

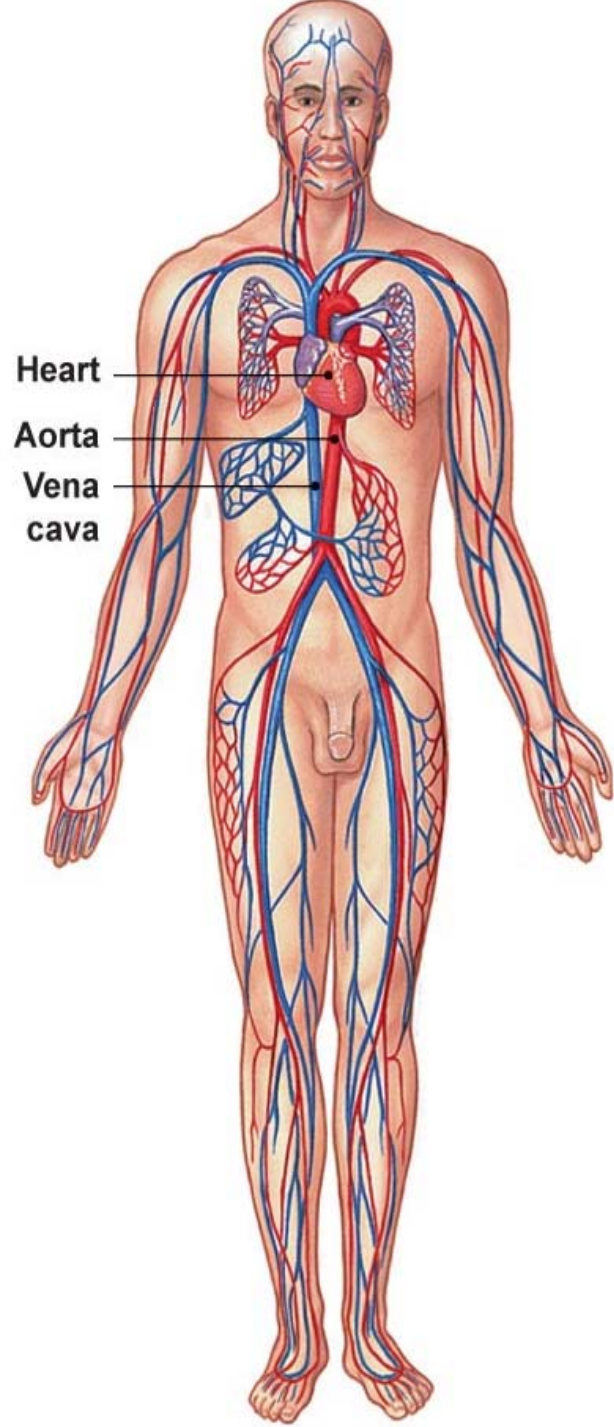
Topics to Review

- Diffusion
- Skeletal muscle fiber (cell) anatomy
- Membrane potential and action potentials
- Action potential propagation
- Excitation-contraction coupling in skeletal muscle
 - skeletal muscle action potential and molecular mechanism of skeletal muscle contraction
- Tetanus in skeletal muscle
- Norepinephrine, epinephrine and acetylcholine

Cardiovascular System

The **cardiovascular** system is a series of tubes (**blood vessels**) filled with blood connected to a pump (**heart**)

- Pressure generated in the heart continuously moves blood through the system which facilitates the transportation of substances throughout the body
 - nutrients, water and gasses that enter the body from the external environment
 - materials that move from cell to cell within the body
 - wastes that the cells eliminate
- Blood vessels that carry blood away from the heart are called **arteries**, which carry blood to the exchange vessels called **capillaries**
- Blood flowing out of capillaries is returned back to the heart via blood vessels called **veins**



Heart

Aorta

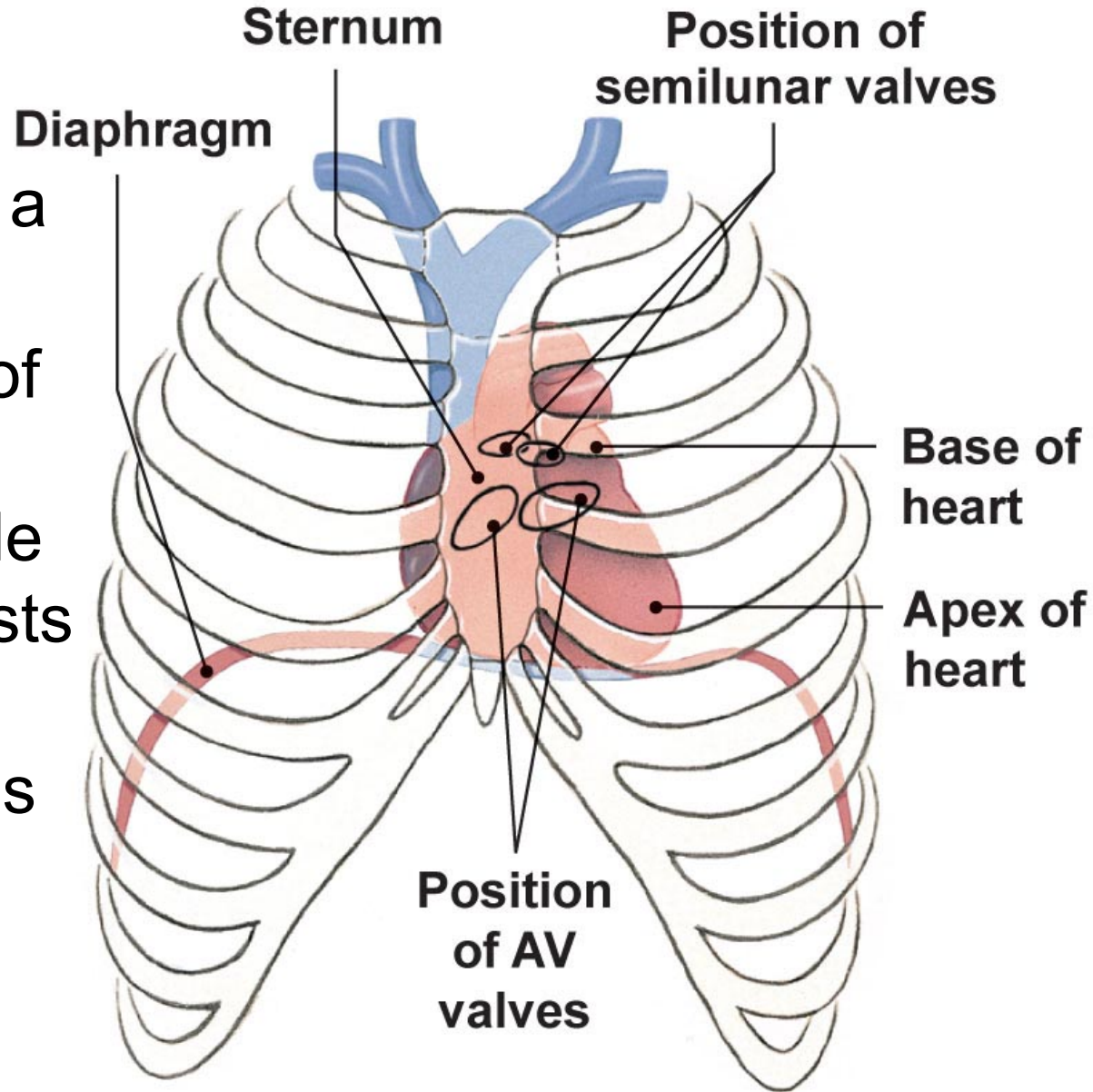
Vena
cava

Why Does Blood Flow?

- Fluids flow down **pressure gradients** (ΔP) from regions of higher pressures to regions of lower pressures
- Blood flows out of the heart when it contracts (region of highest pressure) into the closed loop of blood vessels (region of lower pressure)
- As blood moves through the cardiovascular system, a system of one way **valves** in the heart and veins prevent the flow of blood reversing its direction ensuring that blood **flows in one direction only**

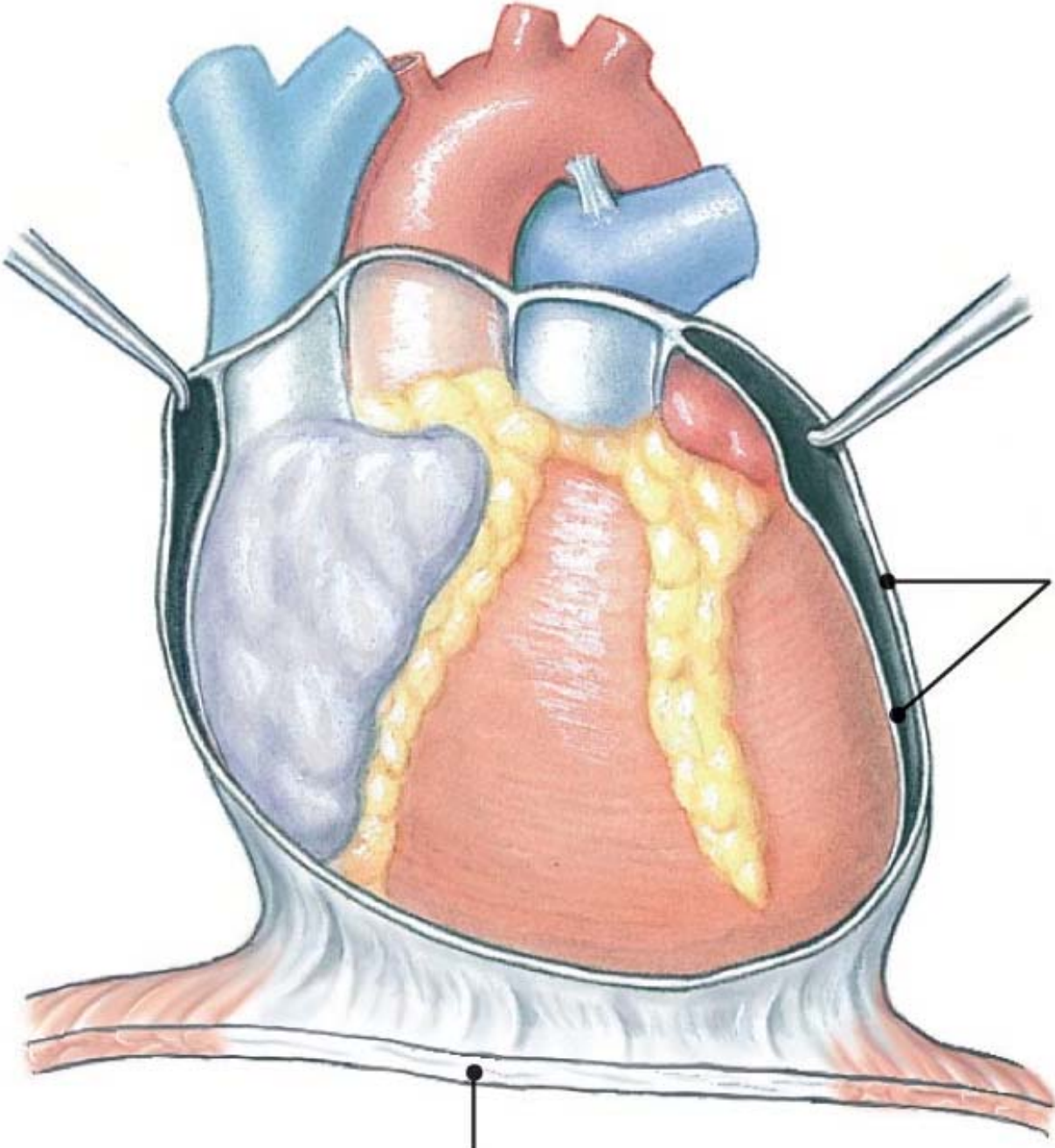
Heart Shape and Position

- The heart is a muscular organ roughly the size of a fist
- The pointed **apex** of the heart angles down to the left side of the body and rests on the diaphragm
- The broad **base** lies just behind the sternum



Heart Covering

- The heart is surrounded by a double membrane **pericardium** made of connective tissue
 - prevents overfilling of the heart with blood
- **Parietal pericardium**
 - fits loosely around the heart
 - attached to the superficial surface of the diaphragm
- **Visceral pericardium** or **epicardium**
 - thin superficial layer of the heart
- Pericardial cavity
 - filled with pericardial fluid
 - allows for the heart to work in a relatively friction-free environment
 - inflammation of the pericardium called **pericarditis** may reduce the lubrication



