Ask Mish

CARDIAC CELL PHYSIOLOGY

- Cardiac Cell Phases: Resting, Depolarization and Repolarization

- Types of Cardiac Cells

- Membrane Potential vs Action Potential

- Ion Channels

- Cardiac Muscle contraction and relaxation

Cardiac Cell Physiology 1

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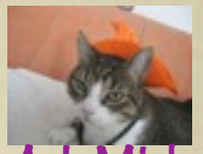
- 3 phases of cardiac cells:
- 1.RESTING
- 2.DEPOLARIZATION
- 3.REPOLARIZATION

- 1.At rest, cell is more negative inside than outside mainly due to ATP pumps, e.g. Na/K pump (3Na out/2K in).Proteins and phosphates are big negative molecules found inside the cell.

Cardiac Cell Physiology 2



- 2.DEPOLARIZATION:cell turns from negative to positive inside.
- The cause of depolarization is an influx of ions of Na and Ca inside the cell.
- Depolarization is propagated from cell to cell producing a wave of depolarization that can be transmitted to the entire heart.This wave represents a flow of electrons(negative charges outside),an electrical current that can be detected by electrodes placed on the surface of the body.
- 3.REPOLARIZATION:cardiac cells restore their resting polarity (negative inside)
- Cause: Na and Ca channels close and K channels open so an efflux of K ions leaves the cell.
- Repolarization can be sensed by recording electrodes.
- All of the different waves that we can see on an EKG are manifestations of these 2 processes: depolarization and repolarization.

Cardiac Cell Physiology 3

	resting	depolarization	repolarization
inside of the cell	negative	positive	negative
due to	proteins phosphates Na/K pump	influx Na, Ca	efflux K
propagation from cell to cell	no	yes	yes

Cardiac Cell Physiology 4

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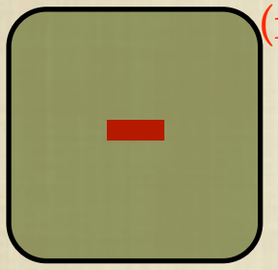
1.Resting cell=polarized cell

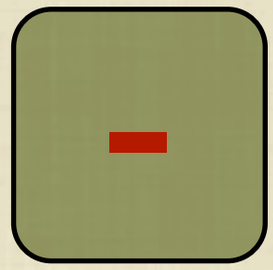


(more negative inside than outside)

2.Depolarization

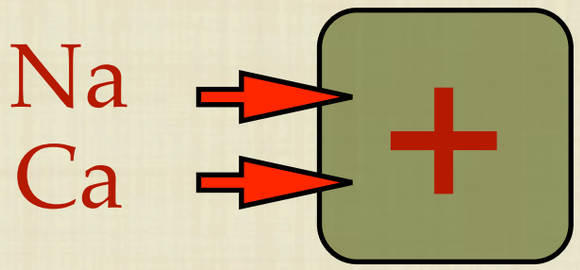
(cell turns positive inside)

3.Repolarizarion

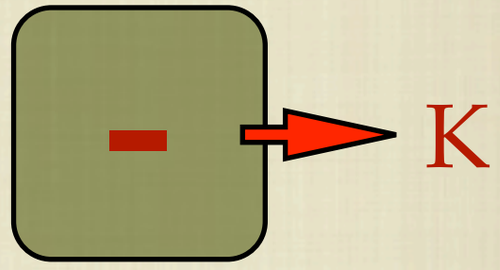


(cell returns to resting polarity)

Due to: Proteins, Phosphates, Na/K pump



influx



efflux

	MEMBRANE POTENTIAL	ACTION POTENTIAL
def	difference in electrical charge (voltage) across the cell membrane in resting state	short living event including Depolarization and Repolarization
cell	ALL CELLS	EXCITATORY CELLS only (nerve,cardiac*,muscle,endocrine)

3 Types of Cardiac Cells

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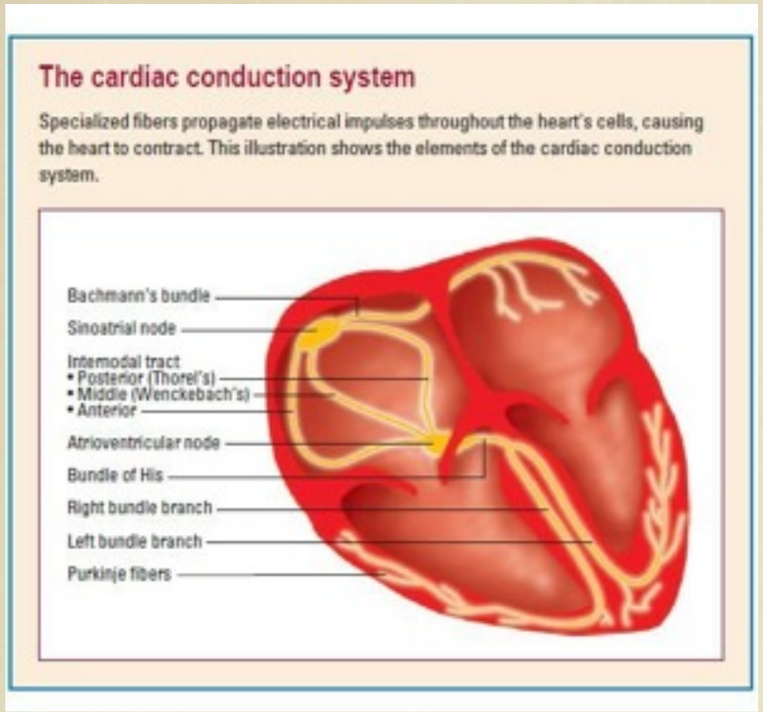

