Cardiovascular

(CVS)

By

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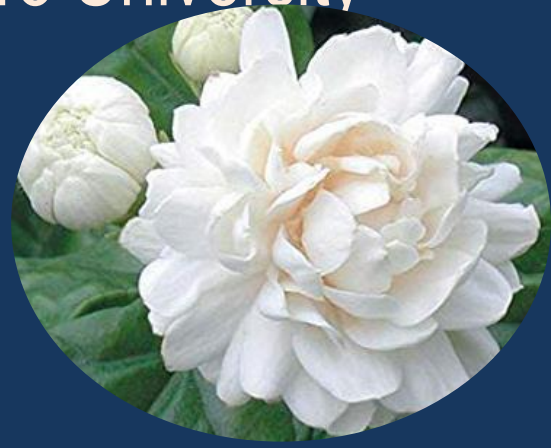

Cardiac properties:

1. Rhythmicity
2. Conductivity
3. Excitability
4. Contractility

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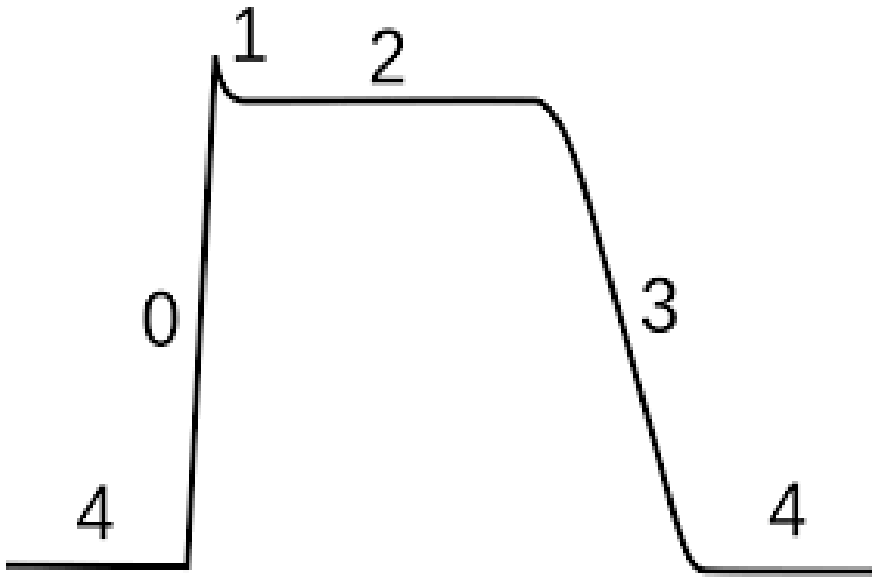
Ability to respond



Ventricular AP

3. Excitability

The ability of cardiac muscle fibers to respond to stimulus of adequate strength and duration

The response is AP

That will be conducted along the muscle fibers

Followed by mechanical response (contraction)

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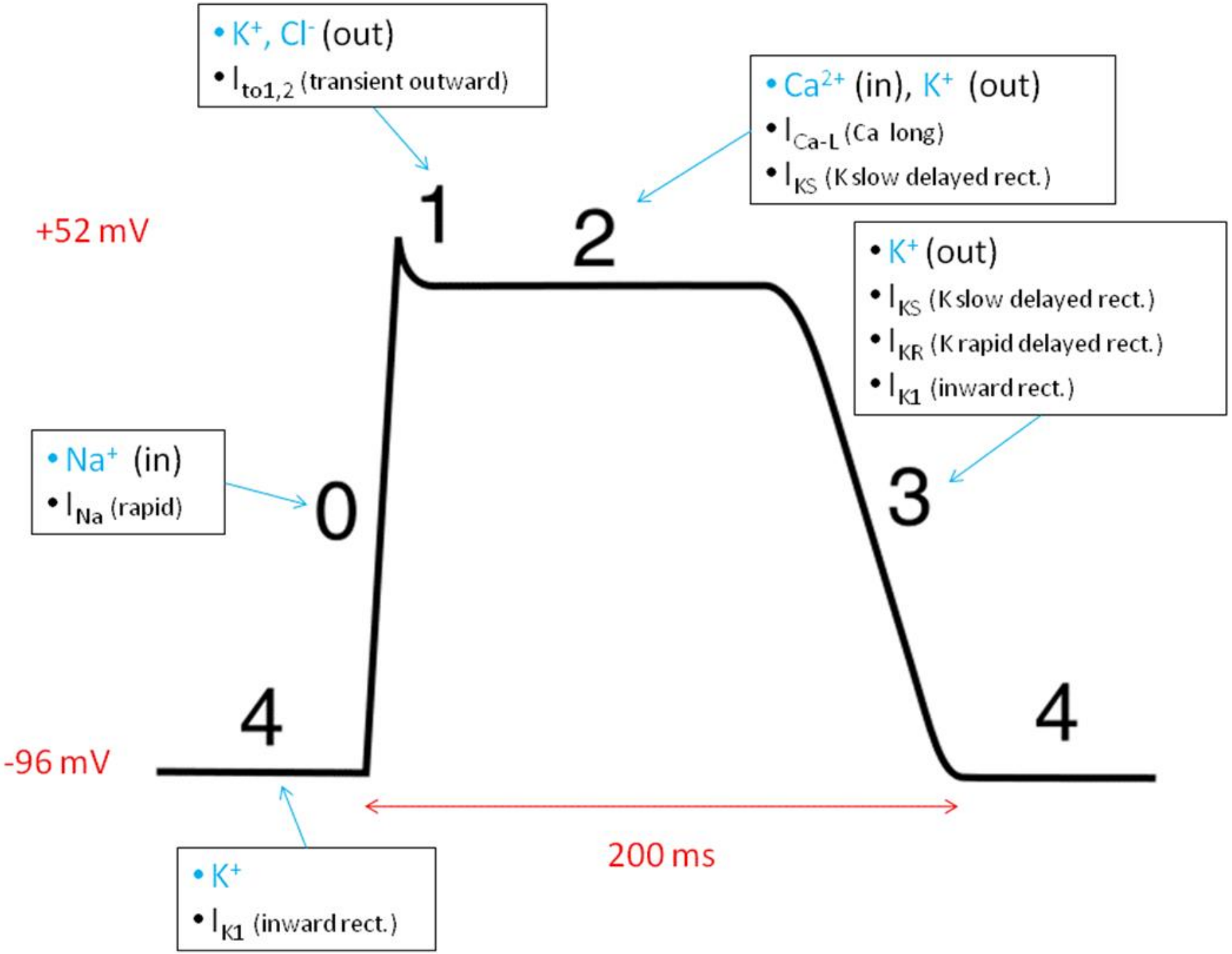
Ventricular AP

- RMP of the cardiac myocyte is -90mV and the firing level (threshold value) is -65mV.
- Ventricular action potential is composed of 5 phases.



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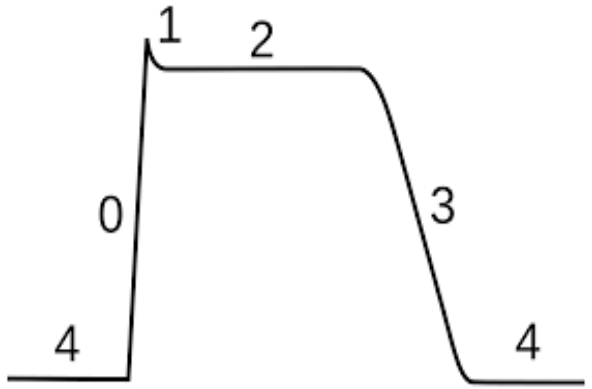
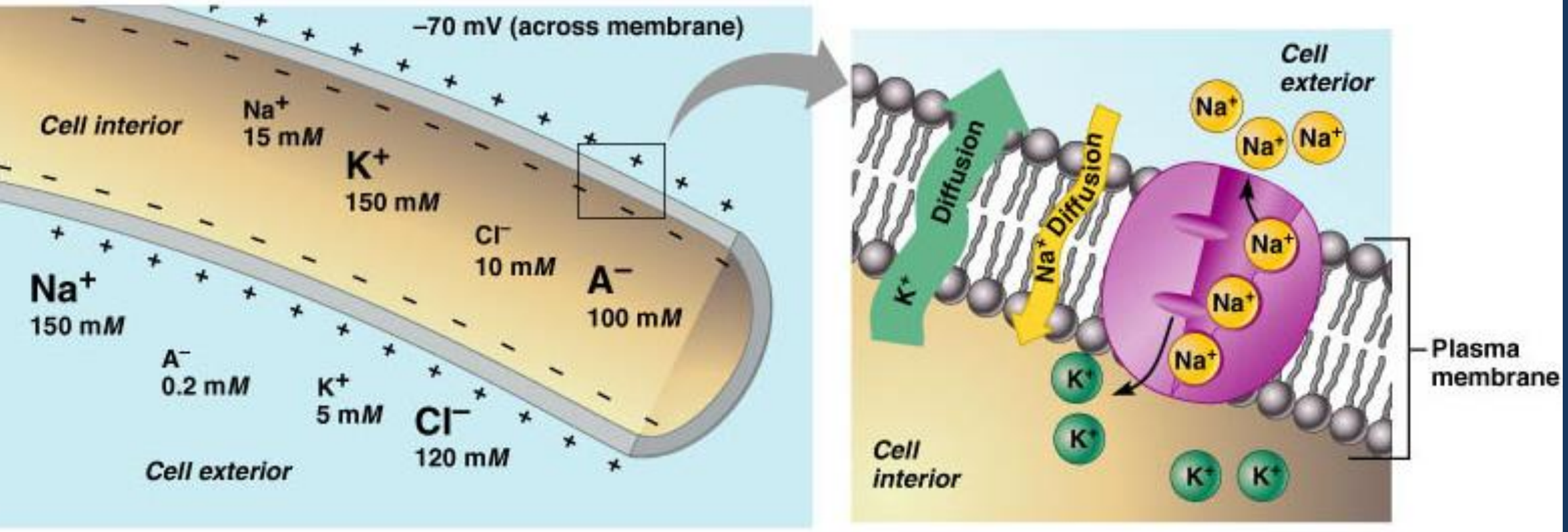
Ventricular AP



- **Phase 4: Resting membrane Potential**

- In general due to: Selective permeability and Na^+/K^+ pump
- Returning to RMP through inward rectifying potassium channels ⟹ outward K+ current maintain the cardiomyocyte RMP.