Pericardium

Diaphragm

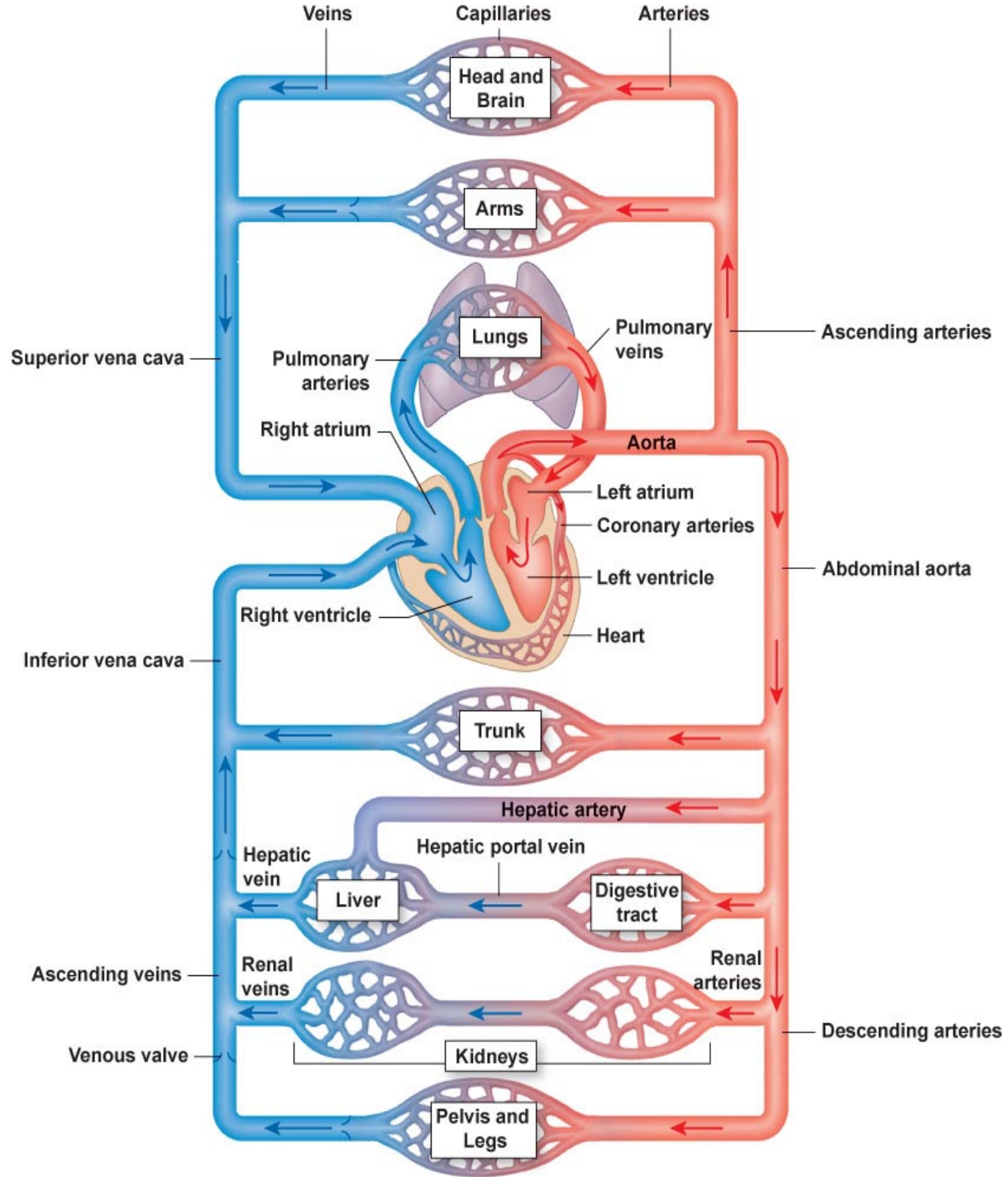
The Pump

- The heart is divided by a central wall (**septum**) into right and left halves
 - the septum serves to separate **oxygenated blood** (**left** half) from **deoxygenated blood** (**right** half)
 - each half consists of a superiorly positioned **atrium** and an inferiorly positioned **ventricle**
 - the **atrium receives** blood returning to the heart from the blood vessels and the **ventricle pumps** blood out into the blood vessels
- The left side of the heart receives newly oxygenated blood from the lungs and pumps it through the **systemic circulation**
- The right side of the heart receives blood from the tissues and pumps it through the **pulmonary circulation**

[Pulmonary and Systemic Circuits](#)

Systemic Circulation

- From the **left atrium**, blood flows into the **left ventricle** and then is pumped into the **aorta** which branch into smaller arteries to bring blood to systemic **capillaries** all over the body for exchange
 - the first branch is the **coronary artery** which nourishes the heart itself
- From the systemic capillaries, blood flows into veins
 - blood from the capillaries of the heart flow into the **coronary vein** which empties into the **right atrium**
 - veins from the upper part of the body join to form the **superior vena cava** and empty into the **right atrium**
 - veins from the lower part of the body join to form the **inferior vena cava** and empty into the **right atrium**



Pulmonary Circulation

- From the **right atrium**, blood flows into the **right ventricle** and then is pumped into the **pulmonary trunk**
 - the pulmonary trunk divides into right and left **pulmonary arteries** which branch into smaller arteries to bring blood to pulmonary **capillaries** in the lungs for gas exchange
 - from the pulmonary capillaries, blood flows through the **pulmonary veins** and empty into the **left atrium**

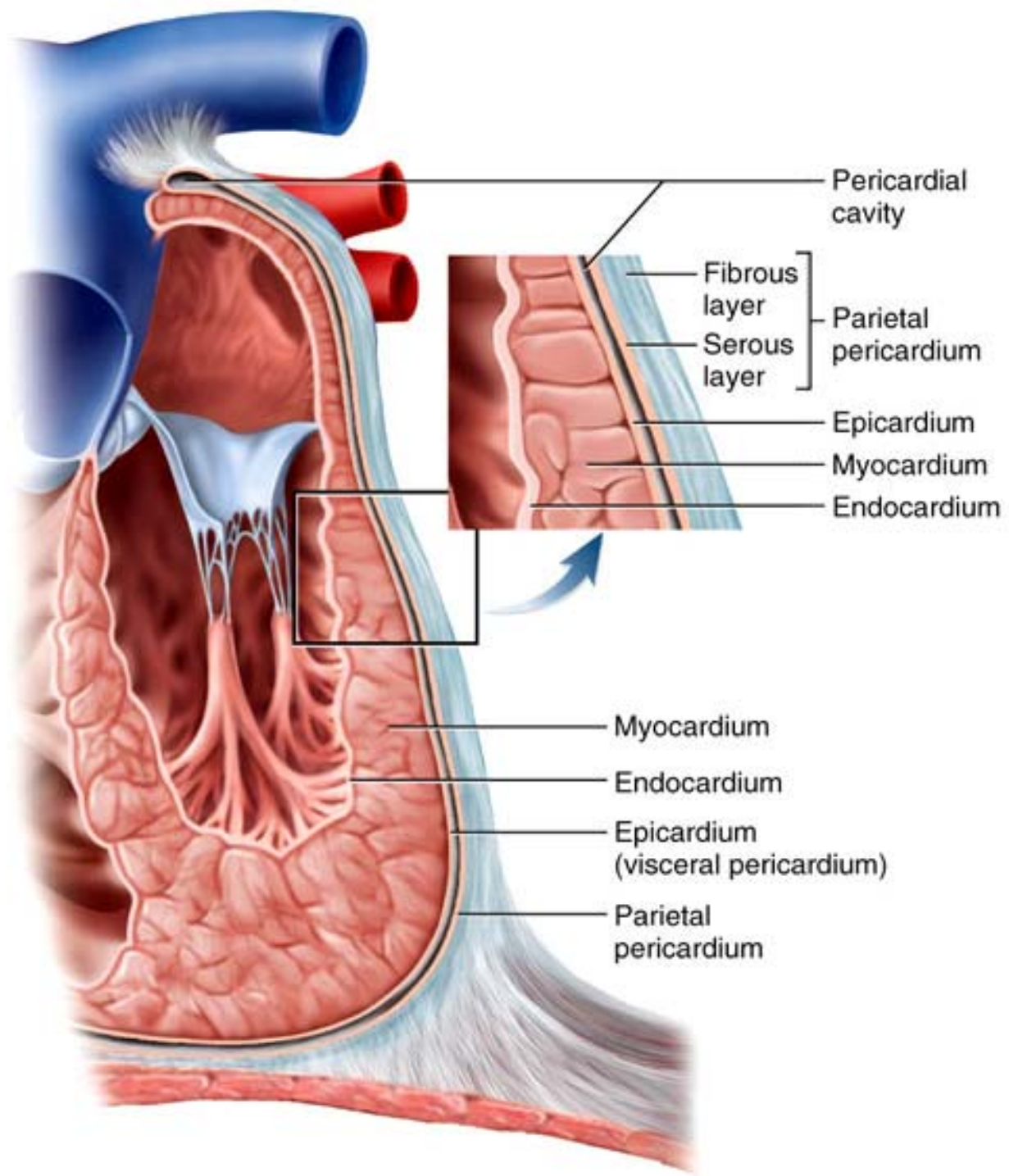
Blue type indicates structures containing blood with lower oxygen content; red type indicates well-oxygenated blood.

	RECEIVES BLOOD FROM	SENDS BLOOD TO
Heart		
Right atrium	Venae cavae	Right ventricle
Right ventricle	Right atrium	Lungs
Left atrium	Pulmonary veins	Left ventricle
Left ventricle	Left atrium	Body except for lungs
Vessels		
Venae cavae	Systemic veins	Right atrium
Pulmonary trunk (artery)	Right ventricle	Lungs
Pulmonary vein	Veins of the lungs	Left atrium
Aorta	Left ventricle	Systemic arteries

Heart Wall

- The heart is composed mostly of cardiac muscle (or **myocardium**) which is covered by thin outer and inner layers of connective tissue (**epicardium** or visceral layer of the pericardium) and epithelial tissue (**endocardium**), respectively
- The myocardium of the 2 atria and 2 ventricles contract (**systole**) and relax (**diastole**) in a coordinated fashion to pump blood through the pulmonary and systemic circulations
 - first the atria contract together (while the ventricles relax), then the ventricles contract together (while the atria relax)
 - this pattern repeats each heartbeat in what is called the **cardiac cycle**

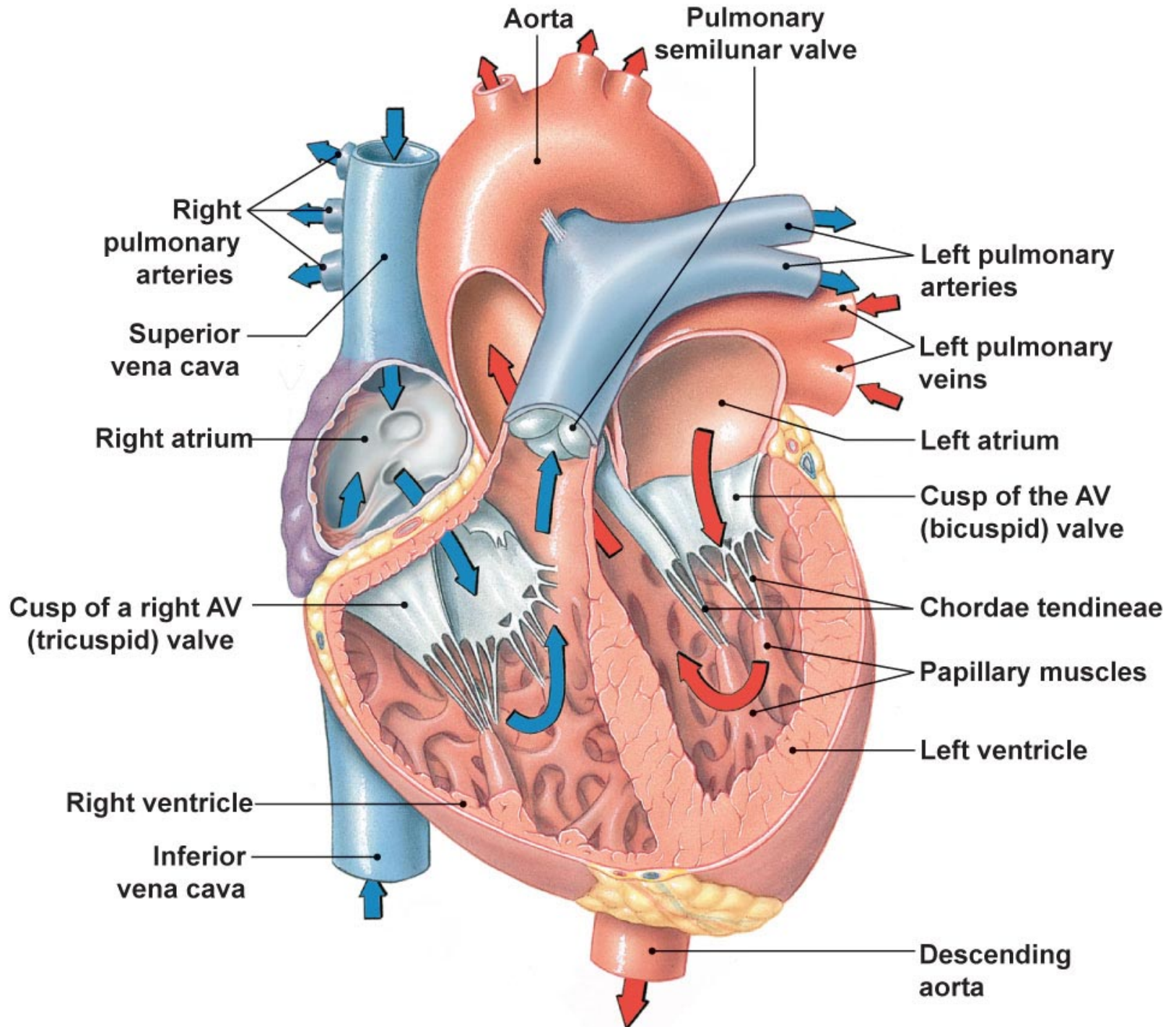
Pericardium and Heart Wall



Heart Valves

- The heart contains 2 pairs of valves (4) which ensure a unidirectional blood flow through the heart
- 2 **atrioventricular** valves are located between the atria and ventricles
- 2 **semilunar** valves are located between the ventricles and the arteries

- An open valve allows blood flow
- A closed valve prevents blood flow
- A valve will open and close due to a blood pressure gradient across it



