Cardiovascular Physiology

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Cardiovascular System Function

- Functional components of the cardiovascular system:
  - Heart
  - Blood Vessels
  - Blood
- General functions these provide
  - Transportation
    - Everything transported by the blood
  - Regulation
    - Of the cardiovascular system
      - Intrinsic v extrinsic
  - Protection
    - Against blood loss
  - Production/Synthesis

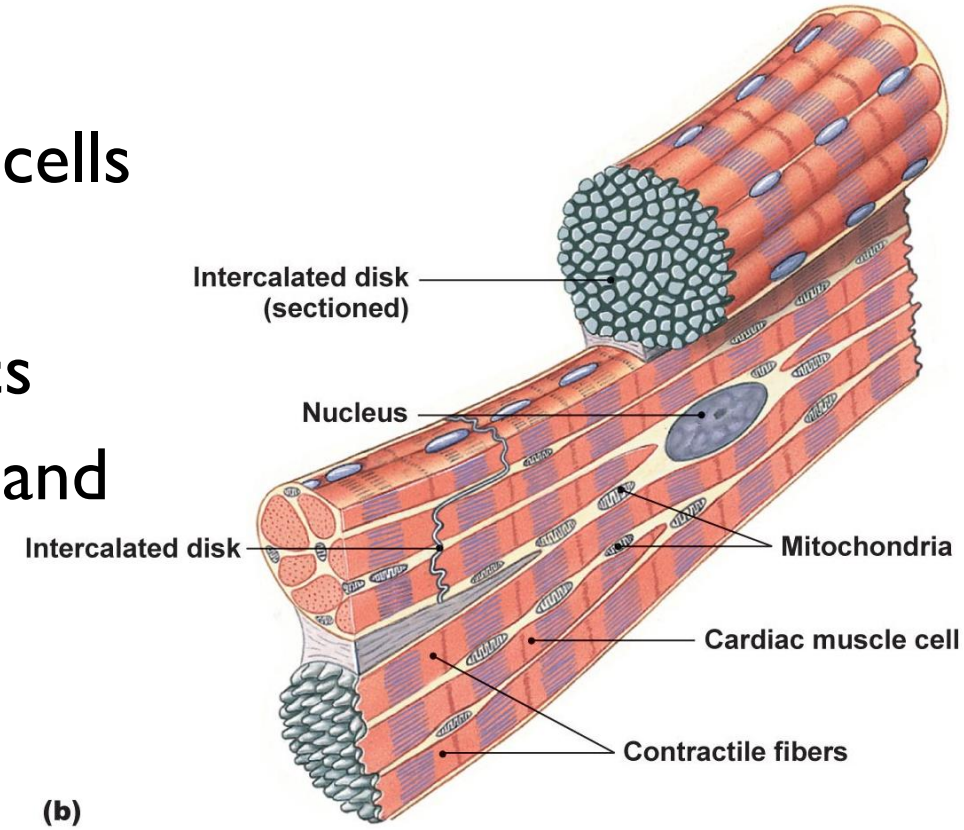
Cardiovascular System Function

- To create the "pump" we have to examine the Functional Anatomy
  - Cardiac muscle
  - Chambers
  - Valves
  - Intrinsic Conduction System

