Chapter 12:
Cardiovascular Physiology

System Overview

Components of the cardiovascular system:

- **Heart**
- **Vascular system**
- **Blood**

Figure 12-1

Plasma includes
water, ions, proteins,
nutrients, hormones,
wastes, etc.

The hematocrit is a
rapid assessment
of blood composition.
It is the percent of the
blood volume that is
composed of RBCs
(red blood cells).

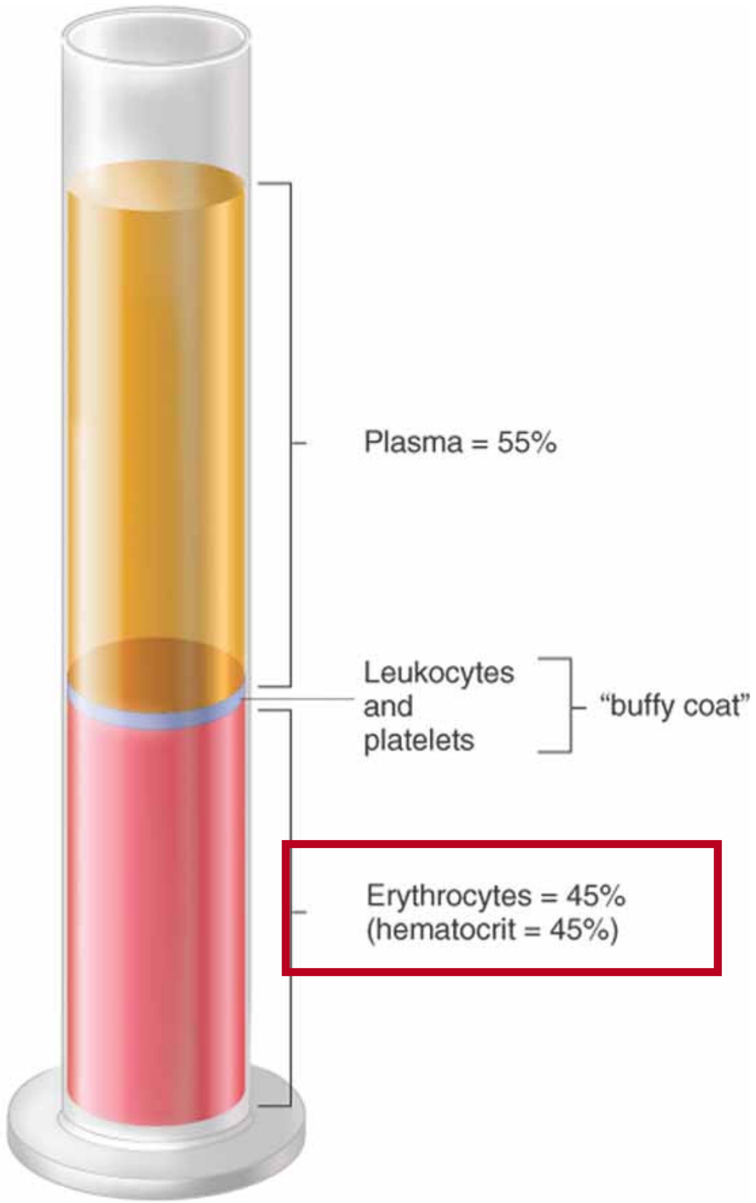

Figure 12-2

The heart is the pump that propels the blood through the systemic and pulmonary circuits.

Red color indicates blood that is fully oxygenated.

Blue color represents blood that is only partially oxygenated.

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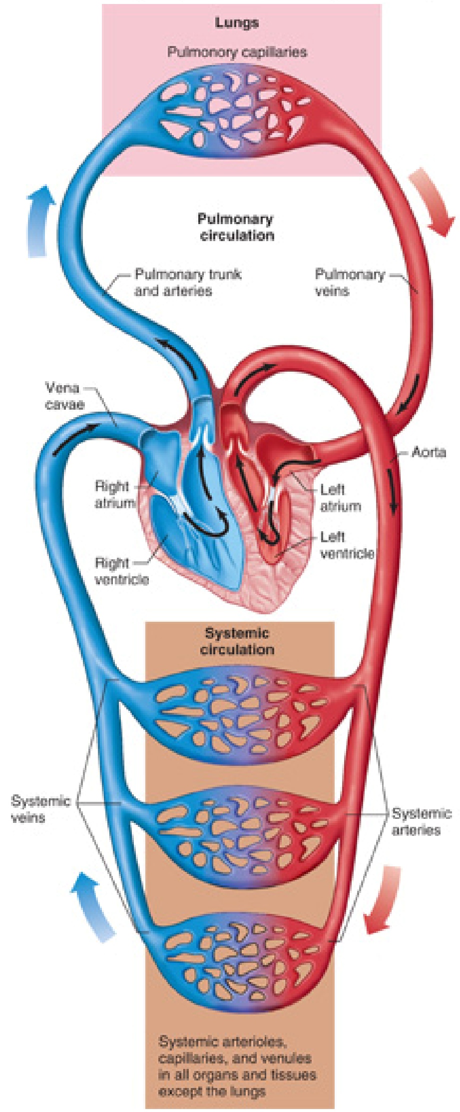


Figure 12-3

The distribution of blood in a comfortable, resting person is shown here.

Dynamic adjustments in blood delivery allow a person to respond to widely varying circumstances, including emergencies.

Organ	Flow at rest ml/min
Brain	650 (13%)
Heart	215 (4%)
Skeletal muscle	1030 (20%)
Skin	430 (9%)
Kidney	950 (20%)
Abdominal organs	1200 (24%)
Other	525 (10%)
Total	5000 (100%)

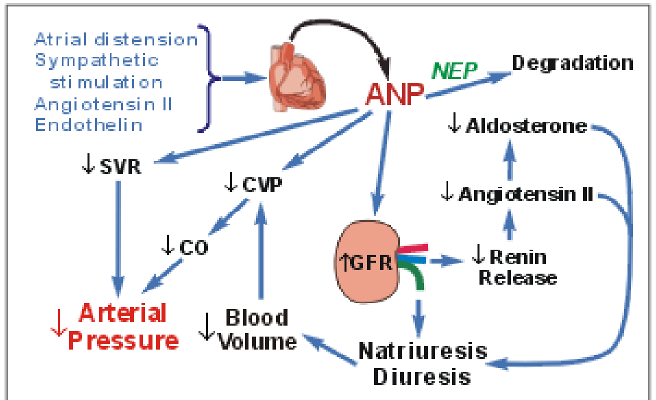
Adapted from Chapman and Mitchell.

TABLE 12–1 The Cardiovascular System

COMPONENT	FUNCTION
Heart	
Atria	Chambers through which blood flows from veins to ventricles. Atrial contraction adds to ventricular filling but is not essential for it.
Ventricles	Chambers whose contractions produce the pressures that drive blood through the pulmonary and systemic vascular systems and back to the heart.
Vascular system	
Arteries	Low-resistance tubes conducting blood to the various organs with little loss in pressure. They also act as pressure reservoirs for maintaining blood flow during ventricular relaxation.
Arterioles	Major sites of resistance to flow; responsible for the pattern of blood flow distribution to the various organs; participate in the regulation of arterial blood pressure.
Capillaries	Sites of nutrient, metabolic end product, and fluid exchange between blood and tissues.
Venules	Sites of nutrient, metabolic end product, and fluid exchange between blood and tissues.
Veins	Low-resistance conduits for blood flow back to the heart. Their capacity for blood is adjusted to facilitate this flow.
Blood	
Plasma	Liquid portion of blood that contains dissolved nutrients, ions, wastes, gases, and other substances. Its composition equilibrates with that of interstitial fluid at the capillaries.
Cells	Includes erythrocytes that function mainly in gas transport, leukocytes that function in immune defenses, and platelets (cell fragments) for blood clotting.

Functions of the heart

- Pumping
- Endocrine
  - Atrial natriuretic peptide (ANP)
  - Brain natriuretic peptide (BNP)



Abbreviations: ANP, atrial natriuretic peptide; NEP, neutral endopeptidase; GFR, glomerular filtration rate; CVP, central venous pressure; CO, cardiac output; SVR, systemic vascular resistance.

Figure 12-6

The Heart

The major external and internal parts of the heart are shown in this diagram.

The black arrows indicate the route taken by the blood as it is pumped along.

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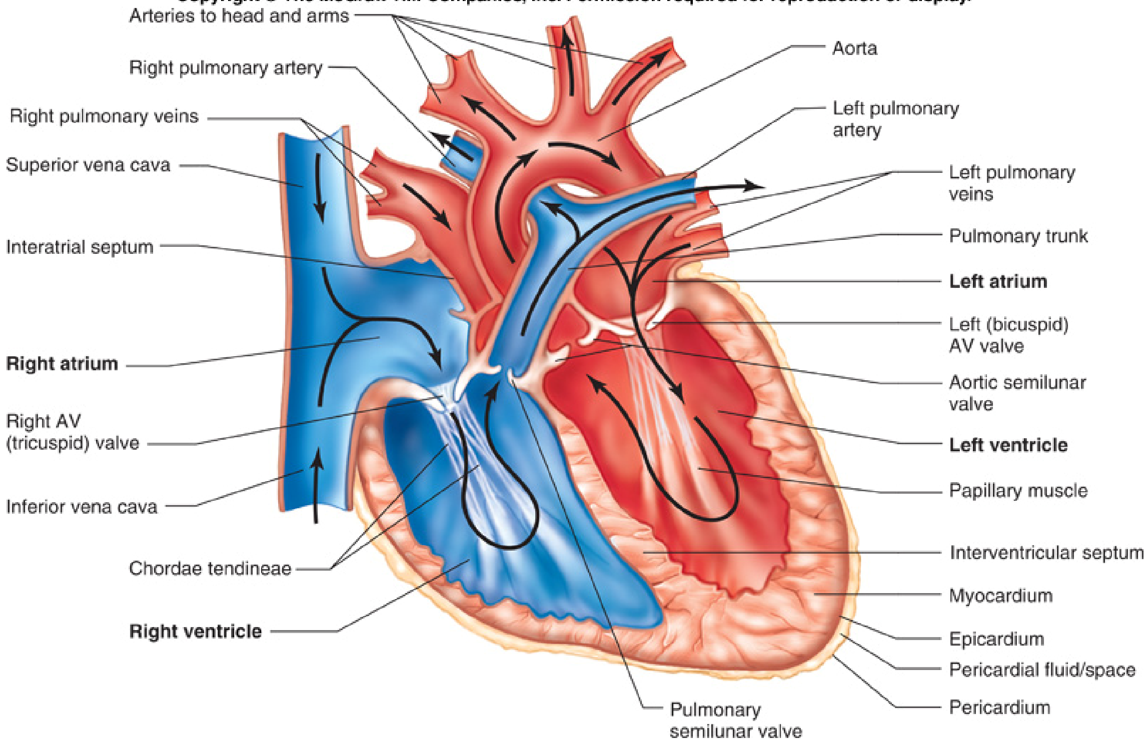
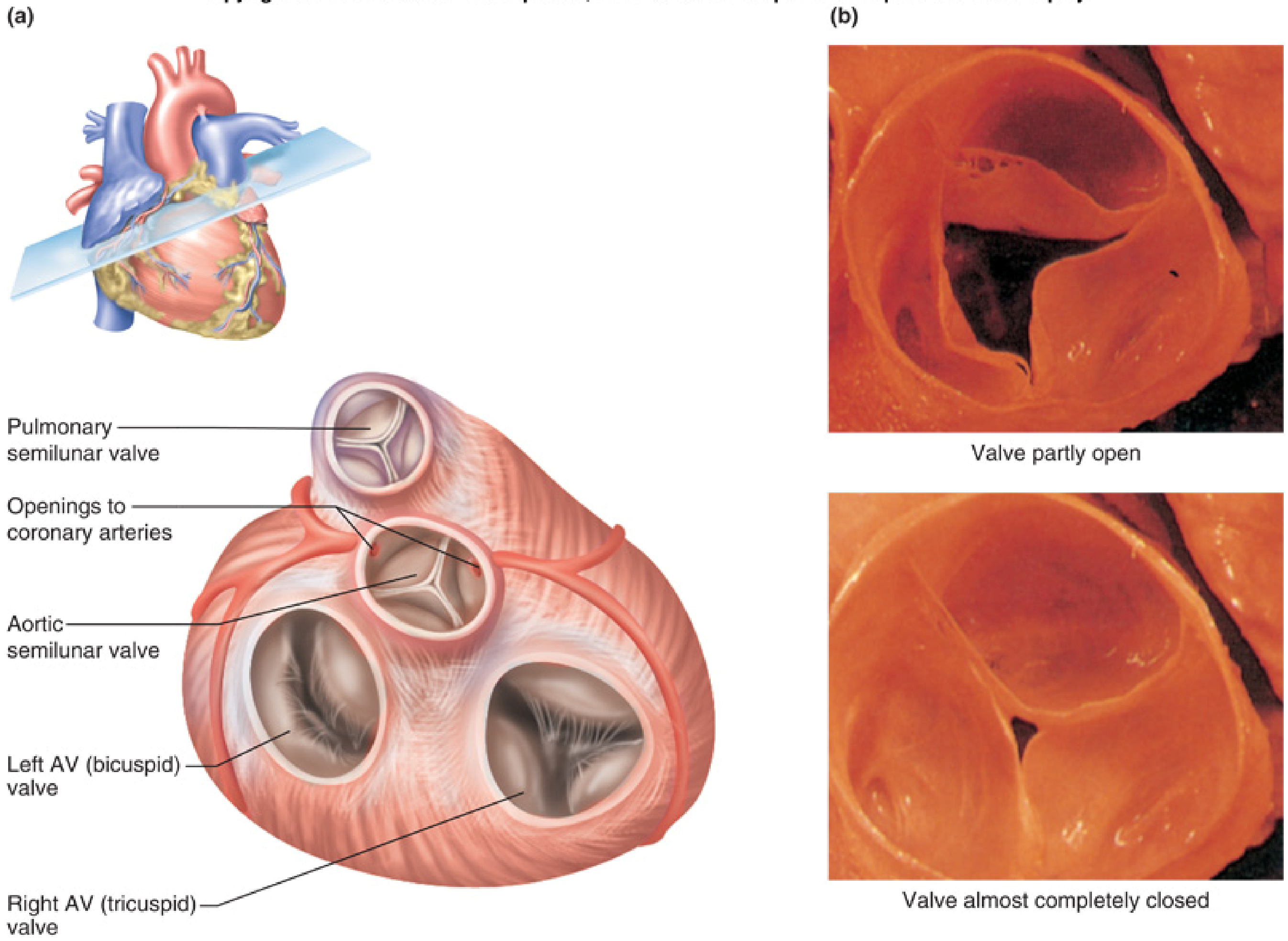


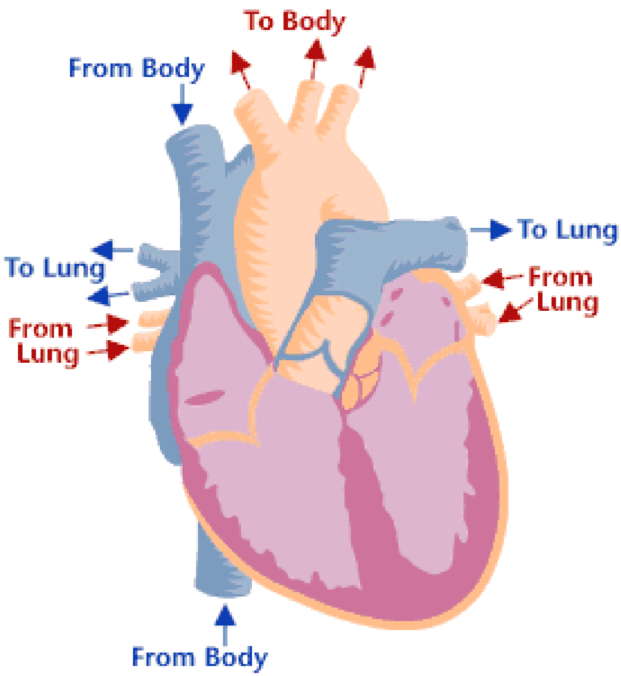


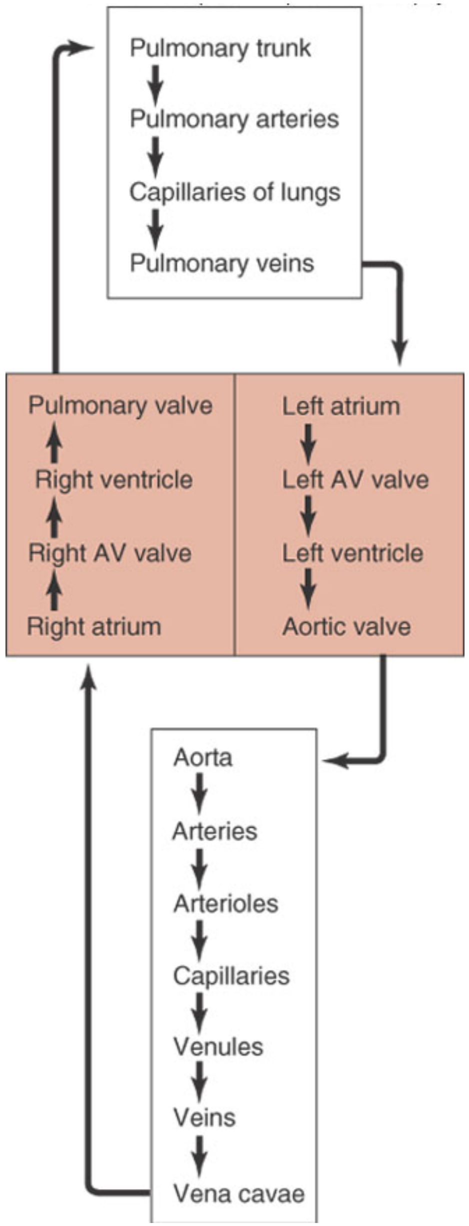
From R. Carola, J. P. Harley, and C. R. Noback, Human Anatomy and Physiology, McGraw-Hill, New York, 1990 (photos by Dr.Wallace McAlpine).

Valves of the heart

Figure 12-8

The general route of the blood through the body is shown, including passage through the heart (colored box).



