Chapter 4.

Circulation System

Dong Jing

Physiology department of medical college of Qingdao university

Email: jingdong8@yahoo.com.cn

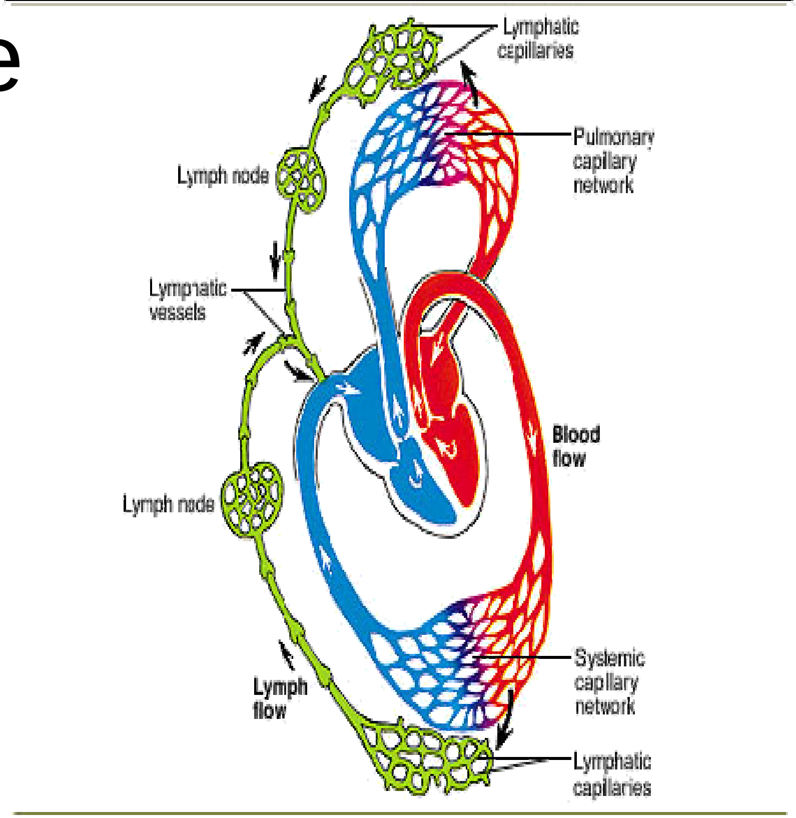
Clinical Investigation

- Jason is a 19-year-old college student who goes to the doctor complaining of chronic fatigue.
- The doctor palpates Jason's radial pulse and discovers that it is fast and weak. An echocardiogram and later coronary arterio graph reveal that he has a ventricular septal defect and mitral stenosis. His electrocardiogram (ECG) indicates that he has sinus tachycardia. When laboratory test results are returned, they indicates that Jason has a very high plasma cholesterol concentration with a high LDL/HDL ratio.
- What can be concluded from these finding, and how are they related to Jason's complaint of chronic fatigue?

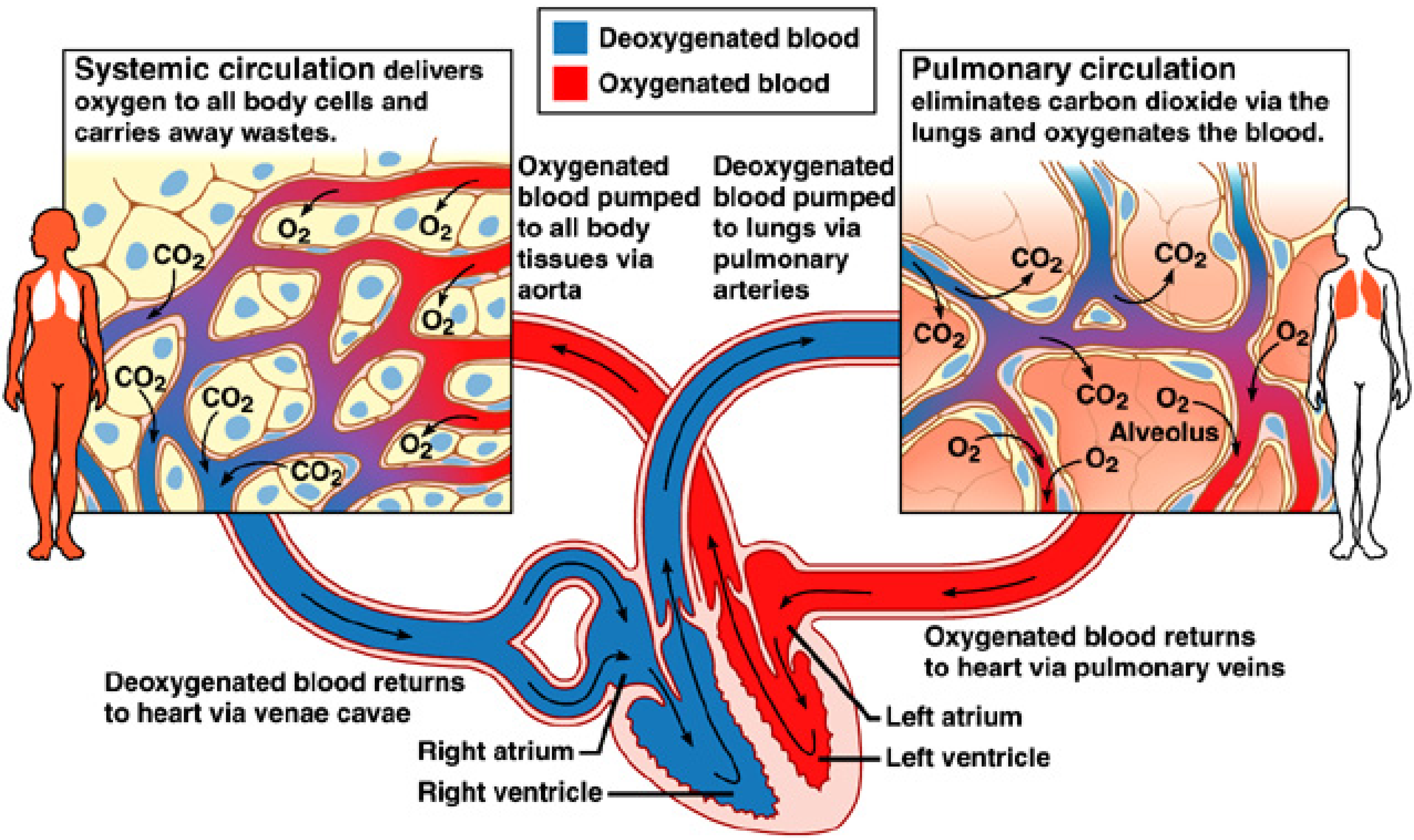
What is the basic anatomy of the heart?

- The heart comprise 2 separate pumps:
  - A right heart and left heart
    - Atrium and ventricle

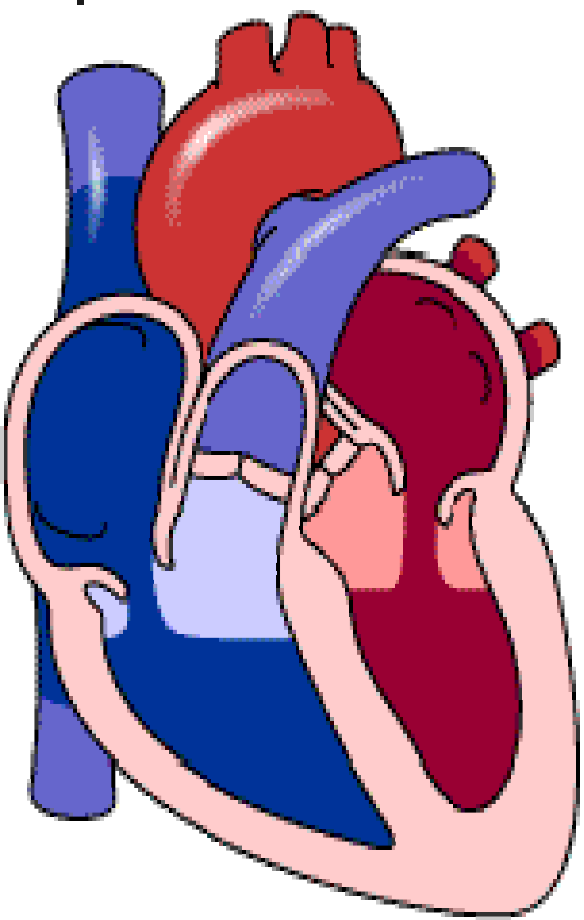
Circulatory system



Lymphatic vessels transport fluid from interstitial spaces to the bloodstream.


Deoxygenated blood
Oxygenated blood
Systemic circulation delivers oxygen to all body cells and carries away wastes.
Pulmonary circulation eliminates carbon dioxide via the lungs and oxygenates the blood.
O_2
CO_2
Oxygenated blood pumped to all body tissues via aorta
Deoxygenated blood pumped to lungs via pulmonary arteries
Alveolus
Oxygenated blood returns to heart via pulmonary veins
Deoxygenated blood returns to heart via venae cavae
Right atrium
Right ventricle
Left atrium
Left ventricle

Overview of the cardiovascular system (list the functions of circulation)



MAIN FUNCTIONS

- ✓Transport and distribute essential substances to the tissues.
- ✓Remove metabolic products.
- ✓Adjustment of oxygen and nutrient supply in different physiologic states.
- ✓Regulation of body temperature.
- ✓Humoral communication.

Chapter 4. Circulation System

- Section 1.

  Bioelectrical activity and physiological characteristics of the heart

- Section 2.

  The pump function of the heart

- Section 3.

  Vascular physiology

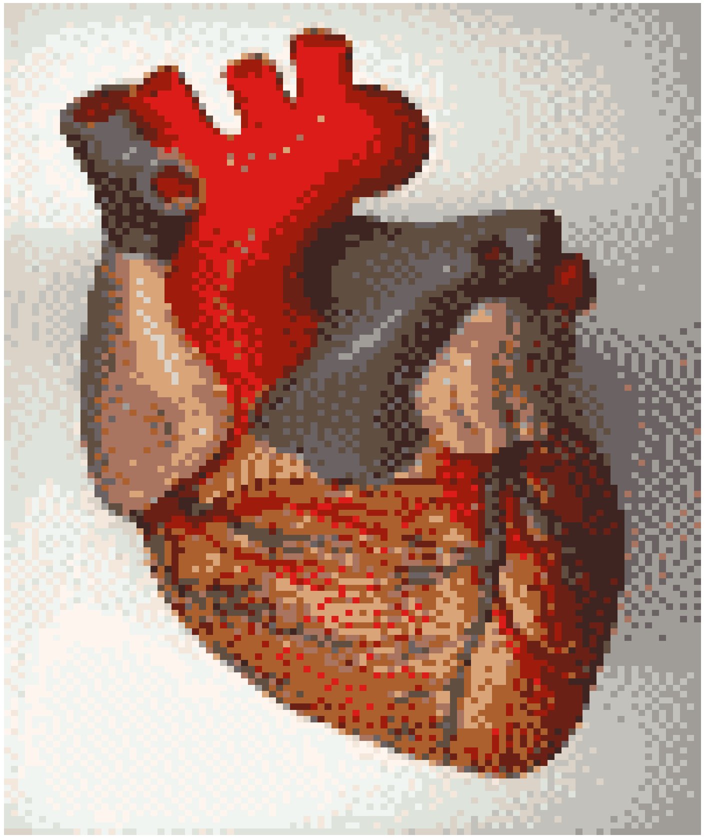
- Section 4.

  The regulation of cardiovascular activity

Section 1.

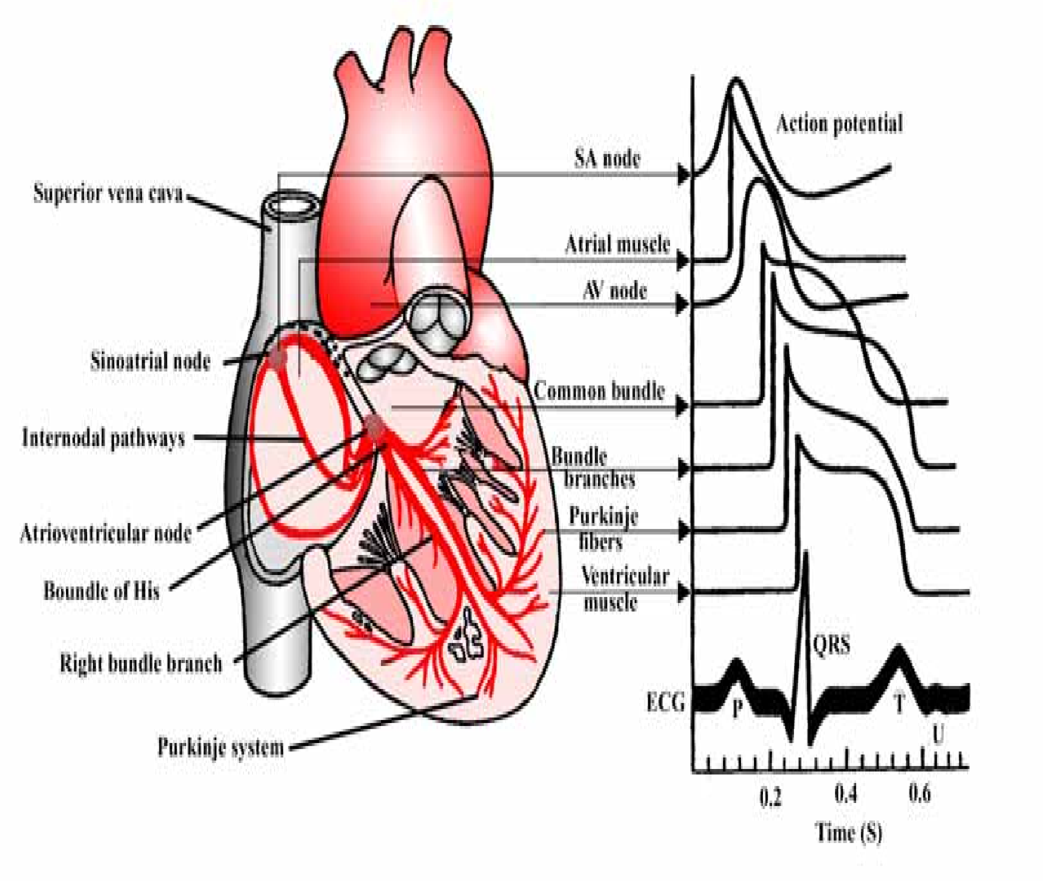
Bioelectrical activity
and physiological characteristics
of the heart

What are the major types of cardiac muscle?



- Atrial muscle
- Ventricular muscle
- Purkinje fibers, a specialized type of conductive fiber found in the wall s of the ventricles

What is responsible for the spontaneous rhythmic excitation of the heart?



- ✓ Cardiac AP starts in SA Node, propagates in an orderly fashion throughout the heart
- ✓ A wave of depolarization that sweeps over the heart from its base to its apex and from the endocardial to the epicardial surface.

The Physiological Properties of Cardiac Cells

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

Myocardial cell

working cardiac cell

Atrial and ventricular

Contractility, excitability, conductivity, no

Autorhythmicity.

Autorhythmic cell: (special conduction system):

Sinus node P cells (pacemaker cell)

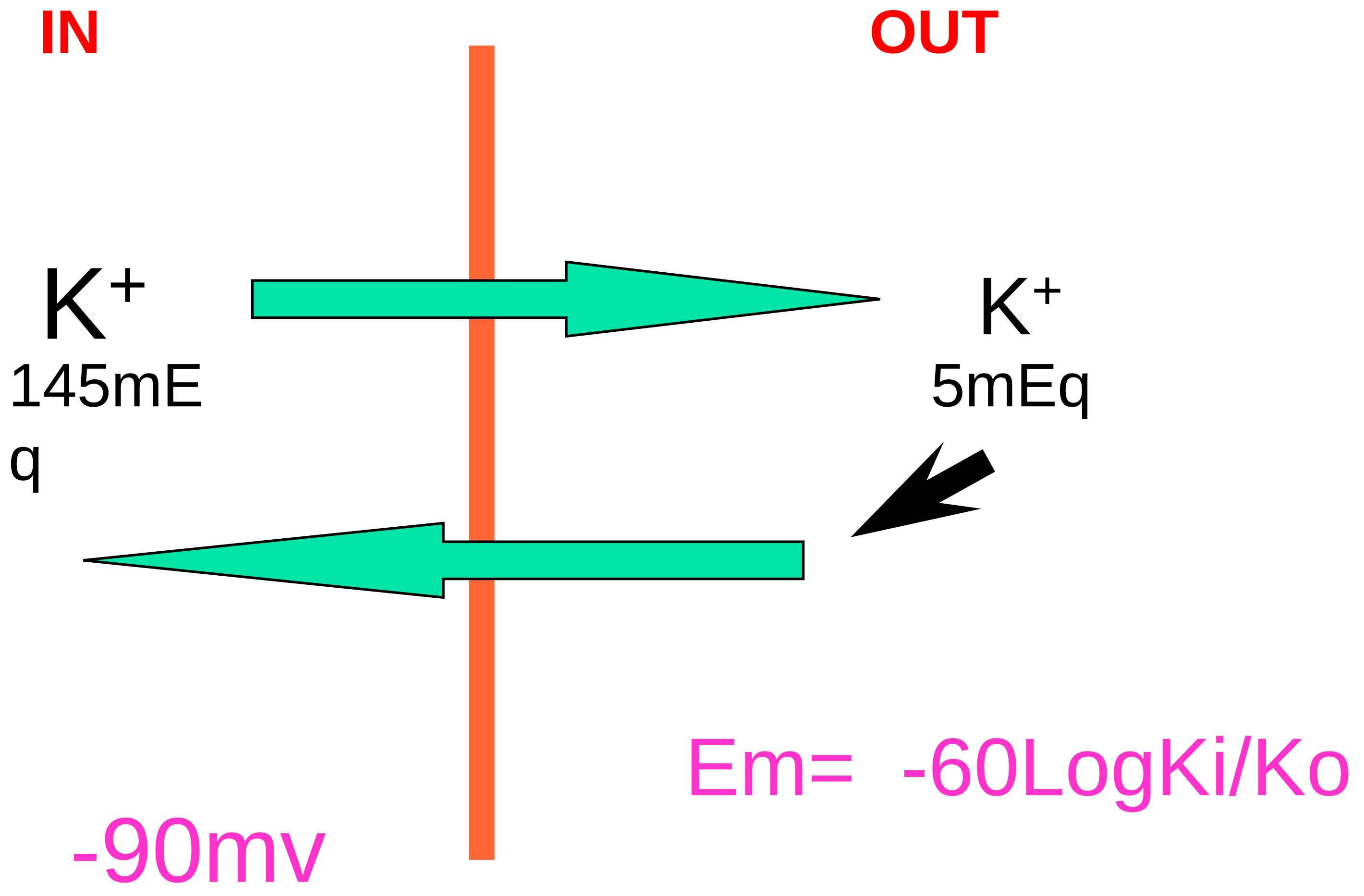
Purkinje cells (Purkinje cell)