Resting membrane potential

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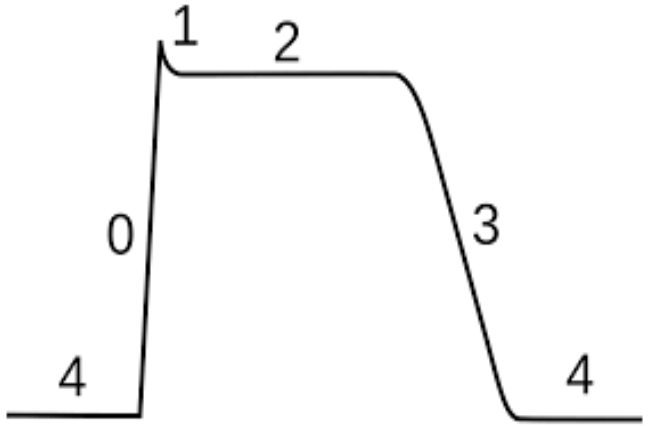
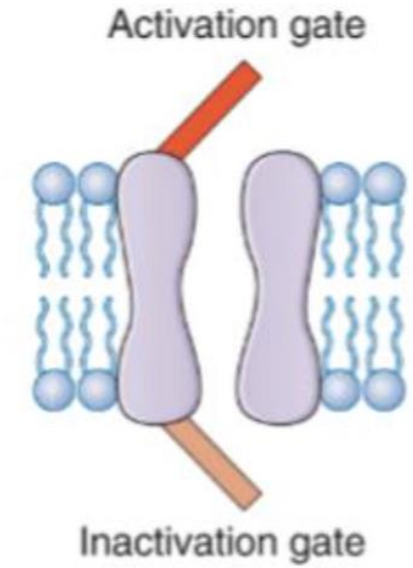
Ventricular AP

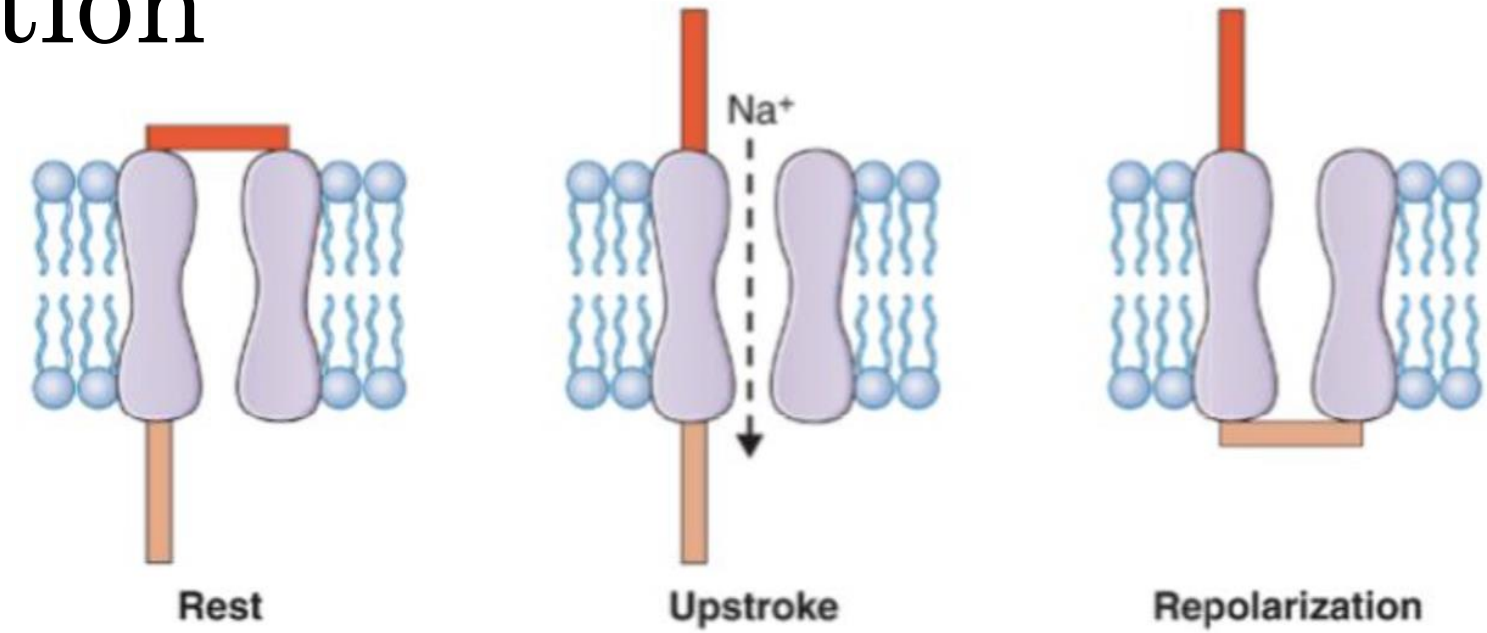


- **<u>Phase 0:</u> Rapid depolarisation phase**
- Rapid upstroke of the action potential passing by the firing level -65mV overshooting to +20mv above zero.
- due to opening of fast voltage gated Na+ channels.
- It opens for short duration (time dependent). At the threshold all Na^+ channels are open.
- Through which Inward Na^+ current ($\boldsymbol{I_{Na}}$) leads to rapid depolarization.
- Outward K+ conductance decreases due to inactivation of inward rectifying K+ channels.

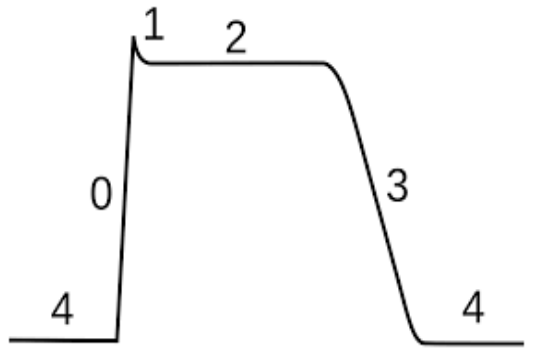
Fast voltage gated Na+ channel With:

- Outer activation gate
- Inner activation gate





Ventricular AP



- **<u>Phase 1:</u> Small Rapid early repolarization phase**
- Due to:

1- **<u>Transient outward K^+ current</u>** due to opening of by voltage- gated K^+ channels, which open transiently in response to depolarization, then quickly inactivate.

2- **<u>Influx of Cl^- current</u>** due to opening of chloride channels.

3- Closure (inactivation) of voltage gated Na+ channels.

Ventricular AP

- Phase 2: Plateau
- Repolarization slows down and the membrane potential is maintained around 0 mV.
- Its duration is average of 200 – 300 msec.

Ventricular AP

- **Phase 2:** Plateau

- Due to:

1- The first part **(Early part)** of the plateau is due to:

a- **Long lasting (L-type) Ca++ channels** inward Ca++ current (I_{CaL}).

b- Delayed rectifier K+ channels that maintain outward K+ current (I_K).

Ventricular AP

- **Phase 2:** Plateau

c- The I_{CaL} counterbalance the I_K and slows down repolarization.

d- So, the outward K+ current gradually increases, until it balances the small, late plateau inward current initiating repolarization (phase 3).