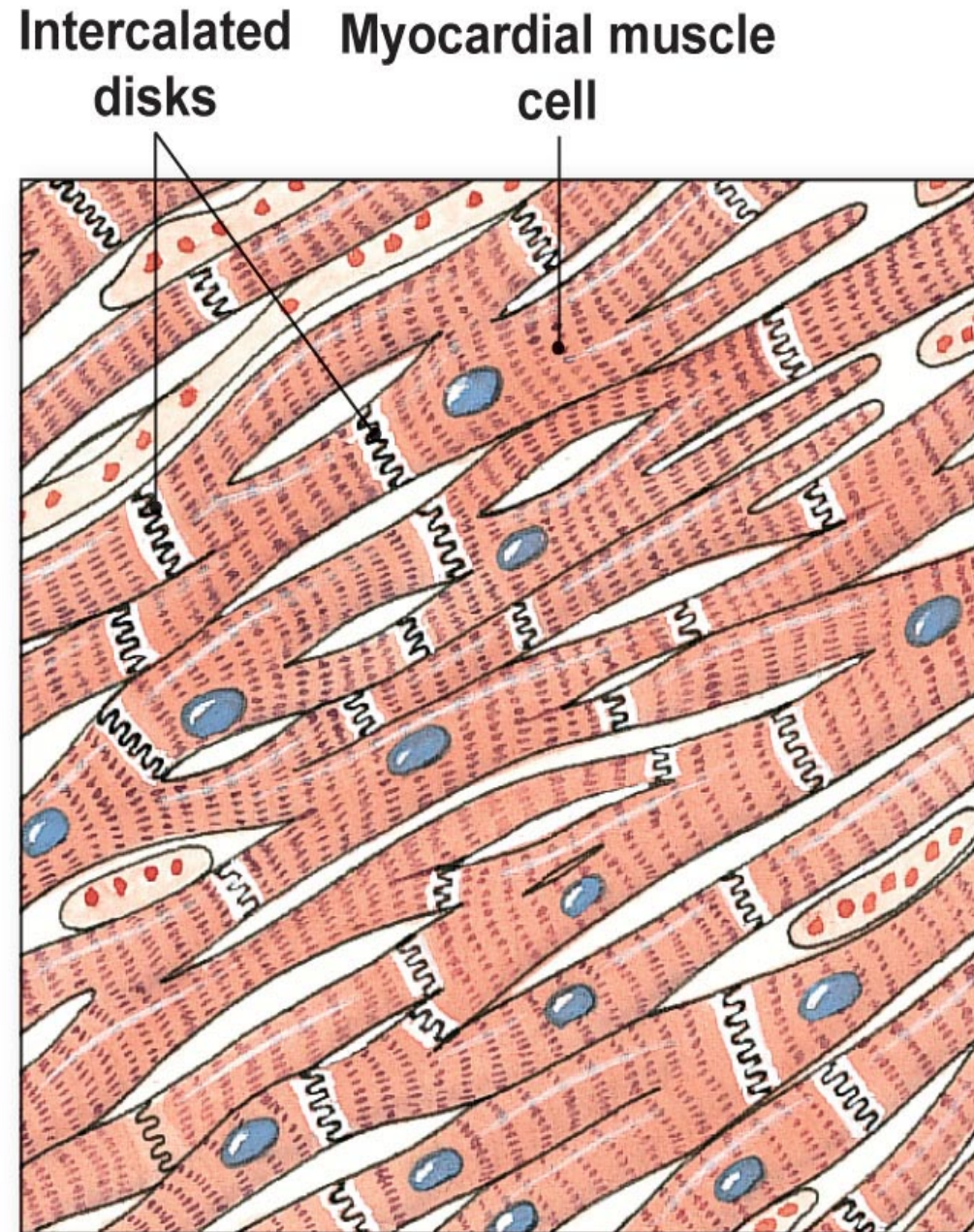
Atrioventricular Valves

- **Atrioventricular** (AV) valves prevent the backflow of blood from the ventricles into the atria
- Formed from thin flaps of tissue joined at the base to a connective tissue ring
 - right AV valve has 3 flaps = **tricuspid**
 - left AV valve has 2 flaps = **bicuspid** or **mitral** valve
- The valves move passively when flowing blood pushes on them during ventricular systole and diastole

Semilunar Valves

- The semilunar valves separate the ventricles from the major arteries and prevent the backflow of blood from the major arteries to the ventricles
 - each semilunar valve has 3 cuplike leaflets
 - left semilunar valve = **aortic** semilunar valve
 - right semilunar valve = **pulmonary** semilunar valve
- The valves move passively when flowing blood pushes on them during ventricular systole and diastole

Histology of the Myocardium



- The myocardium consists of 2 cell types
 - contractile cells
 - conducting cells
- Individual cells branch and join neighboring cells end-to-end at junctions called **intercalated disks**

Intercalated Disks

- Consist of **desmosomes** and **gap junctions**
 - desmosomes are protein complexes that bind adjacent cells together allowing force generated in one cell to be transferred to the adjacent cell
 - gap junctions are protein complexes that form pores between adjacent cells which electrically connect adjacent cells to one another as ions are able to pass freely between cells (**electrical synapse**)
 - allow action potentials to spread rapidly from cell to cell so that the heart muscle cells contract almost simultaneously
 - an AP in one myocyte of the heart will spread to adjacent myocytes until every myocyte of the heart elicits an AP

The Contracting Myocardium

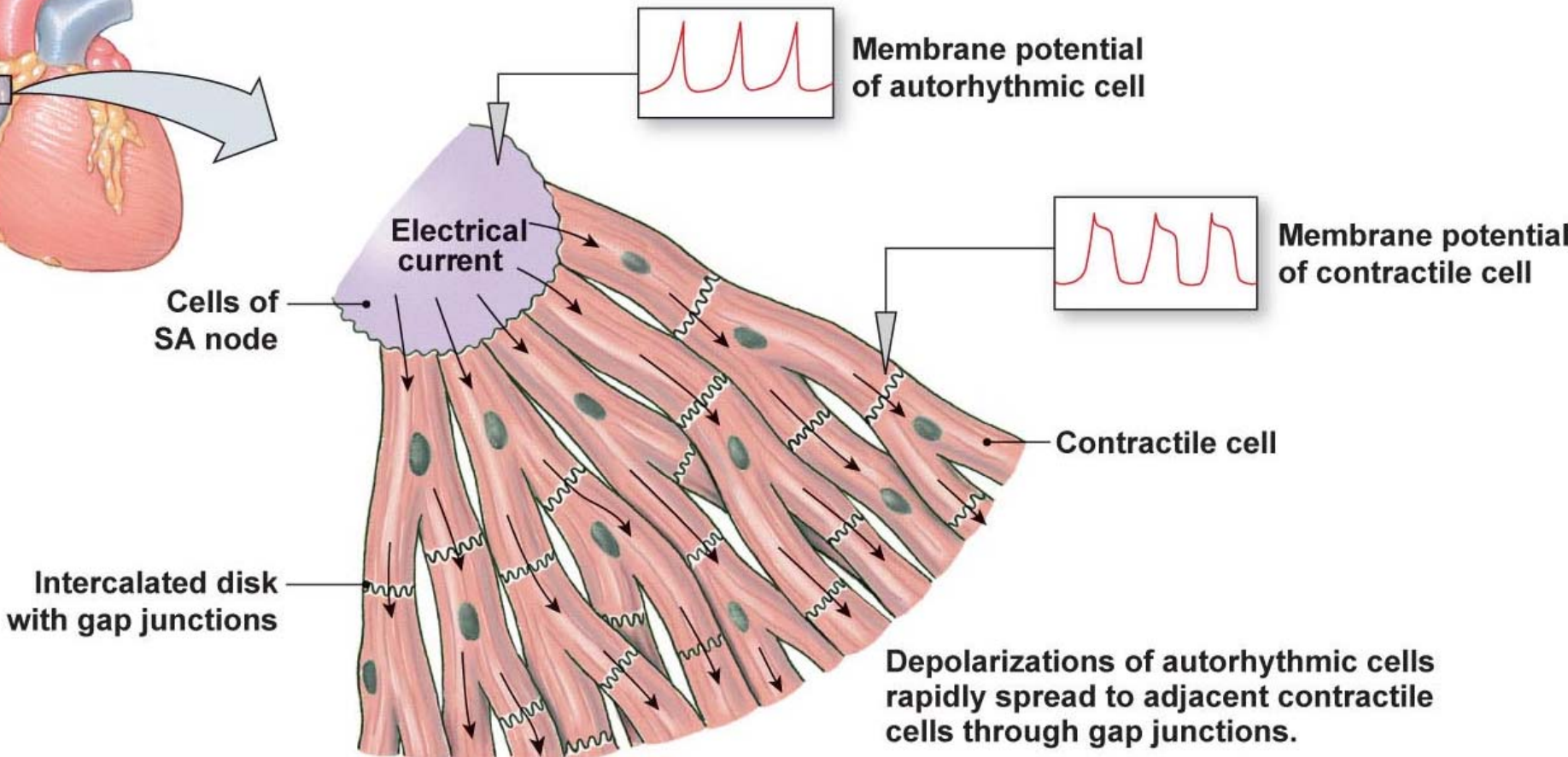
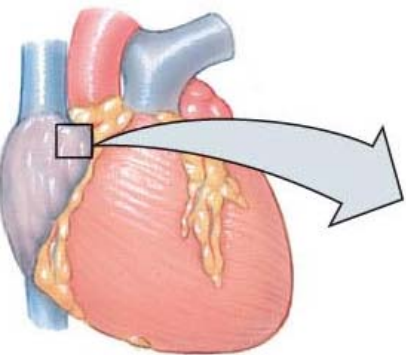
- Contractile cardiac muscle fibers are in some ways similar to and in other ways different than skeletal muscle fibers
 - smaller than skeletal muscle fibers with 1 nucleus
 - striated (contains sarcomeres of actin and myosin)
 - myocardial sarcoplasmic reticulum is smaller than skeletal muscle, reflecting the fact that cardiac muscle depends on extracellular Ca^{2+} to initiate contraction
 - mitochondria occupy ~30% of the cell volume which demonstrates their high energy demand
 - in person at rest, hemoglobin unloads 75% of its delivered oxygen to cardiac muscle

The Conducting Myocardium

- 1% of the myocardium consists of **autorhythmic** or **conducting** myocytes which spontaneously generate action potentials, allowing the heart to beat without any outside signal (**myogenic**)
- Autorhythmic myocytes behave **like neurons**
 - act as pacemakers by setting the rate of the heartbeat at the rate they generate action potentials
 - guide the action potentials travel through the heart
 - cause contraction of contractile myocytes
- 4 distinct groups of autorhythmic cells are in the heart
 - Sinoatrial (SA) node (the primary pacemaker)
 - Atrioventricular (AV) node
 - Bundle of His (and bundle branches)
 - Purkinje fibers

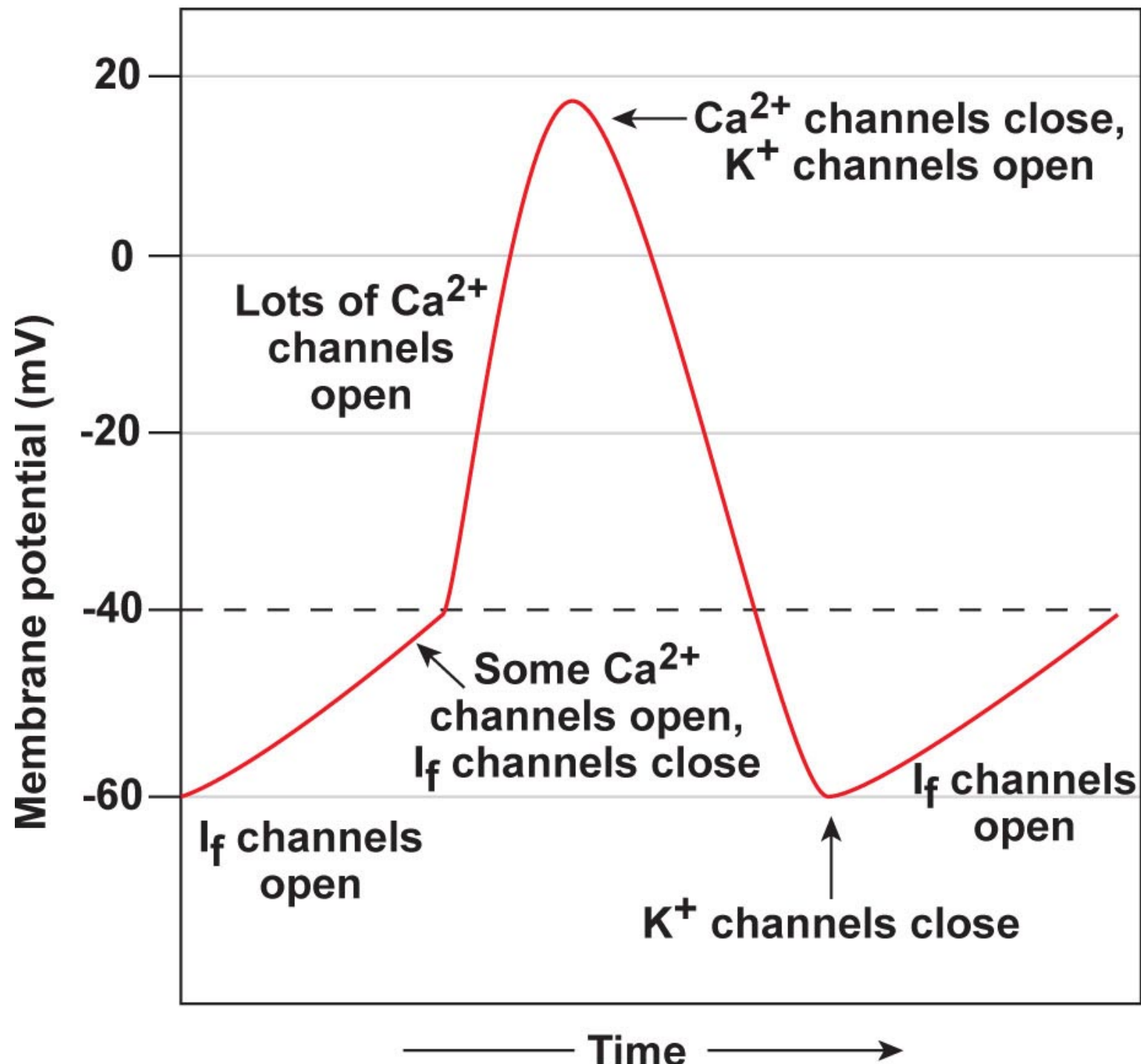
The Heart as a Pump

- In order for individual myocardial cells to produce enough force to move blood around the cardiovascular system they must depolarize and contract in a coordinated fashion
- The heart beat is initiated by an action potential in the SA node that rapidly spreads to adjacent cells through gap junctions in the intercalated disks
- The wave of depolarization that sweeps through the entire heart is followed by a wave contraction that passes across the atria and then move into the ventricles