Functional Anatomy of the Heart

Cardiac Muscle

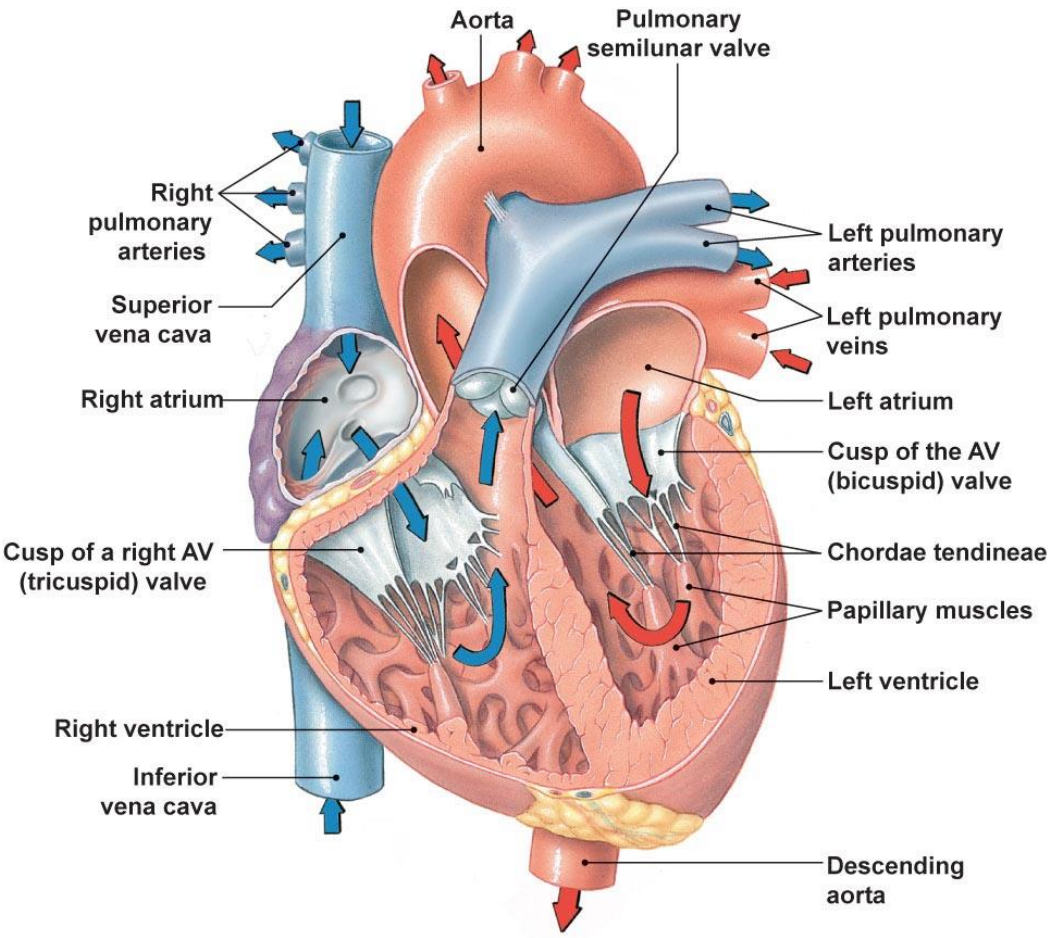
- Characteristics
  - Striated
  - Short branched cells
  - Uninucleate
  - Intercalated discs
  - T-tubules larger and over z-discs



Functional Anatomy of the Heart

Chambers

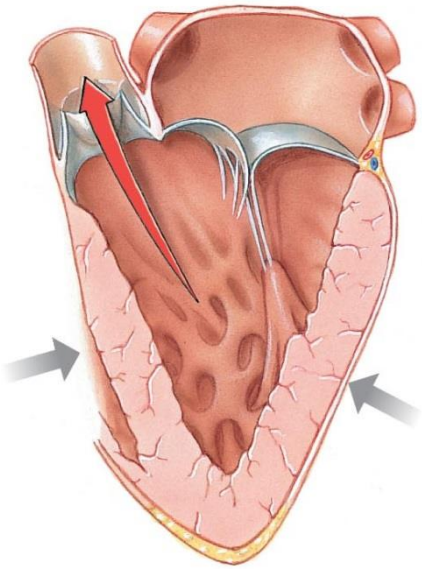
- 4 chambers
  - 2 Atria
  - 2 Ventricles
- 2 systems
  - Pulmonary
  - Systemic

