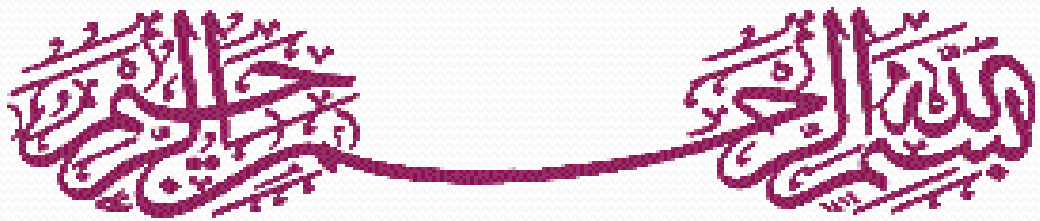

السلام عليكم ورحمة الله وبركاته

Cardiovascular System Block
Contractile Mechanism in Cardiac Muscle
(Physiology)

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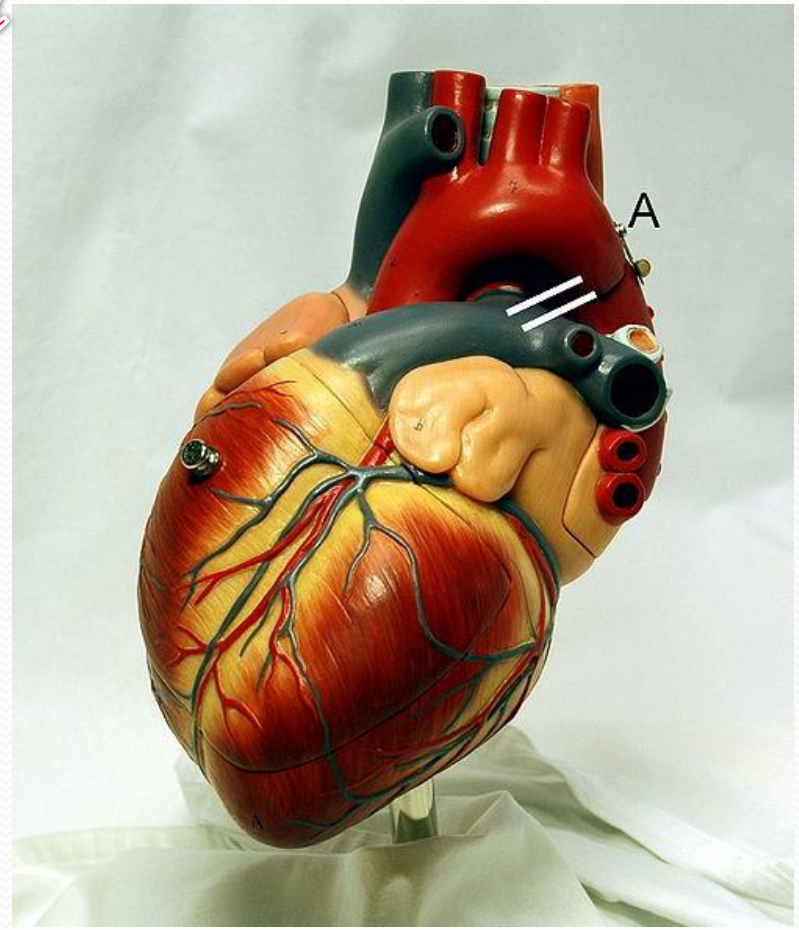


Learning Objectives

- Define cardiac muscle contractility & types of its contraction
- Understand the physiology of cardiac muscle
- Understand the phases of cardiac action potential and the ionic bases
- Identify the refractory period of cardiac muscle
- Discuss the role of Ca^{++} in the regulation of cardiac muscle function
- Describe the mechanism of excitation contraction coupling
- Discuss factors affecting cardiac contractility

The Contractility of the Cardiac Muscle

- **Contractility:** Is the force of contraction for a given fiber length.
- Cardiac muscle fiber contracts when stimulated.
- Strength of contraction determines the pumping power of the heart.
- Cardiac contractile filaments are quite similar to that in skeletal muscle:
  - Thick filaments: (myosin)
  - Thin filaments: (actin, troponin, tropomyocin)
- Ca^{++} regulates contraction: Will be discussed later

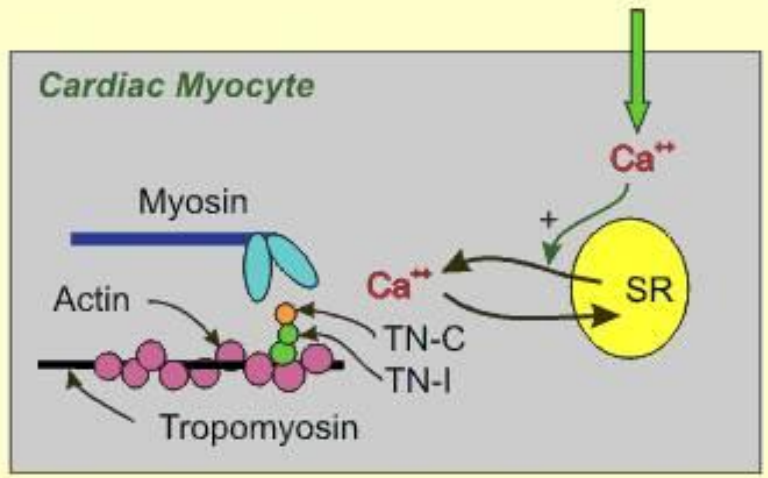


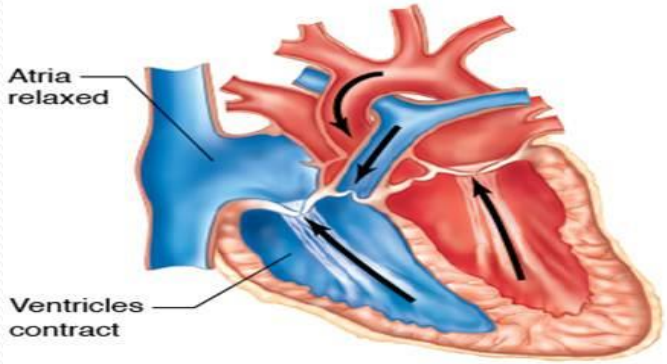
Figure 2. Cardiac myofilaments. Myosin (thick filament) contains two heads having ATPase activity. Thin filament is made up of actin, tropomyosin, and troponin (TN). TN-C binds Ca^{++} released by the sarcoplasmic reticulum (SR). TN-I inhibits actin-myosin binding until Ca^{++} binds to TN-C.

The Contractility of the Cardiac Muscle

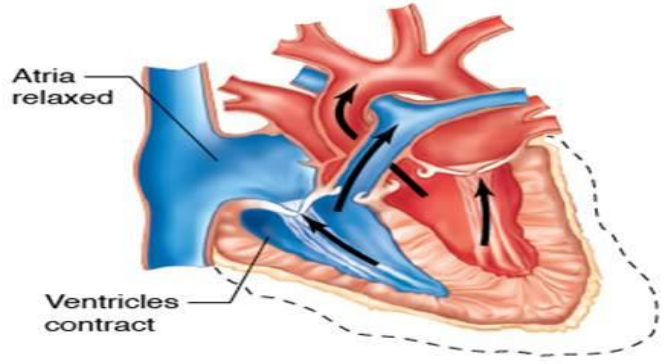
- Cardiac muscle can perform both isometric (isovolumic) & isotonic types of contractions

- ***Isometric contraction***: The stimulated muscle exerts an internal tension but cannot be shortened (NO work with same length). Ventricular pressure rises to high level to open aortic & pulmonary valves.

- ***Isotonic contraction***: The stimulated muscle is allowed to shorten with same tension. Volume of heart diminishes & ventricles pumps blood into lung or body through opened aortic & pulmonary valves.



