جامعة الملك سعود
King Saud University

Please remember that is very important to completely understand physiology.
You may contact the physiology leader for any questions.

Contractile Mechanism in Cardiac muscle

Index:
Red: important Grey: extra information Green: doctor's notes yellow: numbers
Purple: only in female slides Blue: only in male slides

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Revised by

Physiology Team437

MED437
KING SAUD UNIVERSITY

OBJECTIVES

by the end of this lecture you will be able to:

- 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.

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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, tropomyosin).
- Ca++ regulates contraction (Will be discussed later)

  Calcium is the main regulator

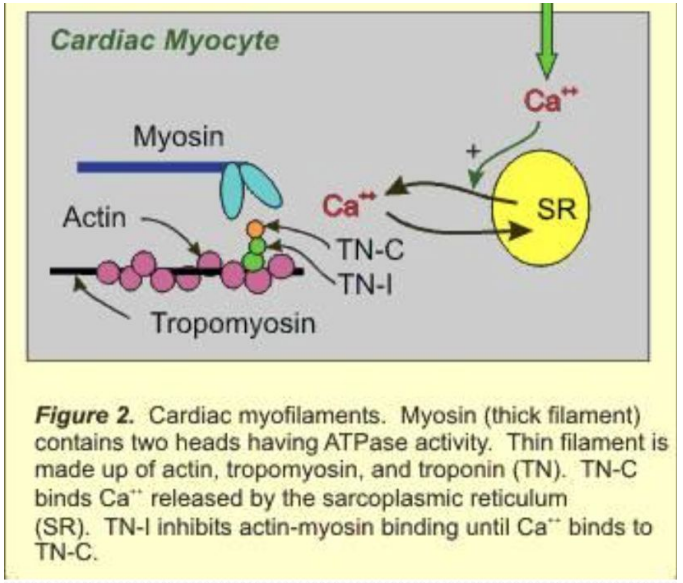
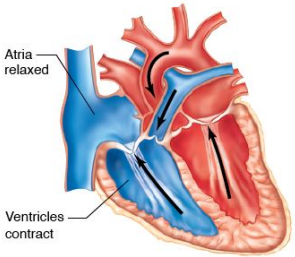


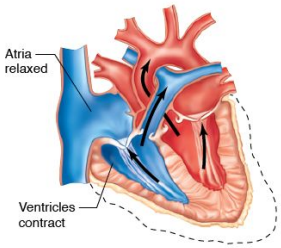
Figure 2. Cardiac myofilaments. Myosin (thick filament) contains two heads having ATPase activity. Thin filament is made up of actin, tropomyosin, and troponin (TN). TN-C binds Ca^{++} released by the sarcoplasmic reticulum (SR). TN-I inhibits actin-myosin binding until Ca^{++} binds to TN-C.

The Contractility of the Cardiac Muscle



AV valves:	Closed
Aortic and pulmonary valves:	Closed

Types of contraction in cardiac muscles



	Closed
	Open

isometric (isovolumic) 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.
muscle contraction without significant shortening or change in distance

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.
muscle contraction without significant change in force of contraction

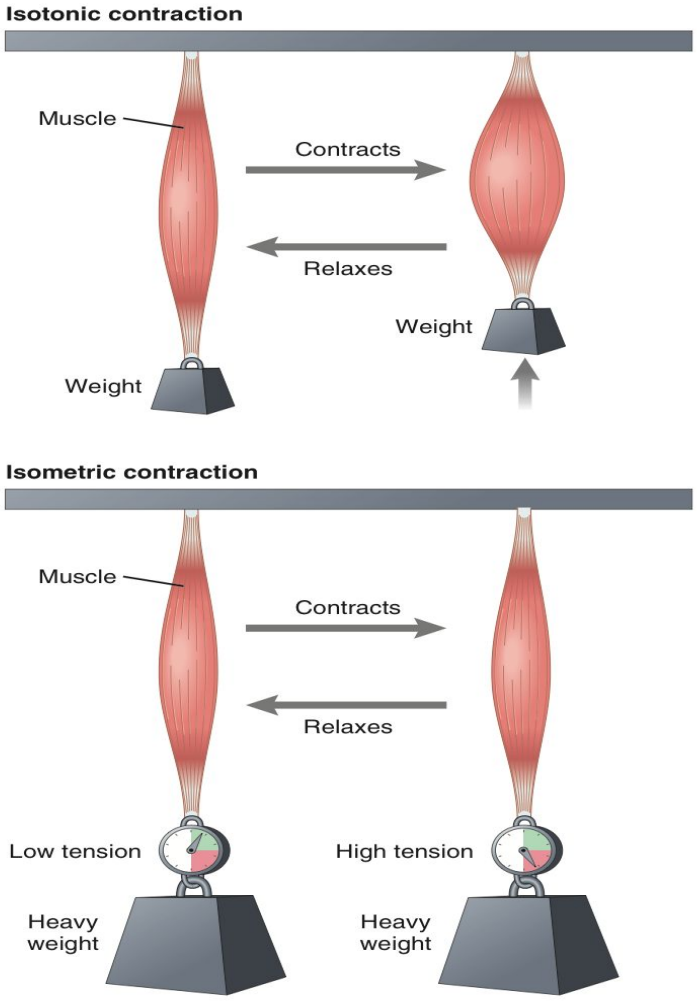
Iso; same / metric; length / tonic; tension (pressure).