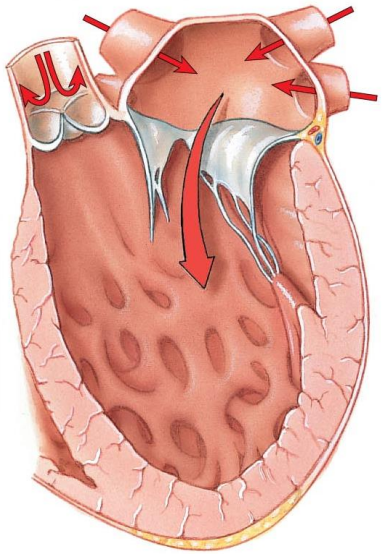


Functional Anatomy of the Heart

Valves

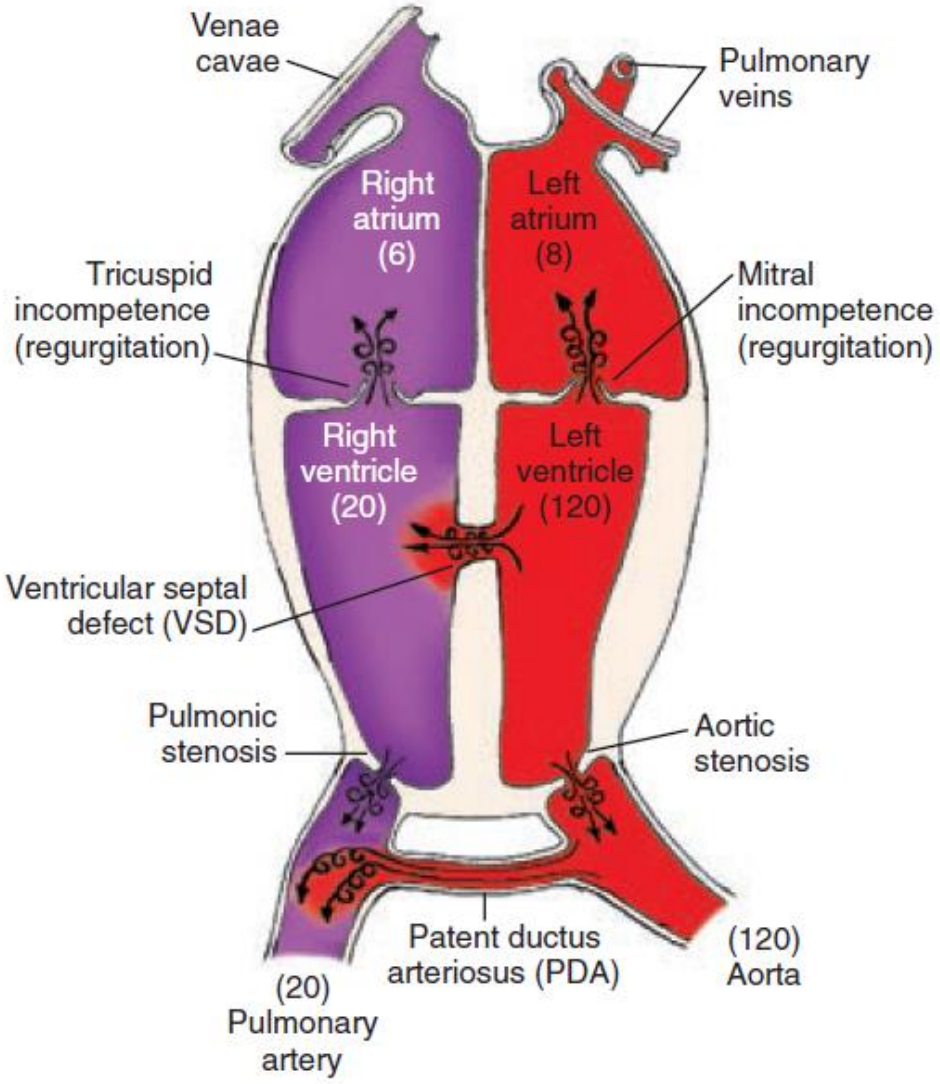
- Function is to prevent backflow
  - Atrioventricular Valves
    - Prevent backflow to the atria
    - Prolapse is prevented by the chordae tendinae
      - Tensioned by the papillary muscles
  - Semilunar Valves
    - Prevent backflow into ventricles





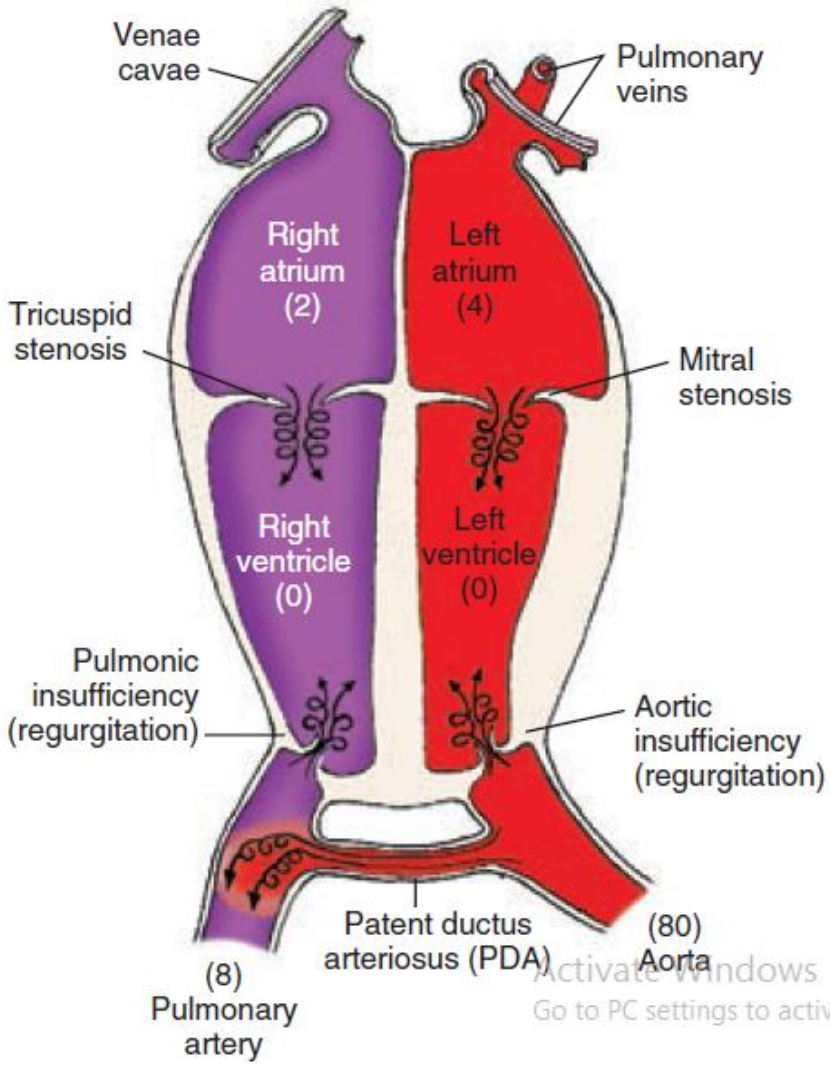
Defects of the Heart

Valves and vessels (systolic murmur)