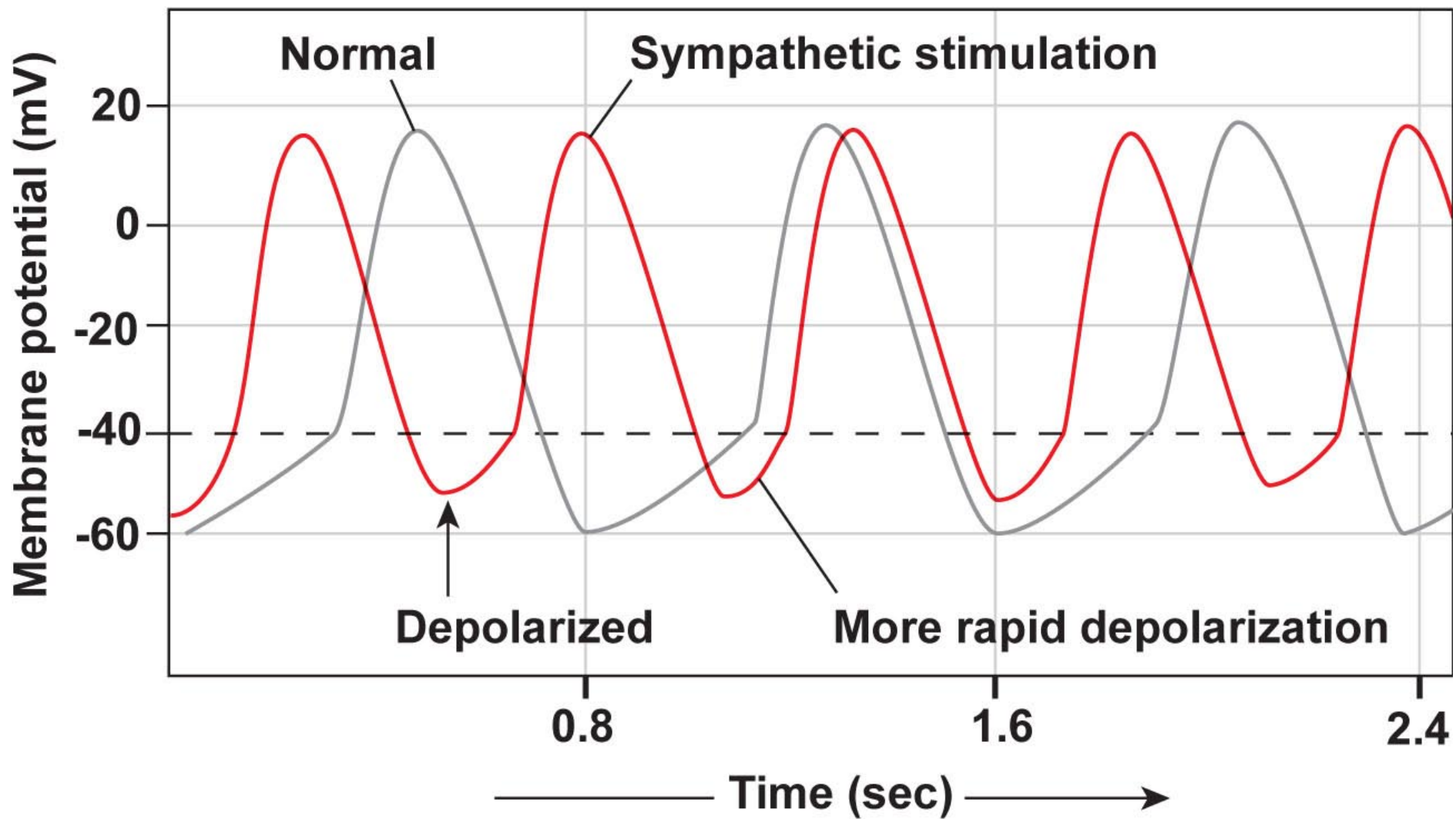
Autorhythmic Action Potentials

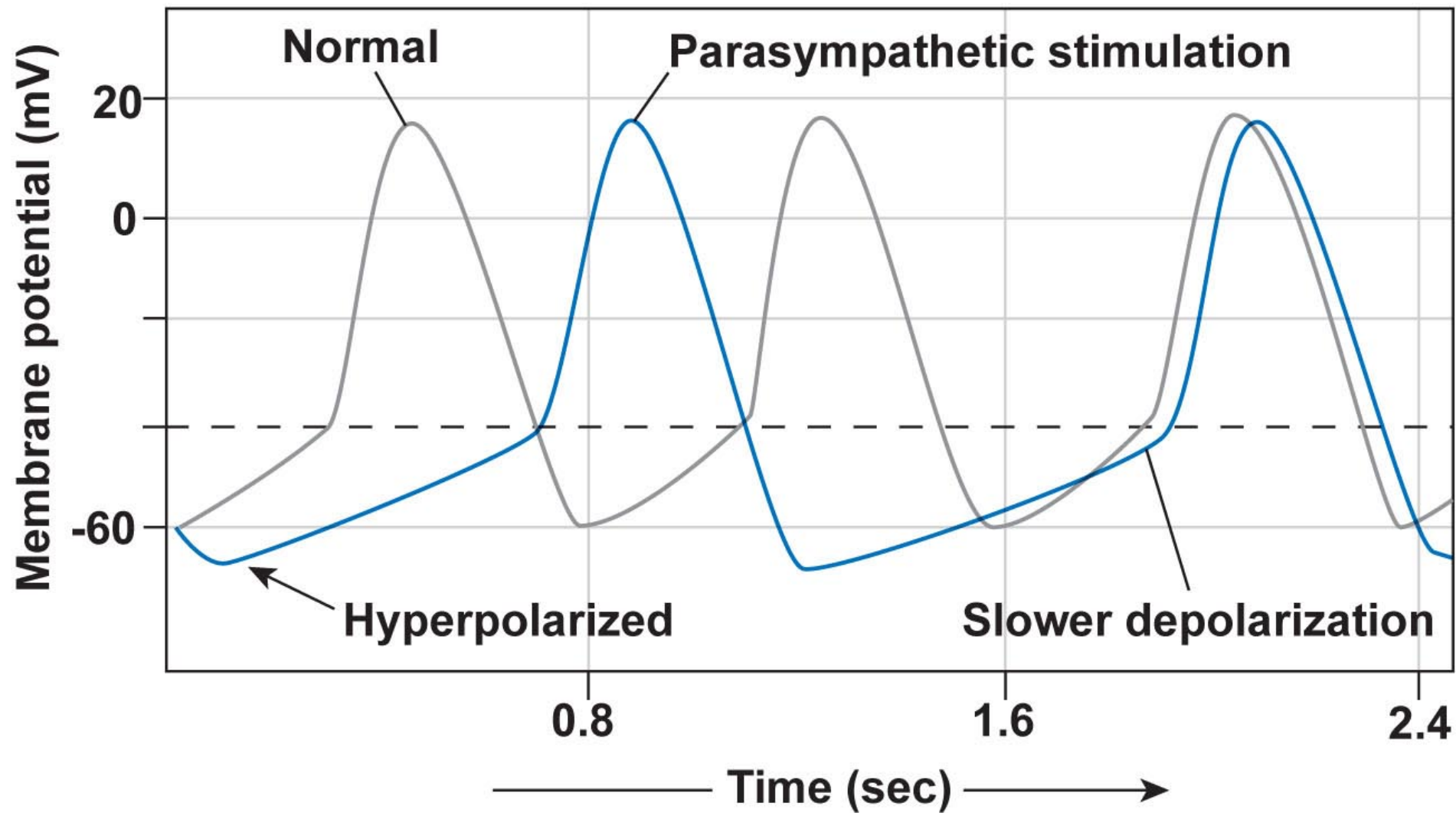
- The ability of autorhythmic cells to pace the beat rate of the heart comes from their ability to spontaneously generate action potentials
- The membrane potential of these cells is always changing, either depolarizing or repolarizing and thus their membrane potential never “rests”
- The ever changing membrane potential begins to slowly depolarize toward threshold from its lowest value of -60 mV
 - when the membrane potential reaches threshold, the cell fires an AP and then repolarizes back to a value of -60 mV



Resting Heart Rate

- In a resting adult the SA node initiates an AP approximately every 0.8 seconds (75 per minute) determining the frequency (**sinus rhythm**) of systole and diastole of the atria and ventricles resulting in a heart rate of 75 beats per minute (bpm)
 - The frequency of the APs can be altered by the antagonistic branches of the ANS to raise or lower the heart rate (HR) when appropriate
 - the **Sympathetic NS** increases HR from rest
 - when $HR > 100$ bpm = **tachycardia**
 - the **Parasympathetic NS** decreases HR from rest
 - when $HR < 60$ bpm = **bradycardia**

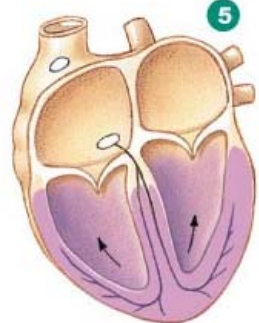
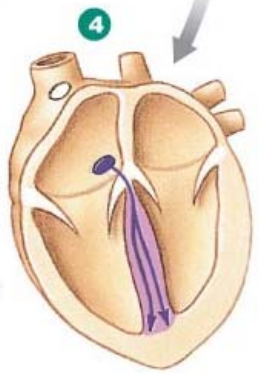
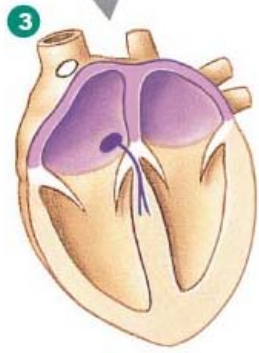
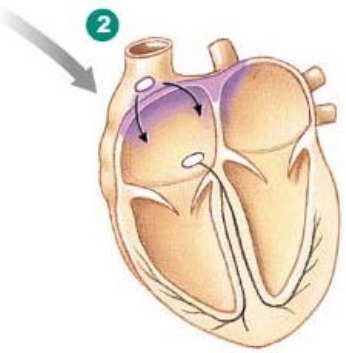
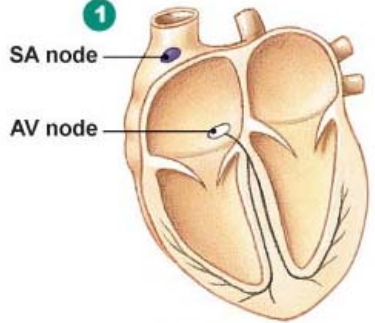
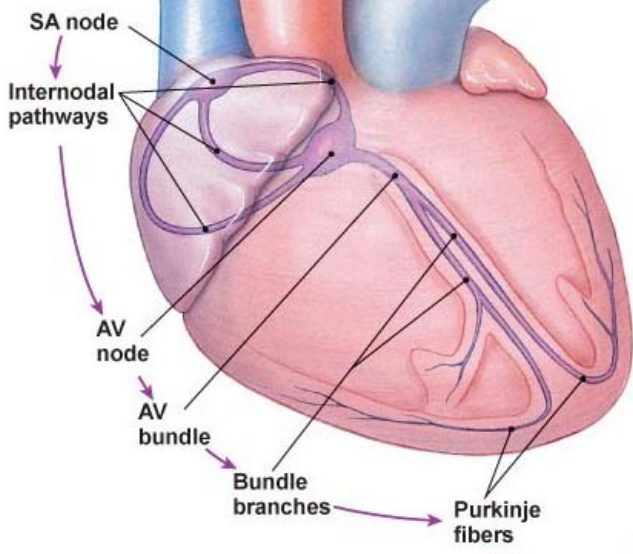




Action Potentials Spread Through Gap Junctions

- The electrical signal for contraction begins as the **sinoatrial (SA) node** fires an action potential
- From the SA node, the AP propagates via gap junctions to the **contractile cells of the atria**, causing **atrial systole** and through branched internodal fibers to the **atrioventricular node** (group of autorhythmic cells at the boundary between the right atrium and the interventricular septum)
 - **only route** for the AP to spread into the ventricles (fibrous skeleton at junction between atria and ventricles prevent transfer of electric signals)
 - **slows** down the speed of the AP propagation
 - ensure that the atria contract **BEFORE** the ventricles contract

THE CONDUCTING SYSTEM OF THE HEART



- 1 SA node depolarizes.
- 2 Electrical activity goes rapidly to AV node via internodal pathways.
- 3 Depolarization spreads more slowly across atria. Conduction slows through AV node.
- 4 Depolarization moves rapidly through ventricular conducting system to the apex of the heart.
- 5 Depolarization wave spreads upward from the apex.

Wave of Depolarization

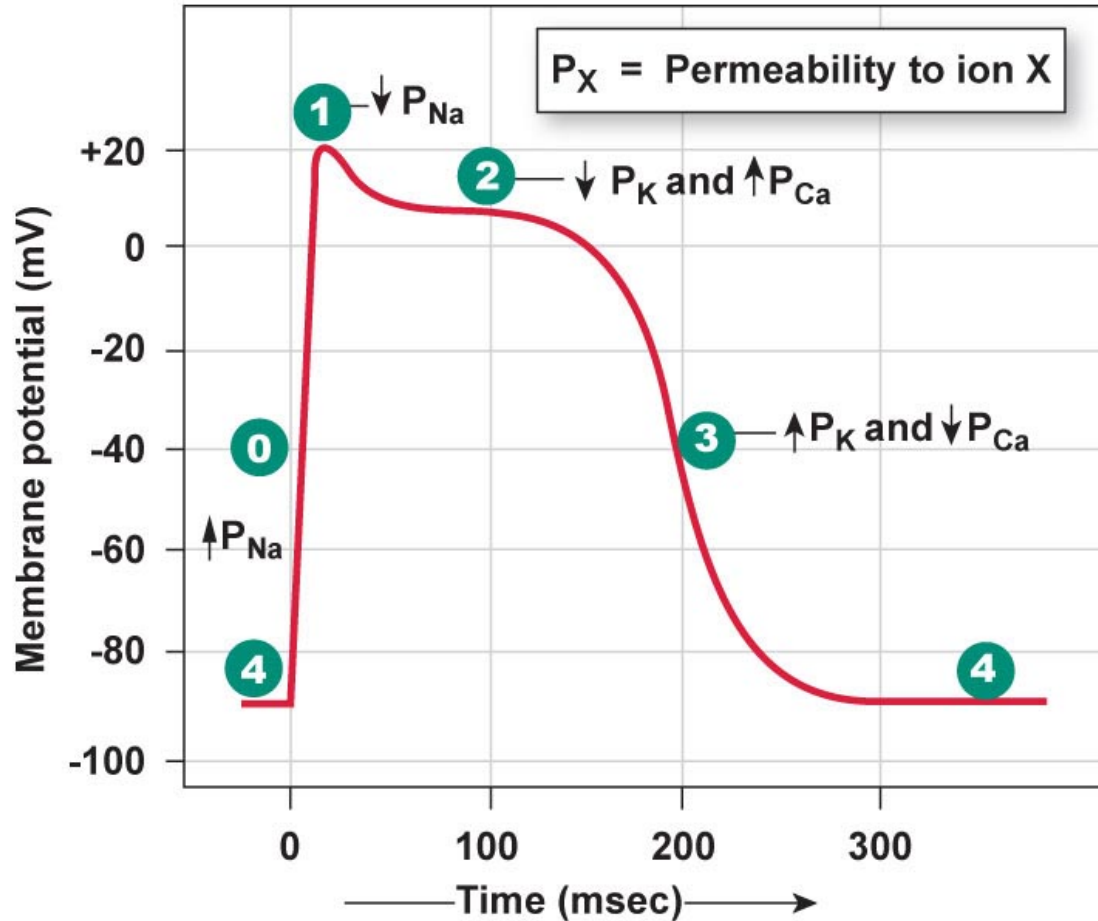
- The AP propagates from the AV node to the **Bundle of His** (and **bundle branches**)
 - located within the interventricular septum
 - **speeds** up the speed of the AP propagation
 - propagates the AP from the AV node through the interventricular septum to the apex of the heart to the **Purkinjie fibers**
 - located within the interventricular septum and the walls of the right and left ventricles
 - propagates the AP from the bundle branches to the contractile cells of the ventricles within the interventricular septum and the outer walls of the right and left ventricles, causing **ventricular systole**