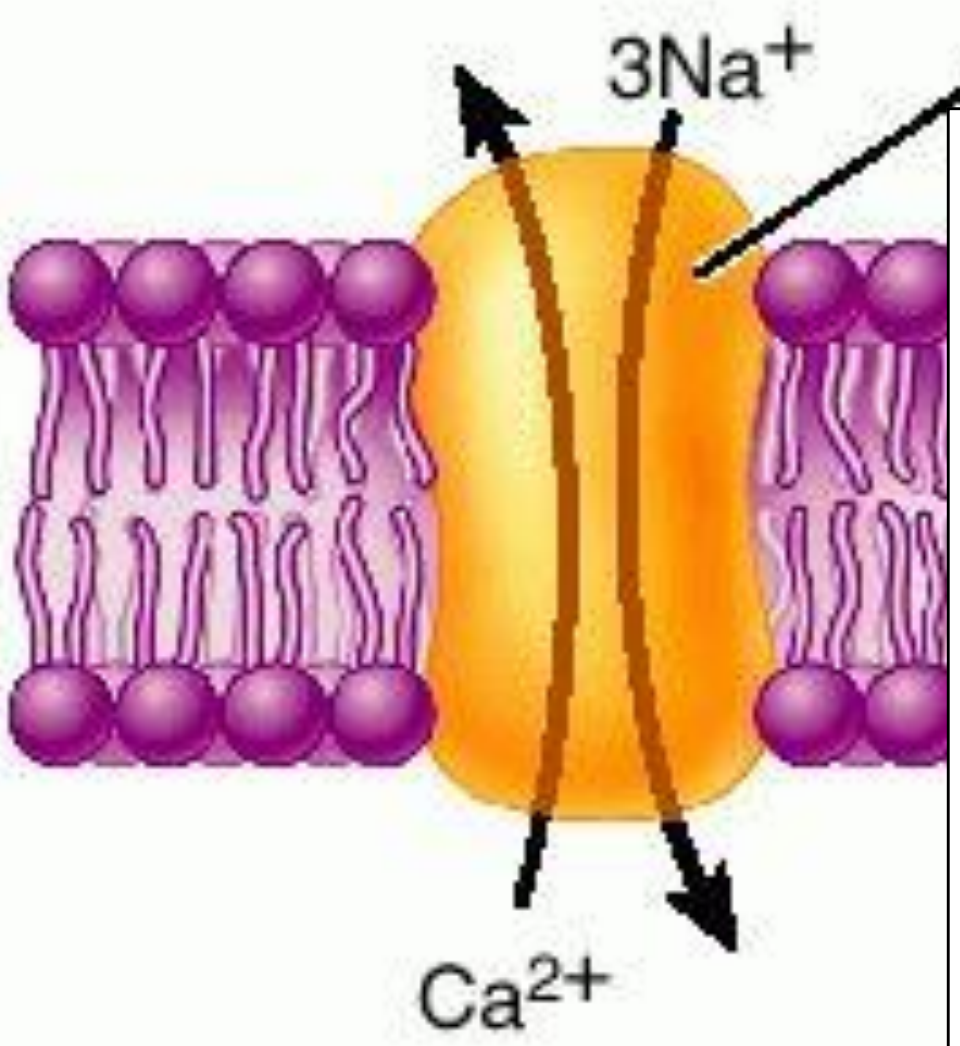
Ventricular AP

- **Phase 2:** Plateau

2- The second part **(Late part)** of the plateau is due to:

- The role played by **Na^+ - Ca^{++} exchanger channels:**

- It is a secondary active type of electrogenic channels. It is responsible for counter transport of Na and Ca ions. Its activity increased by accumulation of intracellular Ca^{++}.



- They help to decrease the intracellular calcium to initiate cardiac muscle relaxation.
- It pumps 1 Ca^{2+} ion outside and 3 Na^{+} ions inside the myocyte maintaining plateau while the L-type Ca^{++} channels are closing.

Ventricular AP

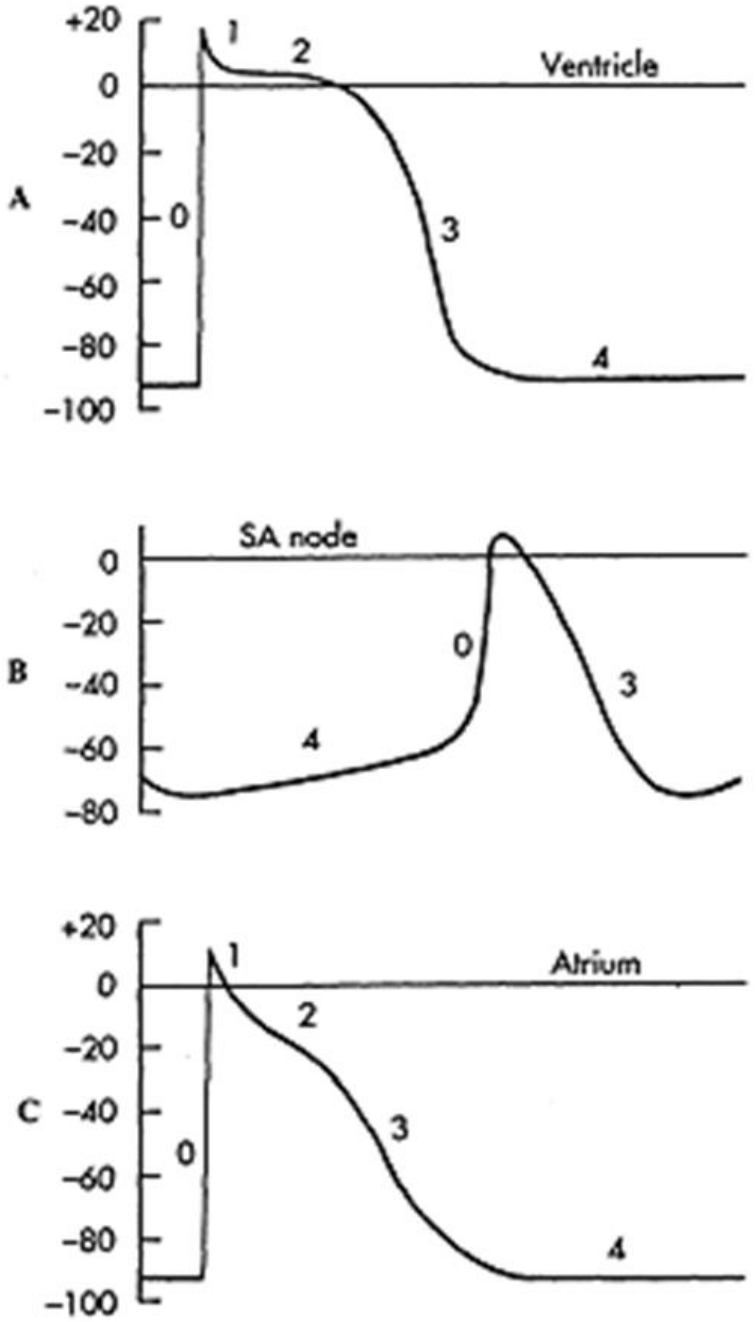
- **Phase 3: Rapid repolarization**
- **Due to:**

- Delayed rectifier K^+ channels become maximally activated and L-type Ca^{++} channels become inactivated leading to unopposed outward K^+ current (I_k) and repolarization continues.

- Reaching RMP: the inward rectifier K^+ channels takes over to maintain RMP (Phase 4) until the next impulse coming from the SAN.

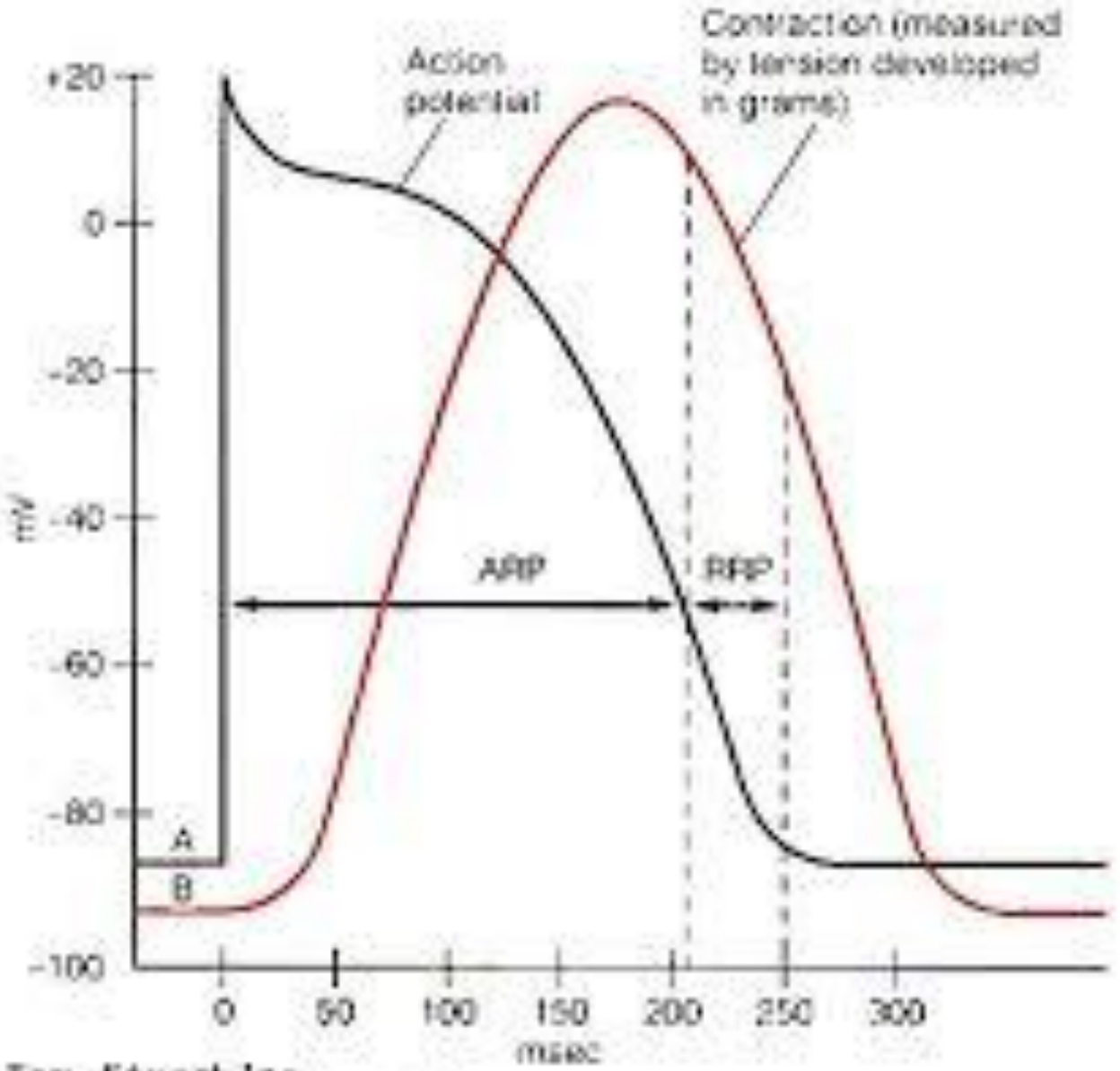
➢ The atrial action potentia versus that of and ventricles:

- **Atrial AP** lasts only 150 ms with less prominent plateau.
- **Ventricular AP** lasts longer (300 - 400 ms) with prolonged plateau at +30 to 0 mV.



