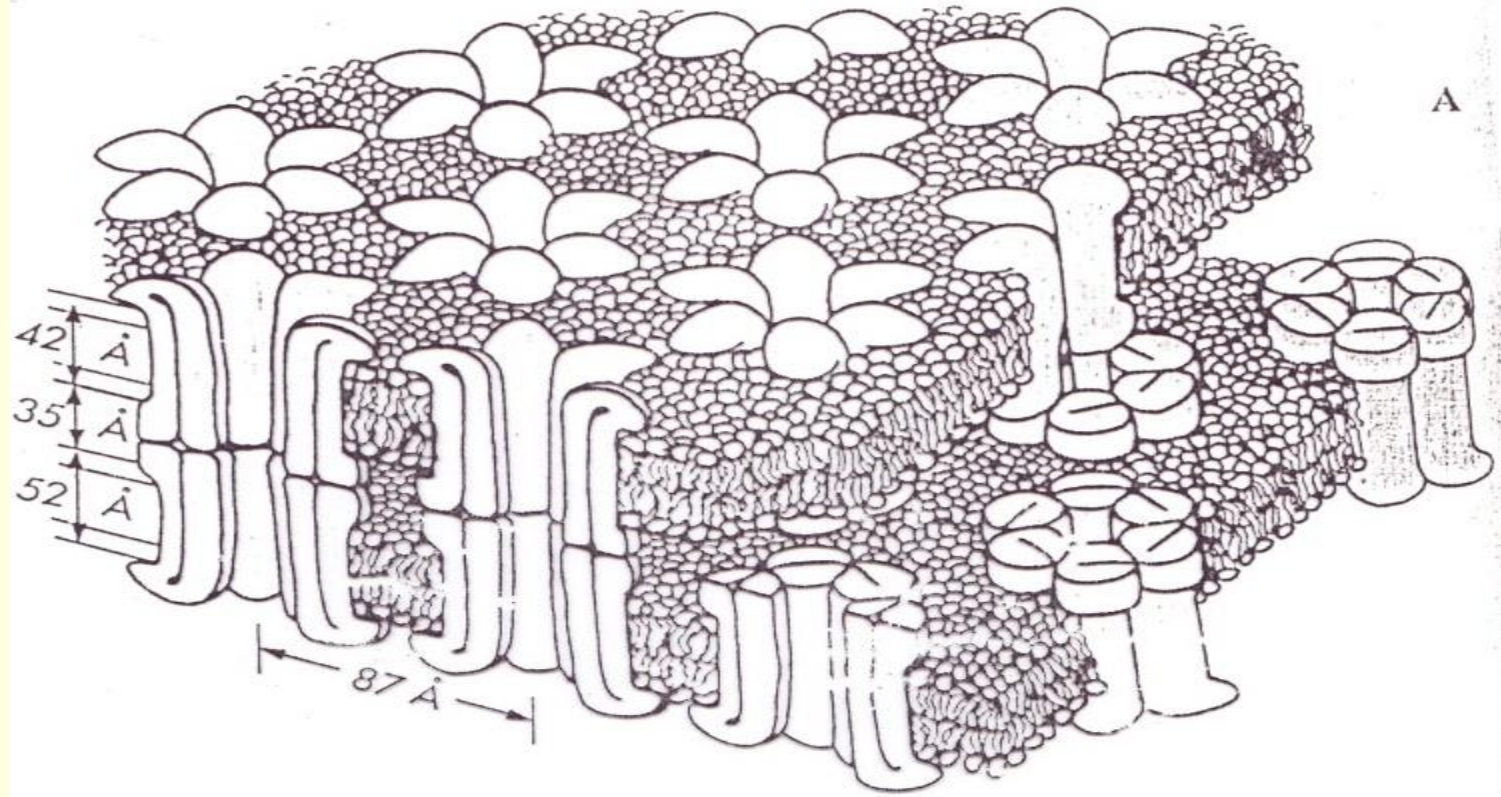


(a) Cardiac muscle fibers

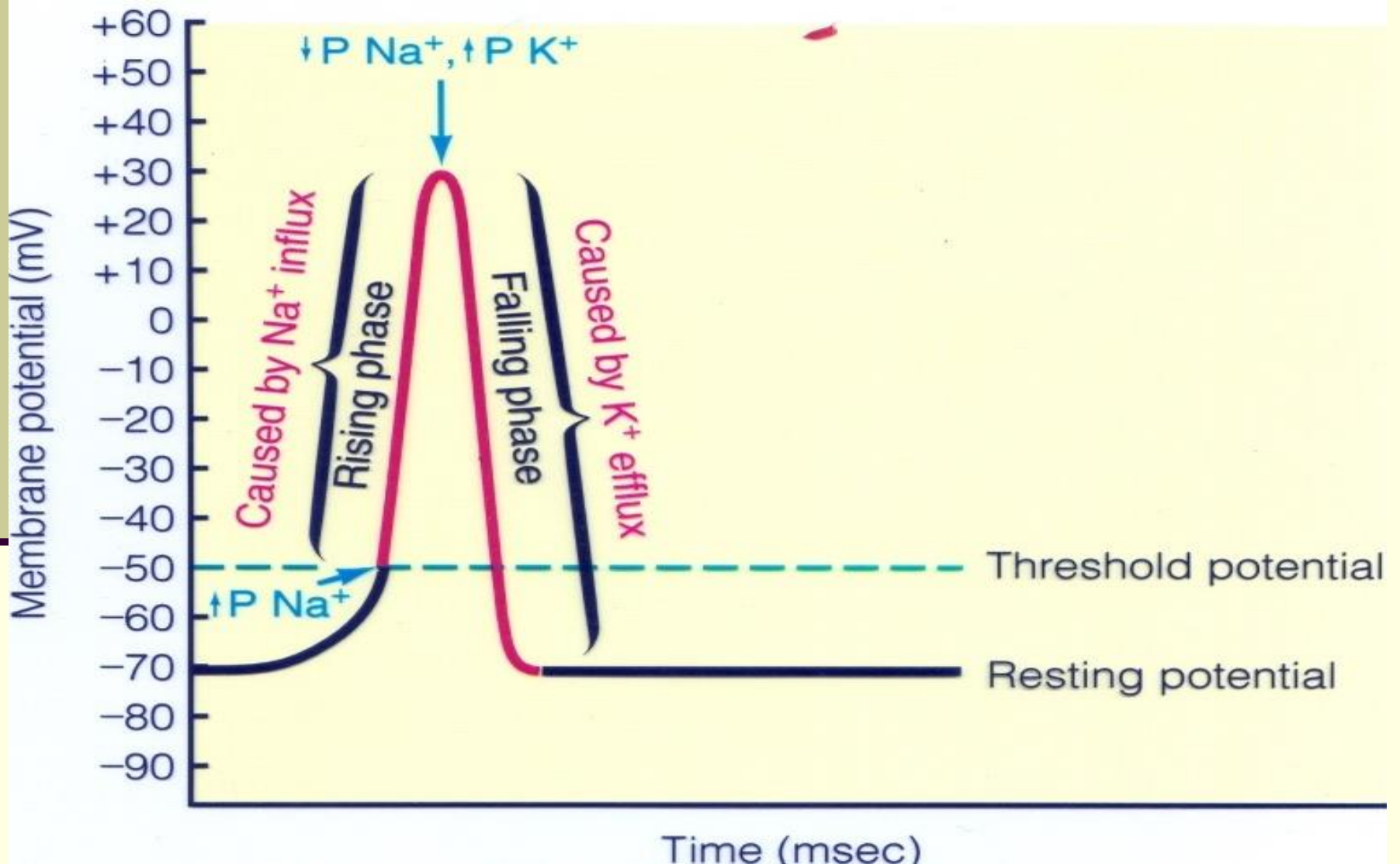


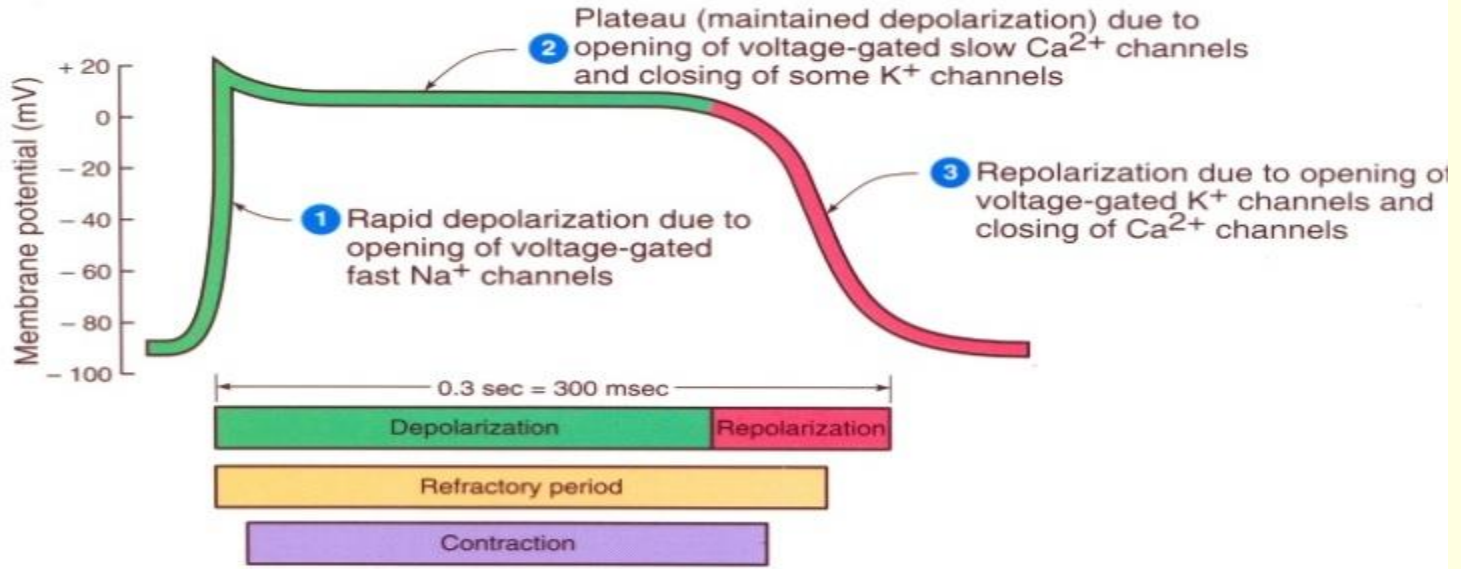
(b) Diagram based on an electron micrograph

Gap junction channels

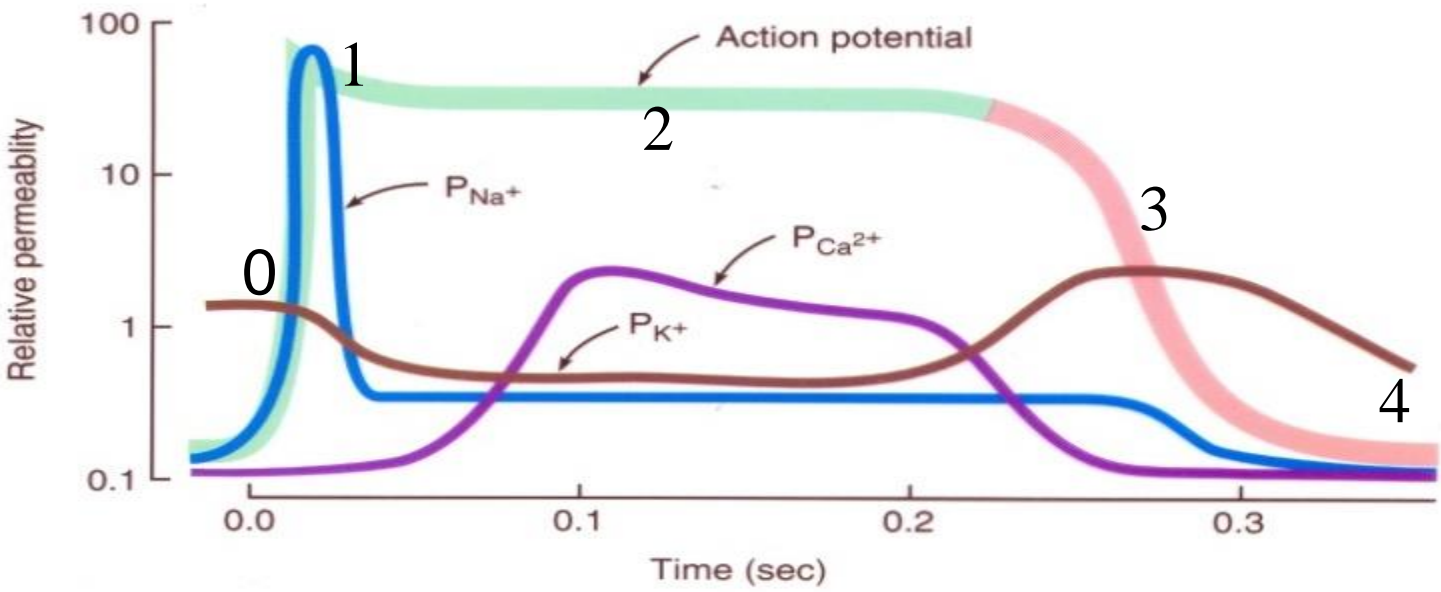


Permeability Changes and Ionic Fluxes During an Action Potential (skeletal Muscle)