Aortic & pulmonary valves closed



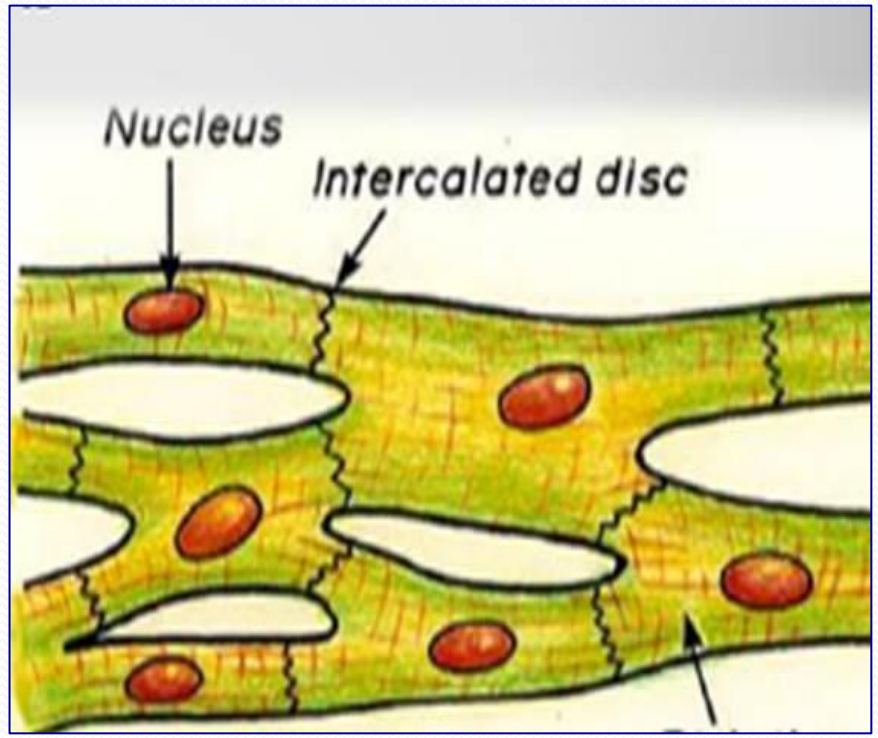
Aortic & pulmonary valves opend

Physiology of Cardiac Muscle

- ✓2 major types of cardiac muscle cells:

  I: Contractile cells.

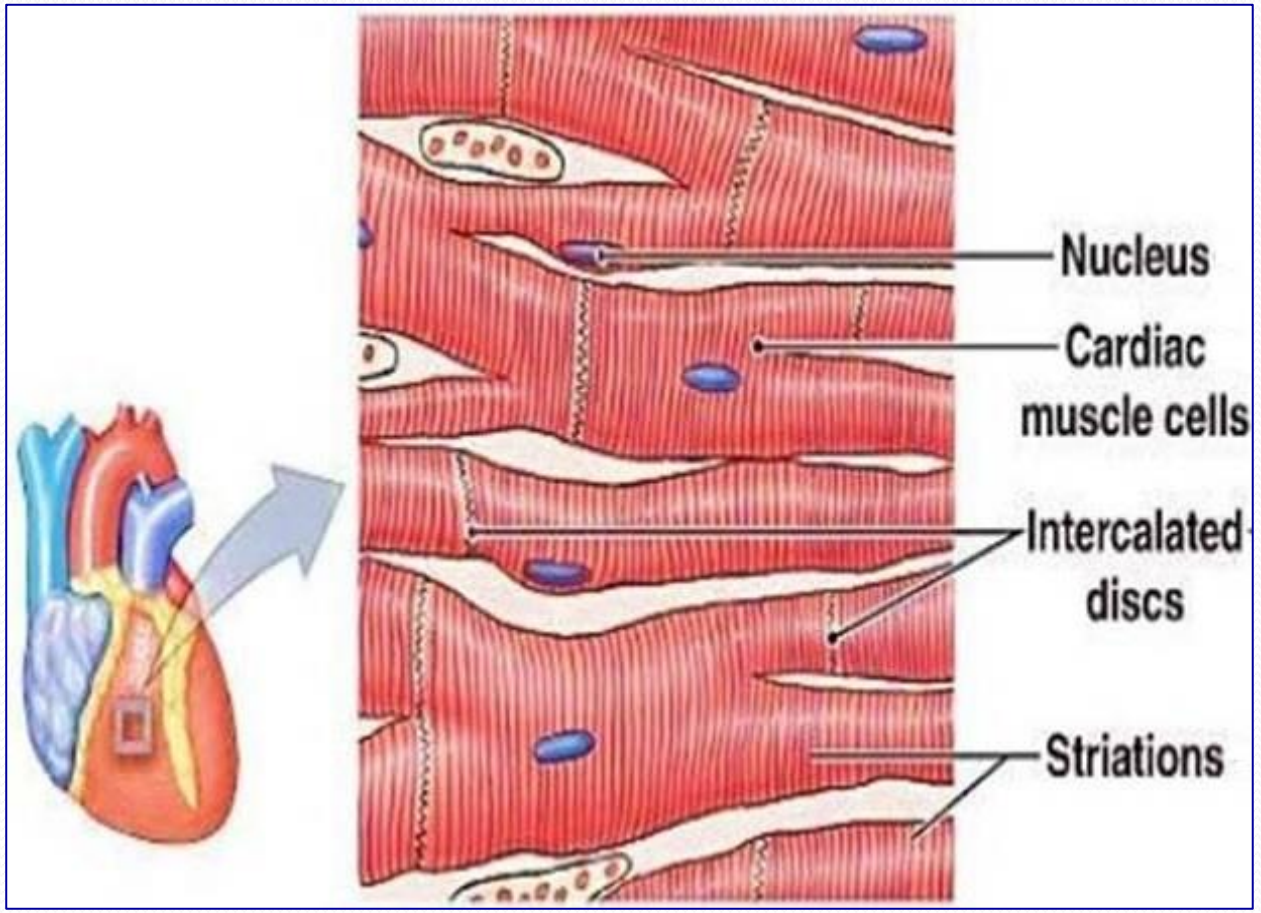
  II: Conducting cells.



I: Contractile Cells

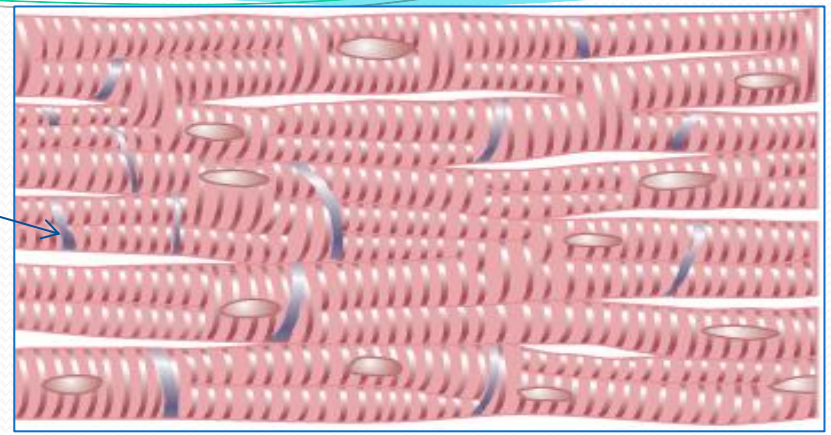
They have special characteristics:

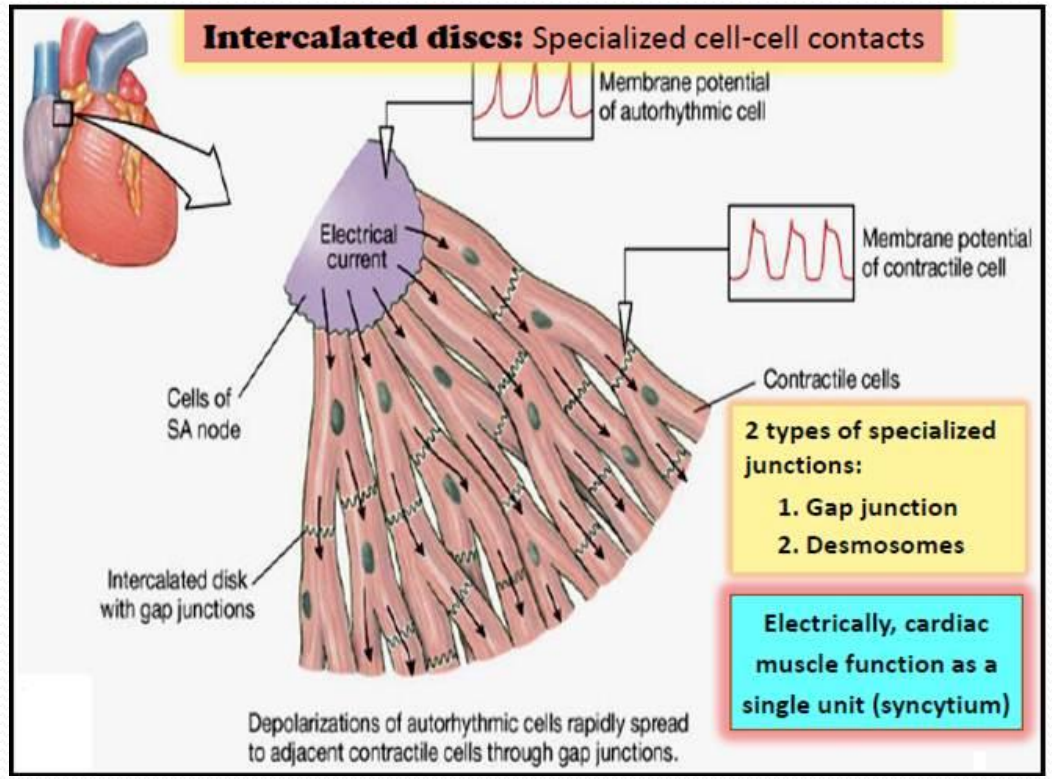
- ✓ Striated.
- ✓ Usually has a single nucleus.
- ✓ Rich in mitochondria (up to 40% of cell volume)
- ✓ Elongated (cylindrical)
- ✓ Branched & interdigitated.
- ✓ A membrane surrounds each fiber i.e. separate fibers.