➢ The relation between action potential and ventricular muscle contraction:

- It lasts about 1.5 times as long as duration of action potential.
- Cardiac muscle contraction (Systole) starts just after the beginning of depolarization and reaches its maximum by the end of the plateau.
- Relaxation (diastole) starts with phase 3 (rapid repolarization).
- Repolarization is completed by the end of the first half of relaxation.



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Excitability changes

1) Absolute refractory period (ARP)
2) Relative refractory period (RRP)
3) Vulnerable period

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Absolute refractory period (ARP):

- It is longer than that of skeletal muscle due to the presence of the plateau
- It coincides with phase 0, 1, 2 and part of phase 3 (during all periods of systole and part of diastole)

Absolute refractory period (ARP):

- The cardiac muscle during this period is completely unexcitable whatever the magnitude of the stimulus because the fast voltage gated sodium channels are still inactivated (i.e. the inner inactivating gates are still closed).
- Significance: the cardiac muscle cannot be tetanized (safety factor).

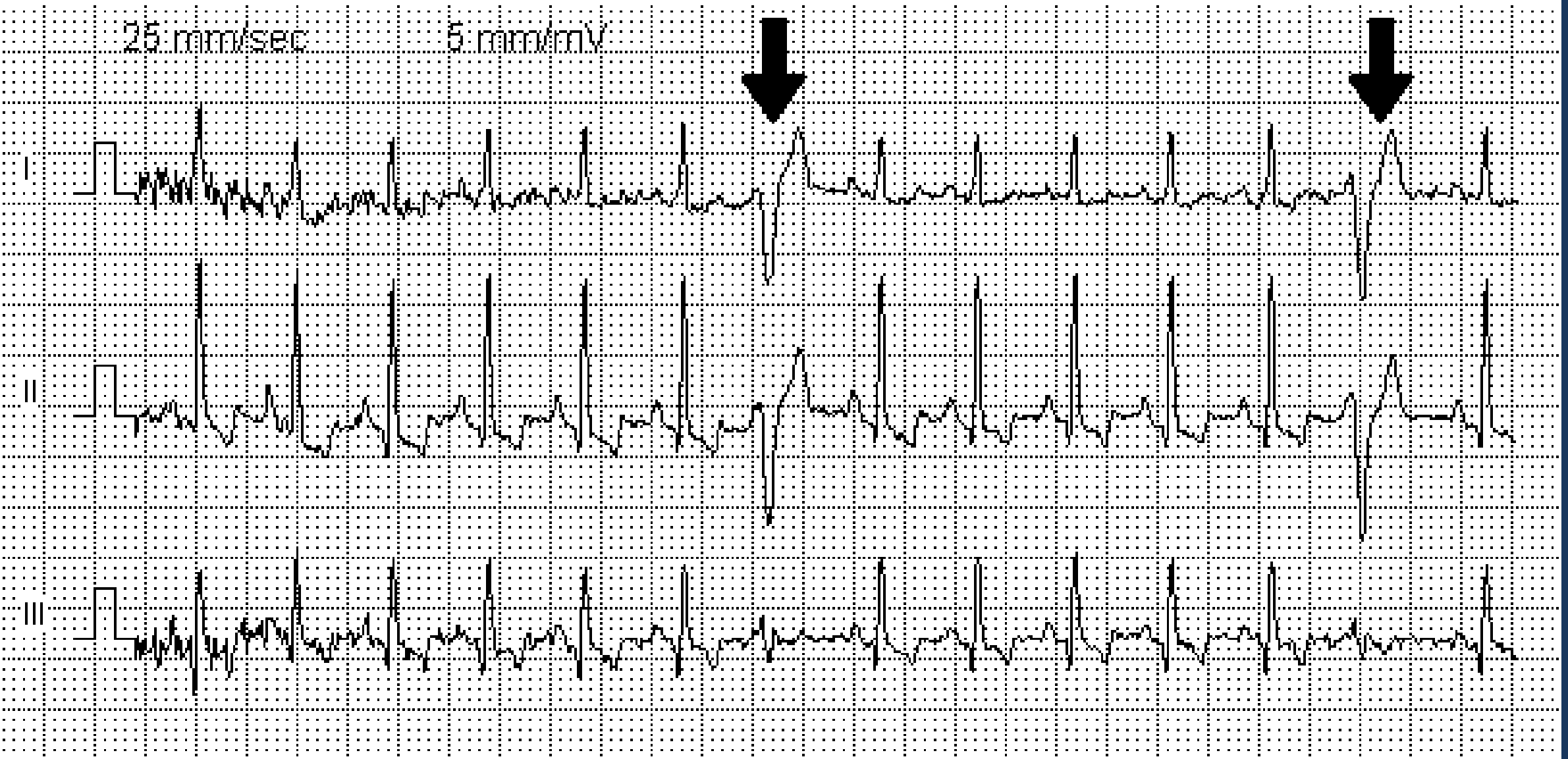
Relative refractory period (RRP):

- It follows the ARP
- The cardiac muscle is partially unexcitable as it can be stimulated by suprathreshold stimulus (strong stimulus).
- It coincides with the rest of phase 3 (coincides with first part of diastole).
- It is the period during which extrasystole may occur.