(a) Action potential, refractory period, and contraction



(b) Membrane permeability (P) changes

The Action Potential in Skeletal and Cardiac Muscle

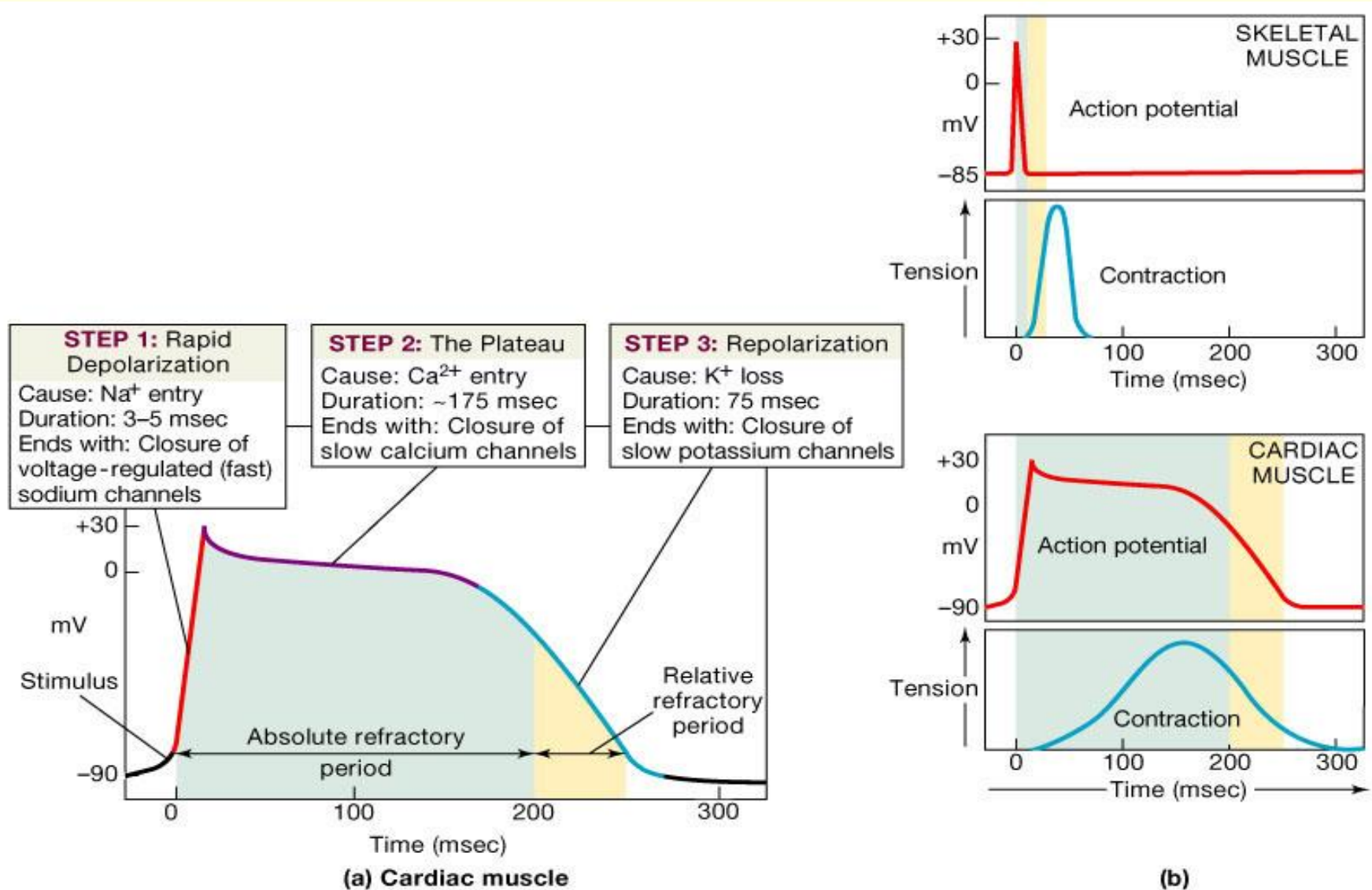
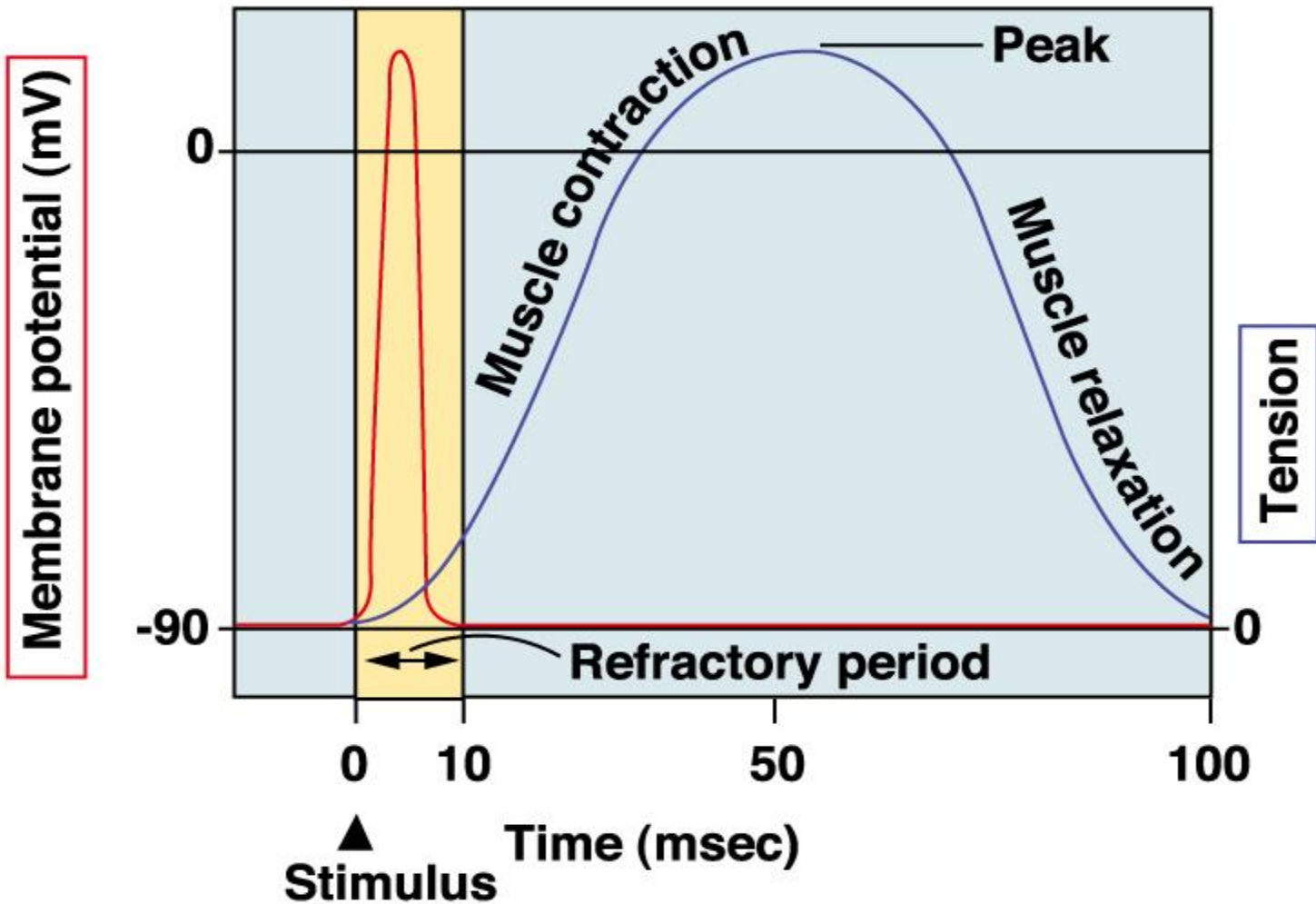
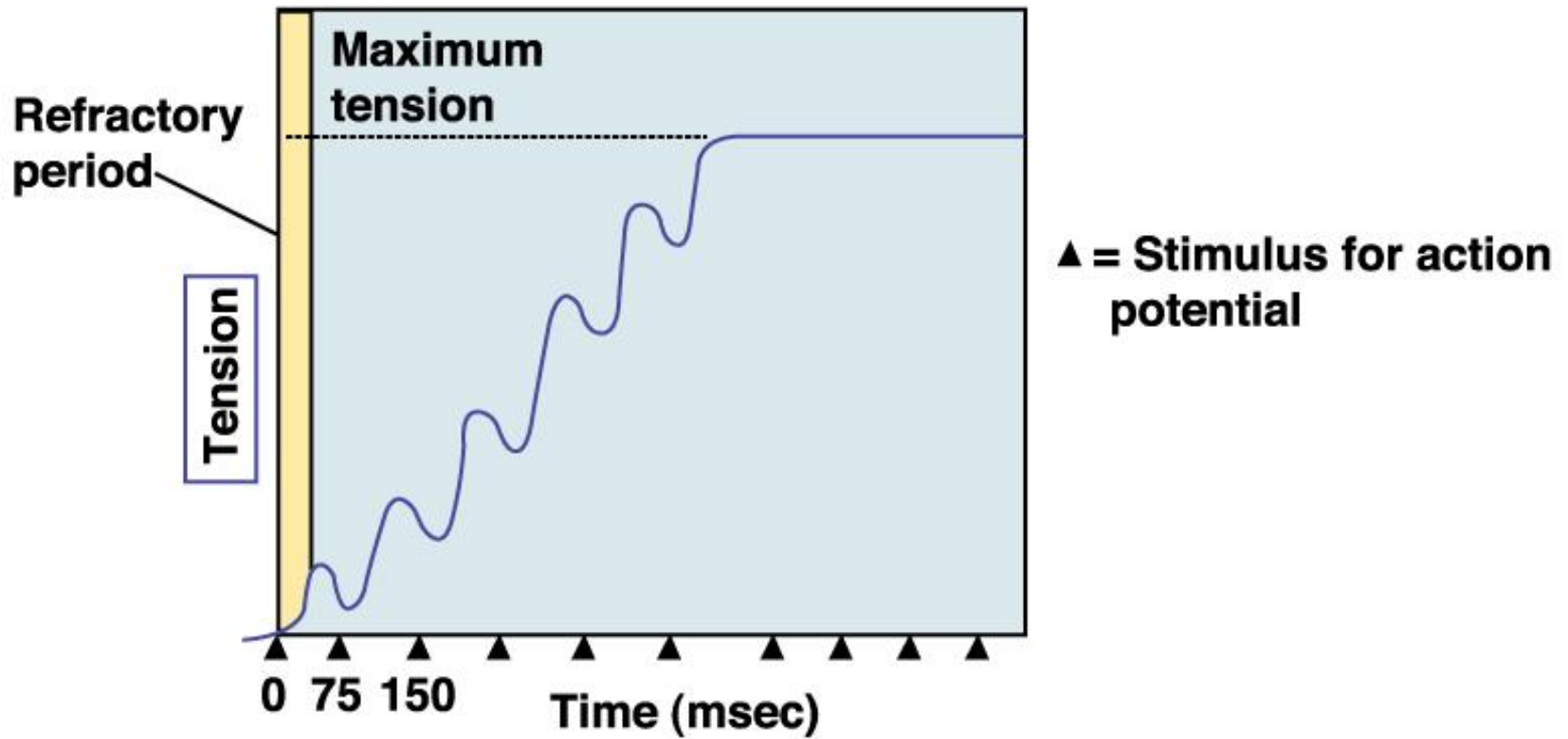