Excitability, conductivity, autorhythmicity,

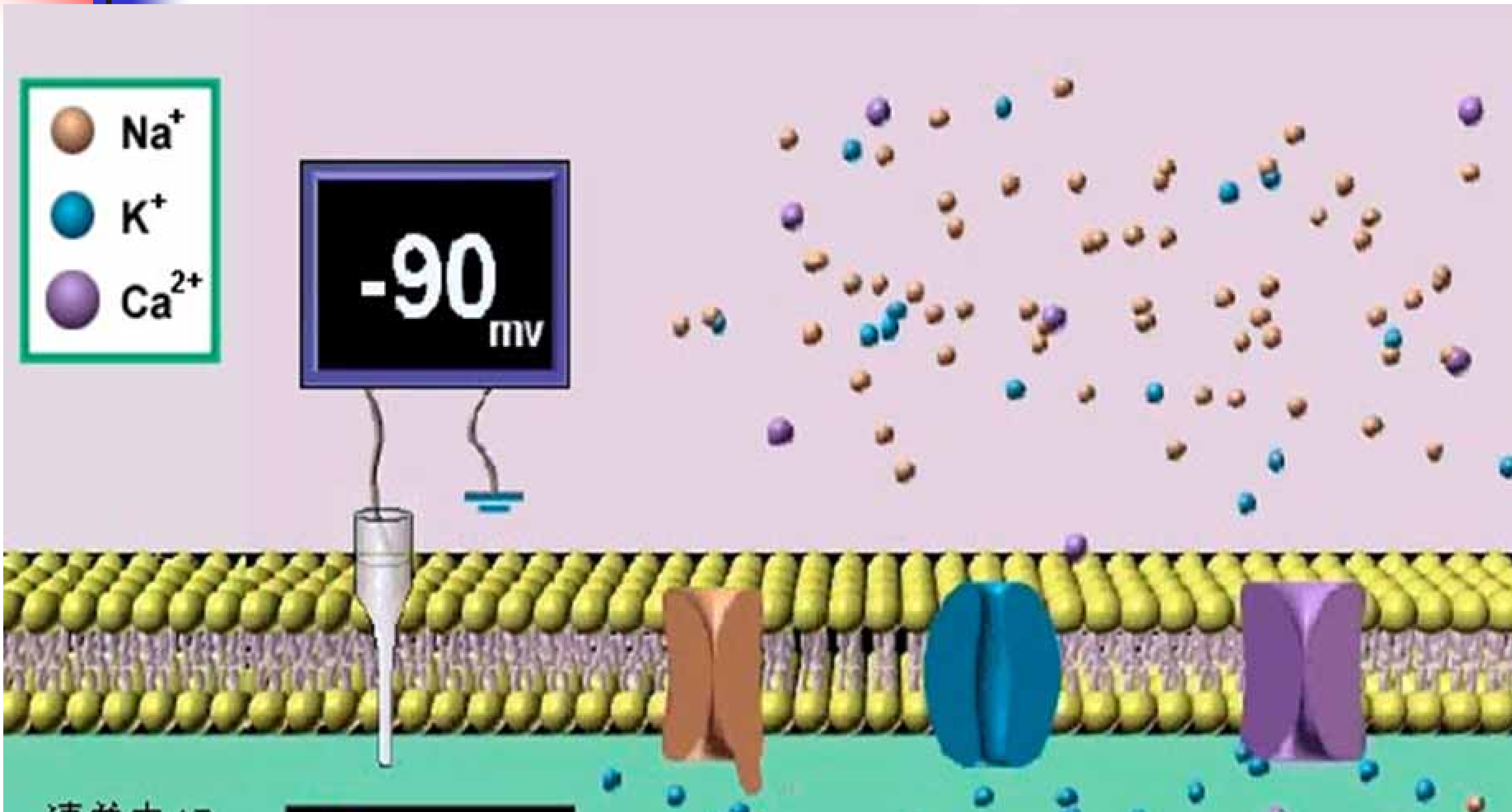
Loss of contractility

Excitability

The Resting Membrane Potential of The Cardiac Cell

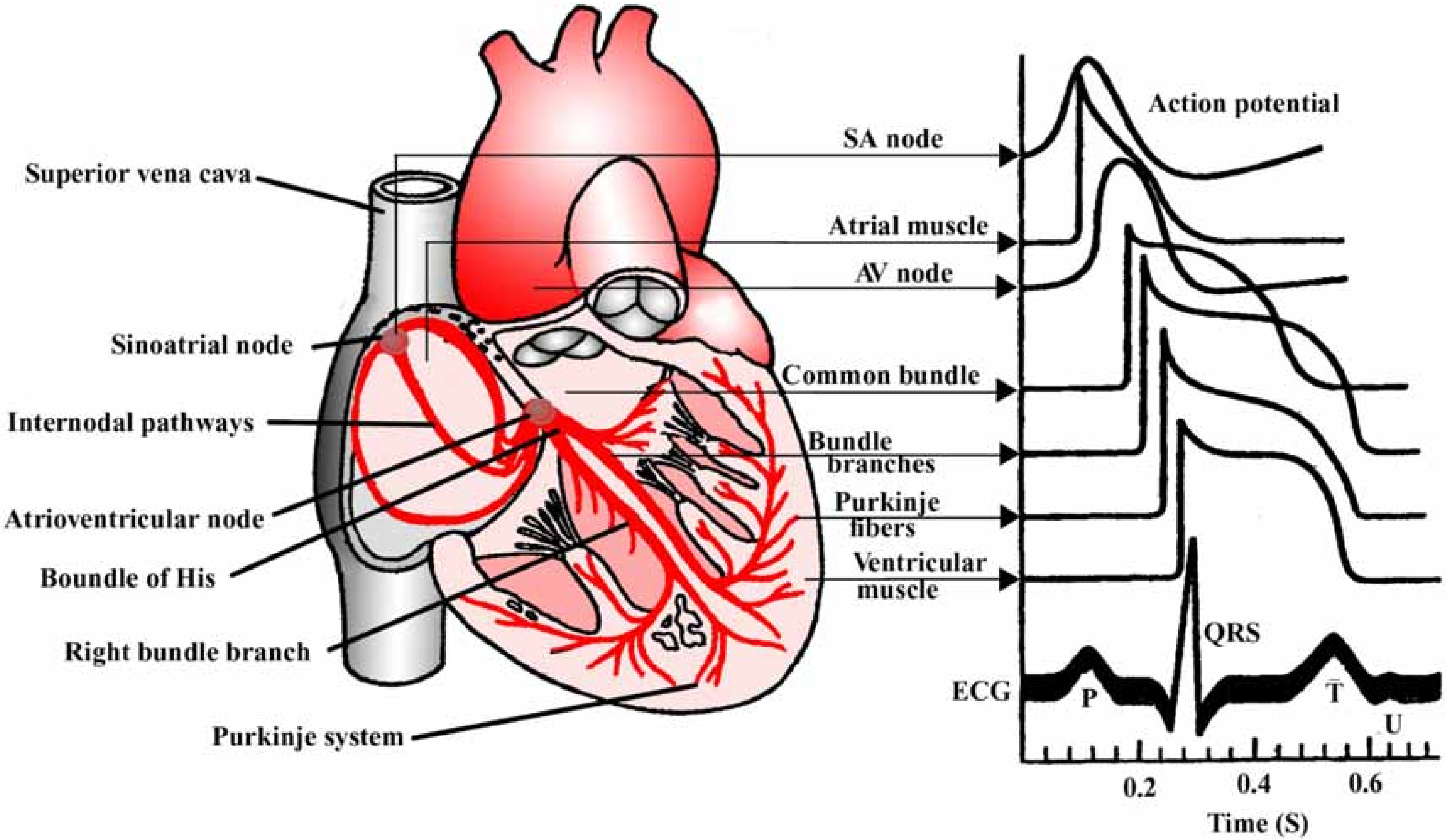


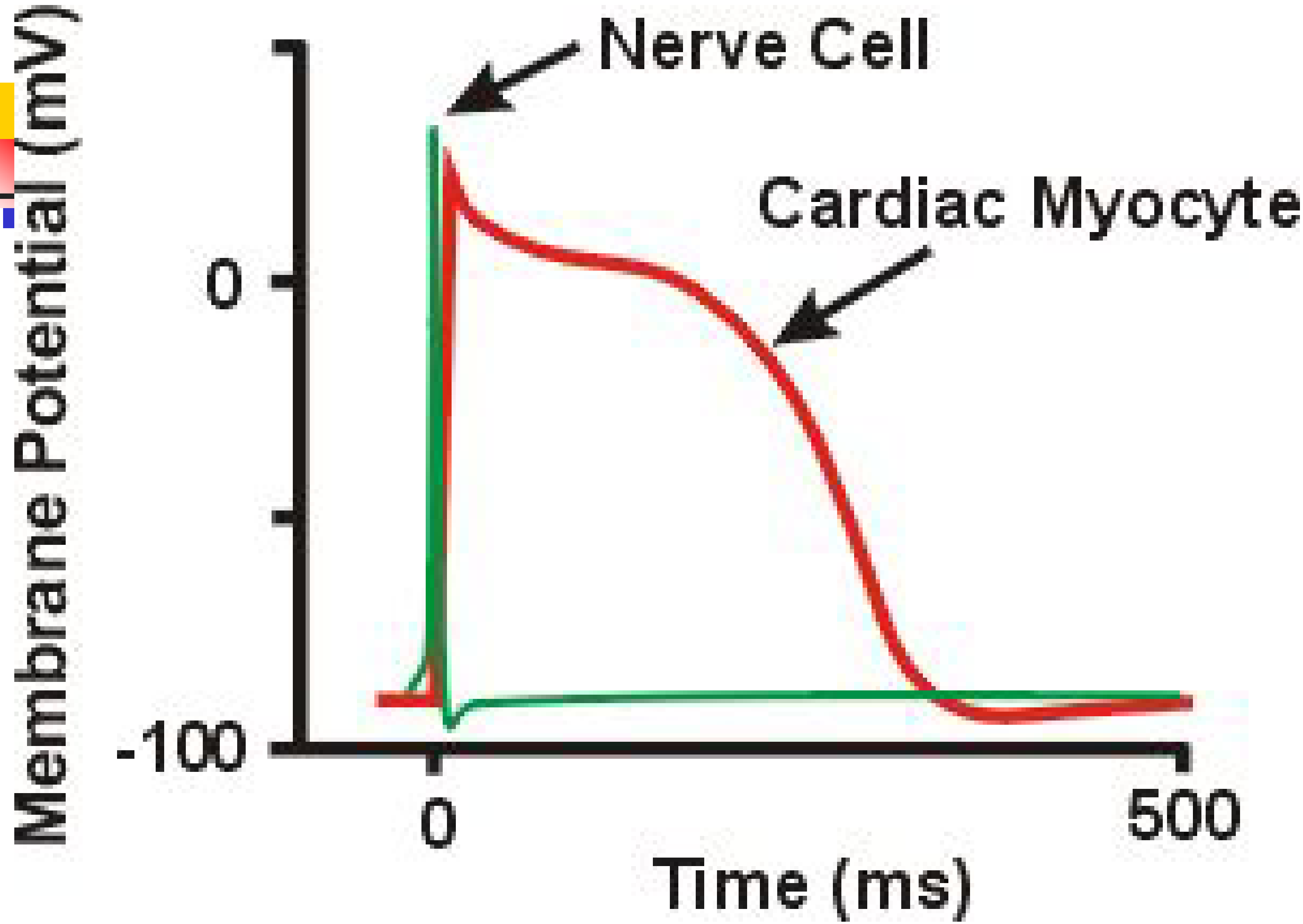
The Resting Membrane Potential of The Cardiac Cell



The Action Membrane Potential of The Cardiac Cell

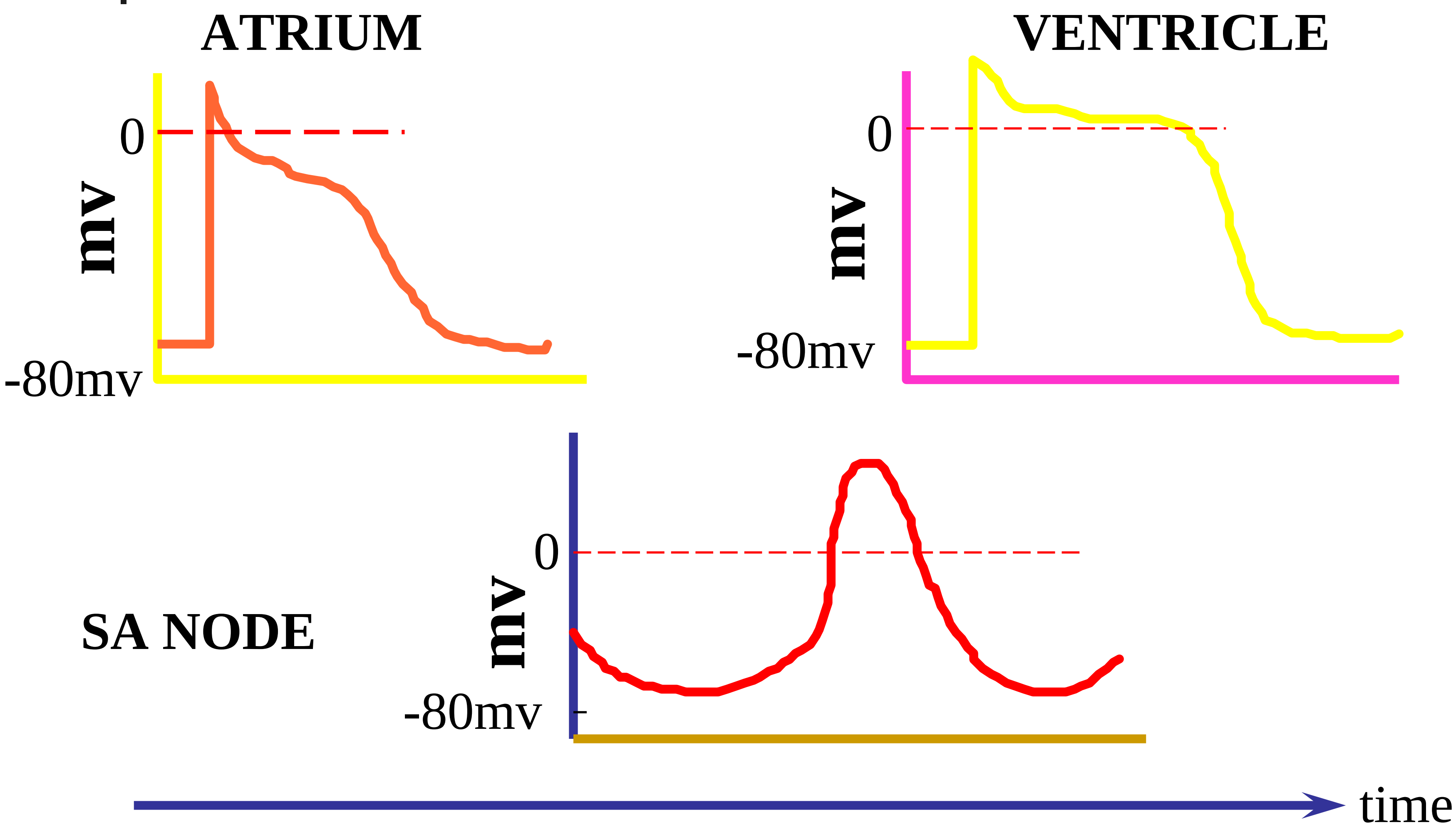
Each part of the heart has special action potential（AP）



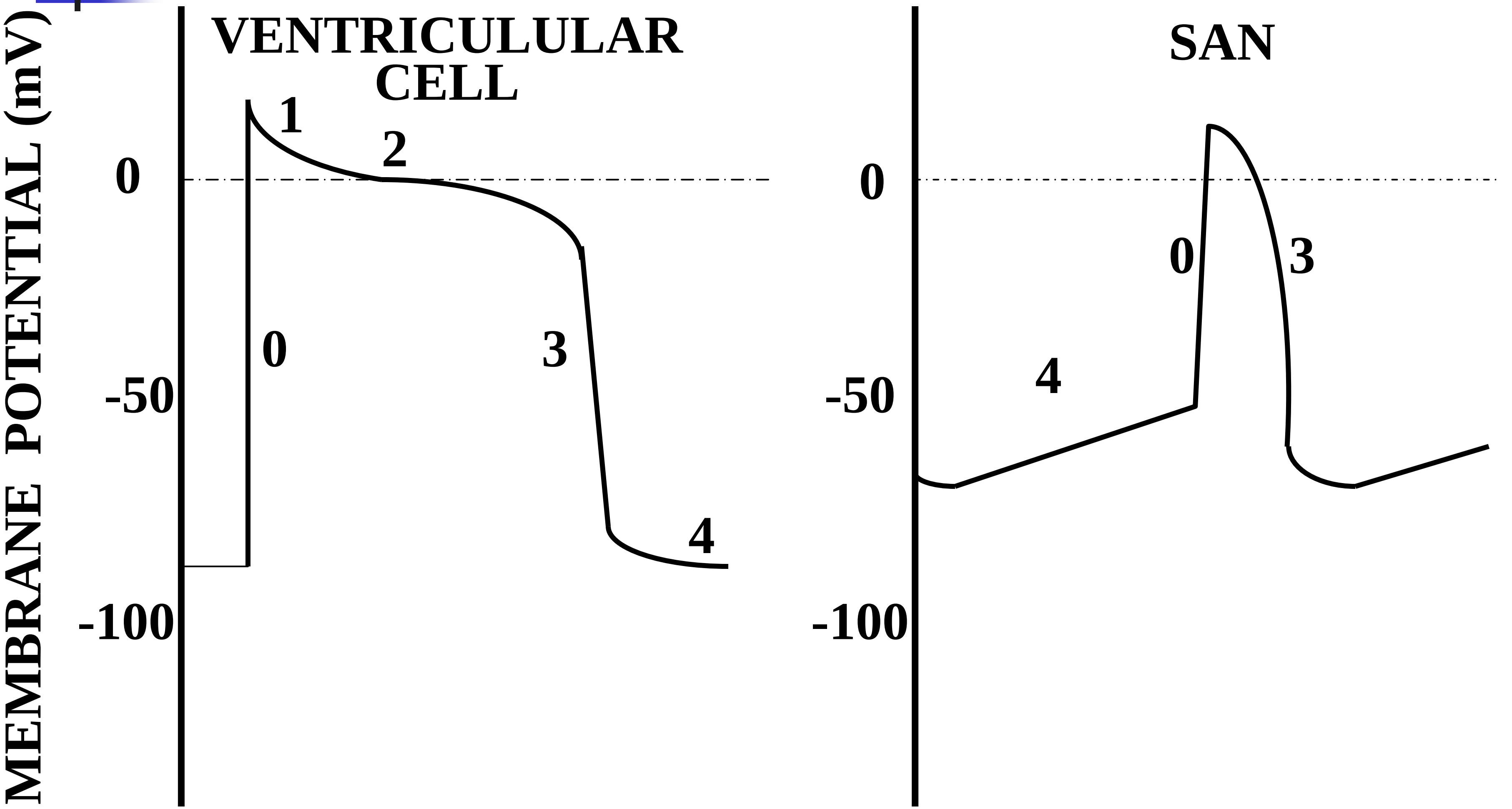


Nerve Cell
Cardiac Myocyte
Membrane Potential (mV)
0
-100
0
500
Time (ms)

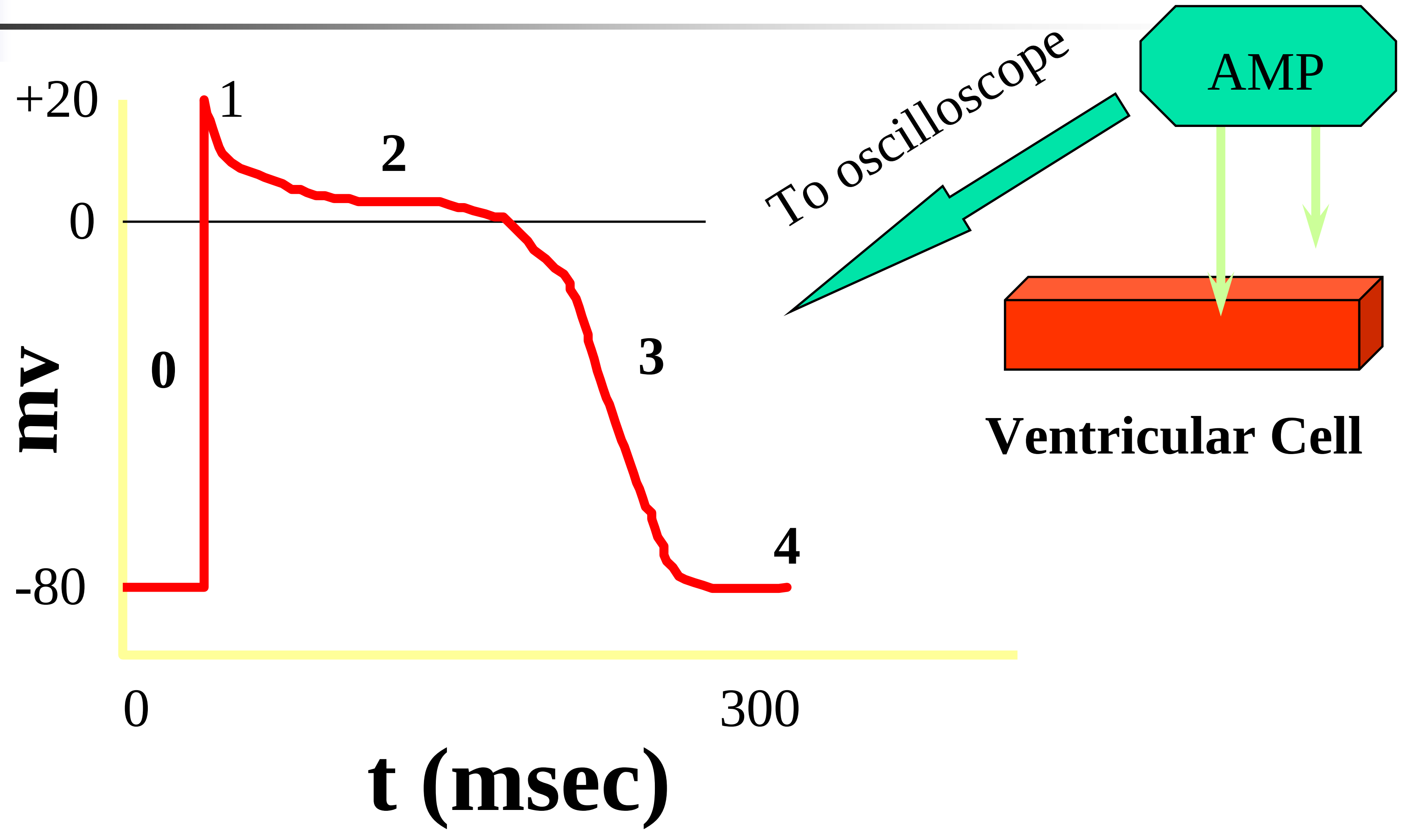
Action Potentials From Different Areas of The Heart



Action Potentials



Electrophysiology of The Fast Response Fiber

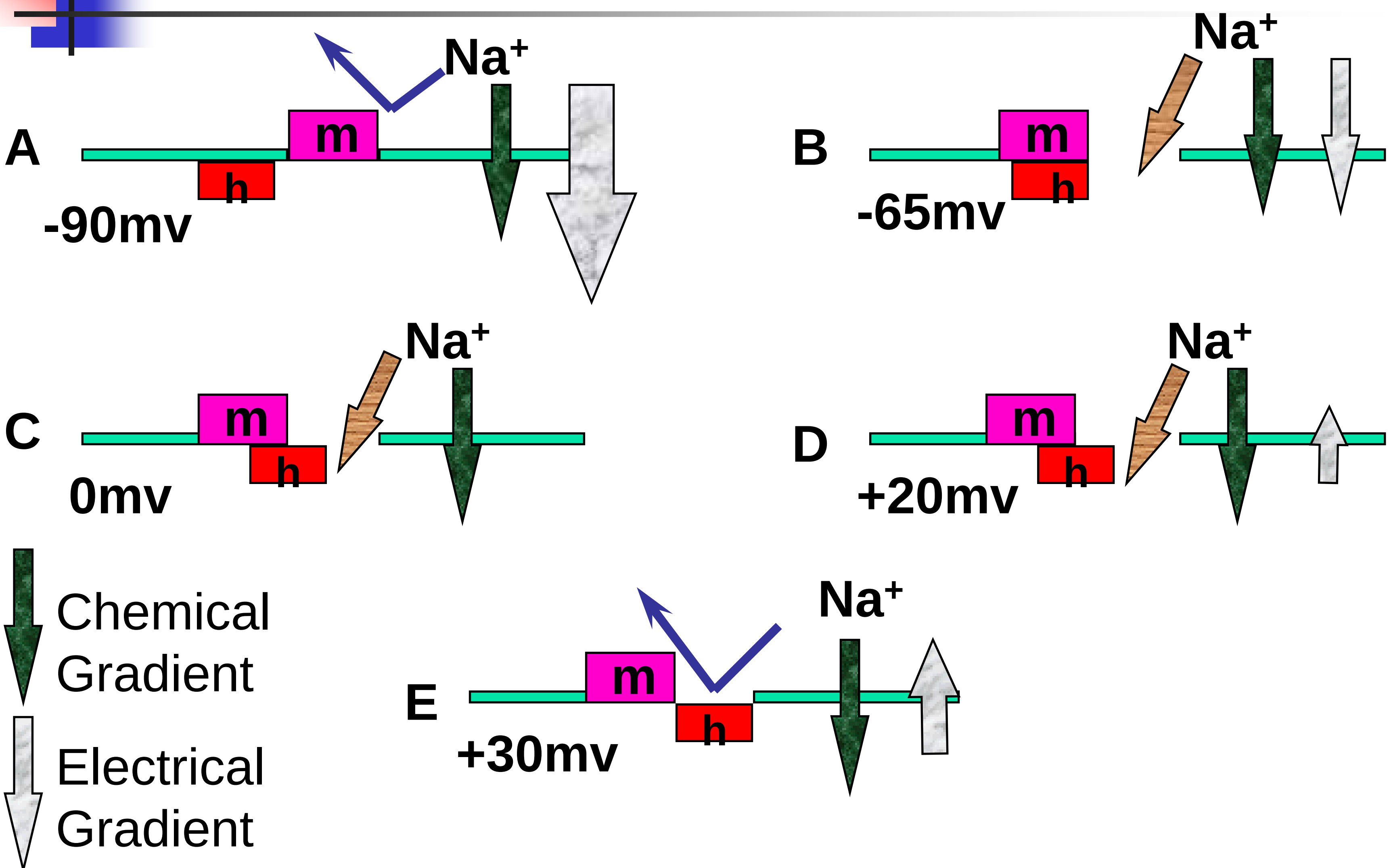


Action potential

- (1) depolarization : 0 (phase 0)
- (2) the repolarization process:

  1, 2 and 3 of (200 - 300 ms)
  - Phase 1: early rapid repolarization
  - Phase 2 : plateau
  - Phase 3 : the later rapid repolarization
- (3) resting period: (Phase4): recovery period. -90mV, active ion transport