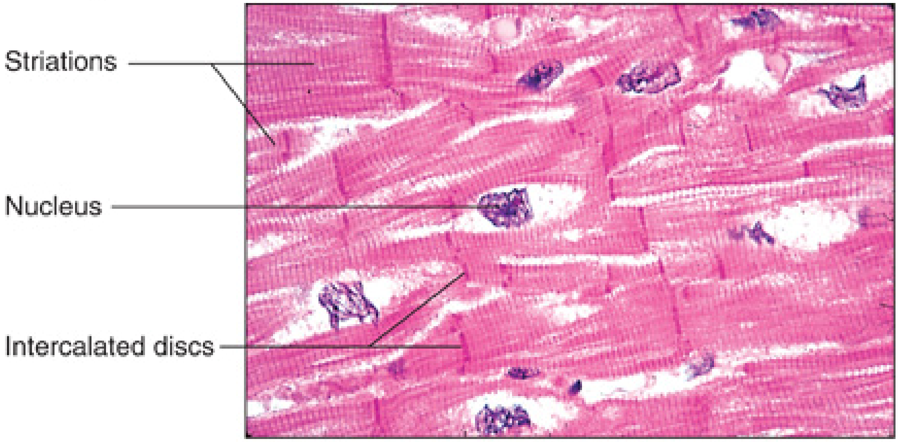


- Three major types of cardiac muscle:
  - Atrial muscle
  - Ventricular muscle
  - Specialized excitatory and conductive muscle

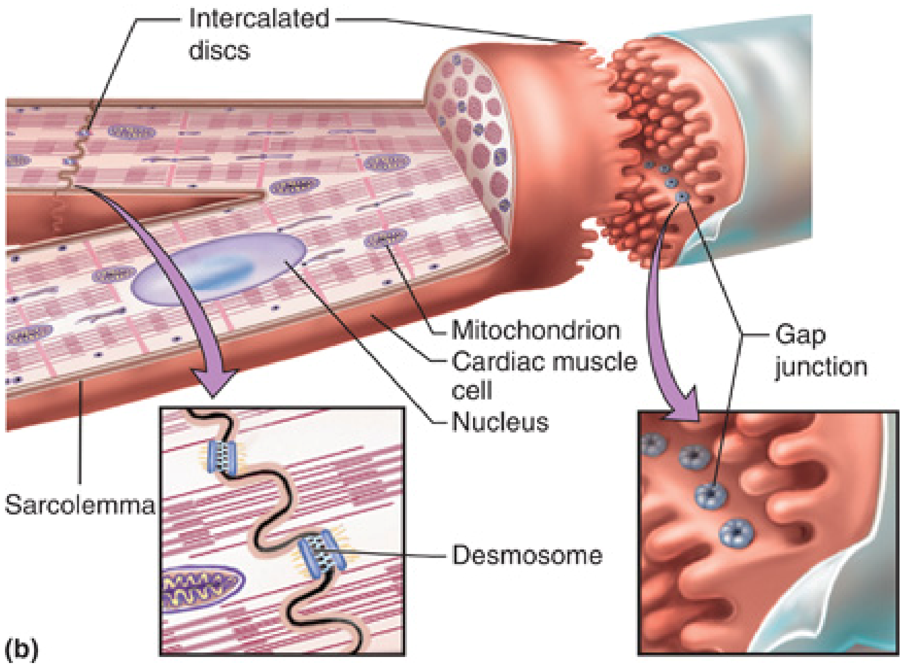
Contractile cells

Autorhythmic cells

Cardiac muscle



(a)



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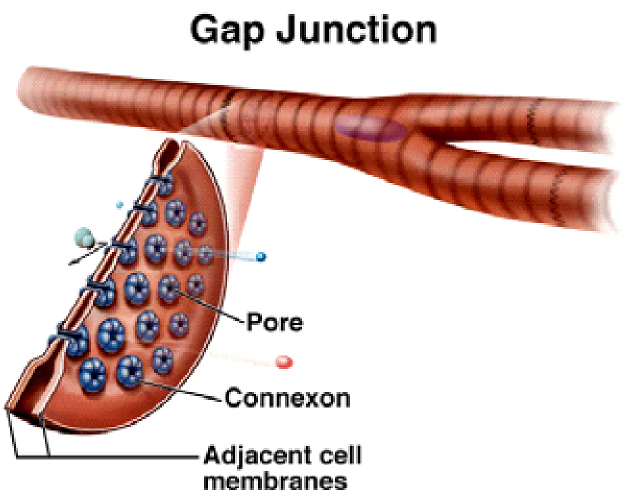
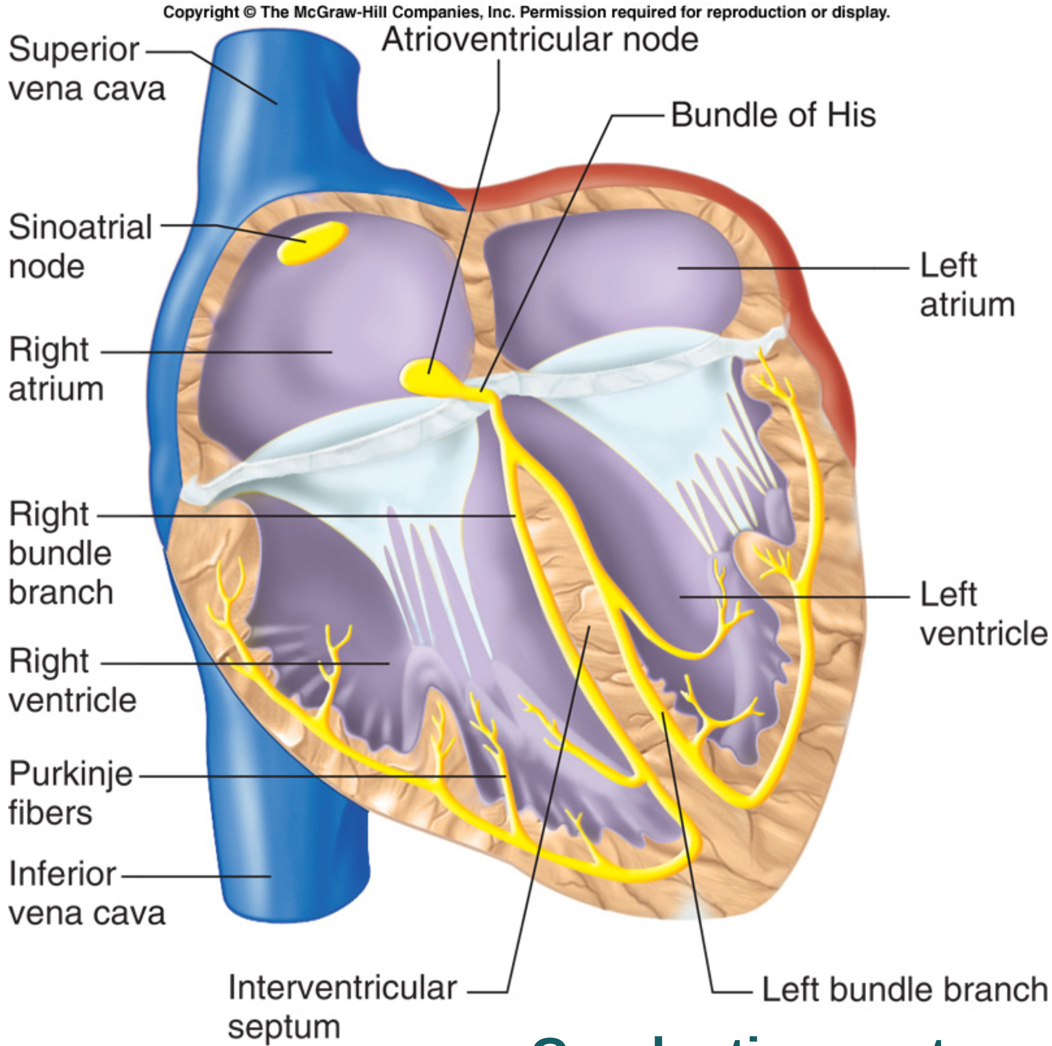


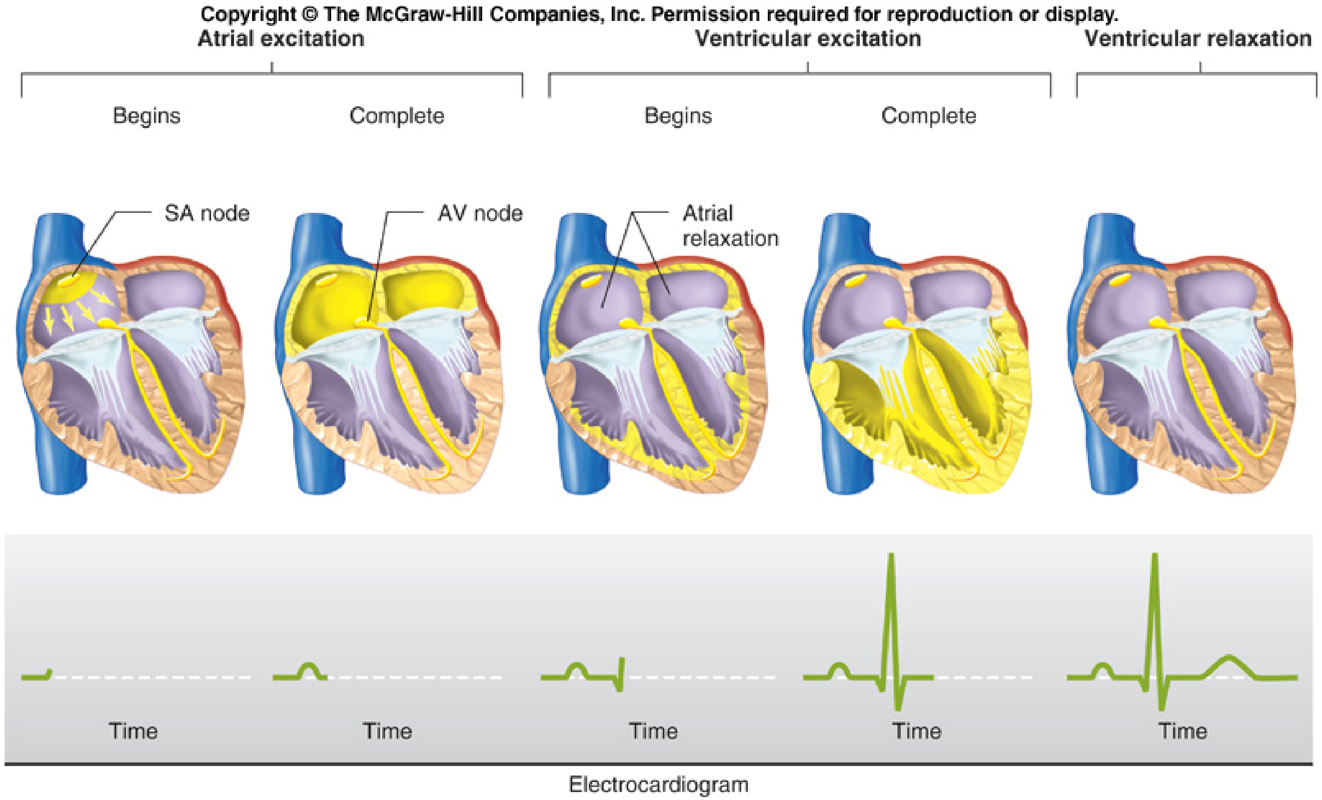
Figure 12-10



Conducting system of the heart

Figure 12-11

Sequence of cardiac excitation



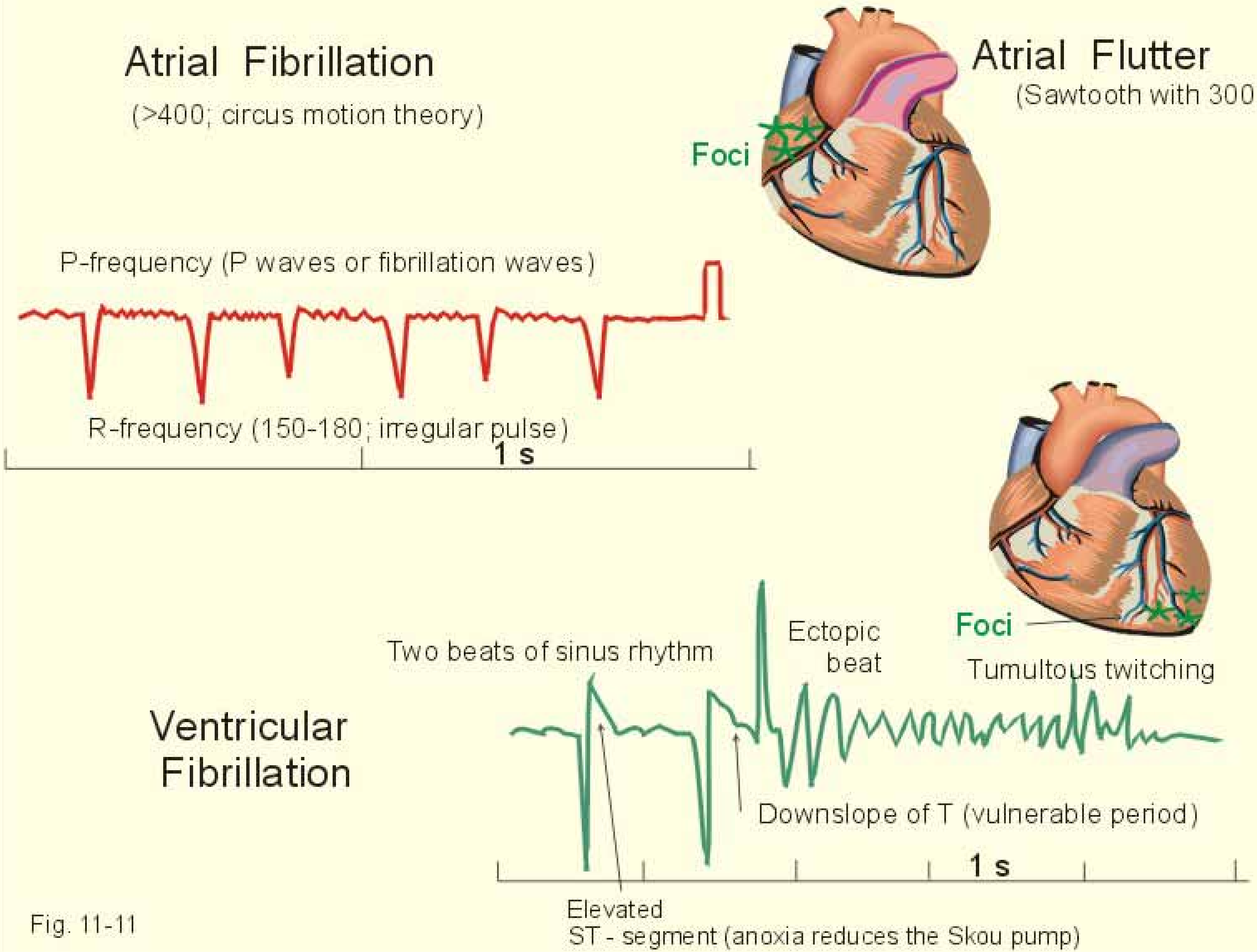
The sinoatrial node is the heart's pacemaker because it initiates each wave of excitation with atrial contraction.

The Bundle of His and other parts of the conducting system deliver the excitation to the apex of the heart so that ventricular contraction occurs in an upward sweep.

General process of excitation and contraction of cardiac muscle

- Initiation of action potentials in sinoatrial node
- Conduction of action potentials along specialized conductive system
- Excitation-contraction coupling
- Muscle contraction

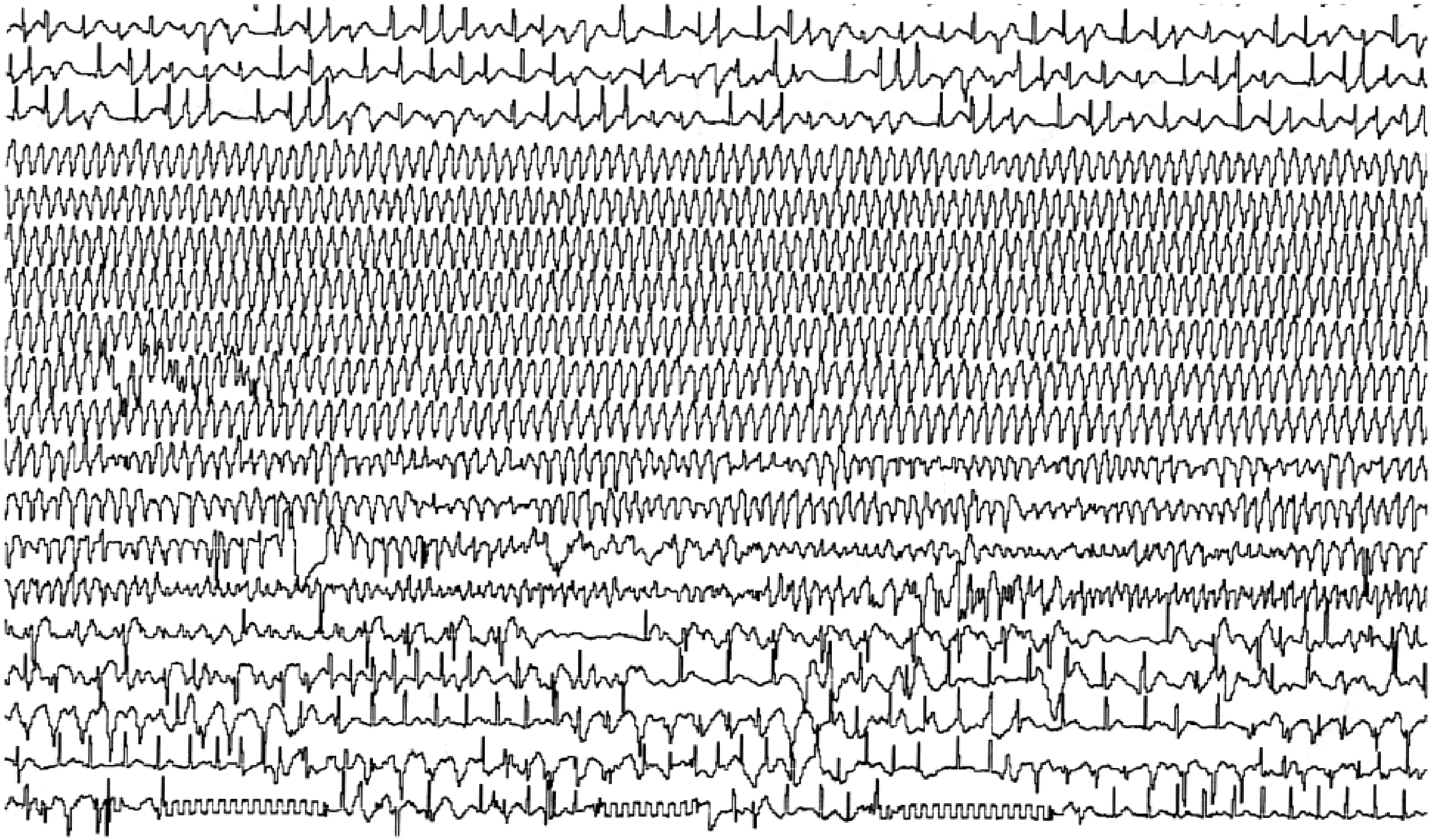
Click here to play the
Conducting System
of the Heart
Flash Animation



Atrial Fibrillation
(>400; circus motion theory)
Foci
Atrial Flutter
(Sawtooth with 300 P)
P-frequency (P waves or fibrillation waves)
R-frequency (150-180; irregular pulse)
1 s
Two beats of sinus rhythm
Ectopic beat
Foci
Tumultous twitching
Ventricular Fibrillation
Downslope of T (vulnerable period)
1 s
Elevated
ST - segment (anoxia reduces the Skou pump)