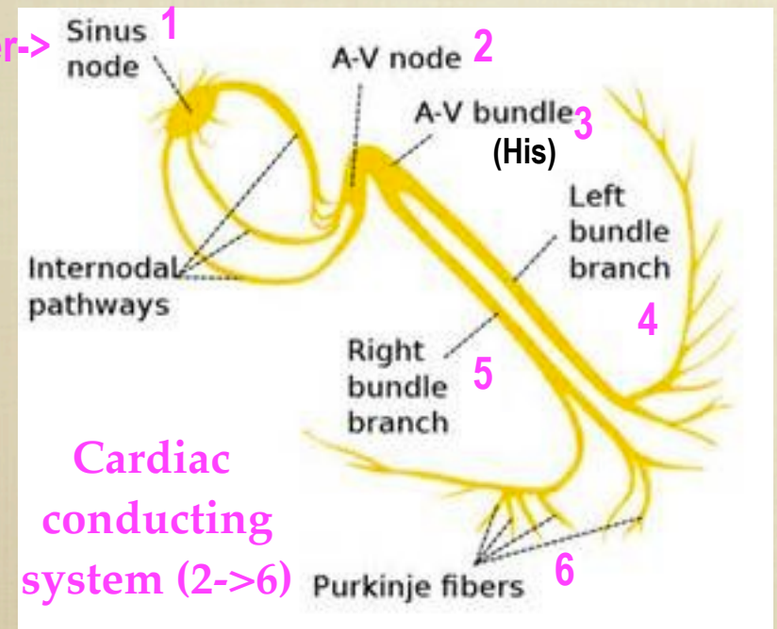

- 3 TYPES of CARDIAC CELLS:
- pacemaker cells
  = electrical power source
  SA node (1) or AV node (2)
- electrical conducting cells
  = wire of the heart
  AV node(2) His bundle(3) with 2 branches(4,5) and Purkinje fibers(6)
- myocardial cells
  = contractile pump of the heart