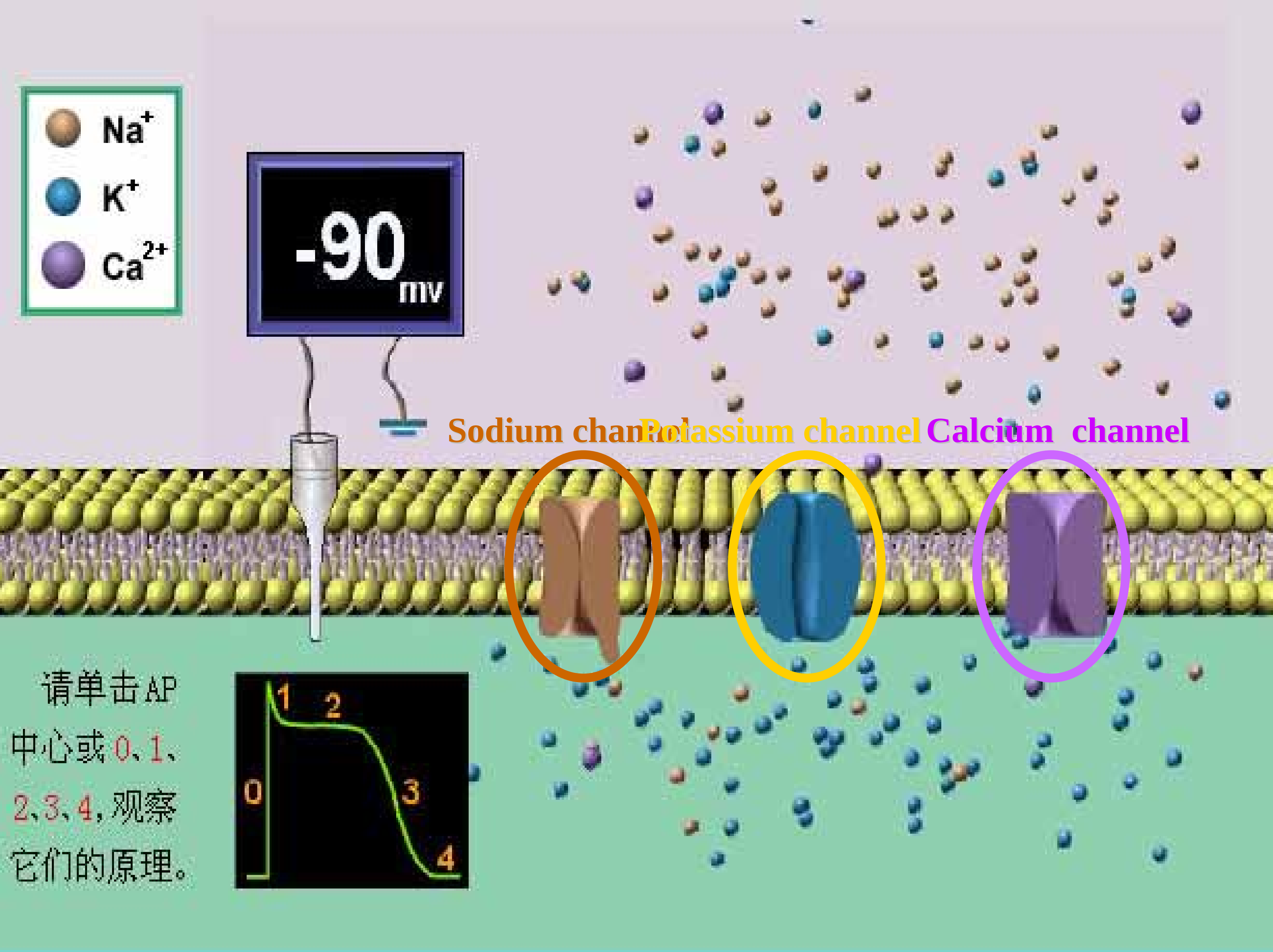
Phase 0 of Action Potential

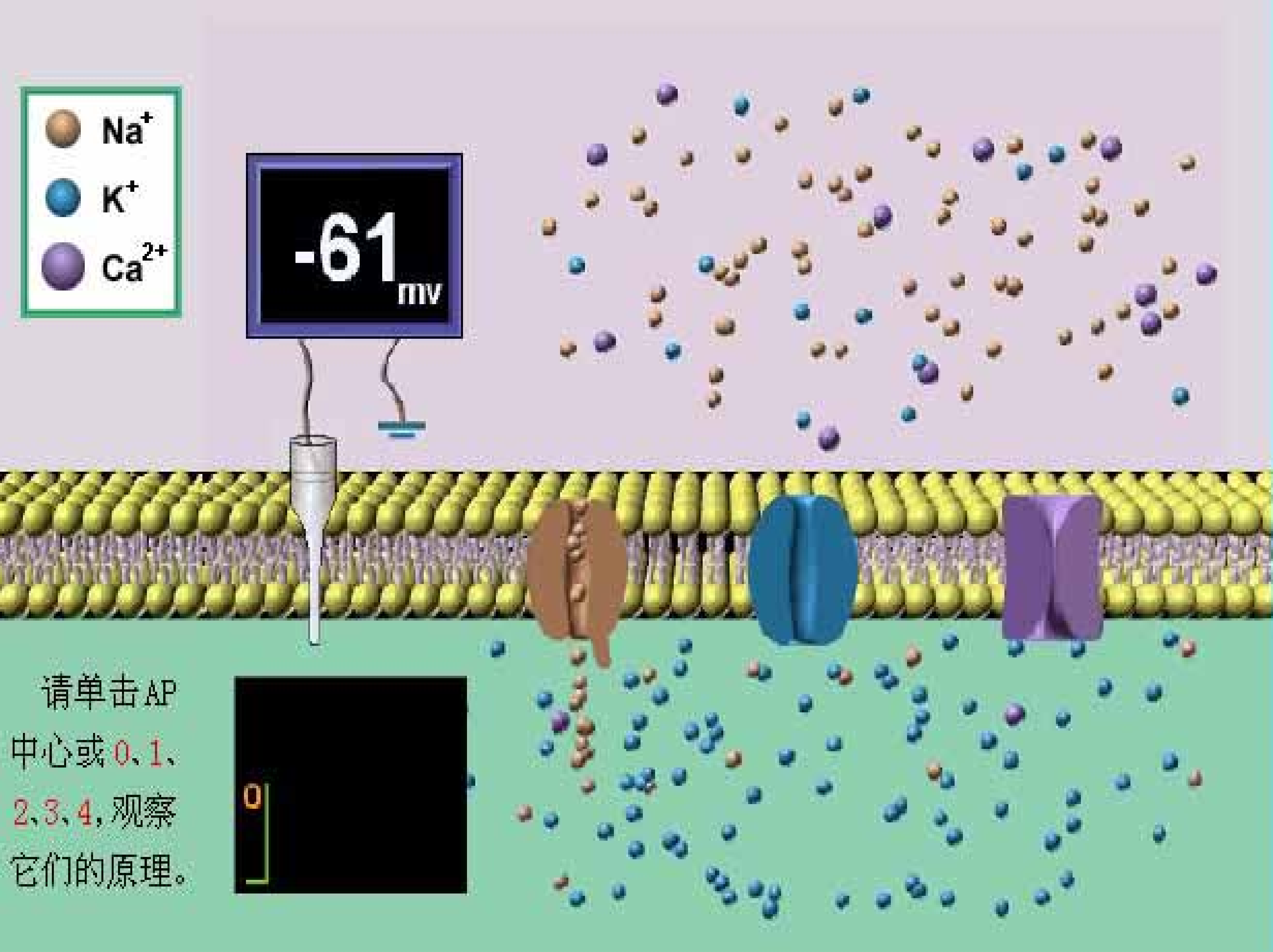


Phase 0 of Action Potential

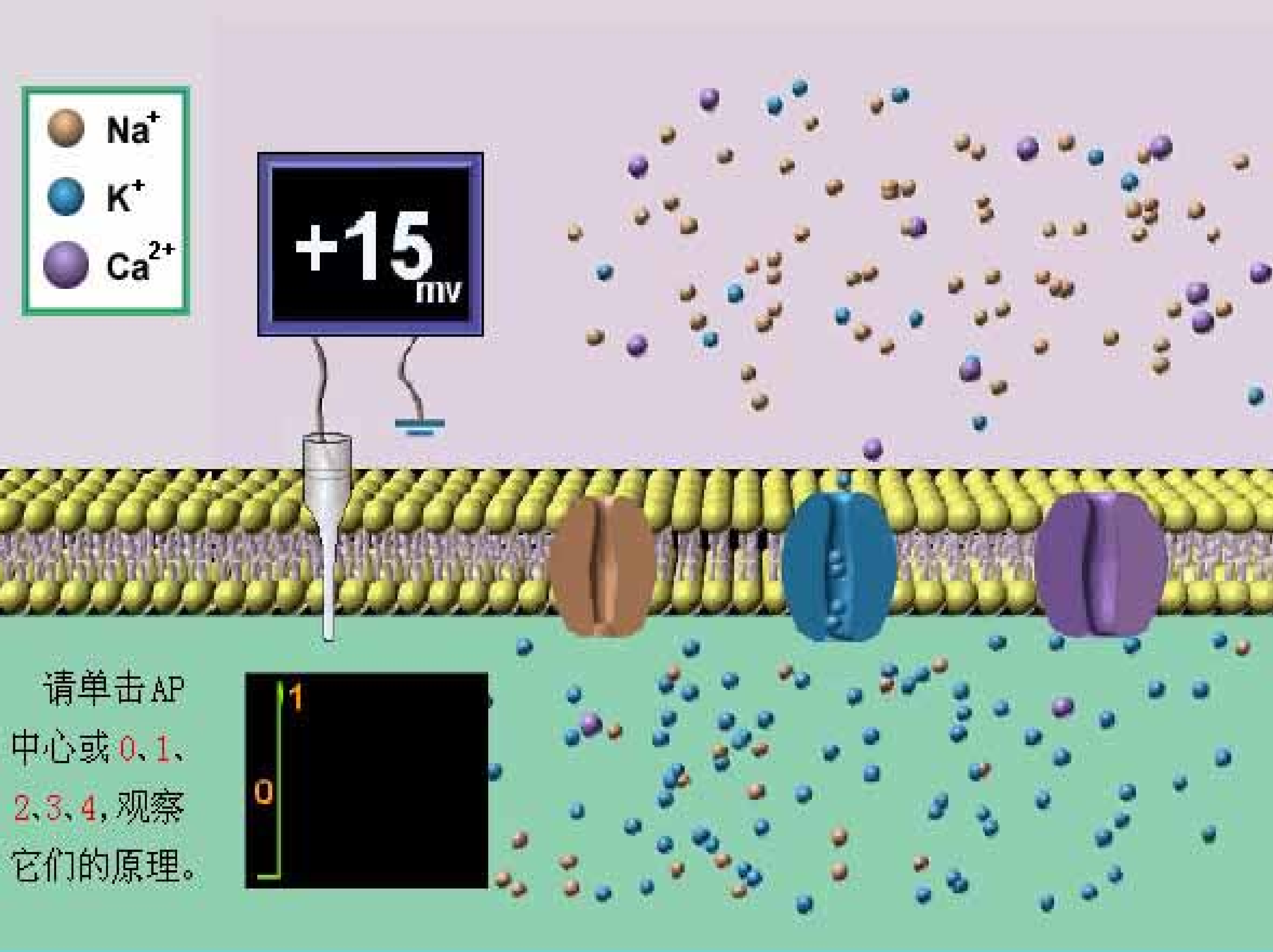
- Na + channel blockers:

  Tetrodotoxin (TTX)


Na+
K+
Ca2+
-90 mv
Sodium channel
Potassium channel
Calcium channel
请单击AP
中心或0、1、
2、3、4，观察
它们的原理。
0
1
2
3
4



Na+
K+
Ca2+
-61mv
请单击AP
中心或0、1、
2、3、4,观察
它们的原理。
0


Na+
K+
Ca2+
+15 mv
1
0
请单击AP
中心或0、1、
2、3、4，观察
它们的原理。

Phase 1

Phase 1： +20 ~ +30mv → 0mv.

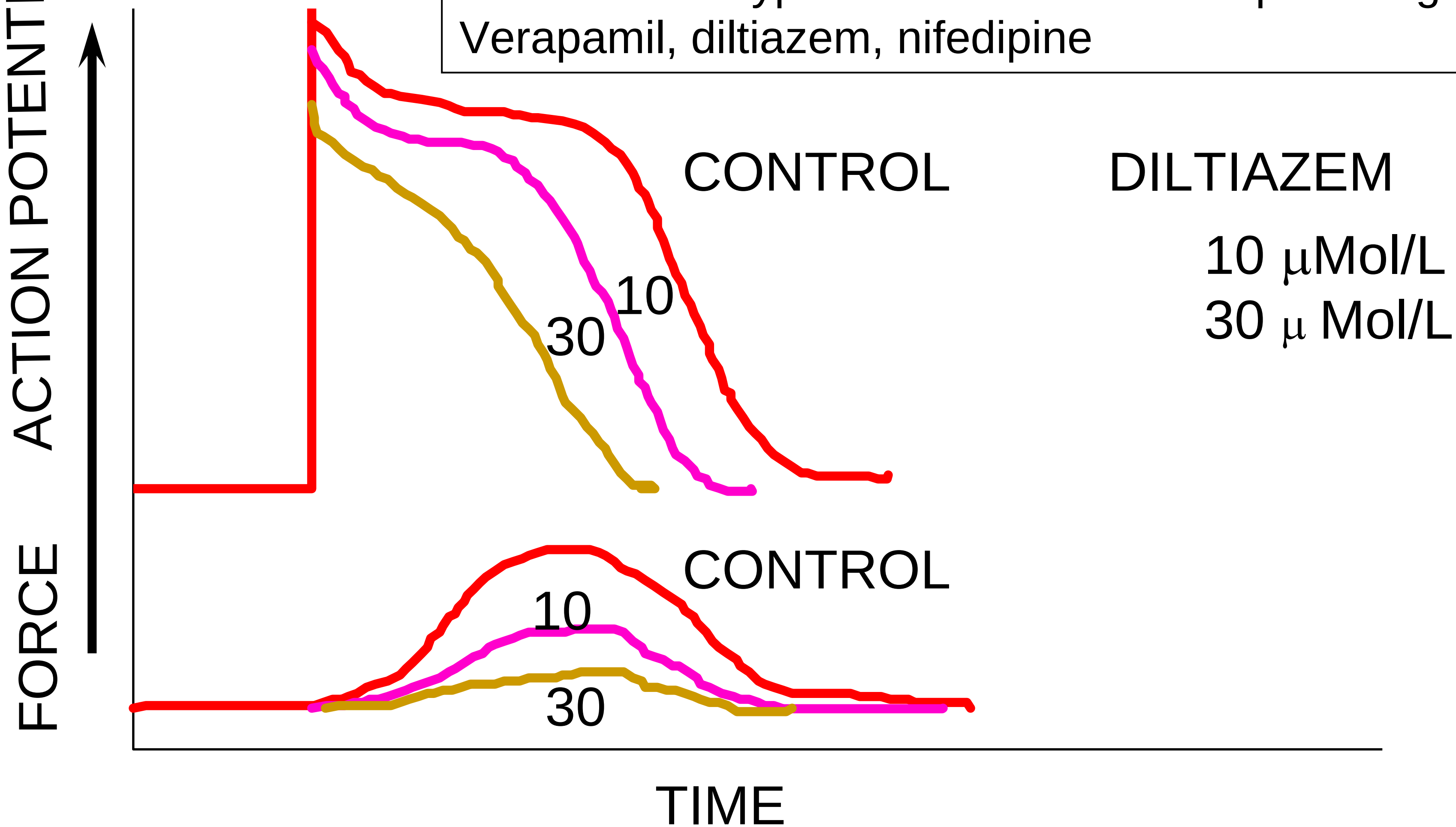
- ✓ Fast Na^+ channels close,
- ✓ transient outward K^+ channel activation (Ito) →
- ✓ K^+ rapid outflow.

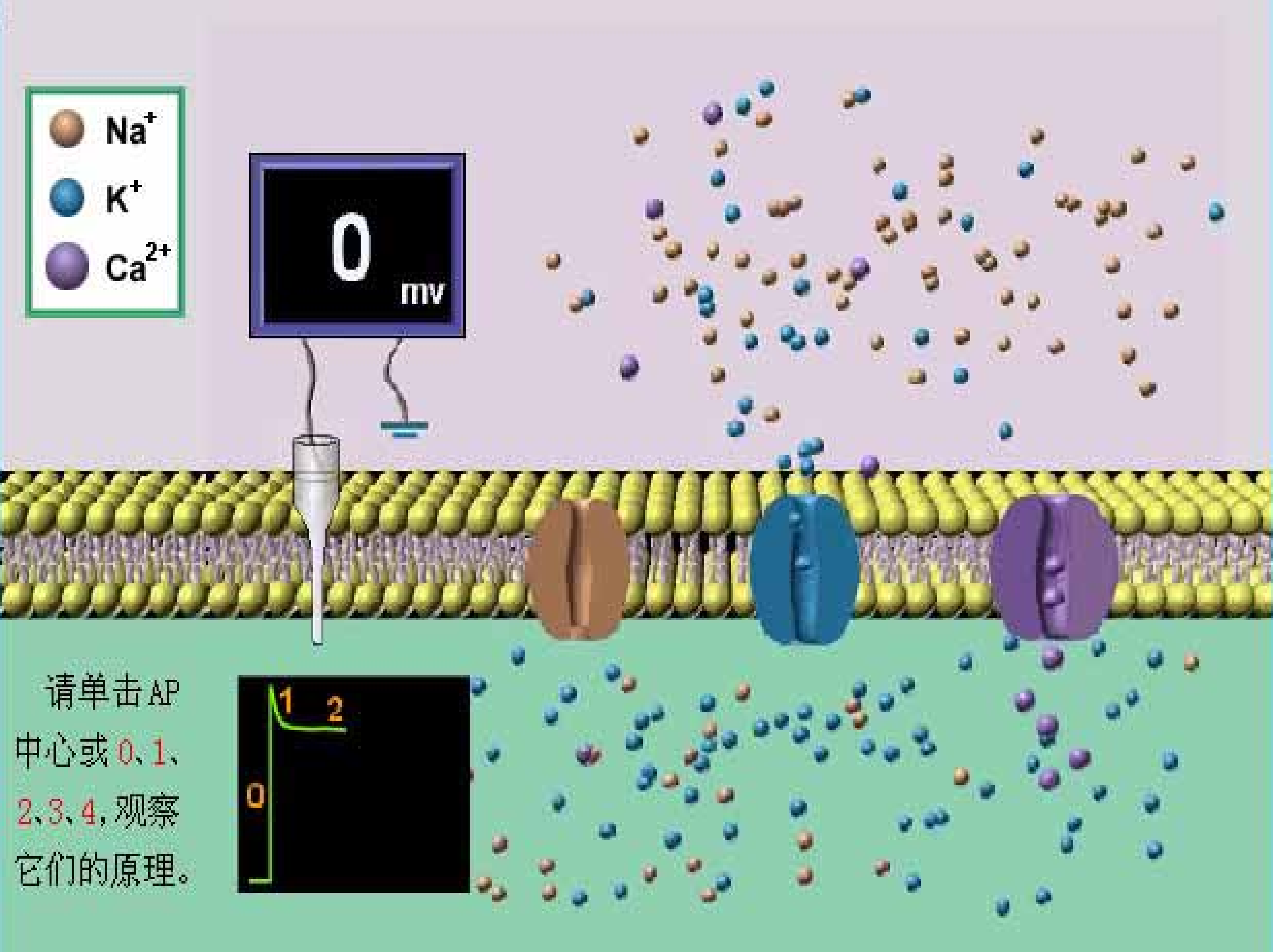
The Plateau Phase and Calcium Ions (Phase 2)

	OPEN	CLINICAL VALUE
L Ca^{++} CHANNELS	+10MV	Ca^{++} BLOCKERS
T Ca^{++} CHANNELS	-20MV	NO (physiological)

Ca^{++} Channel Blockers And The Cardiac Cell Action

Blockers of L-type Ca^{2+} channels–therapeutic agents:
Verapamil, diltiazem, nifedipine

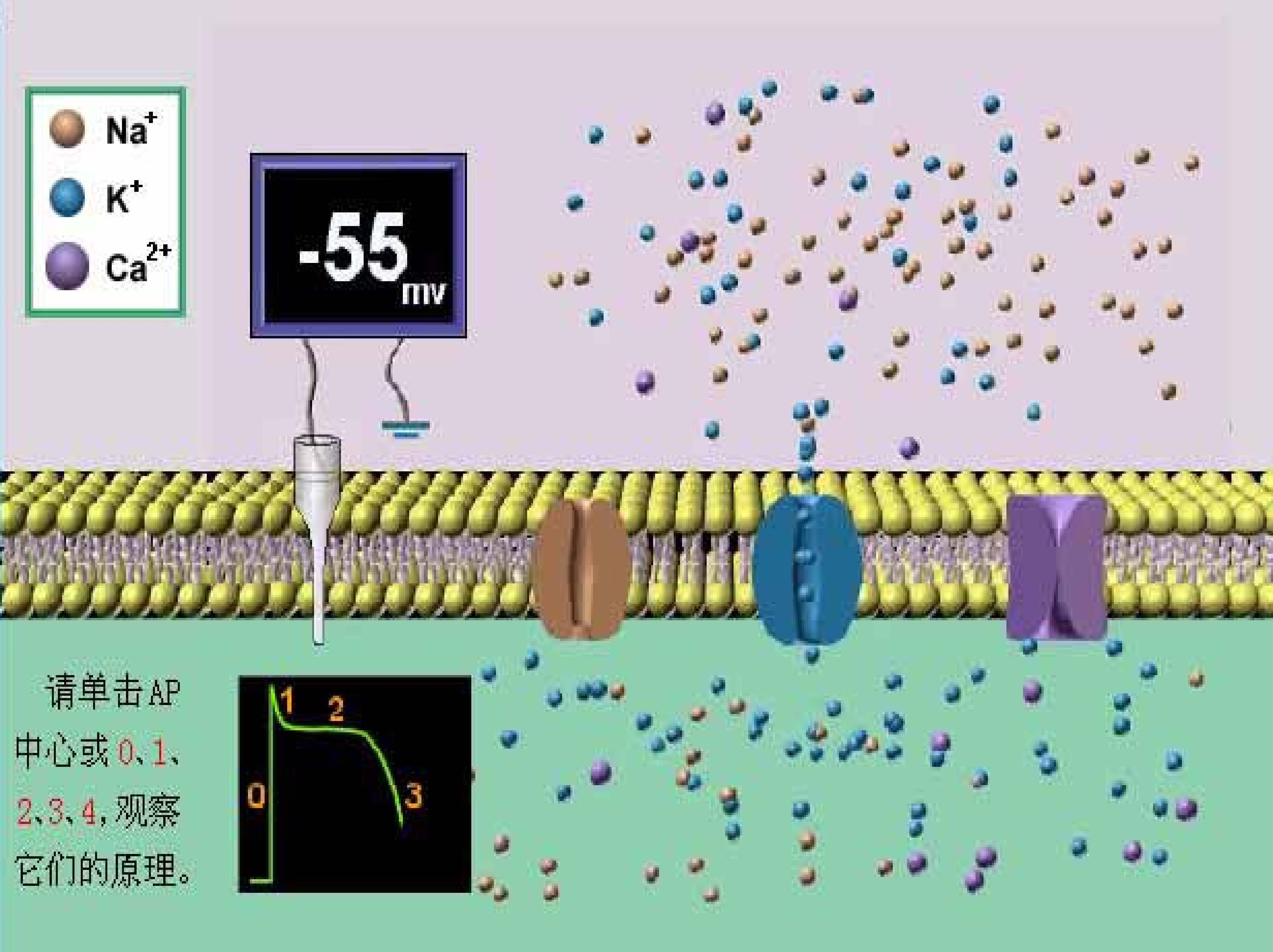



Na+
K+
Ca2+
0
mv
请单击AP
中心或0、1、
2、3、4，观察
它们的原理。
1
2
0

Phase 3

Phase 3: 0mV→-90mV。

- ✓ Late rapid repolarization
  - ✓ Is due to closure of the calcium channels and potassium efflux through various types of potassium channel.