Fig. 11-11

KMc



Ventricular Defibrillation

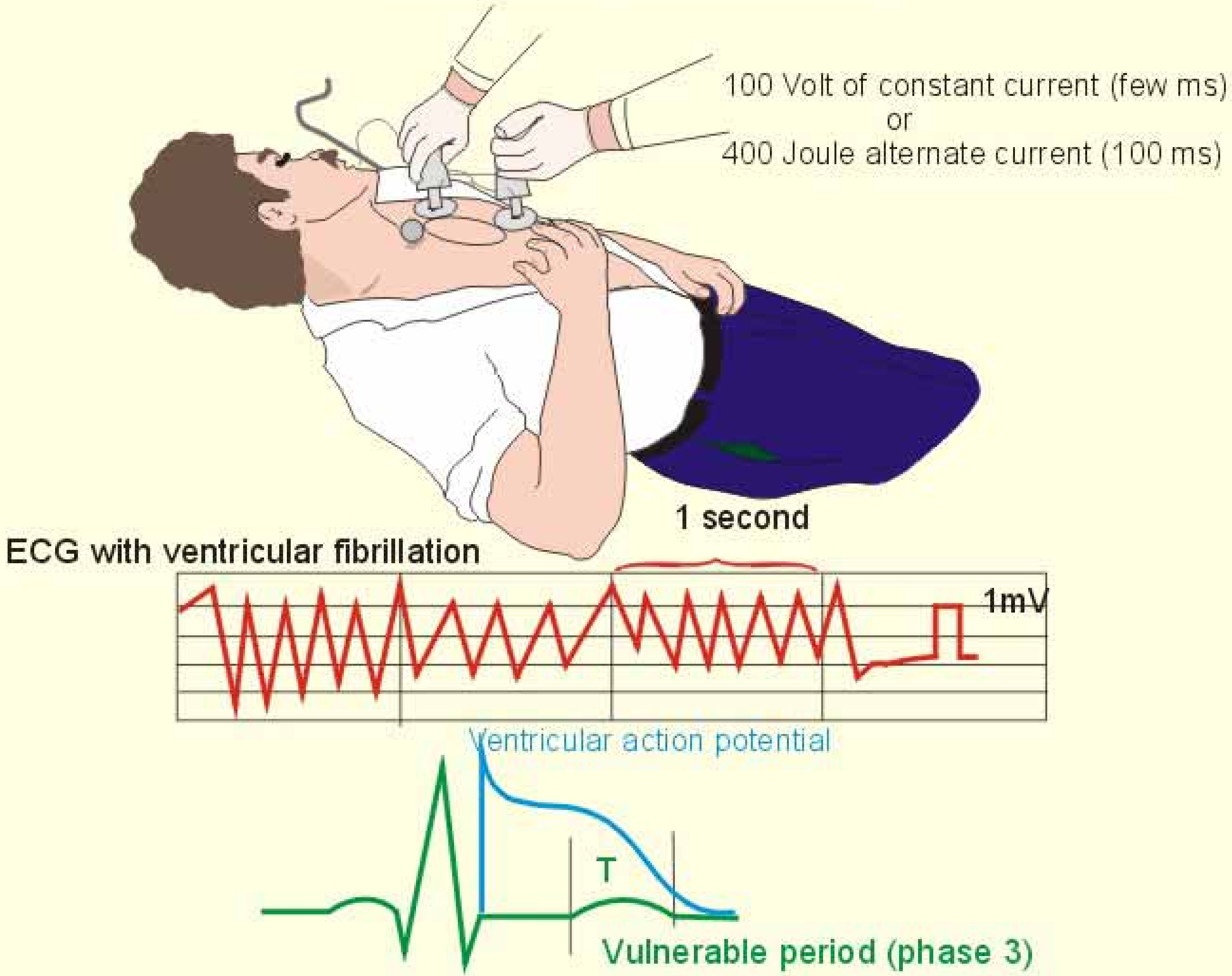
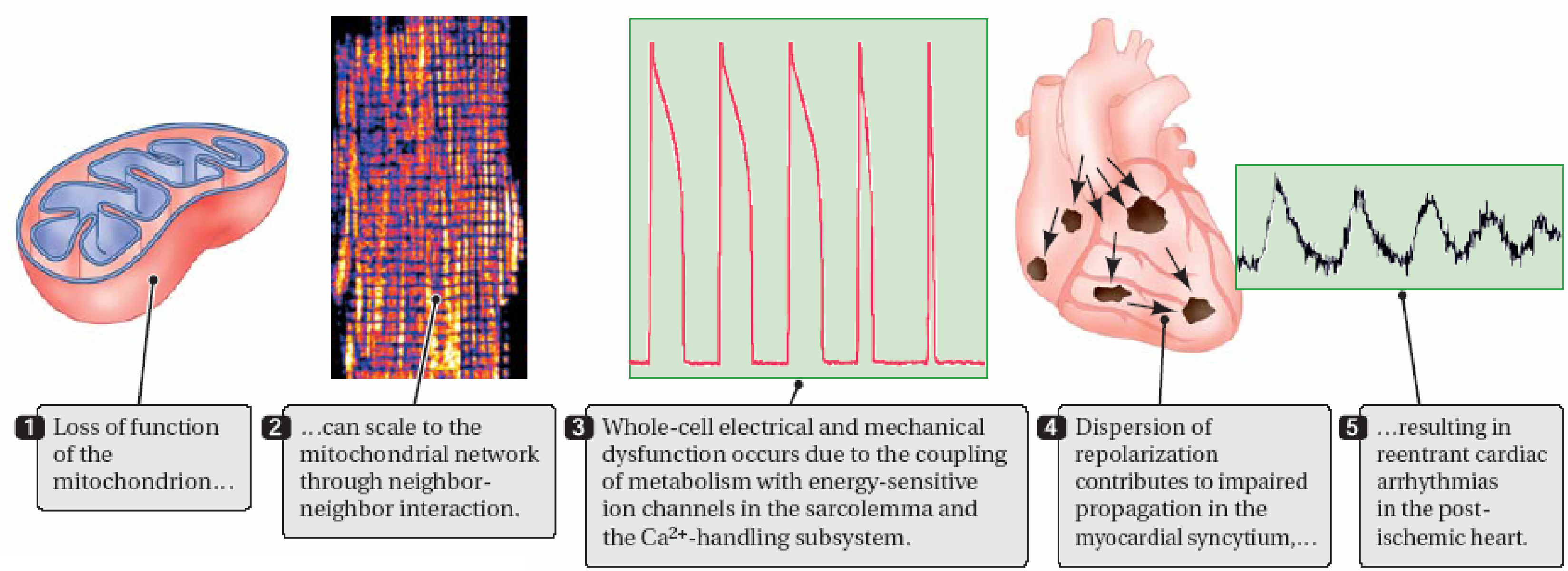
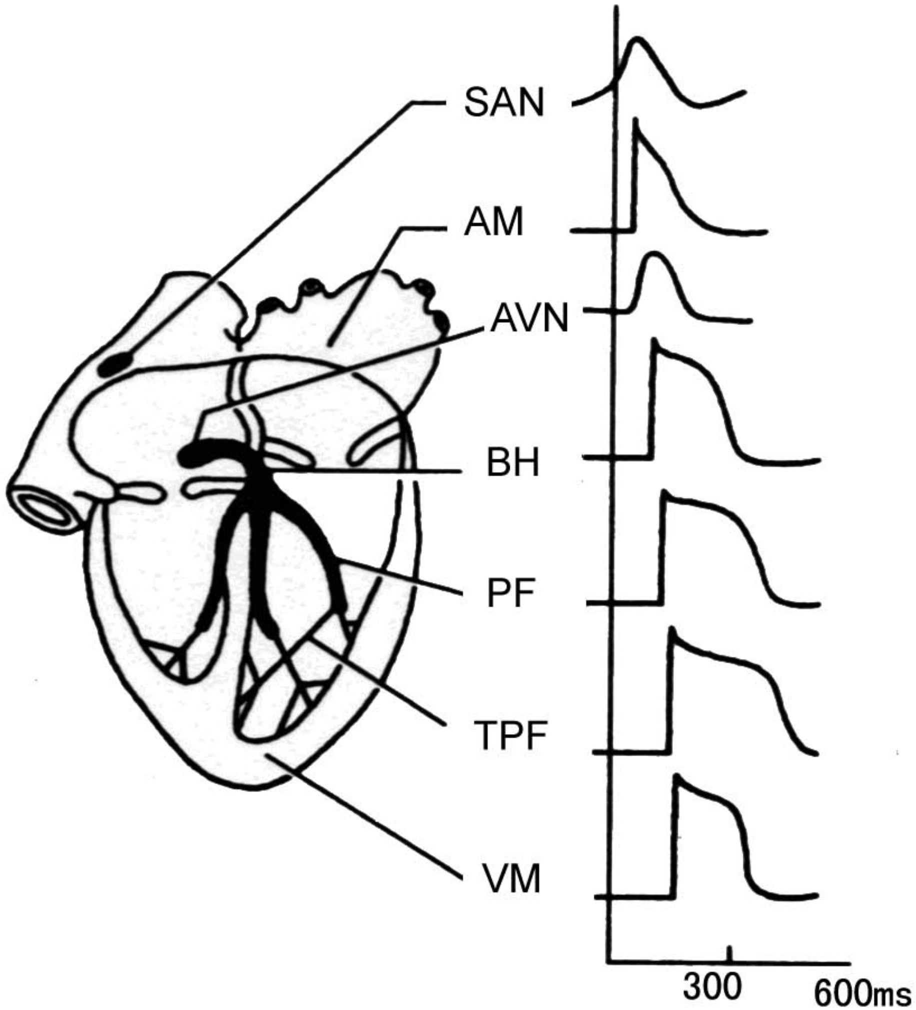


Fig. 11-10

KMc

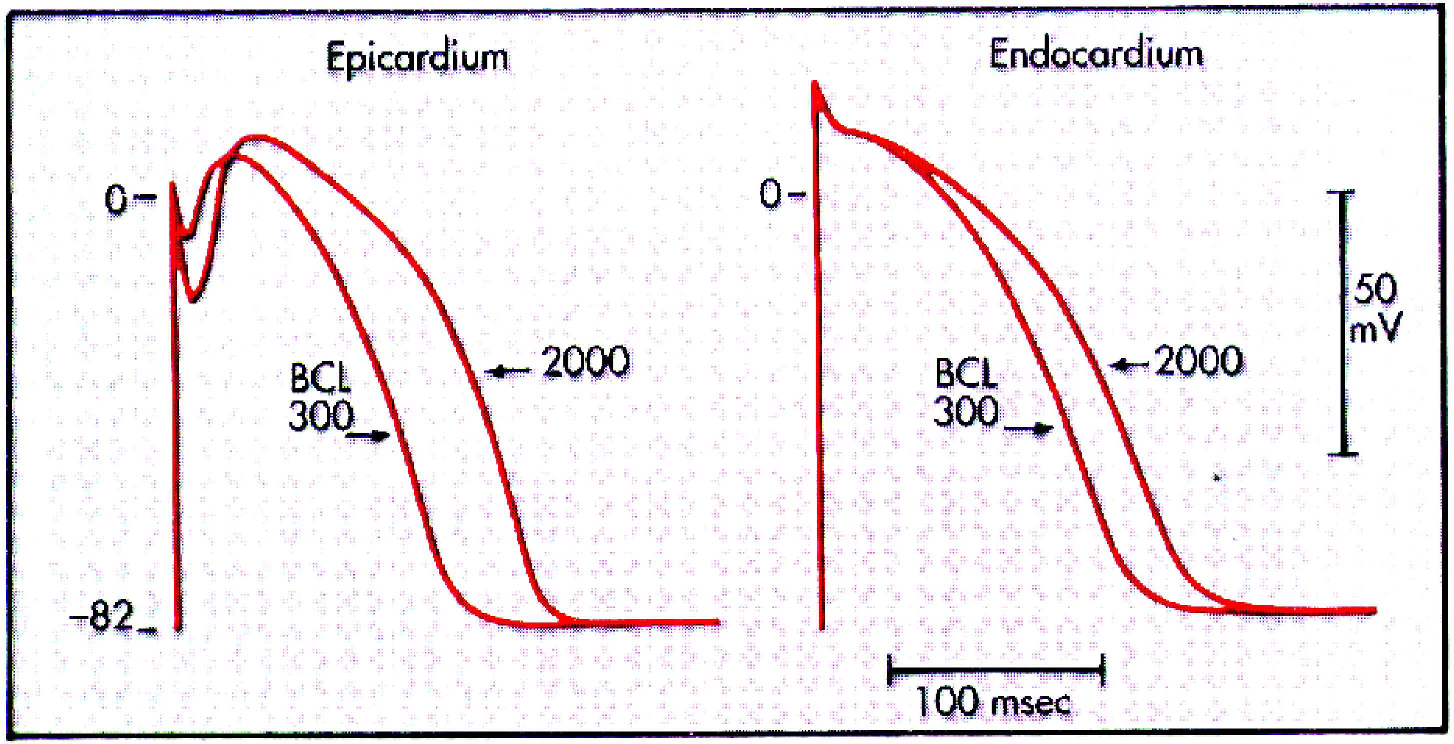


Scaling from the level of the organelle to the organ



Transmembrane potentials recorded in different heart regions

Transmembrane potentials in epicardium and endocardium

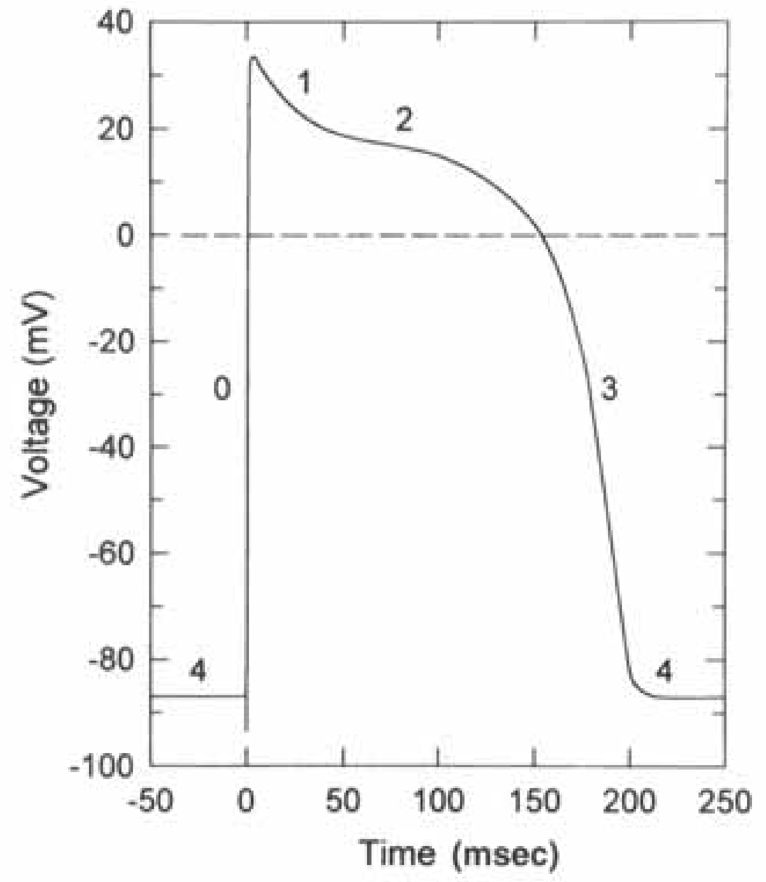


Transmembrane potential of ventricular cells and its ionic mechanisms

Resting Potential: -90 mV

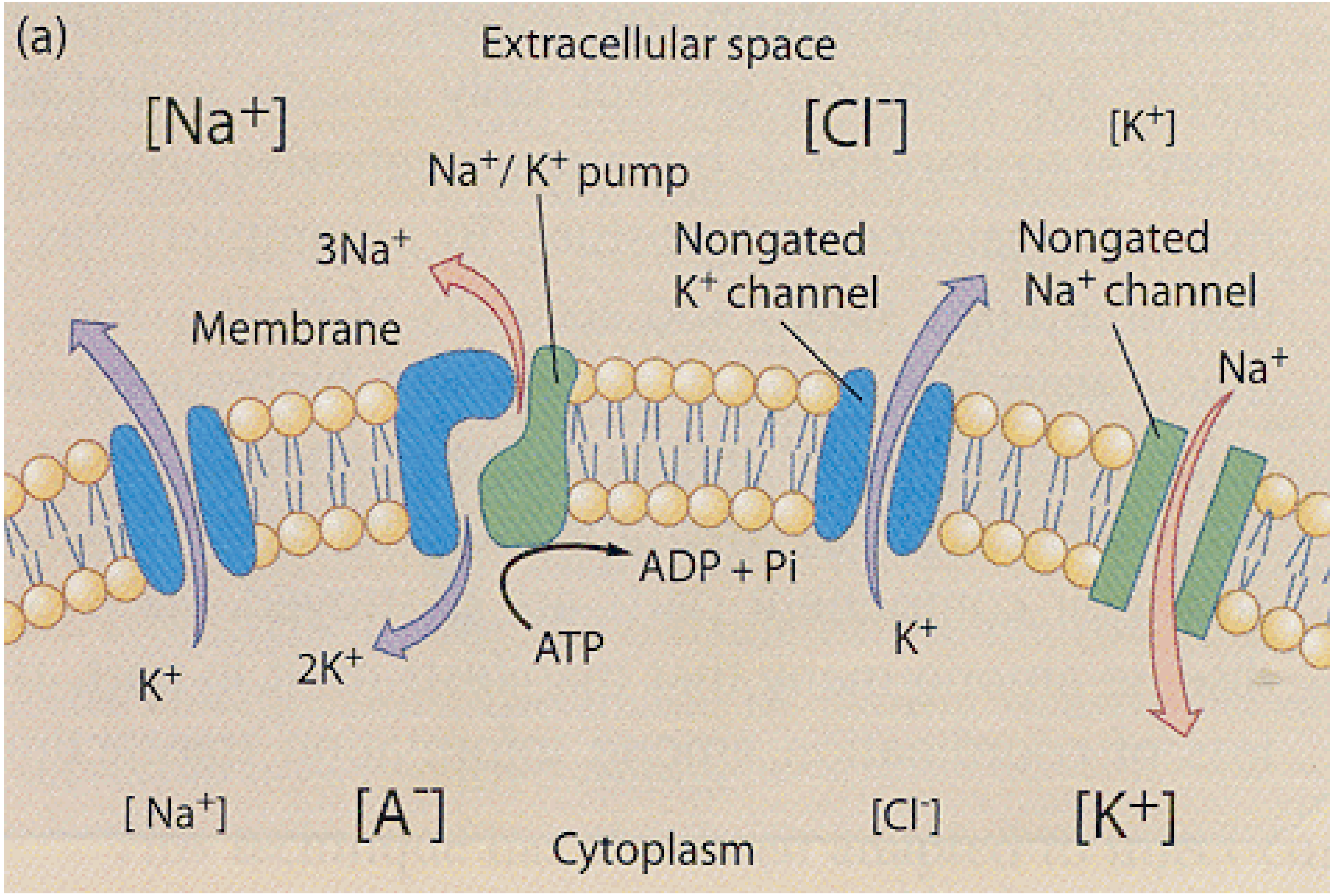
Action Potential

- Phase 0: Depolarization
- Phase 1: Early phase of rapid repolarization
- Phase 2: Plateau
- Phase 3: Late phase of rapid repolarization
- Phase 4: Resting phase



Ionic mechanisms

- Resting potential
  - K^+ equilibrium potential
  - Na^+-inward background current
  - Electrogenic Na^+-K^+ pump


(a)
Extracellular space
[Na+]
[Cl-]
[K+]
Na+/ K+ pump
3Na+
Nongated
K+ channel
Nongated
Na+ channel
Membrane
Na+
ADP + Pi
ATP
K+
2K+
K+
[Na+]
[A-]
Cytoplasm
[Cl-]
[K+]

The action potential of a myocardial pumping cell.

- Phase 0
  - Threshold potential (-70mV)
  - Opening of fast Na^+ channel
  - Regenerative cycle

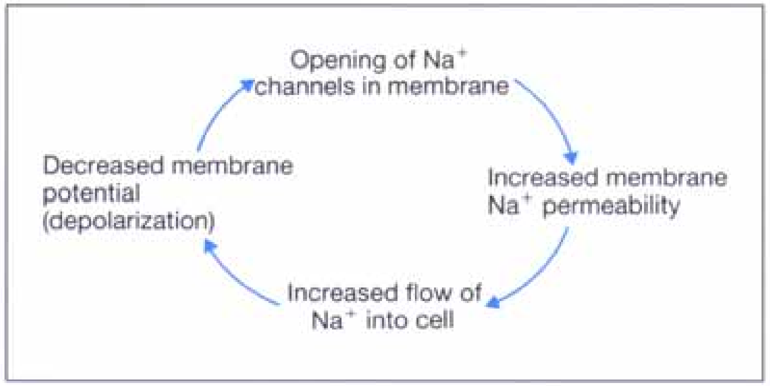
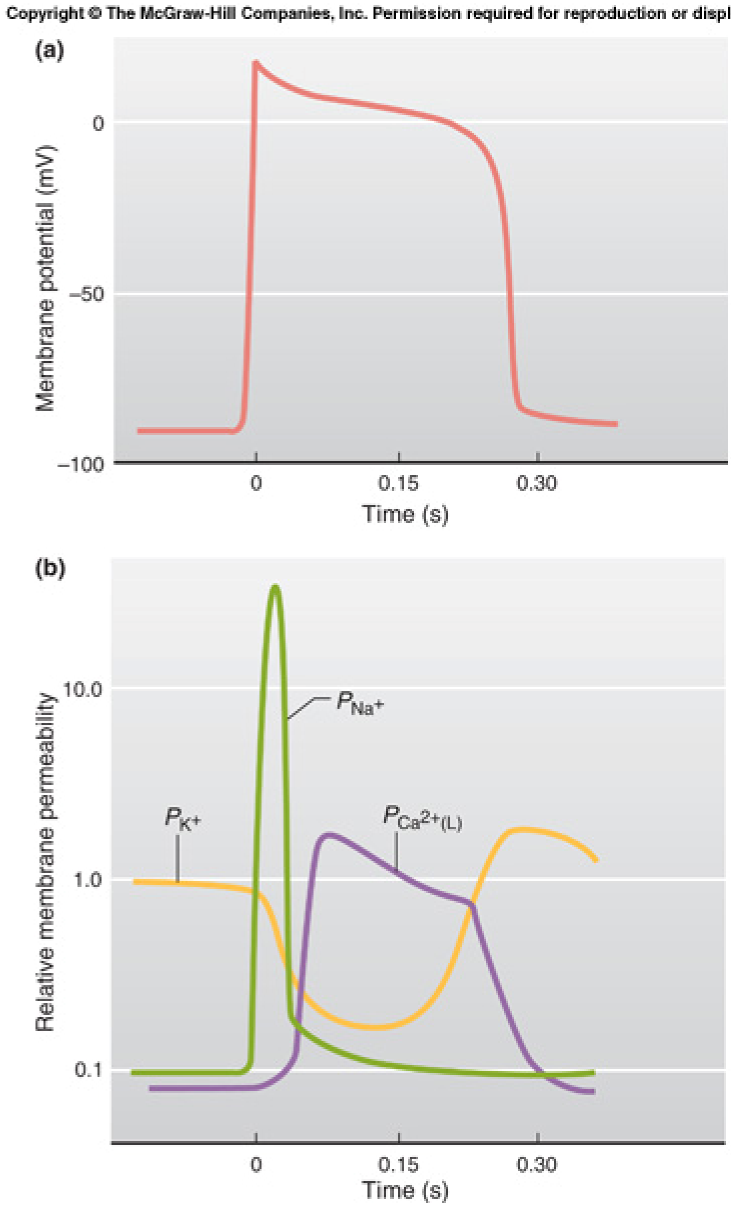