2 Types of Resting Potential

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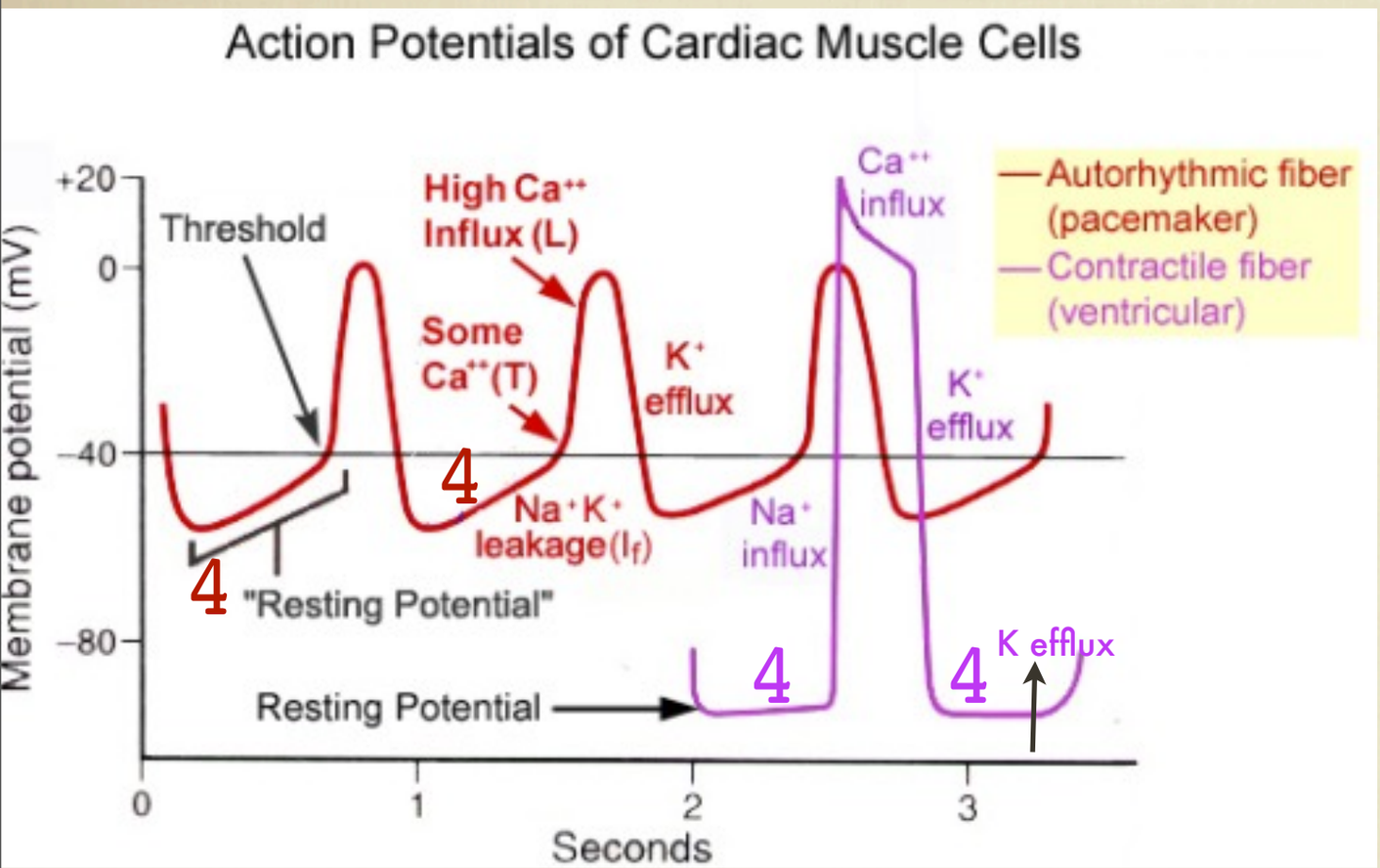
