CARDIOVASCULAR PHYSIOLOGY: HEART, PART II

Engineering Physiology I
BME 365R
Lecture 21
11/13/2014

Announcement

Guest visitor 11/18:

Wesley Hejl, UT BME ‘15

Pamela Combs, MCS Clinical Manager

Seton Heart Specialty Care and Transplant Center

“Ventricular Assist Device (VAD)”

Reading

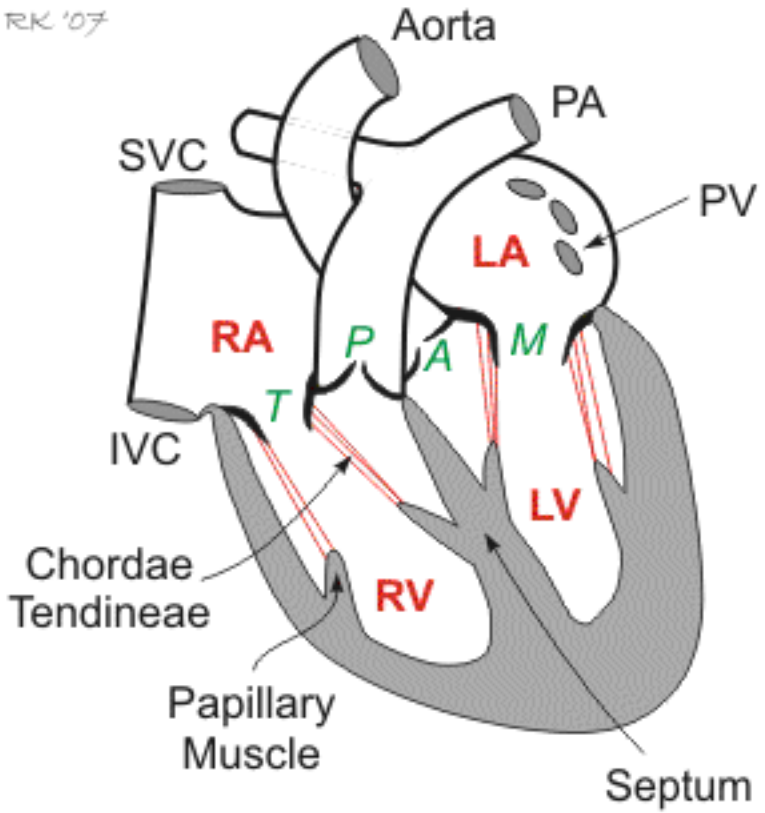
This week Chapter 14.

Next week Chapter 15.

Outline

- Overview of cardiovascular system
- Heart anatomy
- Heart as a pump: mechanical aspects
  - Pressure-Volume loop
  - Frank-Starling Law and stroke volume
  - Preload and afterload
- Heart as a pump: electrical aspects
  - Cardiac muscle cell
  - Action potentials
    - Contractile cells
    - Autorythmic (pacemaker) cells
  - Electrical conduction in the heart
  - Neural modulation of heart rate and contraction

Quick review: Heart Anatomy



Abbreviations: RA, right atrium; RV, right ventricle; LA, left atrium; LV, left ventricle; T, tricuspid valve; P, pulmonic valve; M, mitral valve; A, aortic valve; SVC, superior vena cava; IVC, inferior vena cava; PA, pulmonary artery; PV, pulmonary veins

http://www.cvphysiology.com/

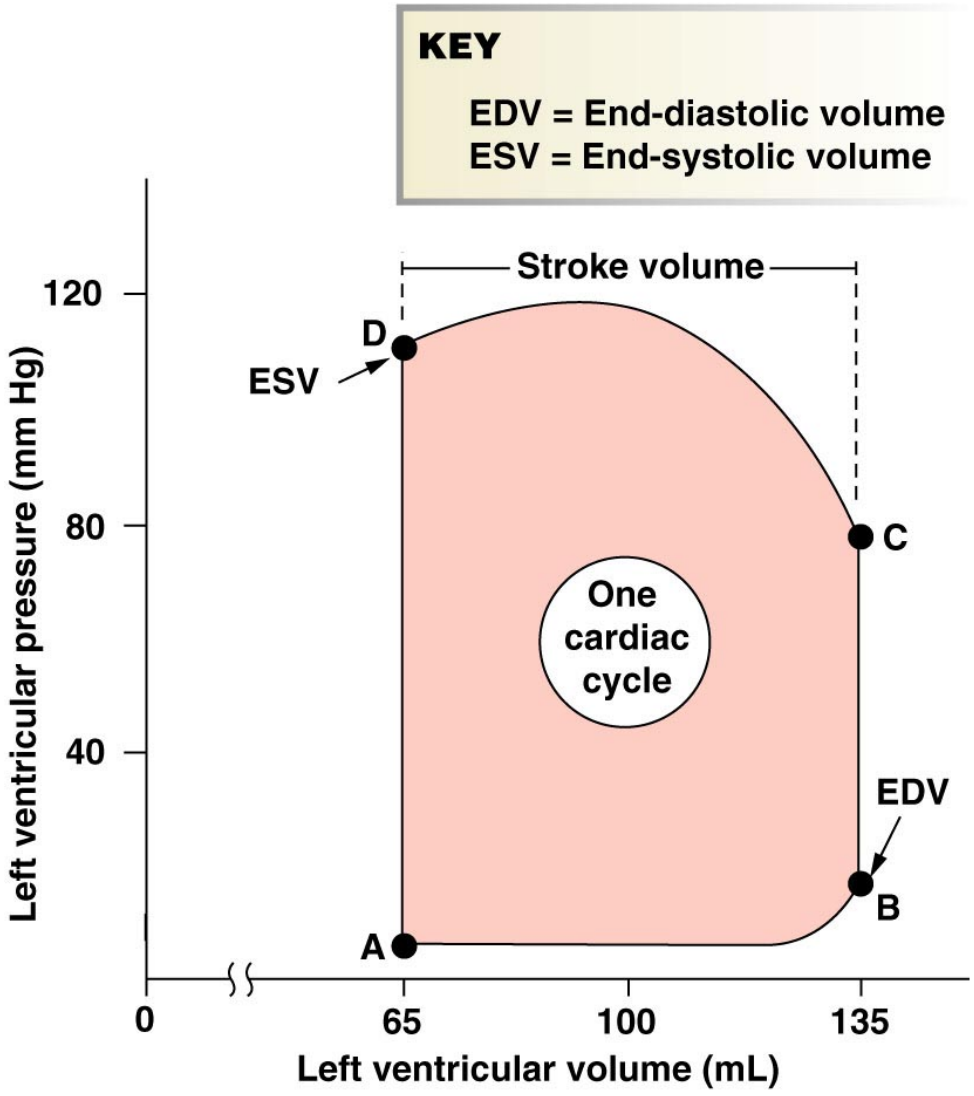
Right Side

- Superior/Inferior Vena Cava
- Right Atrium
- Tricuspid Valve
- Right Ventricle
- Pulmonary Artery

Left Side

- Pulmonary Vein
- Left Atrium (50 – 70ml)
- Mitral Valve
- Left Ventricle (65-135 ml, Cardiac Cycle)
- Aortic Valve
- Aorta

Energetics: Pressure – Volume Loop



Energetics: Pressure – Volume Loop

Stroke volume (SV) is the volume of blood pumped by the heart per beat.

$$SV = EDV - ESV$$

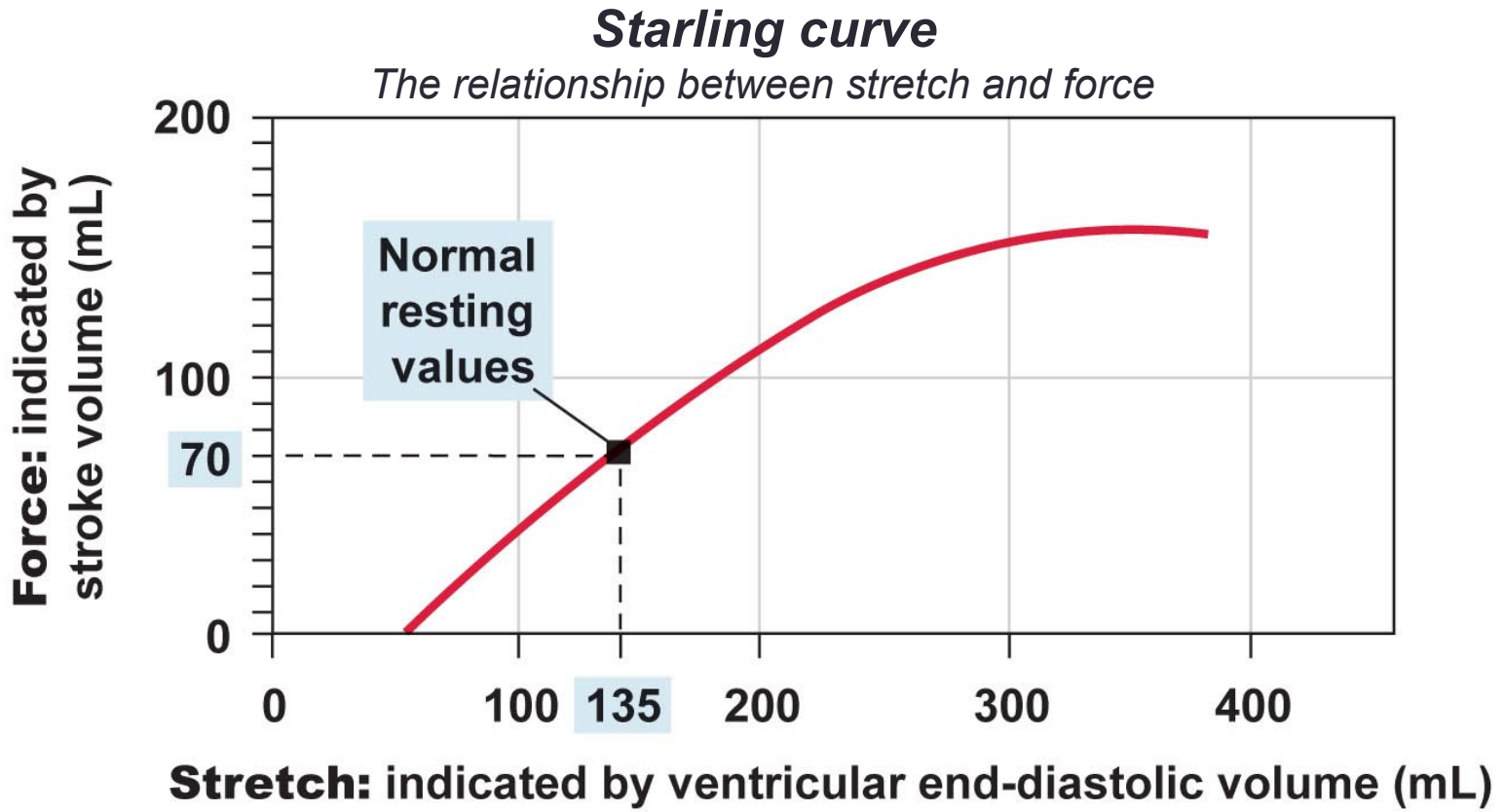
Cardiac output (CO) is the flow rate out of the heart in liters per minute and equal to the stroke volume multiplied by the heart rate.

$$CO = SV \times R$$

Frank-Starling Law of the Heart

Frank-Starling law states: Stroke volume increase as EDV increases.