More explanation for the previous slide

Muscle contraction is said to be **isometric** when the muscle does not shorten during contraction

isotonic when it does shorten but the tension on the muscle remains constant throughout the contraction.

Systems for recording the two types of muscle contraction are shown in Figure



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types of cardiac muscle

- Atrial Muscle
- Ventricular Muscle
- Specialize Excitatory & Conductive Muscle

- The atrial and ventricular muscle contract in same way as skeletal muscle, except duration of contraction is much longer.
- The specialized excitatory and conductive fibers contract weakly because they contain few contractile fibrils

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Physiology of Cardiac Muscle

Types of cardiac muscle cells

- Contractile cells:
  -99%of cardiac muscle cells
  -Do mechanical work of pumping
- Conducting (Autorhythmic) cells:
  -Do not contract
  -Specialized for initiating and conducting action potentials responsible for contraction of working cells

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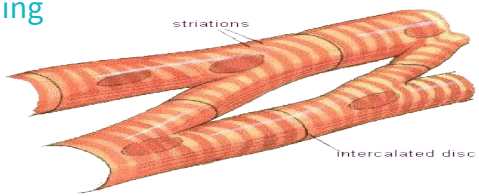
1-Contractile cells

They have special characteristics:

- Striated.
- Sarcomere is the functional unit
- Usually has a single and centrally nucleus.
- Rich in mitochondria (up to 40% of cell volume)
- Elongated (cylindrical)
- Branched , connect to one another at "intercalated discs"
- Contain several gap junctions .
- A membrane surrounds each fiber i.e. separate fibers.
- Sarcoplasmic Reticulum is less abundant than in skeletal muscle, but greater in density than smooth muscle
- Sarcolemma has specialized ion channels that skeletal muscle does not voltage- gated Ca2+ channels
- Fibers are not attached at ends, allows for greater sarcomere shortening and lengthening



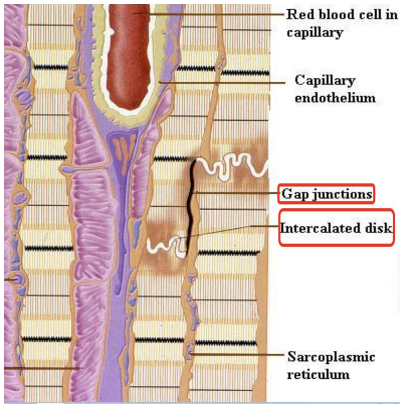
Intercalated Discs and Gap Junctions of Cardiac Muscle Fibers

Interconnected by intercalated discs and form functional syncytia

intercalated discs are the dark areas crossing the cardiac muscle fibers.

They are actually cell membrane that separate individual cardiac muscle cells from one another

There are two kind of membrane junctions: 1- Desmosomes. 2-Gap junctions



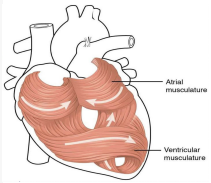
At each intercalated disc the cell membranes fuse with one another and form permeable "communicating" junctions (gap junctions) that allow almost totally free diffusion of ions. from a functional point of view, ions move with ease in the intracellular fluid along the longitudinal axes of the cardiac muscle fibers, so that action potentials travel easily from one cardiac muscle cell to the next, pass the intercalated discs. Thus, cardiac muscle is a syncytium of many heart muscle cells, action potential spreads to all of them.

Functional Syncytium

- Physiological & histological features of cardiac muscle help it to act as TWO functional (not anatomical) syncytia.

Atria syncytium (2 atria)	Ventricular syncytium (2 ventricles)
Both atria work as one unit.	Both ventricles work as one unit.

- Cardiac muscle cells are so tight bound that when one cell become excited, action potential spread rapidly from cell to cell.
- 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).



* a bundle of conductive fibers several mm in diameter will be discussed later in other lecture

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All or none 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
- 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 none rule.

2-Conducting cells: (Automatic/Autorhythmic)

Specialized or modified cardiac muscle cells, containing few contractile fibrils

Self-stimulating & rhythmic: Generate or initiate impulses in a repetitive constant manner

Conductive: Conducts electrical current throughout the heart

Excitatory: Provide an excitatory system to the heart

They don't contract

Specialized for initiating and conducting action potentials responsible for contraction of working cells