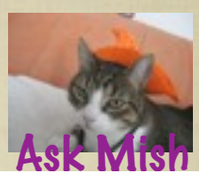
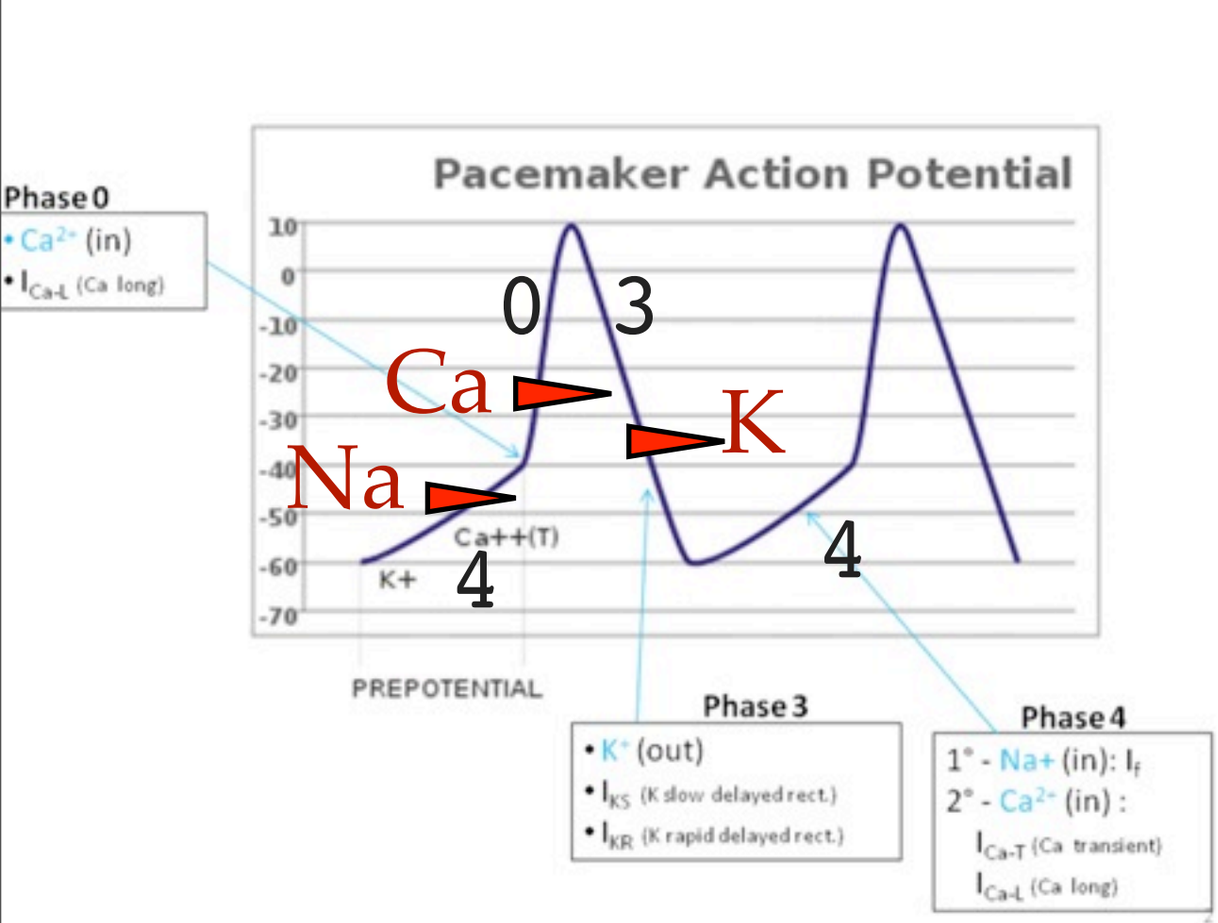
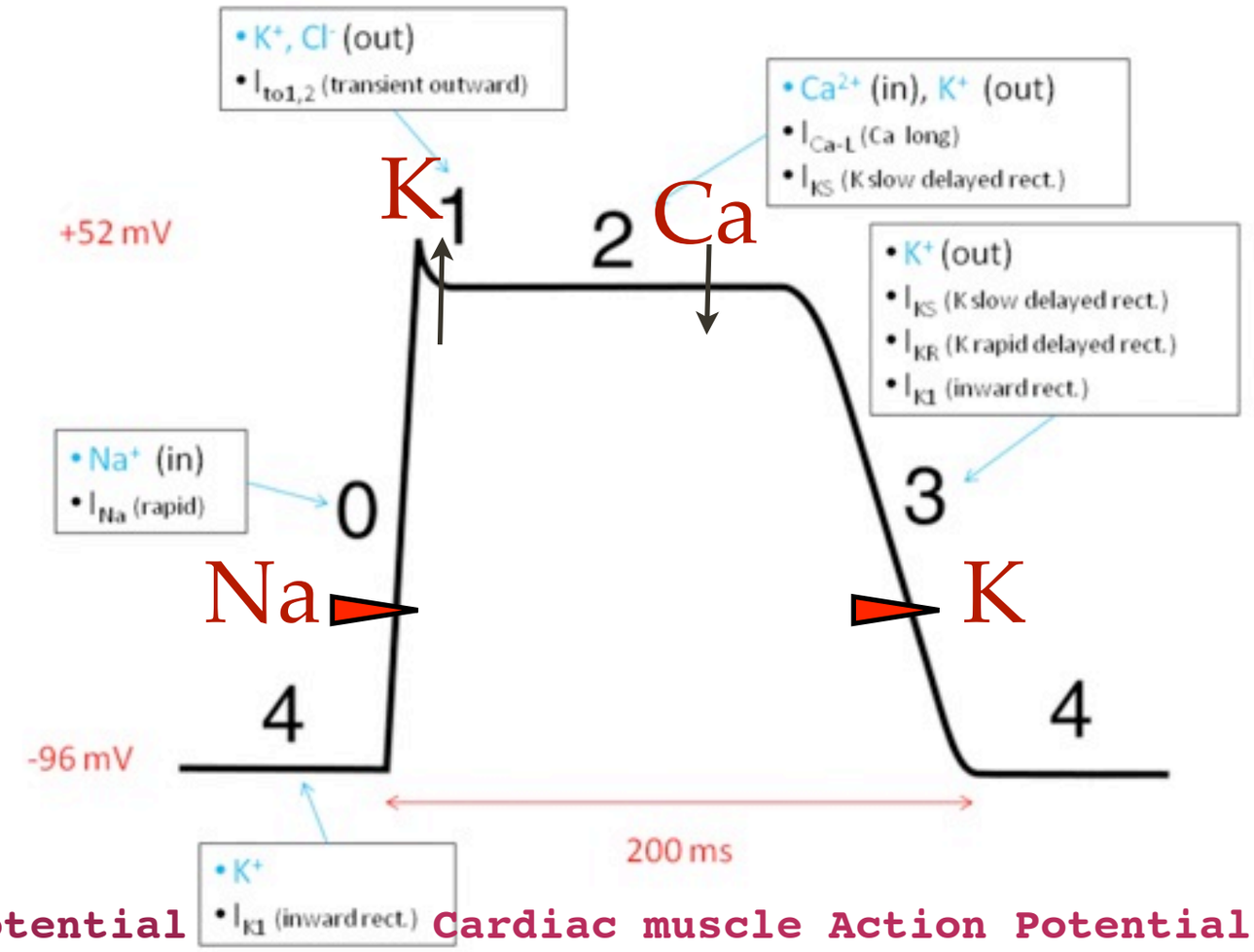