Figure 12-13



- Phase 1
  - Transient outward current, Ito

    K+ current
    - activated at –20 mV
    - opening for 5~10 ms

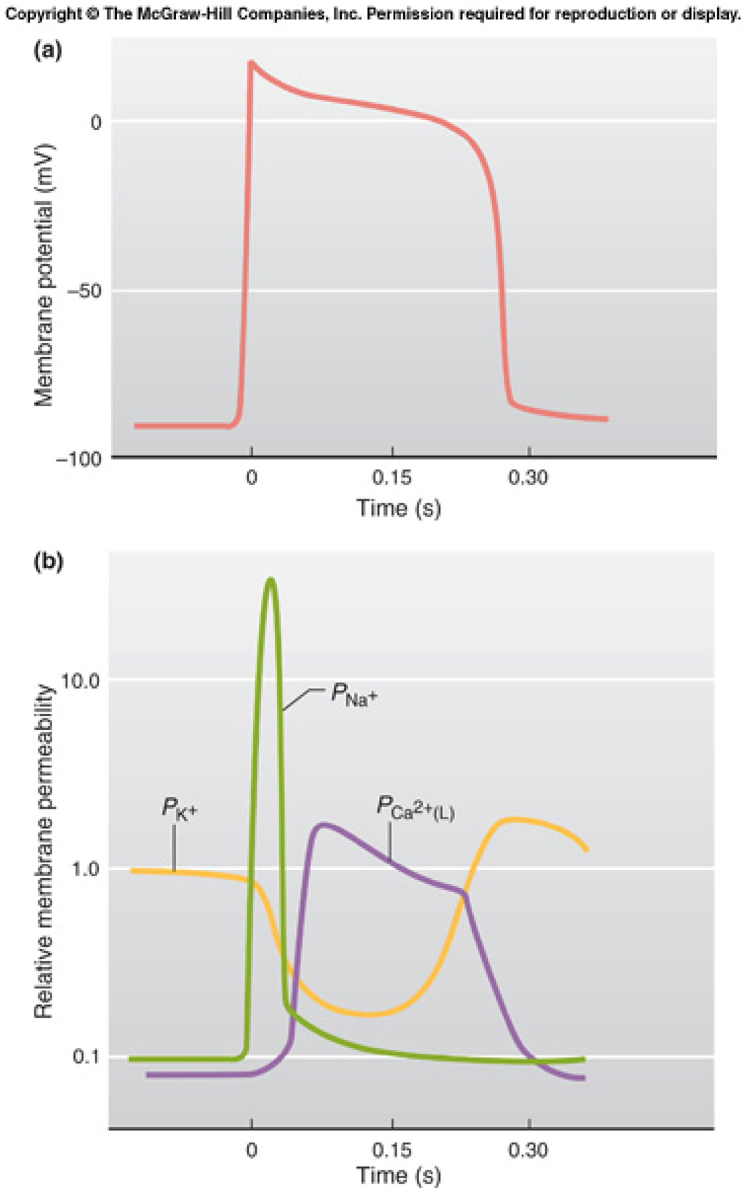


Figure 12-12

- Phase 2

  Inward current ⇄ Outward current

  (Ca^{2+} & Na^{+}) (K^{+} current)

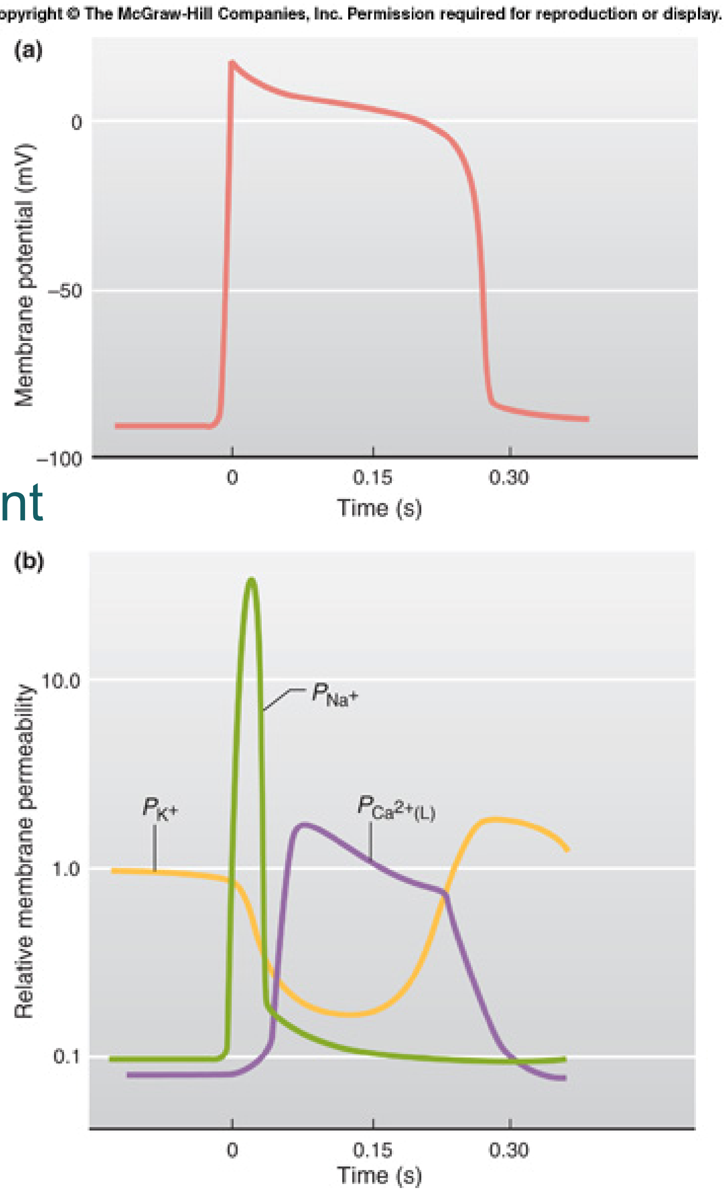


Figure 12-12

Types of Ca^{2+} channels in cardiac cells:

(1) L-type (long-lasting) (Nowycky, 1985)

(2) T-type (transient) (Nowycky, 1985)

	Ca^{2+} channels	
	L-type	**T-type**
Duration of current	long-lasting	transient
Activation kinetics	slower	faster
Inactivation kinetics	slower	faster
Threshold	high (-35mV)	Low (-60mV)
cAMP/cGMP-regulated	Yes	No
Phosphorylation-regulated	Yes	No
Openers	Bay-K-8644	-
Blockers	varapamil	Tetramethrin
	nifedipine, diltiazem	Ni^{2+}
Inactivation by $[Ca^{2+}]_i$	Yes	slight
Patch-clamp recording	run-down	relatively stable

Outward current (K^+ current):

(1) inward rectifier K^+ current (I_{K1})

(2) delayed rectifier K^+ current (I_K)

- Phase 3

  Inactivation of Ca^{2+} channel

  Outward K^+ current dominates

  I_K: Progressively increased

  I_{K1}: Regenerative K+ Outward Current

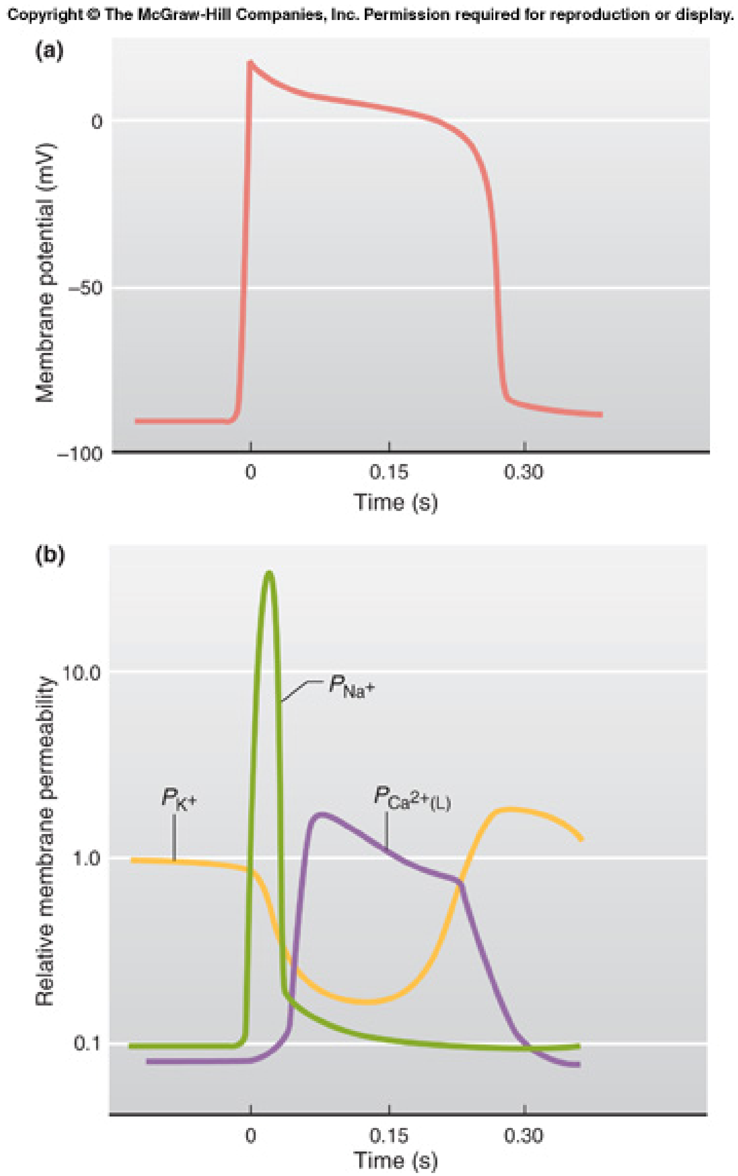


Figure 12-12

- Phase 4
  - Na^+-Ca^{2+} exchange
    - Sarcolemmal Ca^{2+} pump
    - SR Ca^{2+} pump
    - Na^+-K^+ pump

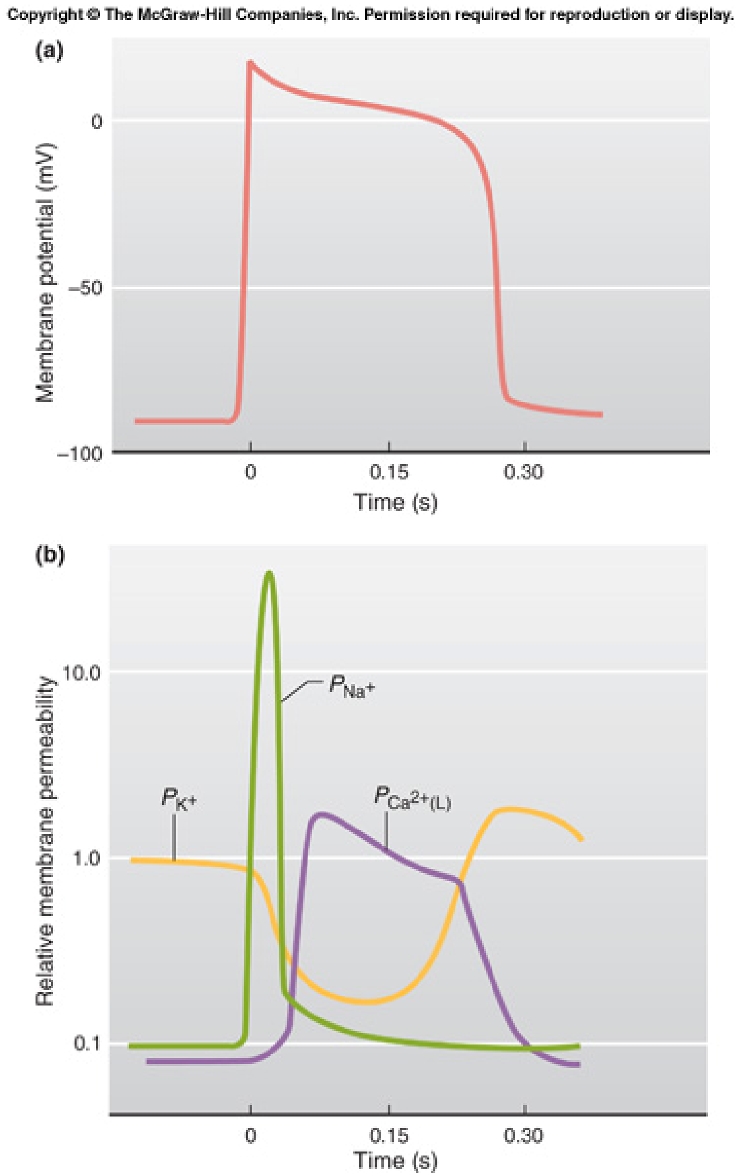
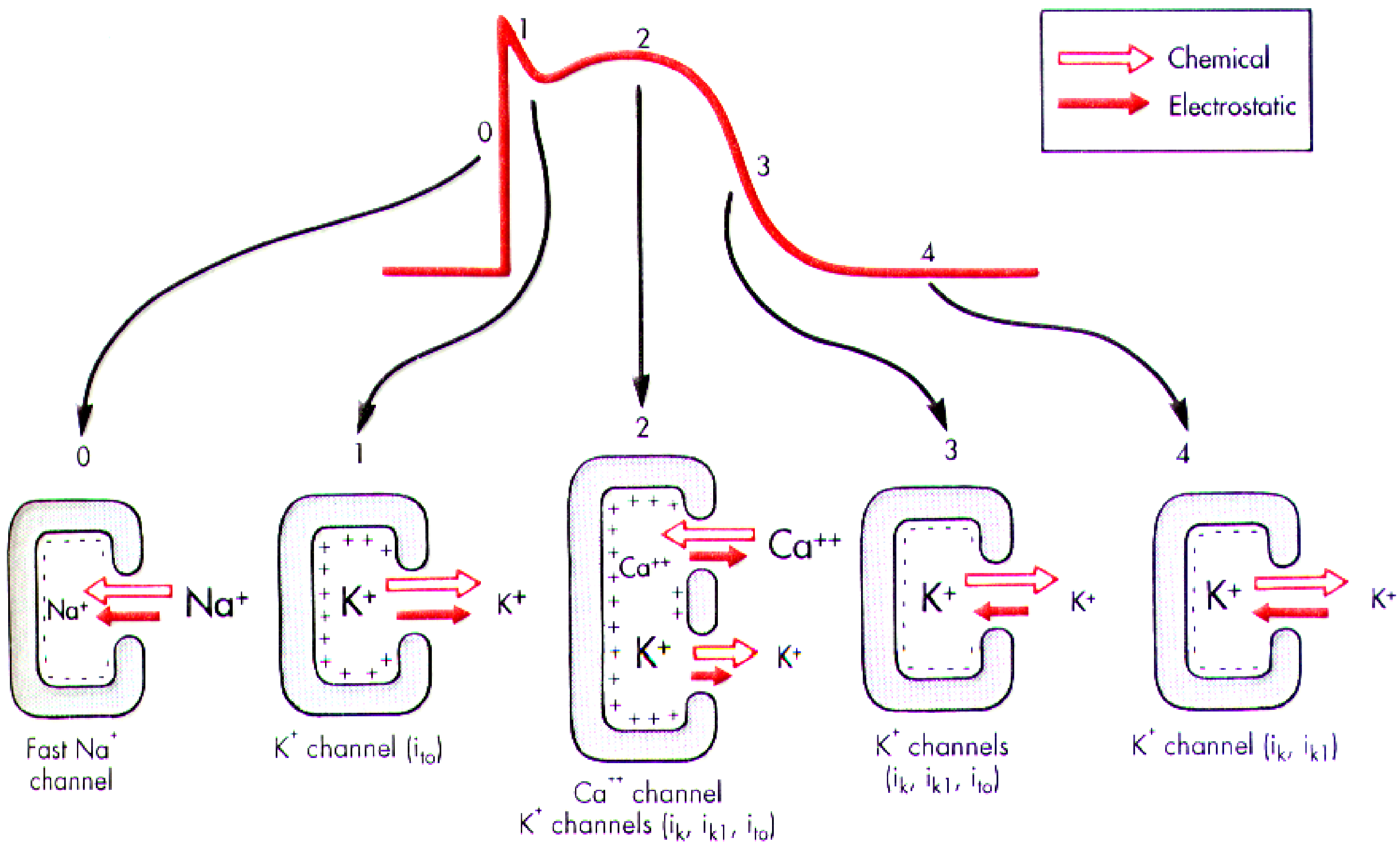
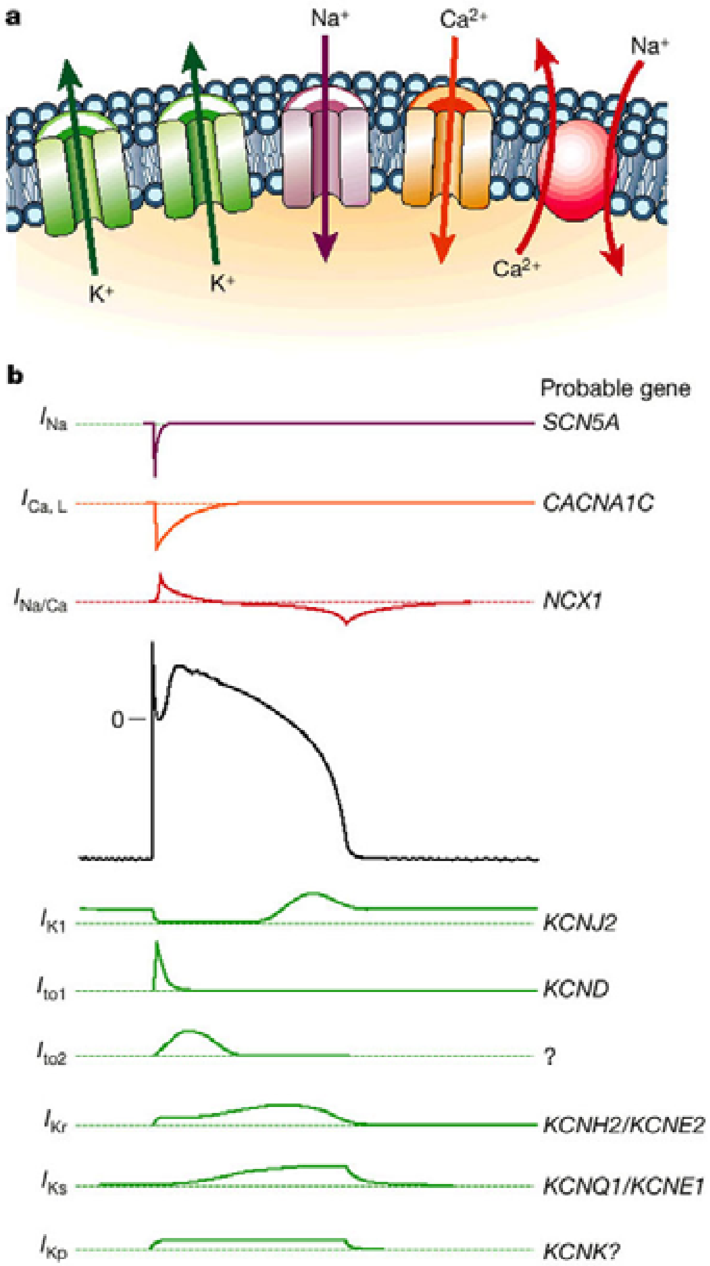


Figure 12-12



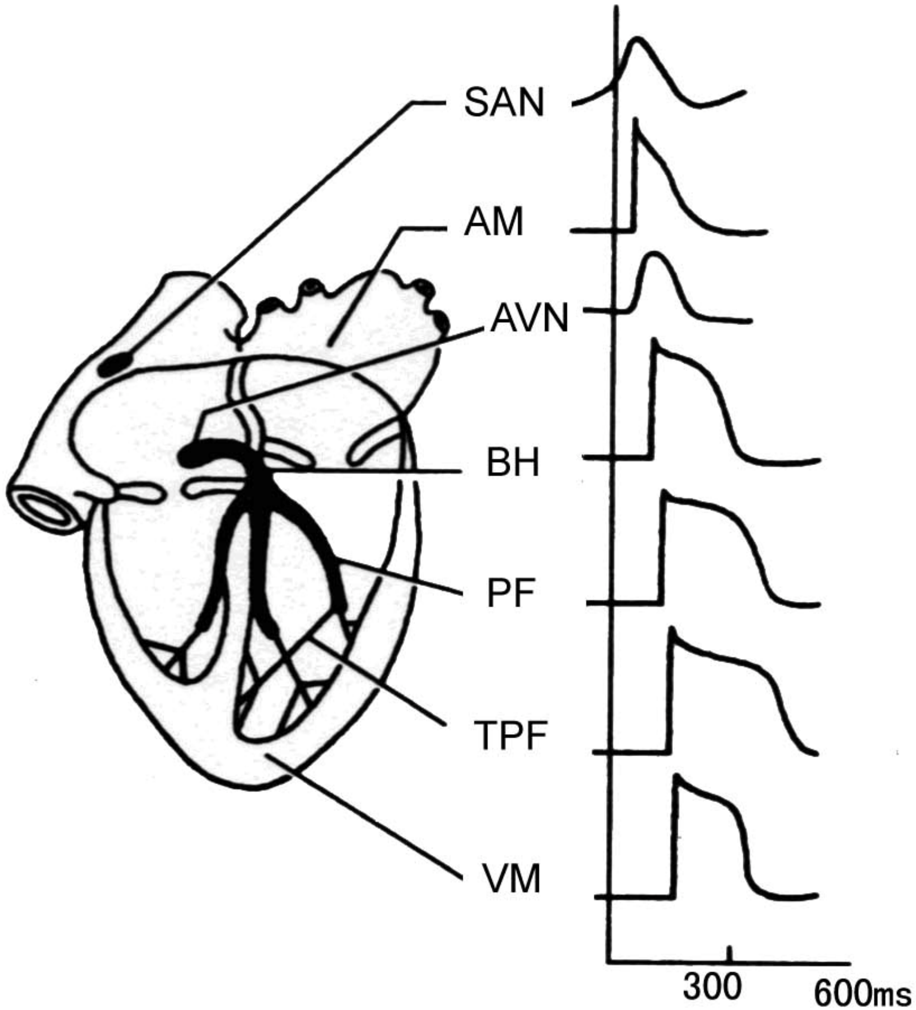
Chemical
Electrostatic
0
1
2
3
4
Na+
Na+
K+
K+
Ca++
Ca++
K+
K+
K+
K+
K+
K+
Fast Na+ channel
K+ channel (ito)
Ca++ channel
K+ channels (ik, ik1, ito)
K+ channels (ik, ik1, ito)
K+ channel (ik, ik1)



a, The key ion channels (and an electrogenic transporter) in cardiac cells. K+ channels (green) mediate K+ efflux from the cell; Na+ channels (purple) and Ca2+ channels (yellow) mediate Na+ and Ca2+ influx, respectively. The Na+/Ca2+ exchanger (red) is electrogenic, as it transports three Na+ ions for each Ca2+ ion across the surface membrane.
b, Ionic currents and genes underlying the cardiac action potential. Top, depolarizing currents as functions of time, and their corresponding genes; centre, a ventricular action potential; bottom, repolarizing currents and their corresponding genes.