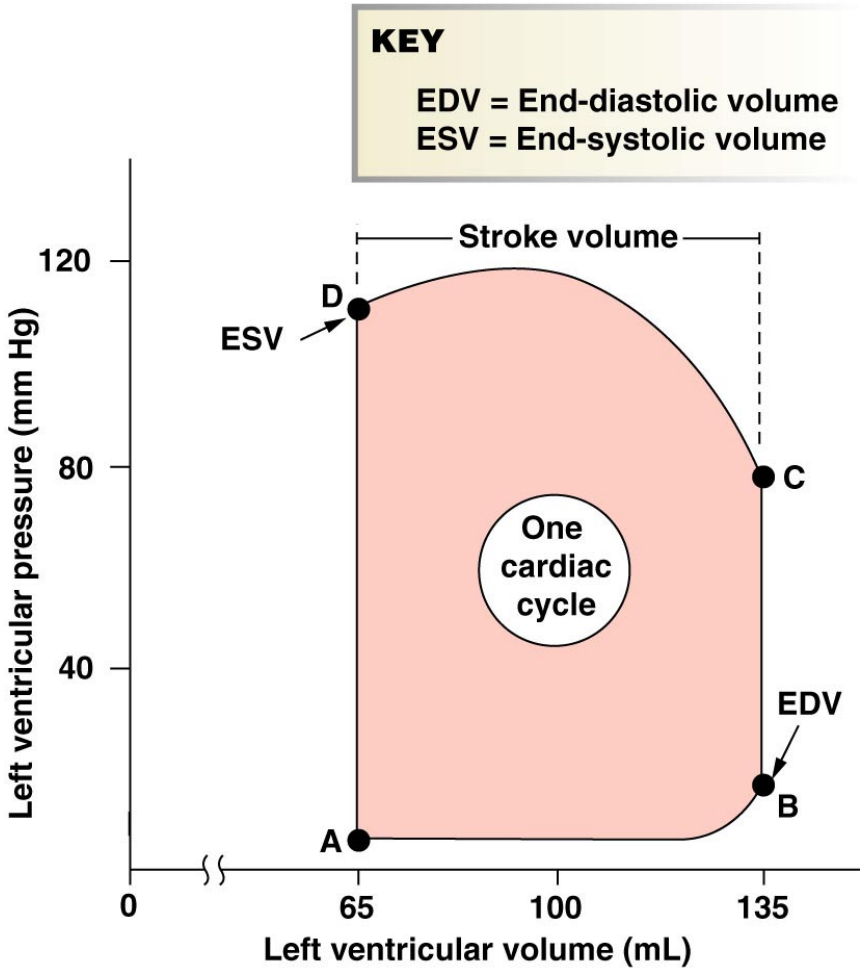
Preload – the degree of myocardial stretch before contraction begins.



Stroke Volume Control via Venous Return

- Stroke volume increase as EDV increases
- EDV is affected by venous return
- Venous return is affected by:
  - *Skeletal muscle pump*: skeletal muscle contractions squeeze veins pushing blood toward the heart
  - *Respiratory pump*: decrease in pressure of the thoracic cavity during inspiration draws blood more blood into vena cava from veins in the abdomen.
  - *Sympathetic innervation*: constriction of veins by sympathetic activity.

Preload and Afterload



Preload – stretch of muscle fibers in the left or right ventricle at the EDV (is measured in pressure units)

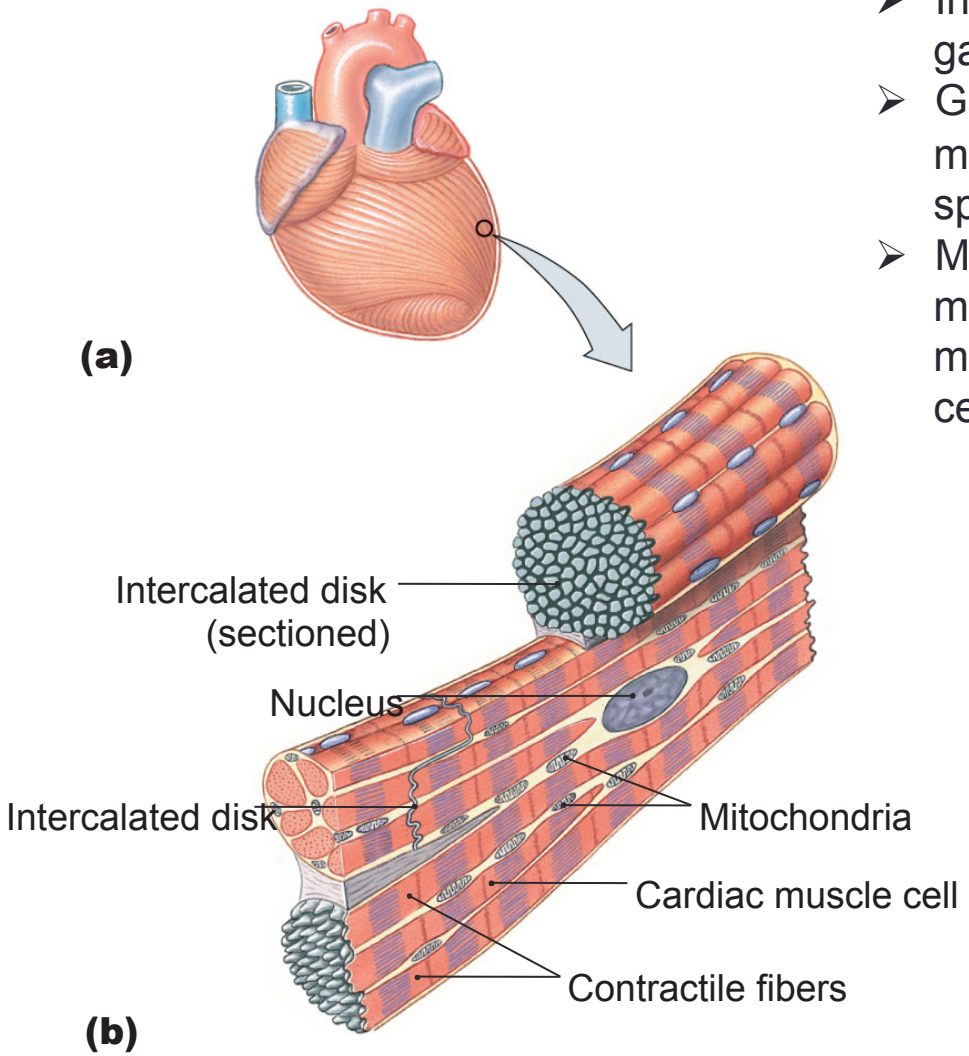
Afterload – pressure in the right of left ventricle when aortic valve opens.

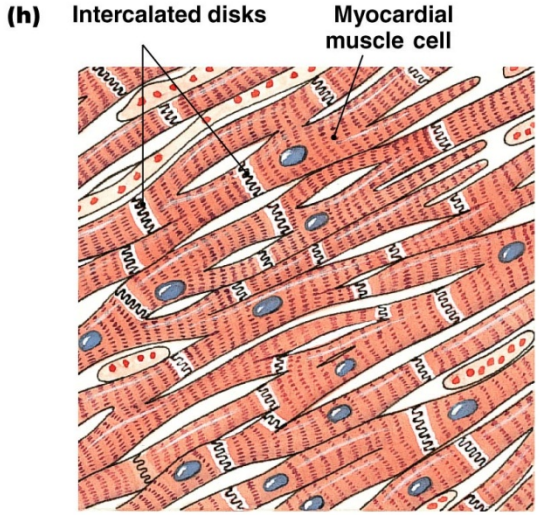
HEART AS A PUMP

Electrical Aspects and Reflex Control

Cardiac muscle cells: Myocardium

- Cardiac muscles are connected by intercalated discs.
- Intercalated discs consist of desmosomes and gap junctions.
- Gap junctions electrically connect cardiac muscle cells allowing waves of depolarization to spread rapidly from cell to cell.
- Mitochondria occupy 1/3 the cell volume; cardiac muscle consumes 70-80% of delivered oxygen – more than twice the amount extracted by other cells.





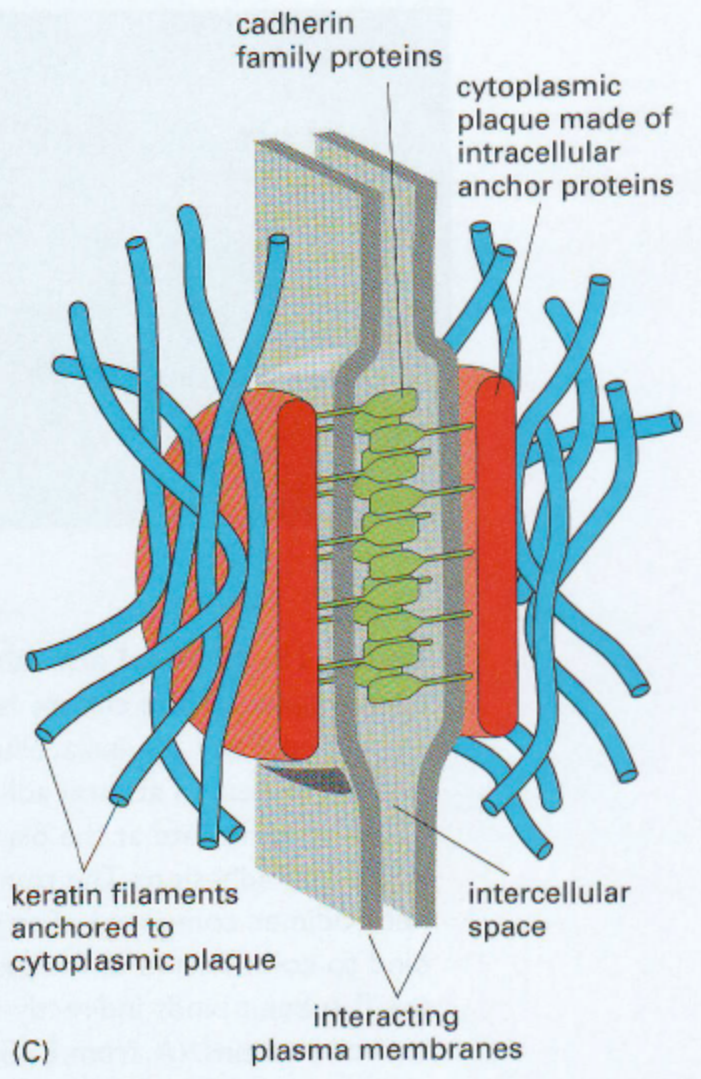
Myocardial muscle cells are branched, have a single nucleus, and are attached to each other by specialized junctions known as intercalated disks.

Desmosomes

Cell-Cell Adhesions:

Desmosomes: Cell-Cell Anchoring Junctions

- **Adherens junctions** sometimes from punctuated or streaked lines. In epithelia they can form an adhesion belt just below the tight junctions.
- **Desmosomes** can link a large number of cells into strings using intermediate filaments inside the cells. They provide large tensile strength.
- **Intermediate filaments** are made of keratin (most epithelial cells), or desmin (heart).