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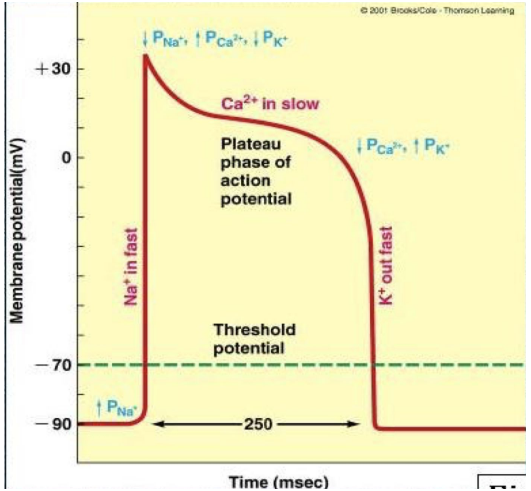
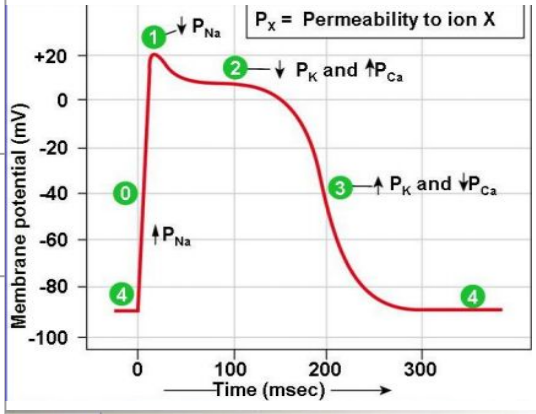
Action Potential of Contractile Cardiac Muscle Fibers

- Resting membrane potential of contractile myocardial fibers is stable "-90 mV".
- Duration of action potential is 300-400 ms. "0.3-0.4 sec"
- 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 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.



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

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

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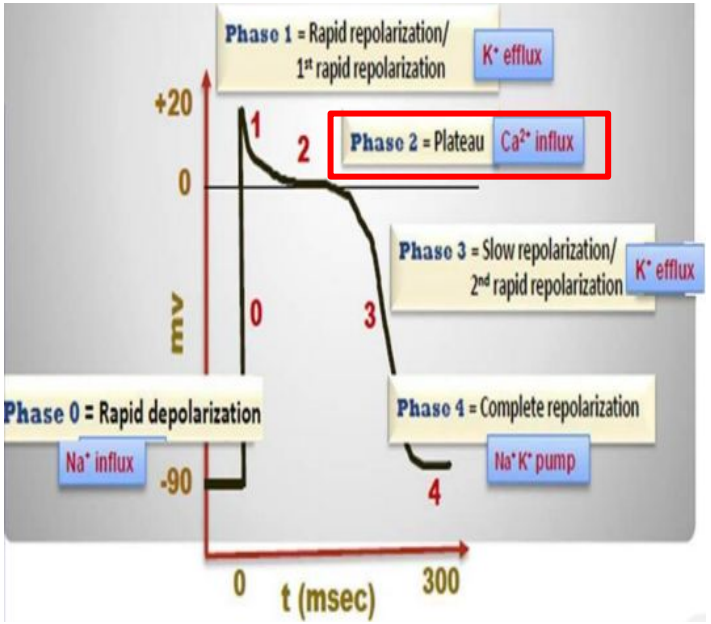
What causes the Plateau in the Action Potential?

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.



Extra information to help you understand the prolonged action potential

Why is the action potential of cardiac muscle so long and have a plateau, while skeletal muscle doesn't have a plateau?

First, the action potential of skeletal muscle is caused almost entirely by the sudden opening of large numbers of *fast Na channels* that allow tremendous number of Na ions to enter the skeletal muscle fibers from the ECF. these channels are called "fast" channels because they remain open for only a few 1/1000 of a second or so. In cardiac muscle, the action potential is caused by opening of TWO types of channels: (1) the same voltage-activated fast Na channels as those in skeletal muscle and (2) another entirely different population of L-type Ca channels (slow channels), which are also called Ca-Na channels. They are slower to open and, even more important, remain open for several 1/10 of a second. During this time, a large quantity of both Ca & Na ions flows to the interior of cardiac muscle fiber, and this activity maintains a prolonged period of depolarization, causing the plateau. Further, the Ca ions that enter during this plateau phase activate the muscle contractile process, whereas the Ca ions that cause skeletal muscle contraction are from intracellular sarcoplasmic reticulum.

Second, immediately after the onset of the action potential, the permeability of the membrane for K decreases about fivefold, an effect that does not occur in skeletal muscle. This decreased K permeability may result from the excess Ca influx. Regardless of the cause, the decreased K permeability greatly decrease the outflux of positively charged K ions during the action potential plateau and thereby prevents early return of the action potential voltage to its resting level. When the slow Ca-Na channels do close at the end of 0.2 to 0.3 second and the influx of Ca and Na ceases, the membrane permeability for K ions also increases rapidly; this rapid loss of K from the fiber immediately returns the membrane potential to its resting level, thus ending the action potential.