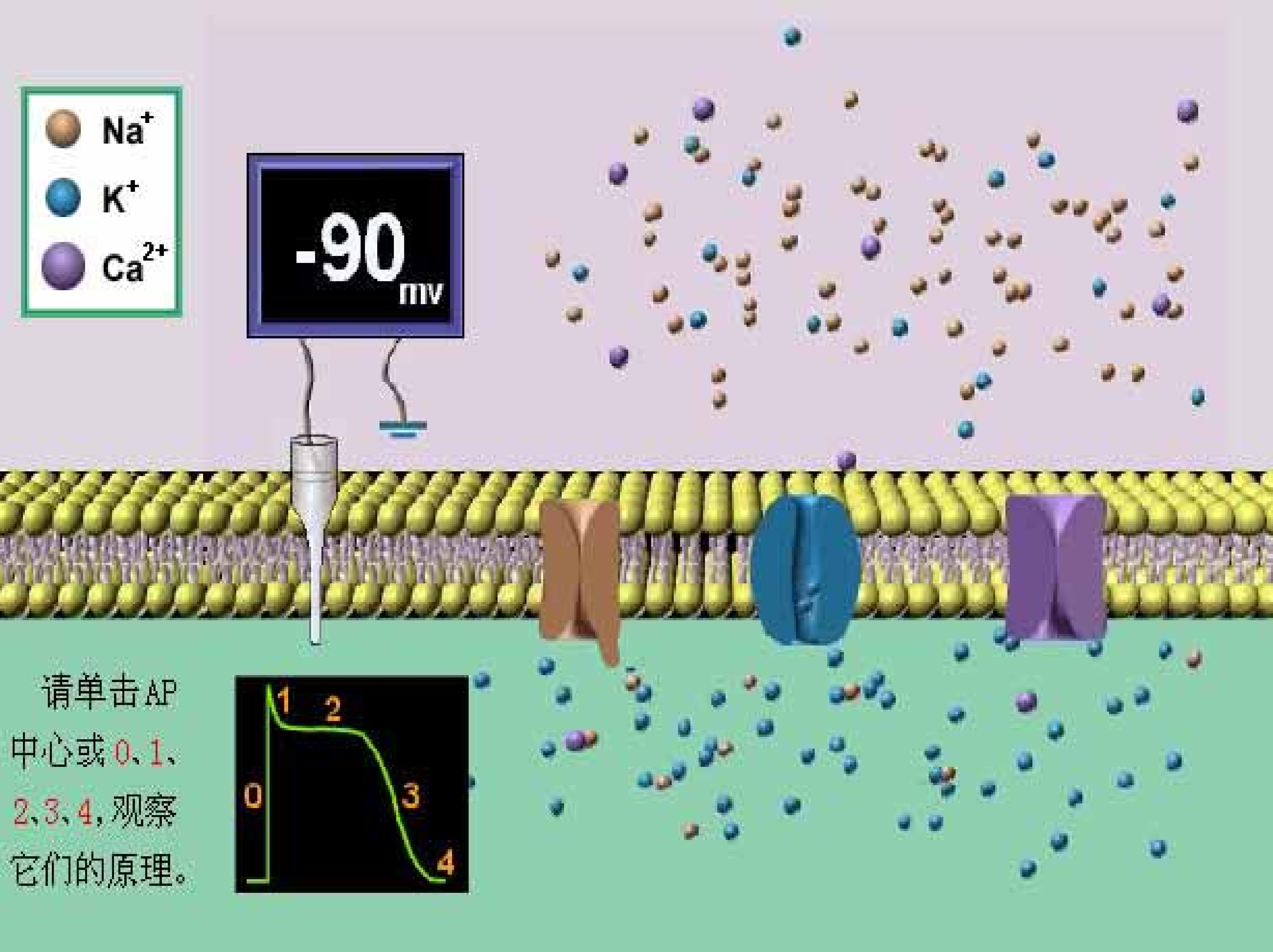

Na+
K+
Ca2+
-55 mv
1
2
0
3
请单击AP中心或0、1、2、3、4，观察它们的原理。

Phase 4

Active ion transport:

Na^+-K^+ pum

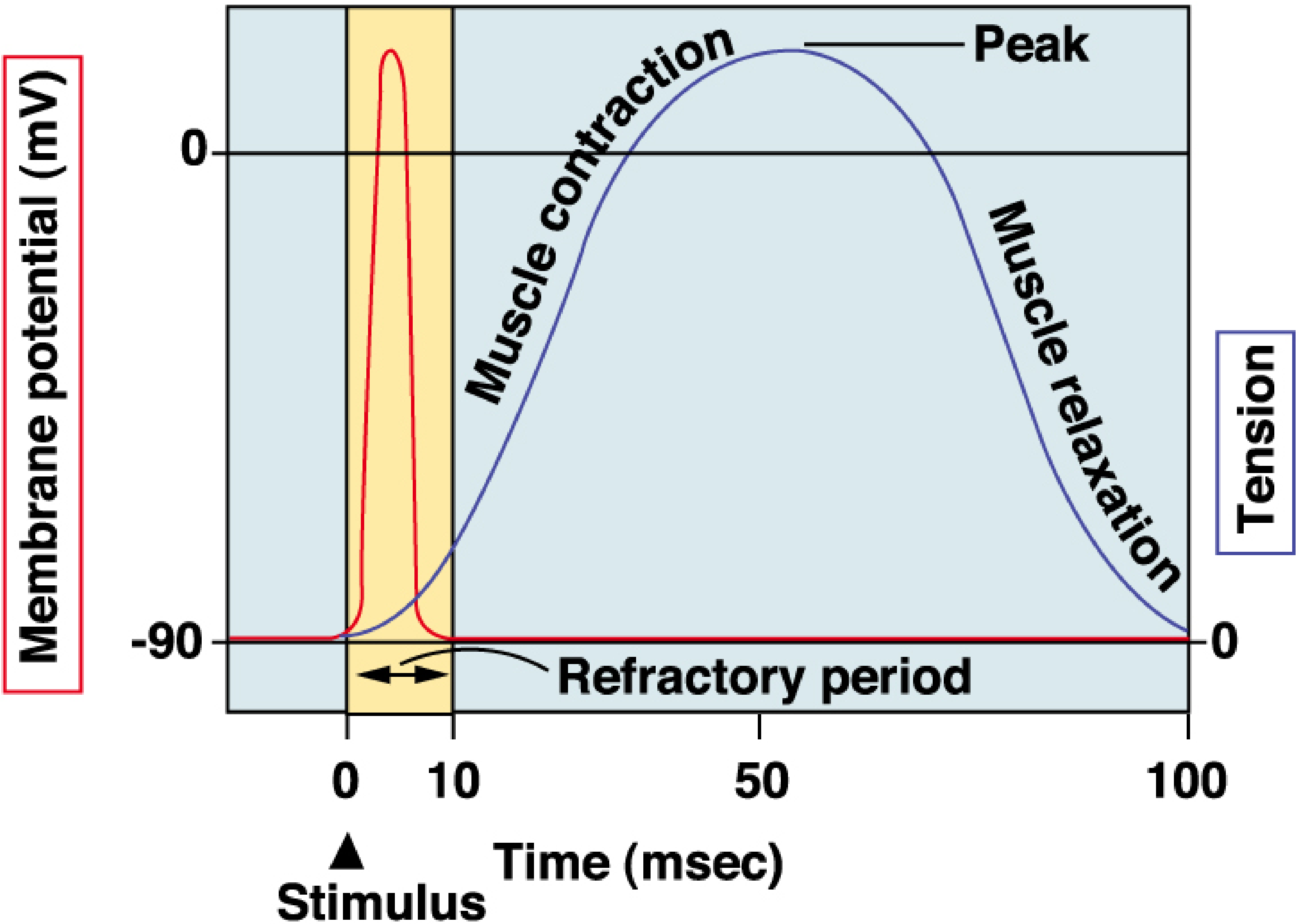
Na^+ - Ca^{2+} exchange

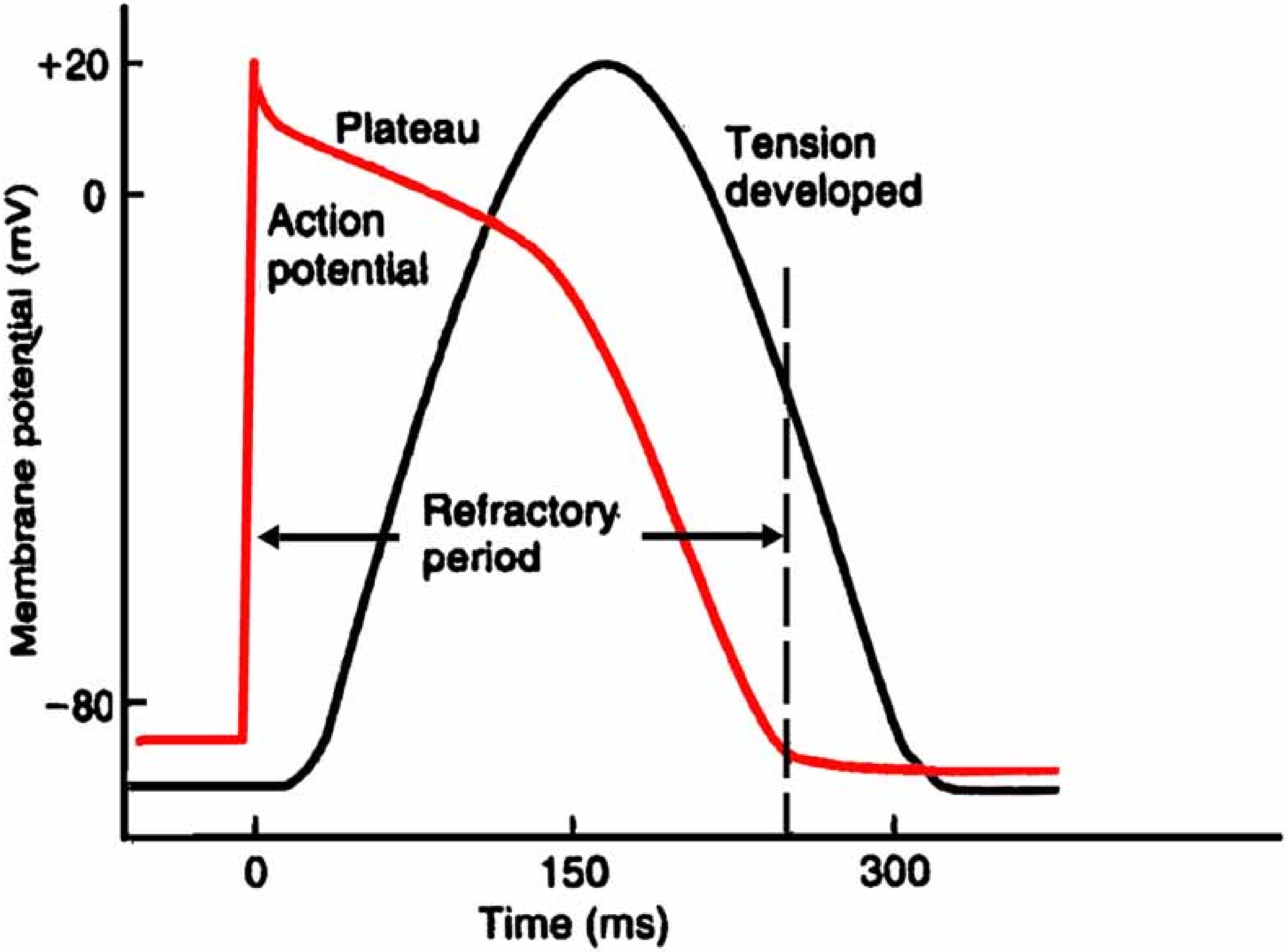

Na+
K+
Ca2+
-90 mv
1
2
0
3
4
请单击AP中心或0、1、2、3、4，观察它们的原理。

1. Excitability: Refractory Period

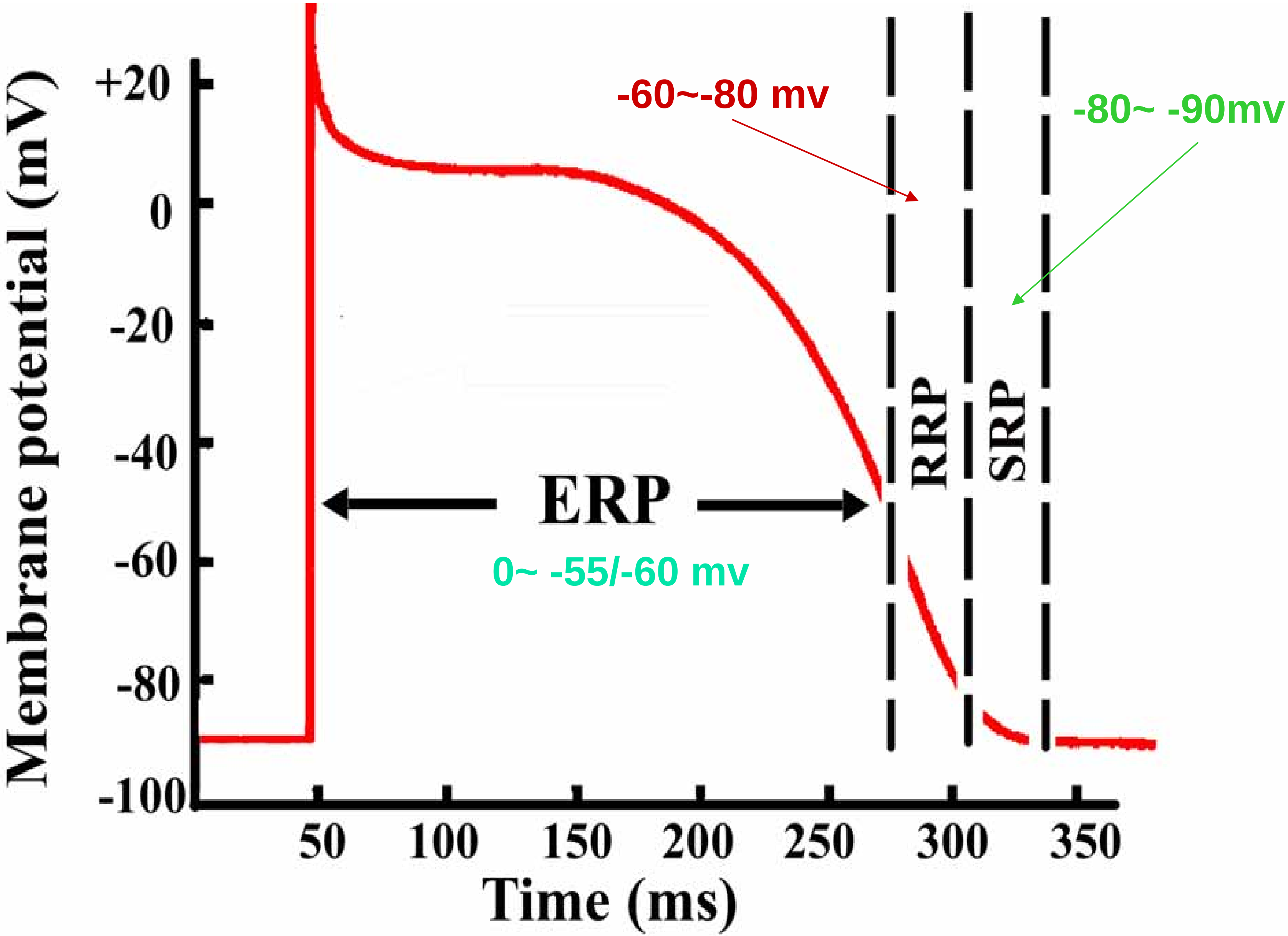
- Absolute refractory period: the muscle cannot be stimulated again (phase 0~ -55 mv, I_{Na} inactivated), effective refractory period: 0~ -60 mv
- Relative refractory period: -60 ~ -80 mv
- Supernormal period: -80 ~ -90mv,cell is easier to stimulate, g_k is still a bit lower than normal; AP is smaller than normal because not all Na channels from Phase 0 have had to ‘reset’.
- Exrasystole/premature systole, compensatory pause

Skeletal muscle fast-twitch fiber



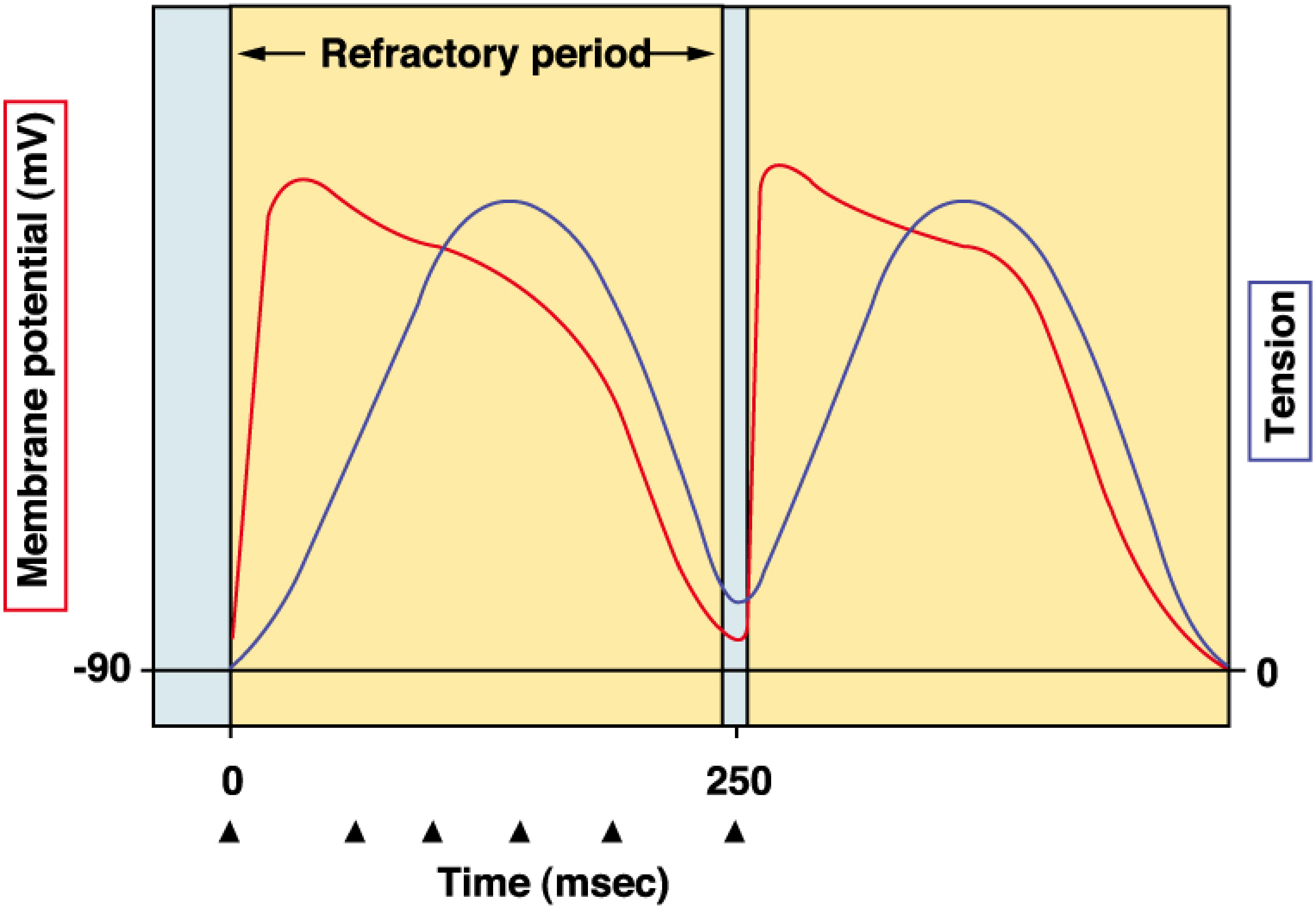


+20
0
−80
Membrane potential (mV)
Plateau
Action potential
Tension developed
Refractory period
0
150
300
Time (ms)



-60~-80 mv
-80~ -90mv
ERP
0~ -55/-60 mv
RRP
SRP
Membrane potential (mV)
+20
0
-20
-40
-60
-80
-100
50
100
150
200
250
300
350
Time (ms)

Long refractory period in a cardiac muscle prevents tetanus.



Prevention of tetanus in the heart is important because cardiac muscles must relax between contractions so the ventricle can fill with blood

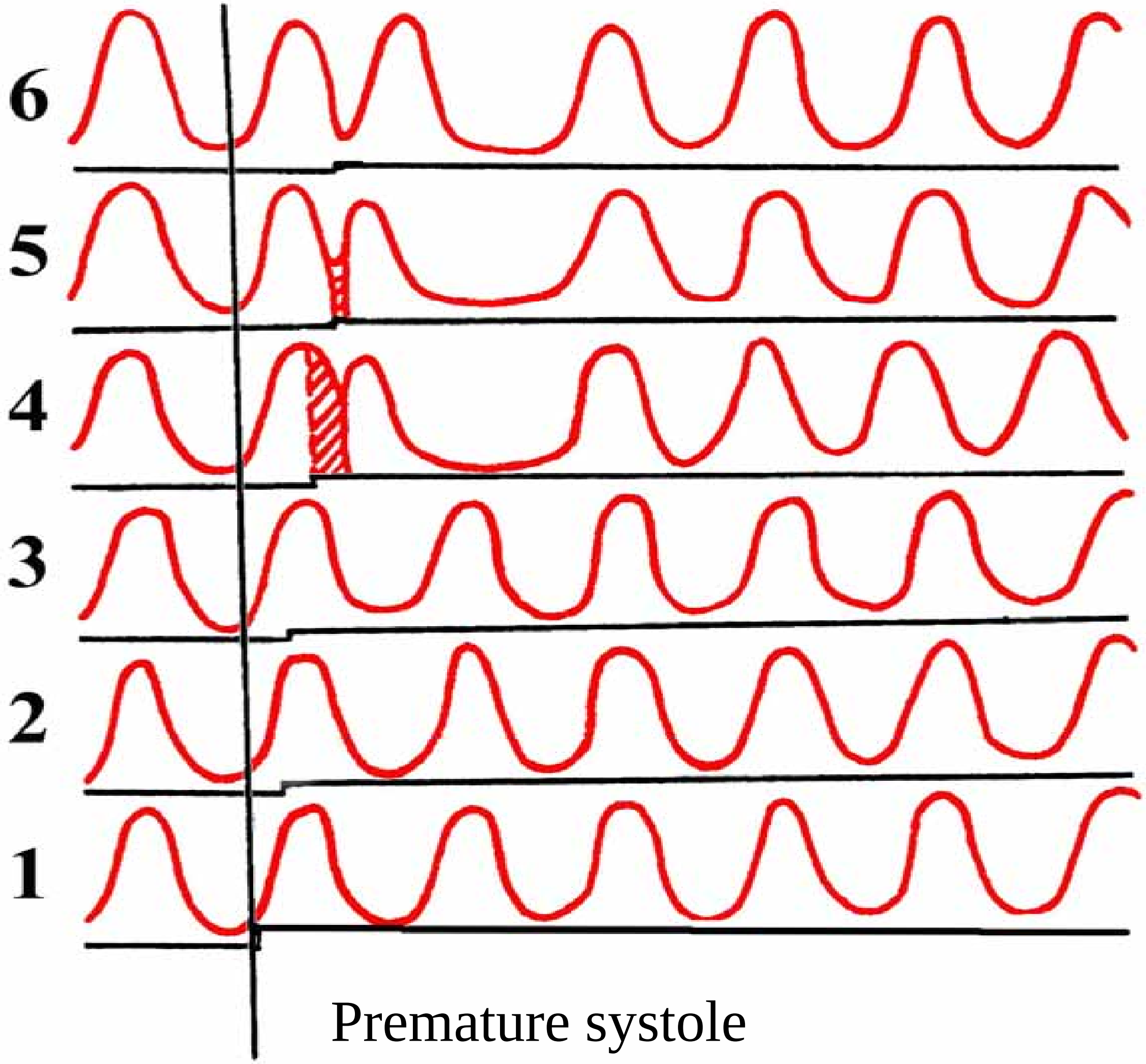
Premature systole Compensatory pause

Premature systole:

Are extra beats that occur when an autorhythmic cell other than the SA node jumps in and fires an action potential out of sequence.

Compensatory pause

The pause following an extrasystole, when the pause is long enough to compensate for the prematurity of the extrasystole; the short cycle ending with the extrasystole plus the pause following the extrasystole together equal two of theregular cycles.