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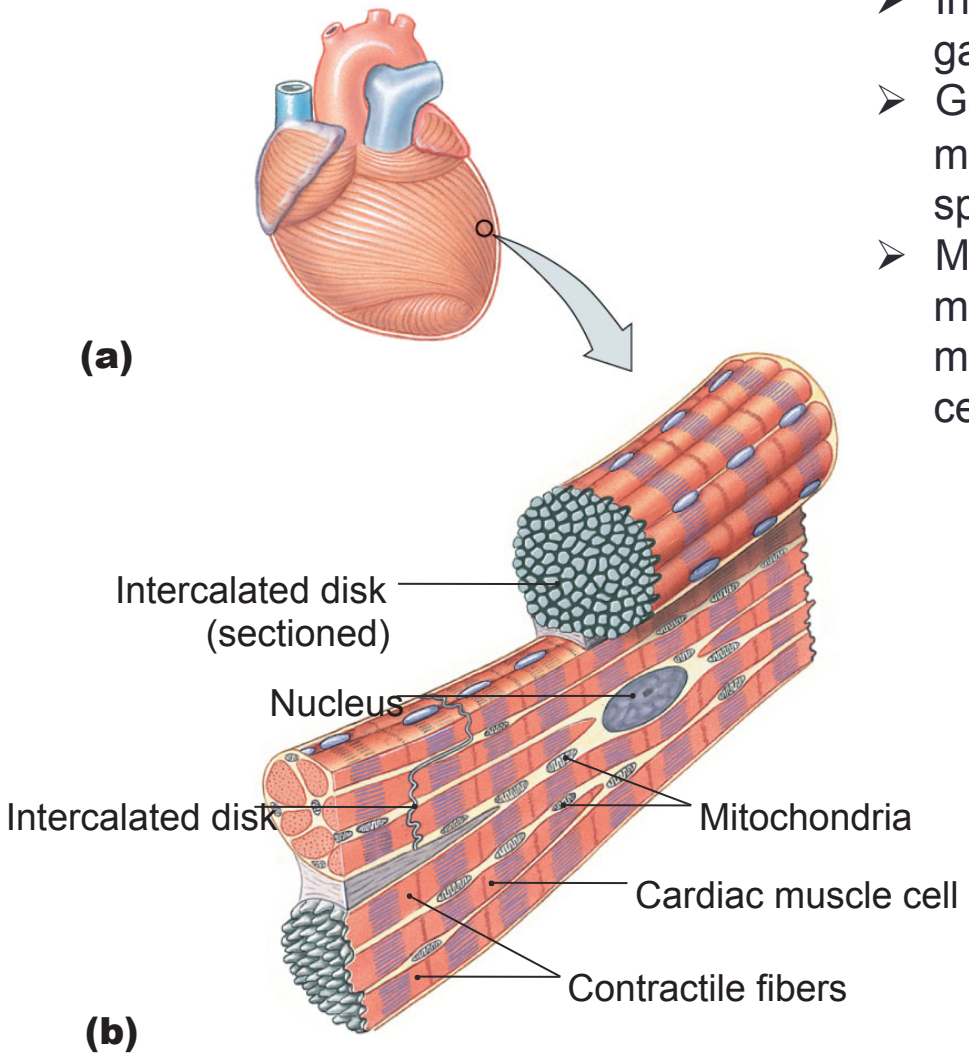

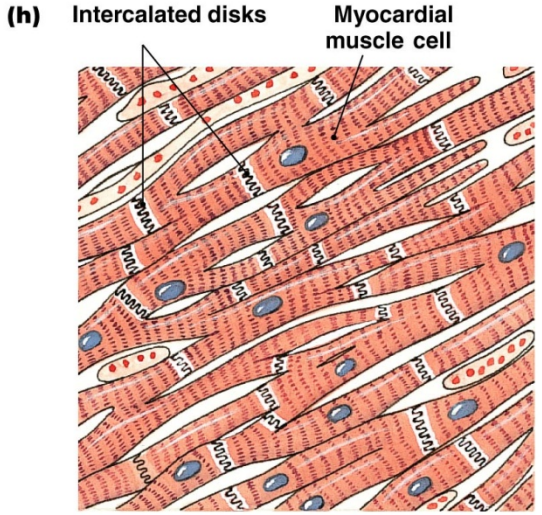

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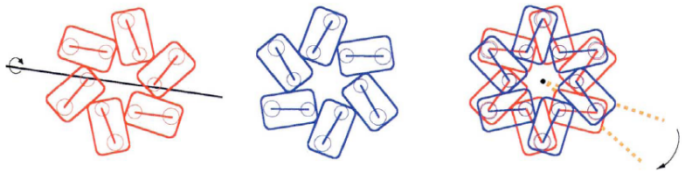
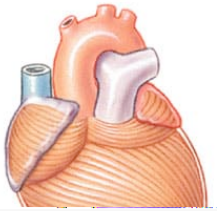
Gap Junctions