Figure 20.13

Skeletal muscle fast-twitch fiber

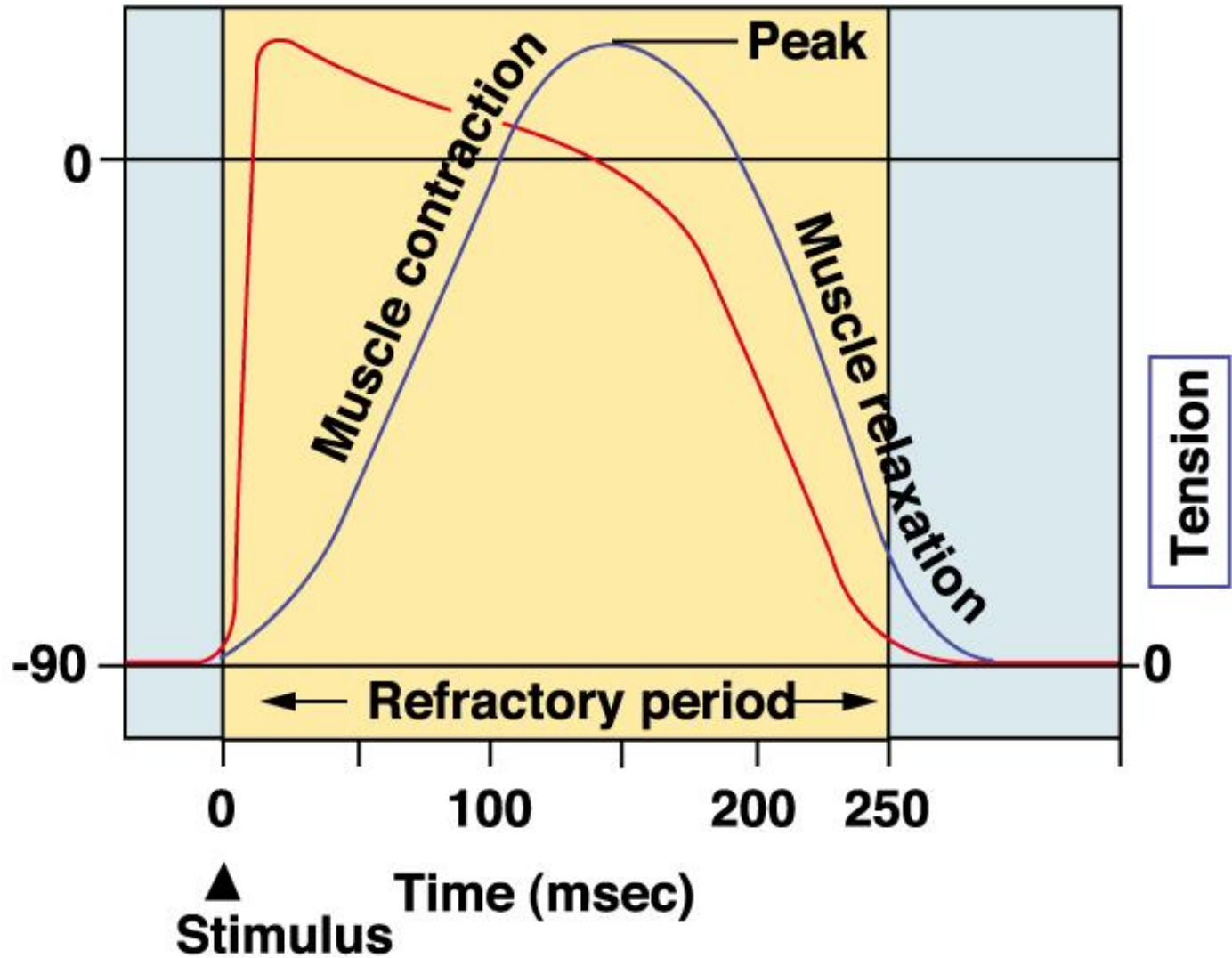


**Tetanus in a skeletal muscle.
Action potentials not shown.**

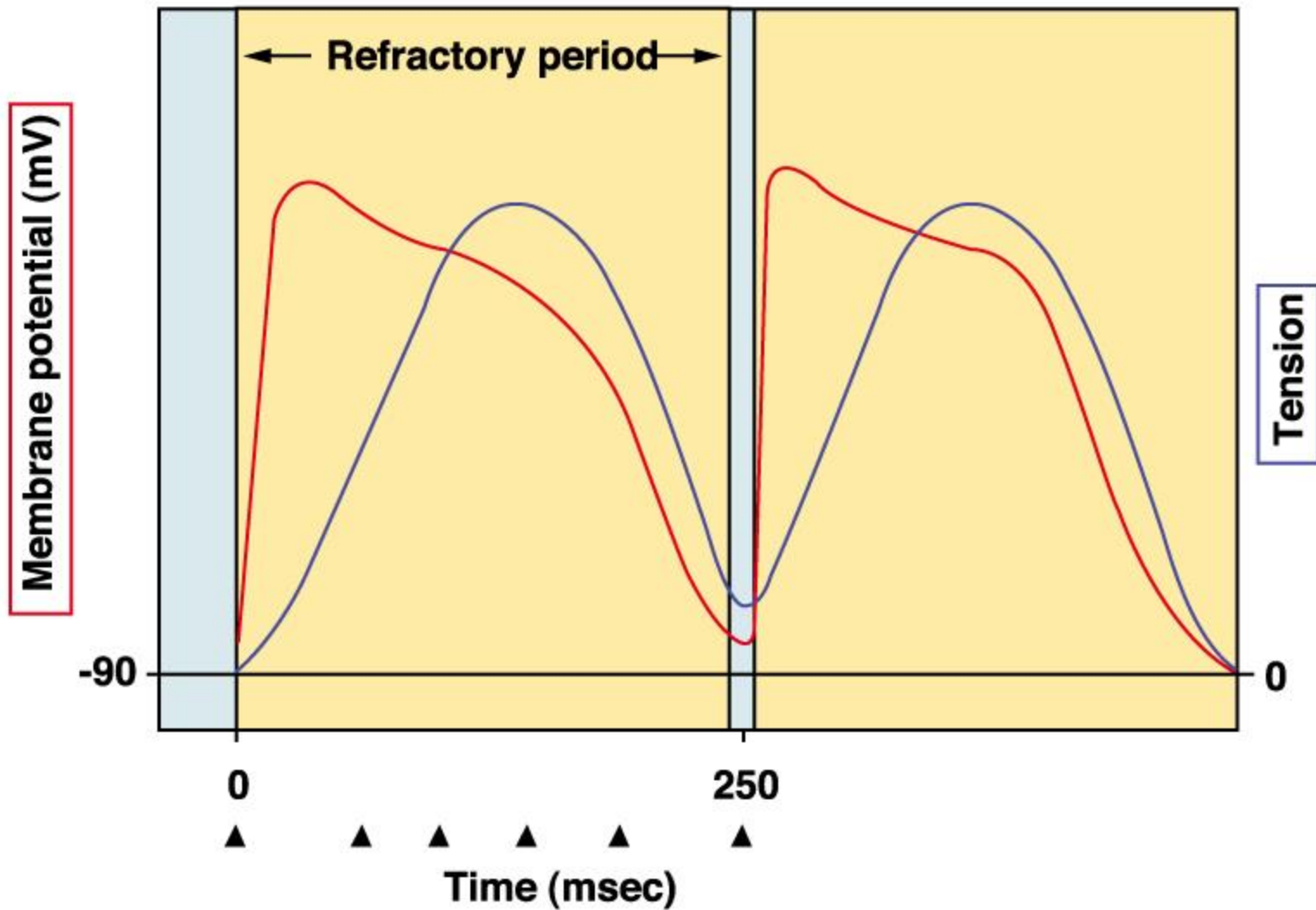


Cardiac muscle fiber

Membrane potential (mV)



Long refractory period in a cardiac muscle prevents tetanus.



Cardiac and Skeletal Muscles

Differences

Skeletal muscle

- Neurogenic
(motor neuron-end plate-acetylcholine)
- Insulated from each other
- Short action potential

Cardiac Muscle

- Myogenic
(action potential originates within the muscle)
- Gap-junctions
- Action potential is longer

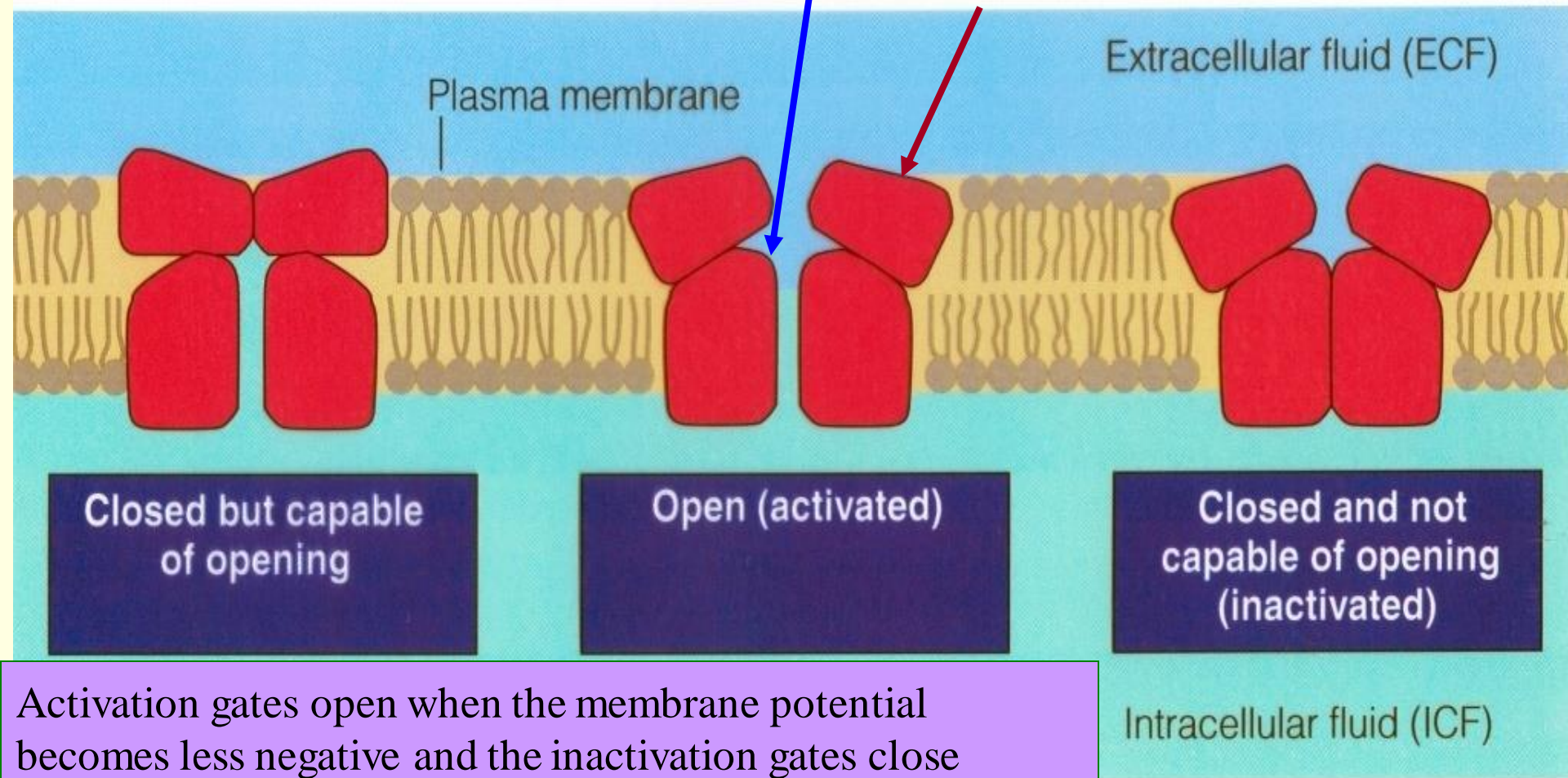
Functional importance of Cardiac action potential

- The decrease in conductance (permeability) of potassium at phase 0 and 1 of the cardiac action potential contributes to the maintenance of depolarization in phase 2 (plateau)
- The long absolute refractory period prevent the occurrence of tetanus (maintained contraction without a period of relaxation) in the cardiac muscle.
- Skeletal muscle action potential is short that allows tetanus to occur

Conformations of a Voltage-Gated Na⁺ Channel

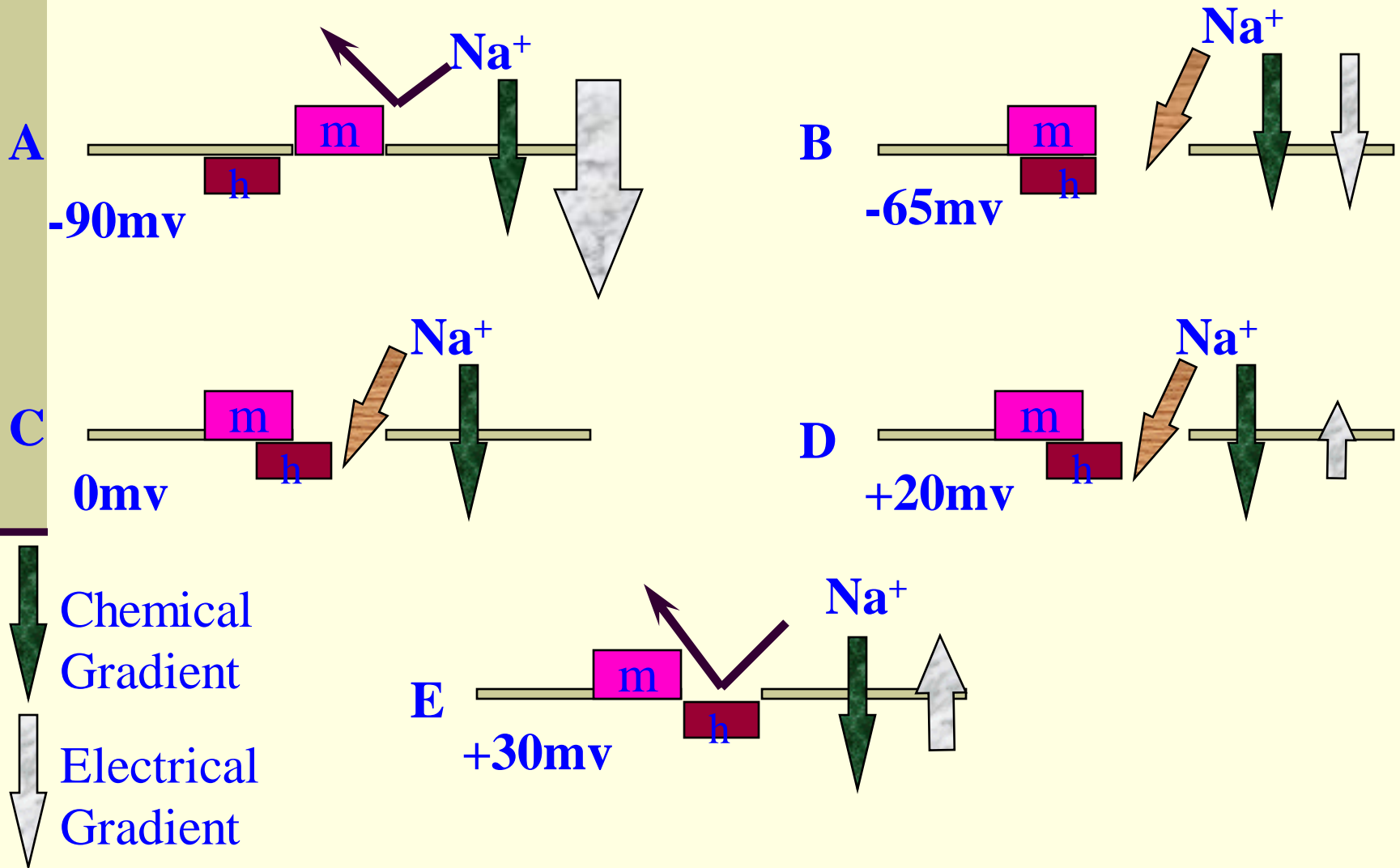
(inactivation gate) h Gate

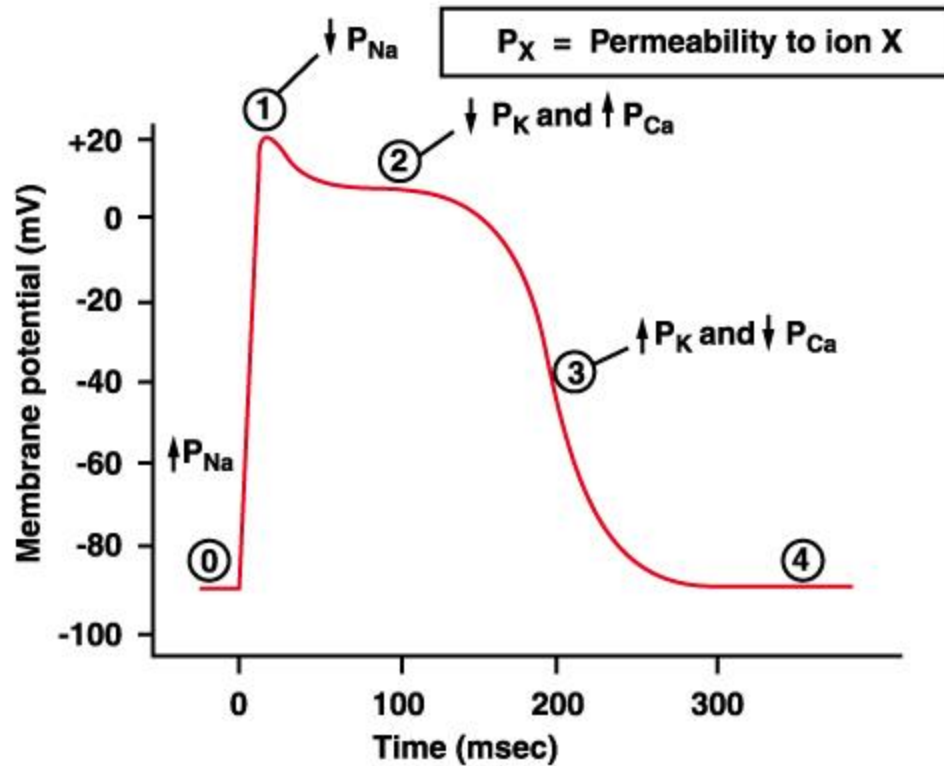
(activation gate) m Gate



Activation gates open when the membrane potential becomes less negative and the inactivation gates close when the potential becomes less negative. The activation gate is fast but the inactivation is slow responding