E-C of Contractile Cardiac Myocytes

- Just like skeletal muscle fibers, contractile cardiac myocytes will contract in response to an action potential in the cell
 - note that the **electrical event (AP)** in the cell **ALWAYS** causes the **mechanical event (contraction)** and is called **excitation-contraction coupling** (to join)
- The action potential in cardiac myocytes originates spontaneously in the autorhythmic cells and spreads into contractile cells through gap junctions

Contractile Myocyte Action Potential

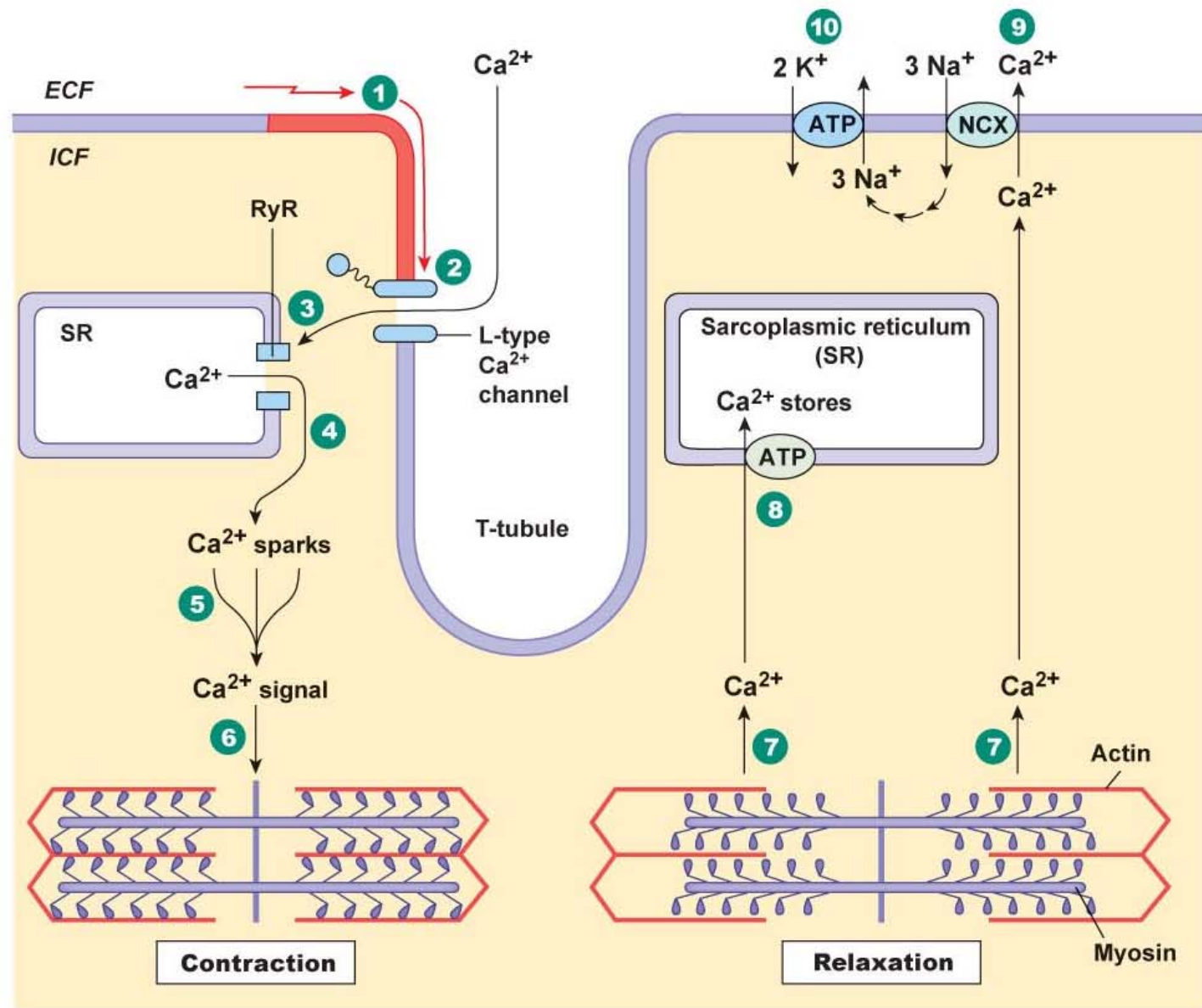
- The action potential has 5 distinct phases
0. Rapid depolarization due to the opening of voltage gated Na^+ channels (inward Na^+ flux)
 1. Slight repolarization due to closing of voltage gated Na^+ channels (inward Na^+ flux stops)
 2. Plateau phase due to the opening of voltage gated Ca^{2+} channels (**inward Ca^{2+} flux**)
 3. Repolarization phase due to the opening of voltage gated K^+ channels (outward K^+ flux) and closing of voltage gated Ca^{2+} channels (inward Ca^{2+} flux stops)
 4. Resting phase due to the voltage-gated channels being closed
- The influx of Ca^{2+} during the plateau phase lengthens the duration of the AP and the refractory period



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

E-C of Contractile Cardiac Myocytes

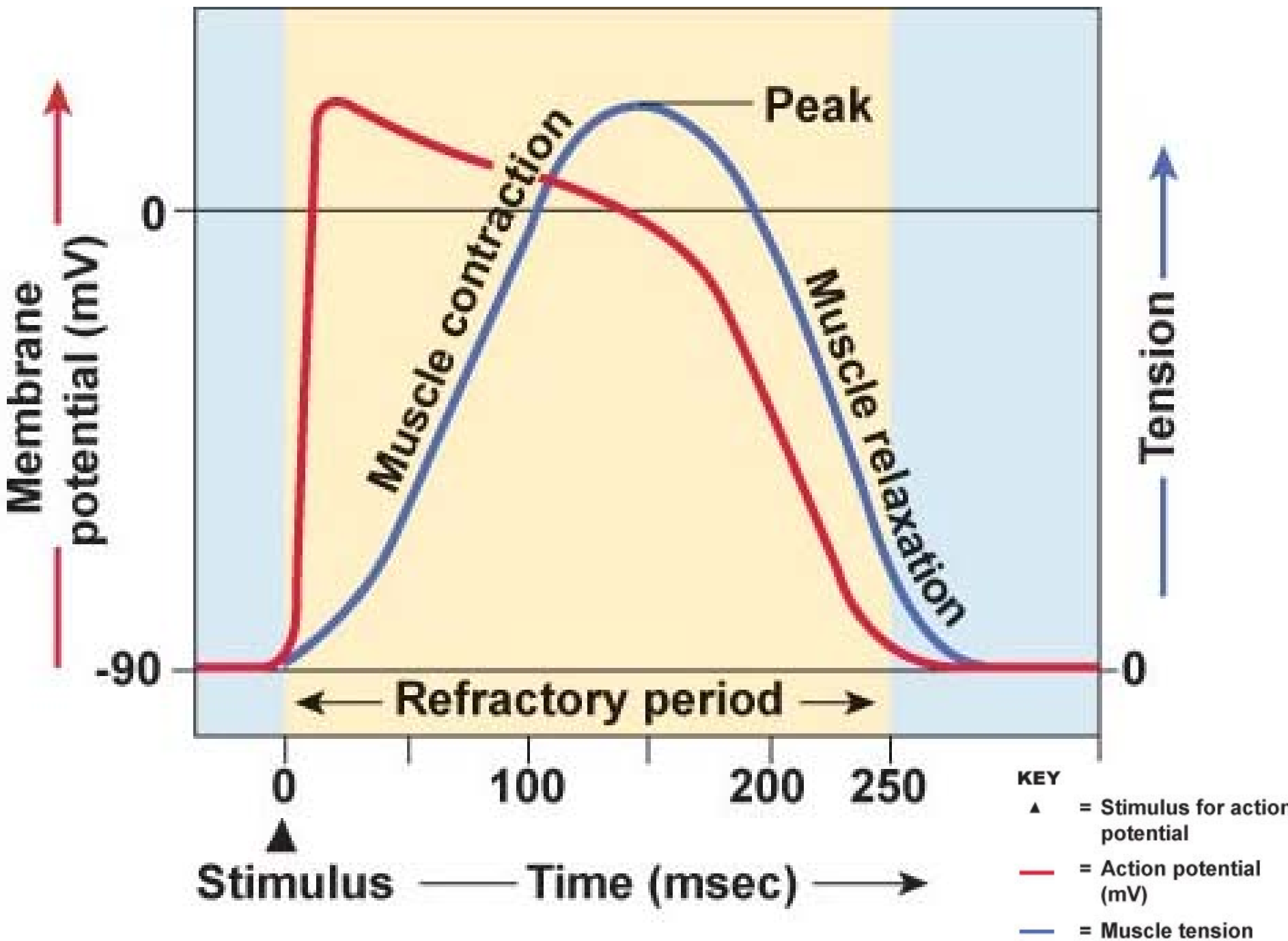
- An action potential that propagates into the t-tubules opens voltage-gated Ca^{2+} channels and Ca^{2+} enters the cell (plateau phase)
- The Ca^{2+} that diffuses into the sarcoplasm binds to and opens Ca^{2+} channels in the of the sarcoplasmic reticulum (SR) membrane causing stored Ca^{2+} in the SR to move into the sarcoplasm creating a **Ca^{2+} spark**
 - known as **calcium induced calcium release (CICR)**
 - multiple sparks summate to create a Ca^{2+} signal
 - Ca^{2+} from the SR provides 90% of the Ca^{2+} needed for contraction, the other 10% comes from the ECF
- Ca^{2+} diffuses through the cytosol to the contractile elements and promotes the interaction between actin and myosin (crossbridge cycling) resulting in the contraction (**systole**) of the 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.

Relaxation of a Working Cardiac Myocyte

- Removal of the Ca^{2+} from the sarcoplasm results in the relaxation (**diastole**) of the cell
- Ca^{2+} is removed from the sarcoplasm and returned to the **SR** and **ECF**
 - **Ca^{2+} -ATPase** (primary active transporting protein) in the SR membrane pumps Ca^{2+} out of the sarcoplasm back into the SR (via ATP hydrolysis) to be ready for the next heart beat
 - **Na^+ , Ca^{2+} -exchanger** (secondary active transporting protein) in the sarcolemma which actively transports Ca^{2+} out of the sarcoplasm as Na^+ diffuses into the sarcoplasm



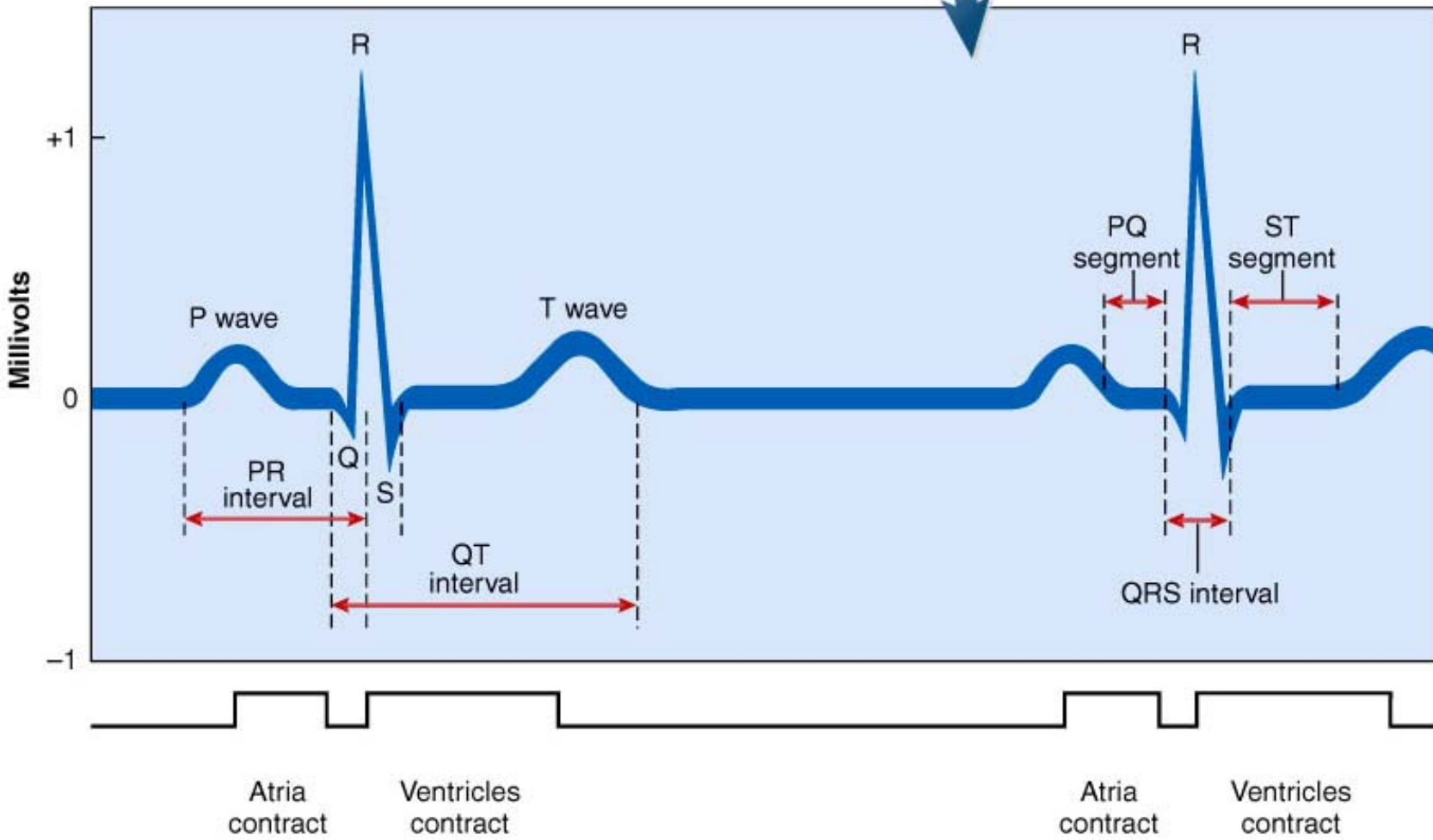
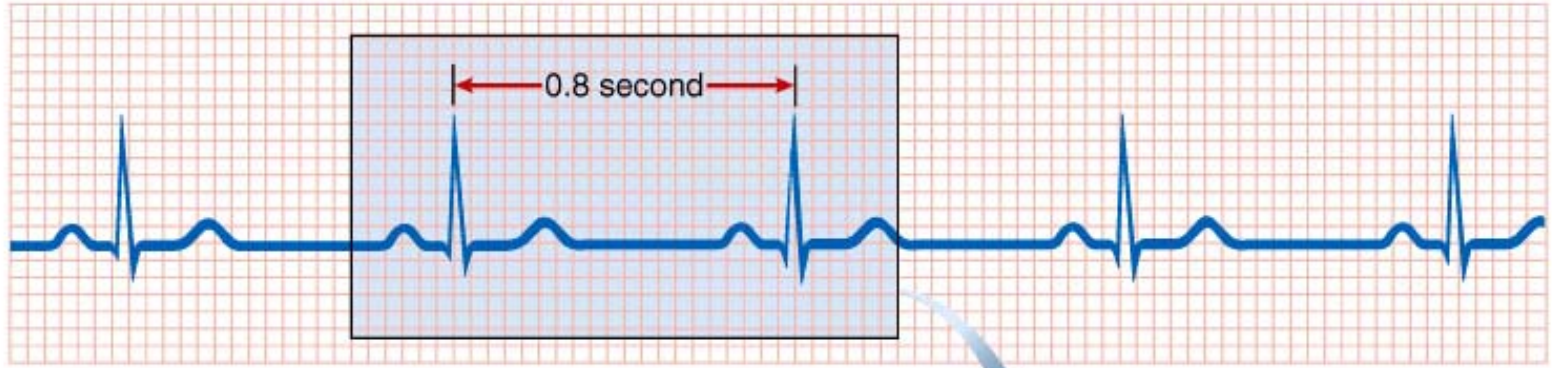
Electrocardiogram