Defects of the Heart

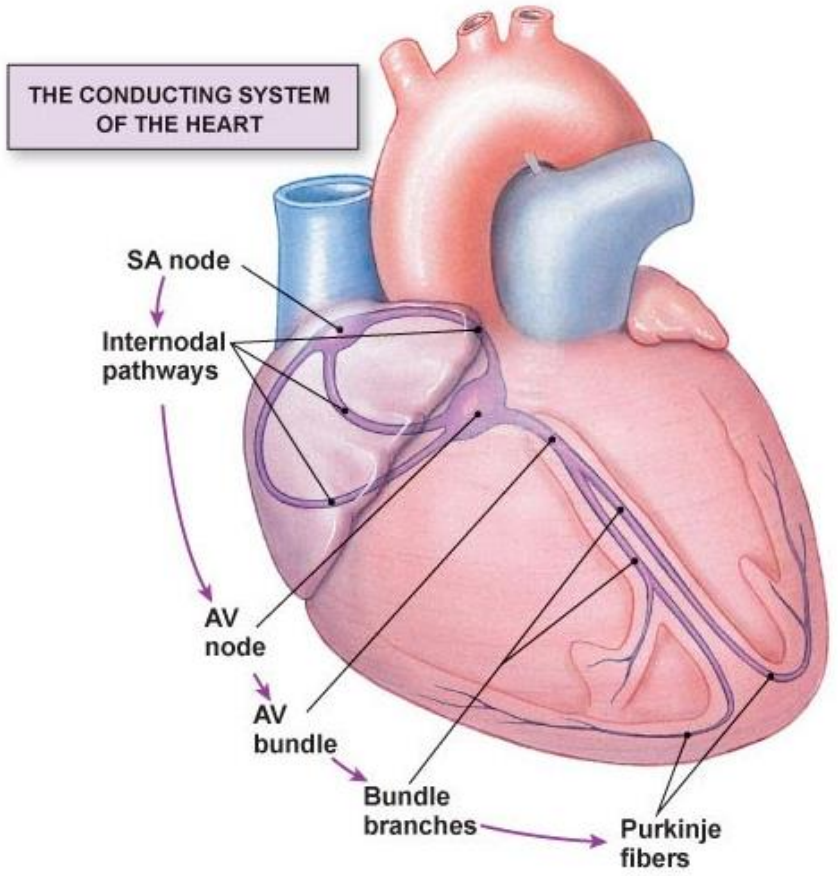
Valves and vessels (diastolic murmur)



Functional Anatomy of the Heart

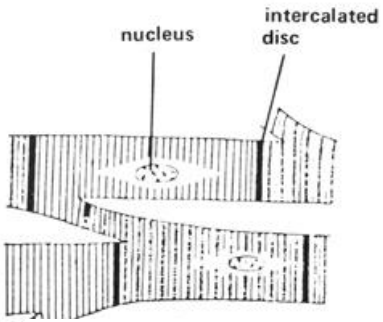
Intrinsic Conduction System

- Consists of "pacemaker" cells and conduction pathways
  - Coordinate the contraction of the atria and ventricles

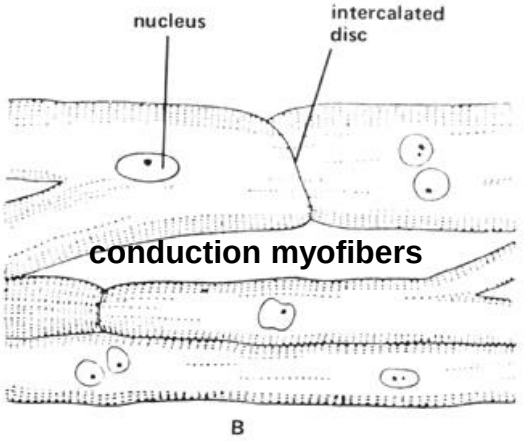


Myocardial Physiology
Autorhythmic Cells (Pacemaker Cells)