	Pacemaker	Cardiac muscle
Resting Potential (4)	variable -60 to-40 mV	stable -96 mV
Due to:	slow influx of Na= "funny current"(I_f) and some CaT (transient)	ions inside vs outside the cell; K efflux (I_{K1})

2 Types of Action Potential







SA node, AV node Action Potential — Cardiac muscle Action Potential

0	Depolarization	Ca influx	Na influx
3	Repolarization	K efflux	K efflux
1-2	Rapid repolarization(1) and Plateau (2)	-	K efflux(1) & Ca influx(2)

3 Types of Ion Channels

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	Type of Channels	Description
I	Voltage gated	"GATED" called like this because of an imaginary gate that opens or closes in this case at voltage variation across the cell membrane allowing or not ions inside the cell. There are voltage gated channels for Na, Ca and K, usually more than one type for each ion. When one channel opens (is activated) in one phase, the previous opened channel usually closes (is inactivated). Order of activation/inactivation in action potential: Na -> Ca ->K
II	Receptor gated	"GATE" opens or close in this case in response to a molecule binding to a receptor. e.g. ATP binding to a receptor on a K channel or Acetylcholine binding to a receptor on a K channel
III	Ligand gated (Specific ions and Chemical Ligands)	opens in response to ions influx in the cell e.g. Ca influx in vascular smooth muscle opens a K channel

3 Types of Ion Channels

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I

Na channels	
slow Na I_f	"funny current" in phase 4 of pacemaker potential
fast Na	phase 0 (depolarization) of non-pacemaker cardiac action potential
K channels	
transient outward I_{to}	phase 1 of non-pacemaker cardiac action potential
slow delayed rectifier I_{KS}	phase 3 of cardiac action potential, starts in phase 2
rapid delayed rectifier I_{KR}	phase 3 of cardiac action potential, continues in phase 4
inward rectifier I_{K1} or I_{ir}	phase 4 of cardiac action potential and late 3
Ca channels	
L-type $I_{Ca\text{-}L}$	long-lasting current: phase 0 (depolarization) of pacemaker AP, phase 2 of non-pacemaker cardiac AP
T-type $I_{Ca\text{-}T}$	transient current: phase 4 of pacemaker action potential in SA and AV node