From the following article:
Cardiac channelopathies
Eduardo Marbán
Nature 415, 213-218(10 January 2002)
doi:10.1038/415213a

Click here to play the Action Potential in Cardiac Muscle Cell Flash Animation

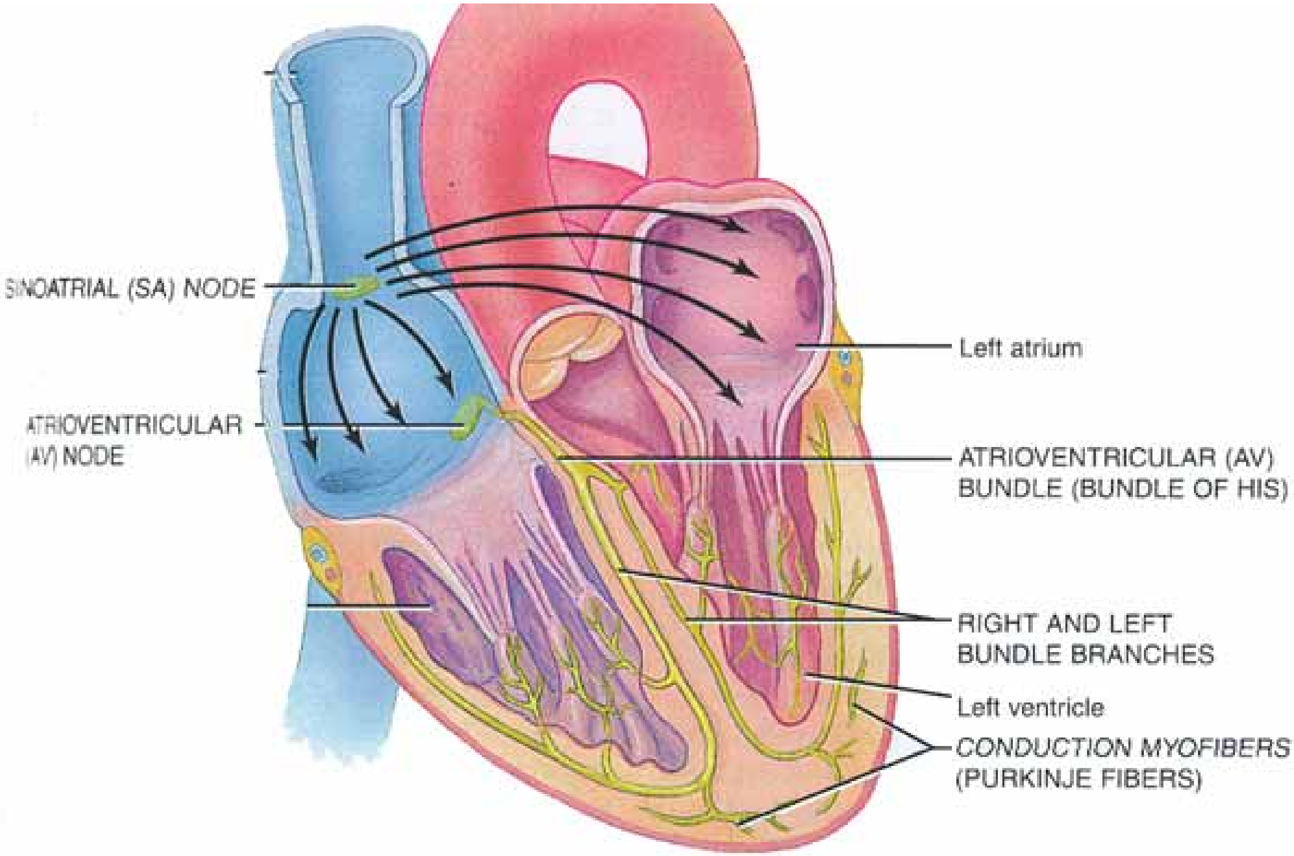


Transmembrane potentials recorded in different heart regions

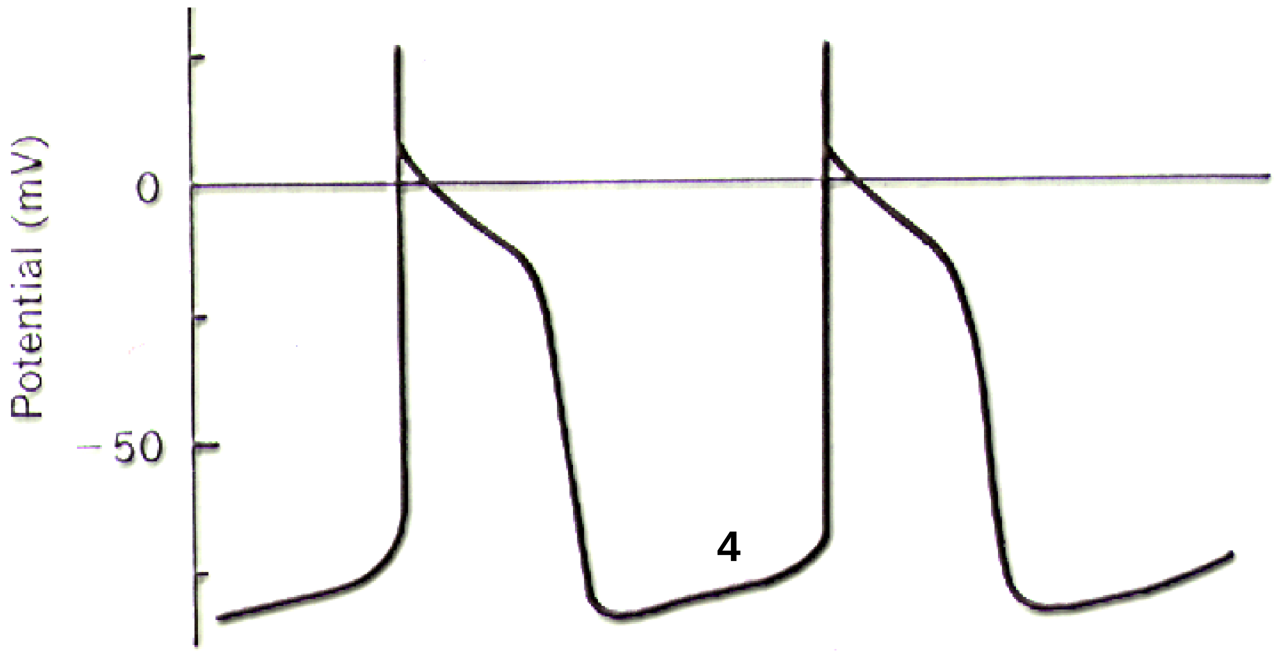
Transmembrane potential of autorhythmic cells and its ionic mechanisms

Contractile cells	Autorhythmic cells
Phase 4 stable potential	Phase 4 spontaneous depolarization
Resting potential	Maximal repolarization potential

Purkinje cells



Purkinje cells: Fast response autorhythmic cells



Ionic mechanism

- Phase 0~3：similar to ventricular cells
- Phase 4：
  - (1) I_f – Funny current, Pacemaker current
  - (2) I_k Decay

Characteristics of I_f channel

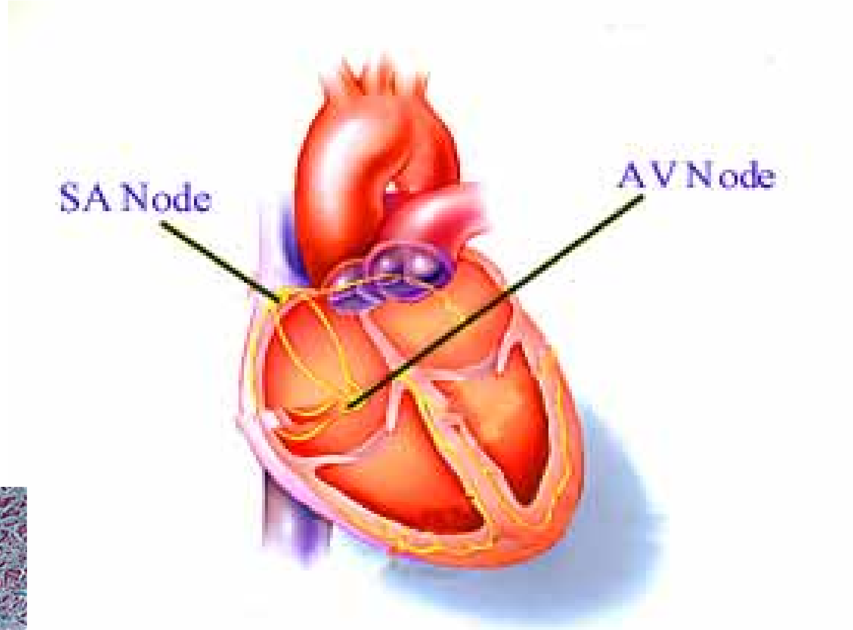
- Na^+, K^+
- Voltage- & time-dependent

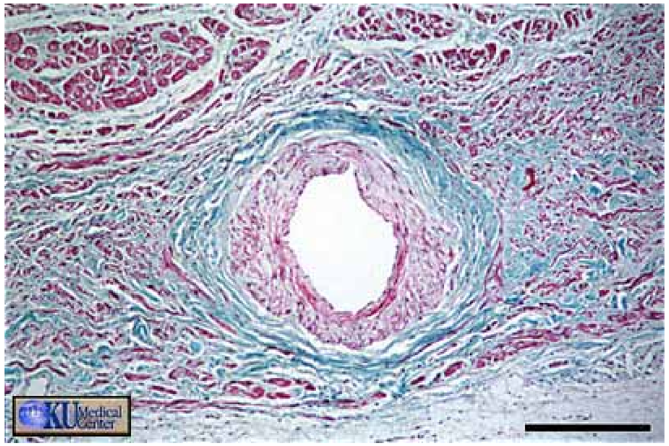
  Activation—— Repolarized to -60mV

  Full activation—— Hyperpolarized to -100mV

  Inactivation—— Depolarized to -50mV
- Blocked by Cs, not by TTX

Sinoatrial cells





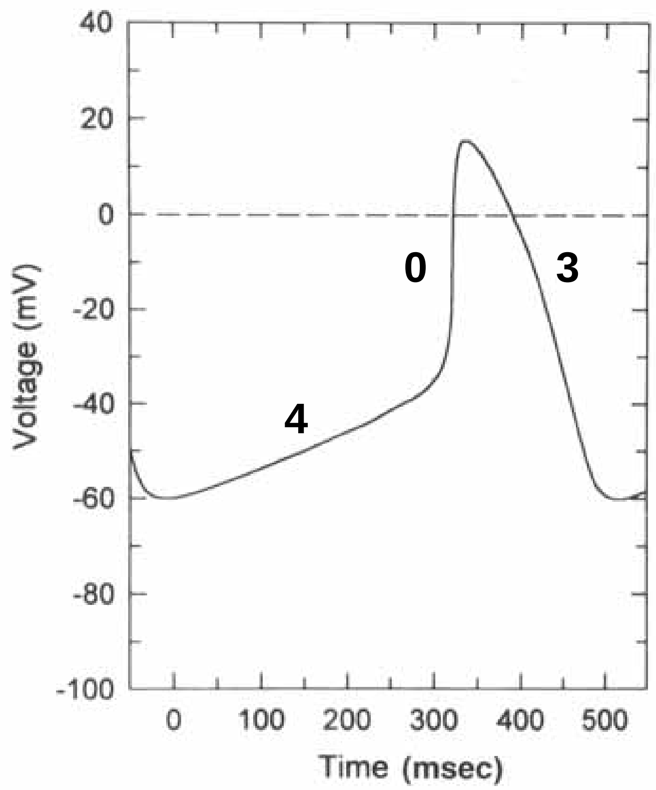
Sinoatrial cells: Slow response autorhythmic cells

- Maximal repolarization

  potential -70mV

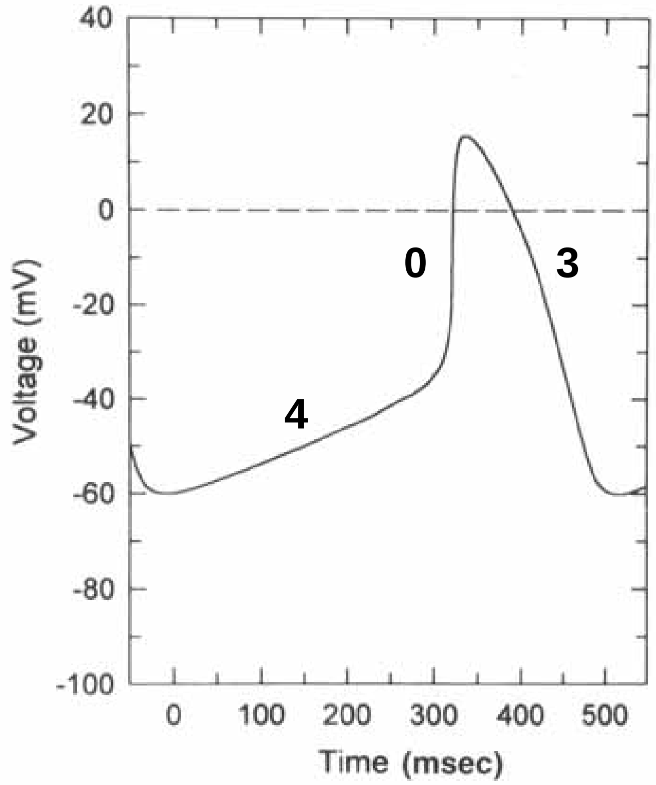
- Threshold potential -40mV

- Phase 0, 3, 4

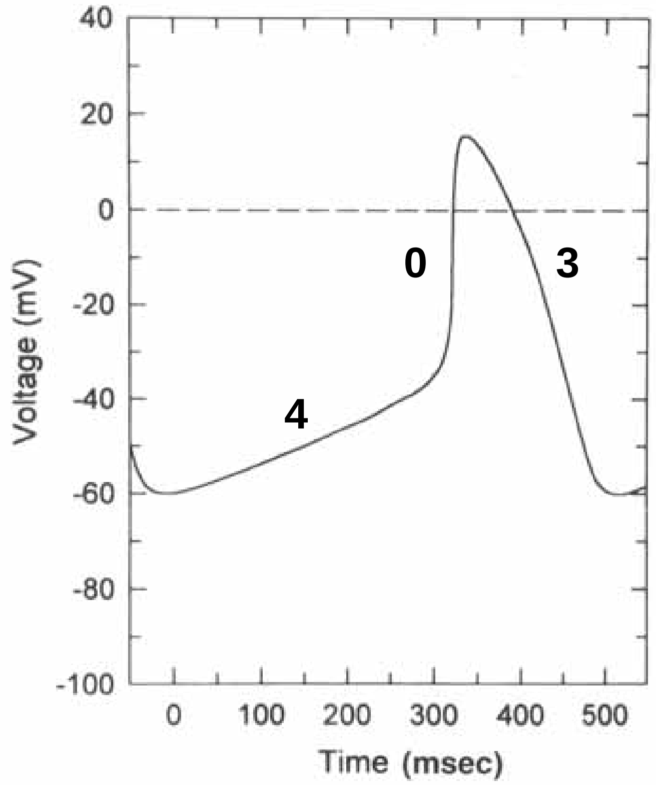


Ionic mechanism

- Phase 0: I_{Ca} ($I_{Ca,L}$)



- Phase 3:
  - Inactivation of L-type Ca^{2+} channel
  - Outward K^+ current (I_k)



- Phase 4：
  - I_k decay

    Inactivated when repolarized to -60mV
  - $I_{Ca,T}$

    Activated when depolarized to -50mV
  - I_f

The action potential of an autorhythmic cardiac cell.

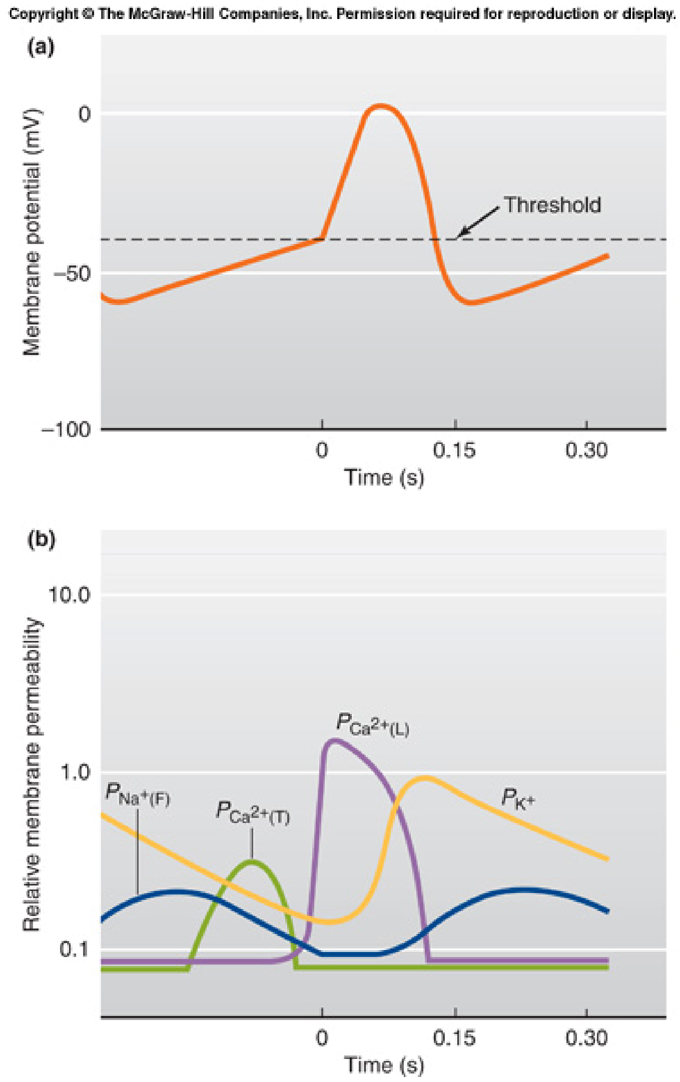
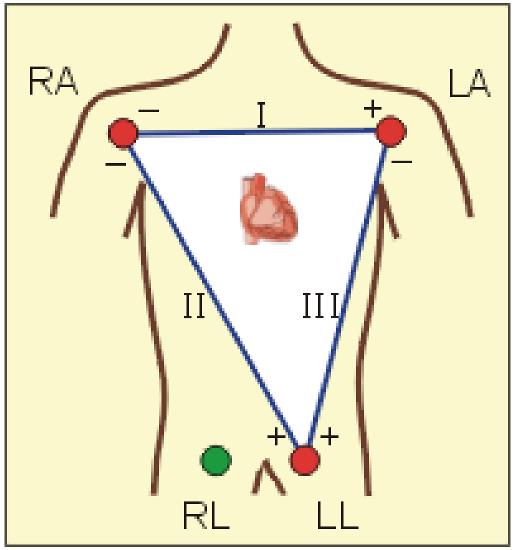
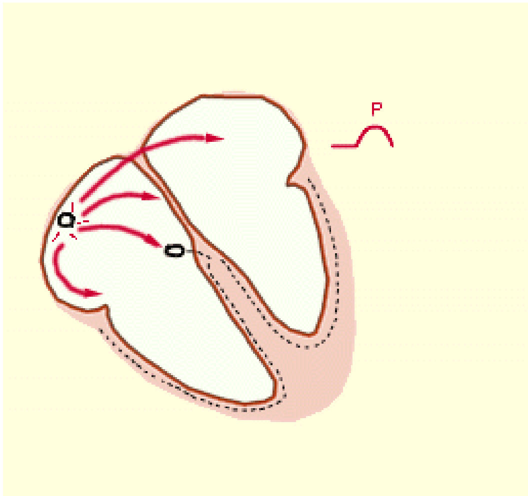