from Guyton 13th edition page 110-111

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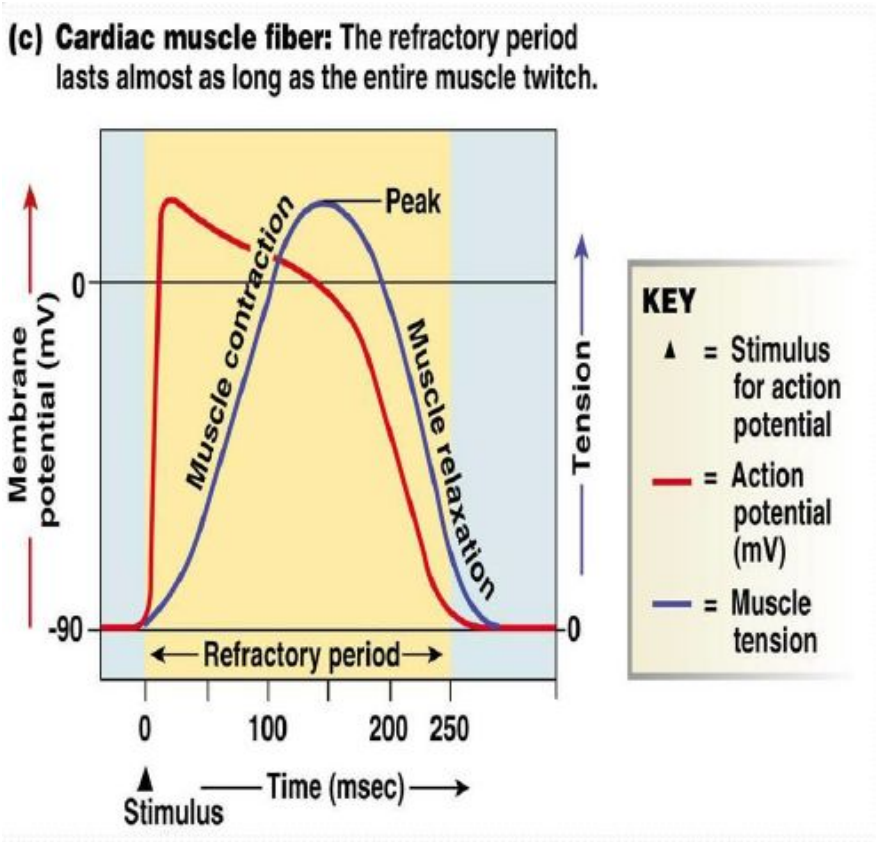
Refractory Period of Cardiac Muscles

- **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.



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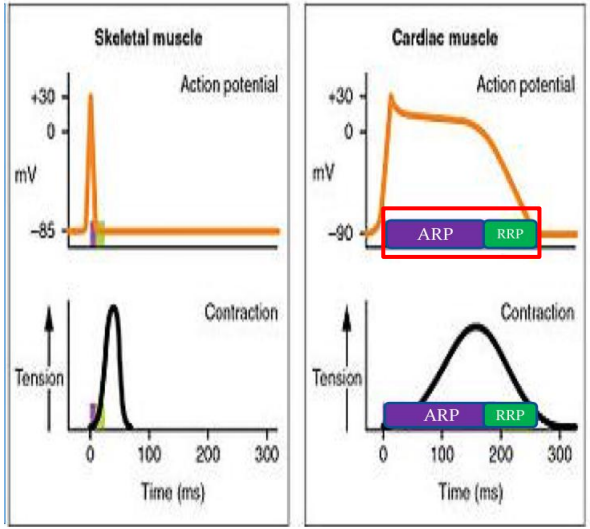
Cardiac Muscle has two Refractory Periods:

1- Absolute refractory period:

- Cardiac muscle cannot be excited while it is contracting (due to complete depolarization)... 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)



2-Relative refractory period:

- Cardiac muscle can be excited by strong stimulus to produce a new systole Called extra -systole
- Time : the last ⅓ of repolarization (the rest of phase 3)
- Mechanically: it occupies the middle of diastole
- Duration: 0.05sec in ventricles and 0.03sec in atria

Excitation-contraction coupling in cardiac muscle

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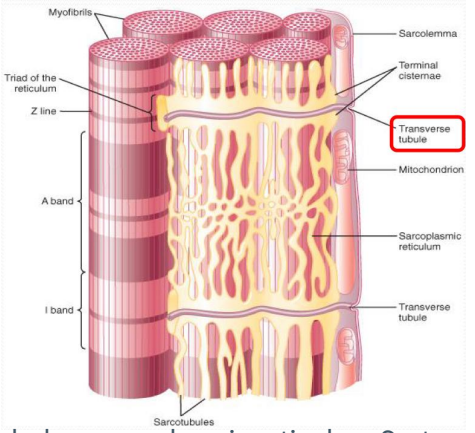
- Excitation-contraction coupling : it is the mechanism by which the action potential causes muscle contraction
- Action potential spreads to the interior of the cardiac muscle fiber along the transverse(T) tubules