- Characteristics of Pacemaker Cells
  - Smaller than contractile cells
  - Don't contain many myofibrils
  - No organized sarcomere structure
    - do not contribute to the contractile force of the heart



normal contractile myocardial cell



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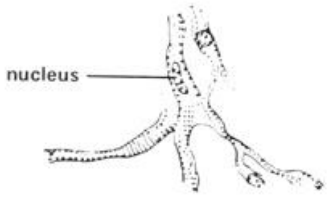
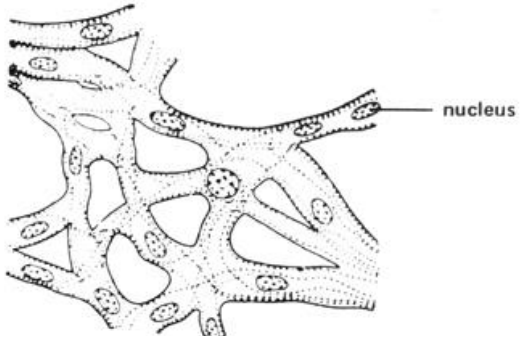


SA node cell



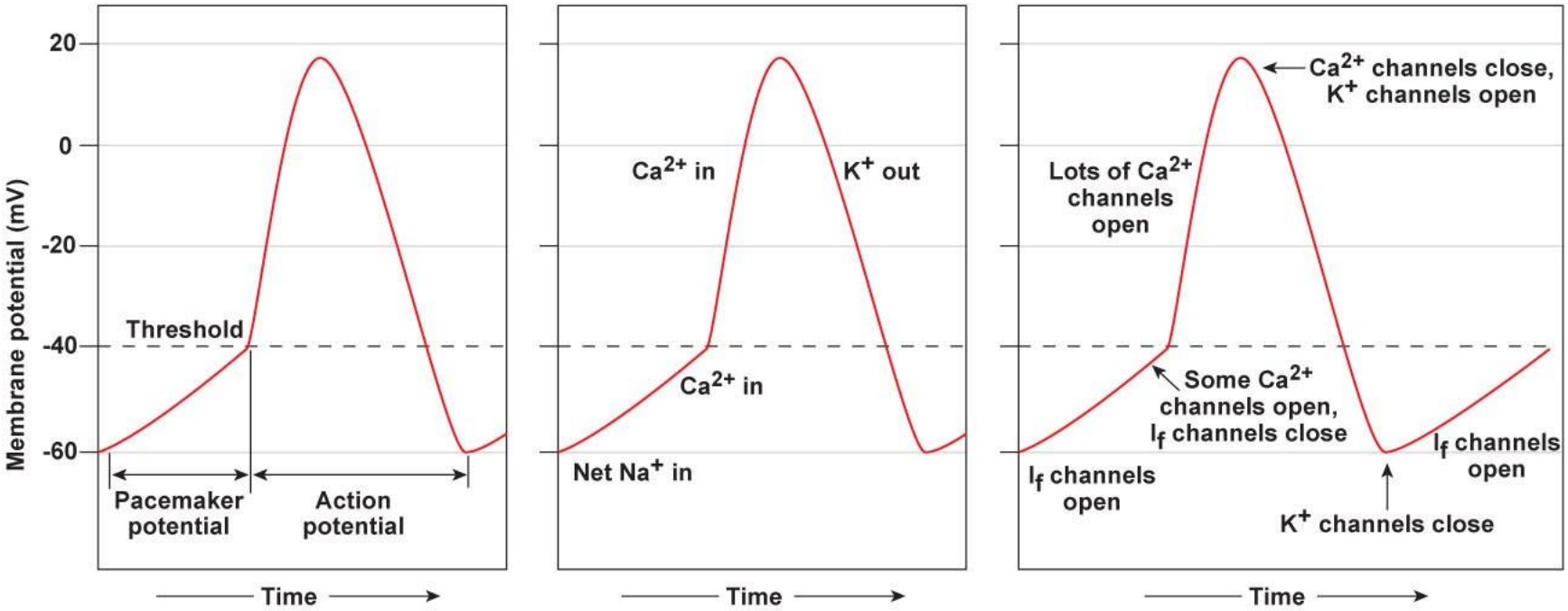
AV node cells

Myocardial Physiology
Autorhythmic Cells (Pacemaker Cells)

- Characteristics of Pacemaker Cells
  - Unstable membrane potential
    - "bottoms out" at -60mV
    - "drifts upward" to -40mV, forming a pacemaker potential
  - Myogenic
    - The upward "drift" allows the membrane to reach threshold potential (-40mV) by itself
    - This is due to
      1. Slow leakage of K^+ out & faster leakage Na^+ in
         - Causes slow depolarization
         - Occurs through I_f channels (f=funny) that open at negative membrane potentials and start closing as membrane approaches threshold potential
      2. Ca^{2+} channels opening as membrane approaches threshold
         - At threshold additional Ca^{2+} ion channels open causing more rapid depolarization
         - These deactivate shortly after and
      3. Slow K^+ channels open as membrane depolarizes causing an efflux of K^+ and a repolarization of membrane

Myocardial Physiology
Autorhythmic Cells (Pacemaker Cells)