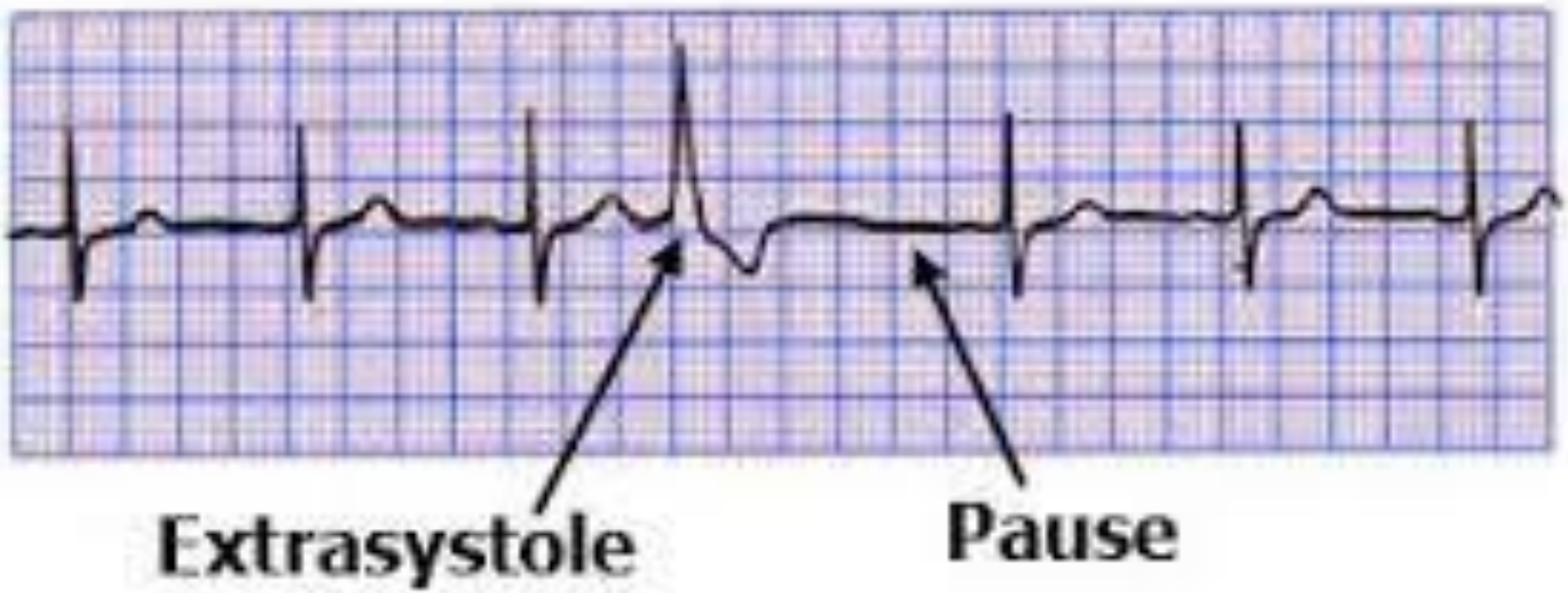
Extrasystole

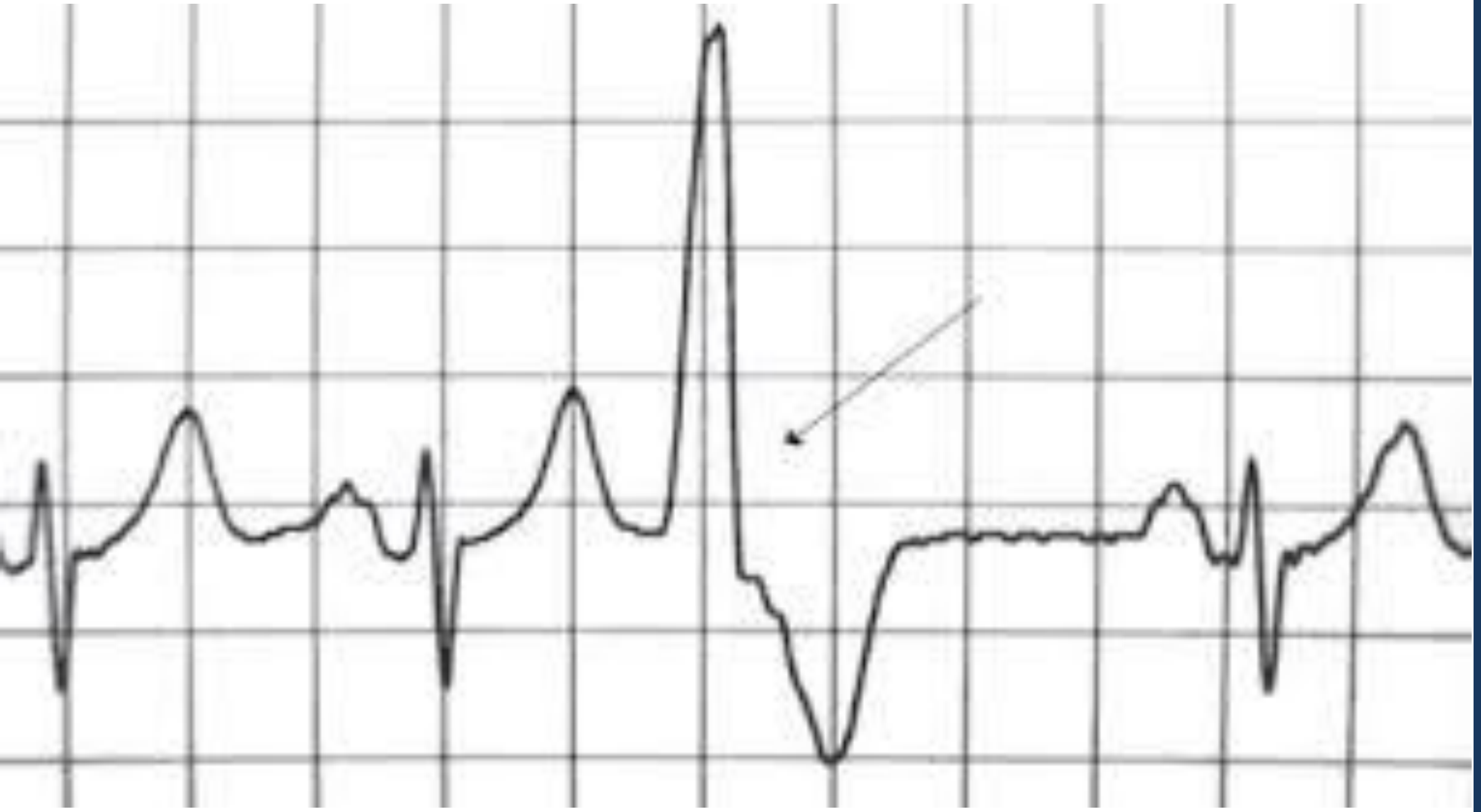
- It is a week contraction resulting from an impulse reaching the heart during RRP.
- Due to presence of ectopic focus or extra discharge from SAN (caffeine, cigarette smoking).
- It has the same excitability changes as normal beating
- Followed by compensatory pause (normal impulse occurs during the ARP of the extrasystole = no response = dropped beat).

Extrasystole



Ventricular Extrasystole





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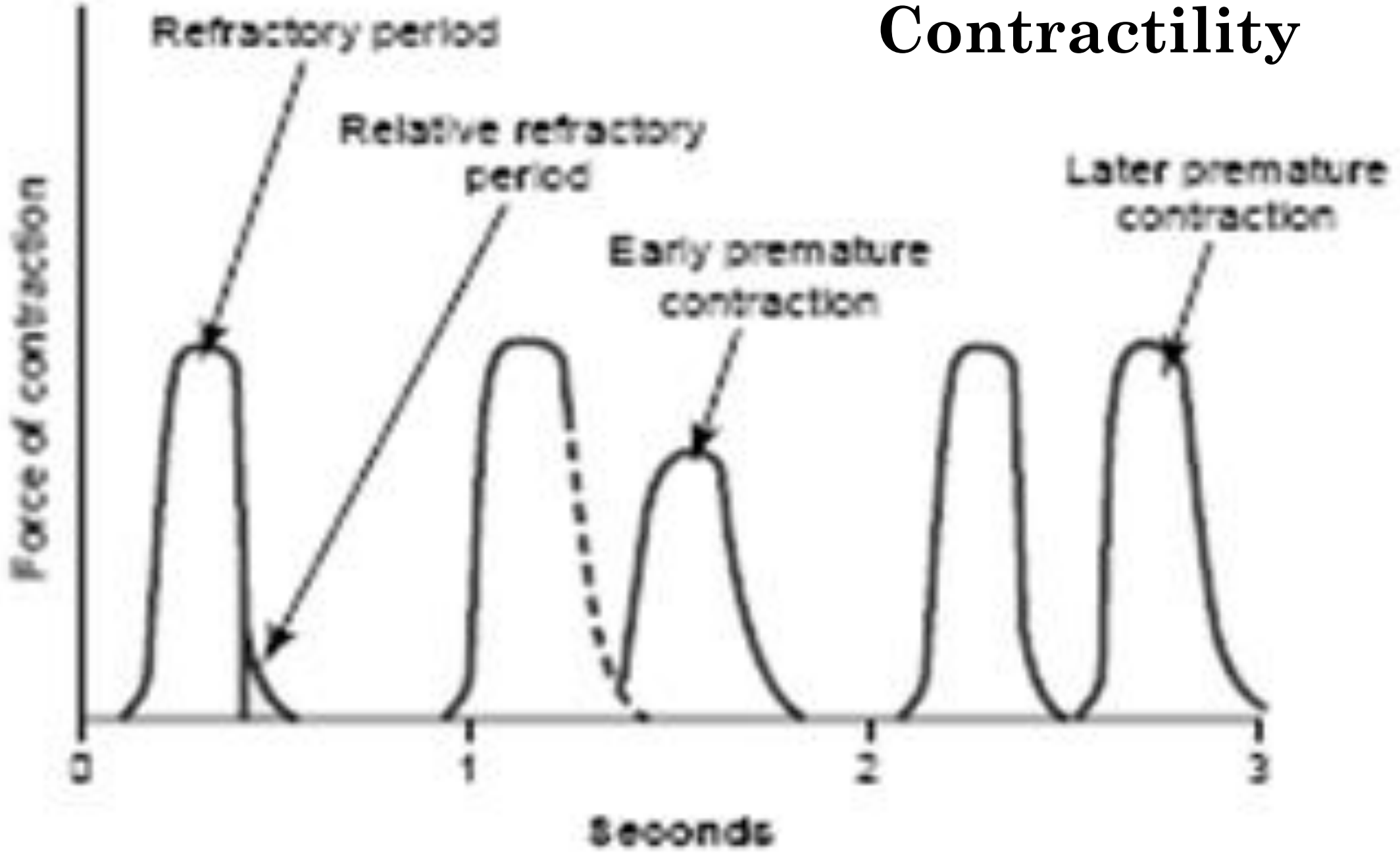
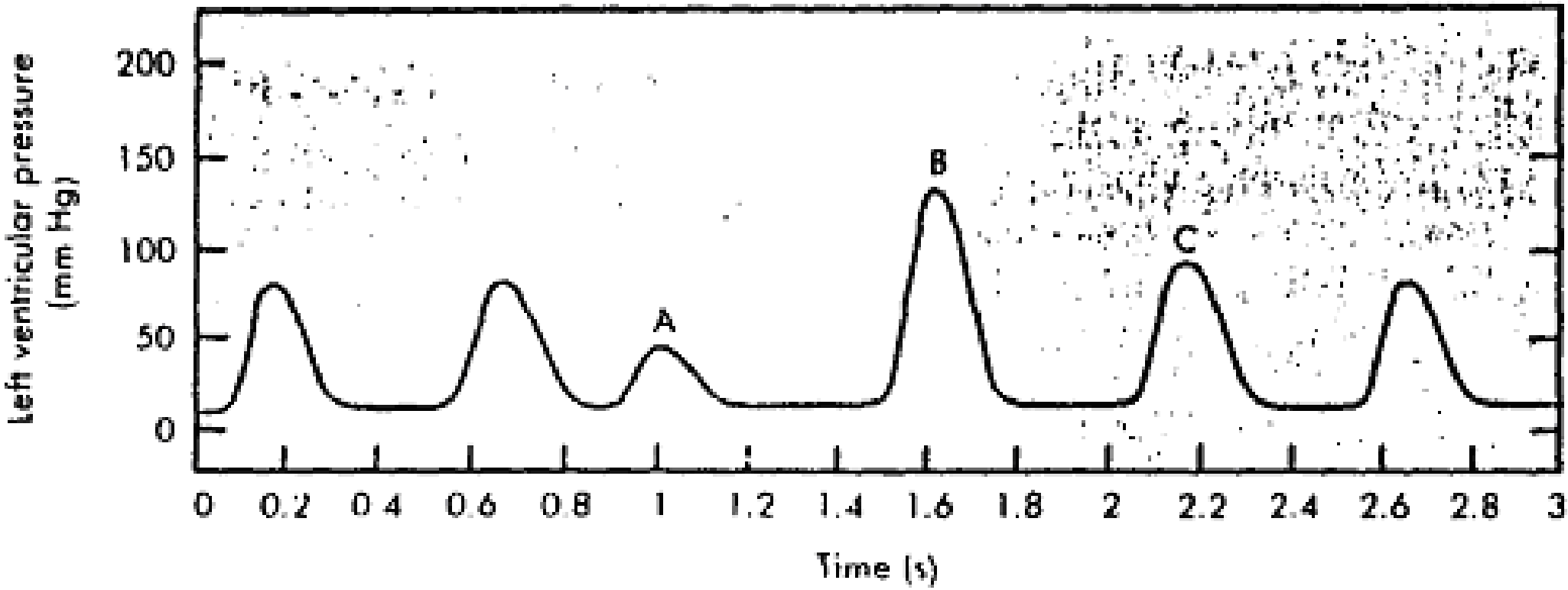
Contractility