Transverse (T) tubules-sarcoplasmic reticulum System

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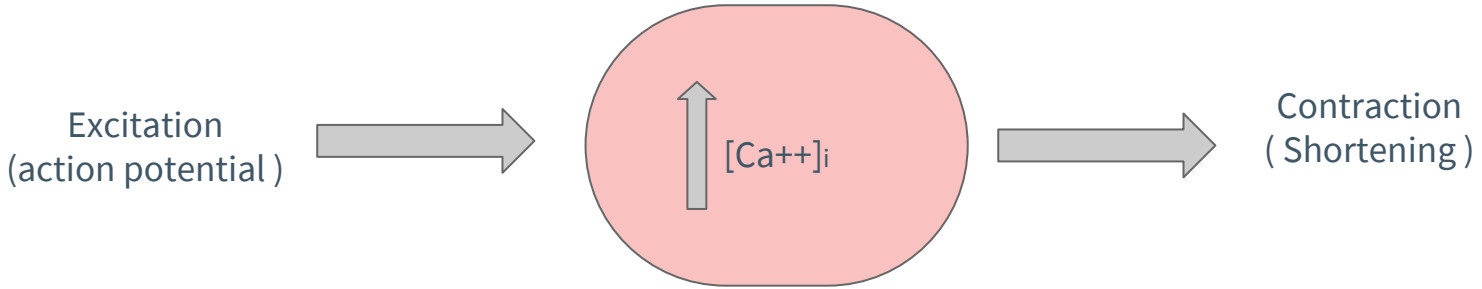
- Excitation of the heart is triggered by electrical impulse rather than neurotransmitters
- Contraction of the heart is triggered by elevation of intracellular calcium influx



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Excitation-contraction coupling in cardiac muscle

1) Action potential spread along the T-tubules

2A) Release of calcium ions from sarcoplasmic reticulum Into the Sarcoplasm.
2B) large quantity of extra Ca++ diffuses into the Sarcoplasm from T-tubules

3) Ca++ binds to troponin causing sliding of actin and myosin filaments

4) Contraction of cardiac muscle fibers

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- Depolarization of myocardial cell stimulates opening of VG Ca++ channels in sarcolemma.
  Ca++ diffuses down gradient into cell —> stimulates opening of Ca++ release channels in SR
  Ca++ binds to troponin and stimulates contraction (same mechanism as in skeletal muscle).

- During repolarization Ca++ actively transported out of the cell via Na+-Ca++ exchanger

Excitation-contraction coupling in cardiac muscle

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- Calcium ions regulate the contraction of cardiac muscle :
  - Entry of extracellular calcium ions causes the release of calcium from the sarcoplasmic reticulum (calcium-induced calcium release) the source of about 95% of the calcium in the cytosol

- 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 skeletal muscle tubules

لأن في القلب نحتاج الكالسيوم اكثر فيكون حجم التبيولز اكبر عشان يجي كالسيوم كثير بزمن قليل

- The strength of contraction of cardiac muscle depends to a great extent on the concentration of Ca^{++}