- Characteristics of Pacemaker Cells



(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

Myocardial Physiology
Autorhythmic Cells (Pacemaker Cells)

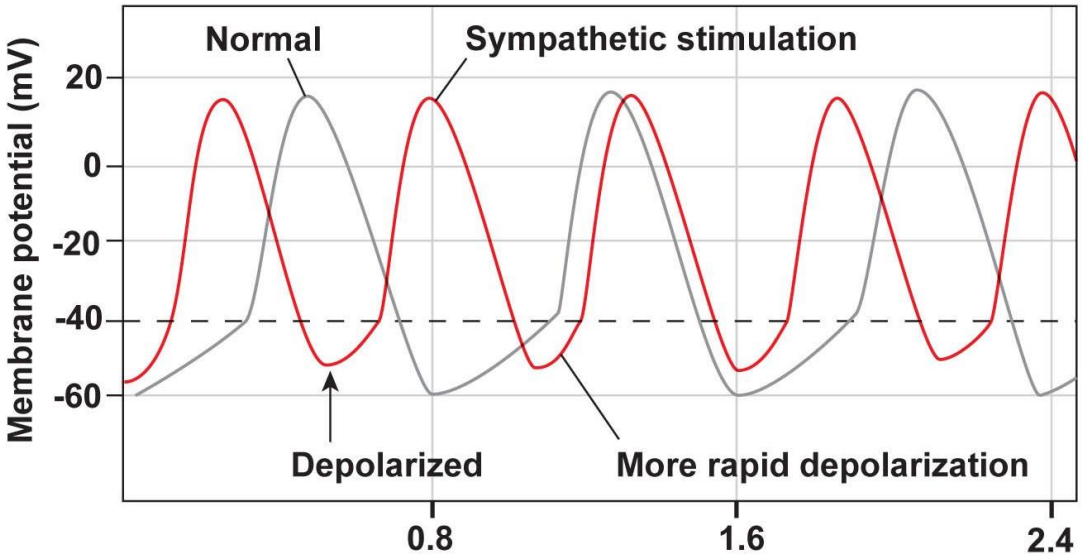
- Altering Activity of Pacemaker Cells
  - Sympathetic activity
    - NE and E increase I_f channel activity
      - Binds to β_1 adrenergic receptors which activate cAMP and increase I_f channel open time
      - Causes more rapid pacemaker potential and faster rate of action potentials

Sympathetic Activity Summary:

increased chronotropic effects
↑heart rate

increased dromotropic effects
↑conduction of APs

increased inotropic effects
↑contractility



Myocardial Physiology
Autorhythmic Cells (Pacemaker Cells)

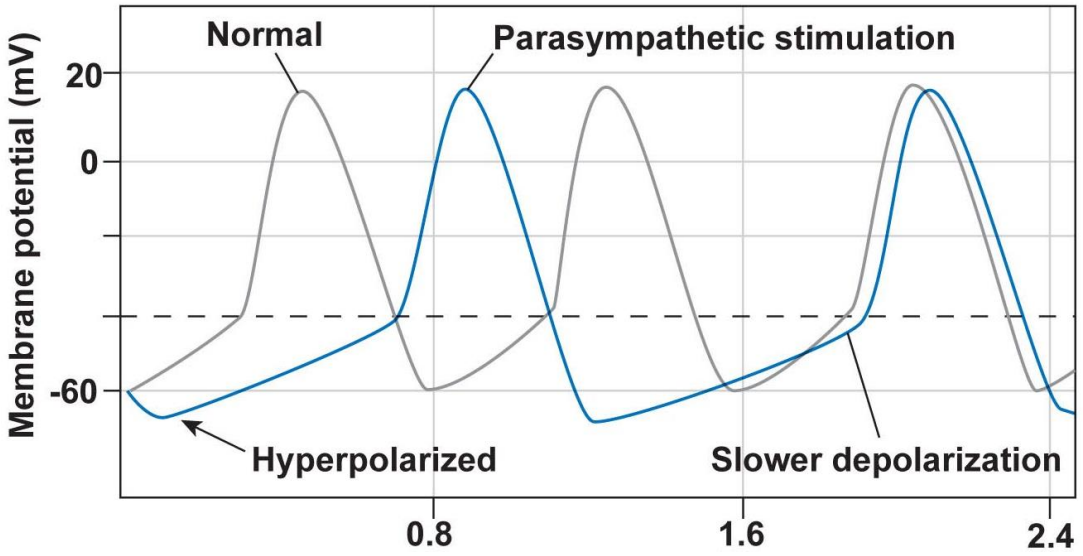
- Altering Activity of Pacemaker Cells
  - Parasympathetic activity
    - ACh binds to muscarinic receptors
      - Increases K^+ permeability and decreases Ca^{2+} permeability = hyperpolarizing the membrane
        - Longer time to threshold = slower rate of action potentials