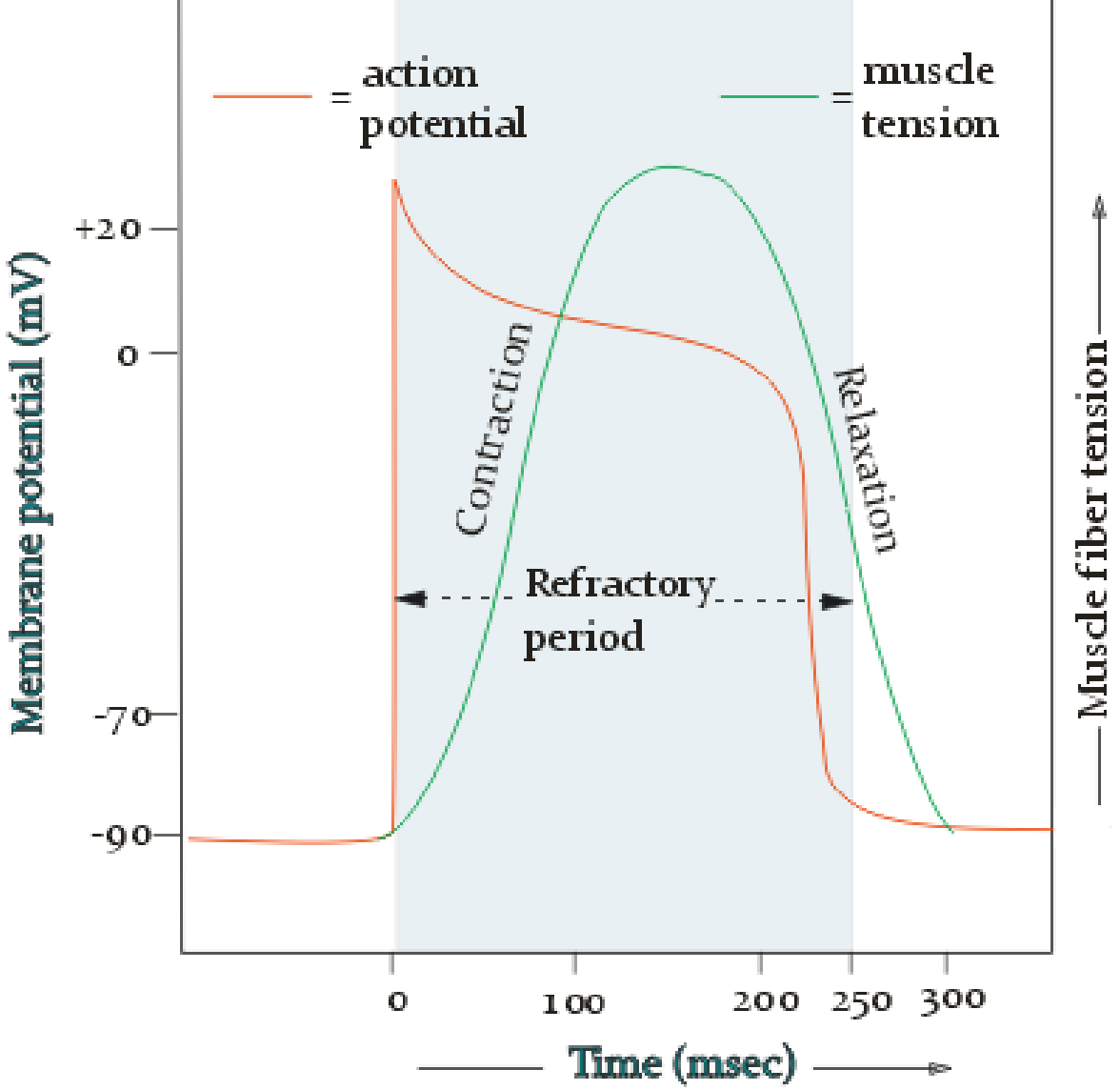




■ **Fig. 25-24** In an isovolumic canine left ventricle preparation a premature ventricular systole (beat *A*) is typically feeble, whereas the postextrasystolic contraction (beat *B*) is characteristically strong, and the enhanced contractility may persist to a diminishing degree over a few beats (e.g., contraction *C*). (From Levy MN: unpublished tracing.)

Excitability changes

The last part of phase 3 and the last half of diastole is known as **Vulnerable period** during which the cardiac response is supra-normal in which it can be excited with weaker stimulus and fatal cardiac arrythmias may occur.



The relationship between an action potential and the refractory period to the duration of the contractile response in cardiac muscle

4. Contractility

Systole and Diastole

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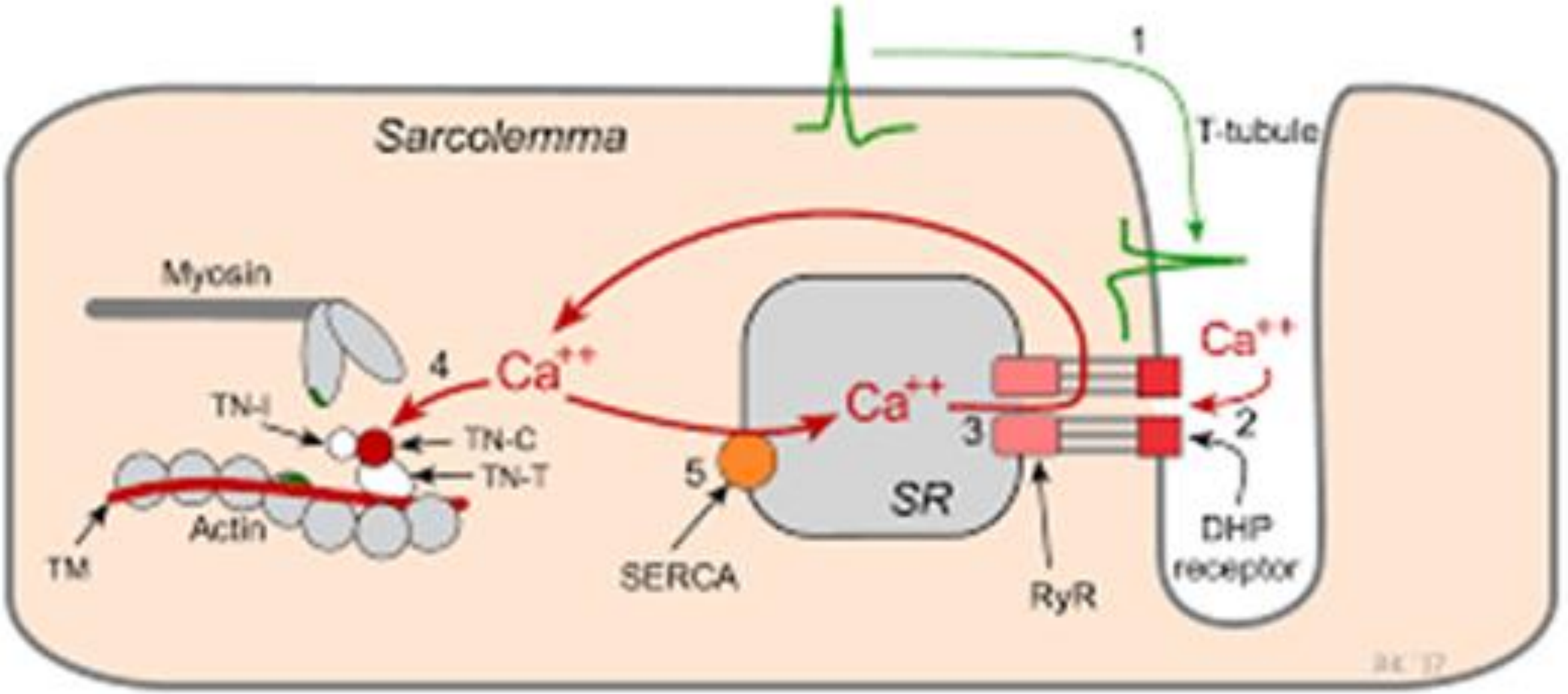
Cardiac muscle contraction:

- **It is the same as skeletal muscle apart from:**

I. Cardiac muscle contract as one syncytium

II. It depends on extracellular and intracellular calcium concentration

Excitation contraction coupling (Inotropic state of heart):



Calcium induced Calcium release

- Ryanodine receptors (RyRs) are ryanodine sensitive calcium channels which will be triggered by the increased intracellular Ca++ causing more release of Ca++ from SR. this process is known as **Calcium induced Calcium release** (CICR).
- Then, Ca++ binds to **Troponin C** and starts sequence of contraction similar to that of skeletal muscle.