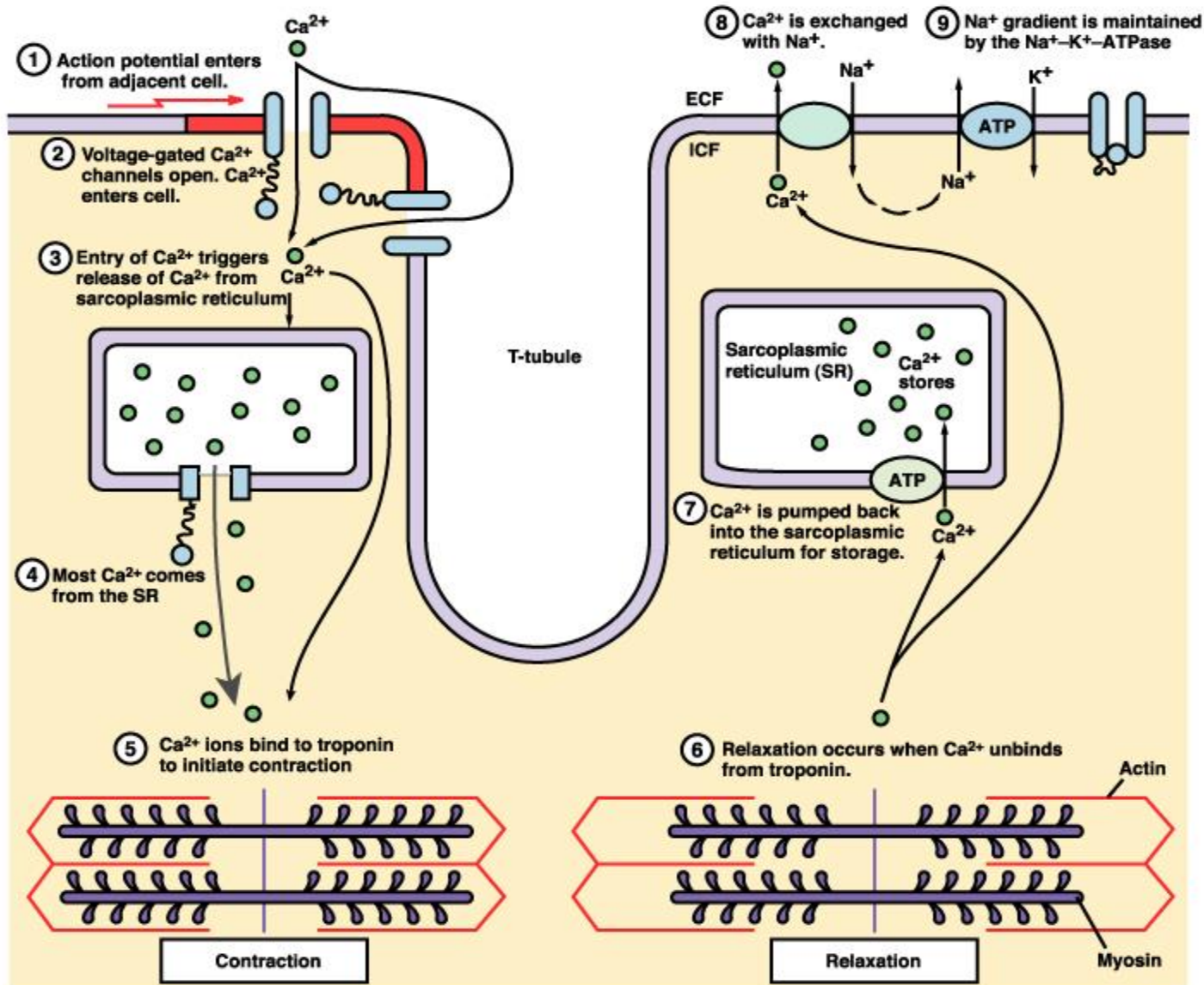
PHASE 0 OF THE FAST FIBER ACTION POTENTIAL



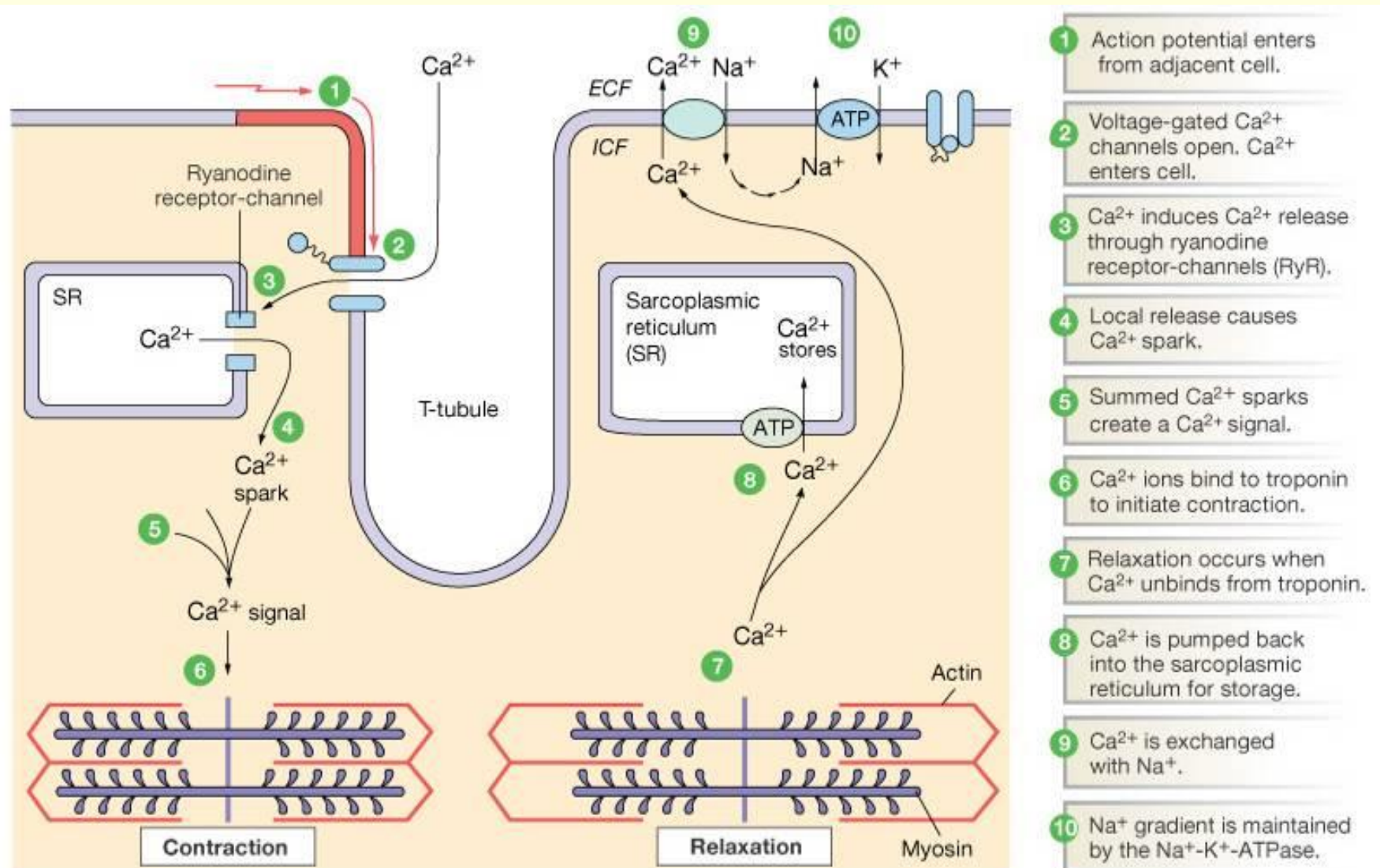


Phase	Membrane channels
①	Na^+ channels open
②	Na^+ channels close
③	Ca^{2+} channels open; fast K^+ channels close
④	Ca^{2+} channels close; slow K^+ channels open
⑤	Resting potential

The importance of calcium influx through the slow voltage gated calcium channels

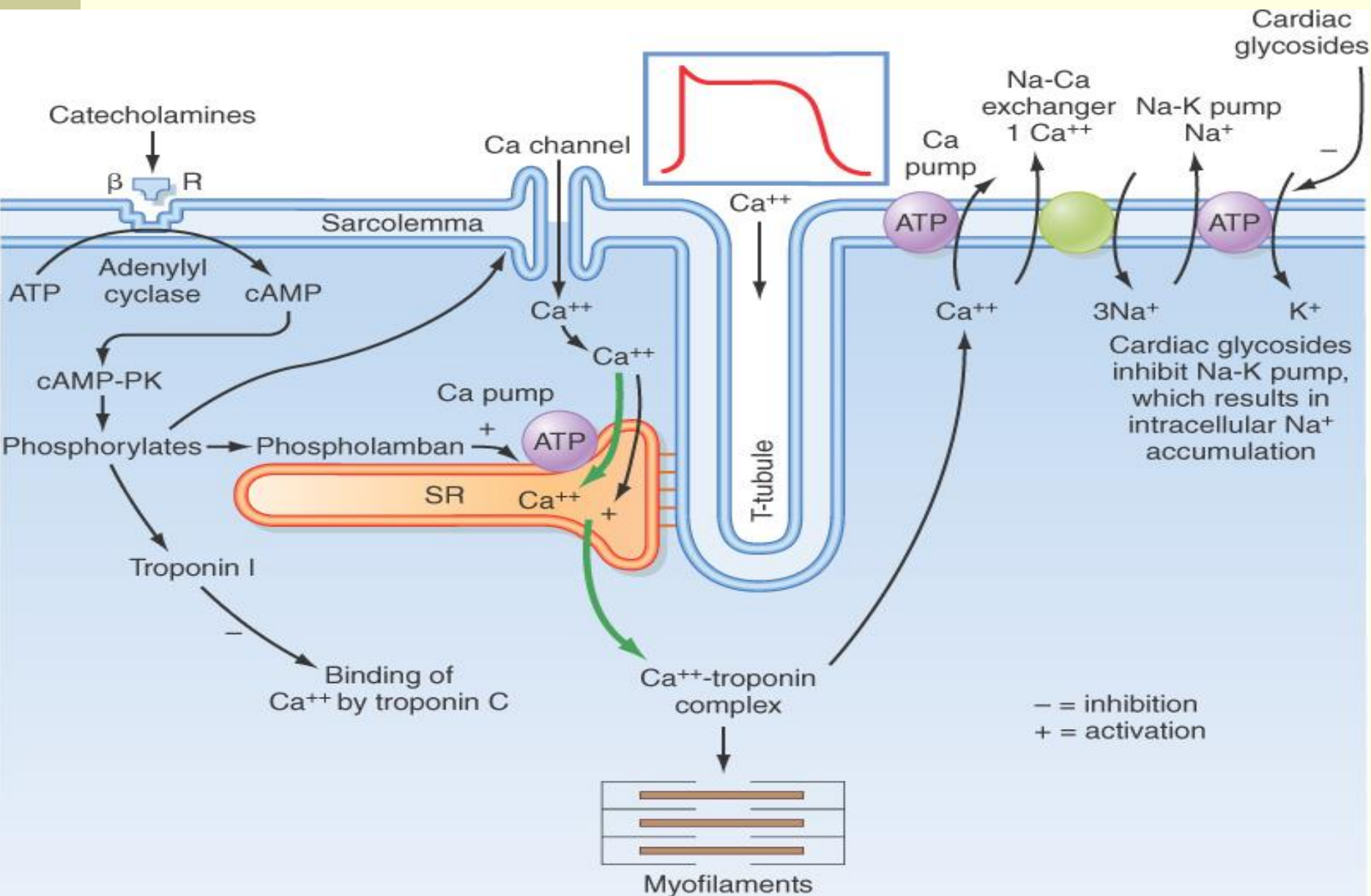


Mechanism of Cardiac Muscle Excitation, Contraction & Relaxation

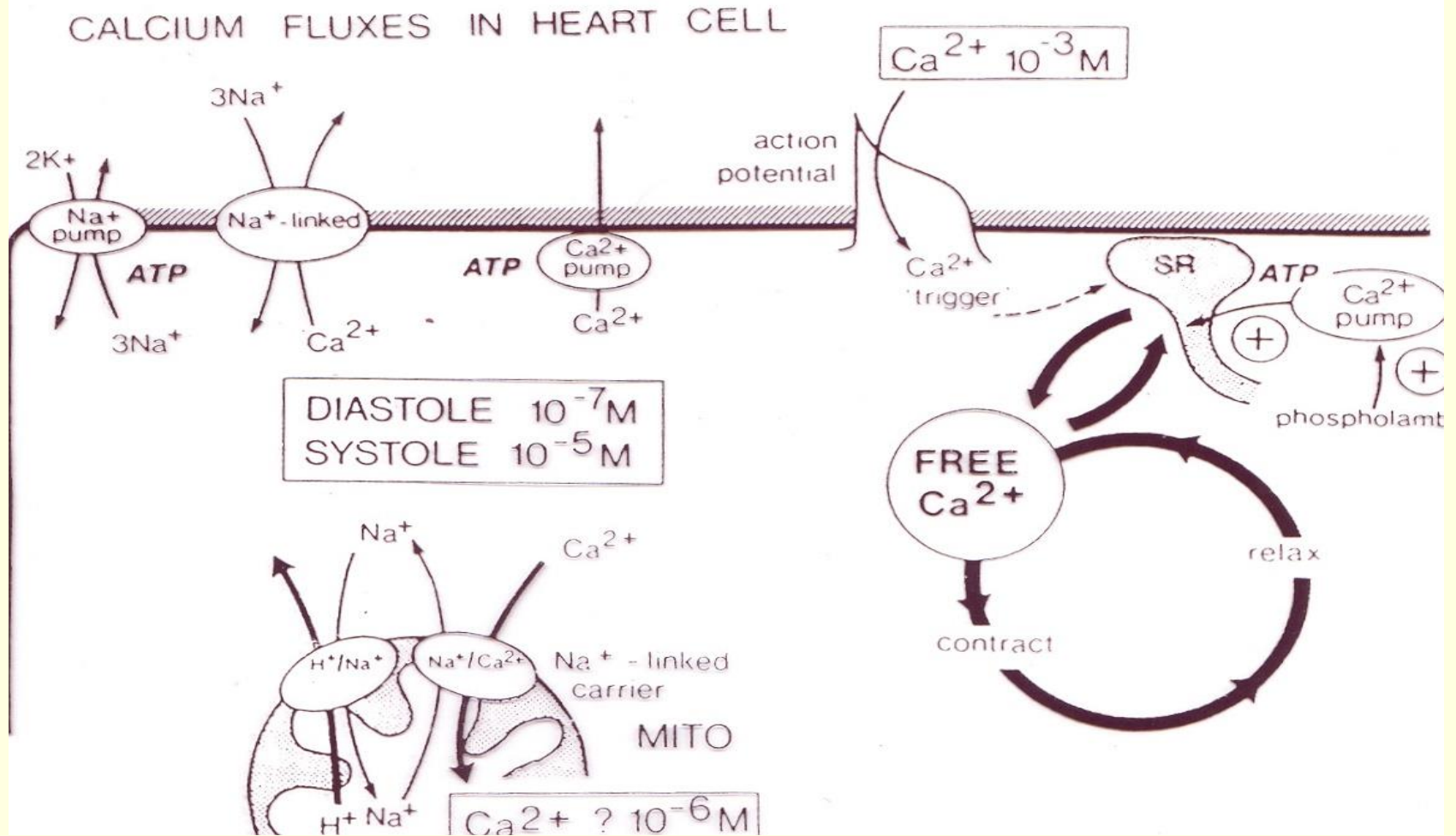


- 1 Action potential enters from adjacent cell.
- 2 Voltage-gated Ca^{2+} channels open. Ca^{2+} enters cell.
- 3 Ca^{2+} induces Ca^{2+} release through ryanodine receptor-channels (RyR).
- 4 Local release causes Ca^{2+} spark.
- 5 Summed Ca^{2+} sparks create a Ca^{2+} signal.
- 6 Ca^{2+} ions bind to troponin to initiate contraction.
- 7 Relaxation occurs when Ca^{2+} unbinds from troponin.
- 8 Ca^{2+} is pumped back into the sarcoplasmic reticulum for storage.
- 9 Ca^{2+} is exchanged with Na^{+} .
- 10 Na^{+} gradient is maintained by the Na^{+} - K^{+} -ATPase.