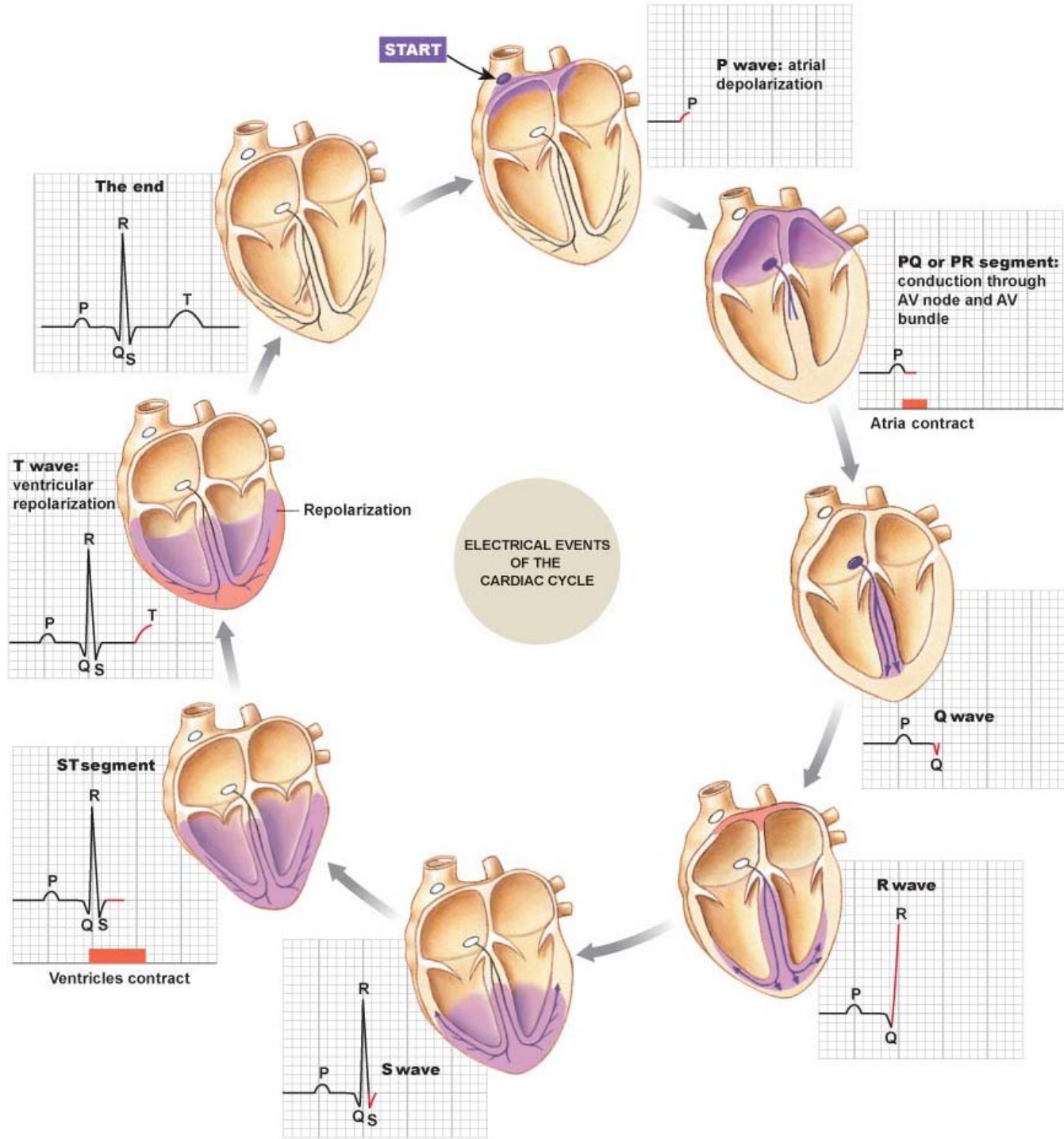
- The **electrocardiogram (ECG)** is a graphical representation of the summation of the APs in the heart
 - relates the depolarization and repolarization of the atria and the ventricles with respect to time
 - since depolarization initiates contraction, these electrical events can be associated with the systole and diastole of the heart chambers
- The 3 major electrical events of an ECG repeat each time the SA node fires an action potential which also results in a single contraction-relaxation cycle of the heart known as the **cardiac cycle**

ECG Waves

- There are 3 major waves of the ECG which, follow in sequence, the spread of the AP from the SA node to the ventricles
 - P wave
 - simultaneous **depolarization** of both atria
 - QRS Complex
 - **depolarization** of both ventricles
 - the **repolarization** both atria occurs at this time but is hidden by much larger ventricular depolarization
 - T wave
 - **repolarization** of all both ventricles
- The mechanical events of the cardiac cycle lag slightly behind the electrical signals just as the contraction of a single muscle cell follows its action potential

ECG





START

P wave: atrial depolarization

PQ or PR segment: conduction through AV node and AV bundle

Atria contract

Q wave

R wave

S wave

ST segment

Ventricles contract

T wave: ventricular repolarization

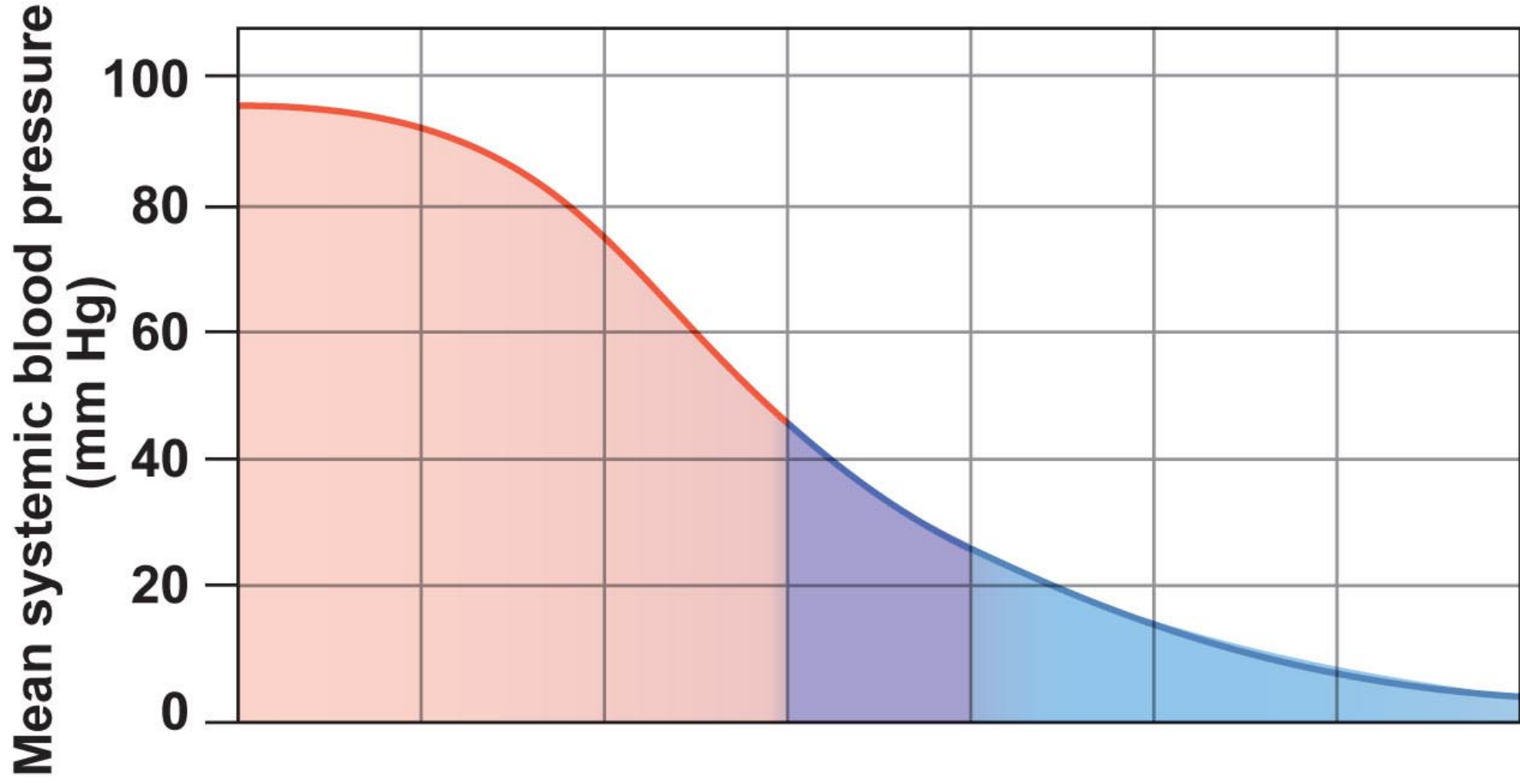
Repolarization

The end

ELECTRICAL EVENTS OF THE CARDIAC CYCLE

How Does the Heart Move Blood?

- Blood can flow in the cardiovascular system if one region develops higher pressure than other regions
- The ventricles are responsible for creating a region of high pressure
- When the blood filled ventricles undergo **systole**, the **pressure** exerted on the blood **increases** and blood flows out of (**empties**) the ventricles into the arteries displacing the lower pressure blood in the vessels
 - as blood moves through the vasculature, pressure is lost due to friction between the blood and the walls of the vessels
- When the blood filled ventricles undergo **diastole**, the **pressure** exerted on the blood **decreases** and blood flows into (**fills**) the ventricles
- The filled ventricle undergoes systole again and repressurizes the blood



The Mechanical Events of the Cardiac Cycle

- The cardiac cycle has 5 phases which are associated with the blood pressure and blood volume changes that occur within the ventricles during ventricular diastole and systole
 1. Passive ventricular filling
 2. Atrial systole
 3. Isovolumetric contraction
 4. Ventricular ejection
 5. Isovolumetric relaxation

[Cardiac Cycle](#)