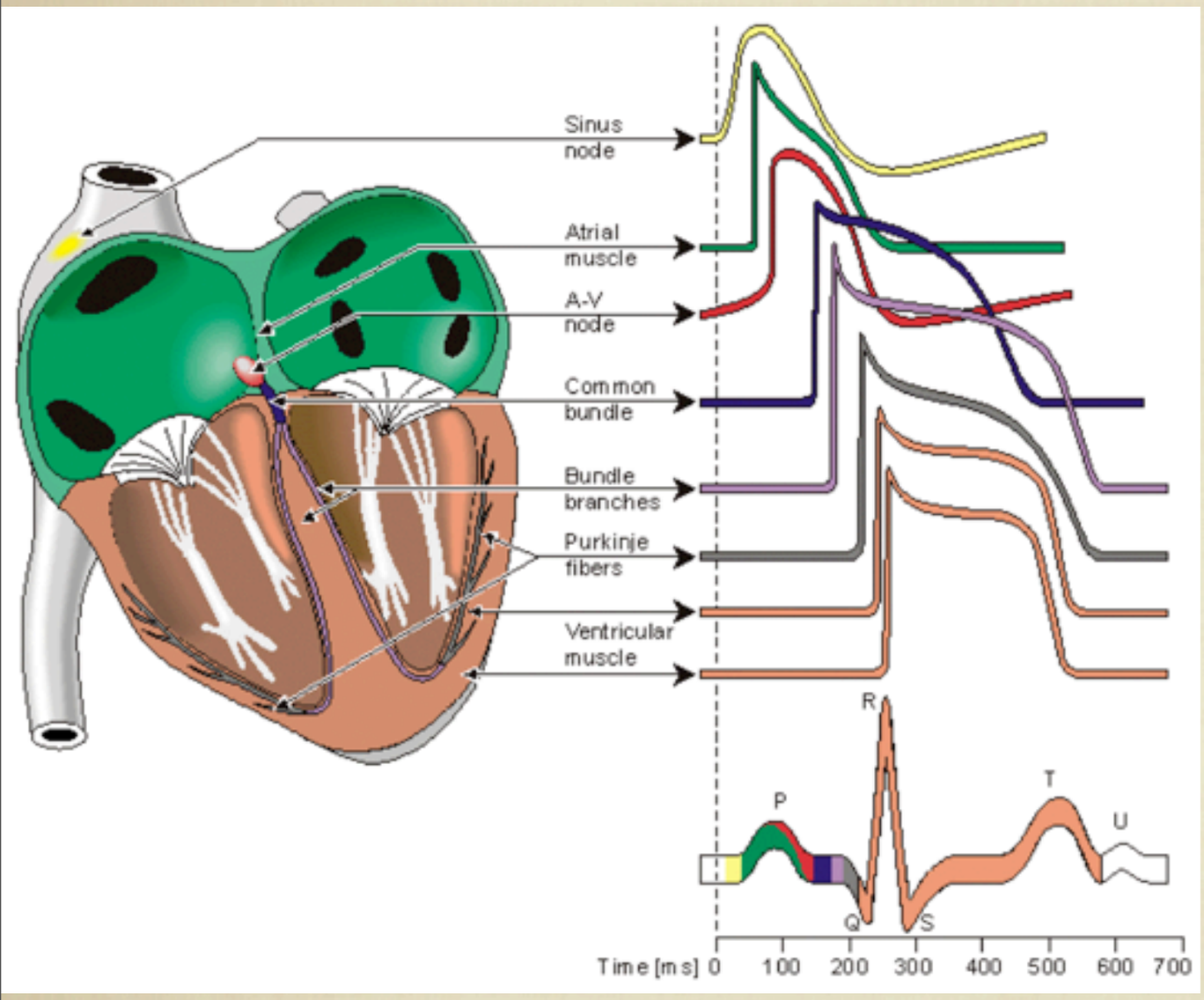
II

K channels	
ATP sensitive $I_{K,\,ATP}$	K_{ATP} channels, inhibited by ATP; in vascular smooth muscle, adenosine (final ATP metabolite) opens K channels resulting hyperpolarization* (more negative repolarization) and vasodilation
Acetylcholine activated $I_{K,\,ACh}$	opened by Acetylcholine; Gi protein coupled

III

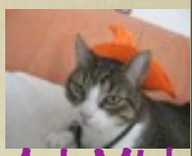
K channels	
Calcium activated $I_{k,\,Ca}$ or BK_{Ca}	open in response to Ca influx in vascular smooth muscle