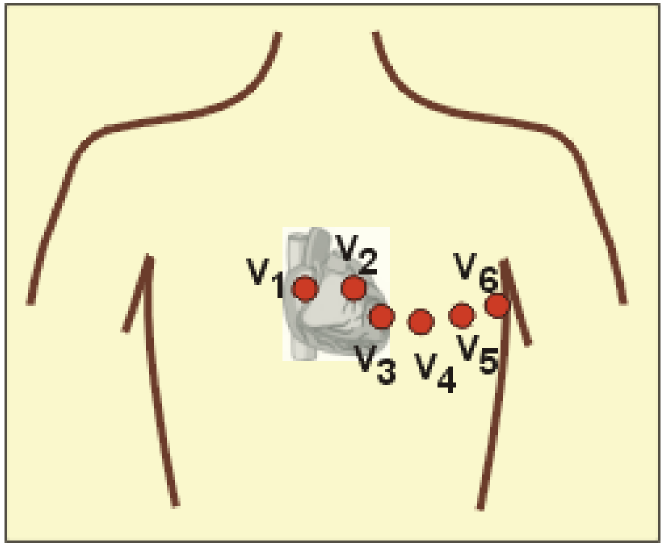
Figure 12-13

Click here to play the Action Potential in SA Node Flash Animation

Electrocardiogram (ECG)







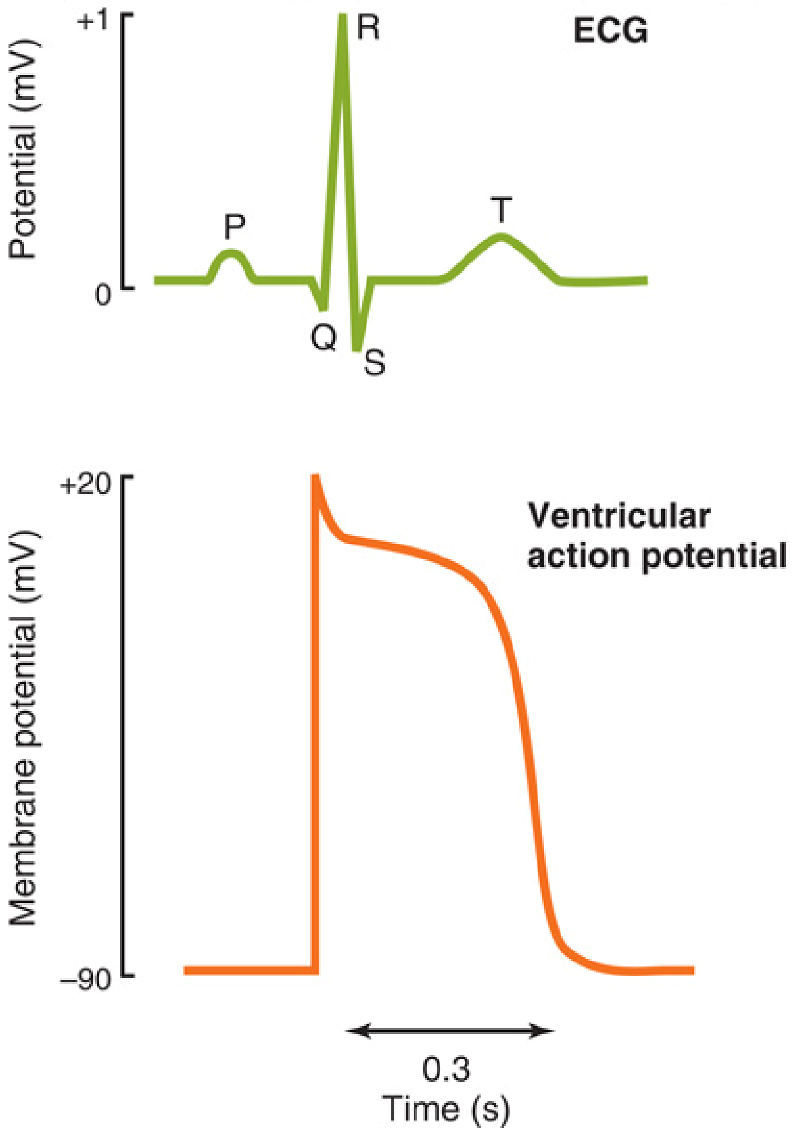
The electrocardiogram (ECG) measures changes in skin electrical voltage/potential caused by electrical currents generated by the heart

Figure 12-14

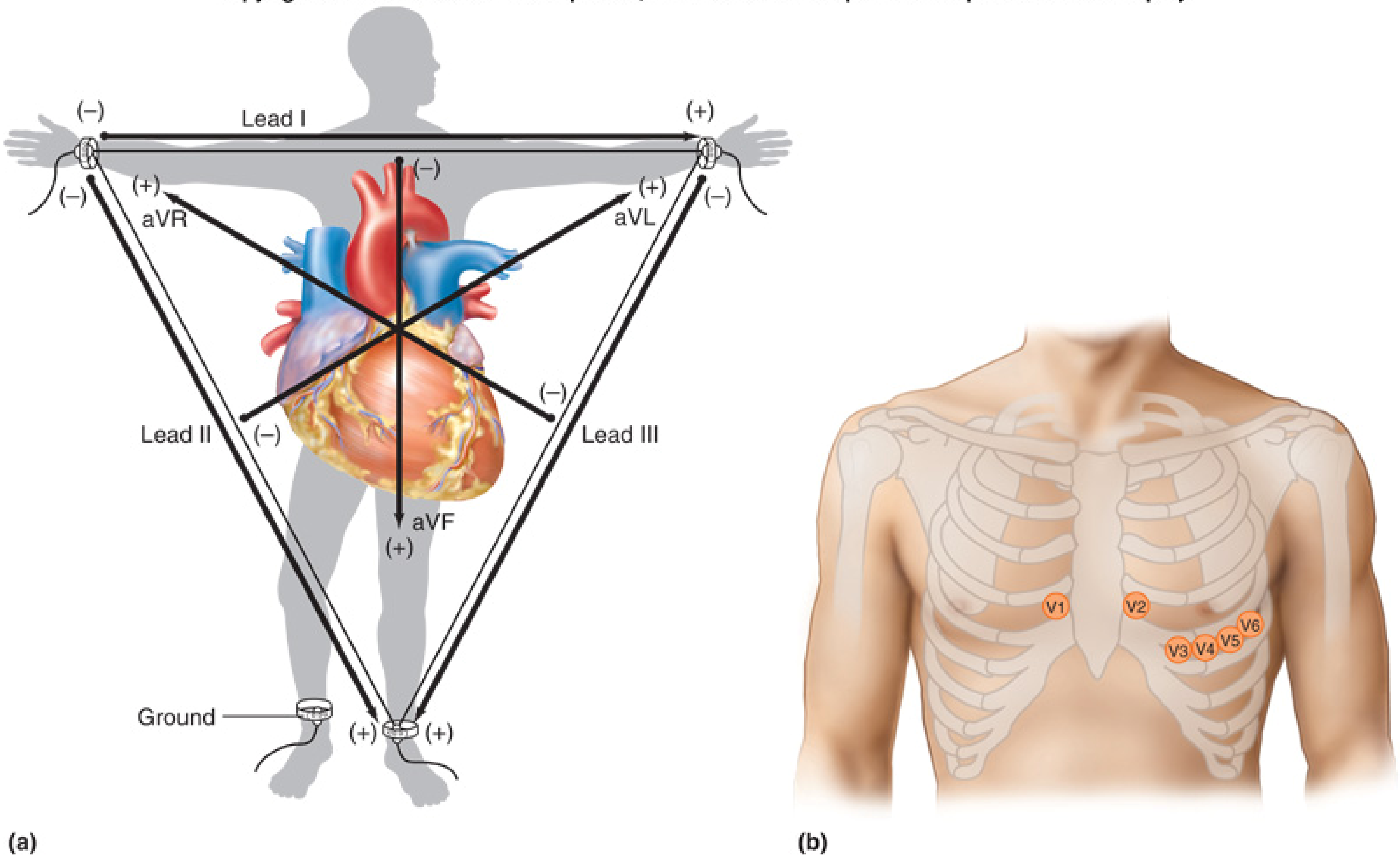
The relationship between the electrocardiogram (ECG), recorded as the difference between currents at the left and right wrists,

and

an action potential typical of ventricular myocardial cells.

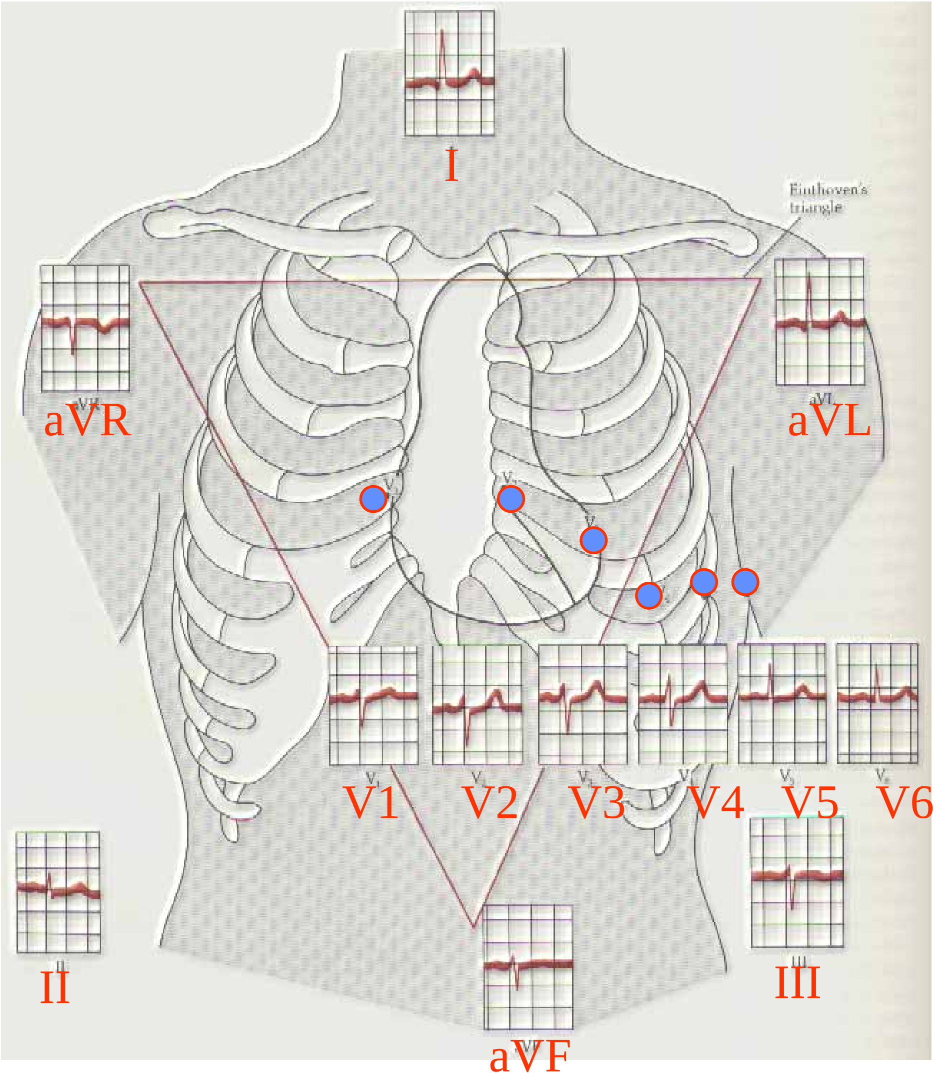


Electrocardiogram (ECG)



Placement of electrodes in electrocardiography

The standard 12 lead ECG



Einthoven's Triangle

Limb leads (Bipolar) (I, II, III)

Augmented limb leads

(Unipolar) (aVR, aVL, aVF)

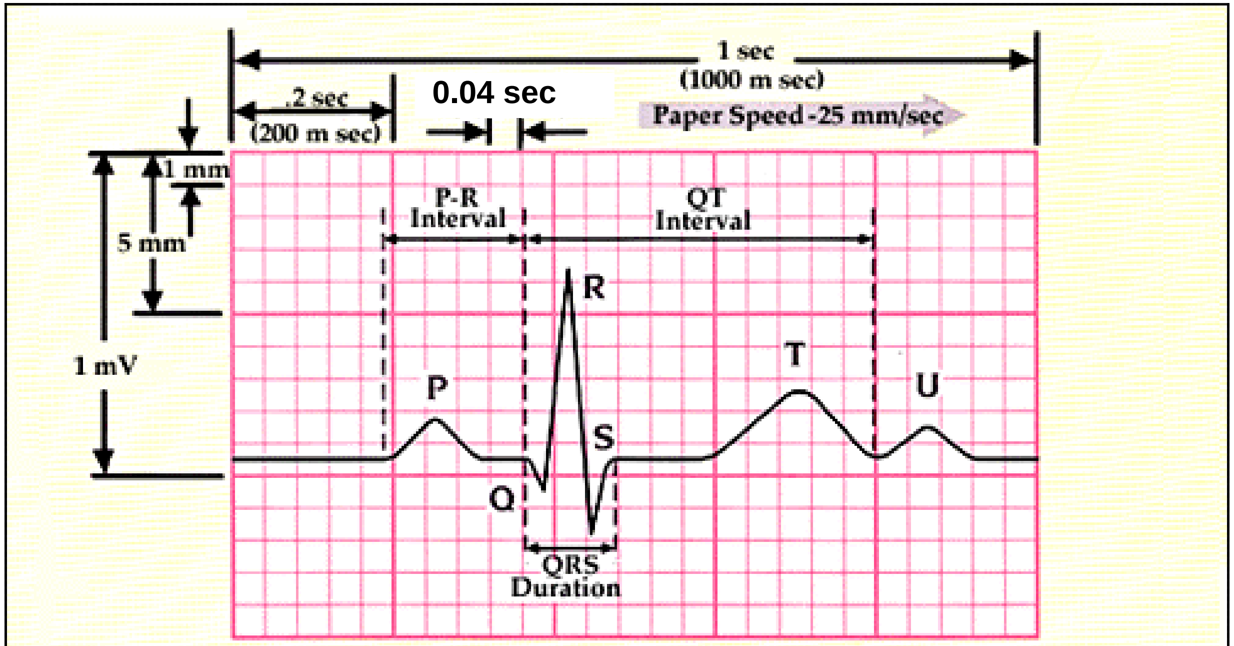
Chest leads (Unipolar) (V1, V2, V3, V4, V5, V6)

TABLE 12–2 Electrocardiography Leads

NAME OF LEAD	ELECTRODE PLACEMENT*	
Standard Limb Leads	*Reference (−) Electrode*	*Recording (+) Electrode*
Lead I	Right arm	Left arm
Lead II	Right arm	Left leg
Lead III	Left arm	Left leg
Augmented Limb Leads		
aVR	Left arm and left leg	Right arm
aVL	Right arm and left leg	Left arm
aVF	Right arm and left arm	Left leg
Precordial (Chest) Leads		
V1	Combined limb leads	4th intercostal space, right of sternum
V2	" " "	4th intercostal space, left of sternum
V3	" " "	5th intercostal space, left of sternum
V4	" " "	5th intercostal space, centered on clavicle
V5	" " "	5th intercostal space, left of V4
V6	" " "	5th intercostal space, under left arm

*In all cases, the right leg is used as an electrical ground. Combining two electrodes forms a reference line between them; combining all limb leads forms a reference plane centered on the heart.

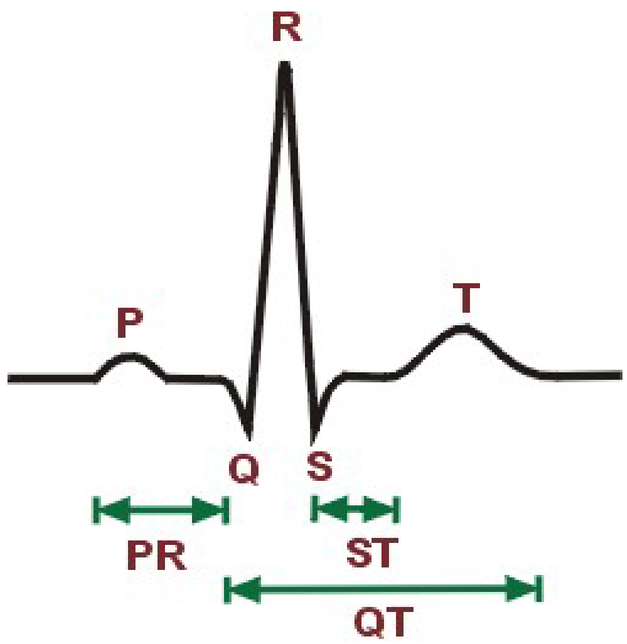
Normal ECG



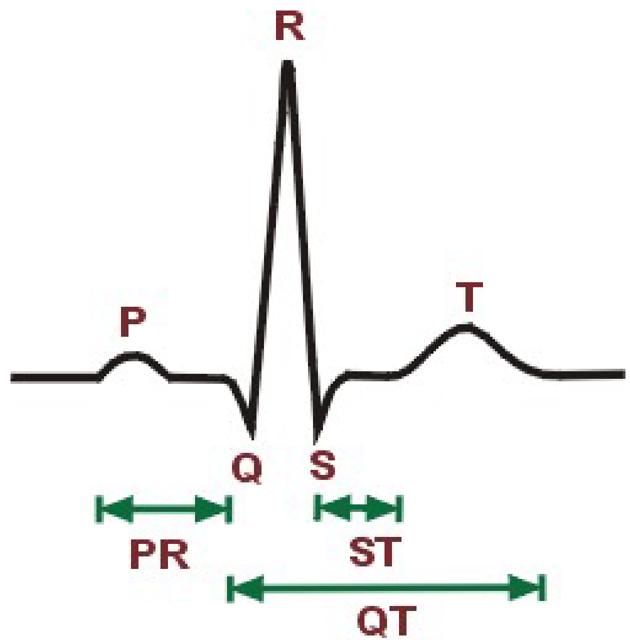
ECG interpretation

- Measurements
- Rhythm analysis
- Conduction analysis
- Waveform description
- Comparison with previous ECG (if any)

- P wave: the sequential depolarization of the right and left atria
- QRS complex: right and left ventricular depolarization
- ST-T wave: ventricular repolarization
- U wave: origin for this wave is not clear - but probably represents "afterdepolarizations" in the ventricles



- PR interval: time interval from onset of atrial depolarization (P wave) to onset of ventricular depolarization (QRS complex)
- QT interval: duration of ventricular depolarization and repolarization
- ST segment: the time period between the end of the QRS complex and the beginning of the T wave, during which each myocyte is in the plateau phase (phase 2) of the action potential



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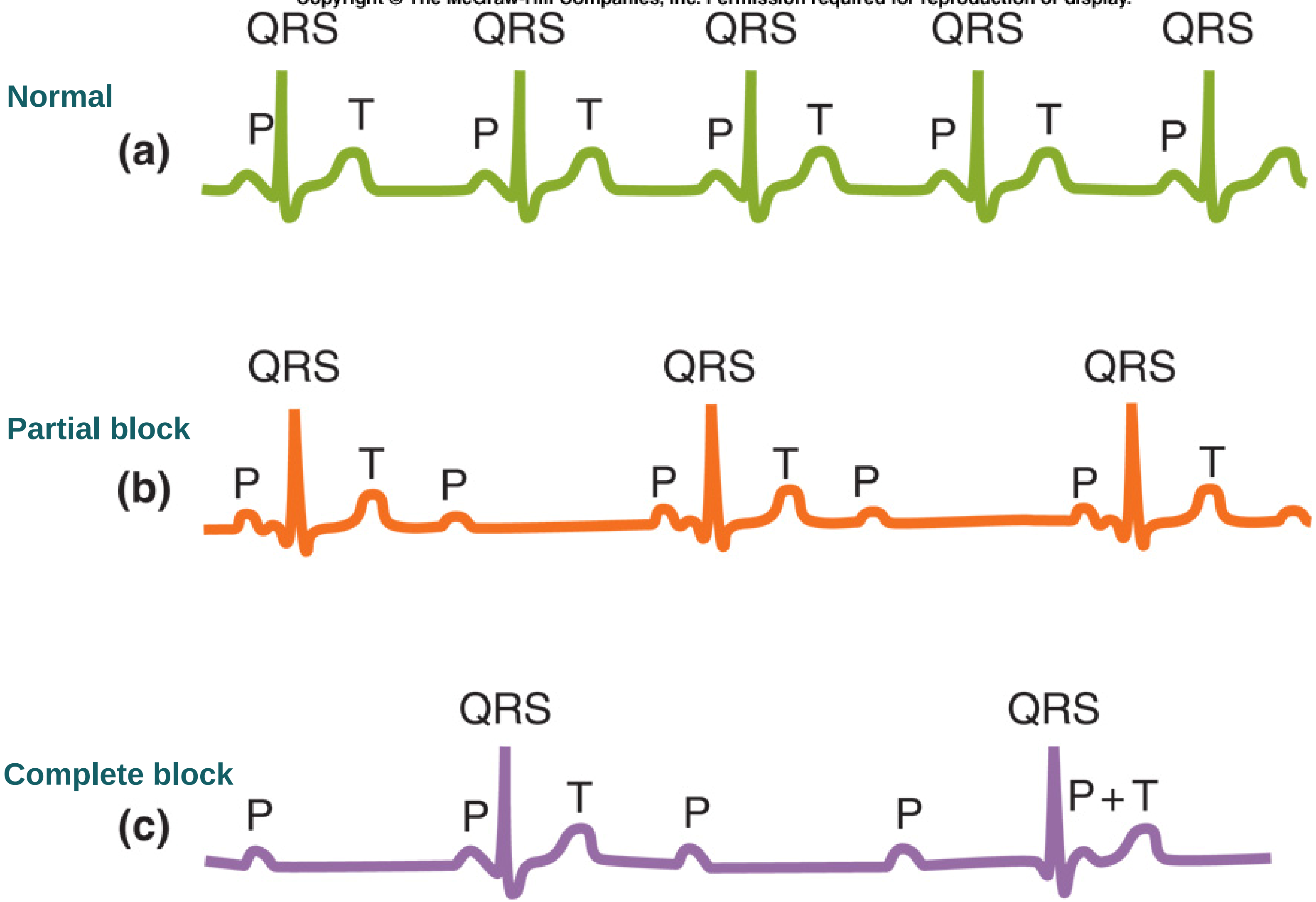


Figure 12-16

The End.