Intracellular Calcium Homeostasis...1



Intracellular Calcium Homeostasis...2



Cardiac Muscle action potential Vs. Skeletal Muscle

- Phase 0 –Depolarization phase (Na^+ influx)
- Phase 1 partial repolarization (Not in skeletal)
- Phase 2 Plateau (~ depolarization not in skeletal) slow calcium channels
- Phase 3 fast repolarization phase (K^+ repolarization)
- Phase 4 resting membrane potential

Thank You



Conduction System of the Heart

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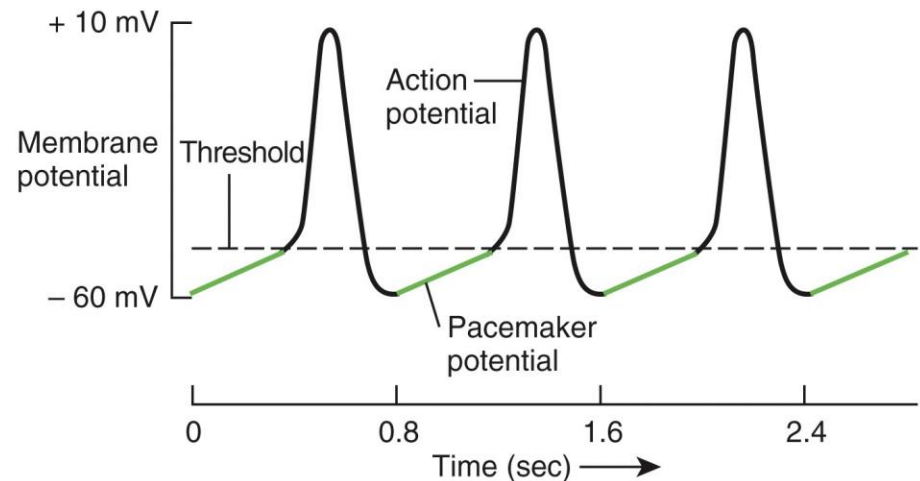


Objectives

- List the parts that comprise the conduction system
- Explain the mechanism of slow response action potential (pacemaker potential)
- Point out the regulation of the conduction system potential by Autonomic Nerves

Autorhythmicity

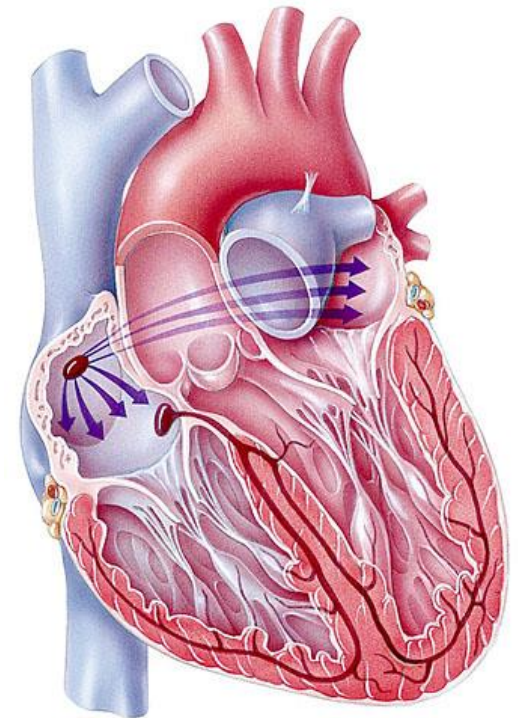
- During embryonic development, about 1% of all of the muscle cells of the heart form a network or pathway called the **cardiac conduction system**.
- This specialized group of **myocytes** is unusual in that they have the ability to spontaneously depolarize.



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

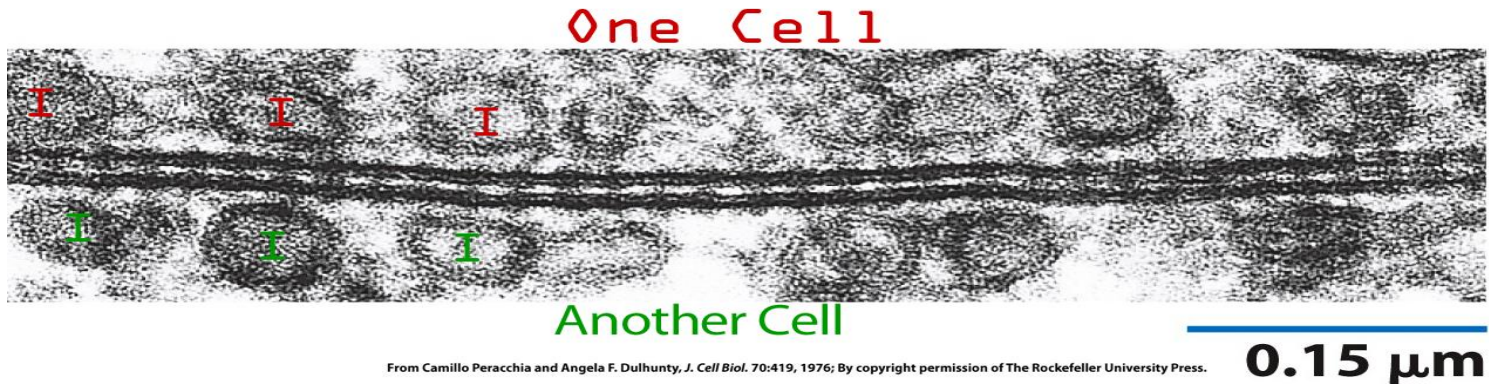
Autorhythmicity

- The rhythmical electrical activity they produce is called **autorhythmicity**.
- It does not rely on the central nervous system to sustain a lifelong heartbeat.



Autorhythmicity

- Autorhythmic cells spontaneously depolarize at a given rate, some groups faster, some groups slower.
- Once a group of autorhythmic cells reaches threshold and starts an action potential (AP), all of the cells in that area of the heart also depolarize.

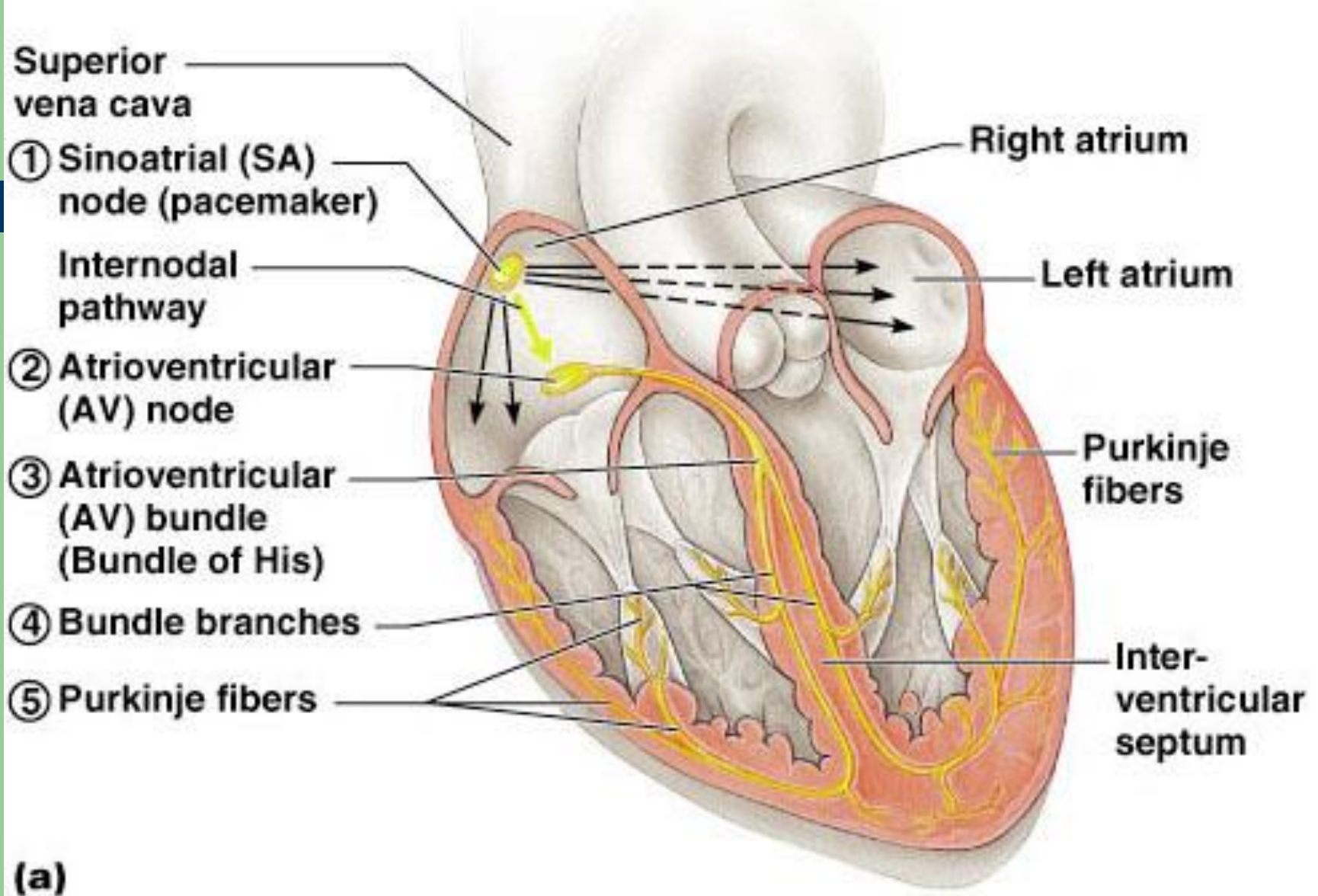


Membrane of two cells clearly seen. The spread of ions through gap junctions of the Intercalated discs (I) allows the AP to pass from cell to cell

Autorhythmic Fibers

- Specialized cardiac muscle fibers
- Self-excitabile
- Repeatedly generate action potentials that trigger heart contractions
- 2 important functions
 1. Act as pacemaker
 2. Form conduction system

Conducting System of Heart



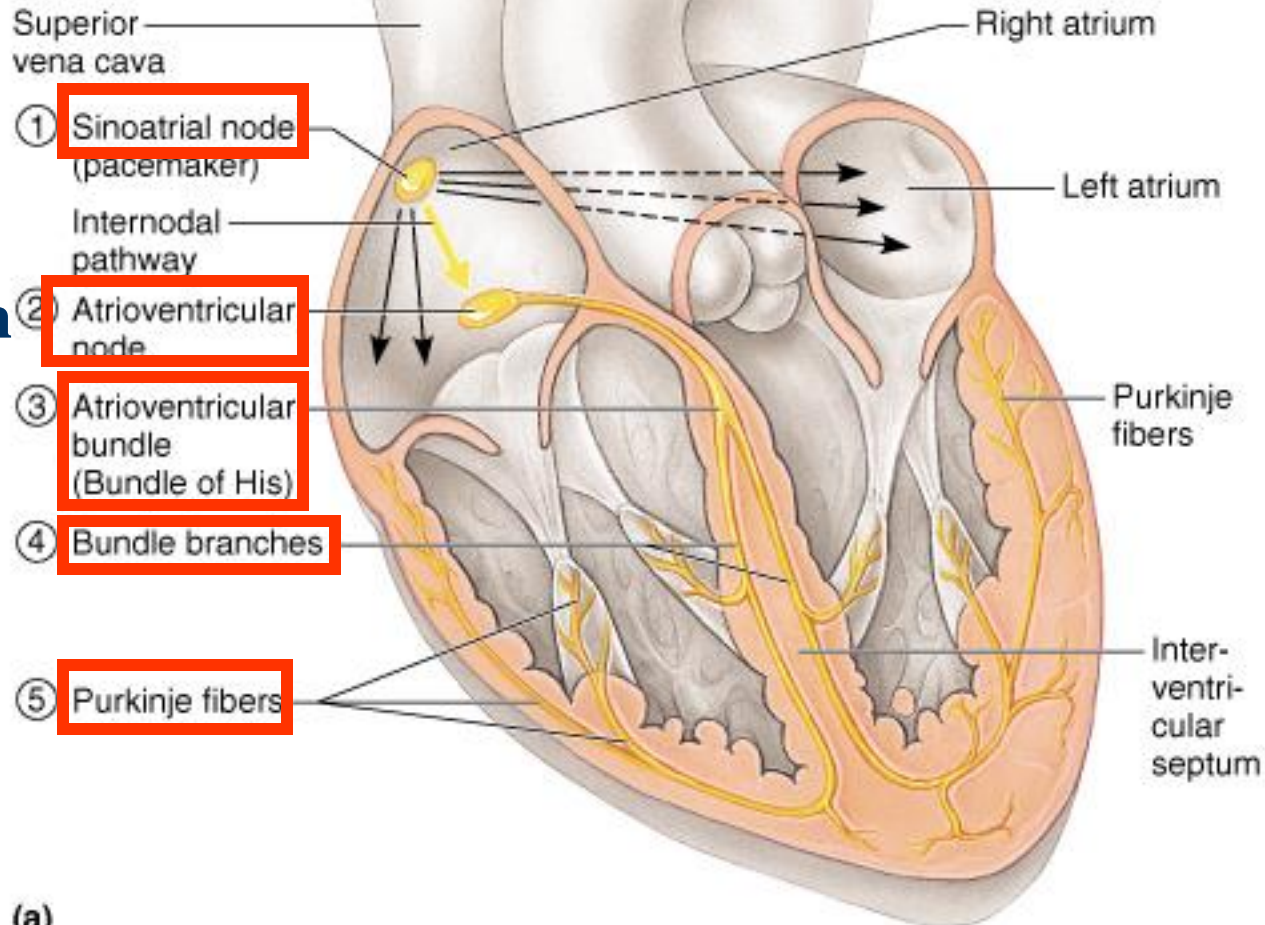
Intrinsic Cardiac Conduction System

Approximately 1% of cardiac muscle cells are autorhythmic rather than contractile