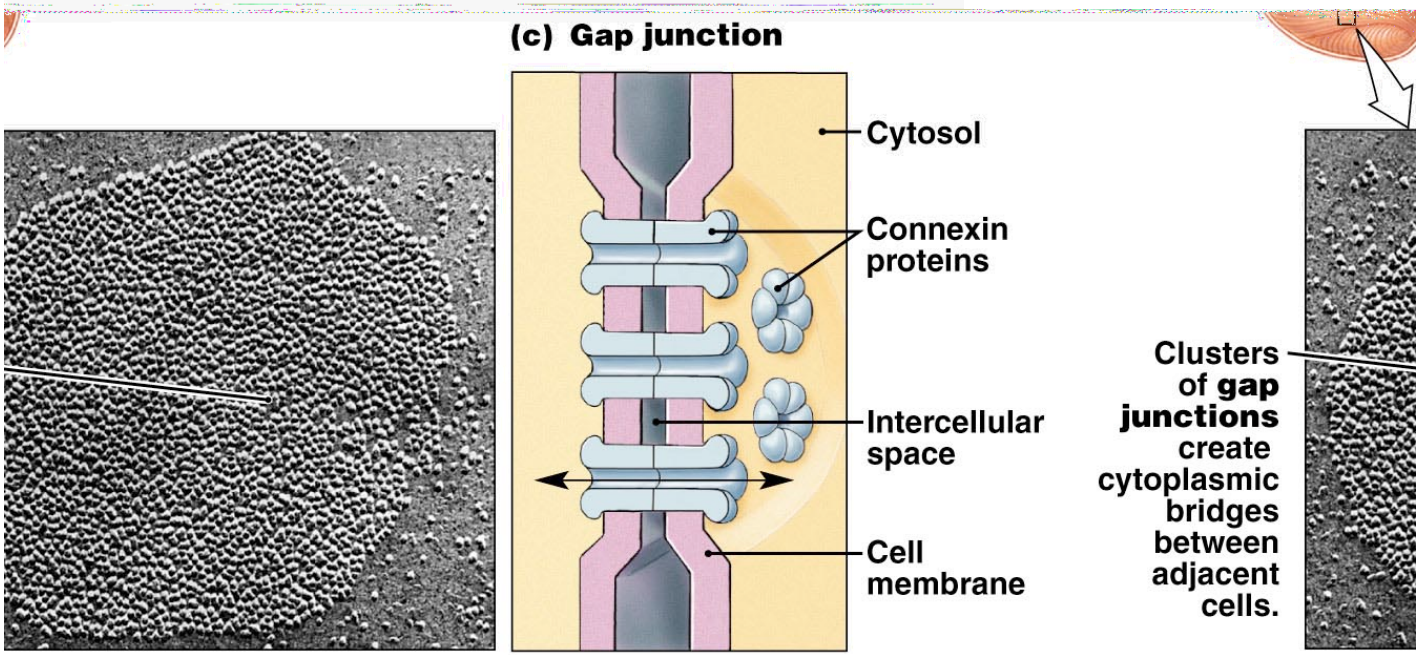
Cell-Cell Adhesions: Gap Junctions

Transmembrane sections are aligned;
each connexin touches 2 on the other side

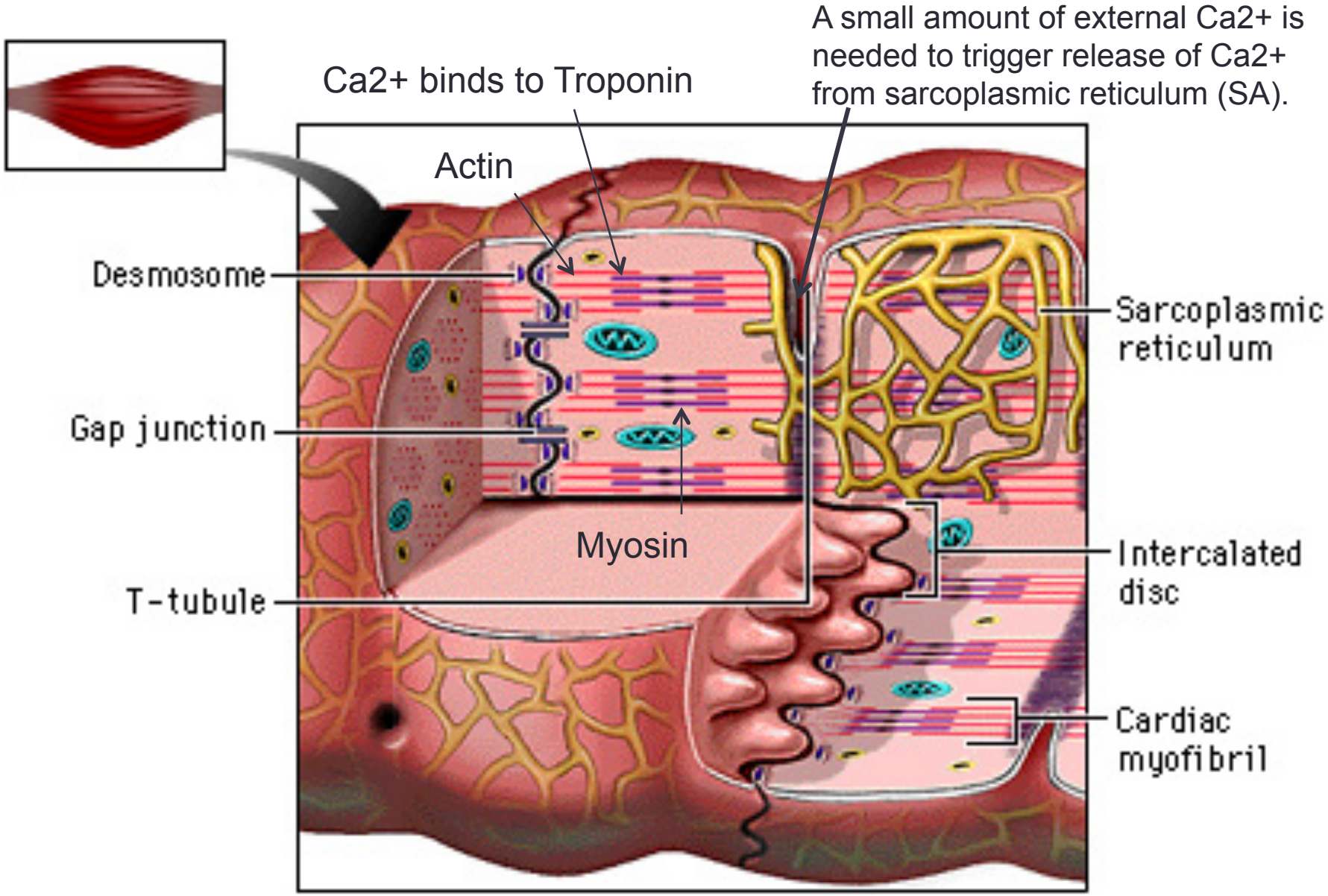




Heart muscle has gap junctions

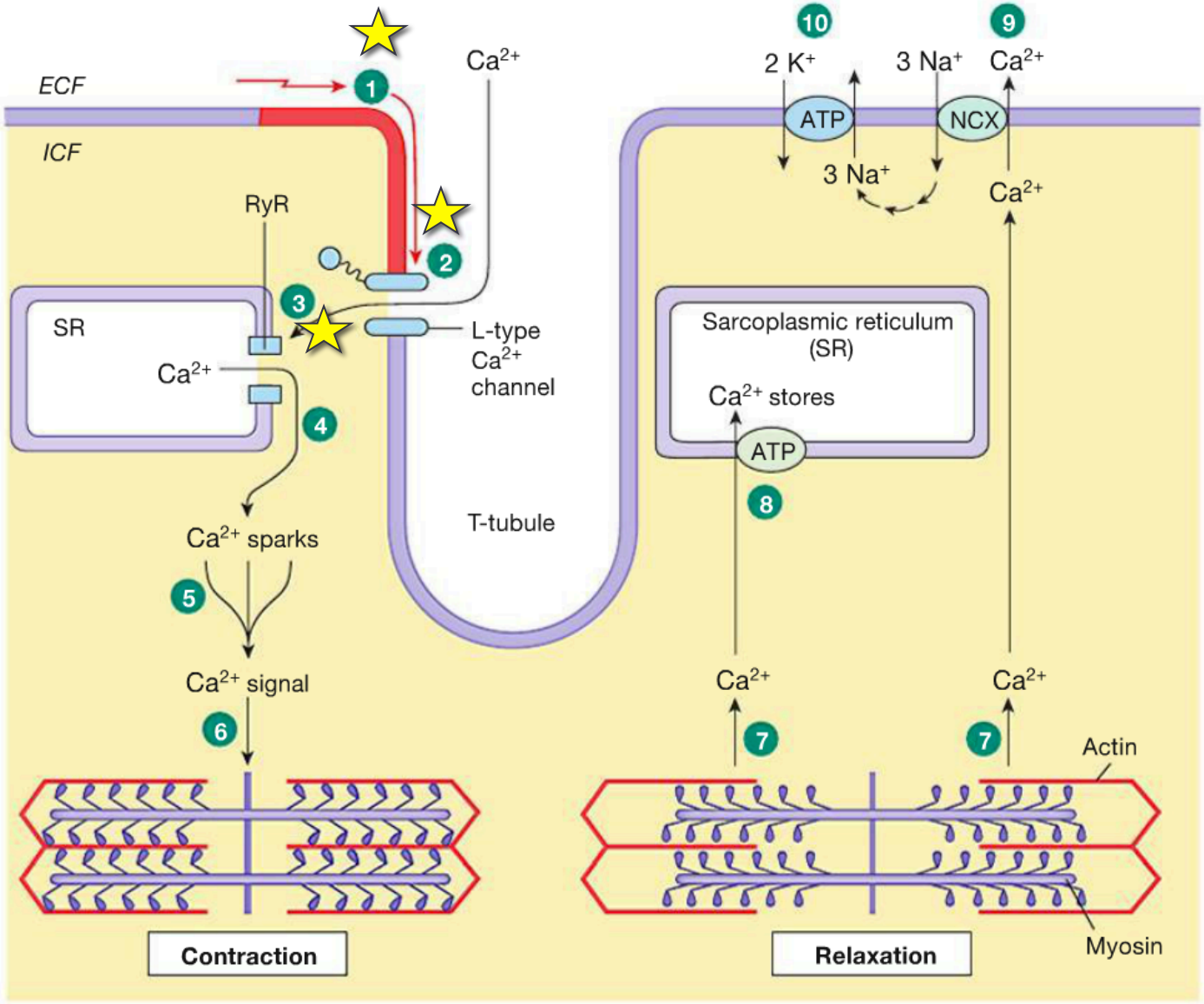


A closer look at the cardiac muscle cell



EC COUPLING IN CARDIAC MUSCLE

This figure shows the cellular events leading to contraction and relaxation in a cardiac contractile cell.



1. Action potential enters from adjacent cell.
2. Voltage-gated Ca^{2+} channels open. Ca^{2+} enters cell.
3. Ca^{2+} induces Ca^{2+} release through ryanodine receptor-channels (RyR).
4. Local release causes Ca^{2+} spark.
5. Summed Ca^{2+} sparks create a Ca^{2+} signal.
6. Ca^{2+} ions bind to troponin to initiate contraction.
7. Relaxation occurs when Ca^{2+} unbinds from troponin.
8. Ca^{2+} is pumped back into the sarcoplasmic reticulum for storage.
9. Ca^{2+} is exchanged with Na^+ by the NCX antiporter.
10. Na^+ gradient is maintained by the Na^+-K^+-ATPase.

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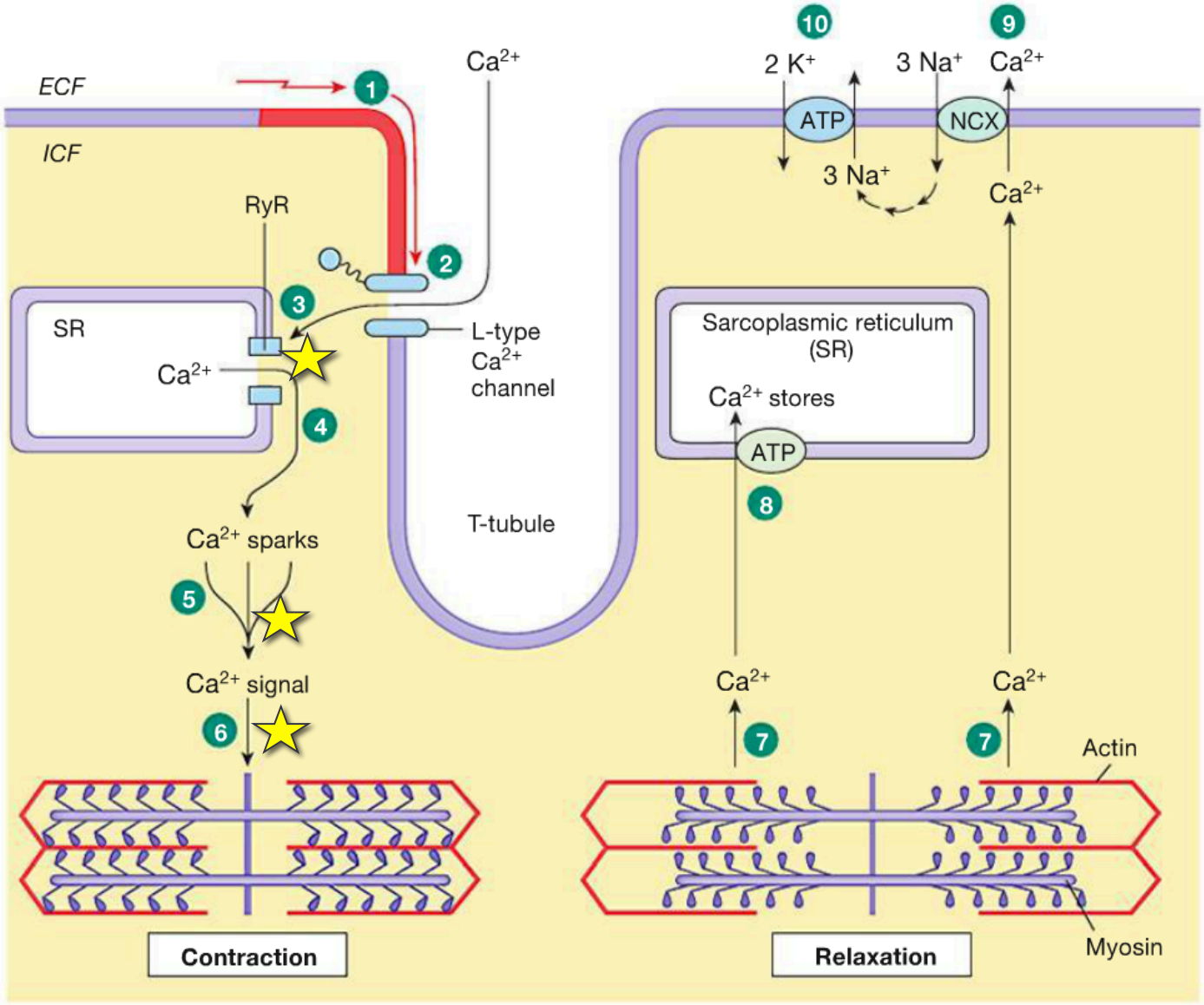

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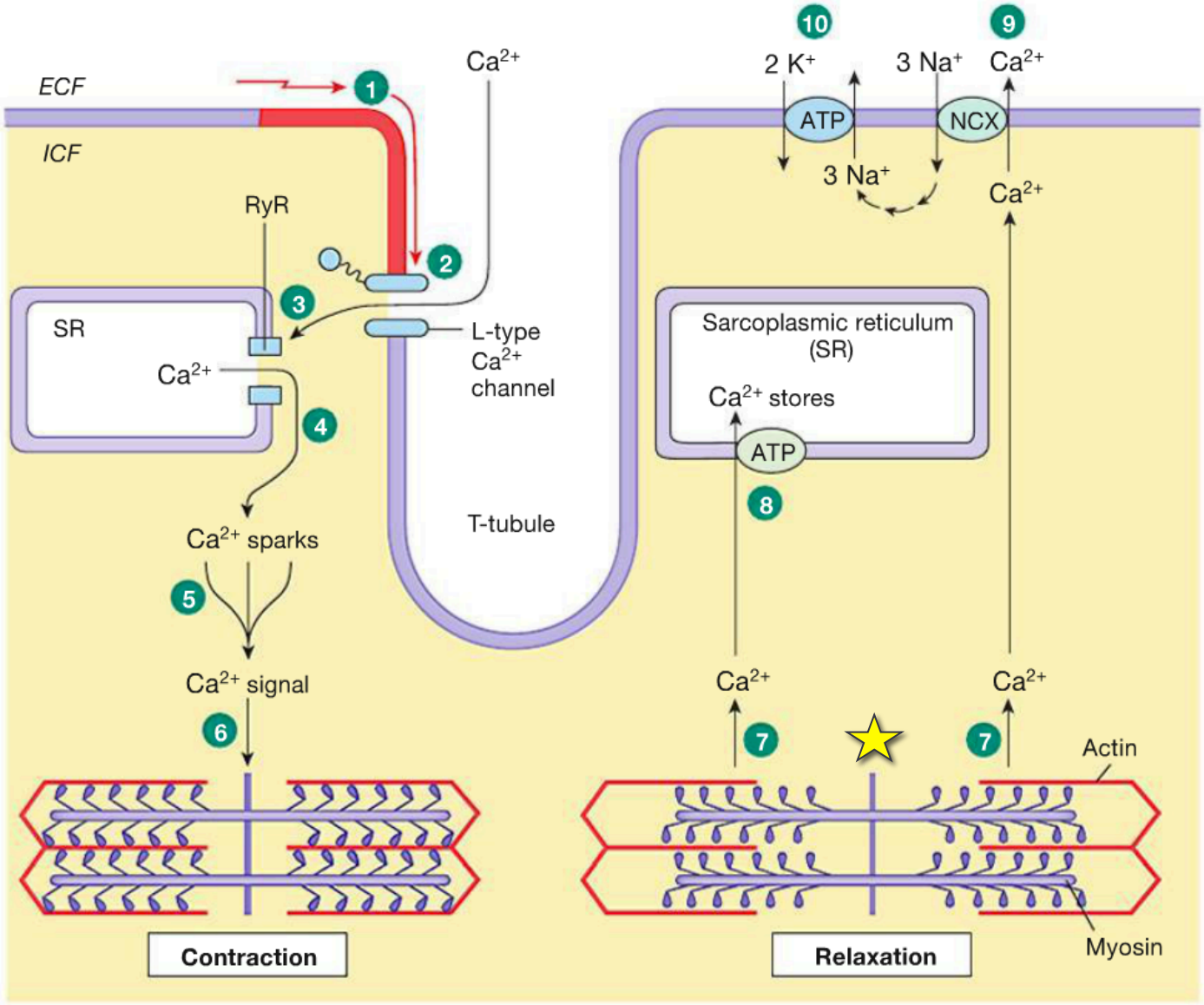