Physiological properties of cardiac cells

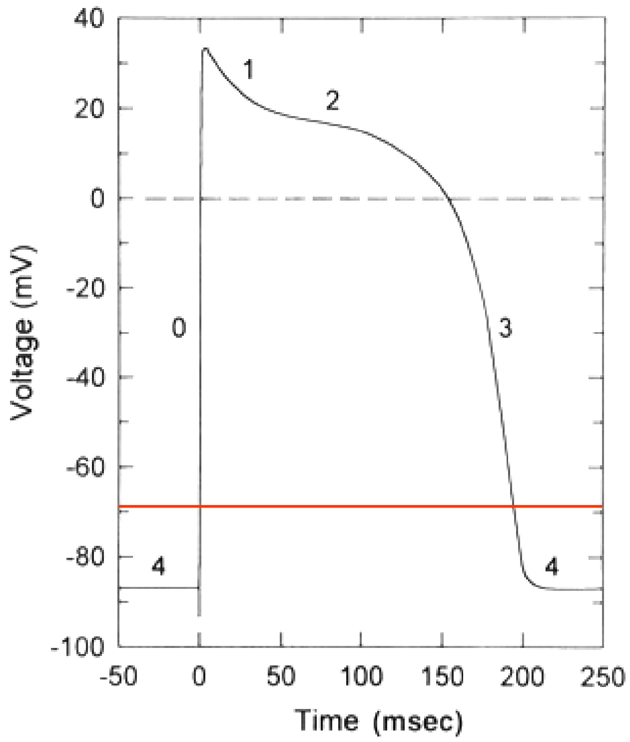
- Excitability
- Autorhythmicity
- Conductivity
- Contractility

Electrophysiological properties

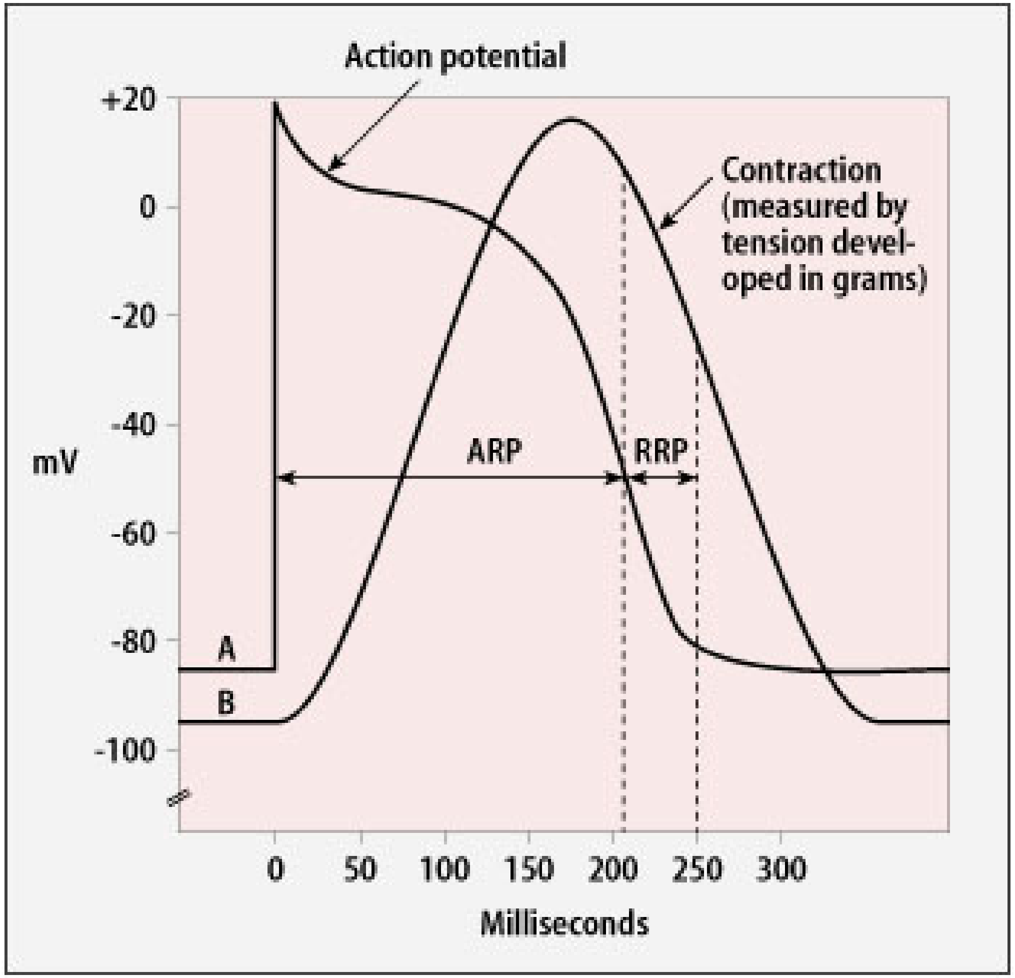
Mechanical property

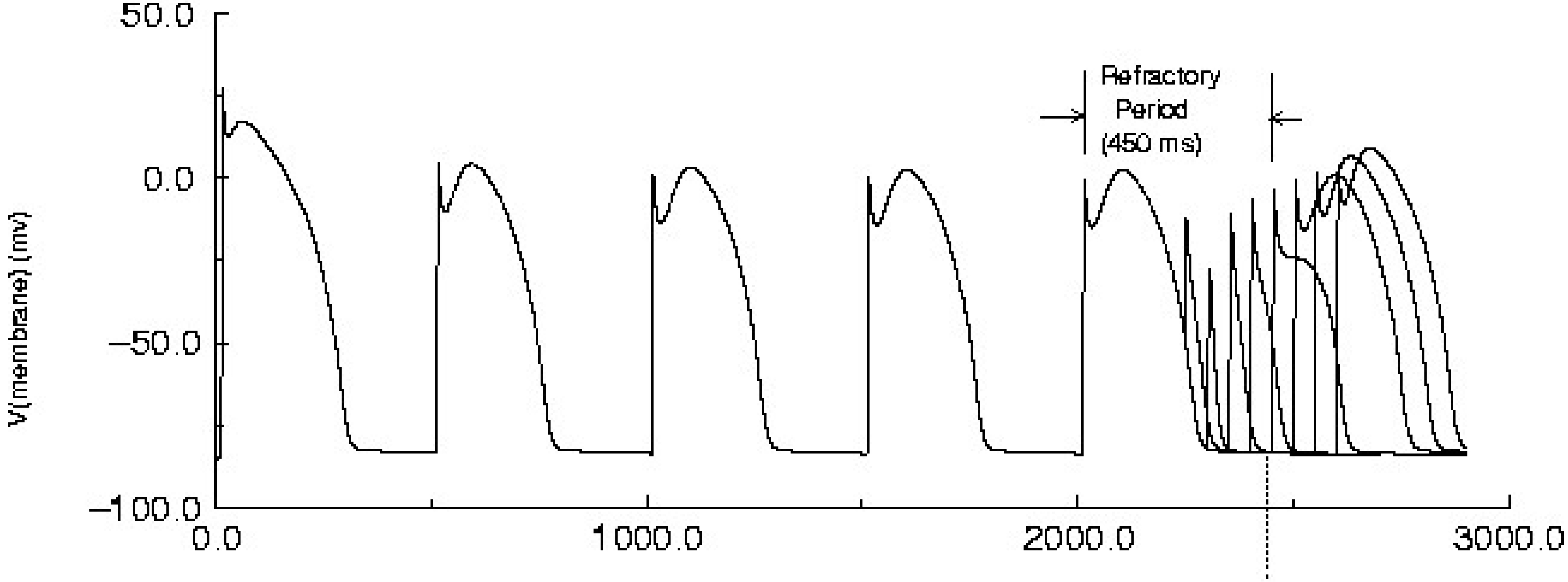
Excitability

- Factors affecting excitability
  - Resting potential
  - Threshold potential
  - Status of Na^{+} or Ca^{2+} channels



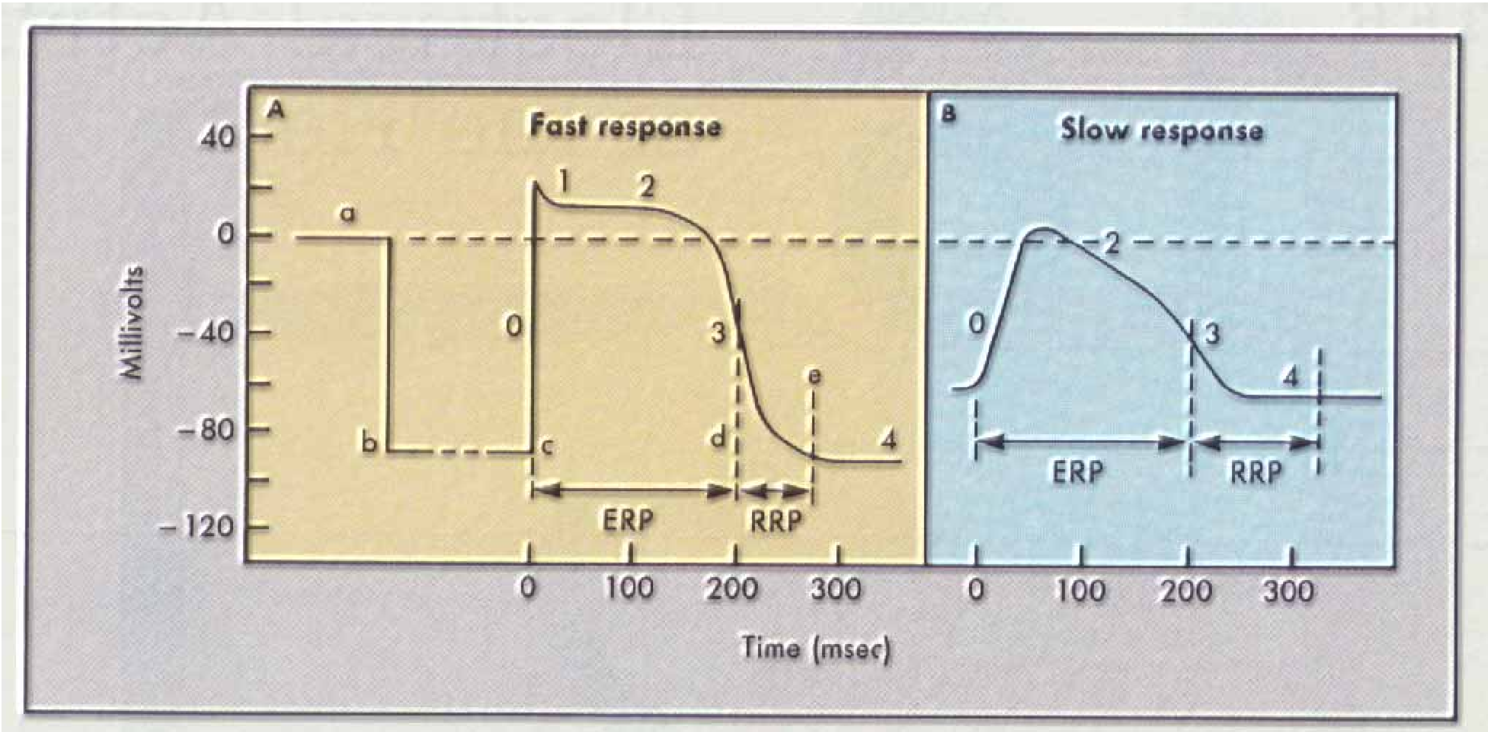
- Periodic changes in excitability

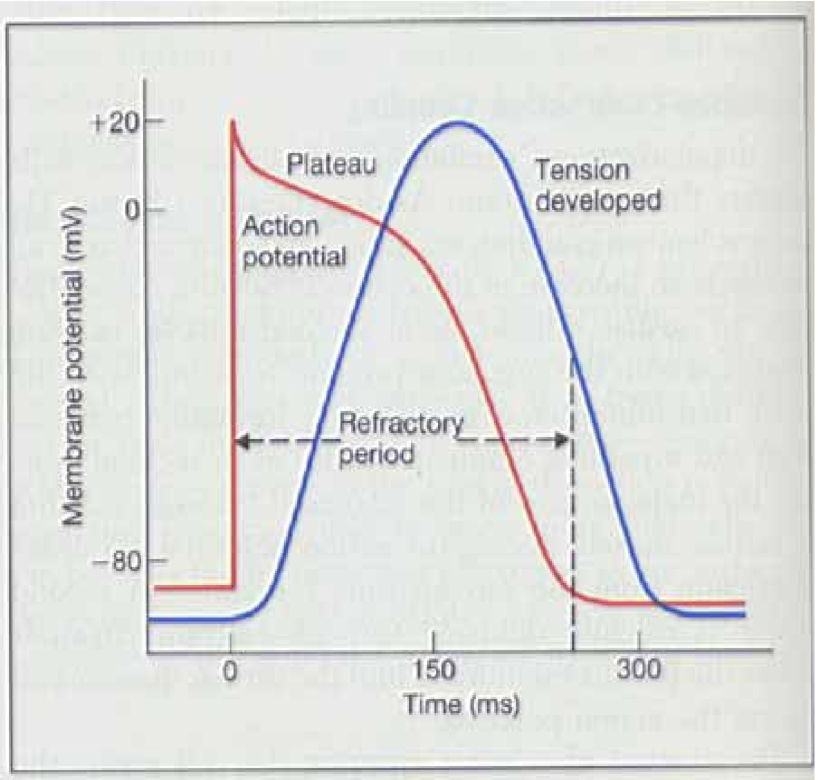




50.0
0.0
−50.0
−100.0
V(membrane) (mv)
0.0
1000.0
2000.0
3000.0
Refractory
Period
(450 ms)

Postrepolarization refractoriness of slow response cells

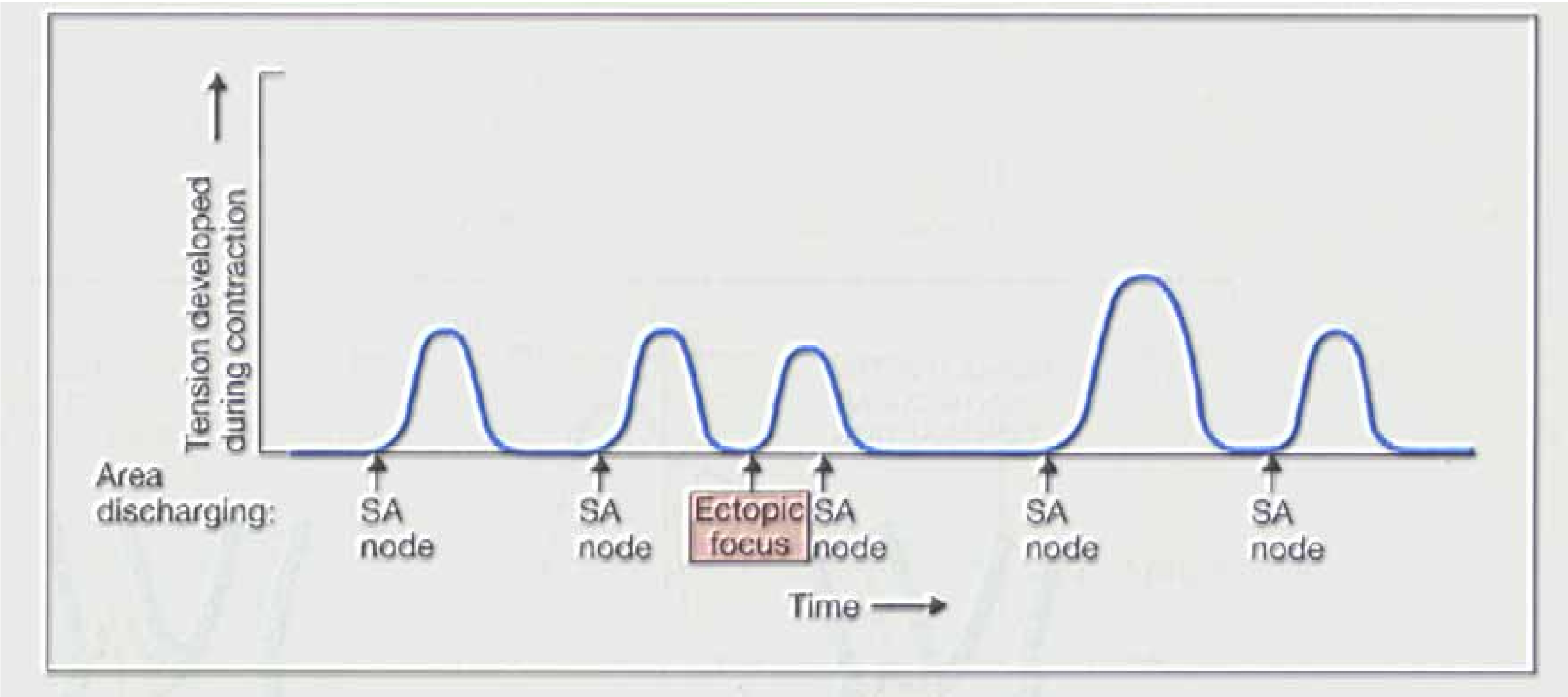




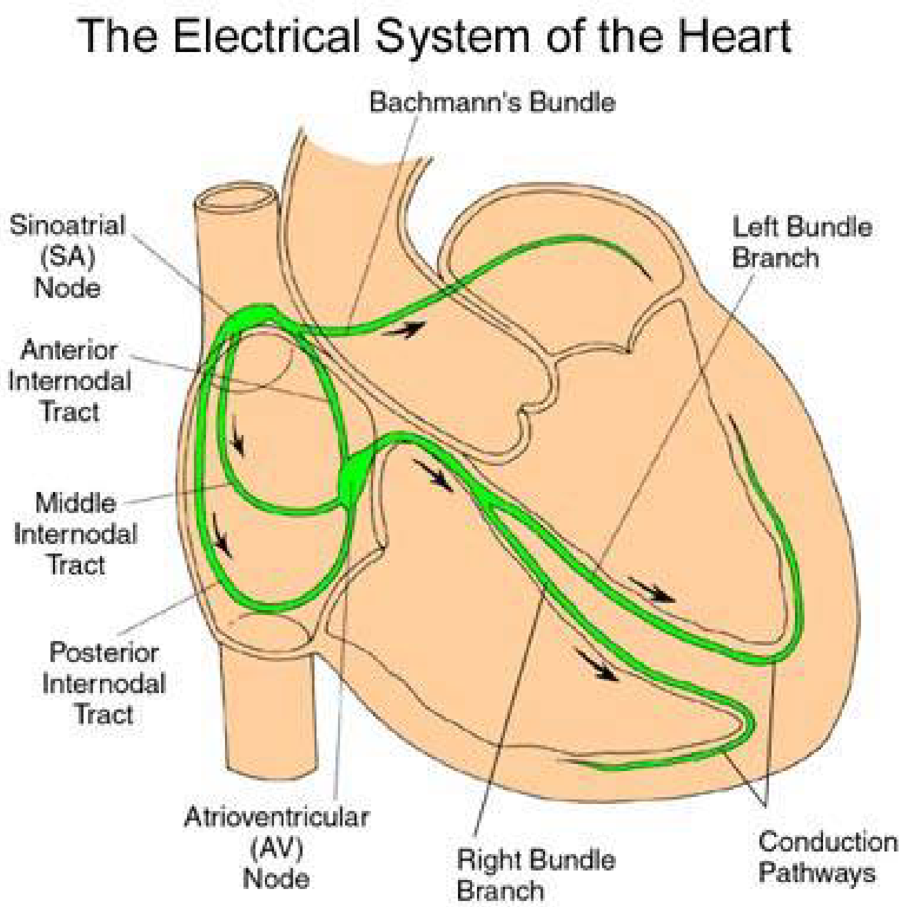
Valuable protective mechanism

- The long refractory period means that cardiac muscle cannot be restimulated until contraction is almost over & this makes summation & tetanus of cardiac muscle impossible