  in the ECF

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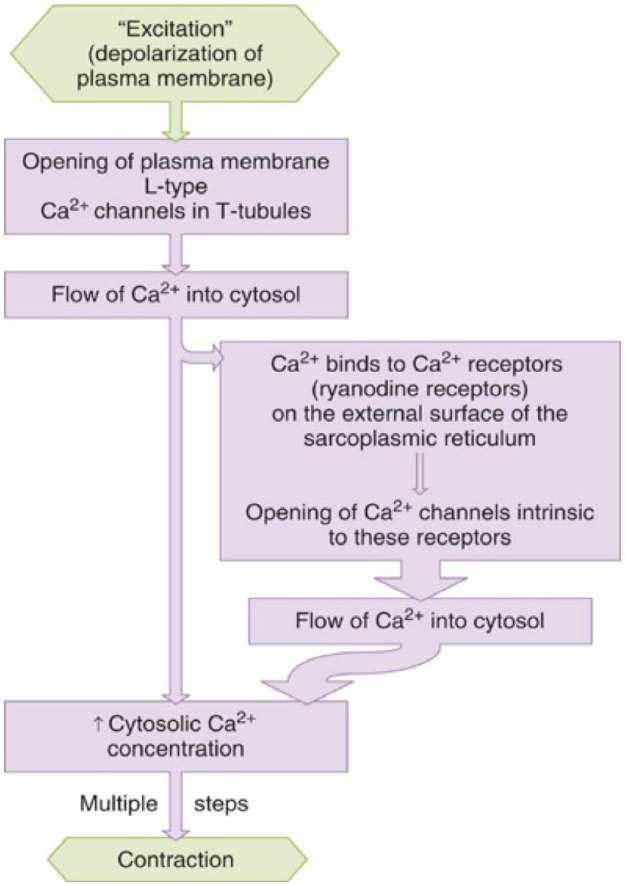
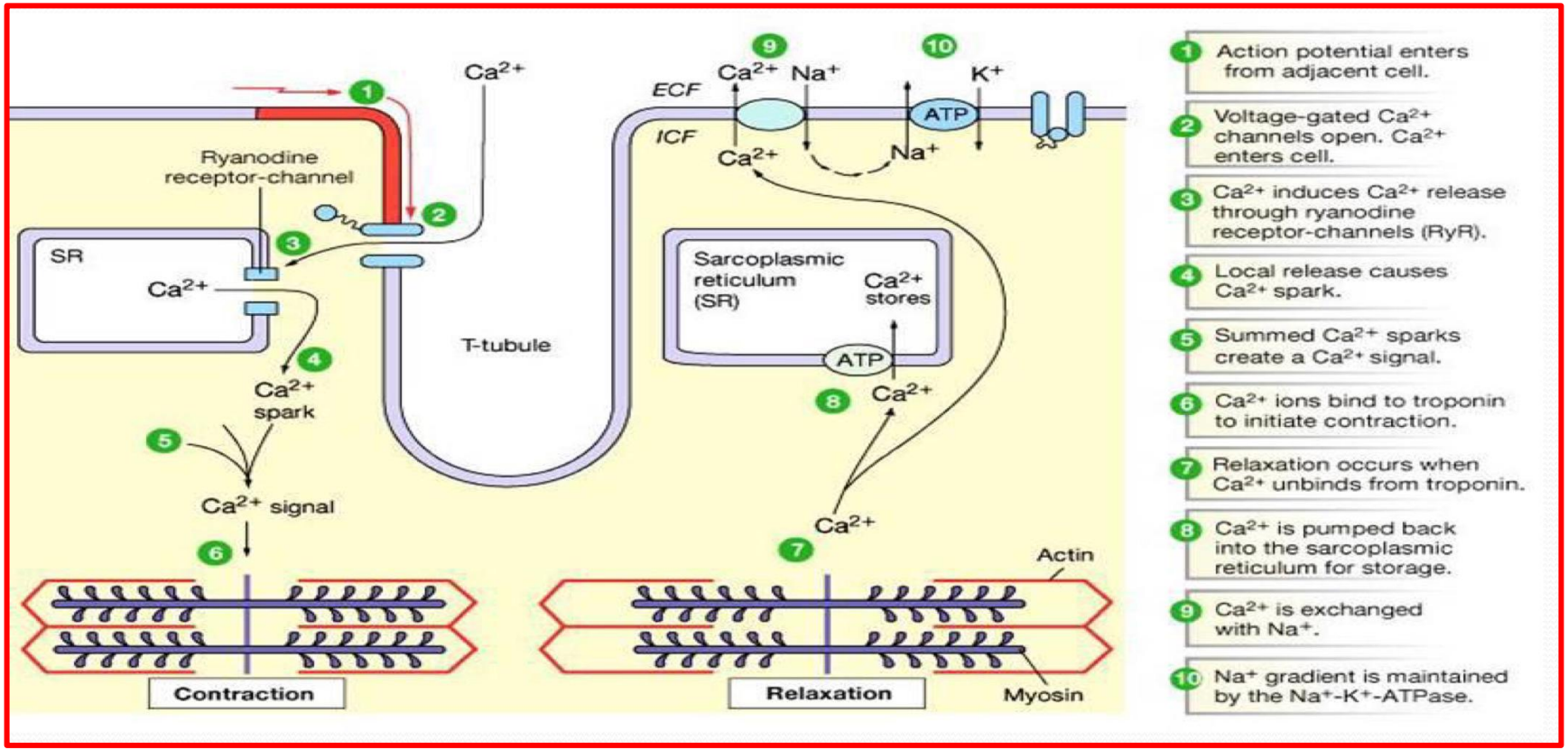


Excitation-contraction coupling in cardiac muscle



The steps are very important

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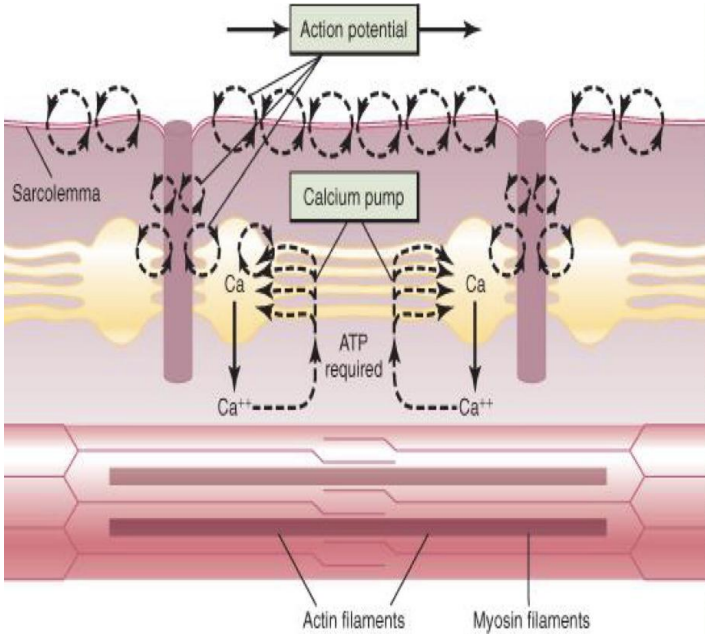
Excitation – Contraction Coupling in Cardiac Muscle

- 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.