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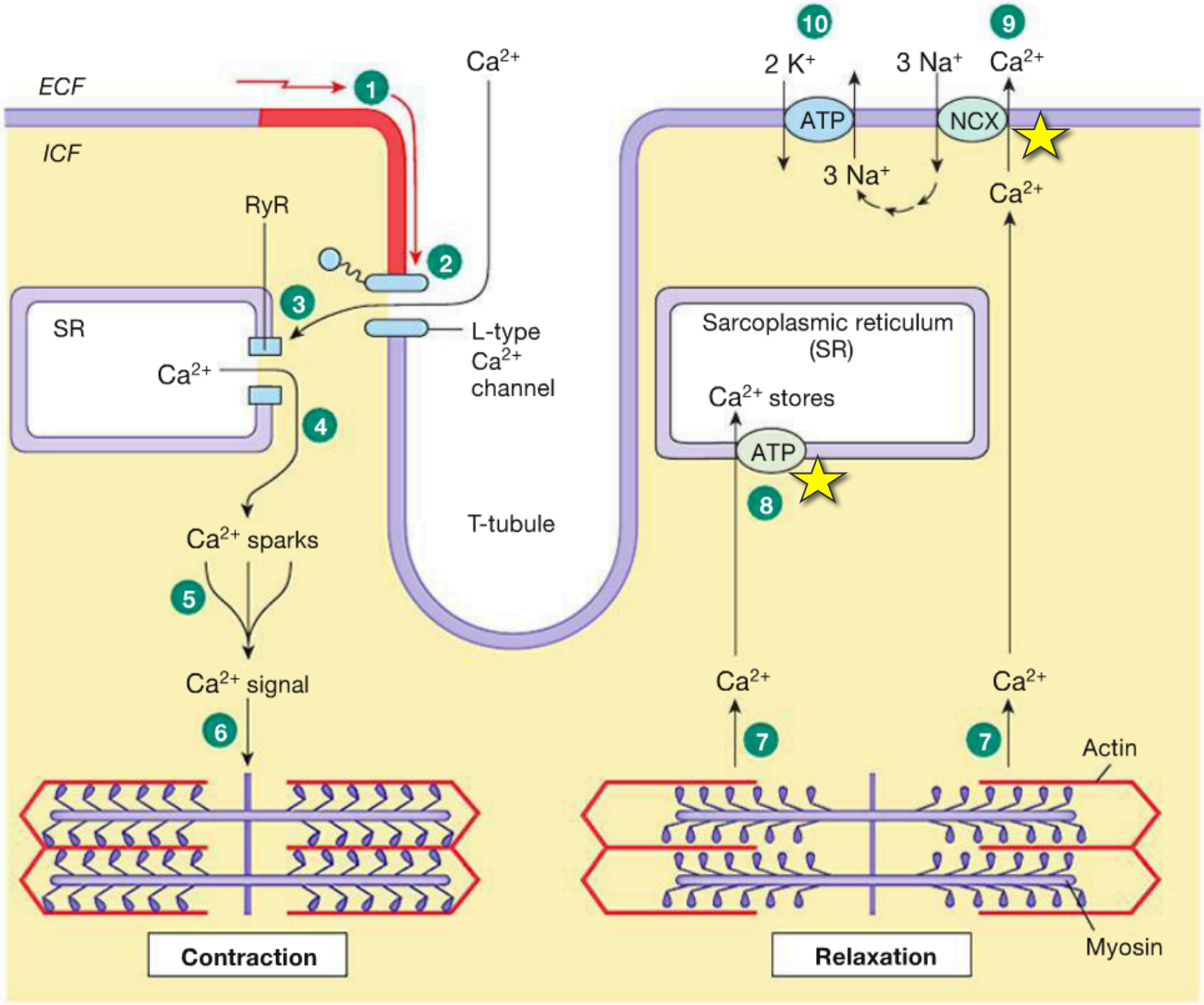

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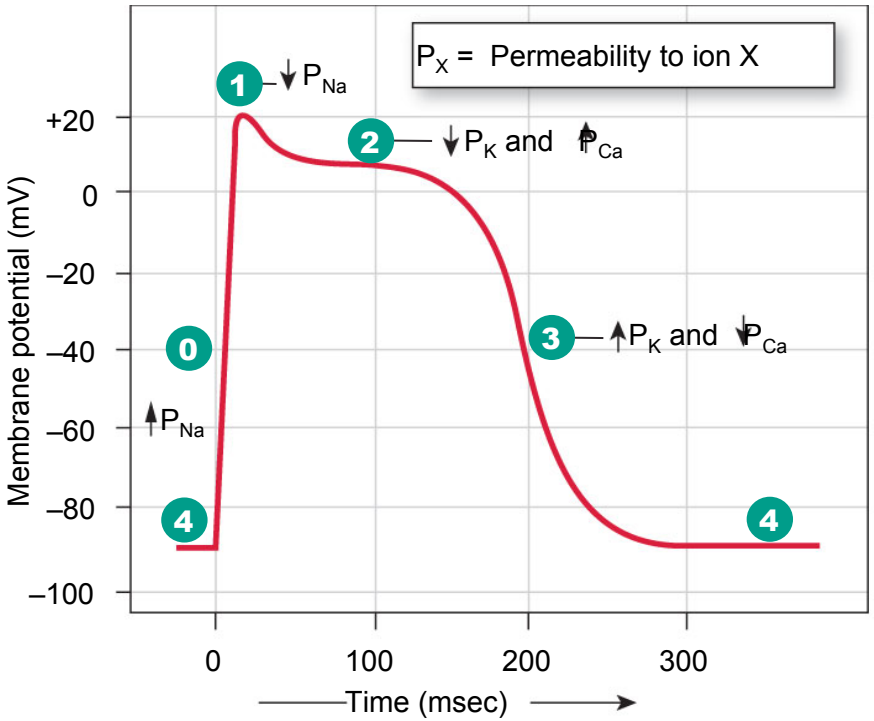
Action potential of cardiac contractile cell



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

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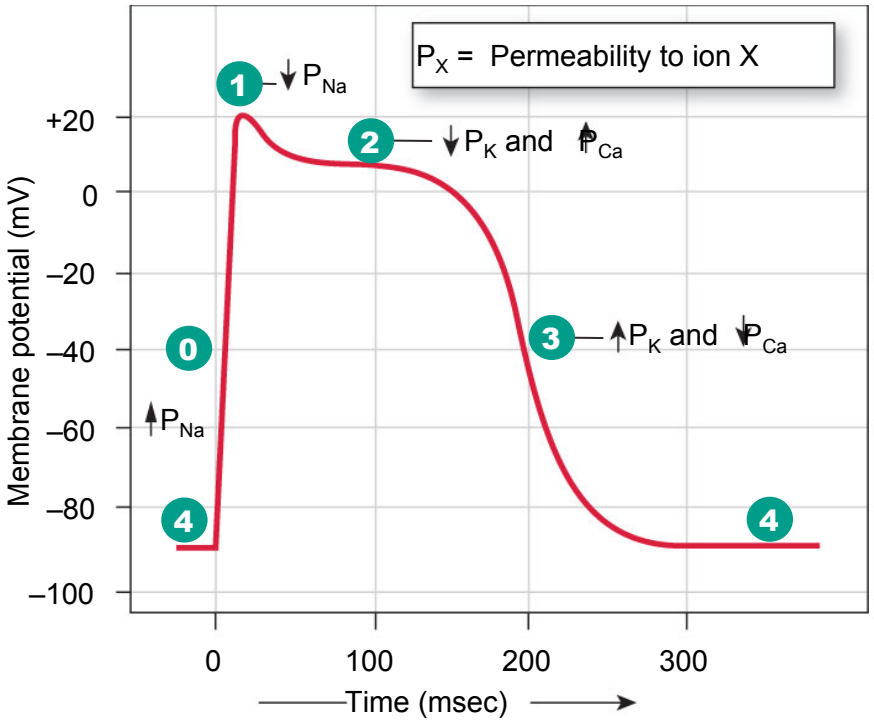

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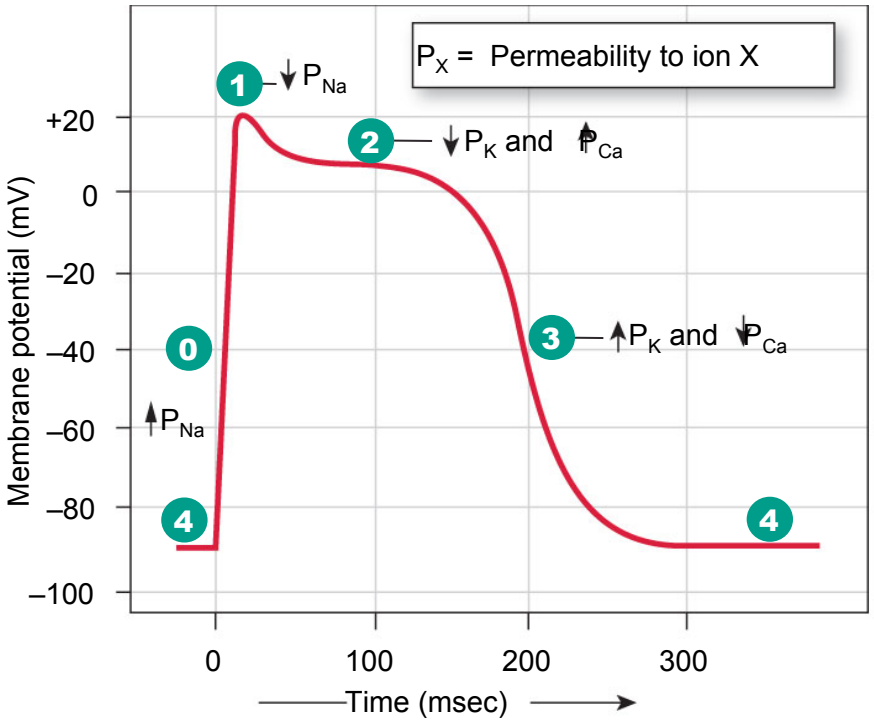