70-80/min

40-60/min

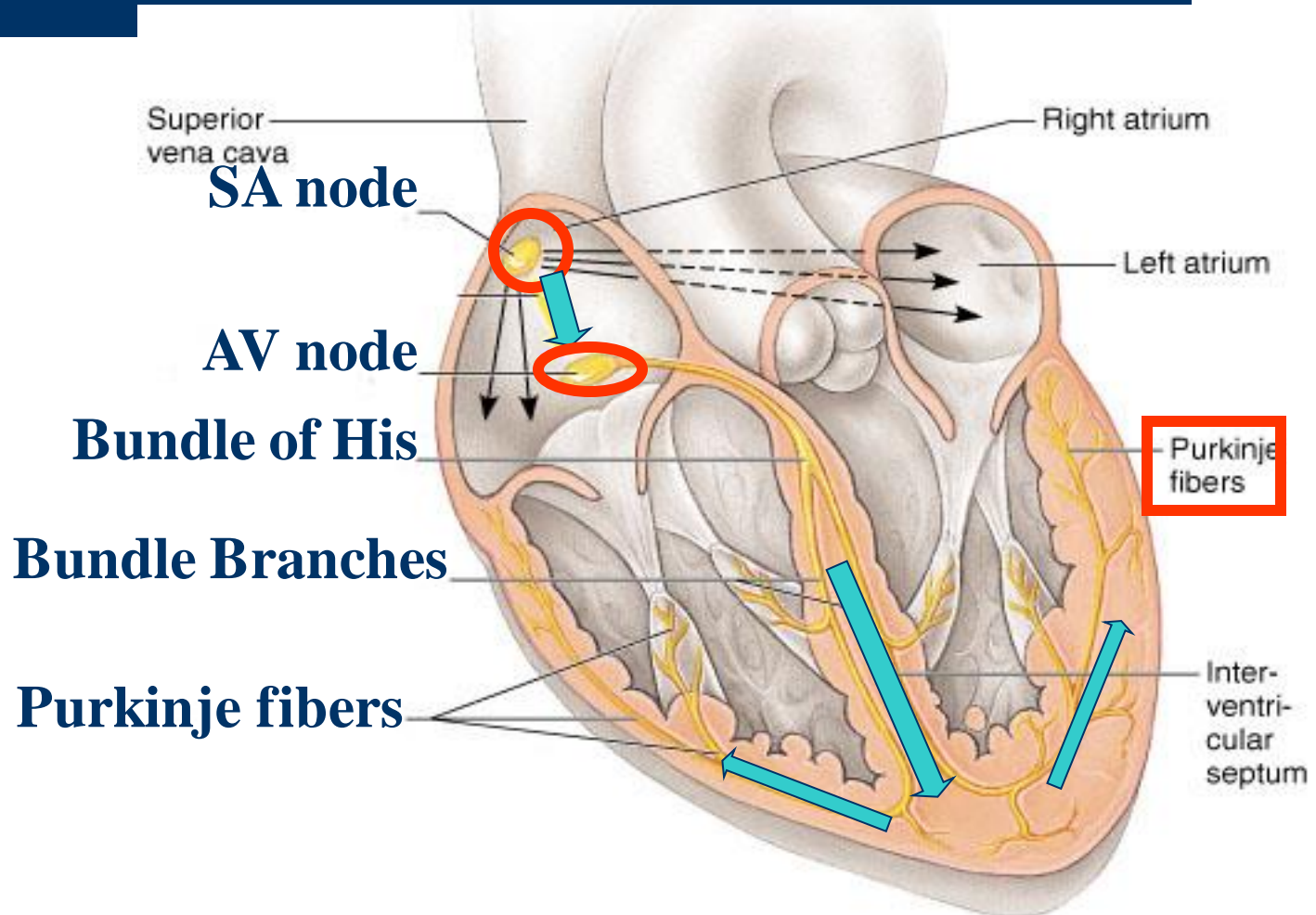
15-40/min



(a)

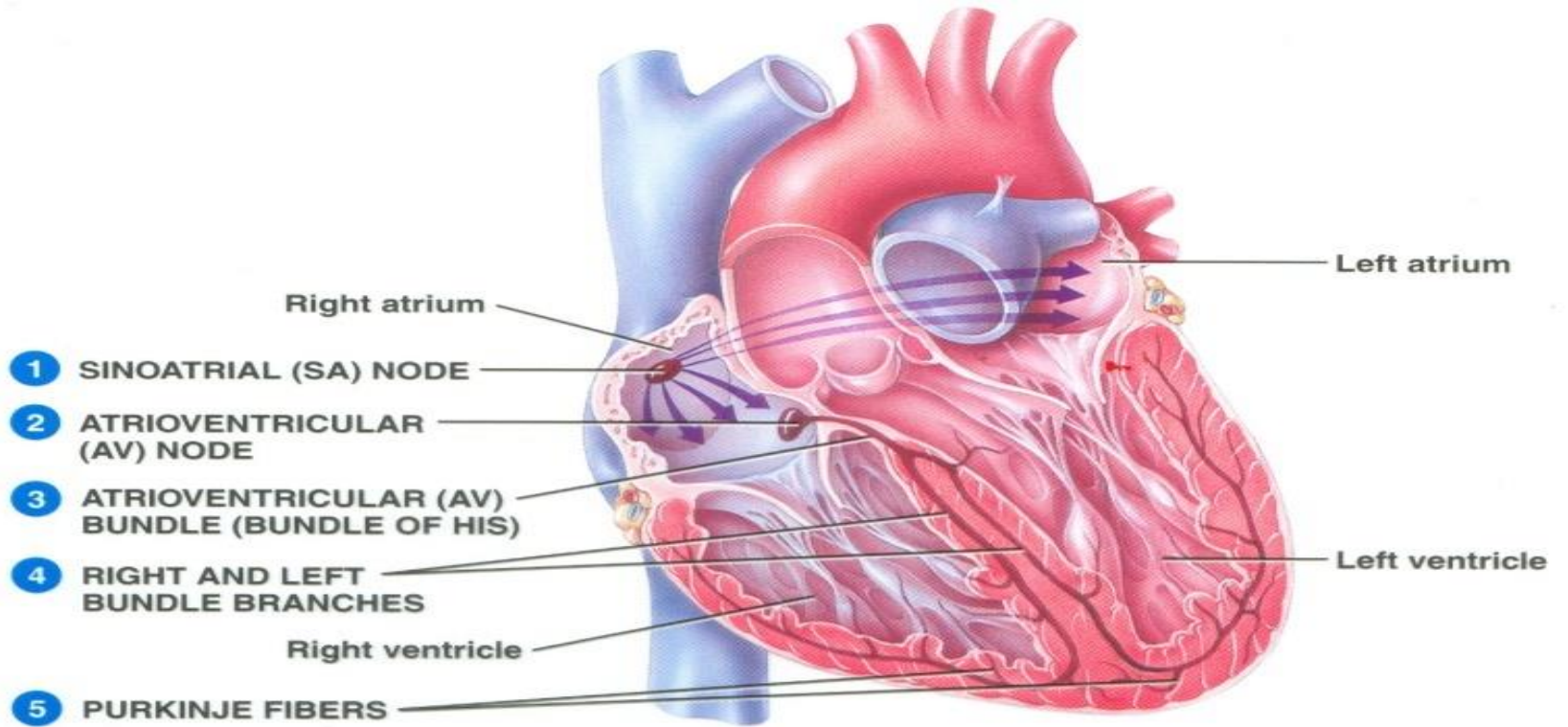
Intrinsic Conduction System

Function: initiate & distribute impulses so heart depolarizes & contracts in orderly manner from atria to ventricles.

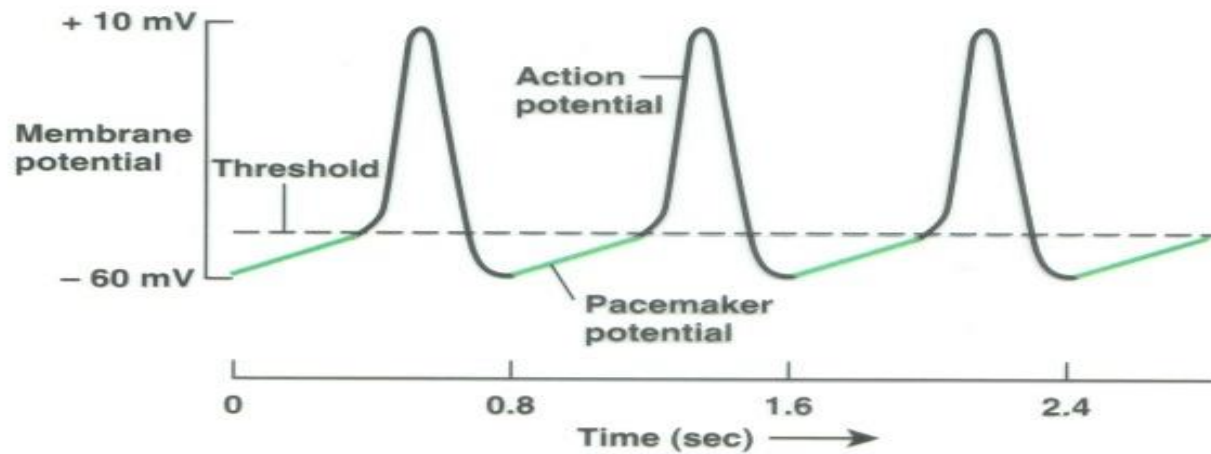


Sinus Node

- 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 .



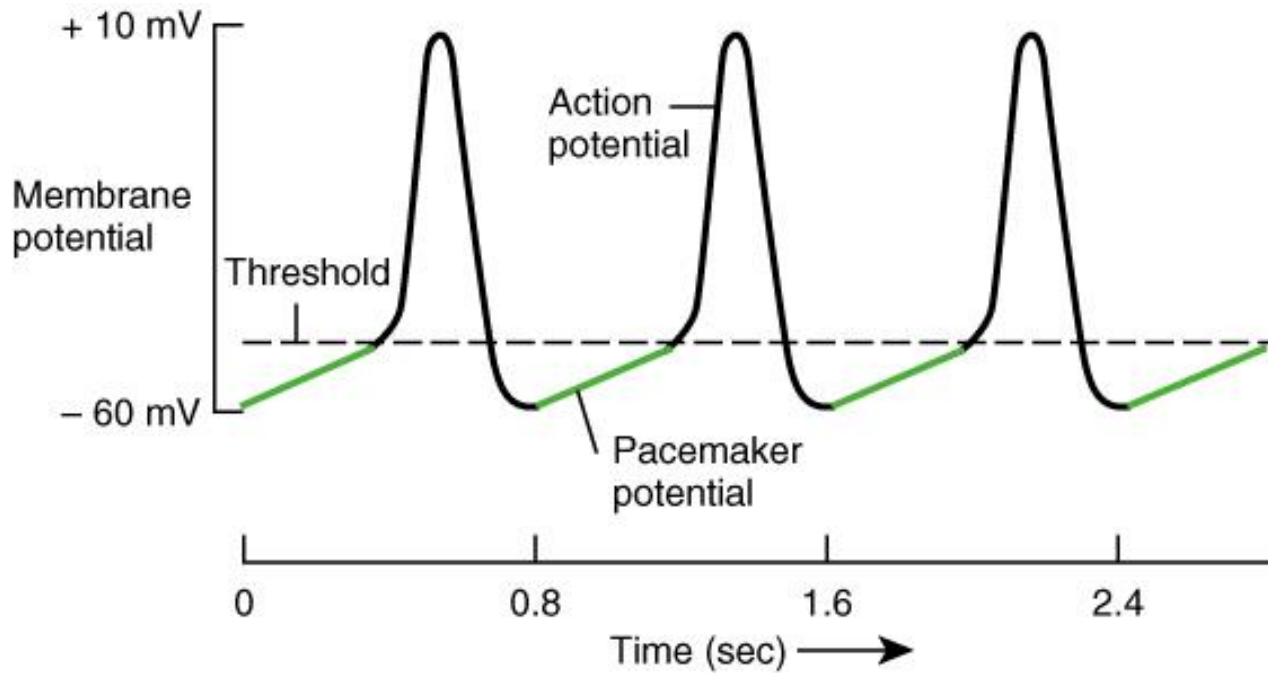
(a) Anterior view of frontal section



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

Conduction System

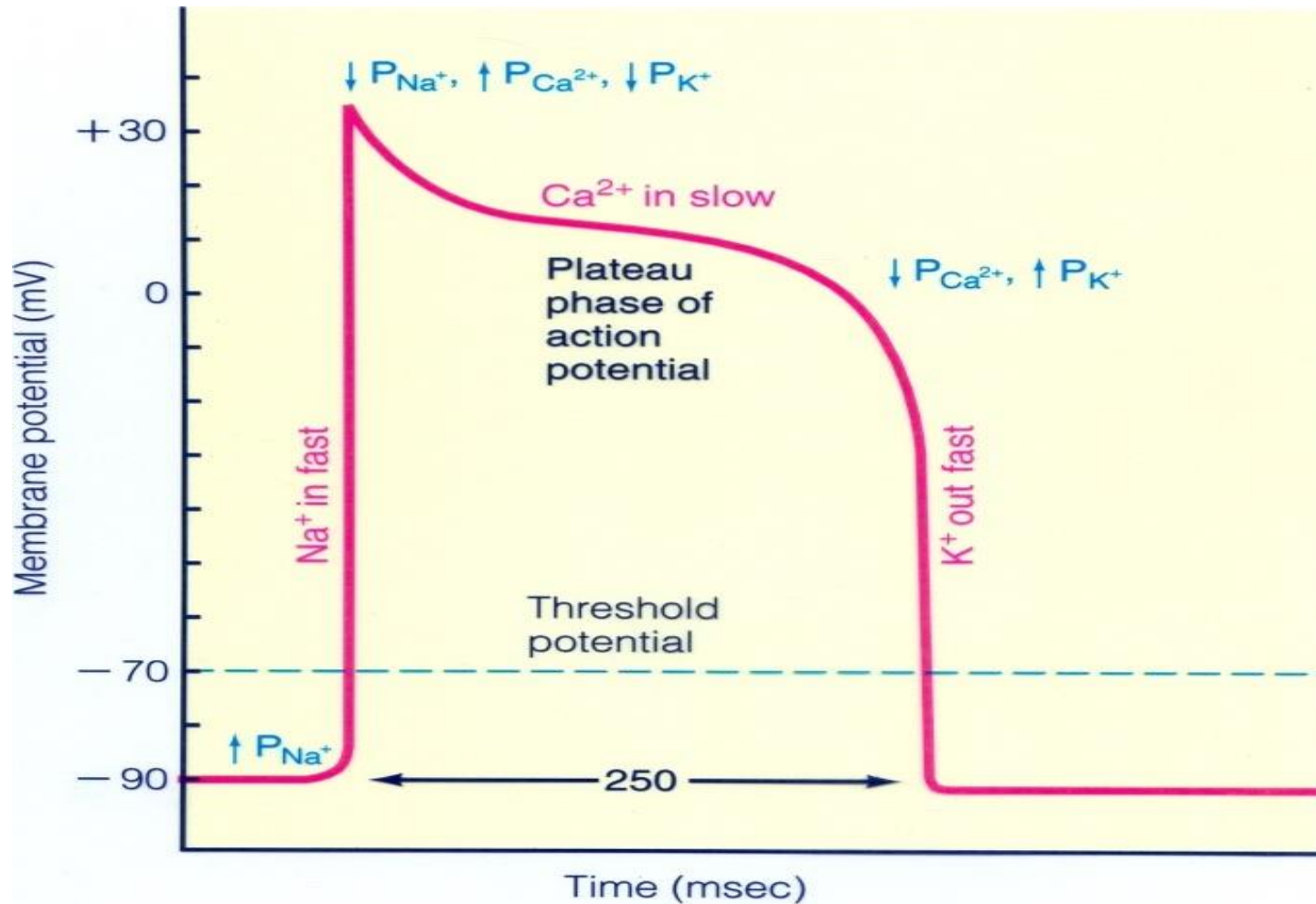
1. Begins in sinoatrial (SA) node in right atrial wall
 - Propagates through atria via gap junctions
 - Atria contract
2. Reaches atrioventricular (AV) node in interatrial septum
3. Enters atrioventricular (AV) bundle (Bundle of His)
 - AV node is the only site where action potentials can conduct from atria to ventricles due to fibrous skeleton
4. Enters right and left bundle branches which extends through interventricular septum toward apex
5. Finally, large diameter Purkinje fibers conduct action potential to remainder of ventricular myocardium
 - Finally, ventricles contract.