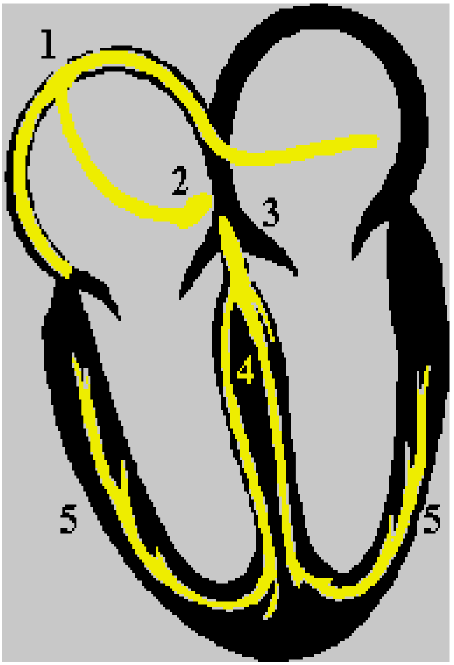
Premature systole & compensatory pause (extrasystole)



- Autorhythmicity



❖ Autorhythmicity



SA node 100 times/min

AV node 50 times/min

Bundle of His 40 times/min

Purkinje fibers 25 times/min

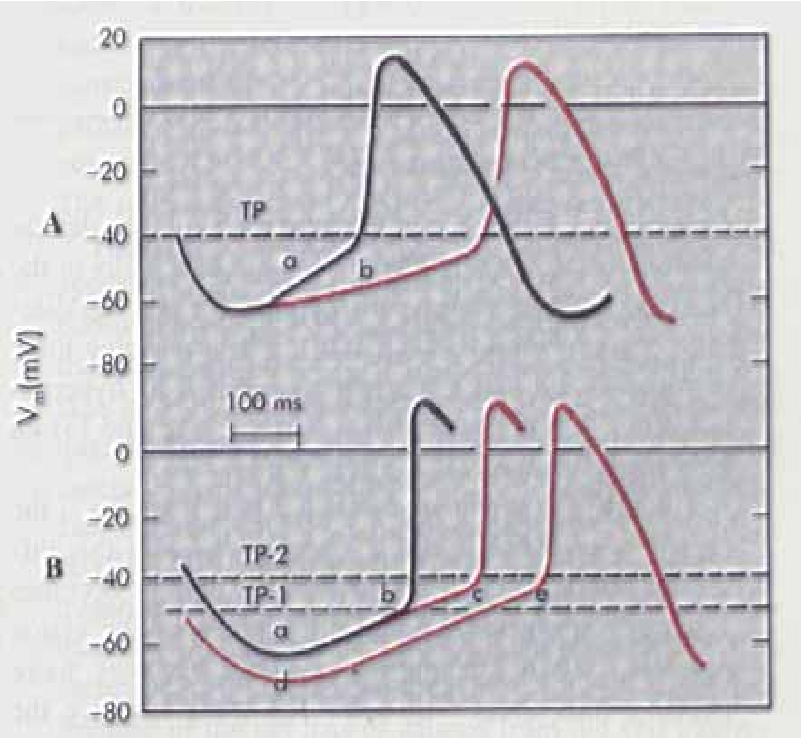
- Normal pacemaker
  - SA node
- Latent pacemaker (Ectopic pacemaker under pathophysiological conditions)
  - AV node
  - Bundle of His
  - Purkinje fibers

The mechanisms of SA node to control latent pacemakers

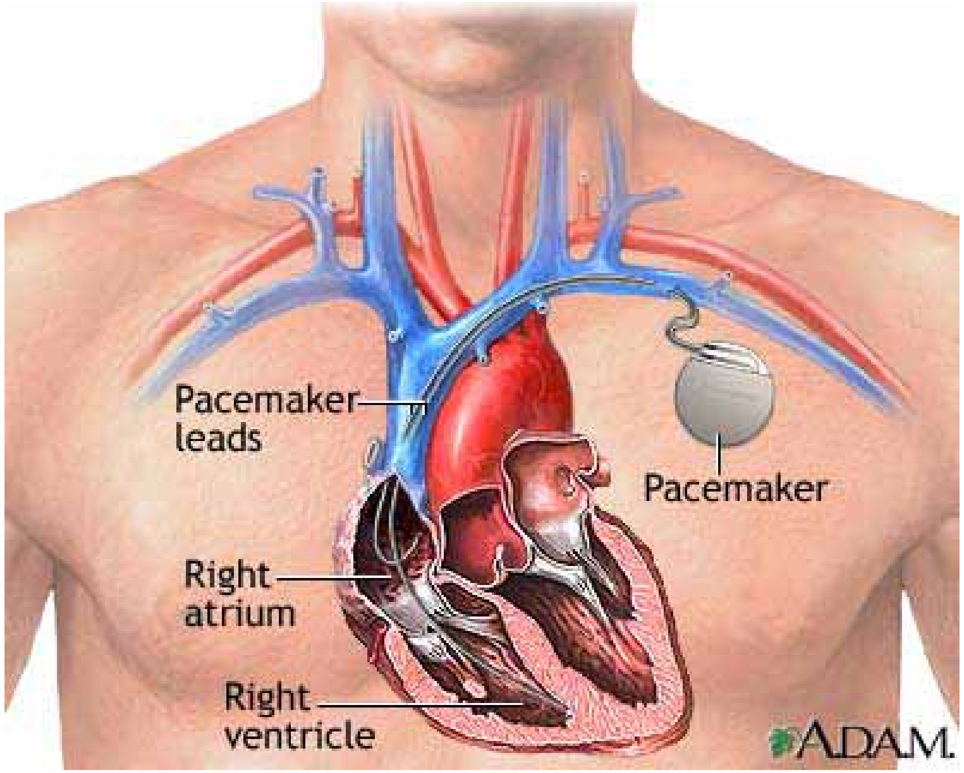
- Capture
- Overdrive suppression

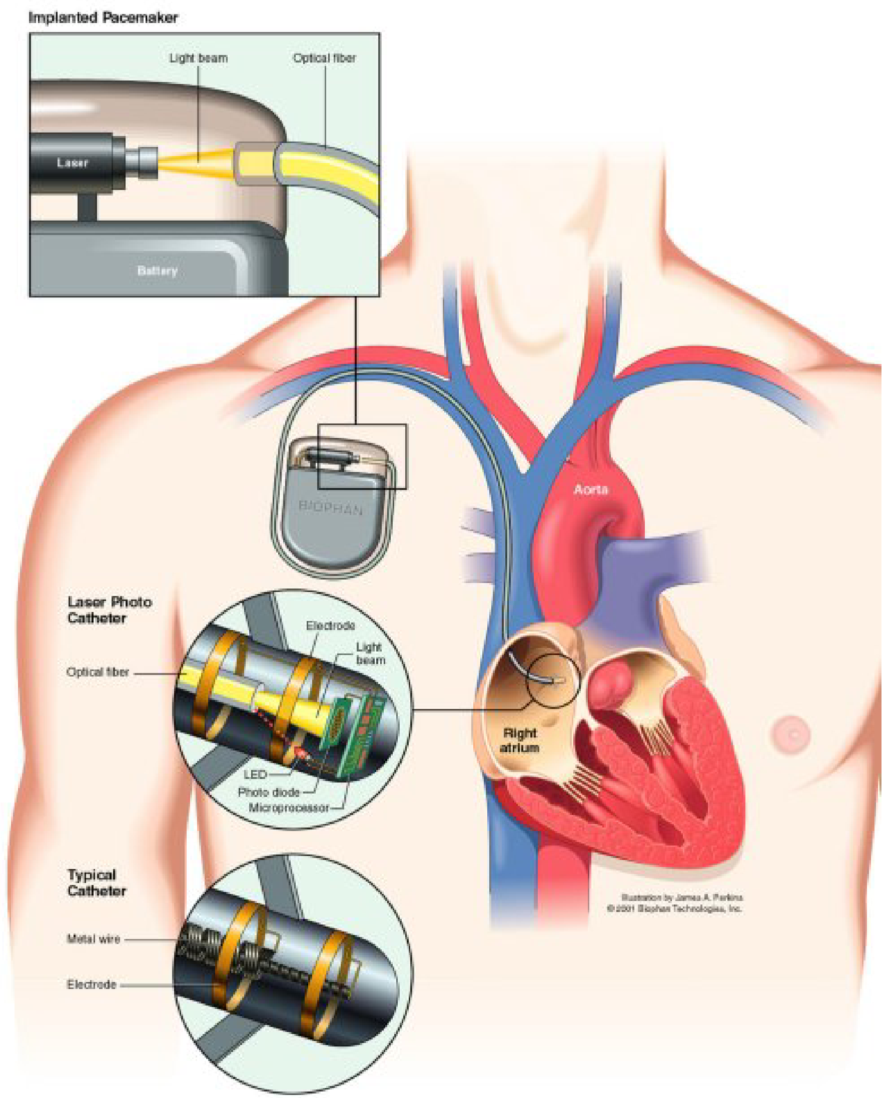
Factors Affecting Autorhythmicity

- Maximal repolarization potential
- Threshold potential
- The rate of phase 4 spontaneous depolarization

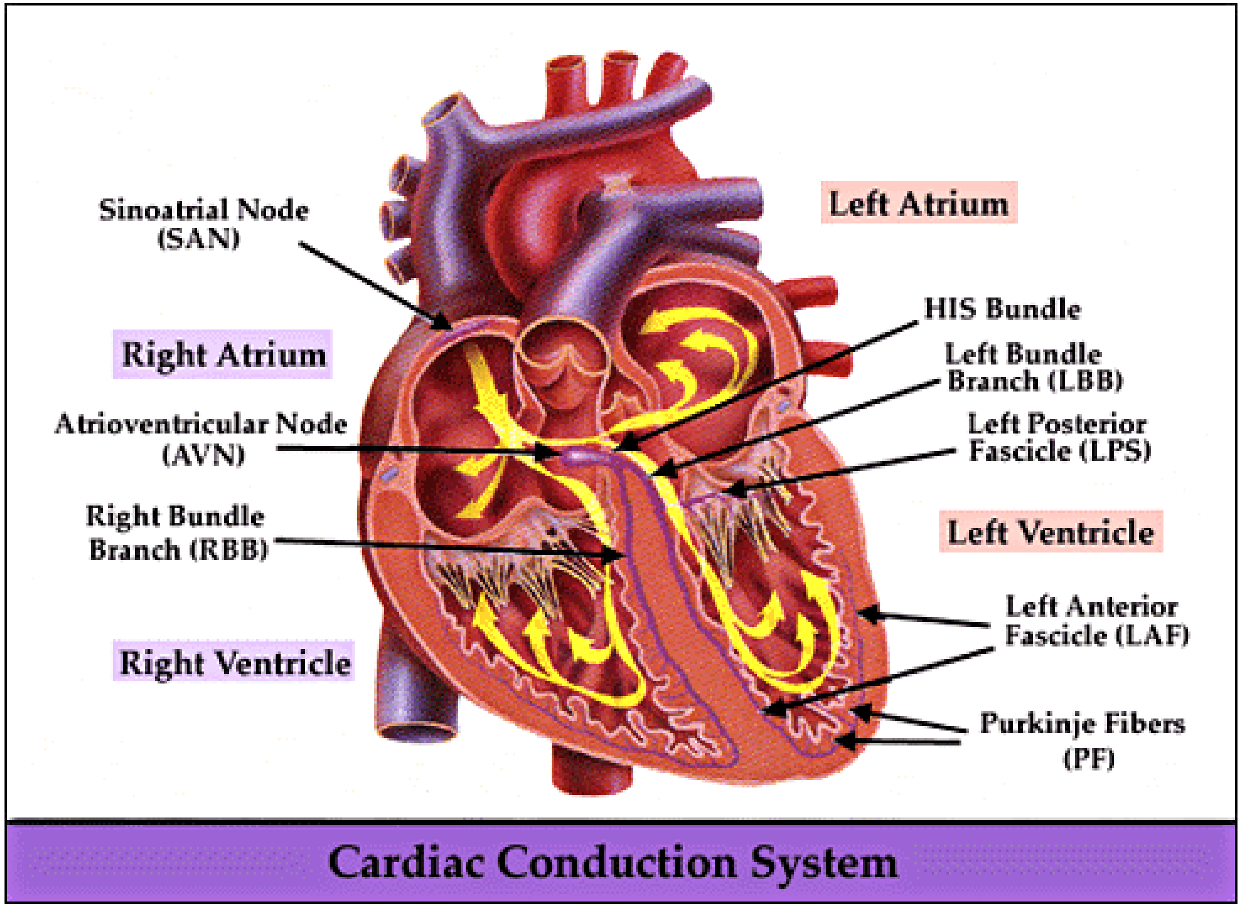


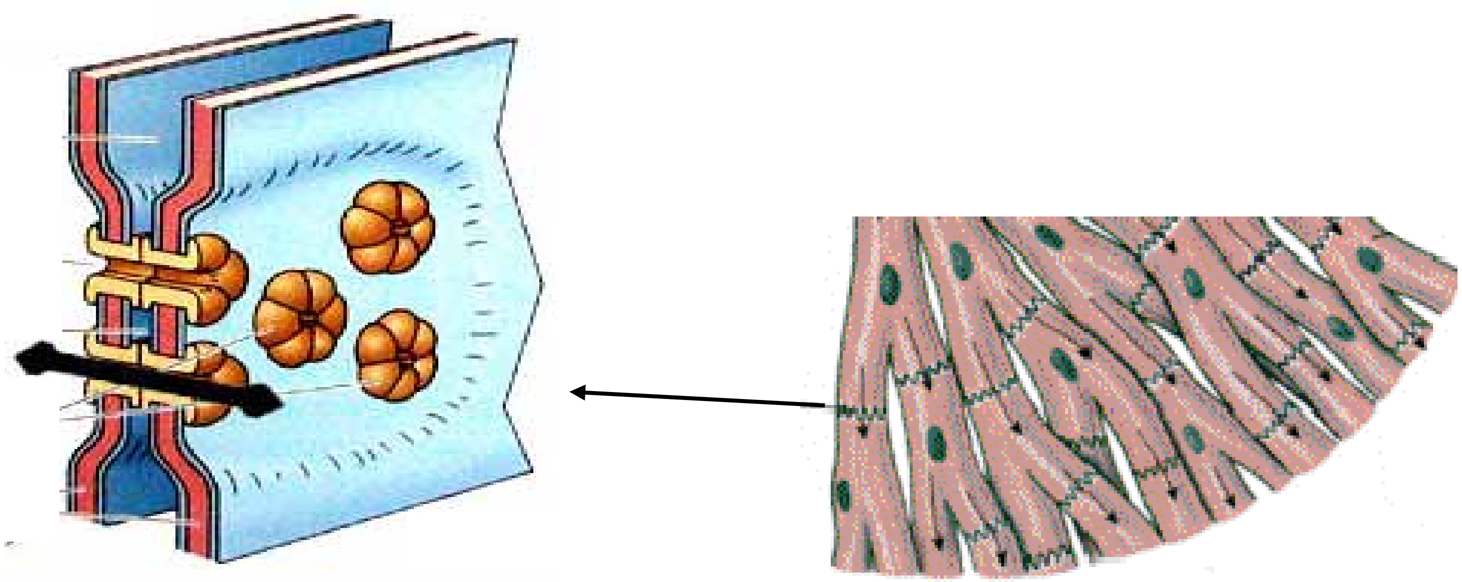
Pacemaker


Pacemaker leads
Pacemaker
Right atrium
Right ventricle
A.D.A.M.


Implanted Pacemaker
Light beam
Optical fiber
Laser
Battery
BIOPHAN
Aorta
Laser Photo Catheter
Electrode
Light beam
Optical fiber
LED
Photo diode
Microprocessor
Right atrium
Typical Catheter
Metal wire
Electrode
Illustration by James A. Perkins
© 2001 Biophan Technologies, Inc.

❖ Conductivity





Gap junction

Conducting velocity

SA node → Atria → A-V node →

0.05 m/s 0.4 m/s 0.02~0.05 m/s

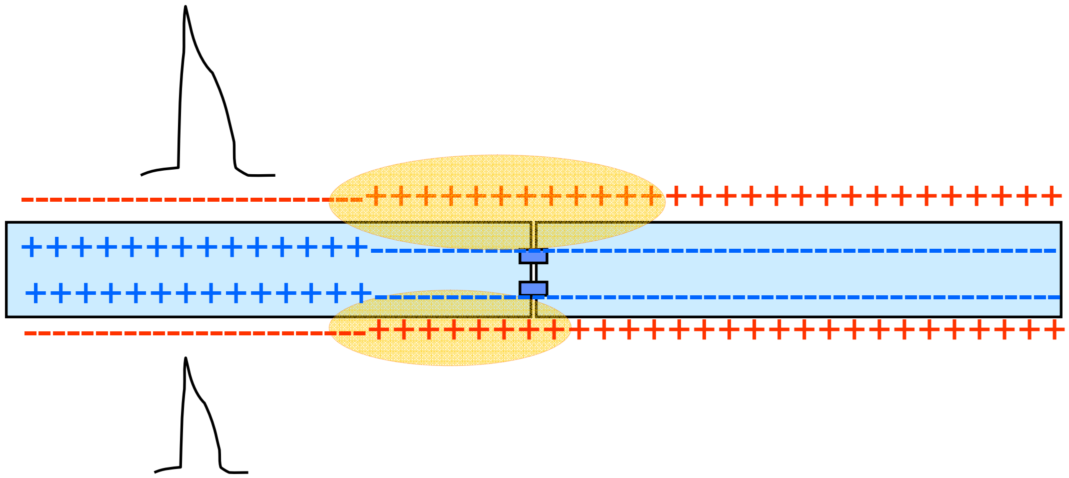
His bundle → Purkinje fiber → Ventricle

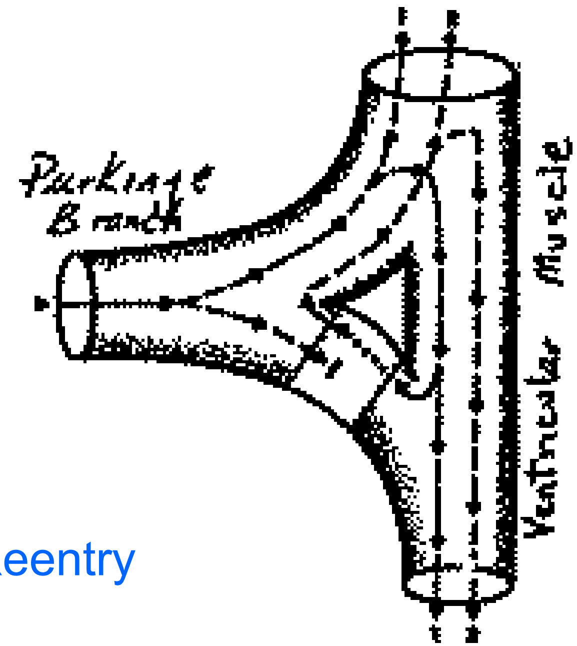
1.2~2.0 m/s 2.0~4.0 m/s 1.0 m/s

Atrioventricular delay: Asynchronization of atrial and ventricular depolarization to provide adequate cardiac output

Factors Affecting Conductivity

- Structural factors
  - Diameter of cardiac cells
  - Gap junctions at Intercalated disk
- Physiological factors
  - The velocity and amplitude of phase 0 depolarization
  - Excitability of adjacent region





Reentry