Parasympathetic Activity Summary:

decreased chronotropic effects
↓heart rate

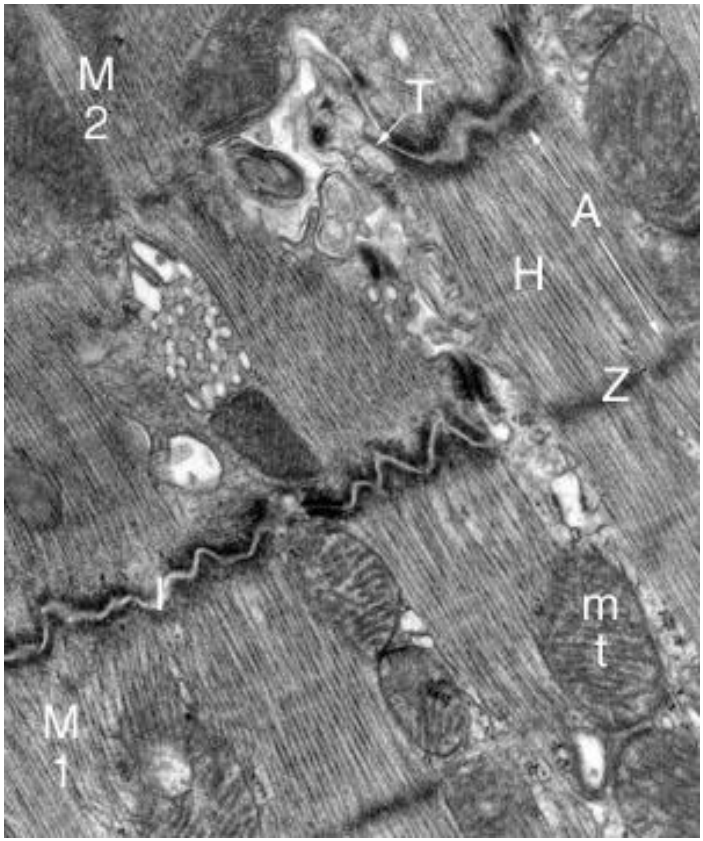
decreased dromotropic effects
↓ conduction of APs

decreased inotropic effects
↓ contractility



Myocardial Physiology
Contractile Cells

- Special aspects
  - Intercalated discs
    - Highly convoluted and interdigitated junctions
      - Joint adjacent cells with
        - Desmosomes & fascia adherens
      - Allow for synticial activity
        - With gap junctions
  - More mitochondria than skeletal muscle
  - Less sarcoplasmic reticulum
    - Ca^{2+} also influxes from ECF reducing storage need
  - Larger t-tubules
    - Internally branching
  - Myocardial contractions are graded!



Myocardial Physiology
Contractile Cells

- Special aspects
  - The action potential of a contractile cell
    - Ca^{2+} plays a major role again
    - Action potential is longer in duration than a "normal" action potential due to Ca^{2+} entry
    - Phases

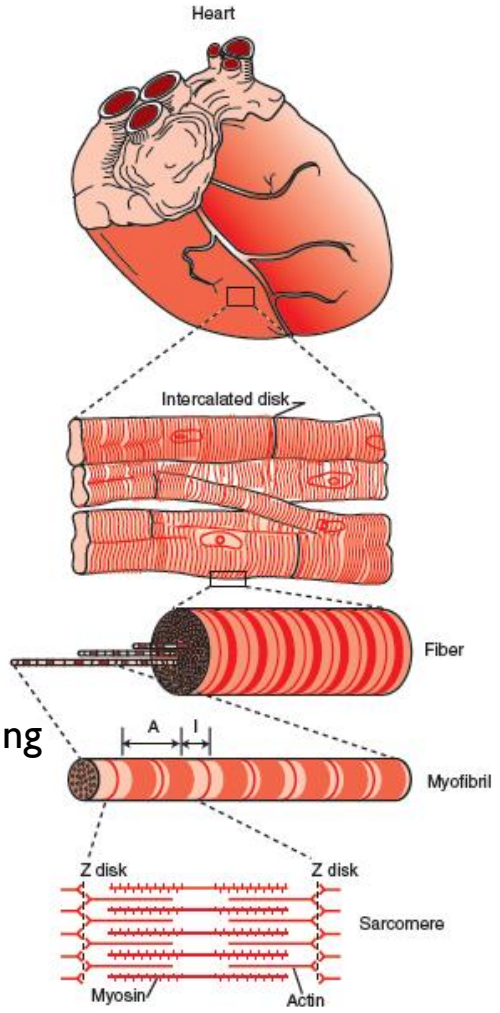
      4 – resting membrane potential @ -90mV

      0 – depolarization
      - Due to gap junctions or conduction fiber action
      - Voltage gated Na^{+} channels open… close at 20mV