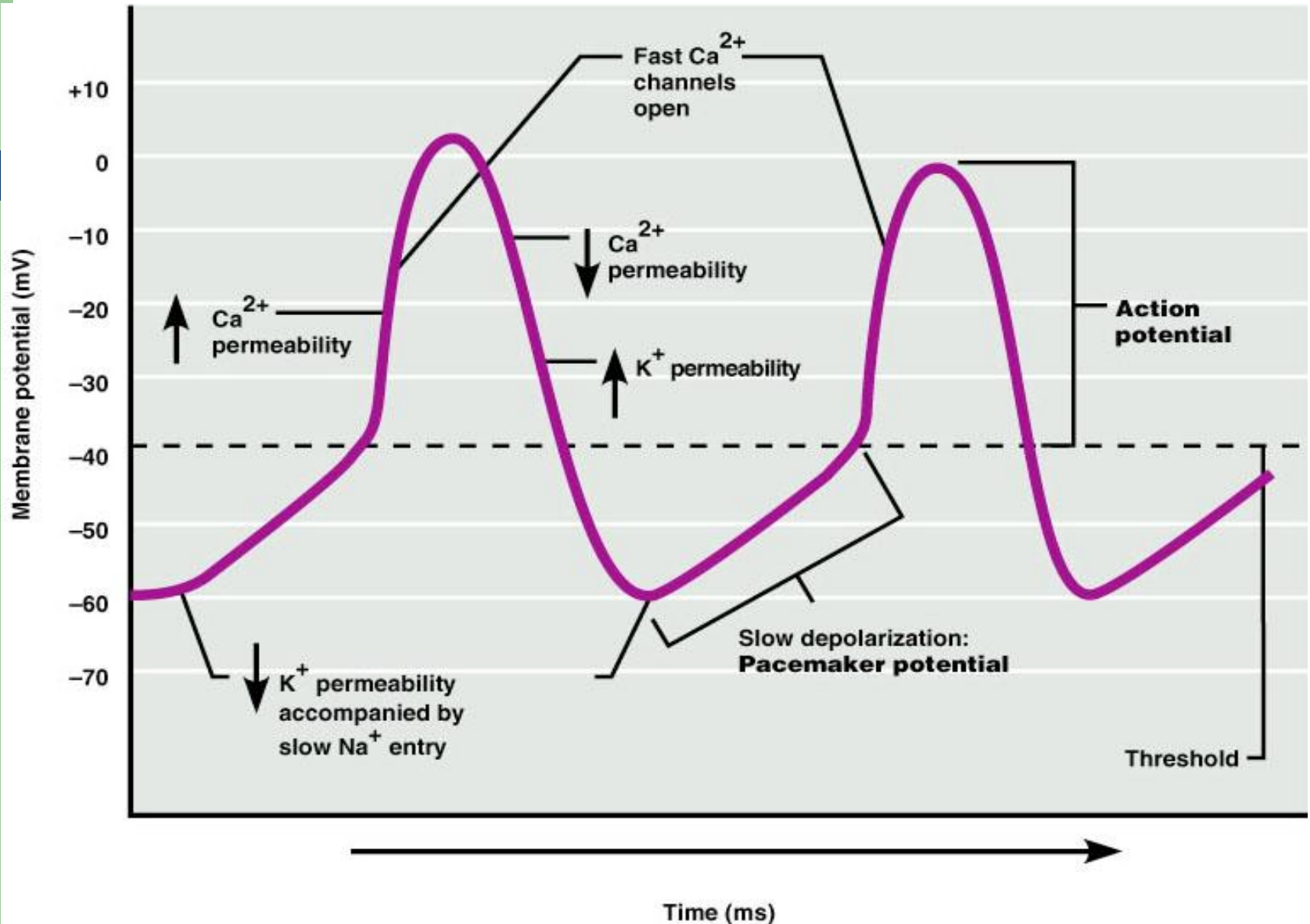
(b) Pacemaker potentials and action potentials in autorhythmic fibers of SA node

20.10b

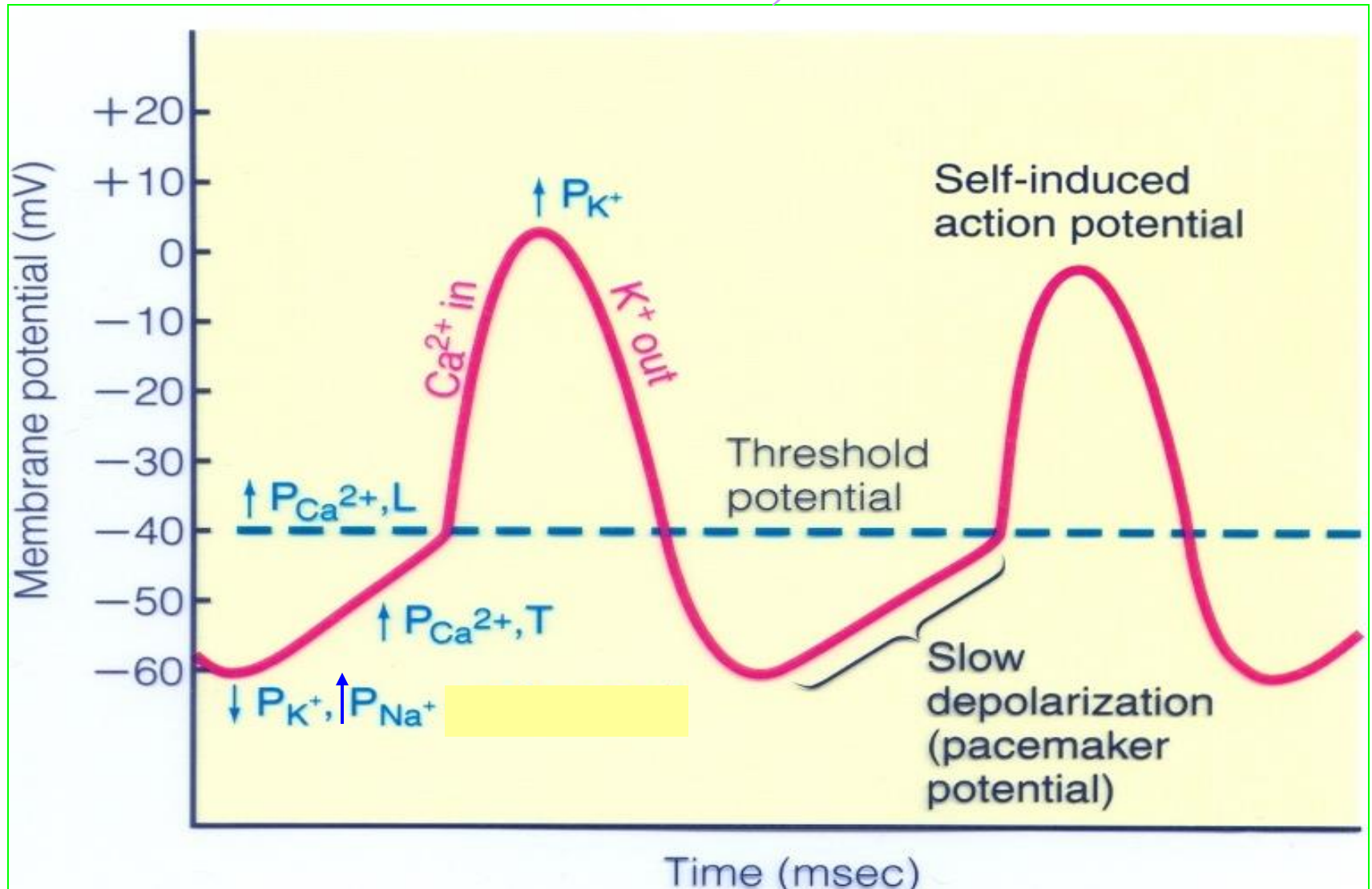
Fast Response Action Potential of Contractile Cardiac Muscle Cell



Pacemaker and Action Potentials of the Heart



Slow Response Action Potential (Pacemaker Potential)



Intrinsic rate and speed of conduction of the components of the system

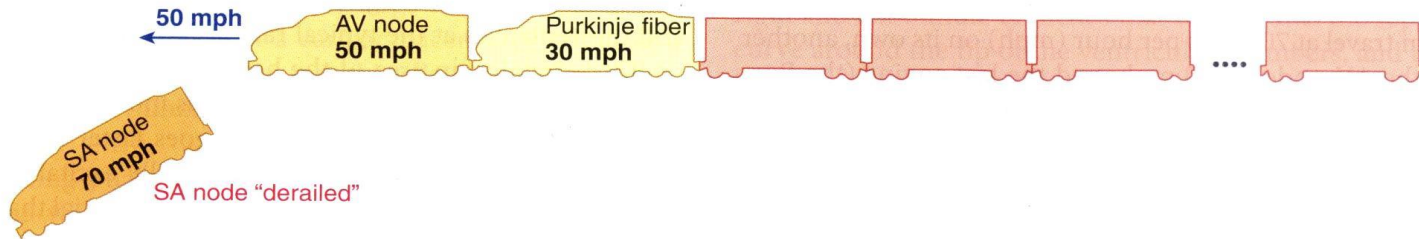
- SA node 60-80 action potential /min (*Pacemaker*)
- AV node 40-60 action potential /min
- Purkinje 15-40 action potential /min

Conduction Speed

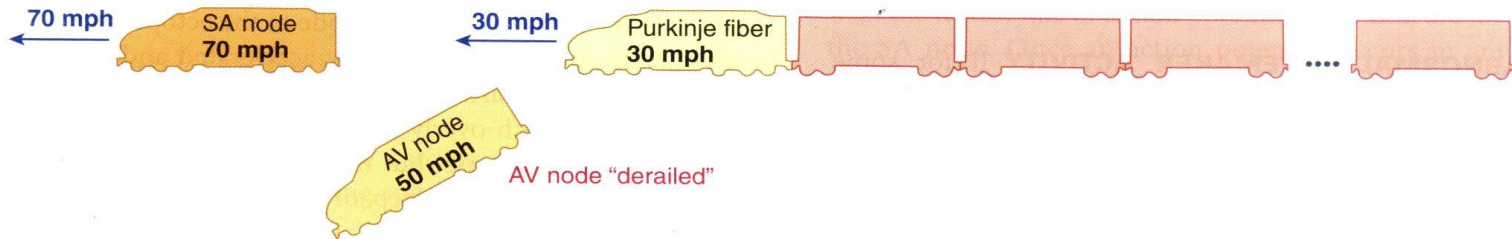
- SA node: slow speed of conduction
- Ventricular and Atrial muscle: Moderate speed
- AV node: slowest speed of conduction
- Purkinje fibers: Fastest speed of conduction
- *Ectopic Pacemaker- Abnormal site of pacemaker*



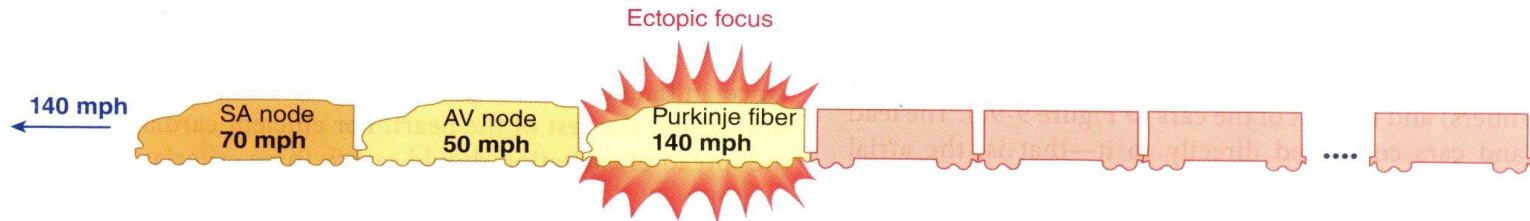
(a) Normal pacemaker activity: Whole train will go **70 mph** (heart rate set by SA node, the fastest autorhythmic tissue).



(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).

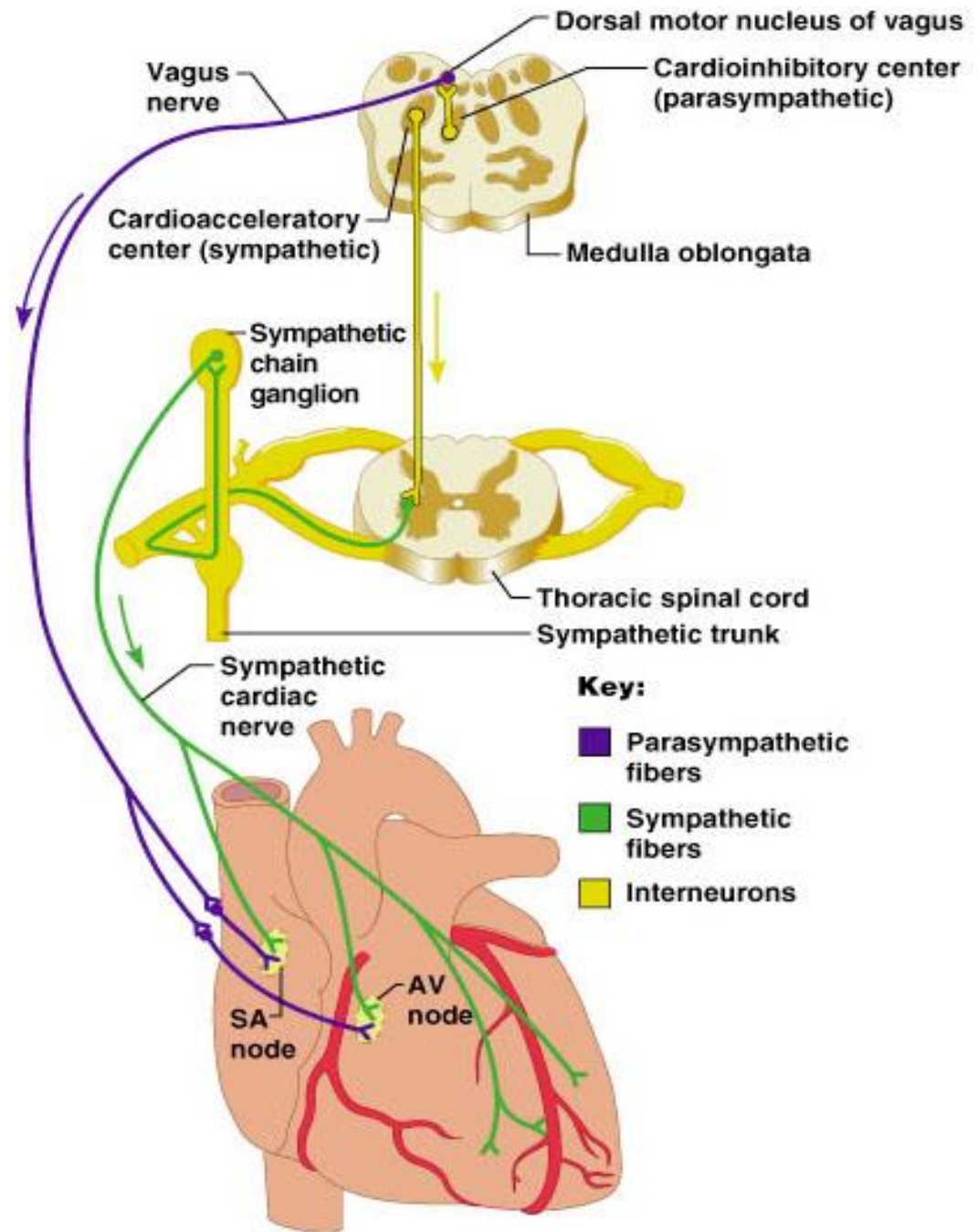


(c) Takeover of ventricular rate by the slower ventricular autorhythmic tissue in complete heart block: First part of train will go **70 mph**; last part will go **30 mph** (atria will be driven by SA node; ventricles will assume own, much slower rhythm).