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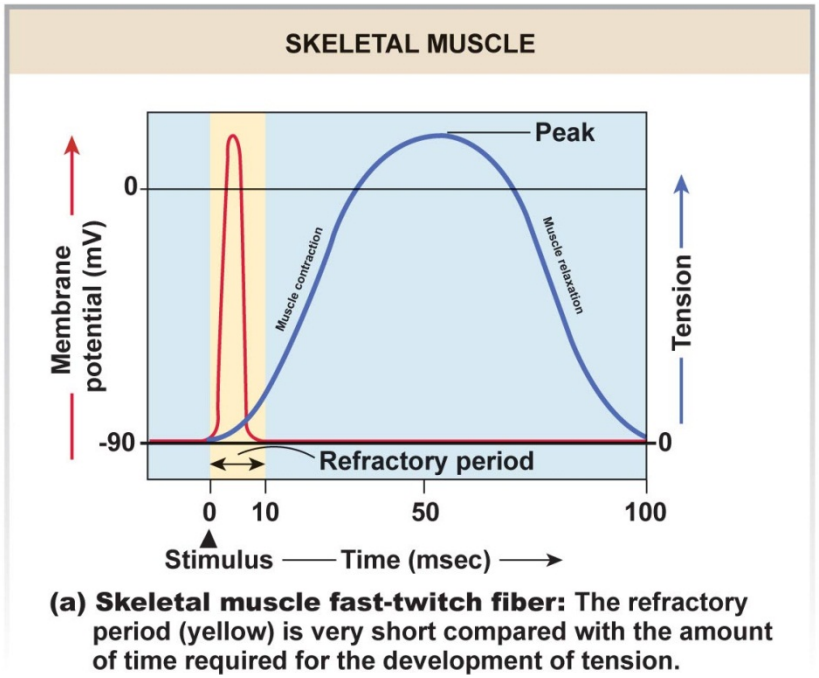
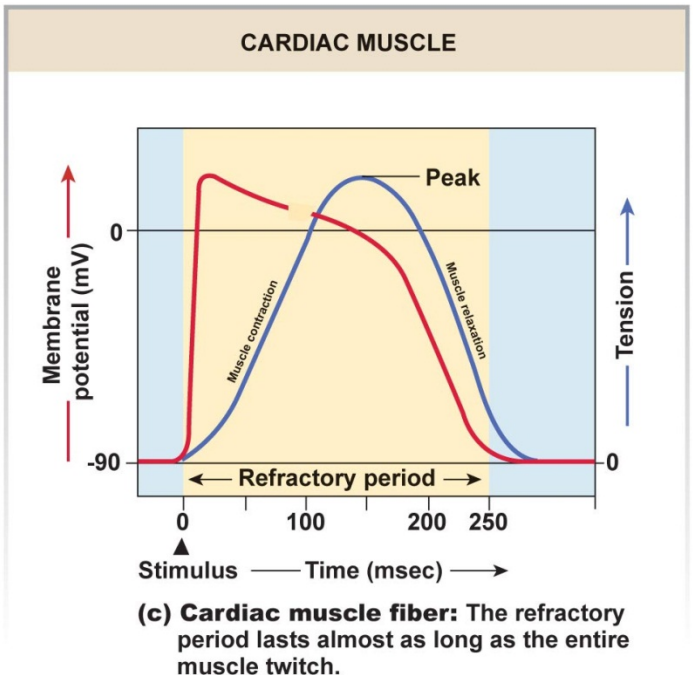
Importance of long refractory period of cardiac muscle cells



(a) Skeletal muscle fast-twitch fiber: The refractory period (yellow) is very short compared with the amount of time required for the development of tension.



(c) Cardiac muscle fiber: The refractory period lasts almost as long as the entire muscle twitch.

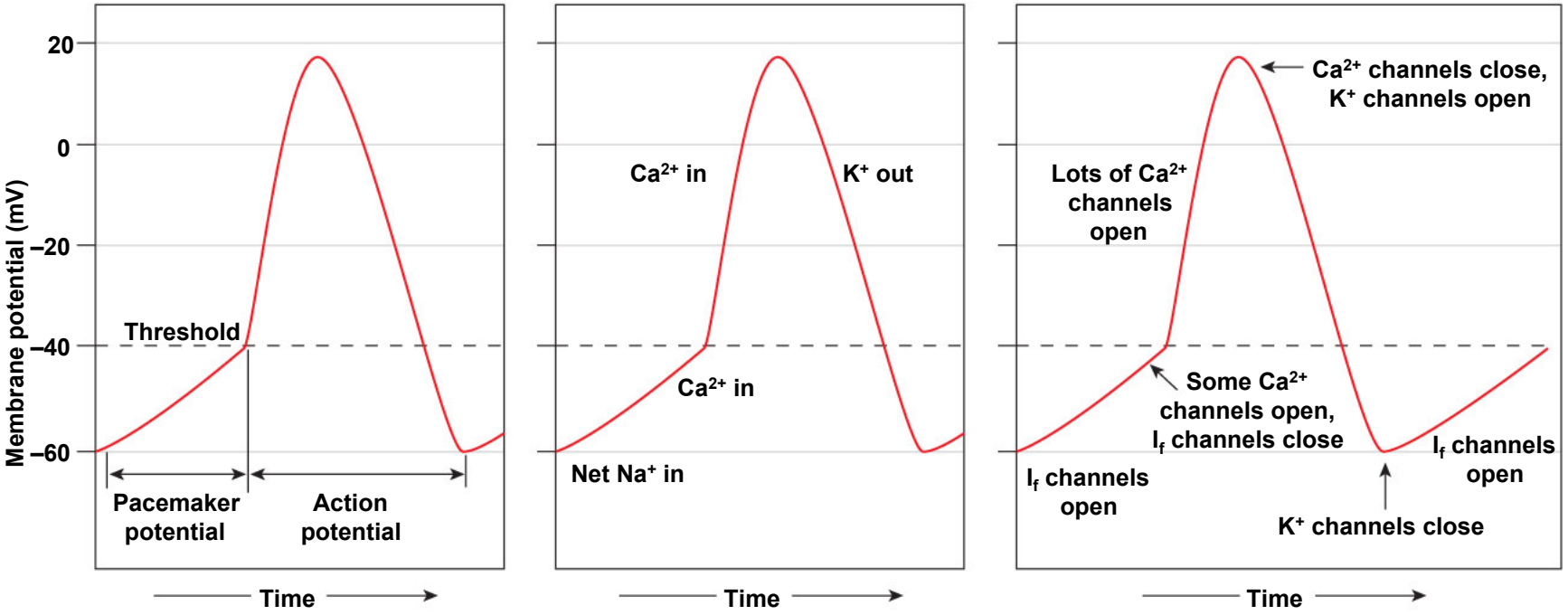
Refractory period – the time required for Na+ channels to reset to their resting positions in order to respond to *an action potential*.

Skeletal muscle – between *1 and 5 msec*

Contractile myocardial cell – 200 msec or more that prevents *tetanus* and, therefore, allows chambers in the heart to be filled with blood.

Action potential in myocardial *autorythmic cells*

Autorythmic cells have unstable membrane potential which starts at -60 mV – *pacemaker potential.*
Unique ***I_f channels*** which are permeable to both K+ and Na+.



(a) The pacemaker potential gradually becomes less negative until it reaches threshold, triggering an action potential.

(b) Ion movements during an action and pacemaker potential

(c) State of various ion channels

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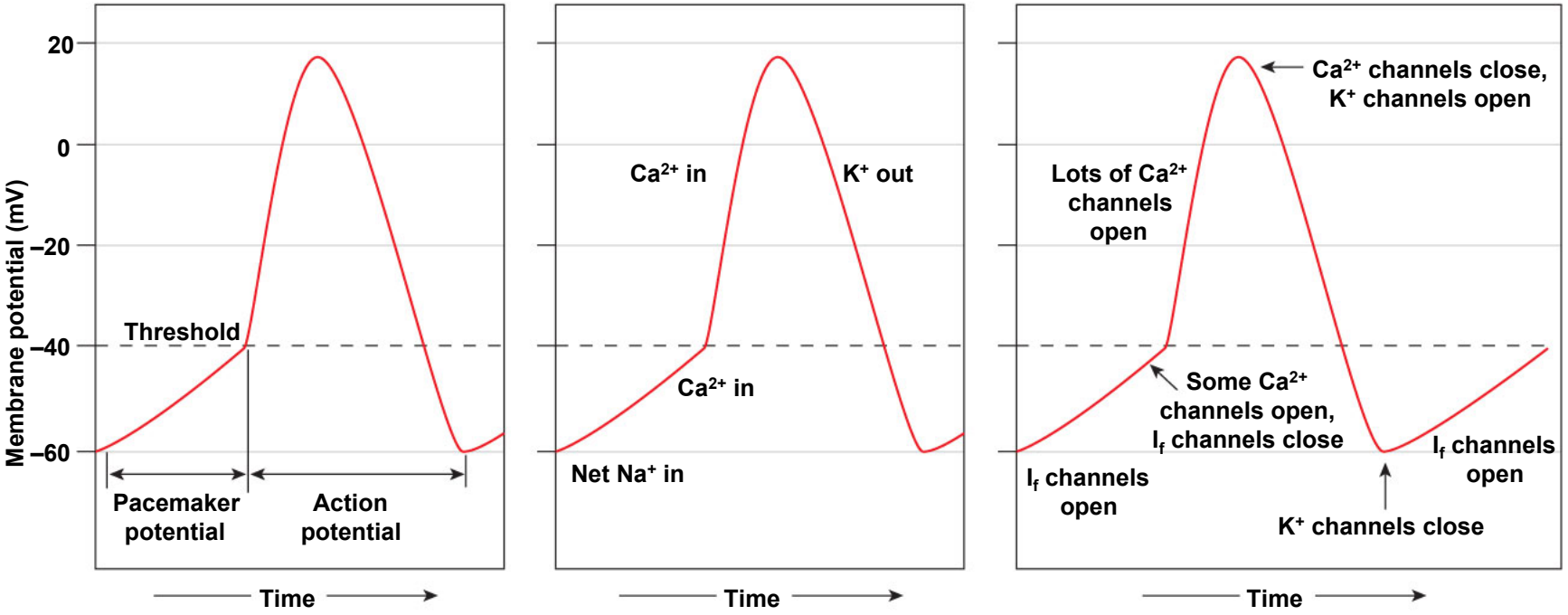

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(b) Ion movements during an action and pacemaker potential

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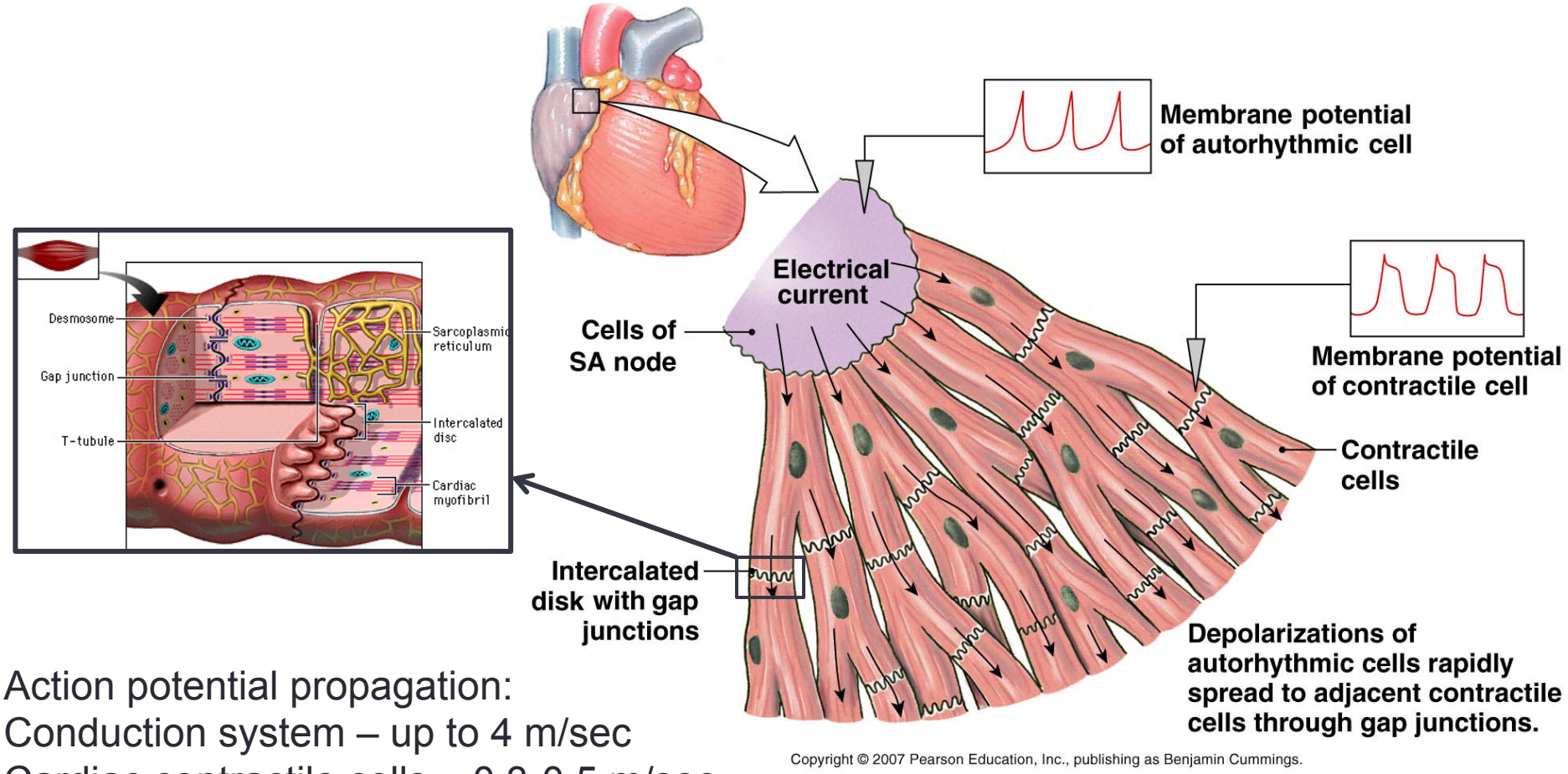
Main characteristics of action potentials