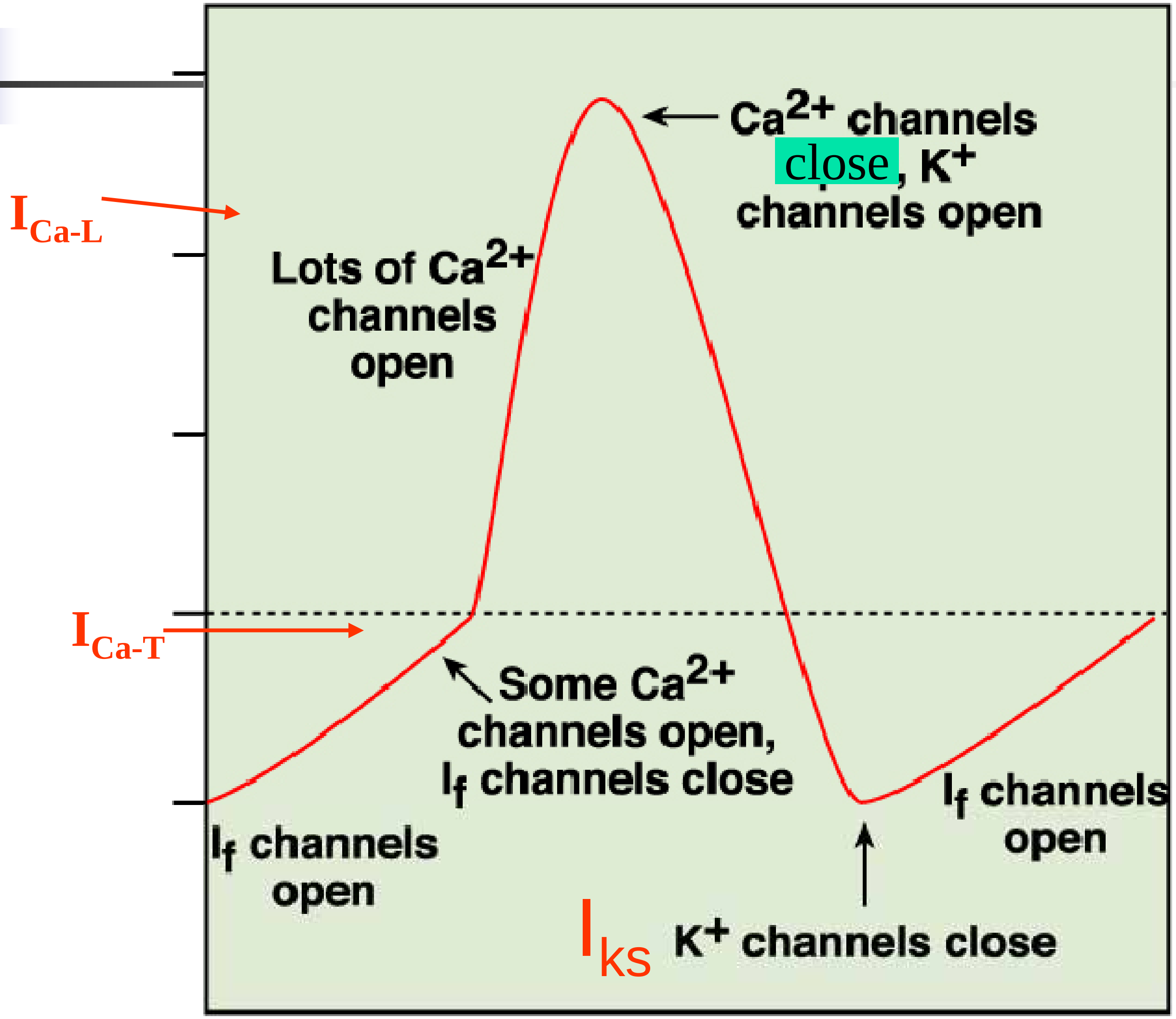


Premature systole
Compensatory pause

The Physiological Properties of Cardiac Cells

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

State of various ion channels

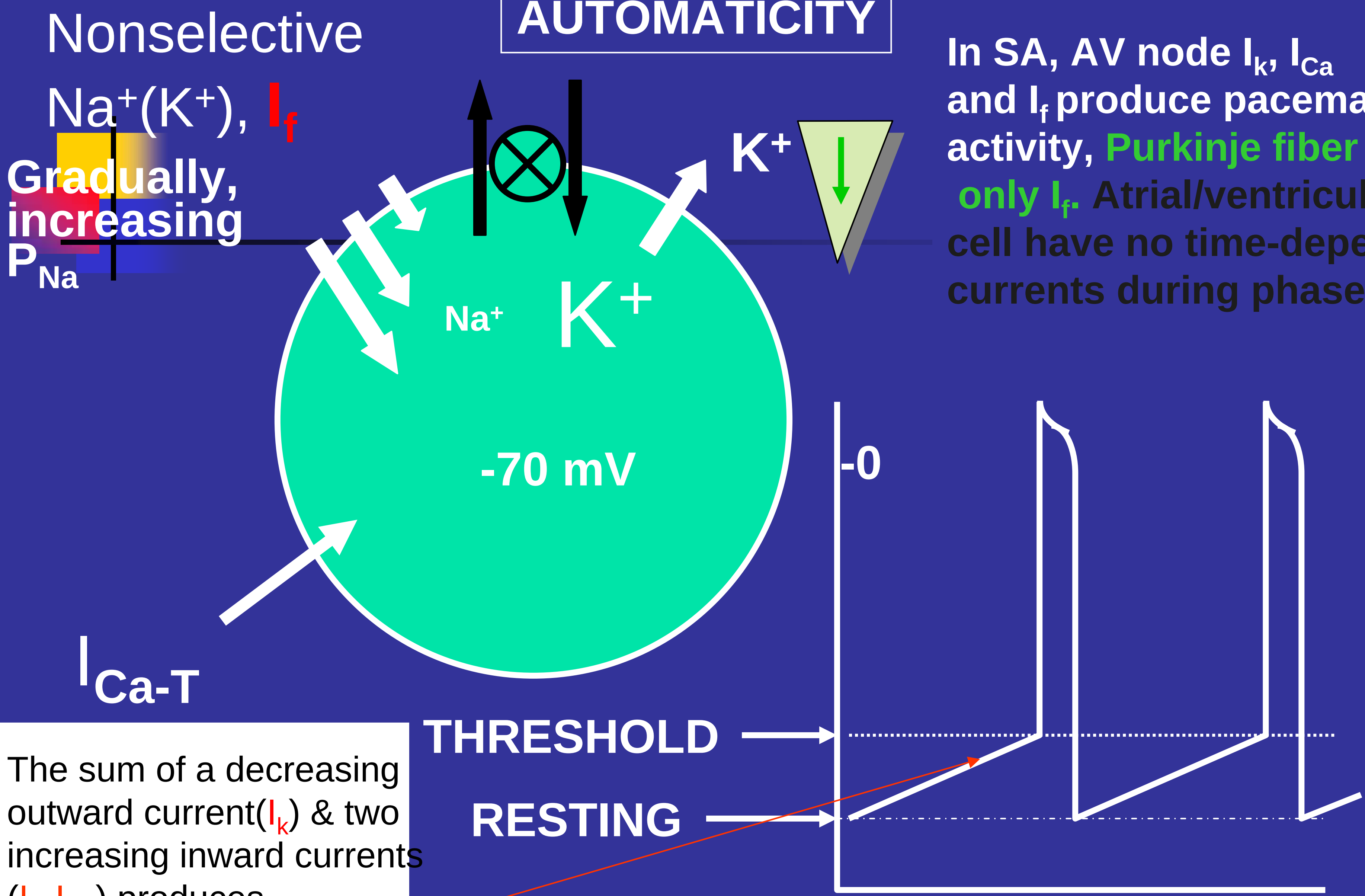


Origin of the Heartbeat : SA nodal action potentials are divided into three phases

- **Phase 0** depolarization is primarily due to gCa^{++} $\uparrow$ "slow inward Ca^{++} channels(**$I_{Ca\text{-}L}$**), slope of Phase 0 is much slower than found in other cardiac cells
- Repolarization occurs (**Phase 3**) as gK^{+} $\uparrow$ and gCa^{++} $\downarrow$
- Spontaneous depolarization (**Phase 4**) is due to ① a fall in gK^{+} as potassium channels close(**I_K deactivation**) ② to a small increase in gCa^{2+} (**$I_{ca\text{-}T}$**). ③A slow inward Na^{+} current also contributes to Phase 4, **"funny" current (I_f).** Once this spontaneous depolarization reaches threshold (about -40 mV), a new action potential is triggered

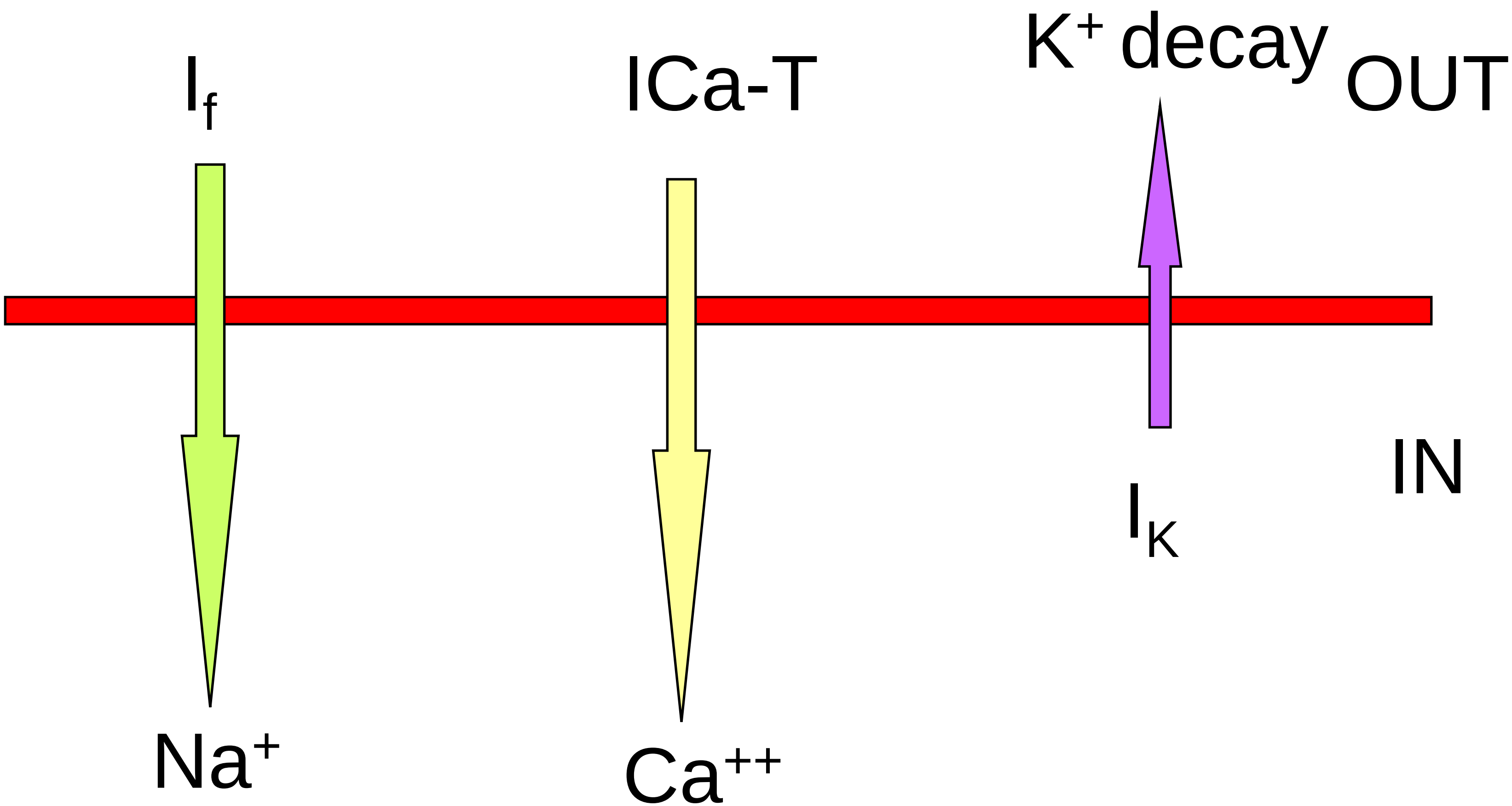
AUTOMATICITY

In SA, AV node I_k, I_{Ca} and I_f produce pacemake activity, Purkinje fiber us only I_f. Atrial/ventricular cell have no time-depend currents during phase 4

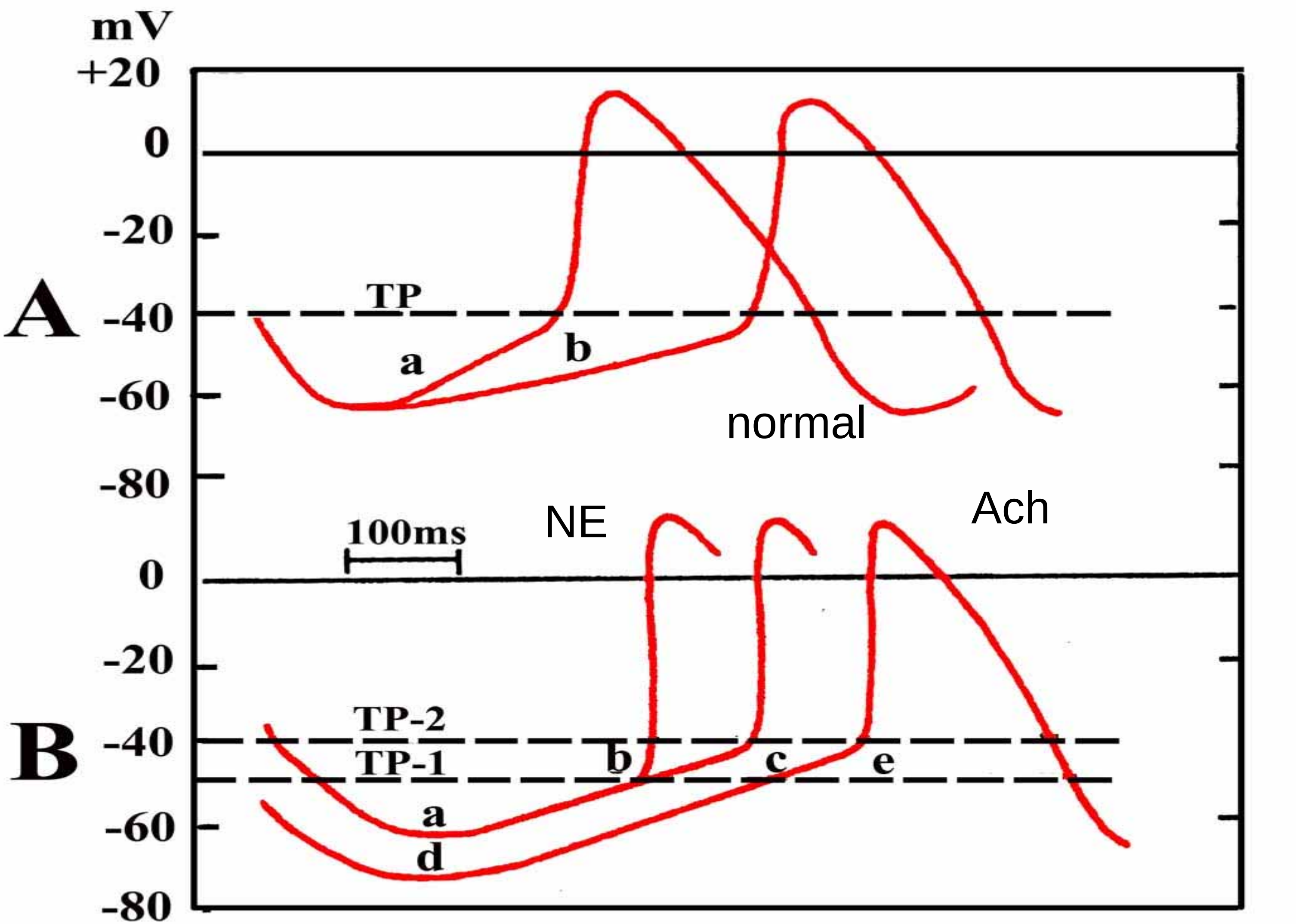


The sum of a decreasing outward current(I_k) & two increasing inward currents (I_f, I_{Ca}) produces **pacemaker potential**

Cause of the pacemarker potential
Phase 4 Spontaneous depolarization , ② Autorhythmicity



Ach & CA Modulate Pacemaker Activity, Conduction V., Contractility. In humans in whom both noradrenergic and cholinergic systems are blocked, the heart rate is approximately 100.



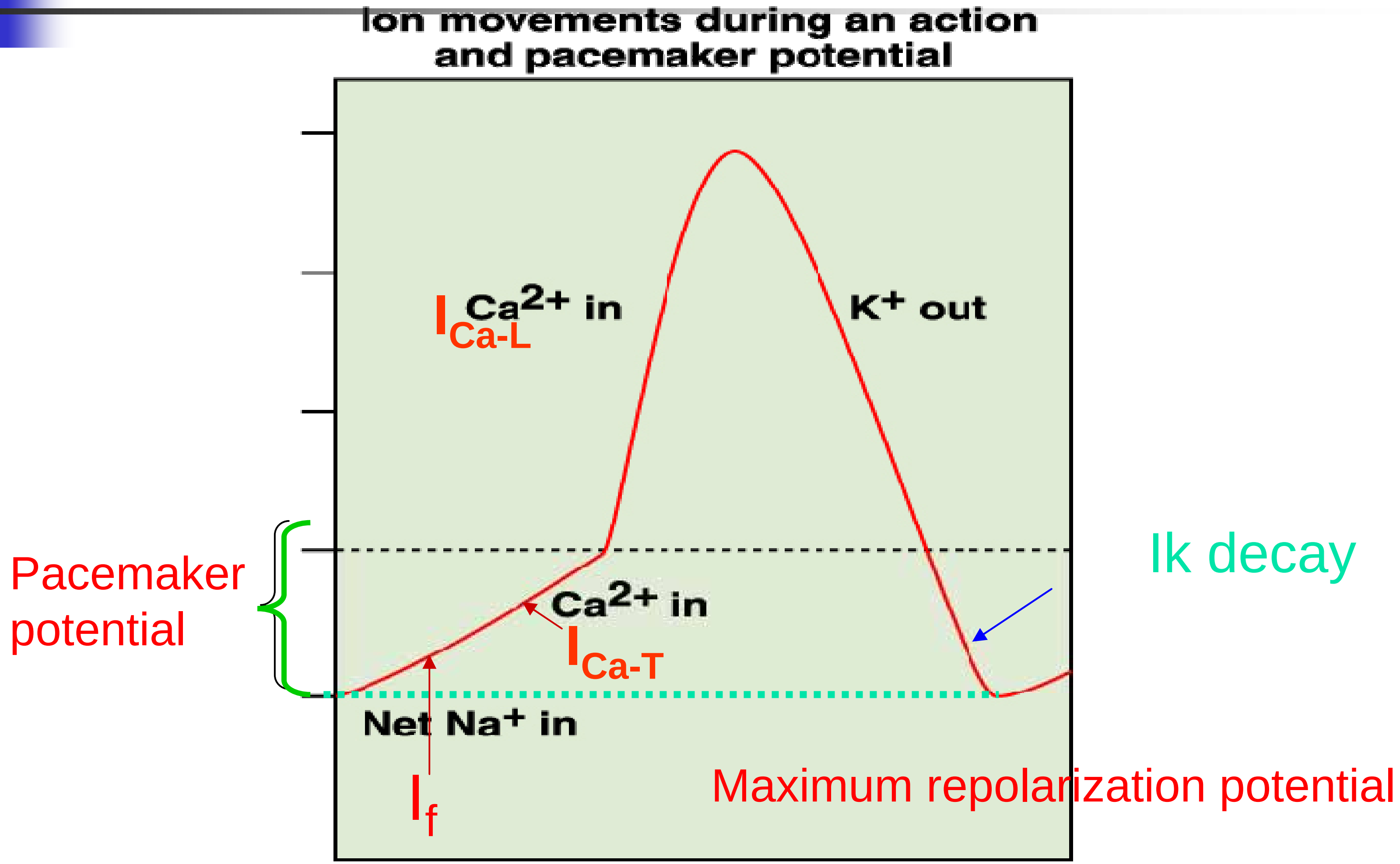
I_f Current: Pacemaker Current

- Nonspecific cation channel, activated by hyperpolarization(-60~ -100mv) at the end of phase 3, activation is slow(100 ms), does not inactivate
- cyclic nucleotide-gated channel, conduct both Na and K, reversal P: -20mv
- ***Interaction among 3 time-dependent, V-G currents control the rhythmicity of SA node*** ***(I_k ↓, I_{Ca-T} ↑, I_f ↑).***
- I_f is blocked by Cs, not by TTX. I_{Ca-T} blocked by miberfradil and Ni^{2+}

SA node: Primary pacemaker Automaticity

- 3 intrinsic pacemaking tissues: SA(dominant P.), AV node,Purkinje fibers, AV node:40/min, latent P, ectopic P.
- SA: the fastest pacemaker is the one to trigger an AP that propagate throughout the heart, sets the heart rate and over-rides all slow pacemakers.
- Maximum diastolic P: -60~ -70mv, few $I_{Na,}$ threshold :-55mv. Upstroke: I_{Ca-L}

Pacemaker activity: Phase 4 spontaneous depolarization

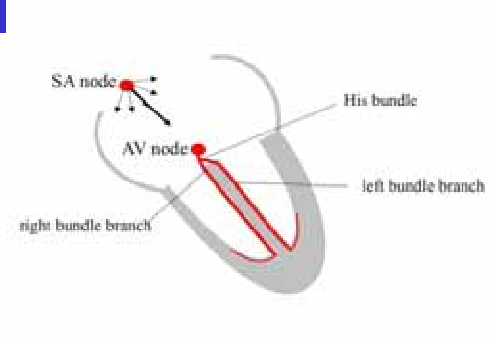


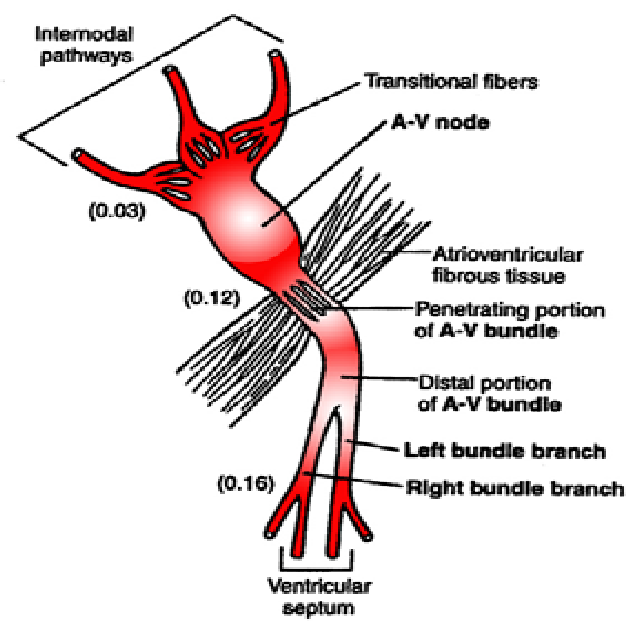
Type / Phase	Fast response cell(atria/ventricle/ Purkinje cells	Slow response Cells(SA/AV node)
Phase 0	Na^+ Channels open	$I_{Ca}L$ channels open
Phase 1	Na^+ Channels close, I_{to}	No
Phase 2 (Plateau)	$I_{Ca}L$ channels open is balanced against efflux of I_{ks}	No
Phase 3	$I_{Ca}L$ channels close, K^+ channels open	K^+ channels open
Phase 4	Steady(except Purkinje Cells)	Spontaneously depolarize, I_K decay, $I_{Ca}T$, I_f
RMP	-90 mv	-50 ~ -60mv

The Physiological Properties of Cardiac Cells

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

Conduction system

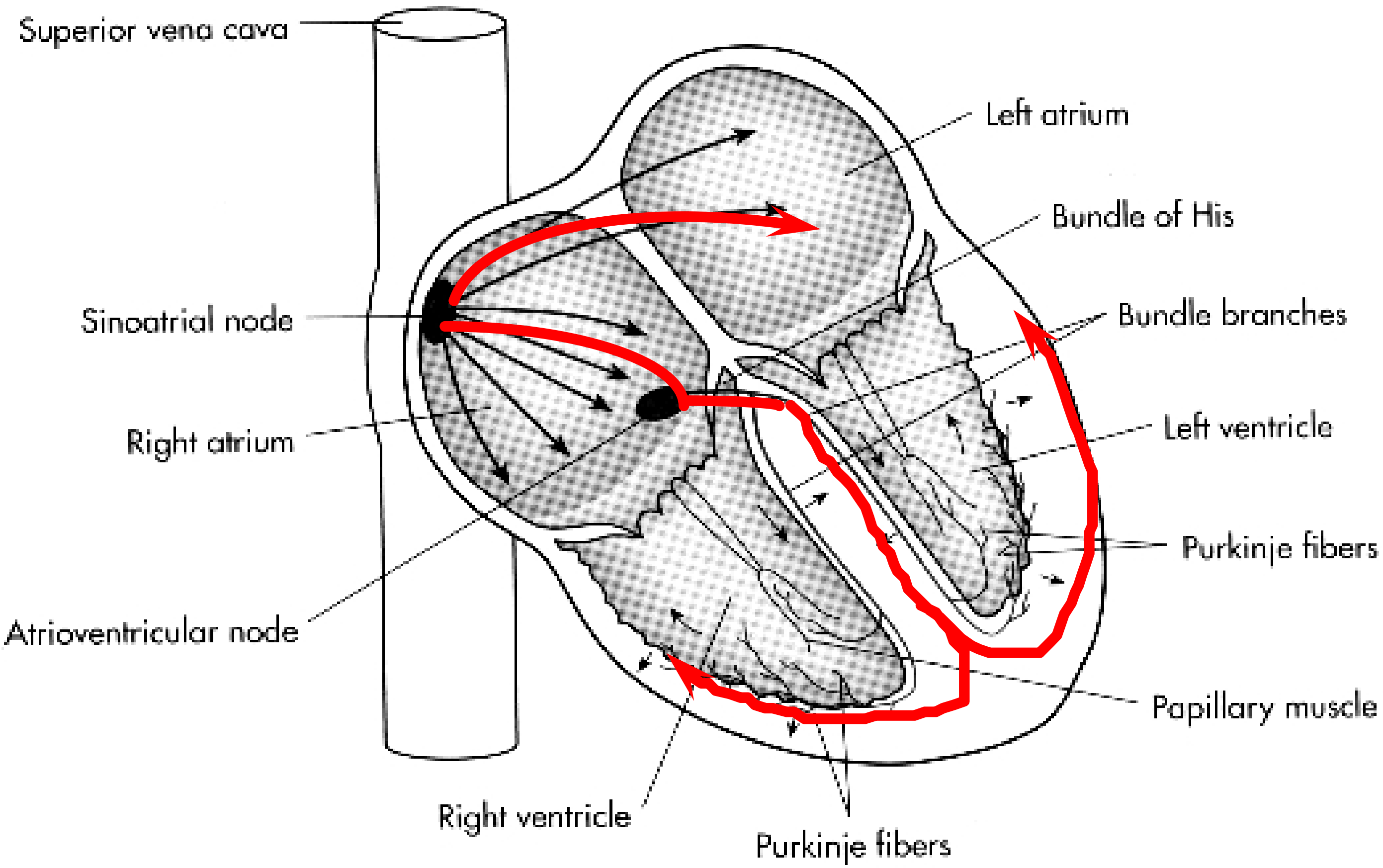




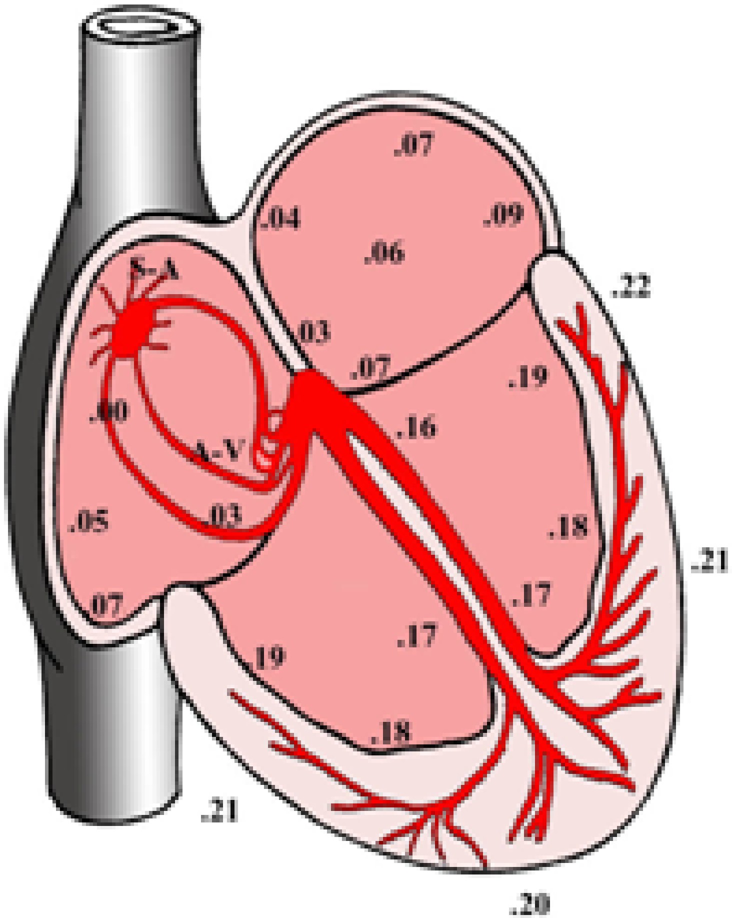
①SA node is located at the junction of the superior vena cava with the right atrium. The AV node is located in the right posterior portion of the interatrial septum.