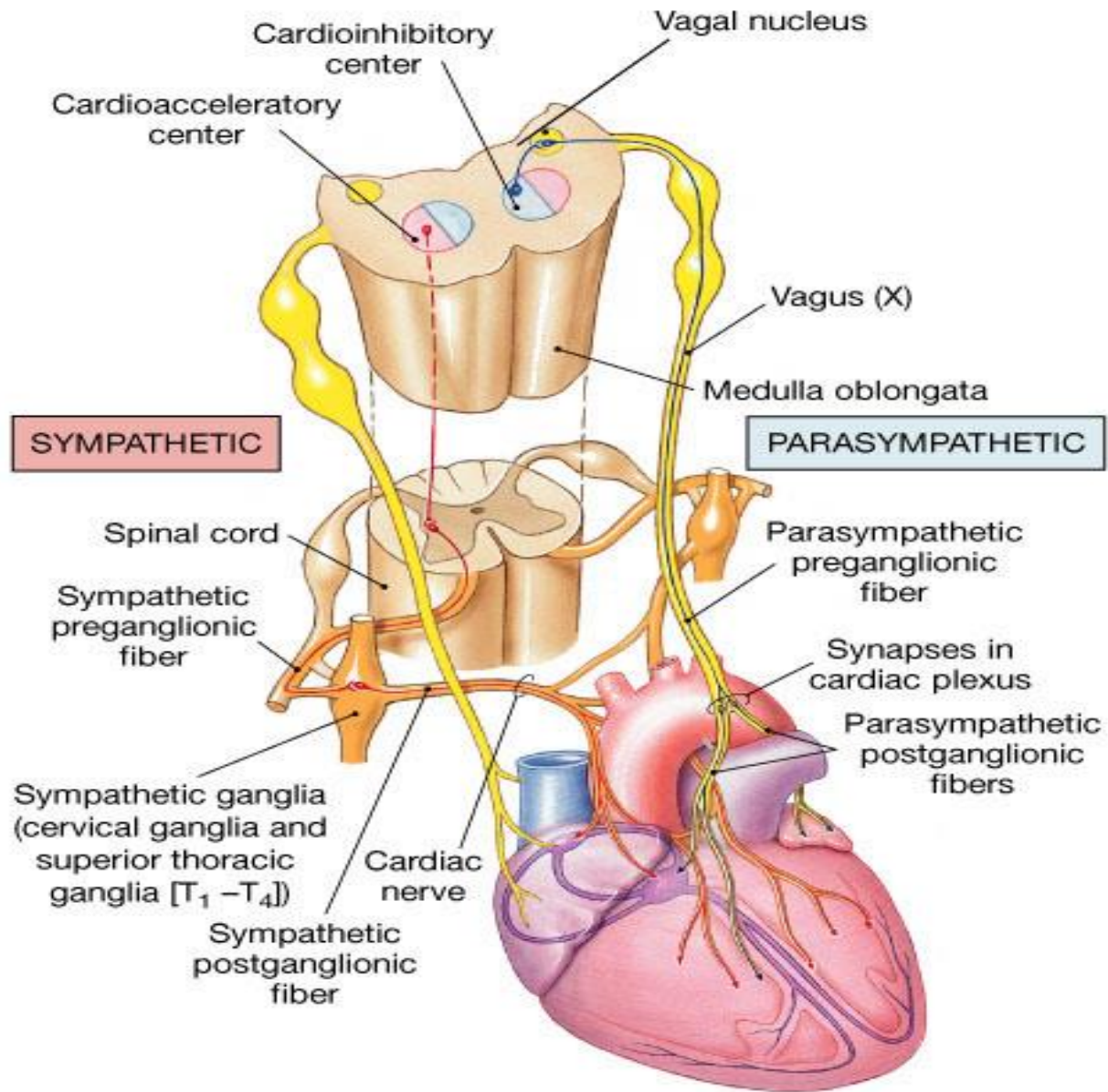


(d) Takeover of pacemaker activity by an ectopic focus: Train will be driven by ectopic focus, which is now going faster than the SA node (the whole heart will be driven more rapidly by an abnormal pacemaker).

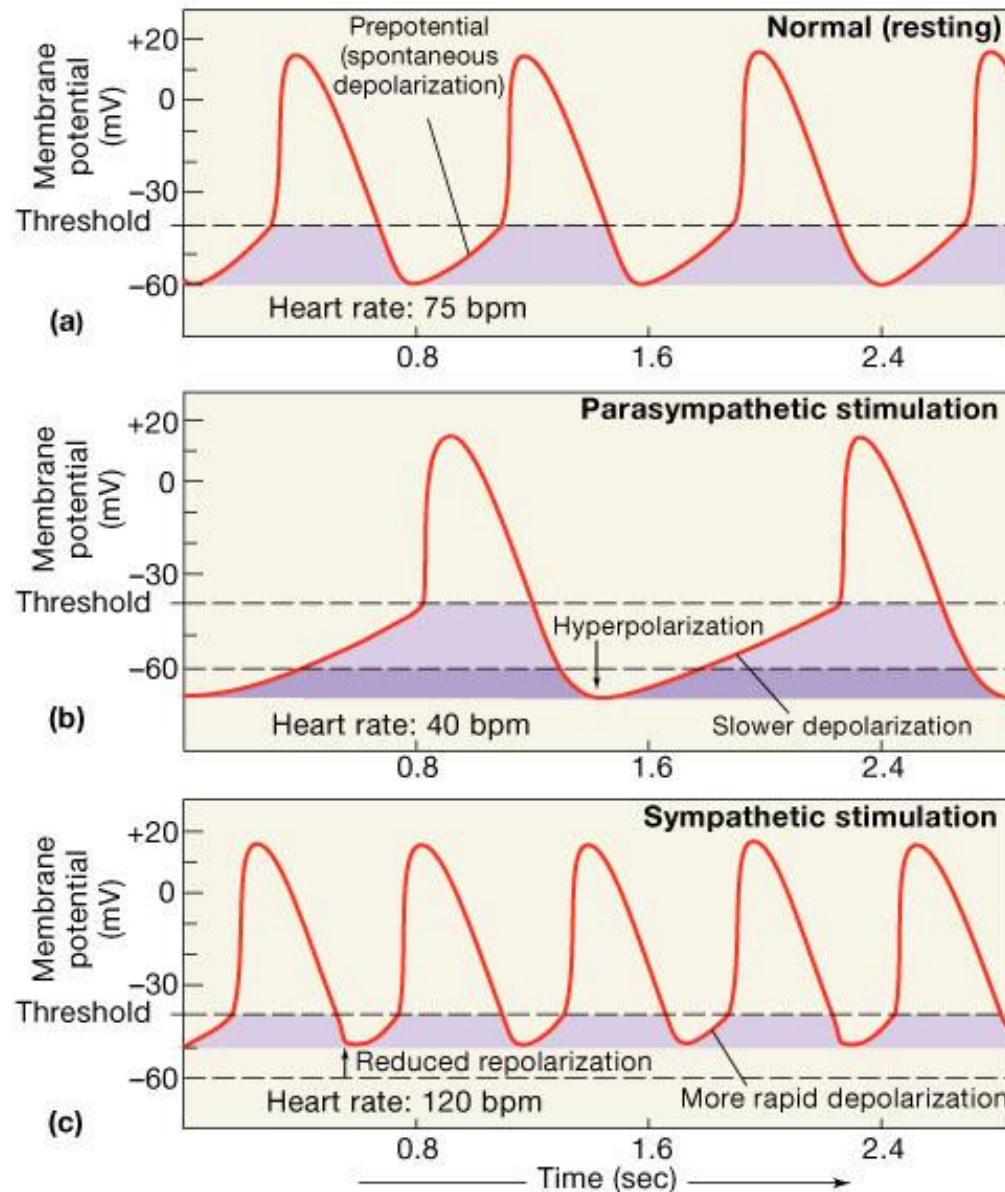
Extrinsic Innervation of the Heart



Heart

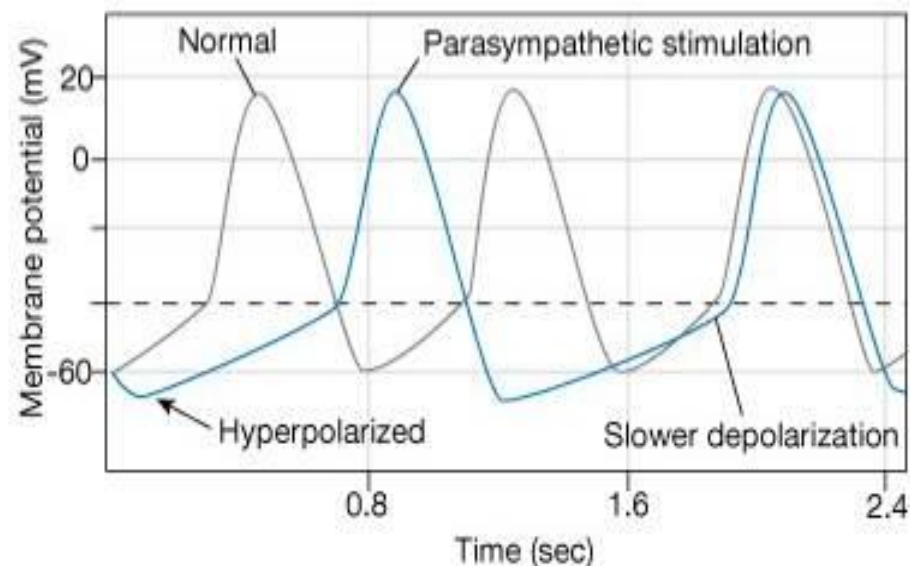
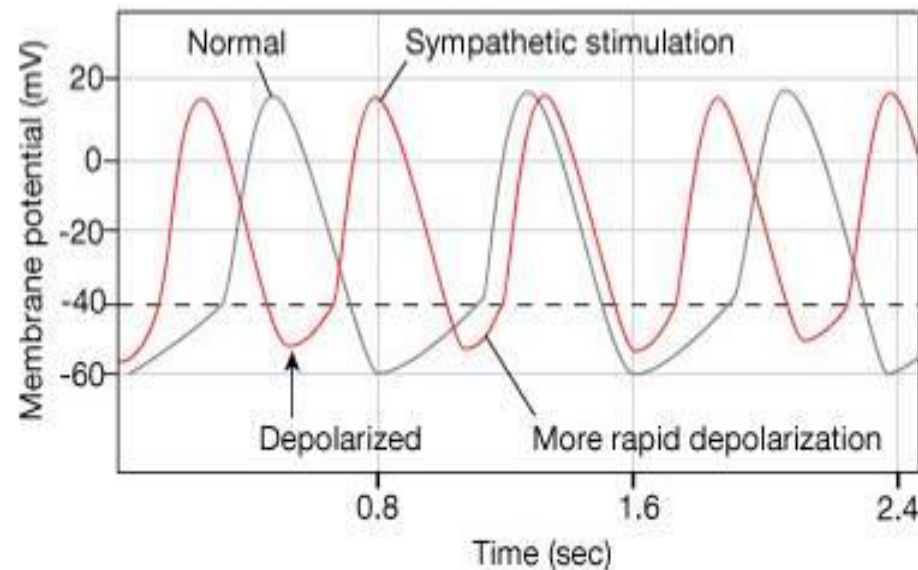


Pacemaker Function



Autonomic neurotransmitters affect ion flow to change rate

- **Sympathetic** – increases heart rate by \uparrow Ca^{+2} & I_f channel (net Na^+) flow
- **Parasympathetic** – decreases rate by \uparrow K^+ efflux & \downarrow Ca^{+2} influx



Regulation of the heart beat

- Sympathetic from the cardiac plexus supplies all parts of the heart (atria, ventricle and all parts of the conduction system)
- Parasympathetic from Vagus nerves supply mainly the atria, SA and AV nodes, very little supply to ventricles
- Sympathetic: increase the permeability of the cardiac cells to Na^+ and Ca^{++} i.e Positive **Chronotropic** and positive **Inotropic** action
- Parasympathetic: Increase the permeability of the cardiac cells to K^+ and decrease its permeability to Na^+ and Ca^{++}

Sinus Node is Cardiac Pacemaker

- Normal rate of discharge in sinus node is 70-80/min.; A-V node - 40-60/min.; Purkinje fibers - 15-40/min.
- Sinus node is pacemaker because of its faster discharge rate
- Intrinsic rate of subsequent parts is suppressed by “Overdrive suppression”

Ectopic Pacemaker

- This is a portion of the heart with a more rapid discharge than the sinus node.
- Also occurs when transmission from sinus node to A-V node is blocked (A-V block).

Parasympathetic Effects on Heart Rate

- Parasympathetic (vagal) nerves, which release acetylcholine at their endings, innervate S-A node and A-V junctional fibers proximal to A-V node.
- Causes hyperpolarization because of increased K^+ permeability in response to acetylcholine.
- This causes decreased transmission of impulses maybe temporarily stopping heart rate.

Sympathetic Effects on Heart Rate

- Releases norepinephrine at sympathetic ending
- Causes increased sinus node discharge (*Chronotropic effect*)
- Increases rate of conduction of impulse (*Dromotropic effect*)
- Increases force of contraction in atria and ventricles (*Inotropic effect*)

Thank You