TABLE 14-3 Comparison of Action Potentials in Cardiac and Skeletal Muscle

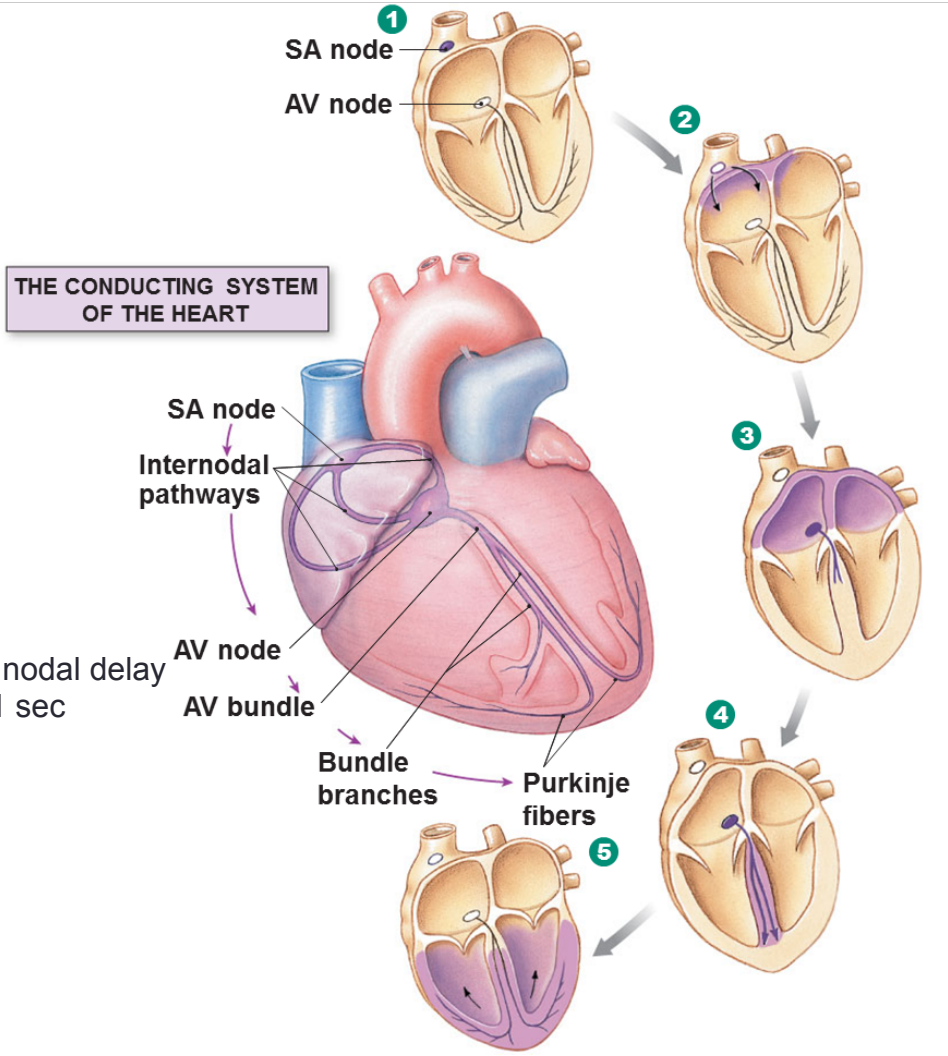
	SKELETAL MUSCLE	CONTRACTILE MYOCARDIUM	AUTORHYTHMIC MYOCARDIUM
Membrane potential	Stable at −70 mV	Stable at −90 mV	Unstable pacemaker potential; usually starts at −60 mV
Events leading to threshold potential	Net Na^+ entry through ACh-operated channels	Depolarization enters via gap junctions	Net Na^+ entry through I_f channels; reinforced by Ca^{2+} entry
Rising phase of action potential	Na^+ entry	Na^+ entry	Ca^{2+} entry
Repolarization phase	Rapid; caused by K^+ efflux	Extended plateau caused by Ca^{2+} entry; rapid phase caused by K^+ efflux	Rapid; caused by K^+ efflux
Hyperpolarization	Due to excessive K^+ efflux at high K^+ permeability when K^+ channels close; leak of K^+ and Na^+ restores potential to resting state	None; resting potential is −90 mV, the equilibrium potential for K^+	Normally none; when repolarization hits −60 mV, the I_f channels open again. ACh can hyperpolarize the cell.
Duration of action potential	Short: 1–2 msec	Extended: 200+ msec	Variable; generally 150+ msec
Refractory period	Generally brief	Long because resetting of Na^+ channel gates delayed until end of action potential	None

Signal conduction in myocardial cells



Action potential propagation:
Conduction system – up to 4 m/sec
Cardiac contractile cells – 0.3-0.5 m/sec

Electrical conduction in the heart: “Action”

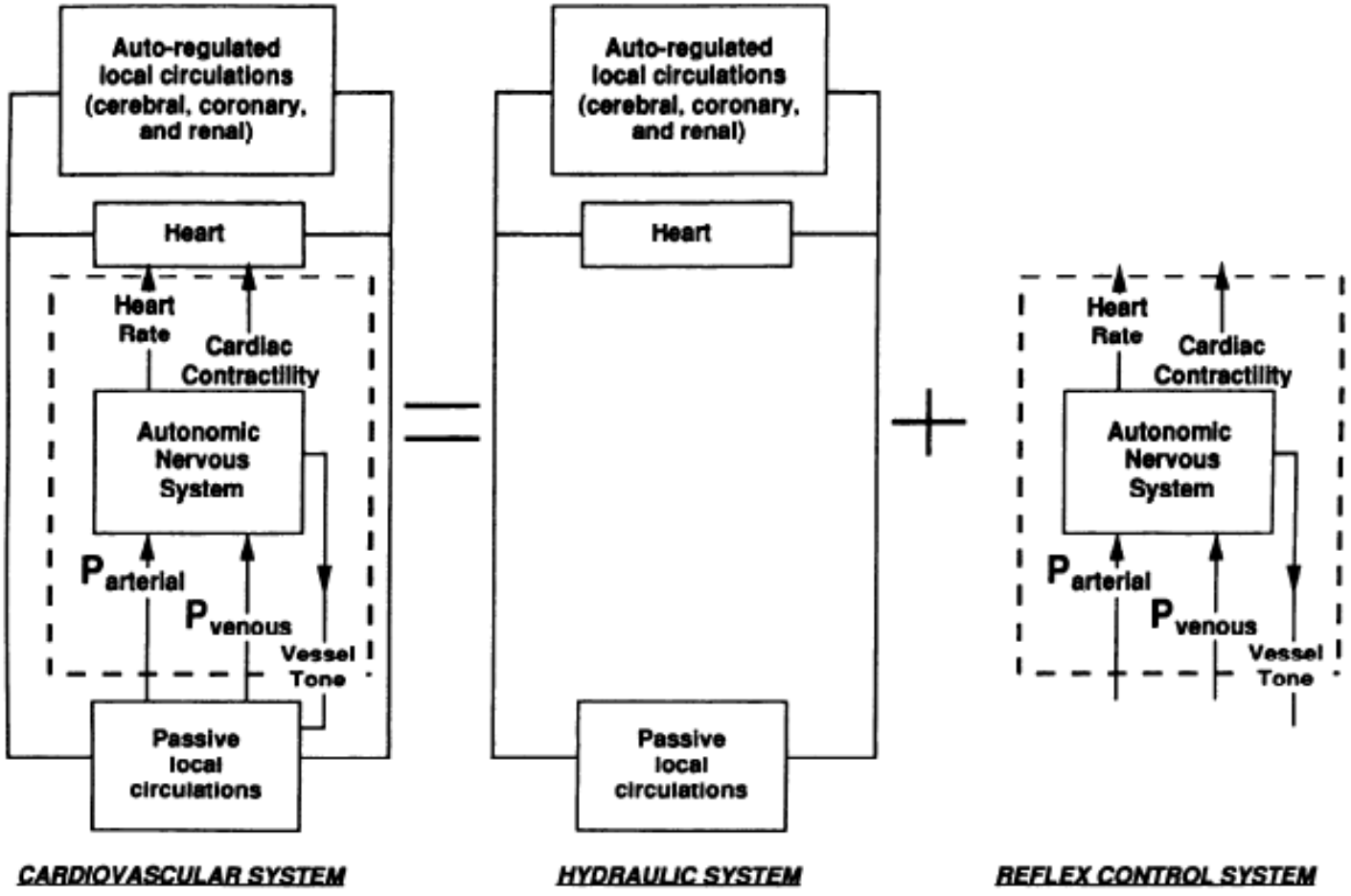


- **Sinoatrial (SA) node: 70 impulses/min**
- **Atrioventricular (AV) node: (50 impulses/min)**
- **AV bundle**
- **L and R bundle branches**
- **Purkinje fibers: (30-40 impulses/min)**

Cardiac conduction system

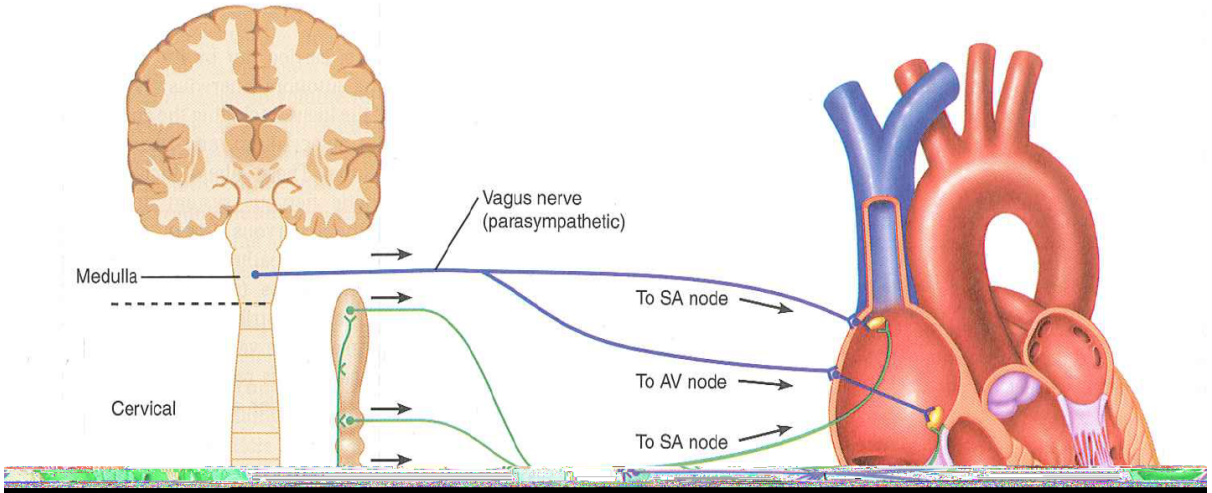
http://www.youtube.com/watch?v=Lt092HZCppo&feature=related