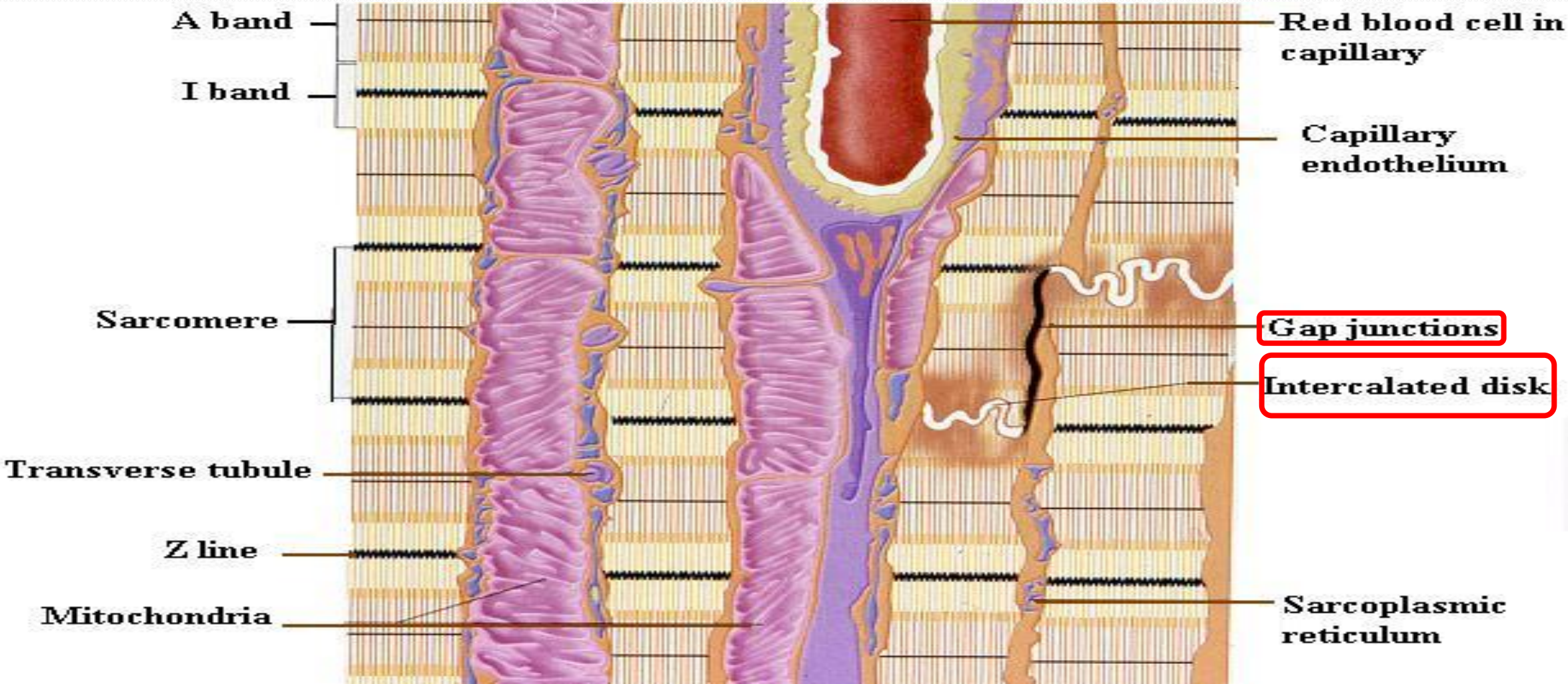
I: Contractile Cells….Cont.

- They have "**Intercalated Discs**": cell membranes, separate individual cardiac muscle cells from one another
- They have "**Gap Junctions**": trans-membrane channel proteins, connecting the cytoplasm of the cells
  - Have low electrical resistance
  - Allow free diffusion of ions
  - Action potentials travel from one cardiac muscle cell to another



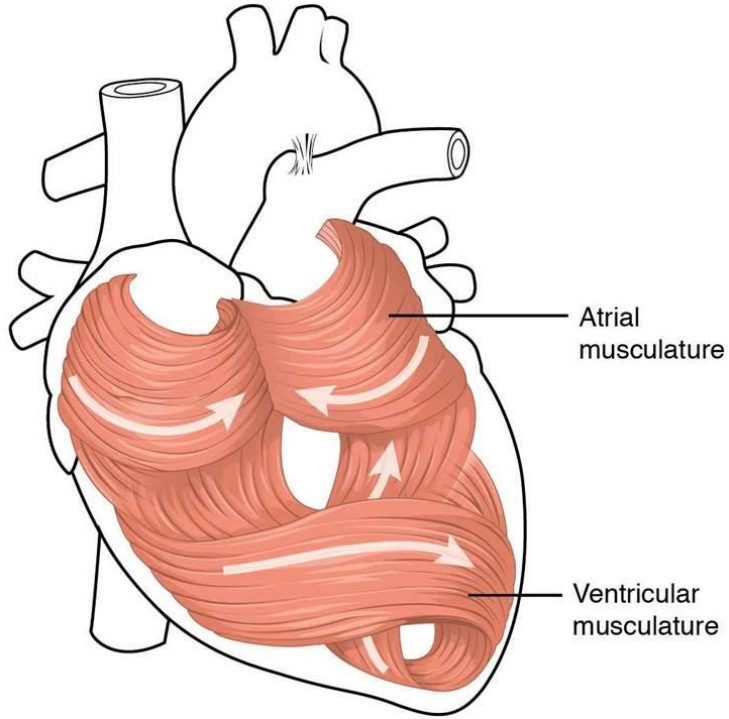


Intercalated Discs and Gap Junctions of Cardiac Muscle Fibers



Functional Syncytia

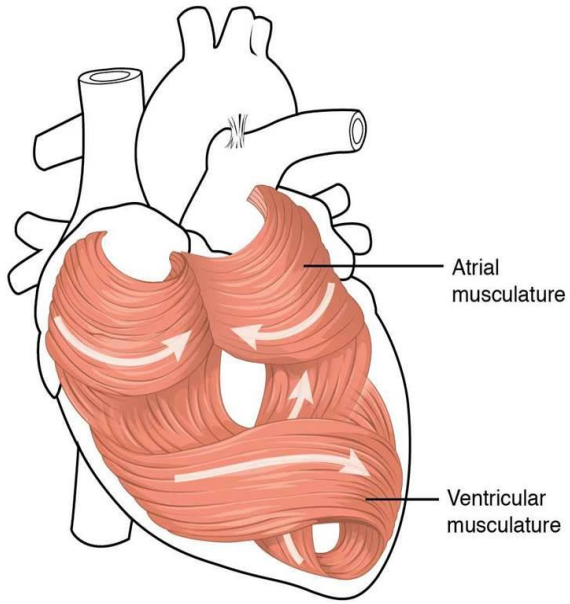
- ✓ Physiological & histological features of cardiac muscle help it to act as a functional (not anatomical) syncytium
- ✓ Cardiac muscle cells are so tight bound that when one cell become excited, action potential spread rapidly from cell to cell.



Functional Syncytia….Cont.

✓ Cardiac muscle tissue forms 2 functional (NOT anatomical) syncytia:

- ***Atria syncytium*** (2 atria): Both atria act as one unit.
- ***Ventricular syncytium*** (2 ventricles): Both ventricles as another unit.
- Action potential can be conducted between them by specialized conducting system "A-V bundle".
- The division of cardiac muscle mass into 2 separate syncytia allows atria to contract before ventricular contraction (for effectiveness of heart pumping).