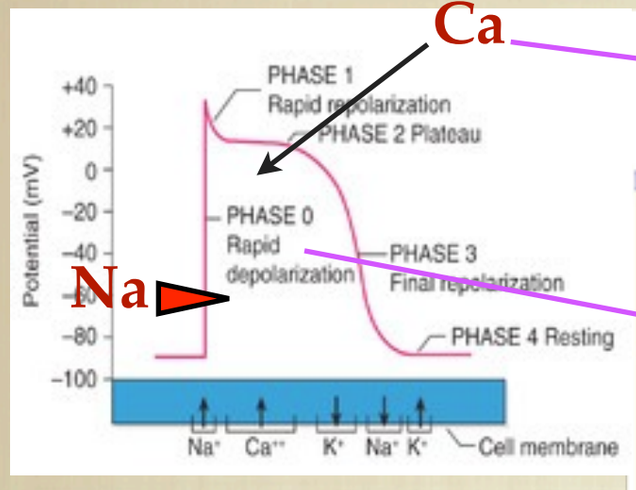
Heart: Action Potentials



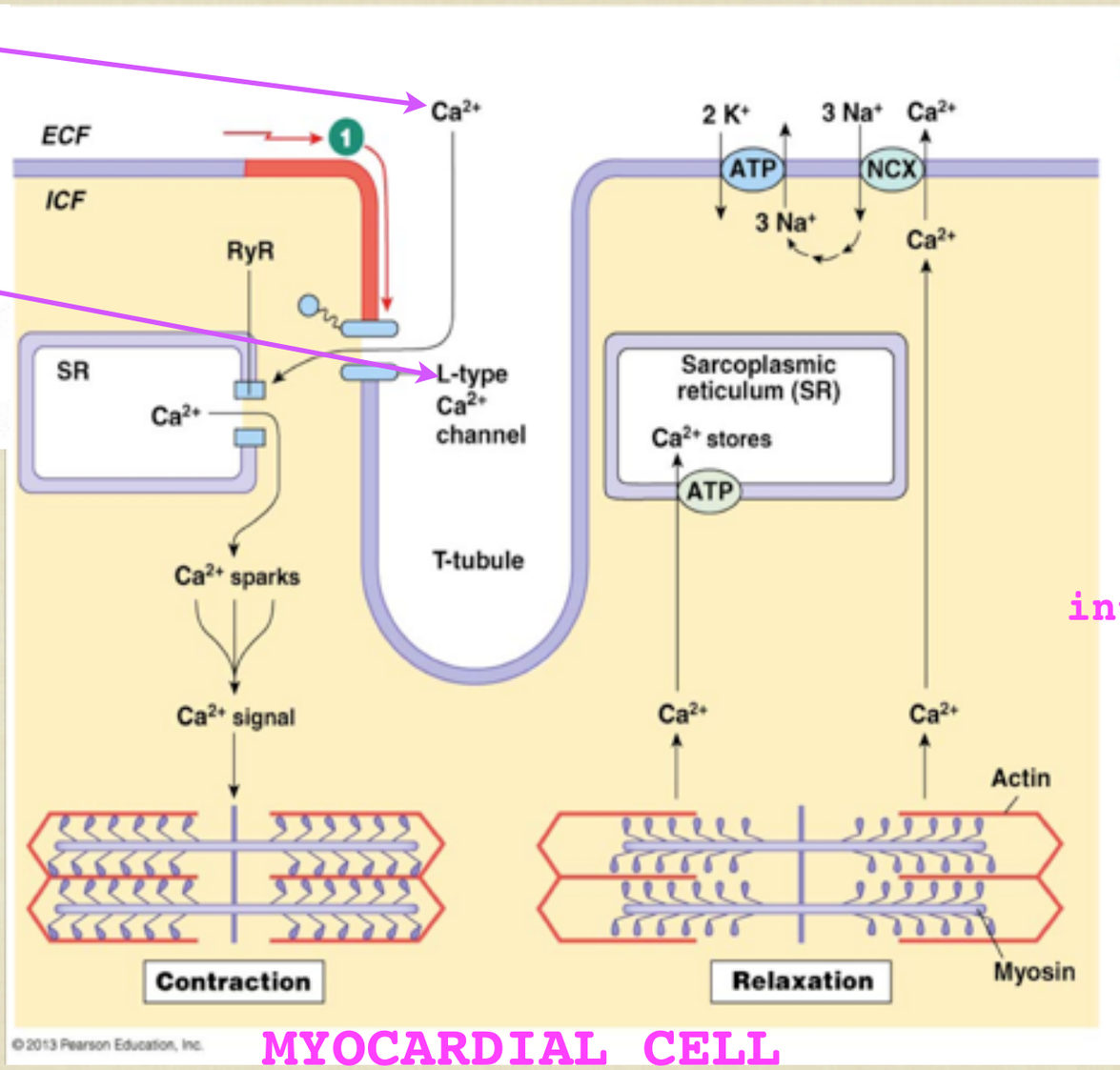
- Action potential (AP) is propagated from cell to cell. It is generated by the pacemaker (sinoatrial node)
- Then is propagated to atrial muscle cells, AV node, bundle of His then bundle branches and finally through Purkinje fibers to the contractile pump which is ventricular myocardium.
- Depolarization and repolarization phases of the action potentials passing through these tissues are recorded on a special paper by electrodes placed on the skin and is called EKG or ECG.

AP:Myocardial Contraction

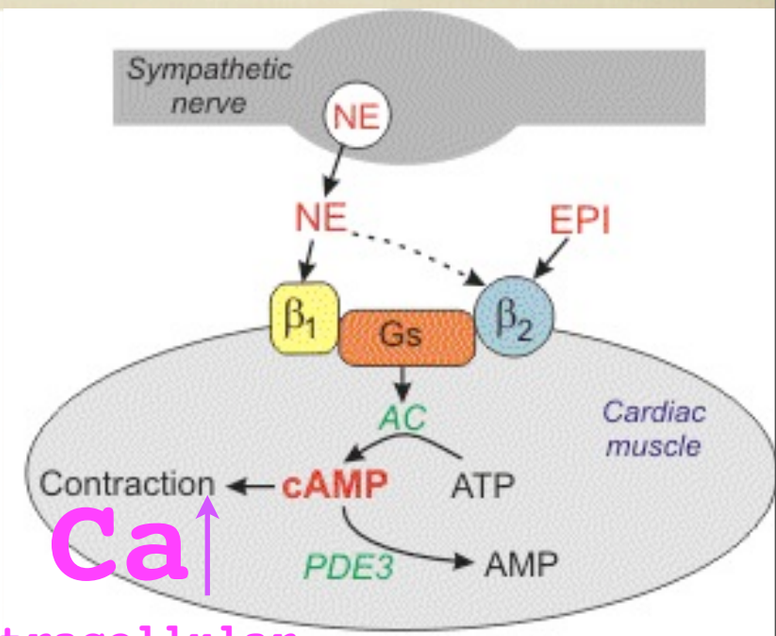




Ca↑ intracellular



MYOCARDIAL CELL



Ca↑ intracellular

Abbreviations: NE, norepinephrine; EPI, epinephrine; Gs, Gs-protein; AC, adenylyl cyclase; PDE3, cGMP-dependent phosphodiesterase (type 3)

AP depolarization(Na in) → activate L typeCa channels

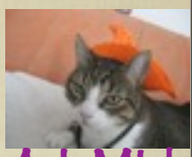
cAMP (NE, EPI) → activate receptor type Ca channels

Ca↑ intracellular

activate ryanodine receptors RyR on SR → **Ca↑ release from SR**

bind troponin C which remove tropomyosin from actin sites → **CONTRACTION** myosin heads(ATP) bind actin free sites

AP: Myocardial Relaxation



Ca^{+2} binds to TnC causing movement of troponin-tropomyosin complex exposing actin's active sites.