Cardiovascular System – Function/ Control Overview

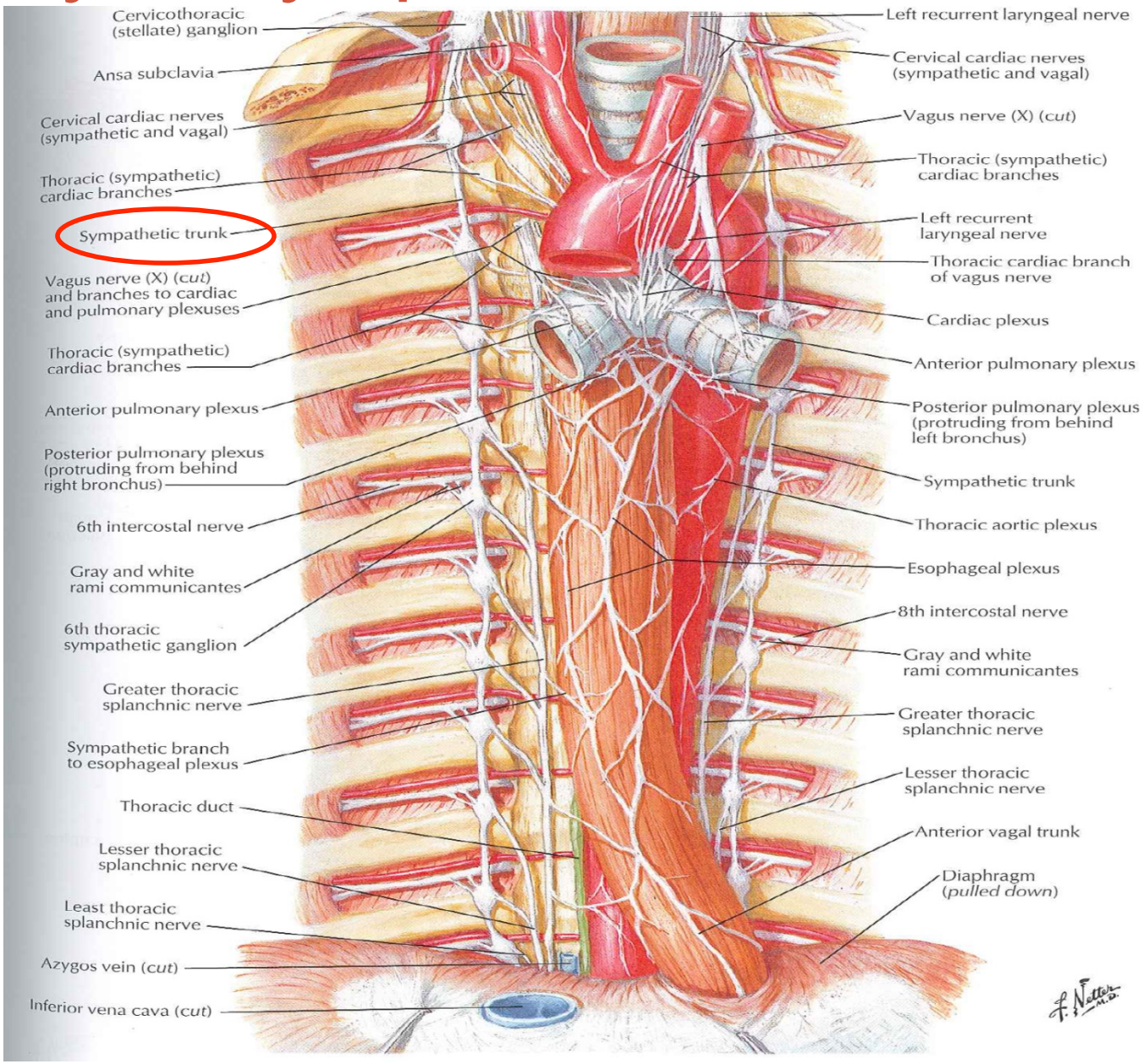


"Mathematical modeling of human cardiovascular system for simulation of orthostatic response," Heart and Circulatory Physiology, H1920 – H1933, 262(6) 1992

Autonomic Inputs to the Heart



Anatomy of Sympathetic Chain



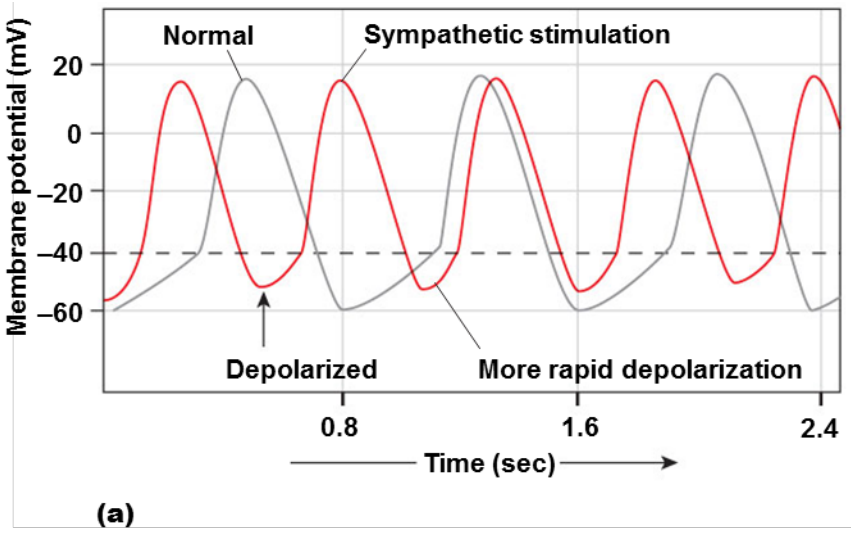
Neural Modulation of Heart Rate: autorythmic cells

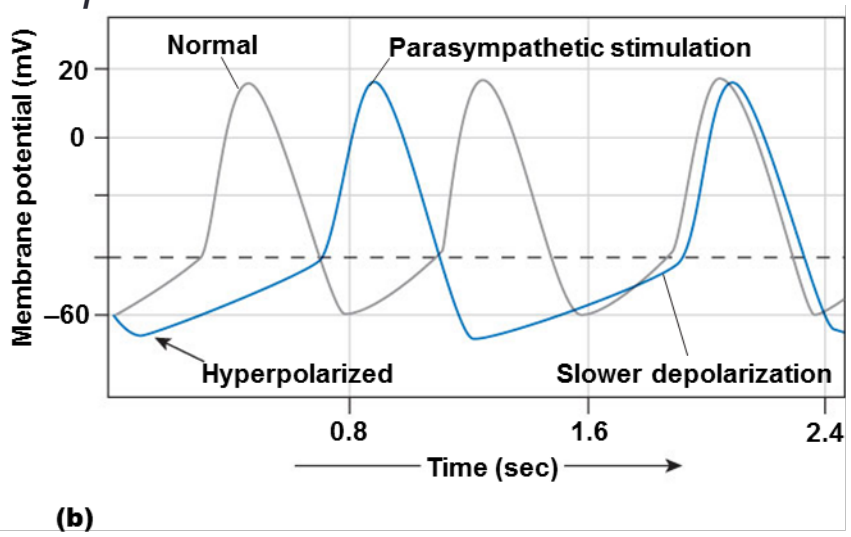
Sympathetic stimulation speeds up heart rate:

- *Norepinephrine* – sympathetic neurons.
- *Epinephrine* – adrenal medulla.
- Bind to *β_1 –adrenergic receptor*.
- Increase in ion flow through *I_f and Ca2+ channels*.

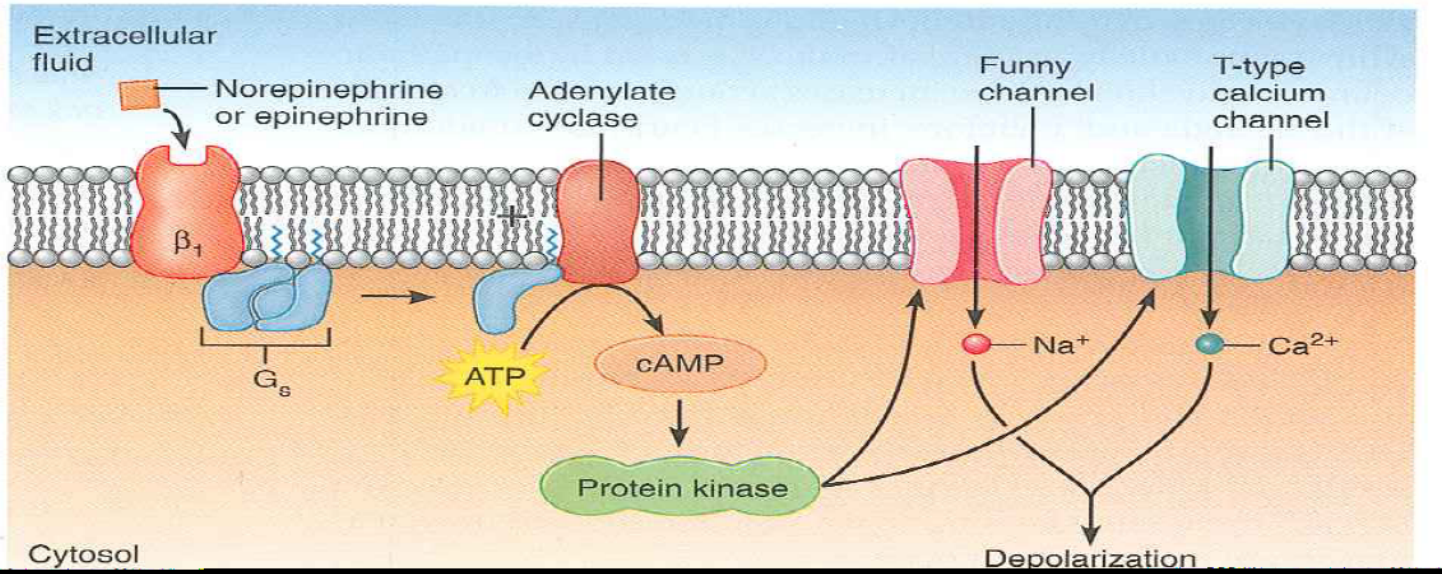
Parasympathetic stimulation decreases heart rate:

- Neurotransmitter *Acetylcholine (ACh)*.
- Activates *muscarinic cholinergic receptors*.
- Increases *K+ permeability* hyperpolarizing the cells.
- Decreases *Ca2+ permeability*.
- Longer time to reach the *threshold potential*.





Molecular mechanism of autonomic neural regulation of SA nodal cells



Neural modulation of cardiac contraction: cardiac muscle cells

- Increase concentration of Ca2+ released inside myocardial muscle cells.
- More active myosin crossbridges.
- Stronger contraction.

In addition:

- Increase speed of Ca2+ -ATPase
- Decrease active time of myosin crossbridges (Why?).
- Briefer muscle twitch.