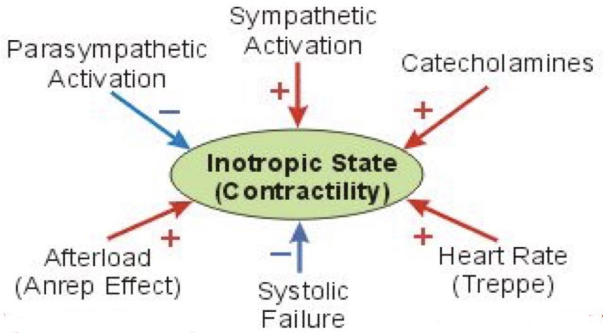
The strength of contraction of cardiac muscle depends to a great extent on the concentration of calcium ions in the extracellular fluids.
The quantity of calcium ions in the T tubule system (i.e., the availability of calcium ions to cause cardiac muscle contraction) depends to a great extent on the extracellular fluid calcium ion concentration.
In contrast, the strength of skeletal muscle contraction is hardly affected by moderate changes in extracellular fluid calcium concentration because skeletal muscle contraction is caused almost entirely by calcium ions released from the sarcoplasmic reticulum inside the skeletal muscle fiber.
From guyton page 112

Factors affecting Cardiac Contractility (Inotropic Effectors)

- **Inotropic 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



Pressure against which heart work to eject the blood during systole.

Myocardial tension increases with increase in heart rate.

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Factors affecting Cardiac Contractility....Cont.

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- **Autonomic innervation:**

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

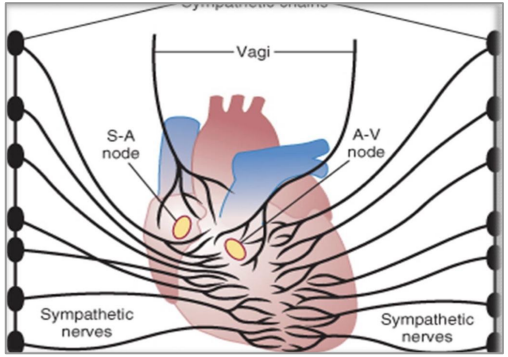

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Table 14.1 Effects of Autonomic Nerve Activity on the Heart

Region Affected	Sympathetic Nerve Effects	Parasympathetic Nerve Effects
SA node	Increased rate of diastolic depolarization; increased cardiac rate	Decreased rate of diastolic depolarization; decreased cardiac rate
AV node	Increased conduction rate	Decreased conduction rate
Atrial muscle	Increased strength of contraction	Decreased strength of contraction
Ventricular muscle	Increased strength of contraction	No significant effect

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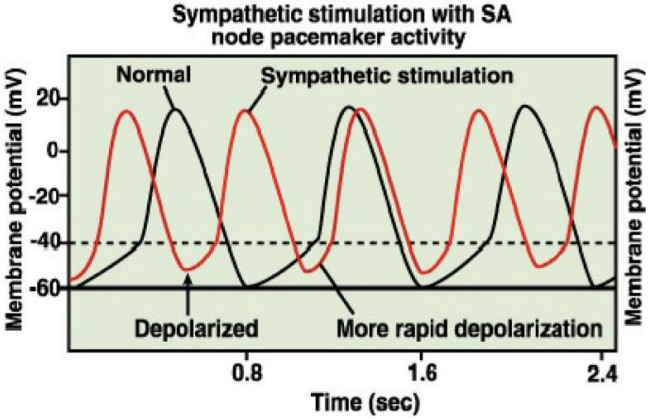
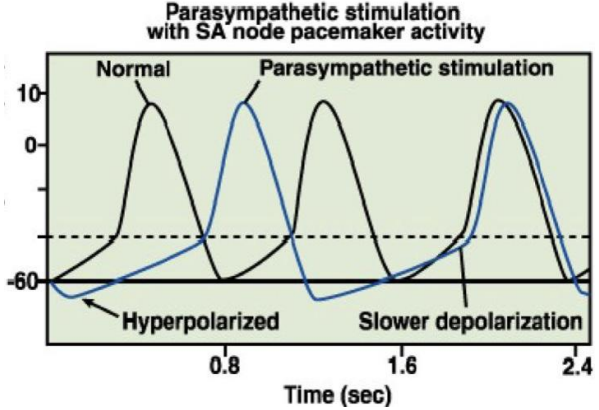
Factors affecting Cardiac Contractility....Cont.

Autonomic nervous system modulates the frequency of depolarization of pacemaker.



- Sympathetic stimulation (neurotransmitter); binds to **b1 receptors** on the SA nodal membranes.



- Parasympathetic stimulation (neurotransmitter); binds to **muscarinic receptors** on nodal membranes; increases conductivity of K+ and decreases conductivity of Ca^{2+}.

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Factors affecting Cardiac Contractility....Cont.