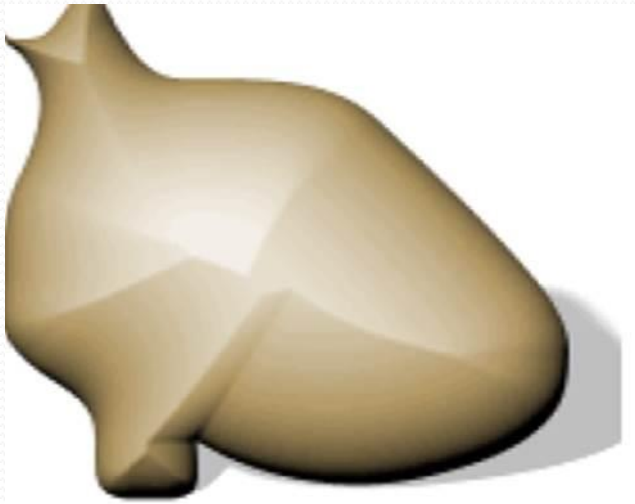


All or non principle as applied to heart

- Stimulation of a single atrial muscle fiber causes action potential to travel over entire atrial mass from cell to cell through the gap junctions leading to contraction of all the muscle fibers
- Also stimulation of any ventricular muscle fiber causes excitation of all ventricular muscle mass.
- So, cardiac muscle sheet behave like a functional syncytium and obeys the all or non rule.

II: Conducting cells: (Automatic/Autorythmic)

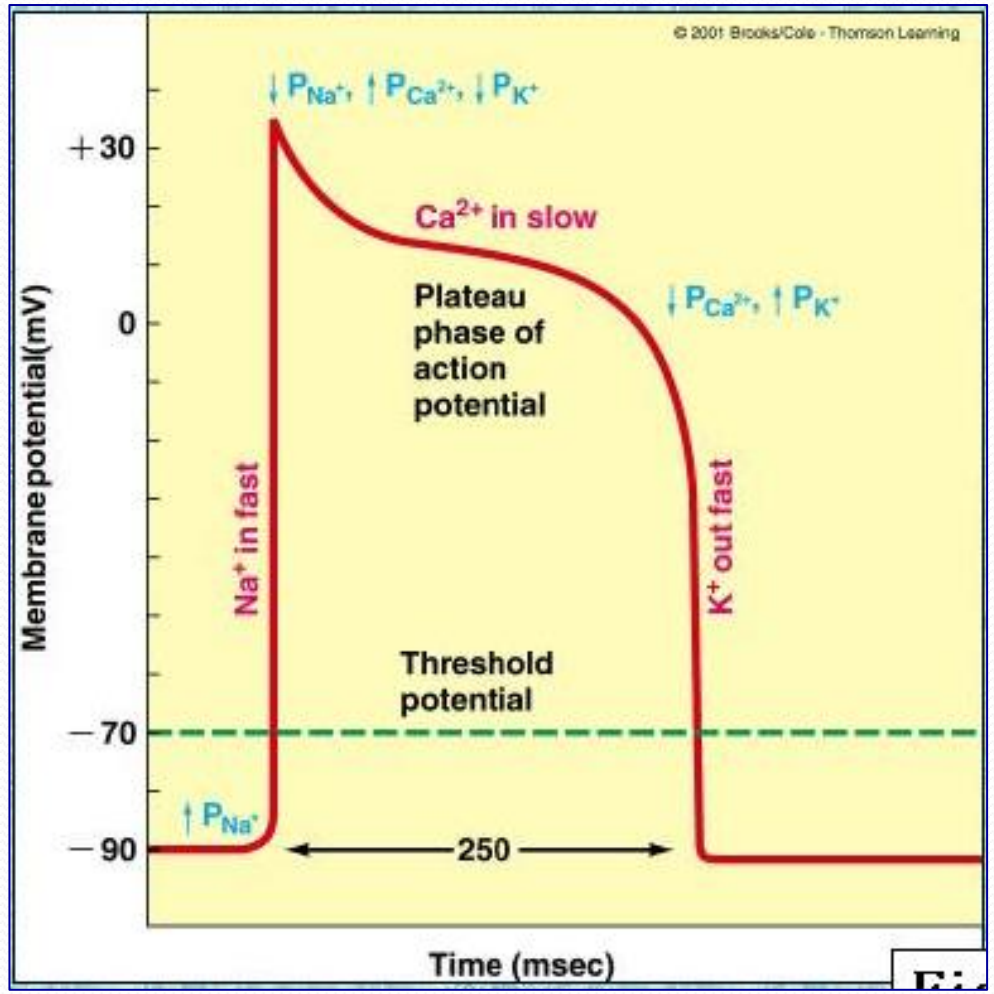
✓ Specialized or modified cardiac muscle cells, containing few contractile fibrils



- Self-stimulating & rhythmic:
  Generate impulses in a repetitive constant manner
- Conductive:
  Conducts electrical current throughout the heart
- Excitatory:
  Provide an excitatory system to the heart

Action Potential iof Contractile Cardiac Muscle Fibers

- Resting membrane potential of contractile myocardial fibers is stable **"-90 mV".**
- Duration of action potential is **300-400 ms.**
- It has 5 phases

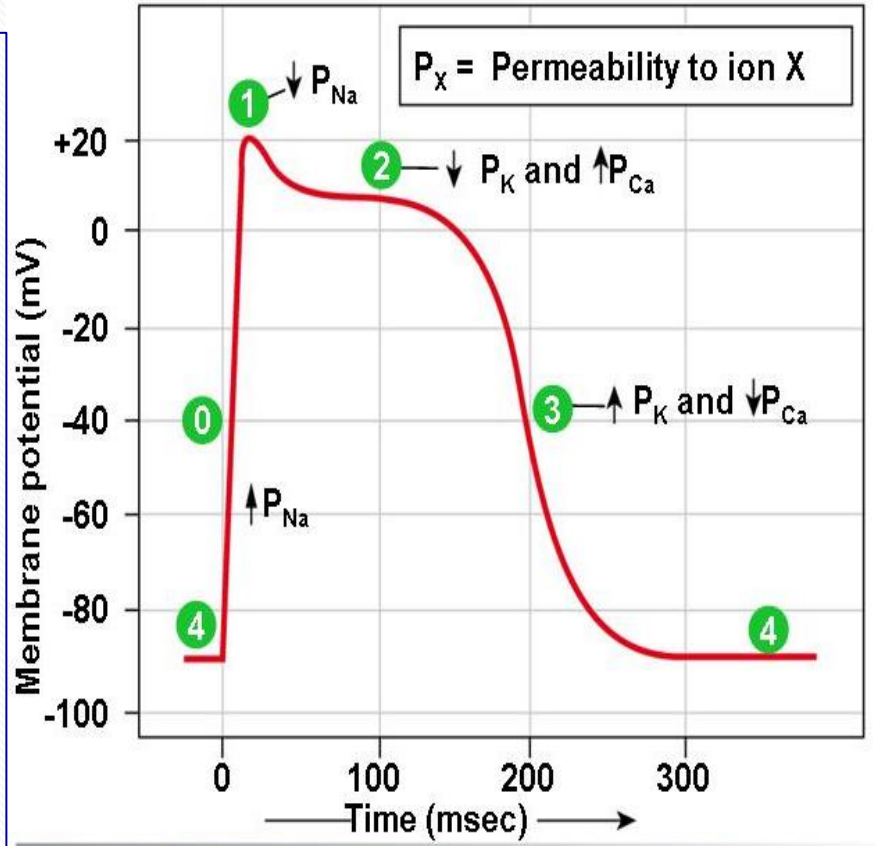


Phases of Action Potential in Cardiac Muscle

Phase 0:- Rapid depolarization (+20 mv), caused by opening of voltage gated Na^+ channels → rapid Na^+ influx into cells. (magnitude = 105-110 mv).

Phase 1:- The early rapid partial repolarization (5-10 mV) due to K^+ efflux. This phase is also caused by closure of Na^+ channels.

Phase 2:- The plateau (near 0 mV), is the flat portion of the curve. It is due to slower but prolonged Ca^{++} influx, balanced by efflux of an equal amount of K^+. Its duration is 0.3 sec in ventricles and 0.2 sec in atria.