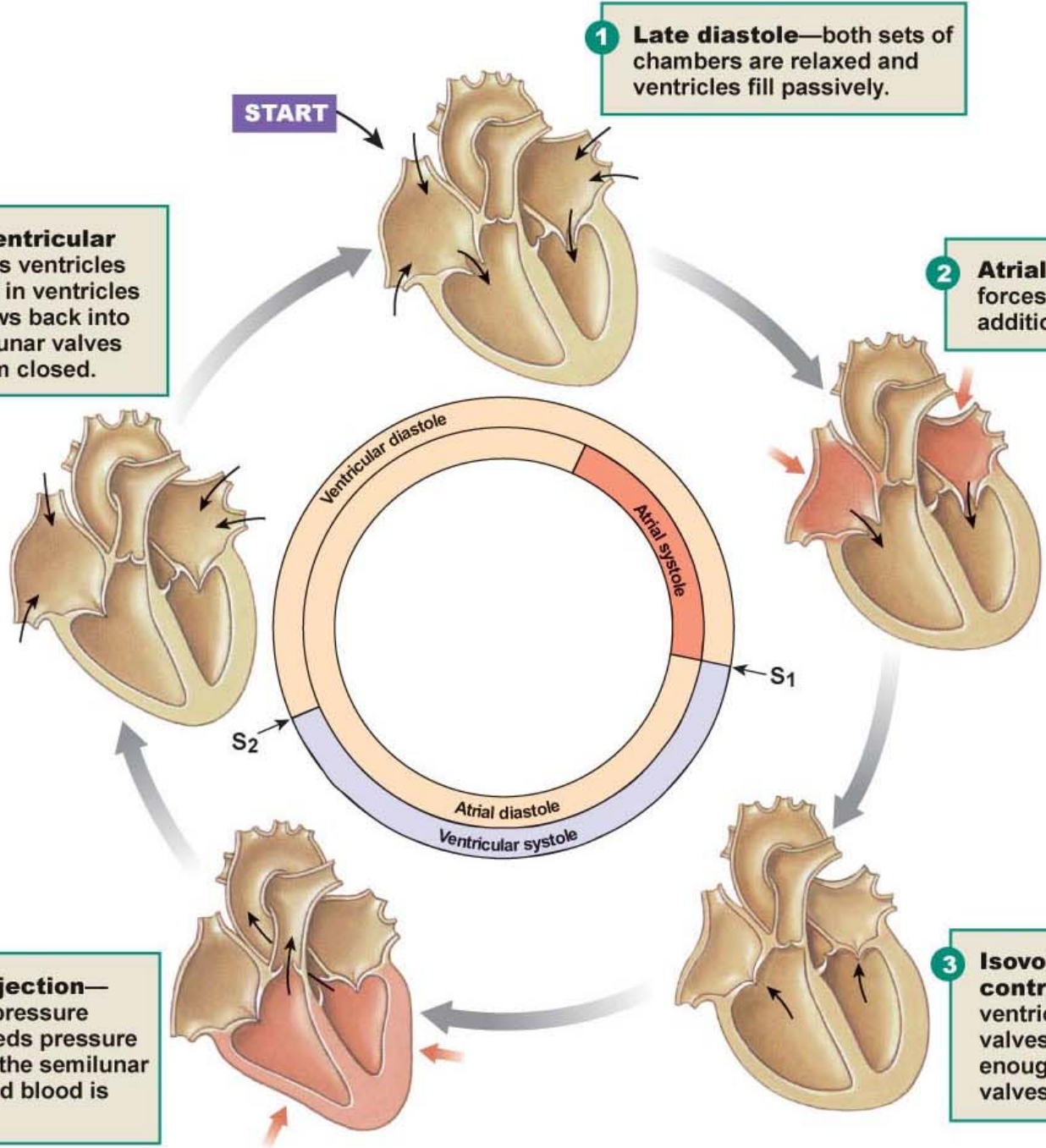
5 Isovolumic ventricular relaxation—as ventricles relax, pressure in ventricles falls, blood flows back into cusps of semilunar valves and snaps them closed.

1 Late diastole—both sets of chambers are relaxed and ventricles fill passively.

2 Atrial systole—atrial contraction forces a small amount of additional blood into ventricles.

3 Isovolumic ventricular contraction—first phase of ventricular contraction pushes AV valves closed but does not create enough pressure to open semilunar valves.

4 Ventricular ejection—as ventricular pressure rises and exceeds pressure in the arteries, the semilunar valves open and blood is ejected.

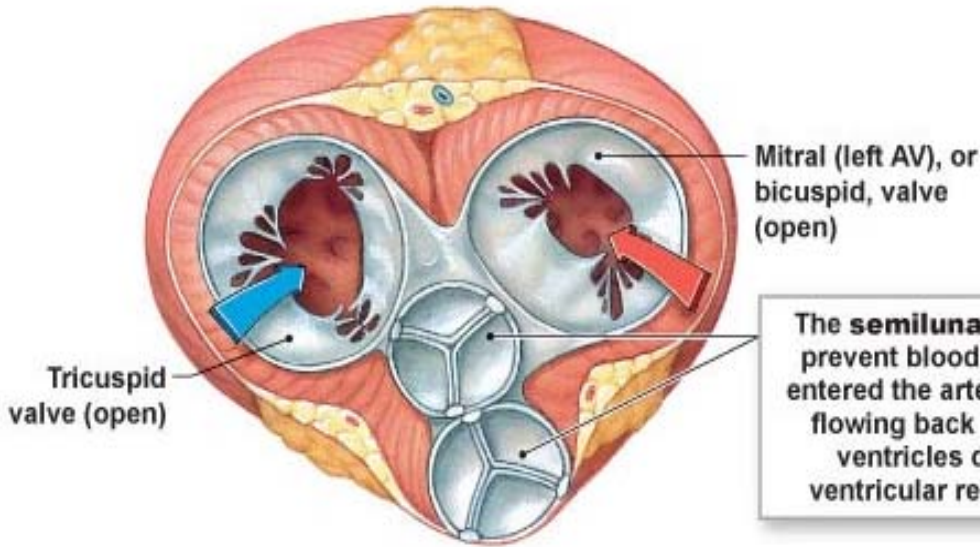


Passive Ventricular Filling

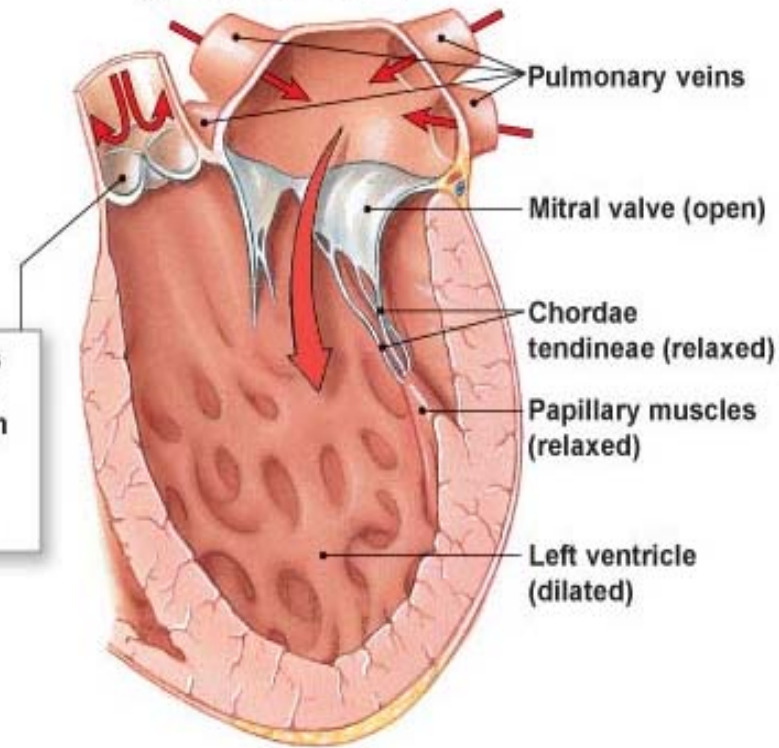
- At the beginning of ventricular filling, the semilunar valves are closed, **BOTH atria and ventricles are in diastole** whereby blood from the great veins pass through the atria through opened AV valves passively filling the ventricles (accounts for 85% of ventricular filling)

VENTRICULAR RELAXATION

(c) Transverse section



(d) Frontal section



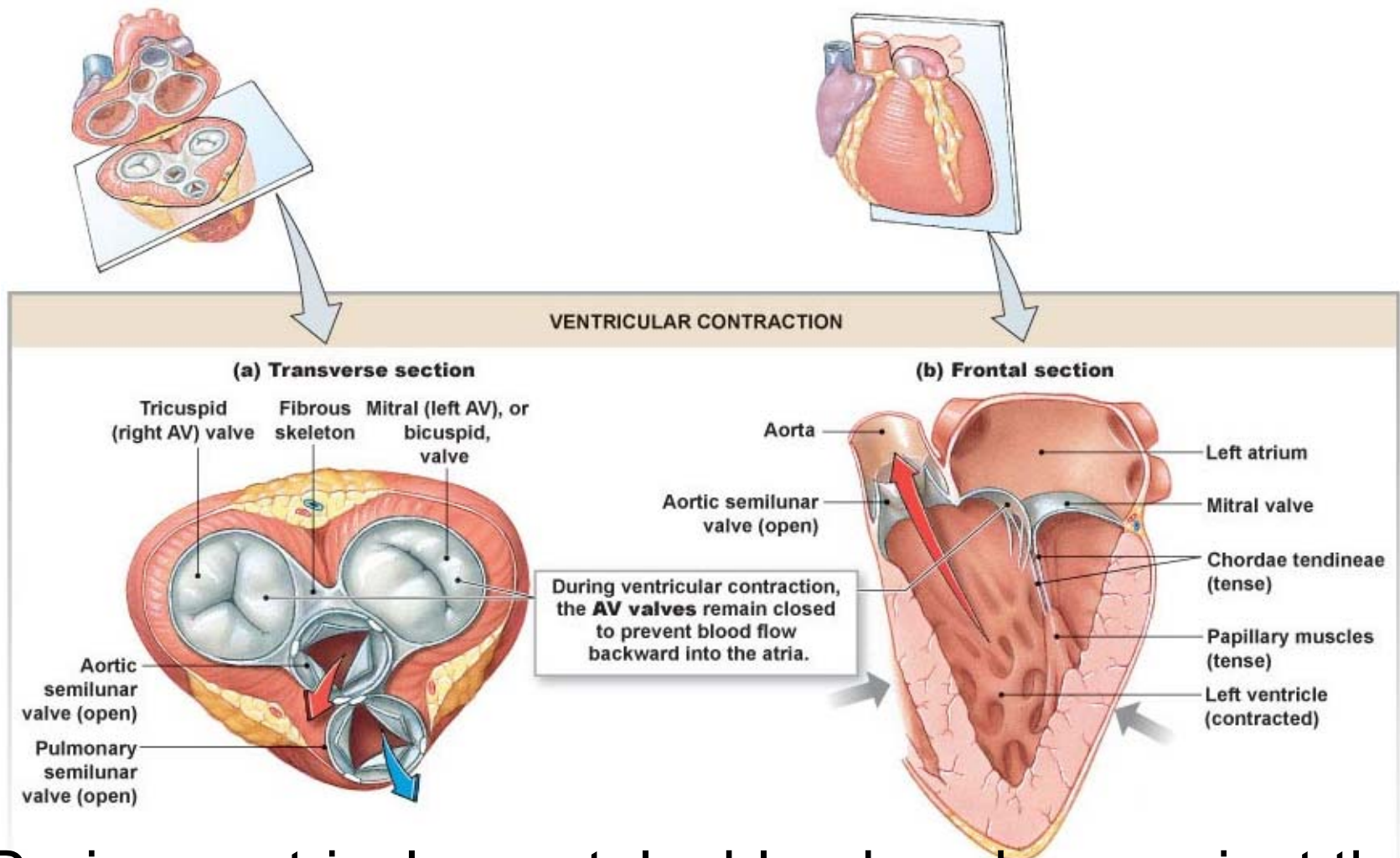
- During ventricular diastole, blood pushes against the top side of the semilunar valves forcing them downward into a closed position producing the **second heart sound (dup)** and against the top side of the AV valves forcing them downward into an opened position

Atrial Systole

- The P wave of the ECG causes atrial systole whereby blood is ejected from the atria to finish the filling of the diastolic ventricles (accounts for 15% of ventricular filling)
- The volume of blood in each ventricle at the end of the filling phase is called End Diastolic Volume (EDV) and is approximately 135 mL

Isovolumetric Contraction

- As atrial systole comes to an end the QRS complex of the ECG causes ventricular systole, which begins with a short **isovolumetric** phase
- The semilunar valves remain closed while ventricular pressure rises above atrial pressure causing the AV valves to close (lub)
 - the ventricle becomes a closed chamber with no blood entering or leaving the ventricle as contraction continues to further increase the pressure in the ventricles



- During ventricular systole, blood pushes against the bottom side of the AV valves forcing them upward into a closed position producing the **first heart sound (lub)** and against the bottom side of the semilunar valves forcing them upward into an opened position

Chordae Tendineae and Papillary Muscles

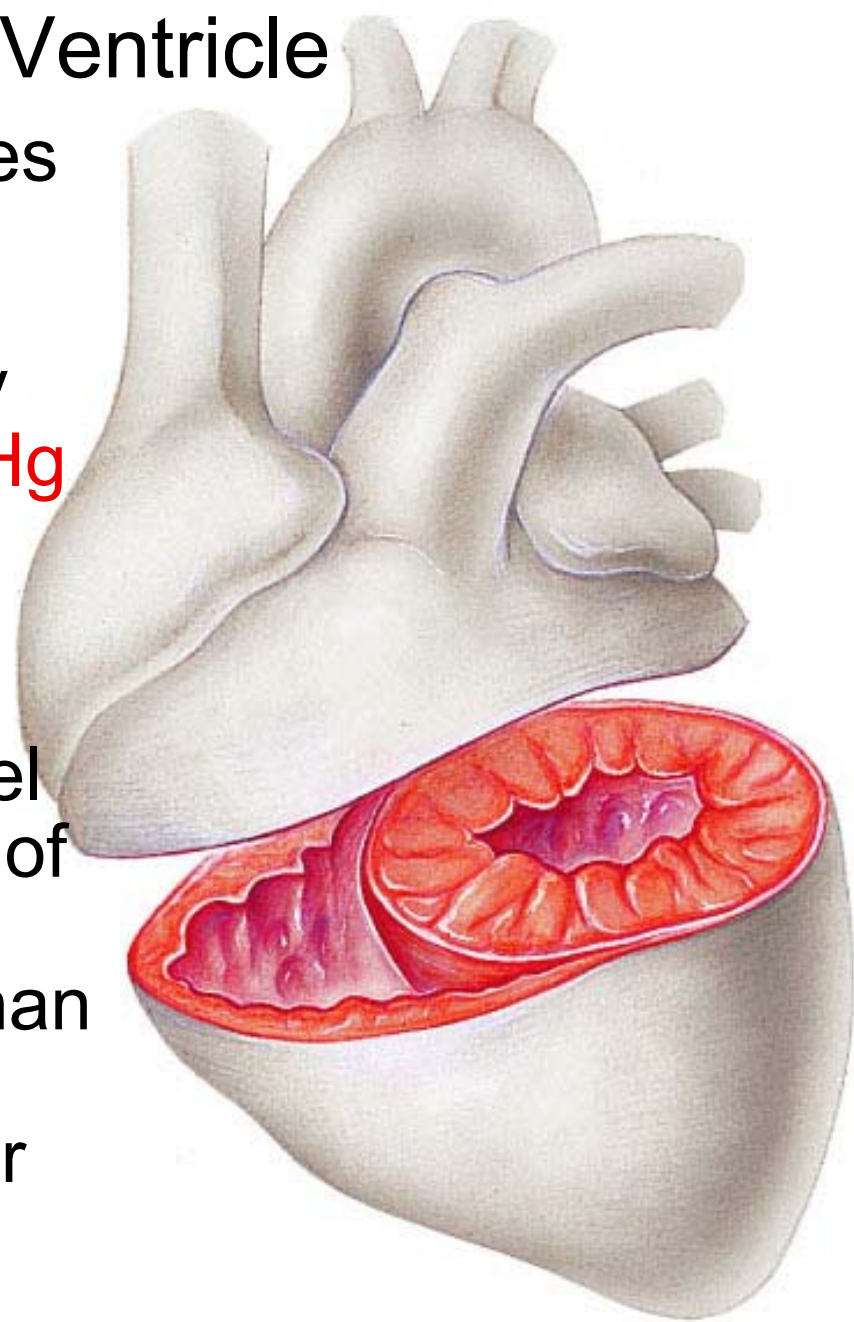
- Flaps of the AV valves connect on the ventricular side to collagenous tendons called **chordae tendineae**
- The opposite ends of the chordae tendineae are tethered to finger-like extensions of the ventricular myocardium called **papillary muscles**
 - these muscles provide stability for the chordae tendineae but cannot actively open or close the AV valves
- During ventricular systole, the chordae tendineae prevent the valve from being pushed back into the atrium
- If the chordae tendineae fail the valve is pushed back into the atrium during ventricular systole and is referred to a **prolapse**