- **Oxygen supply:**

Hypoxia: ↓ Contractility

- **Physical factors:**

Warming: ↑ Contractility
Cooling: ↓ Contractility
Exercise: ↑ Contractility

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

↑$[Ca^{++}]$: ↑Contractility
↑$[K^{+}]$: ↓ Contractility

Very high concentration of Ca^{++} in ECF stops the heart during contractions.
Very high concentration of K^{+} in ECF stops the heart during relaxations.

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Factors affecting Cardiac Contractility....Cont.

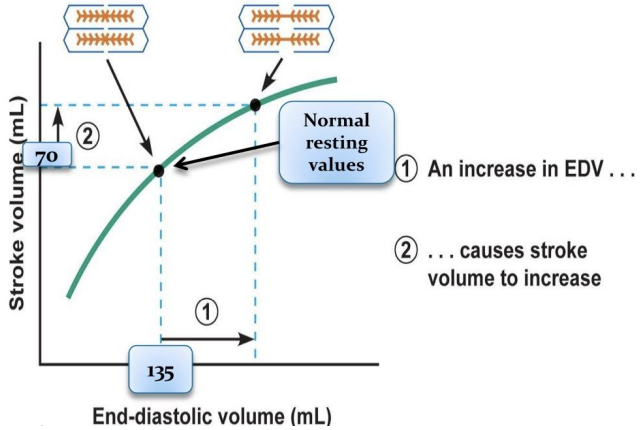
- **Hormonal and chemical factors:**

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)

- **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.



Summary

- Contractility: Is the force of contraction for a given fiber length.
- There are two types of contractions in cardiac muscles,isometric and isotonic.
- There are two types of cardiac muscle cells, contractile and conducting.
- There are three types of cardiac muscles,atrial muscle,ventricular muscle and specialize excitatory(conductive) muscle.
- Intercalated discs are the dark areas crossing the cardiac muscle fiber,and they separate individual cardiac muscle cell from one another.
- Physiological & histological features of cardiac muscle help it to act as a functional (not anatomical) syncytium.
- Resting membrane potential of contractile myocardial fibers is stable “-90 mV”.
- Duration of action potential is 300-400 ms.
- It has 5 phases.
- The refractory period is the interval of time during which a normal cardiac impulse cannot re-excite an already excited area of cardiac muscle.
- The relative refractory period is the interval which the cardiac muscle can be excited by strong stimulus to produce a new systole called extra-systole.
- Excitation – Contraction Coupling is the mechanism by which the action potential causes muscle contraction.

Quiz

1.Which of the following structures will have the slowest
rate of conduction of the cardiac action potential?
A) Atrial muscle
B) Anterior internodal pathway
C) A-V bundle ibers
D) Purkinje fibers
E) Ventricular muscle

2..What is the normal total delay of the cardiac impulse in
the A-V node + bundle?
A) 0.22 second
B) 0.18 second
C) 0.16 second
D) 0.13 second
E) 0.09 second

3,Which condition at the A-V node will cause a decrease in heart rate?
A) Increased sodium permeability
B) Decreased acetylcholine levels
C) Increased norepinephrine levels
D) Increased potassium permeability
E) Increased calcium permeability

4.Which statement best explains how sympathetic stimulation affects the heart?
A) he permeability of the S-A node to sodium decreases
B) he permeability of the A-V node to sodium decreases
C) he permeability of the S-A node to potassium.
D) here is an increased rate of upward drift of the
E) he permeability of the cardiac muscle to calcium increases resting membrane potential of the S-A node decreases

Answers
1.c
2.d
3.d
4.d

Quiz

5. What is the membrane potential (threshold level) at
which the S-A node discharges?
A) −40 millivolt
B) −55 millivolt
C) −65 millivolt
D) −85 millivolt
E) −105 millivolt

6. What is the delay between the S-A node discharge and
arrival of the action potential at the ventricular sep-
tum?
A) 0.80 second
B) 0.16 second
C) 0.13 second
D) 0.09 second
E) 0.03 second

7. If the S-A node discharges at 0.00 seconds, when will the action potential normally arrive at the A-V node?
A) 0.03 second
B) 0.09 second
C) 0.12 second
D) 0.16 second
E) 0.80 second

Answers
5.a
6.b
7.b

Thank you for checking our work

Team Leader:

العنود سلمان

Male Team:

أنس السويداء
أنس السيف
خالد شويل
ريان الموسى
سعد الهداب
سعود العطوي
سيف المشاري
عبدالجبار اليماني
عبدالرحمن آل دحيم
عمر الفوزان
فهد الحسين
نايف المطيري
نواف اللويمي
محمد الحسن
هشام الشايع
خالد العقيلي
سعد الفوزان
عبدالله الزيد

Female Team:

الآء الصويّغ
رناد المقرن
رهف الشنيبر
روان التميمي
روان مشعل
ريم القرني
ليلى الصباغ
فلوة السعوي
نورة بن حسن
نورة الحربي
نورة العثيم
مجد البراك
لينا العوهلي
عهد القرين
مها النهدي
مها بركة
سارة الفليج
هند العريعر
ريناد الغريبي
عائشة الصباغ

Any questions?

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