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

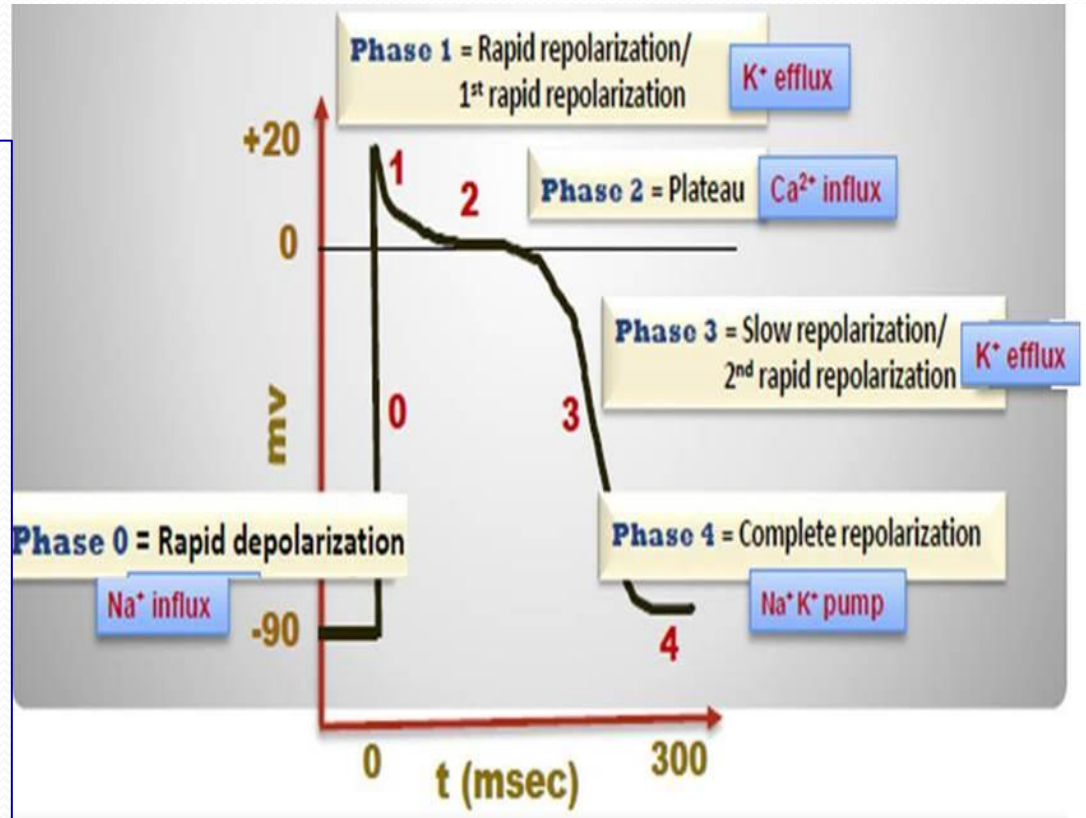
Phases of Action Potential in Cardiac Muscle….Cont.

Phase 3:- Repolarization is caused by sudden increase in K^+ efflux out of cell & closure of Ca^{++} channels.

Phase 4:- Complete repolarization, where membrane goes back to resting levels "-90 mv".

Na^+- K^+ pump works to derive excess Na^+ out and excess K^+ into.

N:B The summated electrical activity of all cardiac muscle fibers is called ECG.



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

What causes the Plateau in the Action Potential?

1. Slow calcium channels: slow to open & remain open for several tenths of a second

   → Large quantity of calcium ions flow to the interior of the cardiac muscle fiber

   → Maintains prolonged period of depolarization

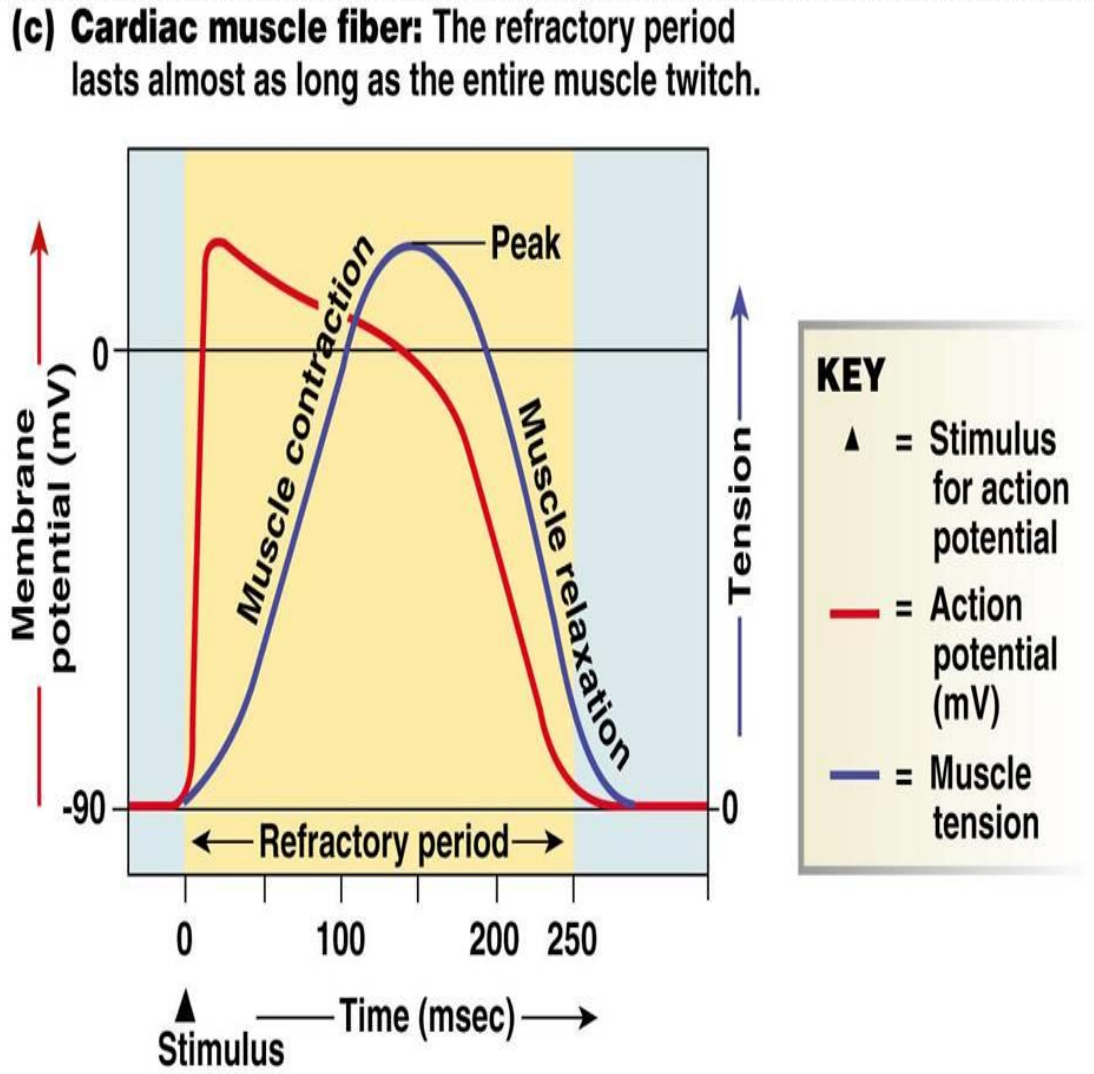
2. Decreased permeability of the cardiac muscle membrane for potassium ions → decrease outflux of potassium ions during the action potential plateau.

- Calcium channels close at the end of the plateau, and membrane permeability for potassium ions increases rapidly, this return the membrane potential to its resting level.

Refractory Period of Cardiac Muscle

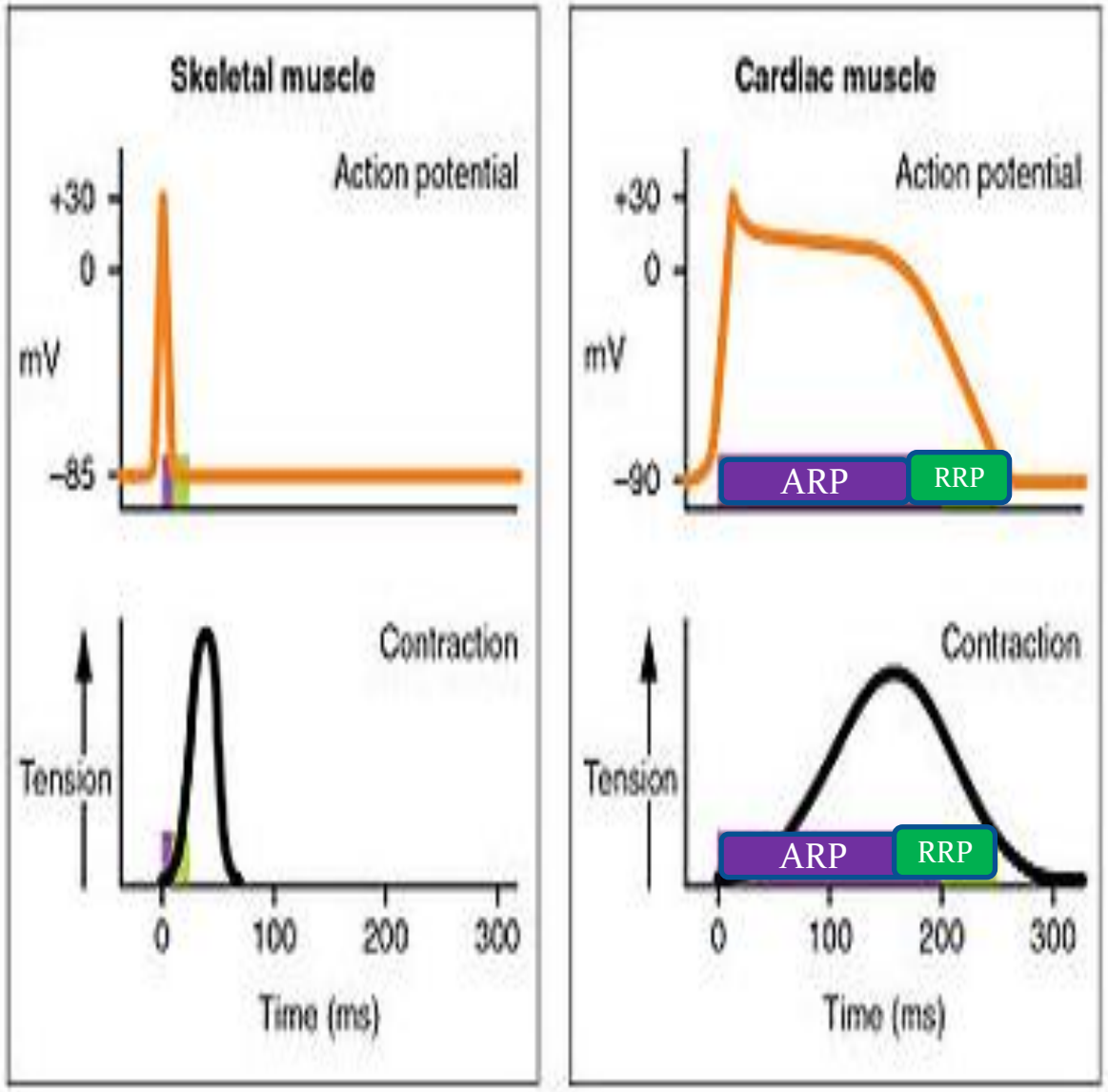
- **The refractory period of the heart:**