Calcium induced Calcium release

When Ca++ binds to Troponin C, starts sequence of contraction similar to that of skeletal muscle:

a- Troponin T undergoes conformational change that leads to removal of tropomyosin from its position covering myosin binding sites on actin.

b- Once uncovering occurs cross bridges of myosin binds to actin and contraction begins by generation of tension.

c- Tension will be generated by the cycling of cross bridges (binding, bending, sliding, detachment and return).

d- Energy (hydrolysis of ATP) is needed for bending to occur.

Factors affecting contractility

1. All or none law
2. Tetanic contraction
3. Length tension relationship (starling law)
4. +ve and –ve Inotropic state

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1. All or none law

- When all the conditions affecting the heart remain constant:
- The cardiac muscle contracts maximally or does not contract at all
- i.e. the minimal stimulus will stimulate all cardiac fibers (whole heart) because it acts as functional syncytium.

1. All or none law

- Changing intensity of the stimulus will not change the strength of contraction (no gradation of muscle contraction)
- While, under normal conditions changing mechanical, nervous or hormonal factors can change force of contraction.

2. Tetanization of the heart would be fatal

- Tetanic contraction **cannot** occur in cardiac muscle due to long ARP

3. Length tension relationship (starling law)

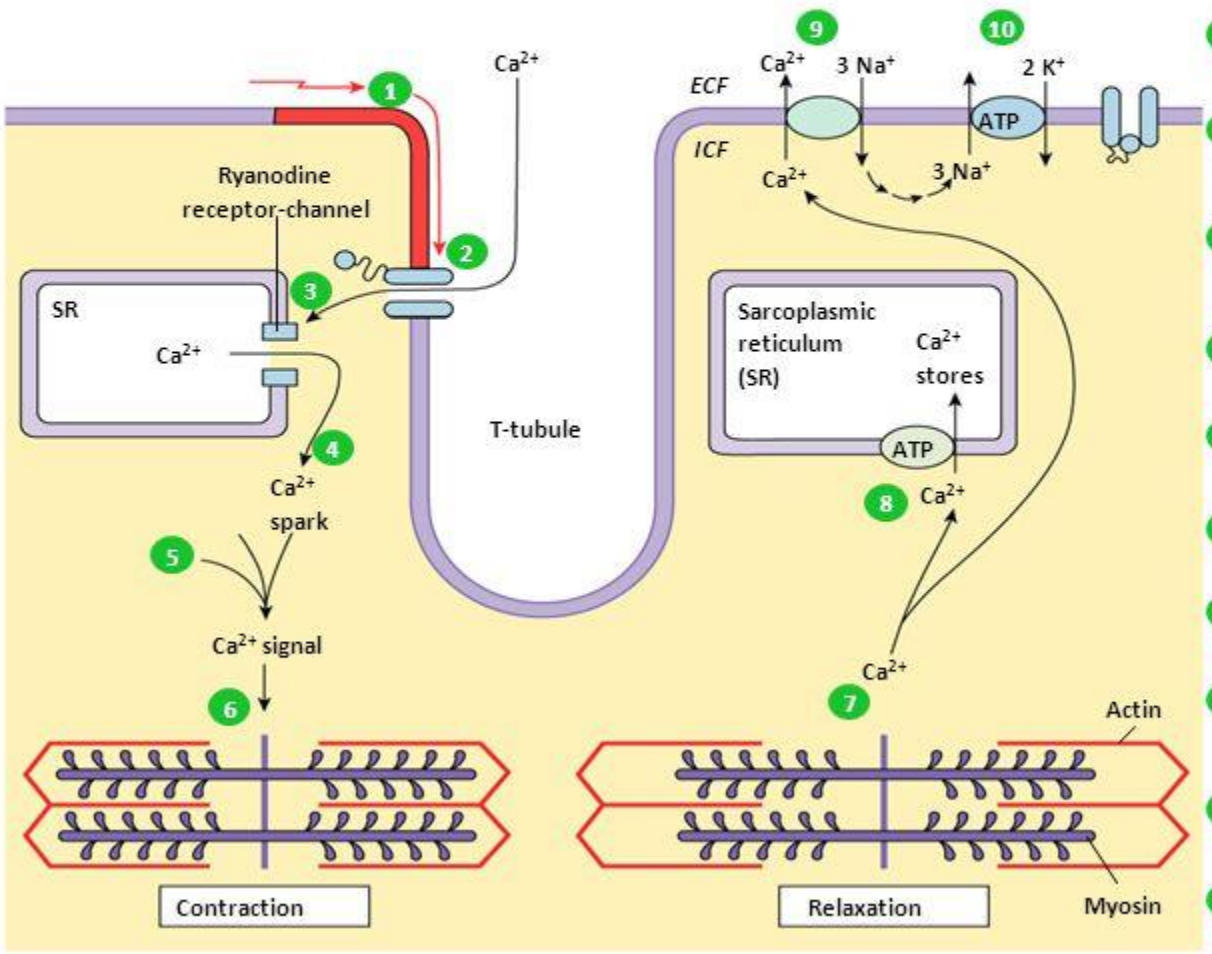
- Within limits, the force of contraction of the heart is directly proportional to the initial length of the cardiac muscle fiber.
- Increasing the initial length of the Cr. Ms. Fiber gradually will increase force of contraction till reaching maximum length (L-max) after which the force of contraction will be decreased.

3. Length tension relationship (starling law)

- L-max (sarcomere length is 2.2 μm) = the number of cross bridges between actin and myosin are increased to maximum (maximum force of contraction)
- Initial length of the ventricular ms. Fiber is determined by the degree of ventricular filling = venous return (VR)
- So, the greater the VR the more the initial length and hence the more will be the force of contraction

Cardiac Muscle

Excitation-contraction coupling and relaxation 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.