Ventricular Ejection

- Ventricular pressure continues to rise until it overcomes the pressure in the arteries opening the semilunar valves and ejecting blood into the arteries
- Approximately 70 mL of the blood in the ventricle is ejected (**stroke volume**) which leaves 65 mL of blood remaining in the ventricles (**End Systolic Volume (ESV)**)

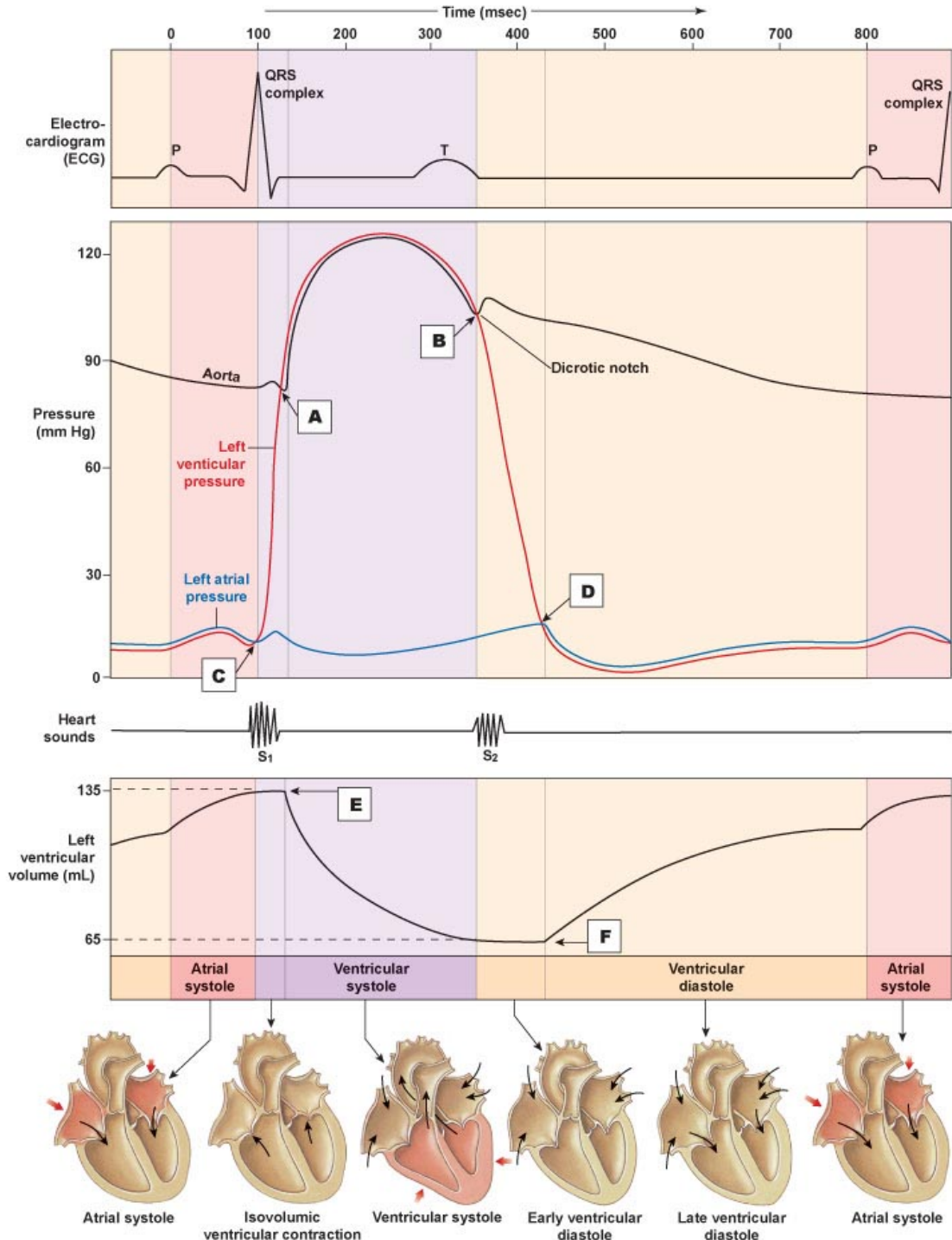
Left vs. Right Ventricle

- The **left** and the **right** ventricles pump the **same volume** of blood into the **systemic** and **pulmonary** circuits but at very different pressures (**120 mmHg** vs. **25 mmHg**)
- Because the blood that is ejected from the left ventricle has a further distance to travel (head to toes), the **outer wall** of the left ventricle is notably thicker (more myocardium) than the right which, when contracted, produces a higher blood pressure capable of moving blood a greater distance.



Isovolumetric Relaxation

- Ventricular contraction comes to an end, whereby ventricular pressure becomes less than the pressure in the great arteries causing a backflow of blood into the ventricles closing the semilunar valves (dup)
 - semilunar valve closure causes a brief rise in the arterial pressure called the **dicrotic notch** as blood rebounds off the valve
- Following the closure of the semilunar valves, the ventricles once again become closed chambers with no blood entering or leaving, as the AV valves remain closed.
- As the ventricles continue to relax, the pressure continues to fall in until it becomes less than the pressure in the atria causing the AV valves to open which ends isovolumetric relaxation and begins passive ventricular filling



Cardiac Output (CO)

- **CO** is the volume of blood pumped by a single ventricle in one minute and is a measure of the cardiac performance
- Directly related to both the **heart rate** (HR) and **stroke volume** (SV)
- **HR** is the number of heart beats per minute
 - normal resting HR = 75 beats/min
- **SV** is the volume of blood ejected out by a ventricle each systole (beat) = EDV – ESV
 - normal resting SV = 70 ml/beat
- **HR x SV = CO**
- (75 beats/min) x (70 ml/beat) = 5250 ml/min
= 5.25 L/min
 - the entire blood volume is completely circulated around the body every minute
- During exercise CO can increase to 30 L/min

The Need to Control Cardiac Output

- The CO can be altered to meet the needs of your body
 - deliver O_2 , nutrients, hormones... to the cells of the body as quickly as they are used
 - remove CO_2 , urea, lactic acid... from the cells of the body as quickly as they are produced
- At certain times, the needs of your body change
 - skeletal muscles during exercise use O_2 and produce CO_2 faster requiring an increase in the delivery rate of O_2 and removal rate of CO_2
 - during sleep, O_2 is used and CO_2 is produced more slowly requiring a decrease in the delivery rate of O_2 and removal rate of CO_2

Alteration of Cardiac Output

- CO can be changed by either changing HR or SV
- If **HR** or **SV increases**, the **CO increases**, sending blood through the cardiovascular system faster
- If **HR** or **SV decreases**, the **CO decreases**, sending blood through the cardiovascular system slower
- Both HR and SV are controlled by the 2 antagonistic branches of the Autonomic Nervous System
- **Cardioacceleratory** (sympathetic) **center** in the medulla oblongata can **increase** both the HR and SV
- **Cardioinhibitory** (parasympathetic) **center** in the medulla oblongata can **decrease** the HR only

Cardiac Centers and Regulation of HR

- APs from the **cardioacceleratory** center propagate along the **sympathetic cardiac nerve** which synapse with the SA node
 - sympathetic neurons exocytose **norepinephrine** (an **adrenergic** agent) onto the SA node
 - norepinephrine binds to β -(beta) adrenergic receptors of SA nodal cells resulting in an **increase** in the frequency of APs in the SA node
- APs from the **cardioinhibitory** center propagate along the **Vagus nerve** which synapses with the SA node
 - releases the neurotransmitter **acetylcholine** (a **cholinergic** agent) onto the SA node
 - acetylcholine binds muscarinic cholinergic receptors of SA nodal cells resulting in a **decrease** in the frequency of APs in the SA node

Regulation of SV

- Ventricular **contractility**
 - the force produced by the working ventricular myocytes during systole
 - controlled by hormones, neurotransmitters and other chemical substances (drugs)
- The **preload** on the ventricles
 - the force applied to working ventricular myocytes **before** they contract
 - the amount of pressure in the ventricles at the end of ventricular filling
 - aids ejection of blood out of the ventricles
- The **afterload** on the ventricles
 - the force applied to working ventricular myocytes **after** they begin to contract
 - the amount of pressure in the arteries pushing on the closed semilunar valves
 - opposes ejection of blood out of the ventricles

Ventricular Contractility and SV

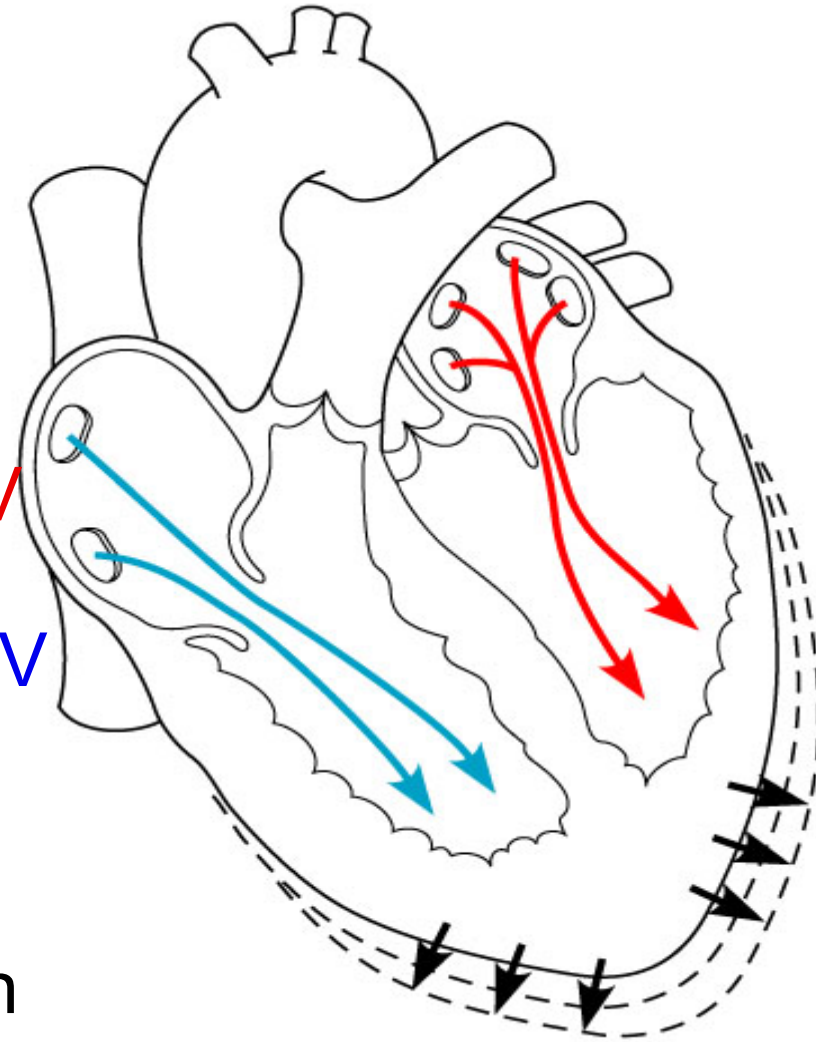
- The amount of force that a cardiac fiber generates can vary and depends on 2 key factors
 - the amount of Ca^{2+} in the cytosol during contraction
 - determines the number of active crossbridges formed during contraction
 - when cytosolic concentrations of Ca^{2+} are low, fewer crossbridges are activated and the force of contraction is small
 - when additional Ca^{2+} enters the cell from the ECF, more Ca^{2+} is released from the SR activating more crossbridges increasing the force of contraction
 - length of the fiber before contraction
 - stretching a fiber before it contracts results in a greater the force of contraction

Chemical Effects on Ventricular Contractility

- **Epinephrine** and **norepinephrine** bind to **β -adrenergic receptors** on working myocytes causing the opening of additional Ca^{2+} channels in the cell membrane
 - **increases** sarcoplasmic Ca^{2+} increasing the SV
- “ **β blockers**” prevent the binding to the β receptors
 - **decreases** intracellular Ca^{2+} decreasing the SV
- “**Cardiac glycosides**” (digoxin/digitalis) inhibits the Na^+, K^+ -ATPase decreasing the Na^+ gradient across the cell membrane of the myocyte
 - decreases the removal of Ca^{2+} from the sarcoplasm by the **$\text{Na}^+, \text{Ca}^{2+}$ -exchanger**
 - **increases** intracellular Ca^{2+} increasing the SV

Preload, the Starling Law of the Heart and SV

- The more working ventricular cardiac myocytes are stretched, the harder they contract. This stretch is determined by the amount of blood in the ventricle before it contracts (EDV).
 - If the EDV **increases** the **SV** will **increase**
 - If the EDV **decreases** the **SV** will **decrease**
- The amount of blood that enters the ventricle during filling depends on factors such as venous pressure, blood volume and atrial contractility



Afterload and the SV

- Arterial blood pressure **opposes** the ejection of blood from the ventricles by pushing against closed semilunar valves
- The afterload and the SV are inversely proportional
 - if the afterload **increases** the SV **decreases**
 - if the afterload **decreases** the SV **increases**
- The arterial blood pressure depends on factors such as blood volume, arterial compliance and arterial vasoconstriction/vasodilation