  Is the interval of time during which a normal cardiac impulse cannot re-excite an already excited area of cardiac muscle.
- Cardiac muscle is refractory to re-stimulation during the action potential
- In cardiac muscle fiber, the refractory period lasts almost as long as the entire muscle contraction.
- ***Significance***: Cardiac muscle can't be tetanized i.e. heart cannot continue systole without diastole. If tetanus in heart continued for few seconds, circulation would stop.



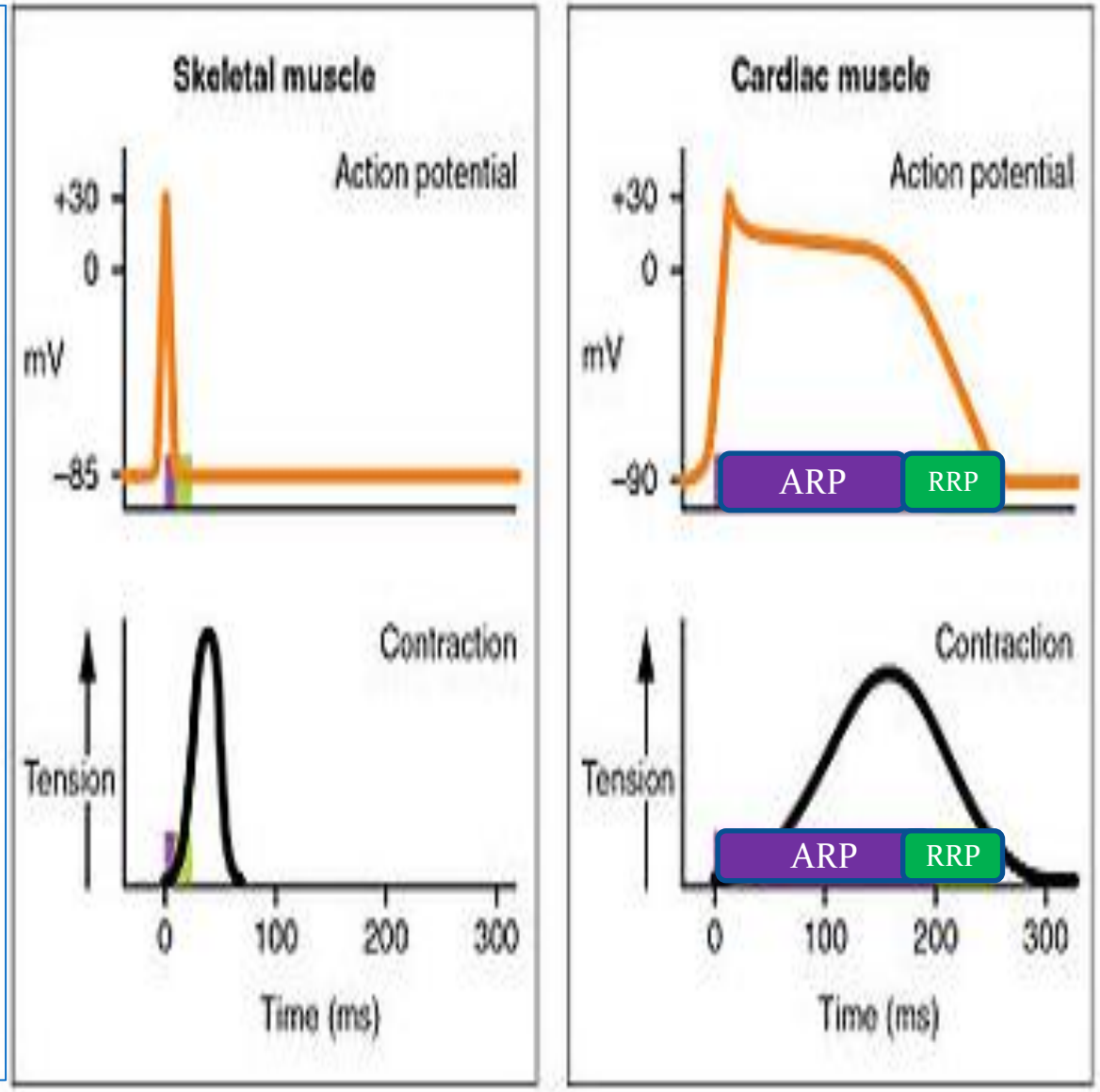
Cardiac Muscle has two Refractory Period s:

- ***Absolute refractory period***
  - Cardiac muscle cannot be excited while it is contracting (due to complete depolarizationa)… benefit?
  - Time: depolarization and the 1st 2/3 of repolarization (phases 0, 1, 2 and beginning of phase 3).
  - Mechanically, it occupies whole period of systole & early diastole.
  - Duration: Long (0.25- 0.3 sec)



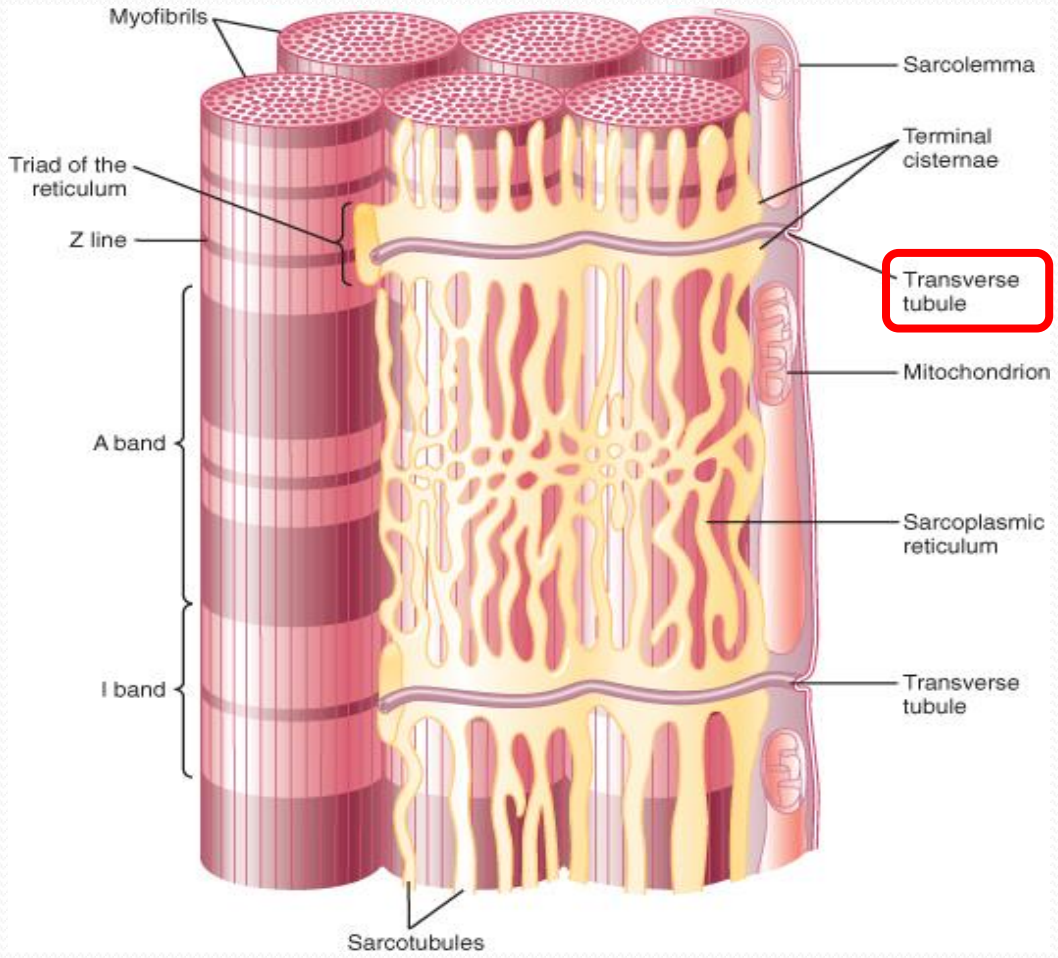
Cardiac Muscle has two Refractory Period s….Cont.