②the internodal atrial pathways
③atrioventricular node (AV node)
④the bundle of His and its branches
⑤the Purkinje system.

The conduction system of the heart



Conductivity



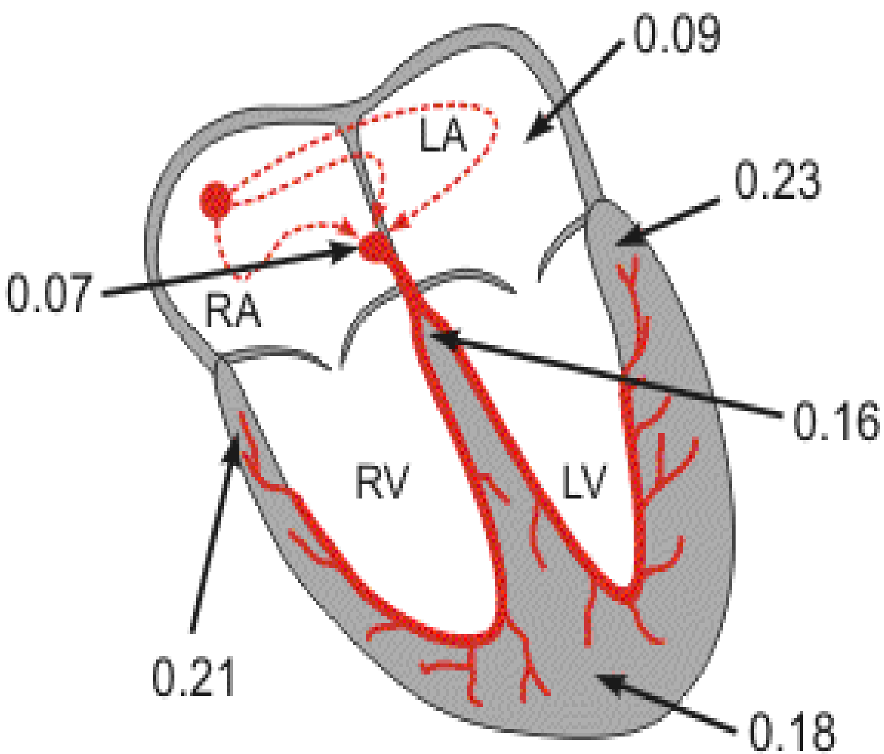
- Brachycardia:

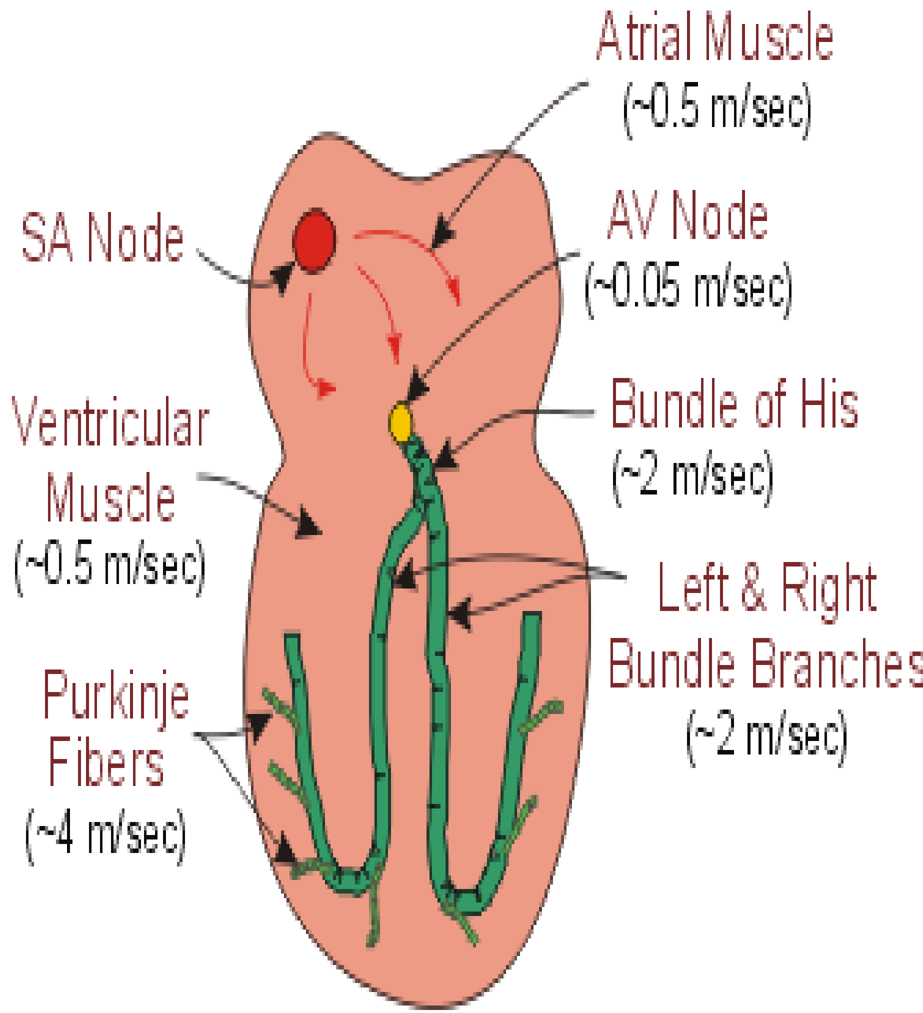
  Resting heart rate<60bpm

- Tachycardia: >100bpm
- *Chronotropic*: affect the heart rate
- *Inotropic*: affect the strength of contraction
- Factors affecting conductivity
- Amplitude & speed of phase 0
- Diametter of fibers

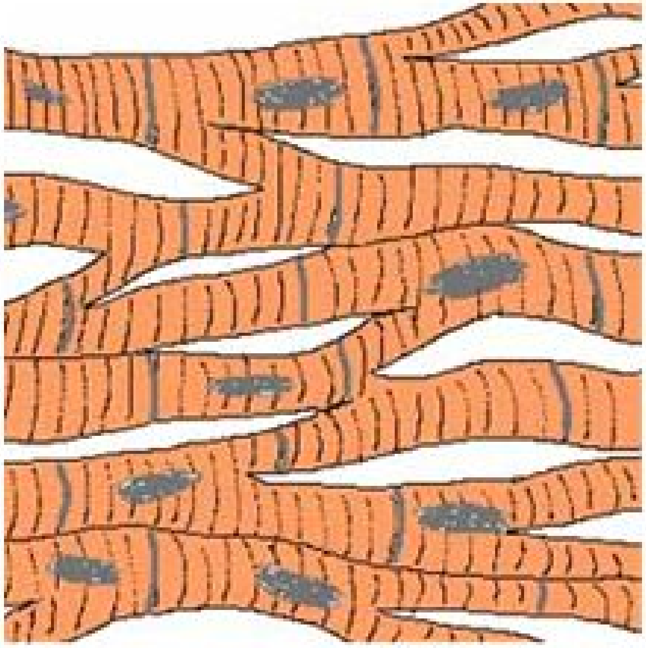
Conductivity

Cardiac Activation Times
(seconds)



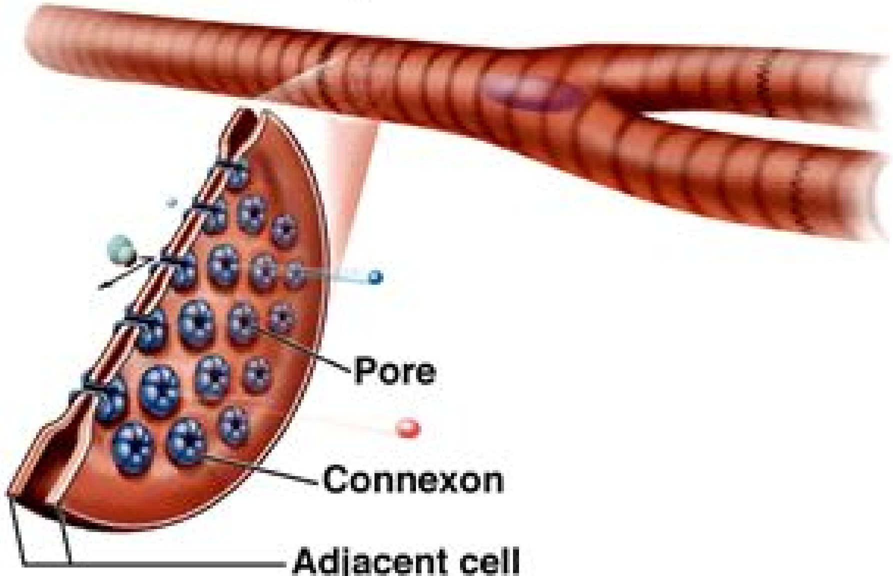


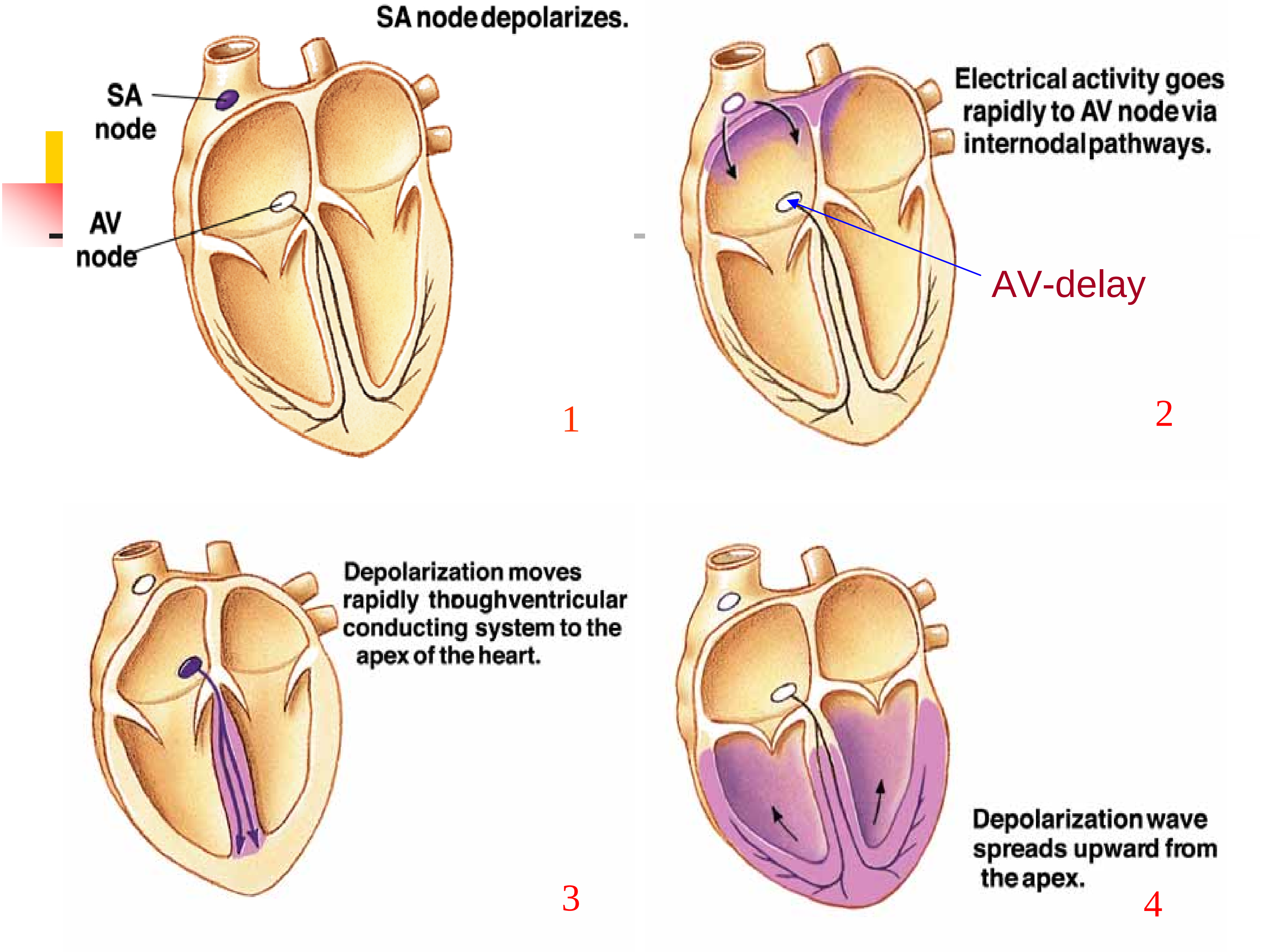
Cardiac muscle as a syncytium

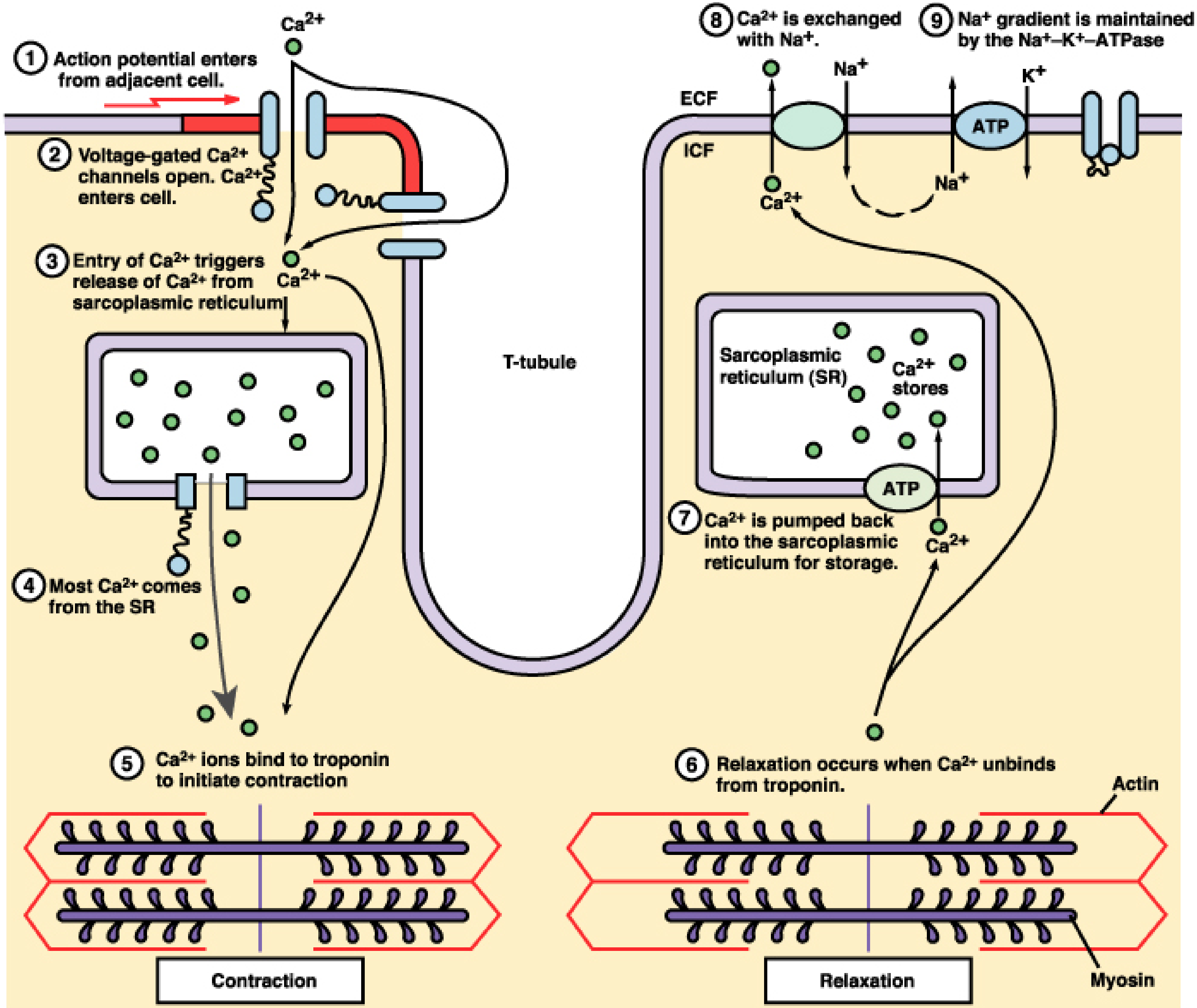


Syncytial

Gap Junction

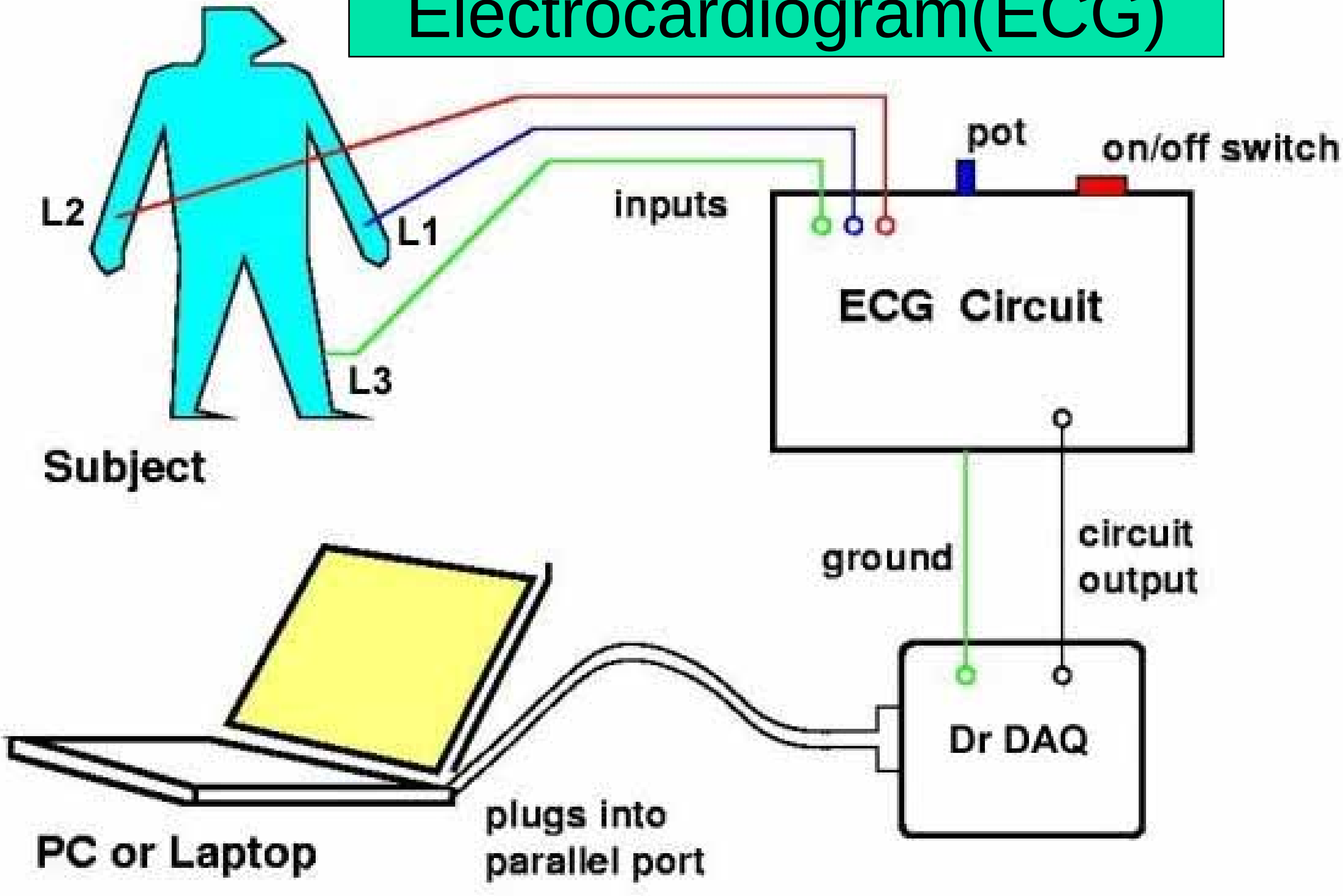



SA node depolarizes.
SA node
AV node
1
Electrical activity goes rapidly to AV node via internodal pathways.
AV-delay
2
Depolarization moves rapidly thoughventricular conducting system to the apex of the heart.
3
Depolarization wave spreads upward from the apex.
4