As soon as the active sites are exposed myosin heads bind to actin

CONTRACTION

RELAXATION

CYCLE

1) Crossbridges Form

CONTRACTION
Shortening

Working Stroke pulls the Z-lines together.

2) Myosin Head Swivels

ADP + Pi released.

3) Crossbridges Detach

ATP is taken up by myosin. Without available ATP crossbridges are unable to detach

Myosin is in a weak binding state

ATP is hydrolyzed and its energy is transfered to the cocked myosin head

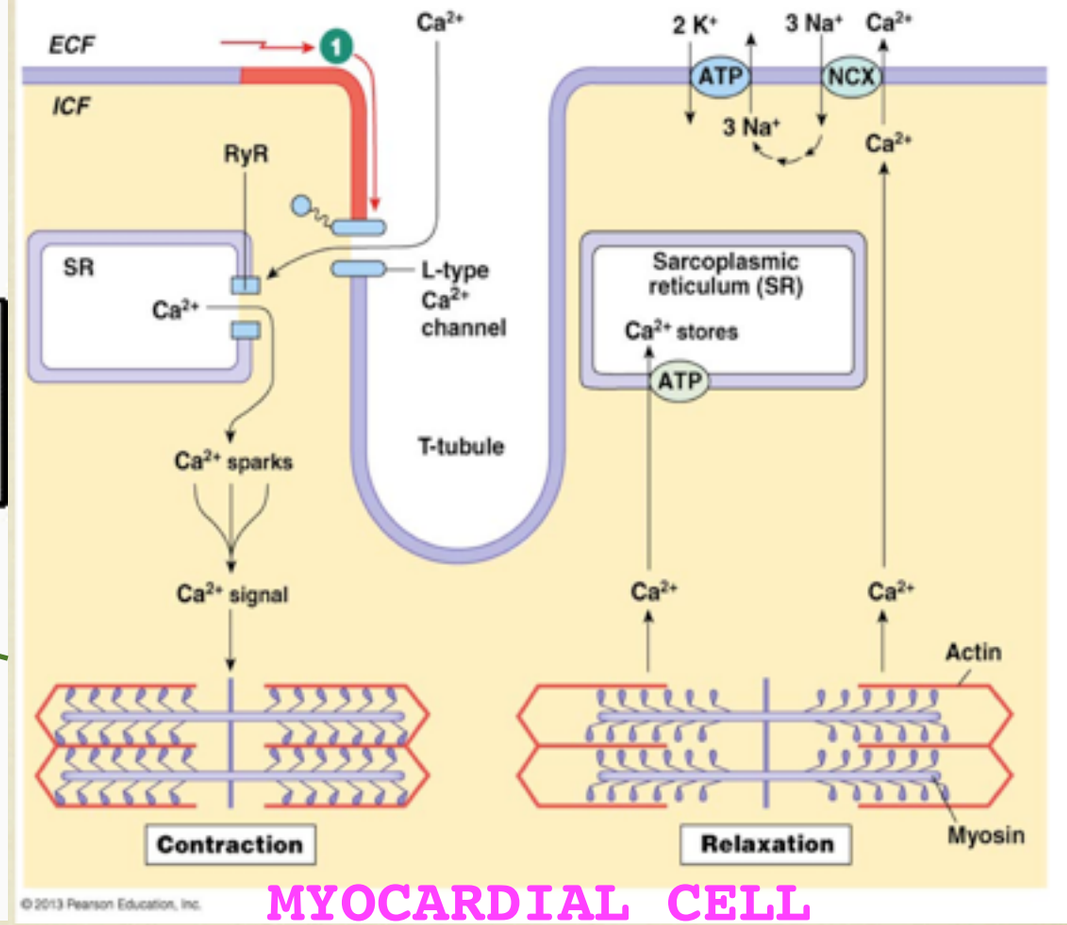
4) Cocked Myosin Head

Ca^{+2}

Myosin is in a strong binding state

(ATP is used to bend myosin head = "cocked")

RELAXATION
(under the green line)



MYOCARDIAL CELL

AP plateau (Ca in) → activate voltage gated K channels

ATP depletion → activate receptor gated K channels (ATP, Ach)

Acetylcholine (Ach) → activate receptor gated K channels (ATP, Ach)

K ↑ extracellular

Ca back to SR → due to ATPase

Ca out of the cell → due to Ca/Na pump driven by the energy from Na/K ATP pump

Ca ↓ intracellular

RELAXATION