- ***Relative refractory period***
  - Cardiac muscle can be excited by strong stimulus to produce a new systole called extra-systole.
  - Time: the last 1/3 of repolarization (the rest of phase 3)
  - Mechanically, it occupies the middle of diastole.
  - Duration: 0.05 sec. in ventricles and 0.03 sec in atria.



Excitation – Contraction Coupling in Cardiac Muscle

- ***Excitation – Contraction Coupling*** is the mechanism by which the action potential causes muscle contraction
- Action potential spreads to the interior of the cardiac muscle fiber along the transverse (T) tubules



Transverse (T) tubule-sarcoplasmic reticulum system

Excitation – Contraction Coupling

Action potential spreads along the T-tubules

↓

1. Release of calcium ions from sarcoplasmic reticulum into the sarcoplasm
2. Large quantity of extra Ca^{++} diffuses into the sarcoplasm from the T tubules

↓

Ca^{++} ions diffuse into the myofibrils

↓

Ca^{++} binds to troponin causing sliding of actin and myosin filaments

↓

Contraction of cardiac muscle fibers

Excitation – Contraction Coupling…Cont.

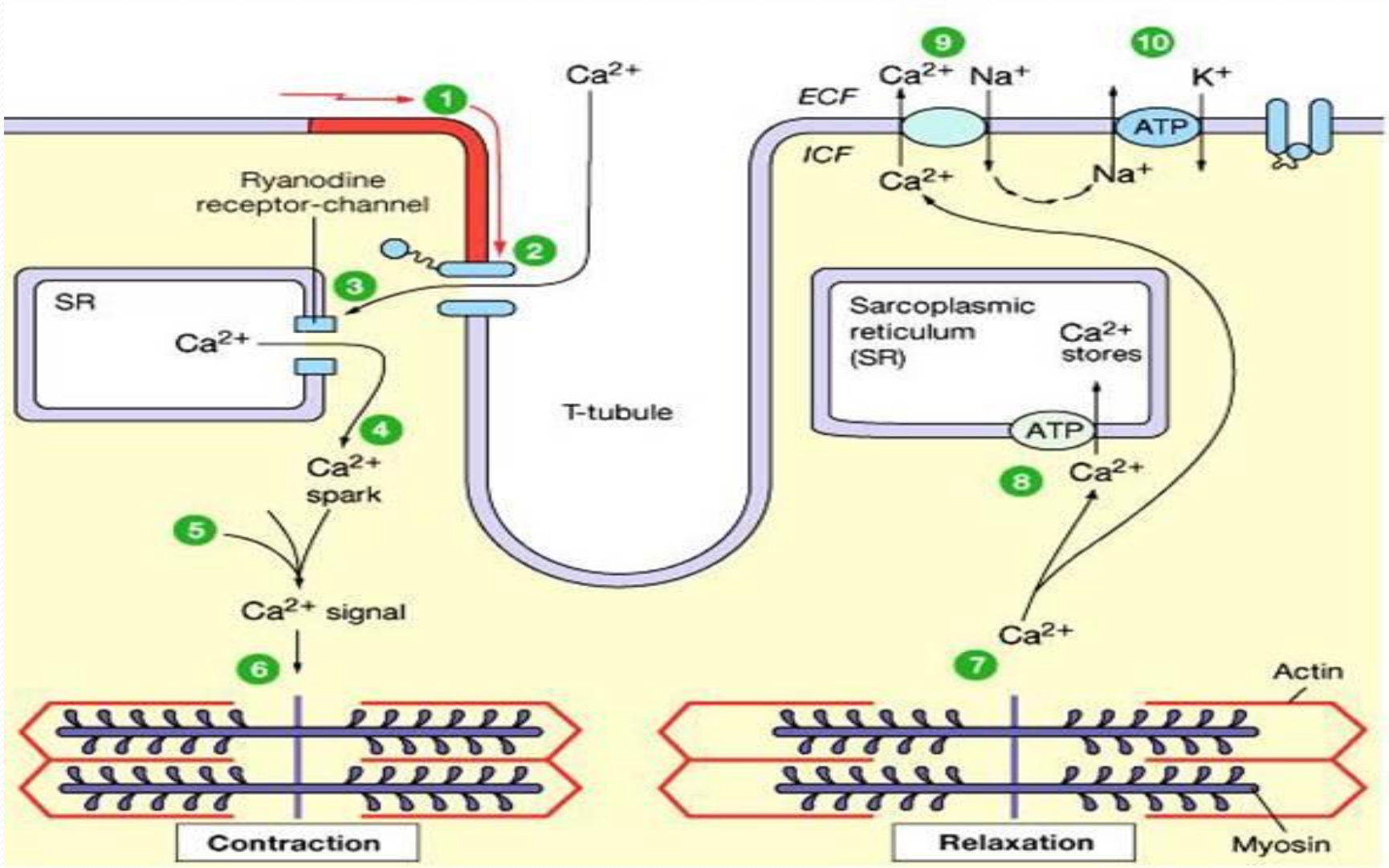
- At the end of the plateau of the action potential

  → calcium ions are pumped back into the sarcoplasmic reticulum and the T-tubules

  → contraction ends (repolarization)

- The T tubules of cardiac muscle have a diameter 5 times as great as that of the skeletal muscle tubules.
- The strength of contraction of cardiac muscle depends to a great extent on the concentration of Ca^{++} in the extracellular fluids

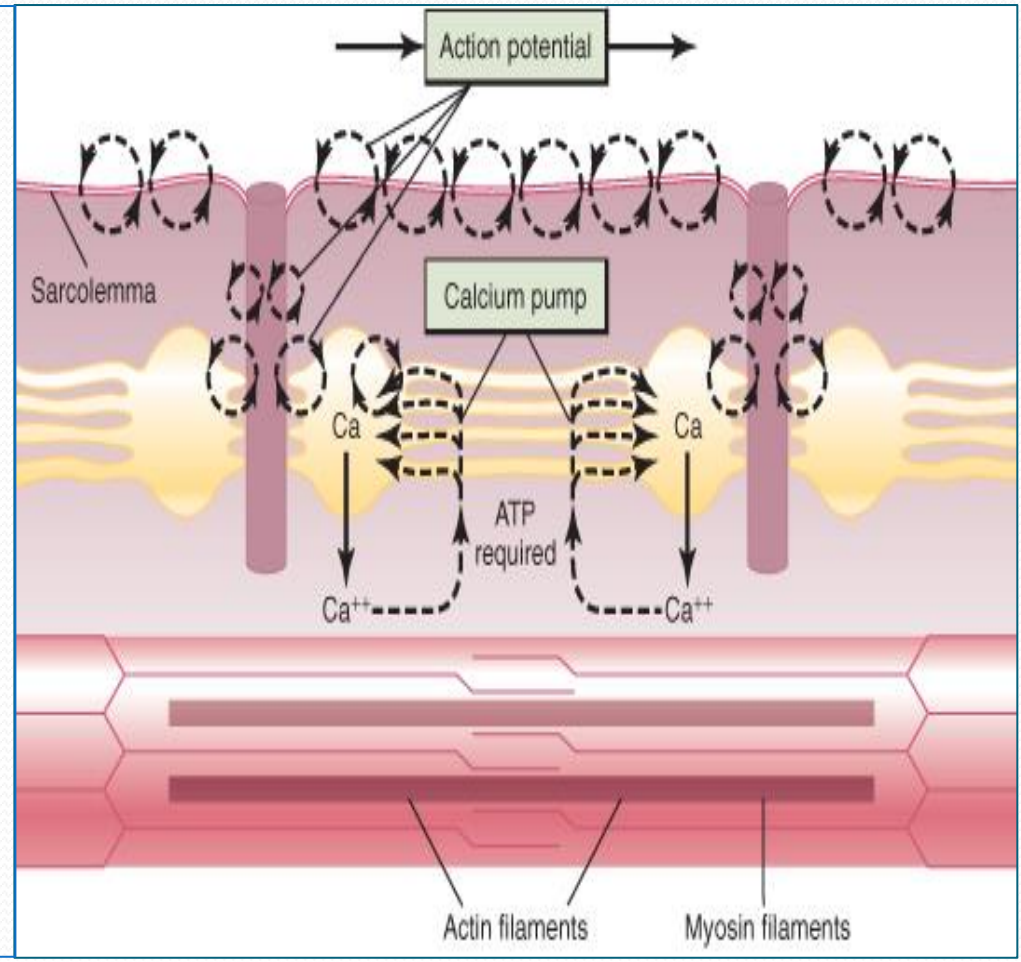
Excitation – Contraction Coupling in Cardiac Muscle



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.