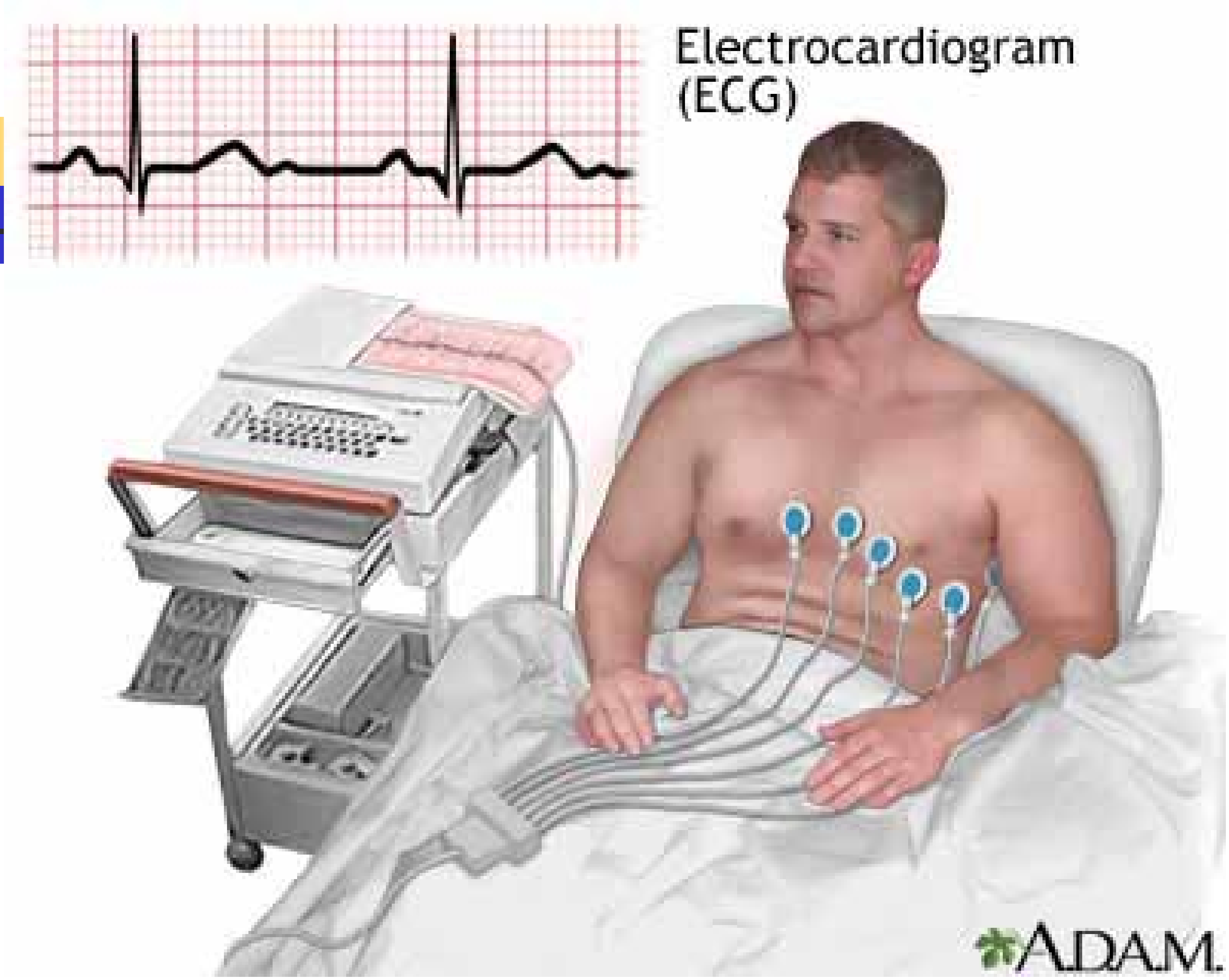


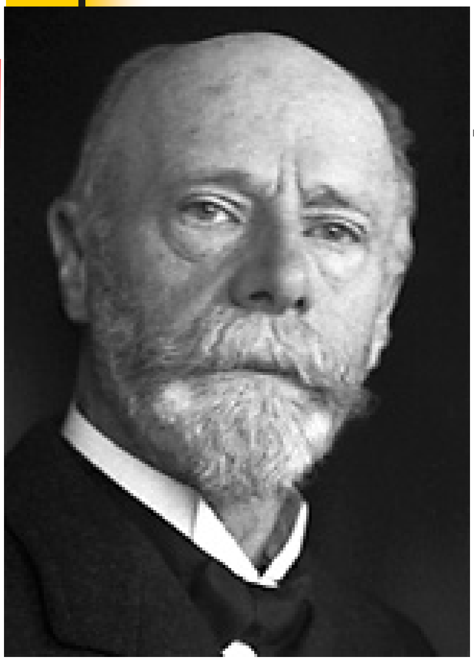
Ca2+
1 Action potential enters from adjacent cell.
2 Voltage-gated Ca2+ channels open. Ca2+ enters cell.
3 Entry of Ca2+ triggers release of Ca2+ from sarcoplasmic reticulum
Ca2+
4 Most Ca2+ comes from the SR
5 Ca2+ ions bind to troponin to initiate contraction
T-tubule
ECF
ICF
8 Ca2+ is exchanged with Na+.
9 Na+ gradient is maintained by the Na+–K+–ATPase
Na+
K+
ATP
Na+
Ca2+
Sarcoplasmic reticulum (SR)
Ca2+ stores
ATP
7 Ca2+ is pumped back into the sarcoplasmic reticulum for storage.
Ca2+
6 Relaxation occurs when Ca2+ unbinds from troponin.
Actin
Myosin
Contraction
Relaxation

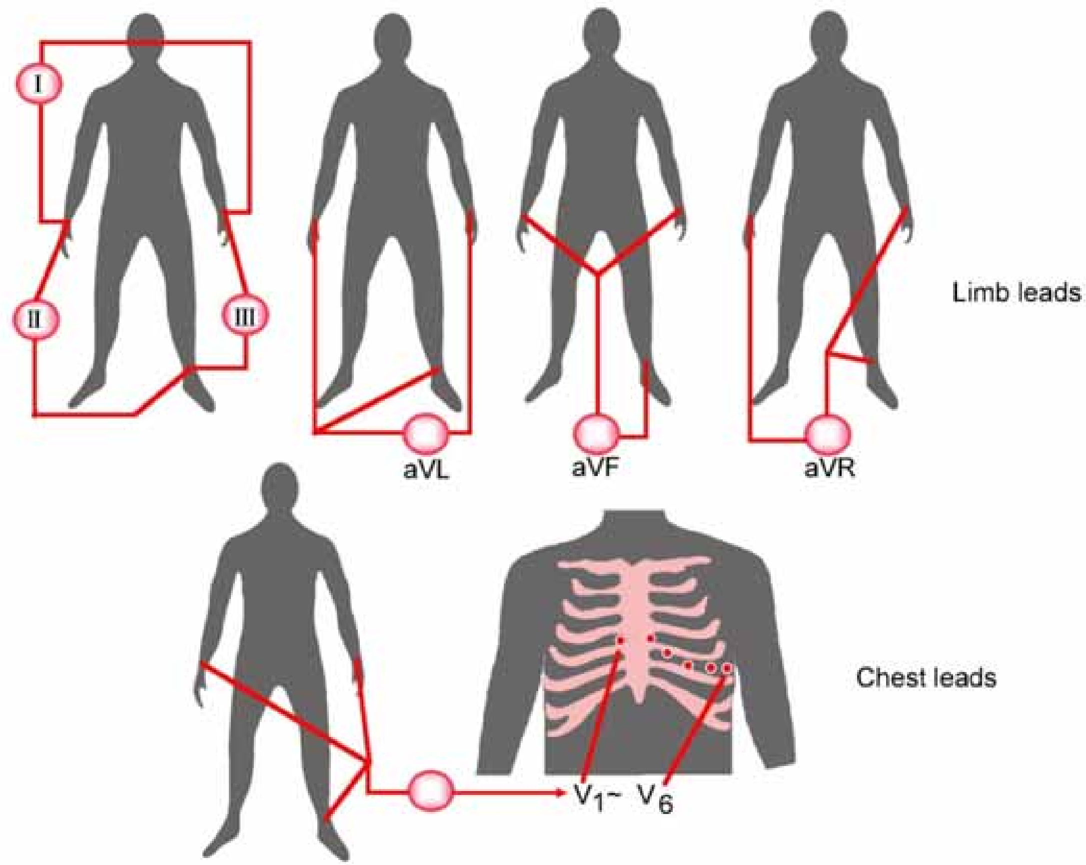
Electrocardiogram(ECG)



DrDAQ ECG project setup


Electrocardiogram
(ECG)
A.D.A.M.



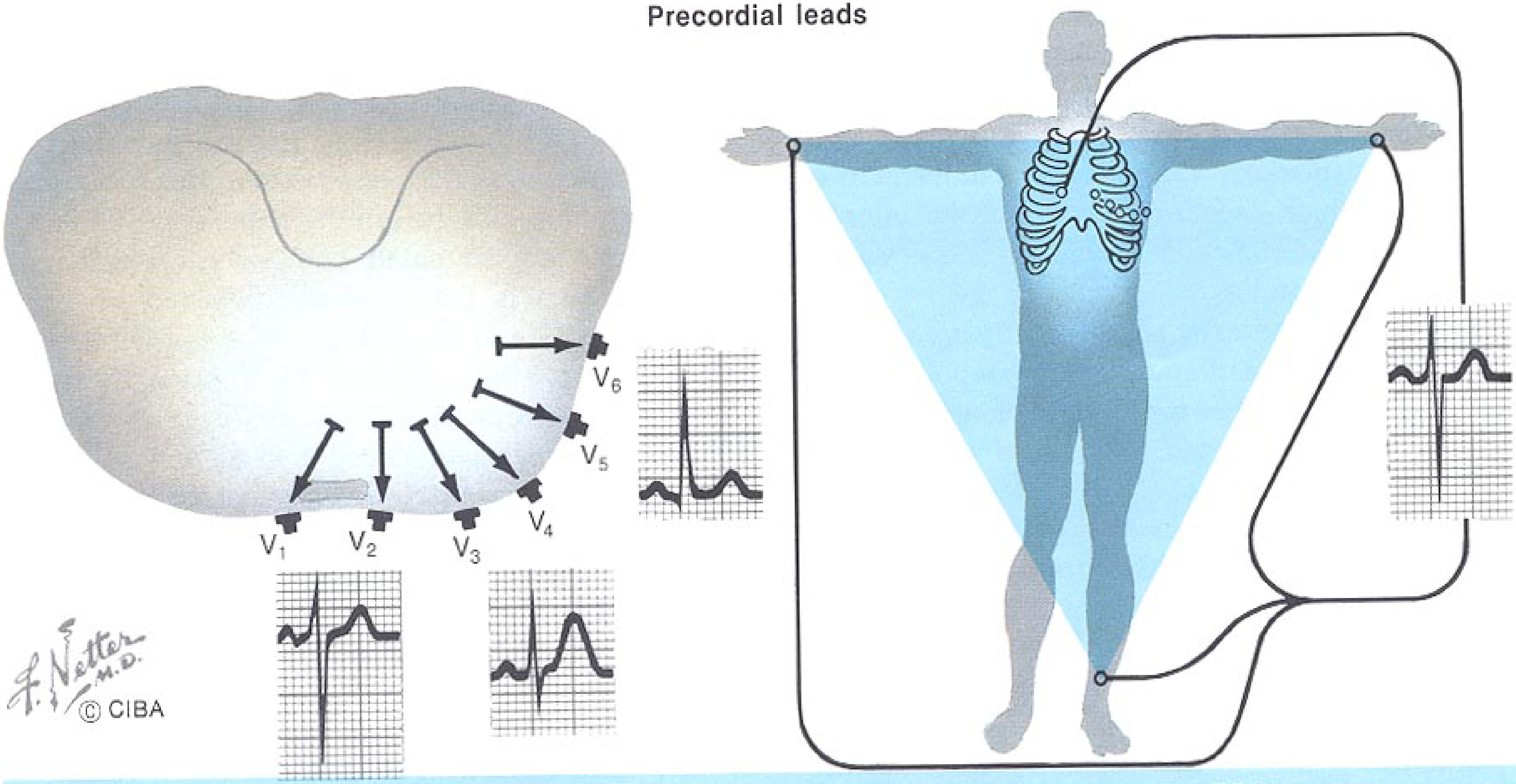


Willem Einthoven

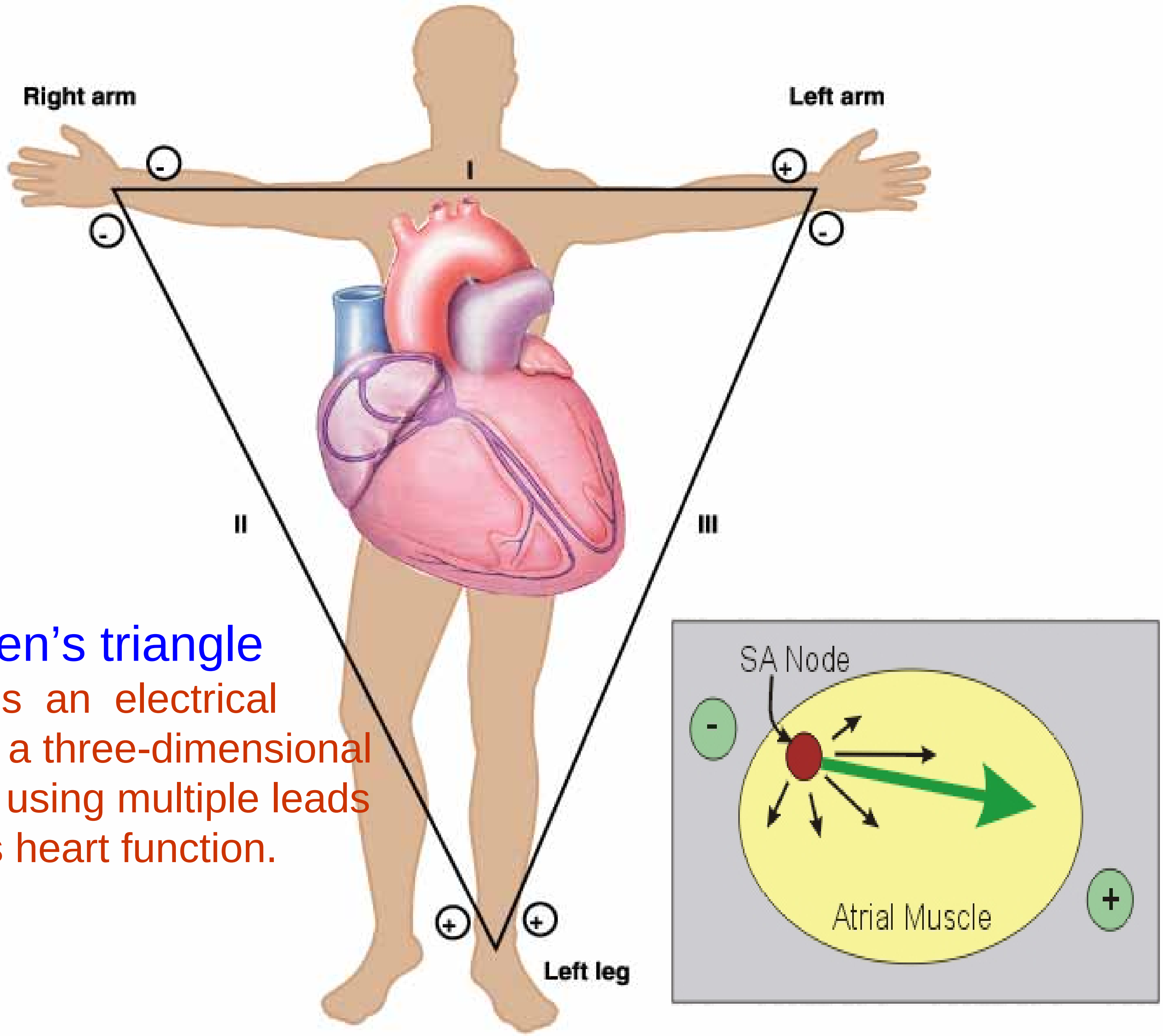
Nobel Prize of Medicine in 1924

Quick, painless, noninvasive

ECG Precordial Leads

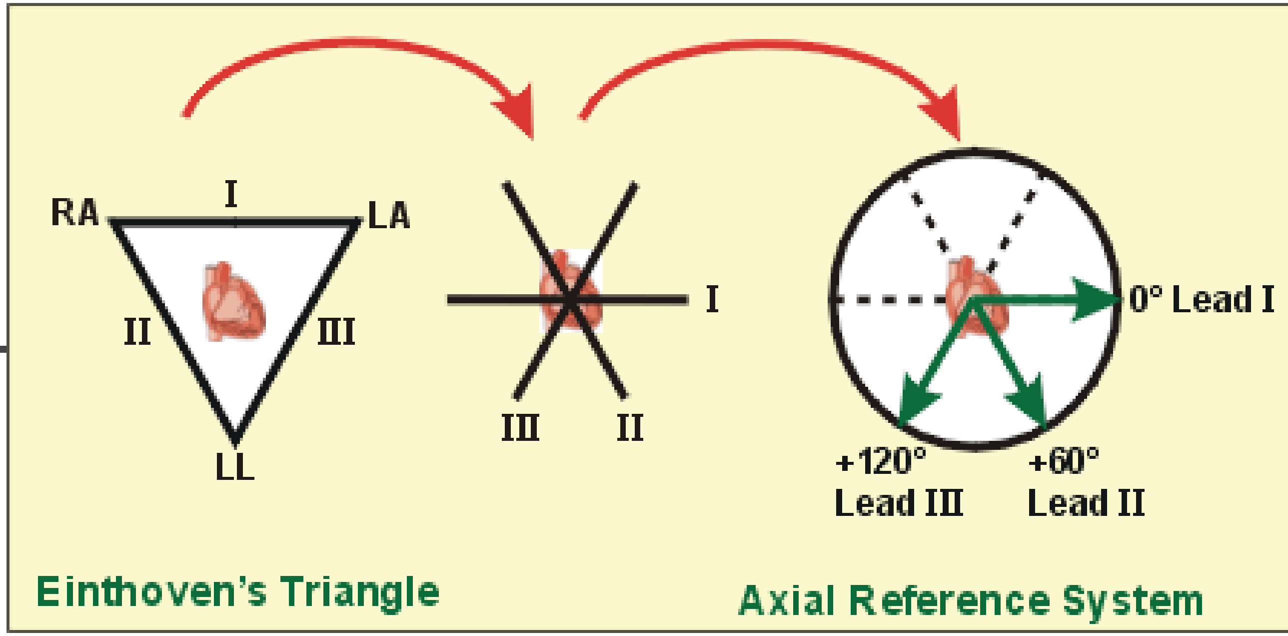


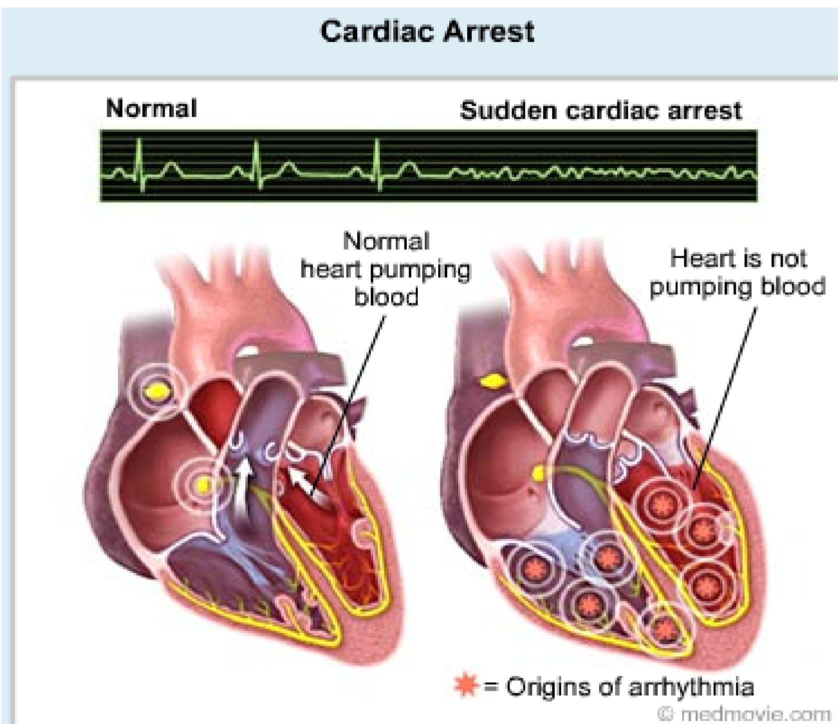
When current flows toward arrowheads (axes), upward deflection occurs in ECG
When current flows away from arrowheads (axes), downward deflection occurs in ECG
When current flows perpendicular to arrows (axes), no deflection occurs

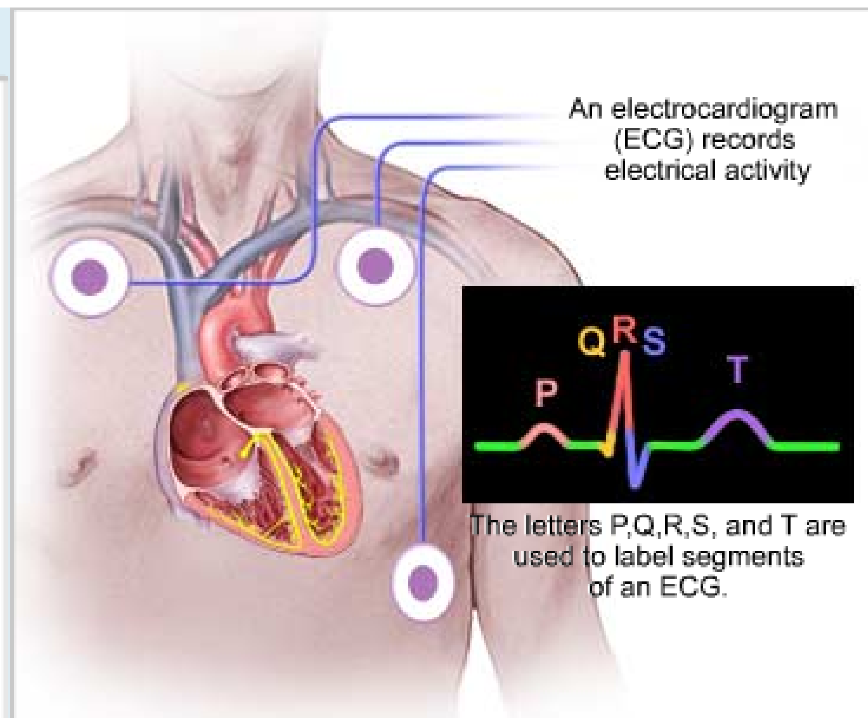


Einthoven's triangle

An ECG is an electrical "view" of a three-dimensional object by using multiple leads to assess heart function.

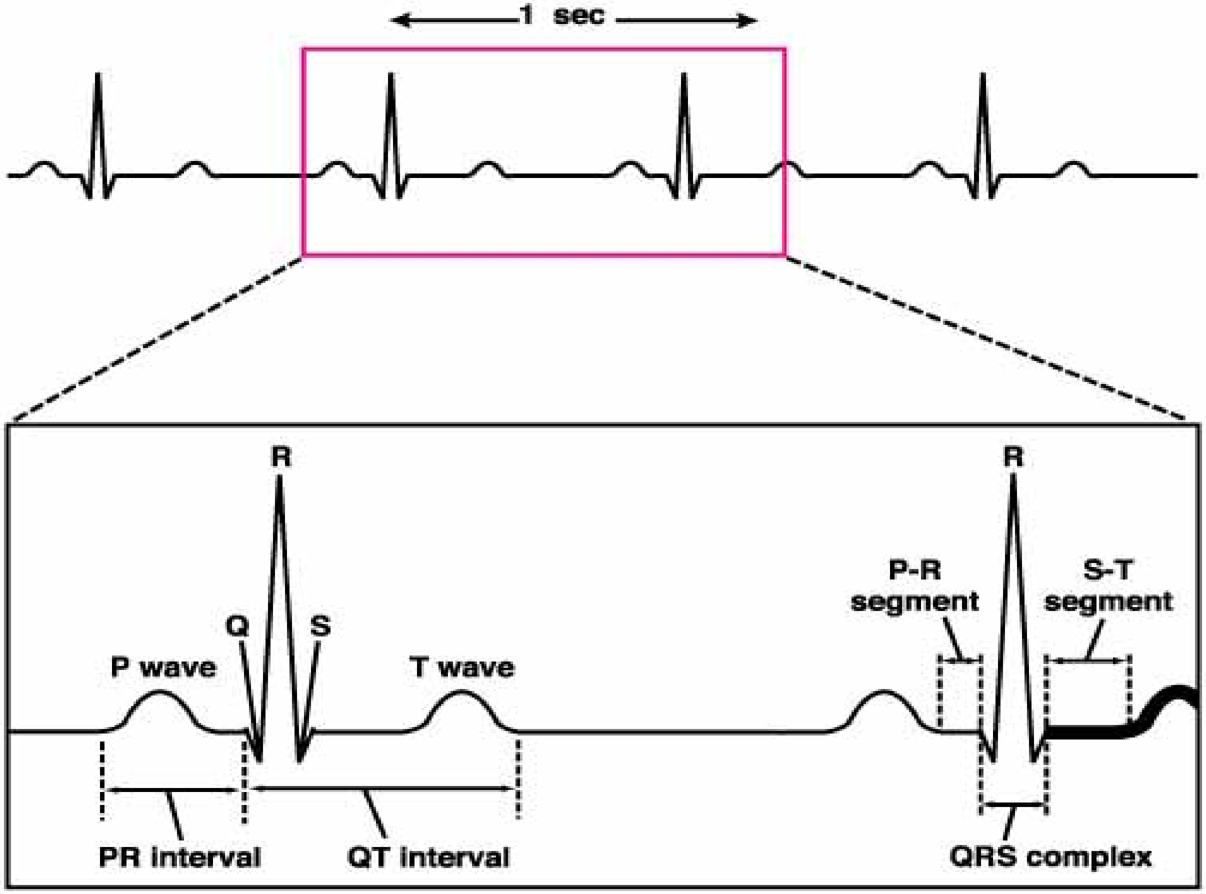

RA
I
LA
II
III
LL
I
III
II
0° Lead I
+120°
Lead III
+60°
Lead II
Einthoven's Triangle
Axial Reference System


Cardiac Arrest
Normal
Sudden cardiac arrest
Normal heart pumping blood
Heart is not pumping blood
= Origins of arrhythmia
© medmovie.com


An electrocardiogram (ECG) records electrical activity
Q
R
S
P
T
The letters P,Q,R,S, and T are used to label segments of an ECG.