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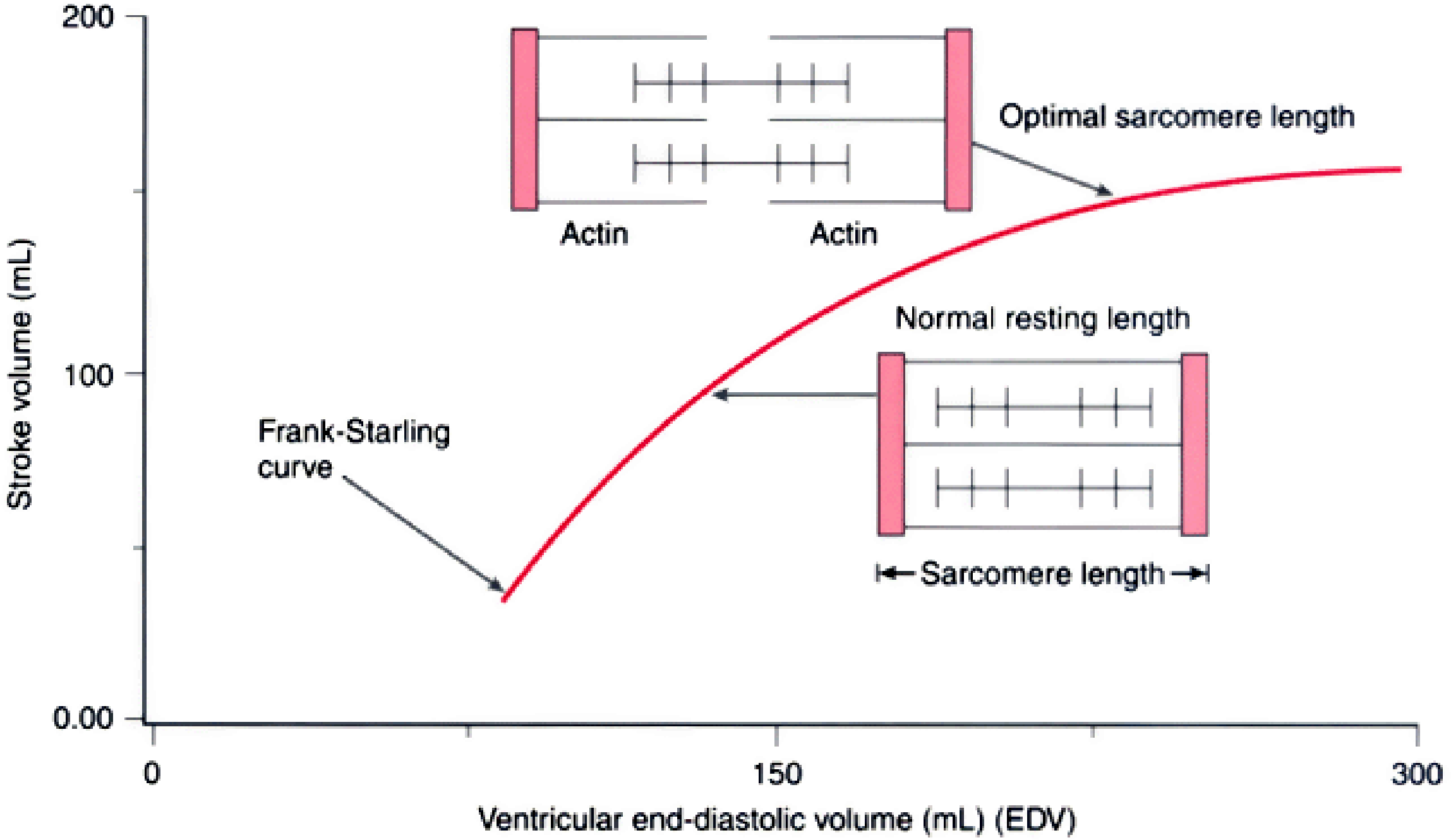
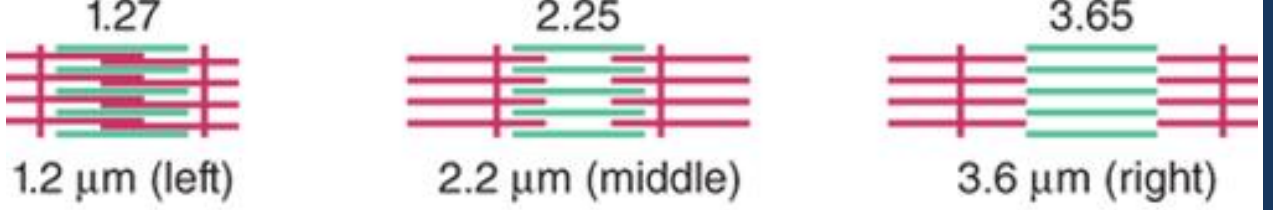
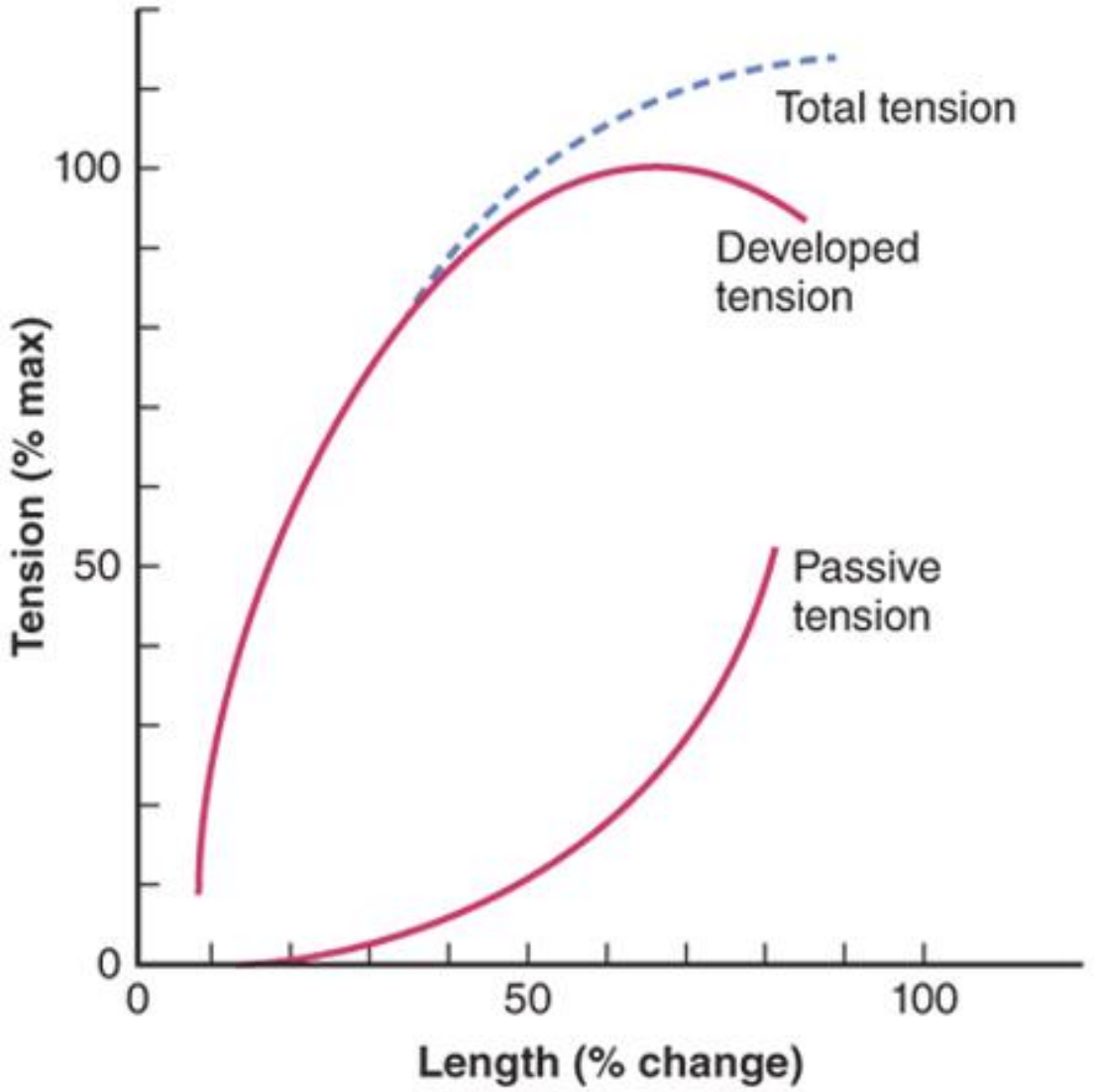


Starling law (wisdom of the heart)





4- Inotropic state of the heart

+ve inotropic state
Increase force of contraction
As:

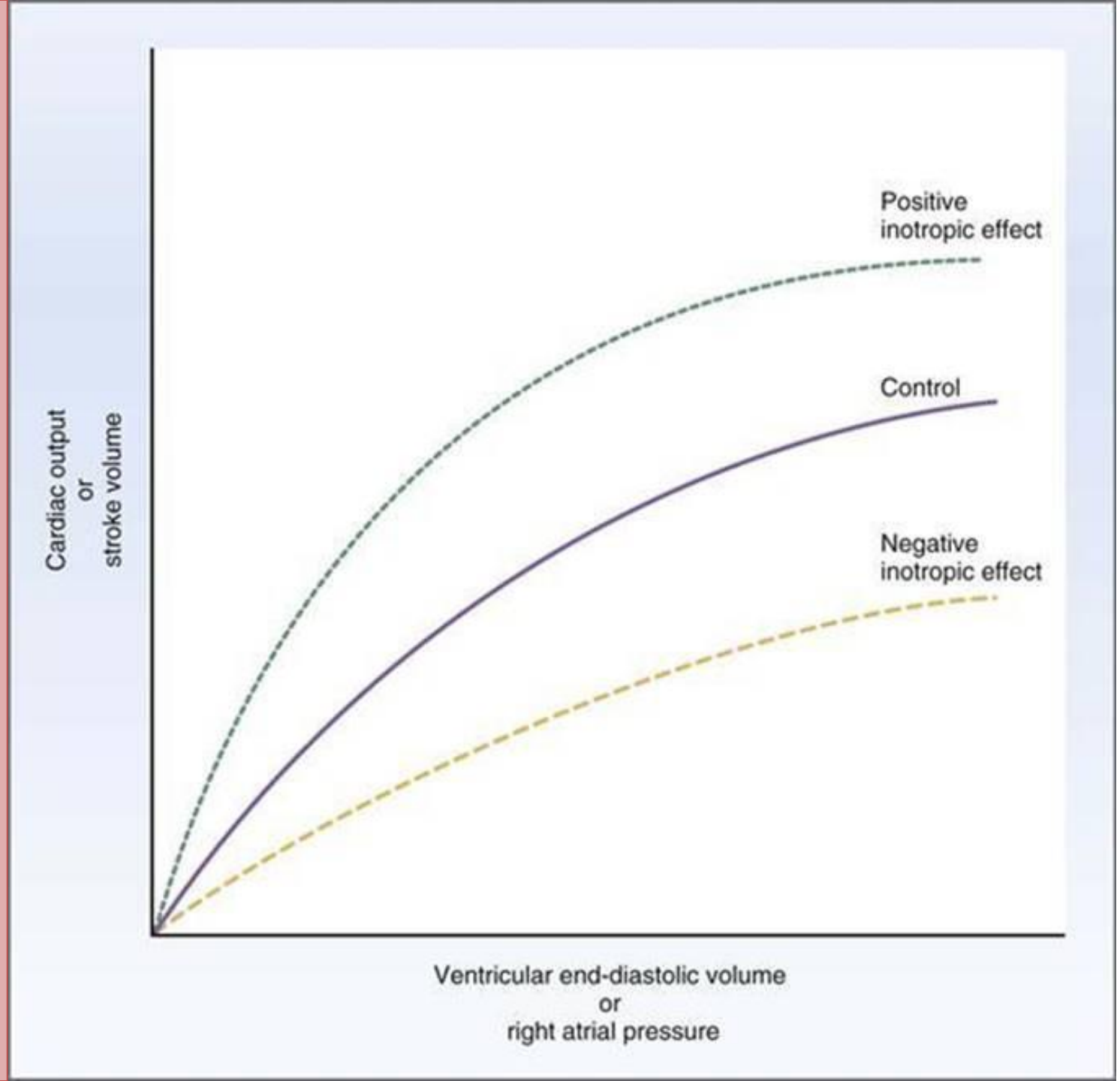
- **Sympathetic stimulation**
- **Drugs as digitalis**

-ve inotropic state
Decrease force of contraction
As:

- **vagal activity on the heart**

At the same initial Length (VR or Ventricular end diastolic volume)

The force of contraction can be increased or decreased




thank you