Excitation – Contraction Coupling in Cardiac Muscle

- Cardiac muscle are continually contracting and require substantial amounts of energy for the process of contraction and sliding mechanism.
- The energy is derived from ATP generated by oxidative phosphorylation in the mitochondria (the myocytes contain large numbers of mitochondria).
- Each contraction involves the hydrolysis of an ATP molecule.



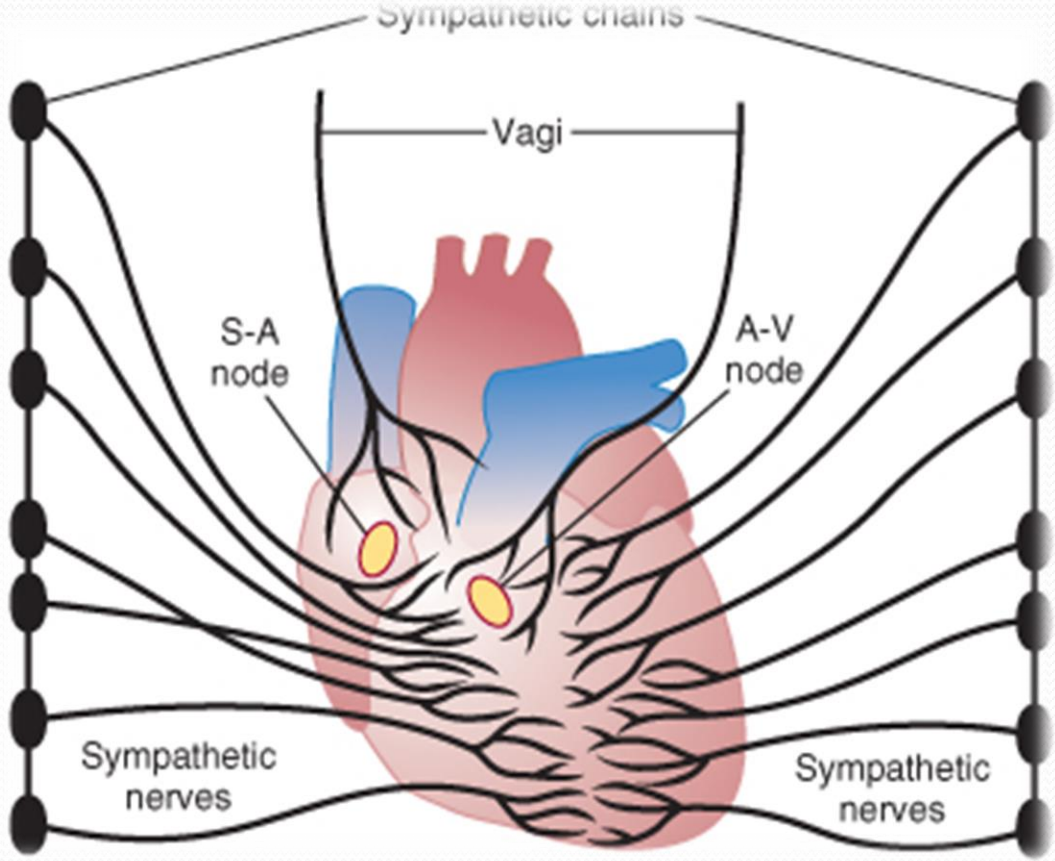
Factors affecting Cardiac Contractility (Inotropic Effectors)

- ***Ionotropic effect:*** mechanism that affect the contractility
- ***Positive Inotropic Effects***: factors that increase the cardiac contractility
  - Sympathetic stimulation
  - Calcium ions
- ***Negative Inotropic Effects***: factors that decrease the cardiac contractility
  - Parasympathetic stimulation
  - Ca^{++} channel blockers

Factors affecting Cardiac Contractility….Cont.

1- ***Autonomic innervation***

- Sympathetic nerves increase the force of contraction (both atria & ventricles)
- In contrast, paraympathetic (vagus) nerves decrease the force of atrial contraction (No significant effect on ventricular muscle).



Factors affecting Cardiac Contractility….Cont.

2- Oxygen supply:

Hypoxia: ↓ Contractility

3- [Ca^{++}]& [K^{+}] ion concentration in ECF:

↑ [Ca^{++}]: ↑ Contractility

↑ [K^{+}]: ↓ Contractility

4- Physical factors:

Warming: ↑ Contractility

Cooling: ↓ Contractility

Exercise: ↑ Contractility

Factors affecting Cardiac Contractility….Cont.

5- Hormonal & Chemical factors:

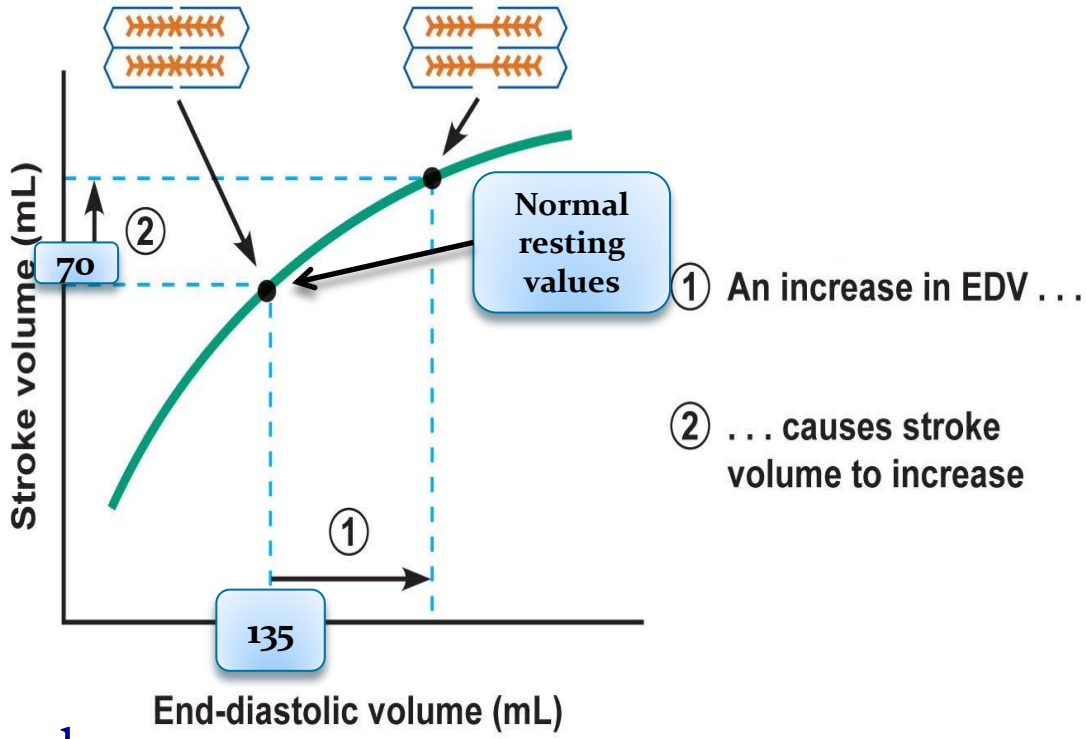
Positive (Increase contractility)	Negative (Decrease contractility)
Digoxin, digitalis	Beta blockers
Adrenaline & noradrenaline	Acetylcholine
Alkalosis	Acidosis
Ca^{++}	Ca^{++} channel blockers
Caffeine	Some bacterial toxins (e.g diphtheria toxins)

Factors affecting Cardiac Contractility….Cont.

6- Mechanical factors

Starling's law of the heart

- The force of contraction is proportional to the initial length of the cardiac muscle within physiological limits



- The initial length depends on end diastolic volume
- Cardiac muscle accommodates itself to the changes in venous return up to certain limits

For further readings and diagrams:

Textbook of Medical Physiology by Guyton & Hall

Chapter 9 (Heart Muscle)


Thank You