ECG intervals

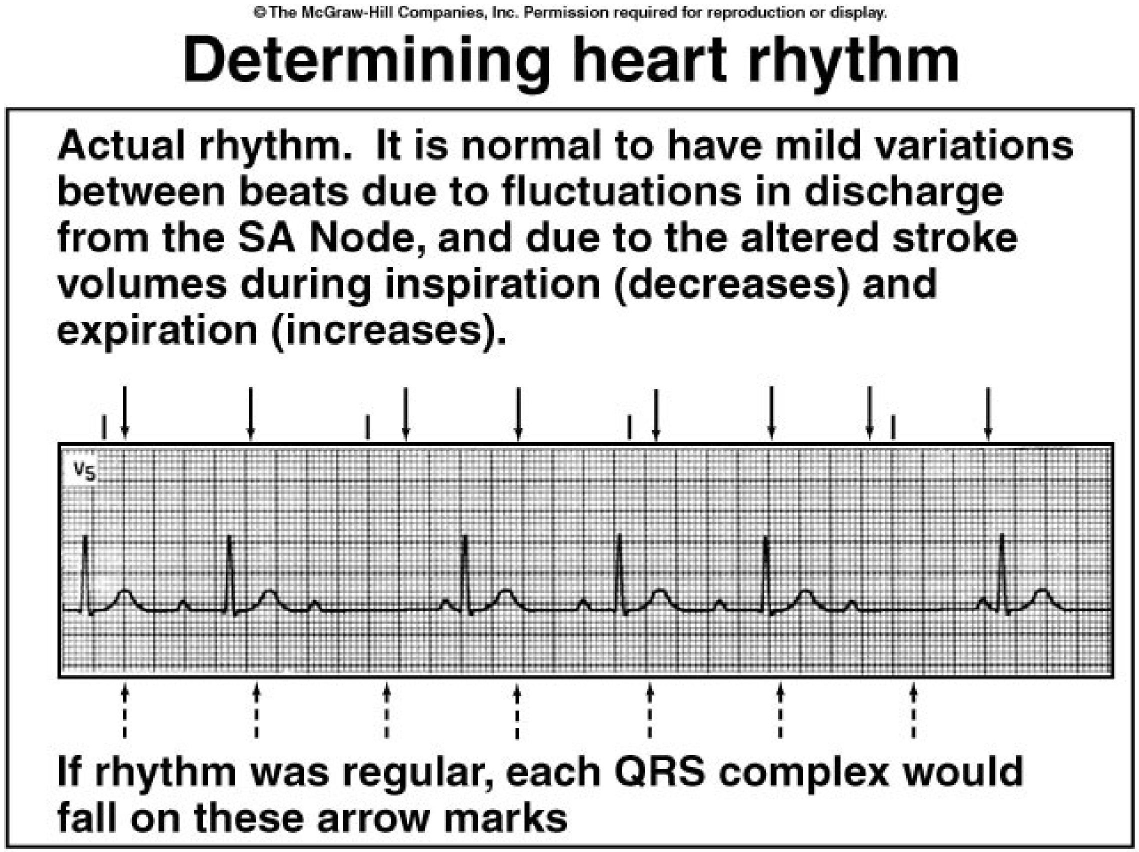
1. When an electrical wave is directed toward the positive electrode, the ECG wave goes up from the baseline.
2. If net charge movement is toward the negative electrode, the wave points downward.



Component	Association in the heart
The P wave	atrial depolarization followed by atrial contraction
The QRS complex	ventricular depolarization followed by ventricular ejection,0.08-0.10s
The T wave	ventricular repolarization
The PR segment	the AV nodal delay,0.12-0.2s
The ST segment	the time it takes for the ventricles to contract and empty,0.32s
The TP interval	the time during which the ventricles are relaxing and filling.
The QT interval	ventricular depolarization plus ventricular repolarization,0.4-0.43s

Interpretation of ECG

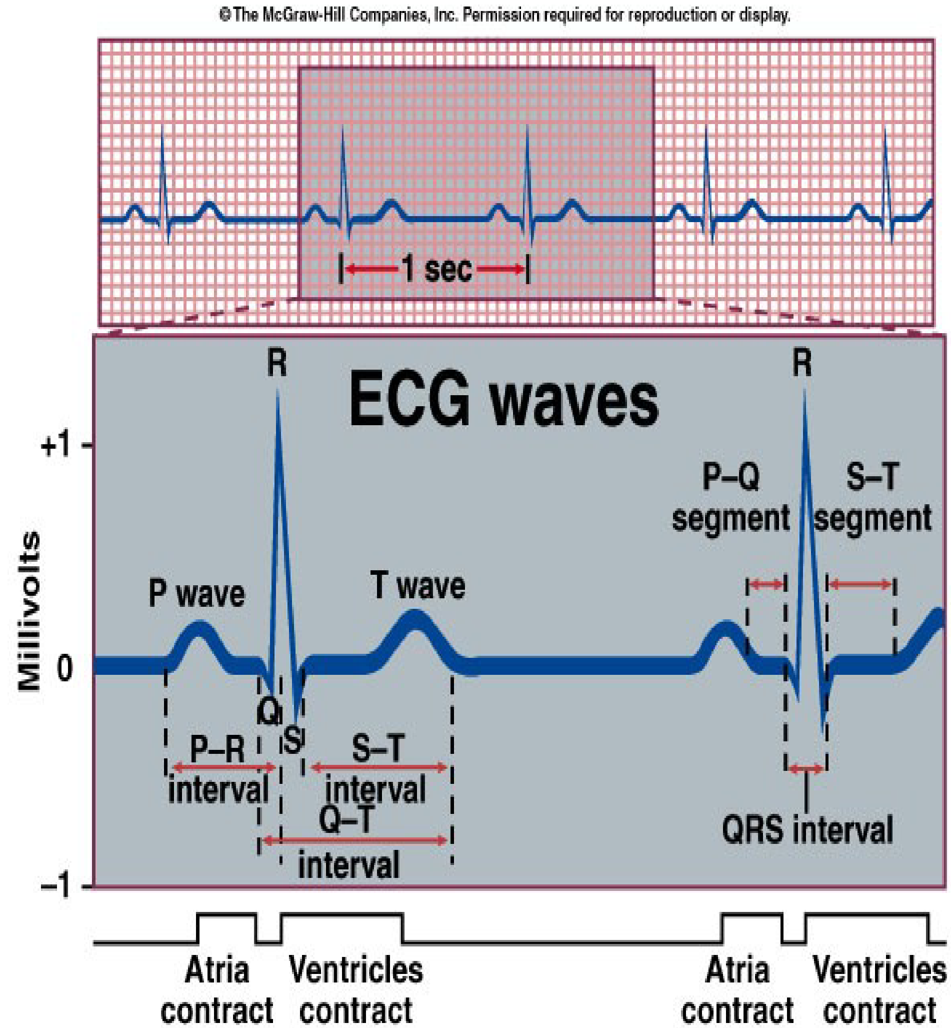
- Normal heart rhythm has consistent R-R interval.
- Mild variations due to breathing also normal

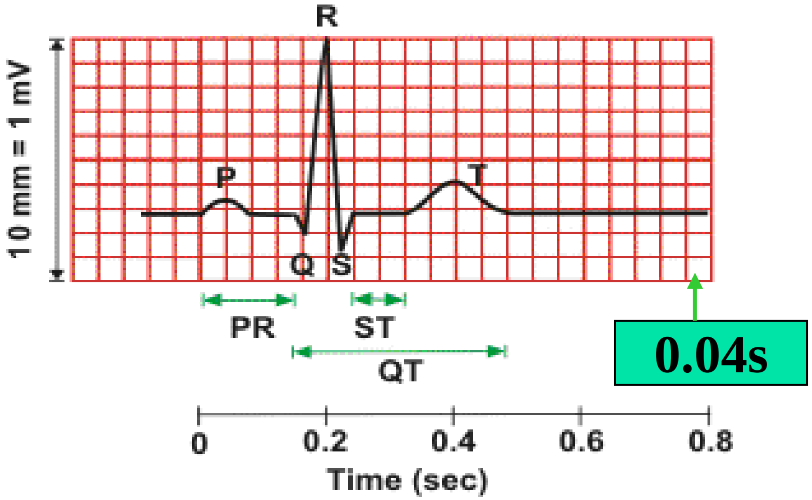


Interpretation of ECG

Normal Sinus Rhythm

- Rate: 60-100 b/min
- Rhythm: regular
- P waves: upright in leads I, II, aV_F
- PR interval: < .20 s
- QRS: < .10 s





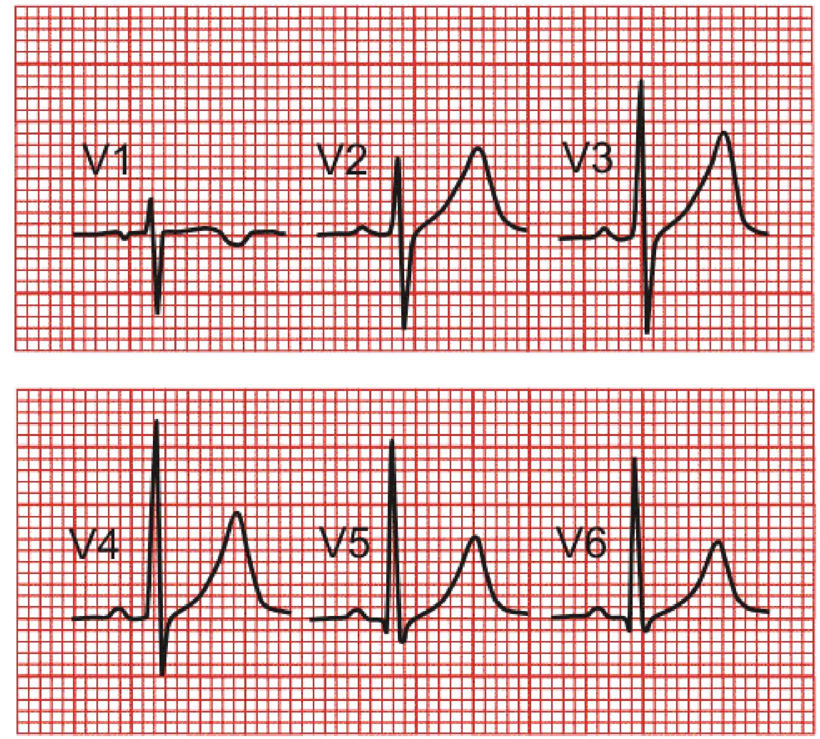
P wave (0.08 - 0.10 s)

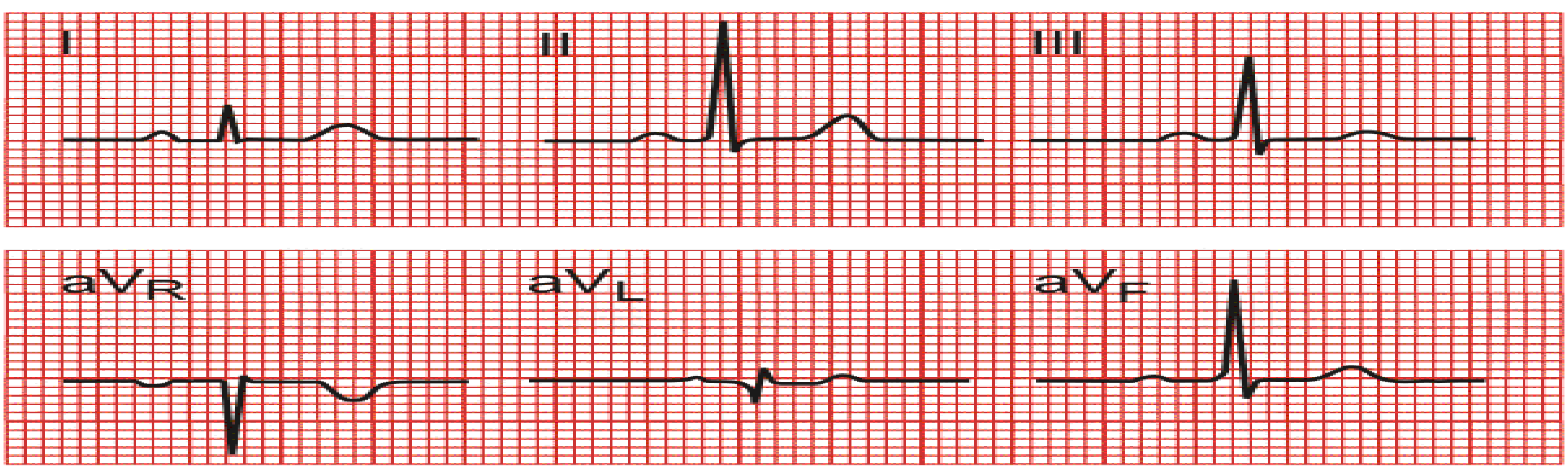
P-R interval (0.12 - 0.20 s)

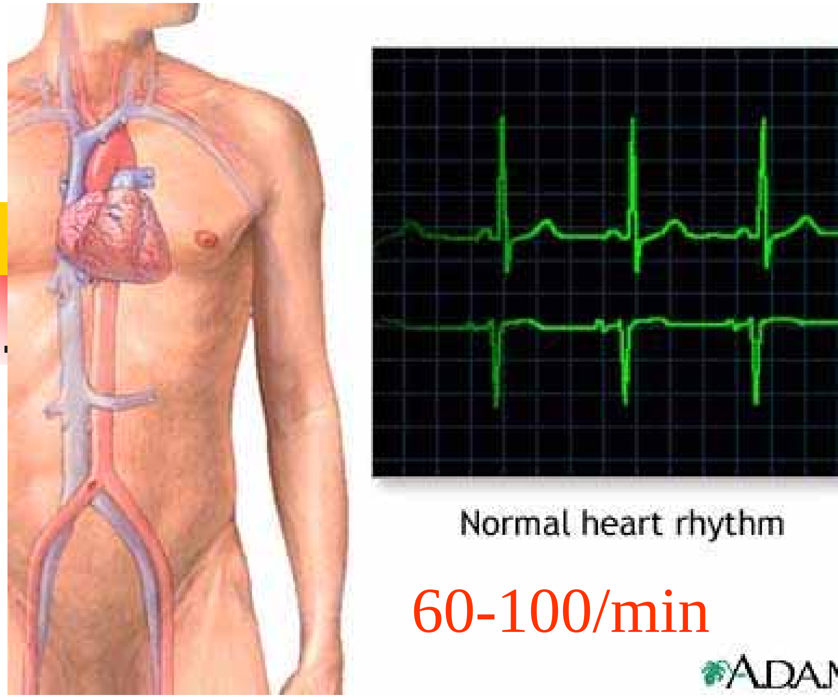
QRS (0.06 - 0.10 s)

$Q\text{-}T_C$ interval ($\leq$ 0.44 s)*

$$^{*}QT_C = QT/\sqrt{RR}$$







Normal heart rhythm

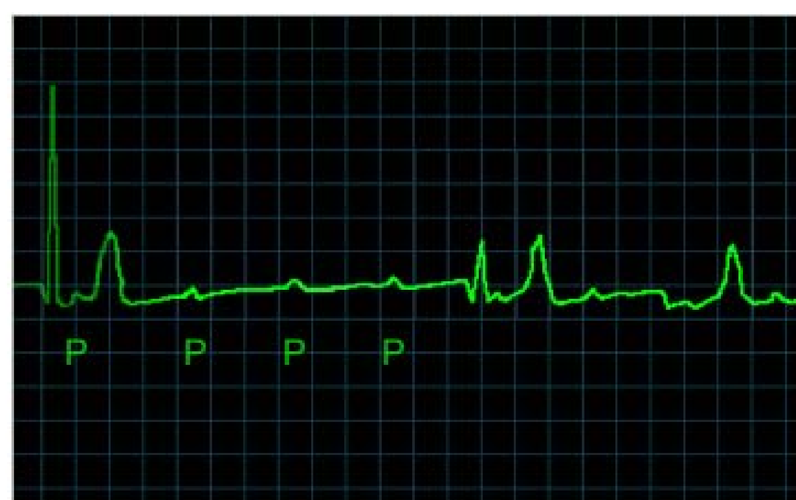
60-100/min

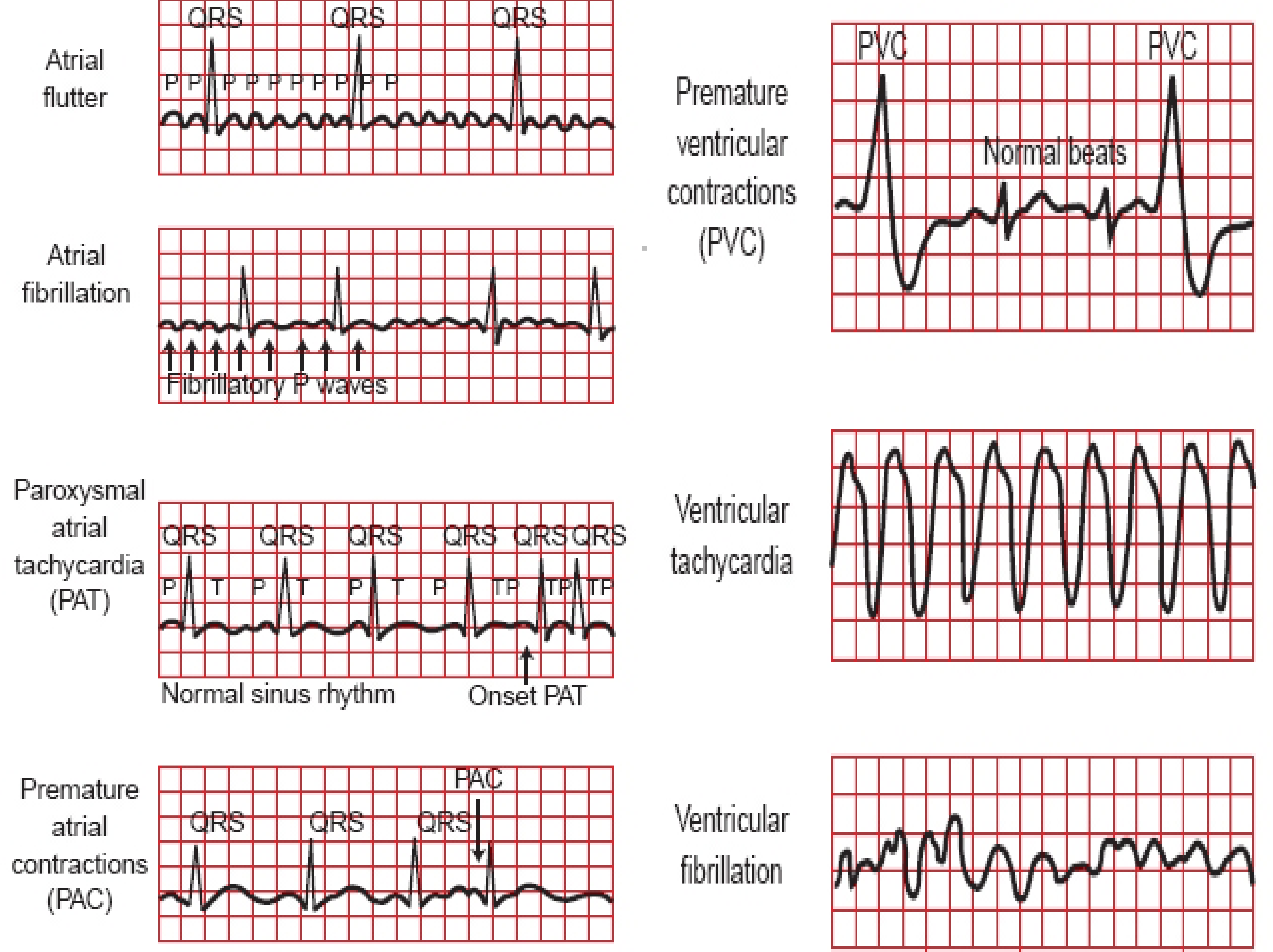
Sinus bradycardia

<60/min

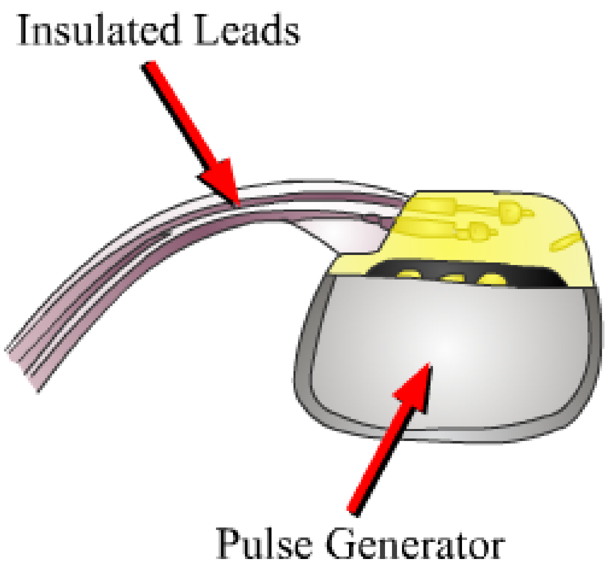
Ventricular tachycardia

Atrioventricular block ECG tracing





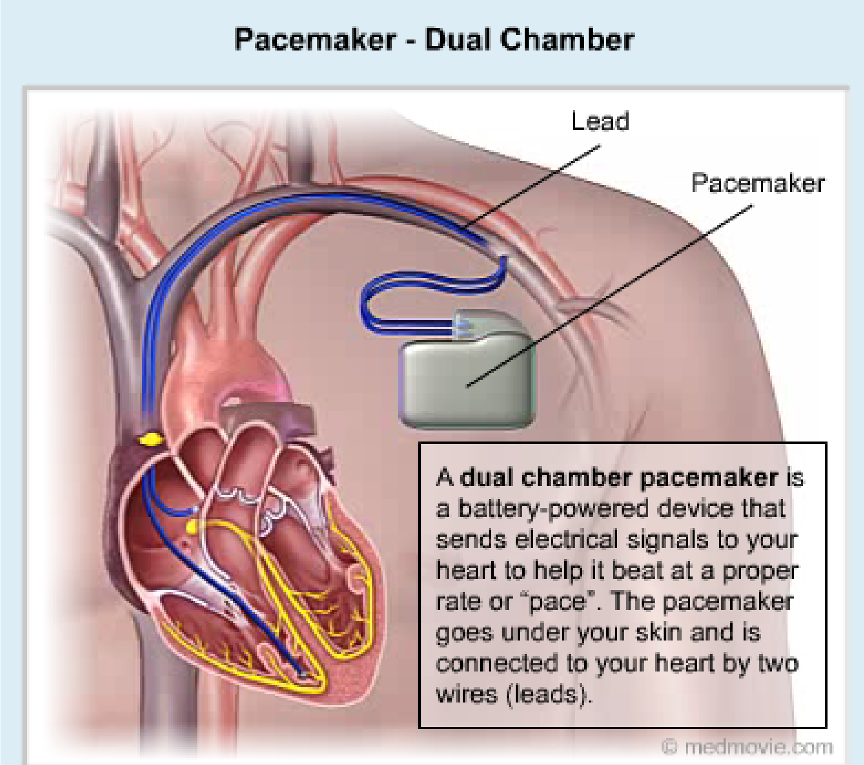
Atrial flutter
QRS
QRS
QRS
P P P P P P P P P P P
Atrial fibrillation
Fibrillatory P waves
Paroxysmal atrial tachycardia (PAT)
QRS
QRS
QRS
QRS
QRS
QRS
P T P T P T P TP TP TP
Normal sinus rhythm
Onset PAT
Premature atrial contractions (PAC)
QRS
QRS
QRS
PAC
Premature ventricular contractions (PVC)
PVC
PVC
Normal beats
Ventricular tachycardia
Ventricular fibrillation



An implanted electronic device that takes over the function of the natural cardiac pacemaker.

a small battery-operated computer, called the pulse generator

It may be surgically implanted or placed externally on the chest.



- **Sick sinus syndrome:**

  refers to the inability of the sinus node to regulate a steady heart rate, caused by damage to the sinus node

  -A heart rate which is too fast or too slow

  -Fatigue

  -Breathlessness

  -Dizziness

  -Loss of consciousness

Summary

- Myocardial contraction results from a change in voltage across the cell membrane (depolarization), which leads to an action potential. Contraction is normally in response to an electrical impulse. This impulse starts in the sinoatrial (SA) node, a collection of pacemaker cells located at the junction of the right atrium and superior vena cava. These specialised cells depolarise spontaneously, and cause a wave of contraction to pass across the atria.
- Following atrial contraction, the impulse is delayed at the atrio-ventricular (AV) node, located in the septal wall of the right atrium. From here His-Purkinje fibres allow rapid conduction of the electrical impulse via right and left branches, causing almost simultaneous depolarisation of both ventricles, approximately 0.2 seconds after the initial impulse has arisen in the sinoatrial node.
- Depolarisation of the myocardial cell membrane causes a large increase in the concentration of calcium within the cell, which in turn causes contraction by a temporary binding between two proteins, actin and myosin.
- The cardiac action potential is much longer than that of skeletal muscle, and during this time the myocardial cells is unresponsive to further excitation.