      1 – temporary repolarization
      - Open K^{+} channels allow some K^{+} to leave the cell

      2 – plateau phase
      - Voltage gated Ca^{2+} channels are fully open (started during initial depolarization)

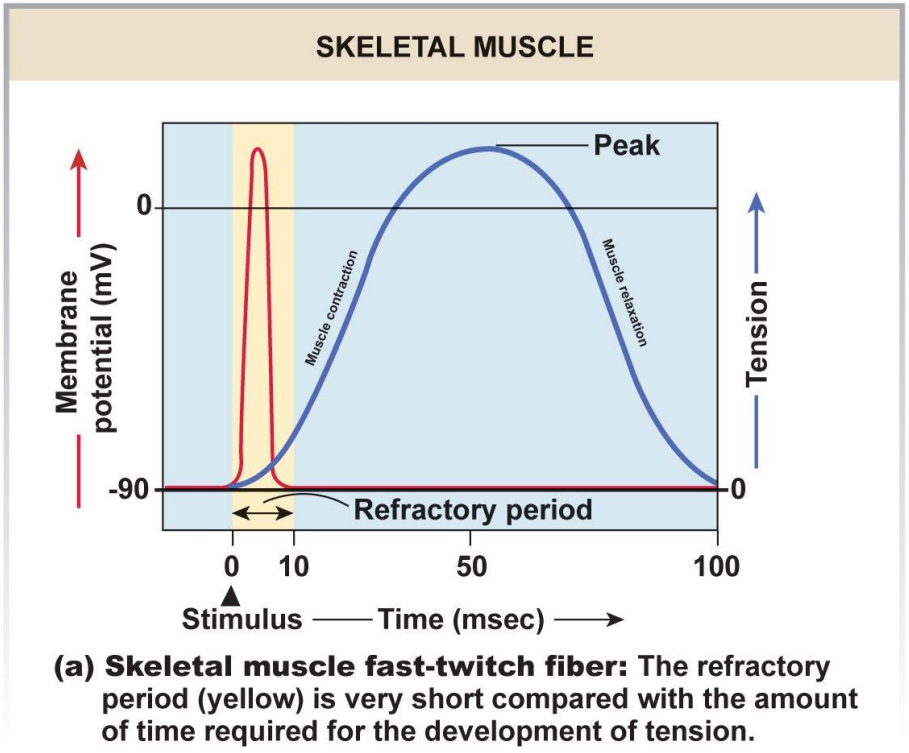
      3 – repolarization
      - Ca2+ channels close and K+ permeability increases as slower activated K+ channels open, causing a quick repolarization
  - What is the significance of the plateau phase?



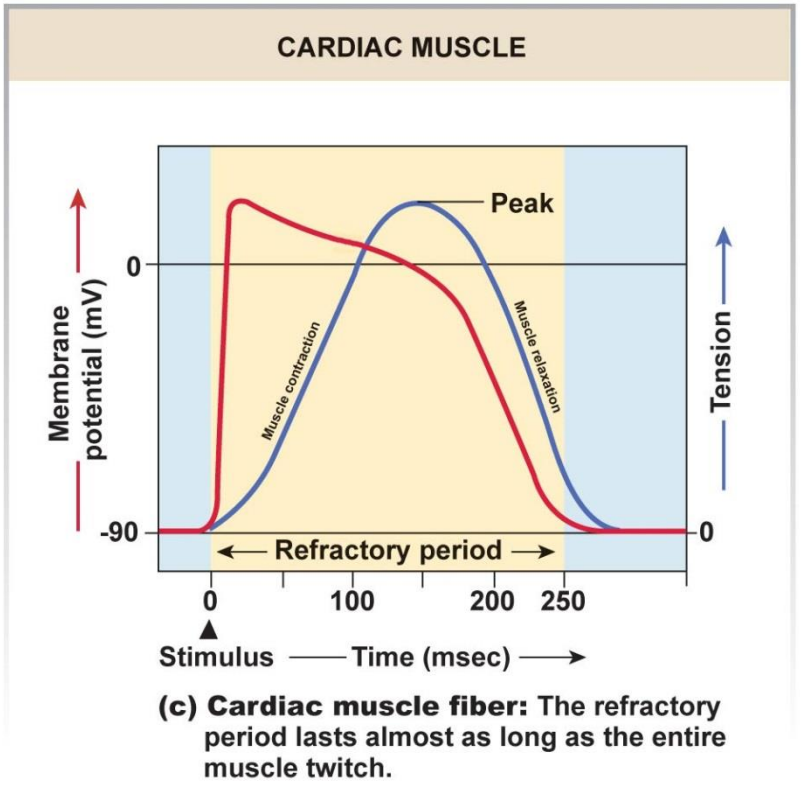
Myocardial Physiology

Contractile Cells

- Skeletal Action Potential vs Contractile Myocardial Action Potential



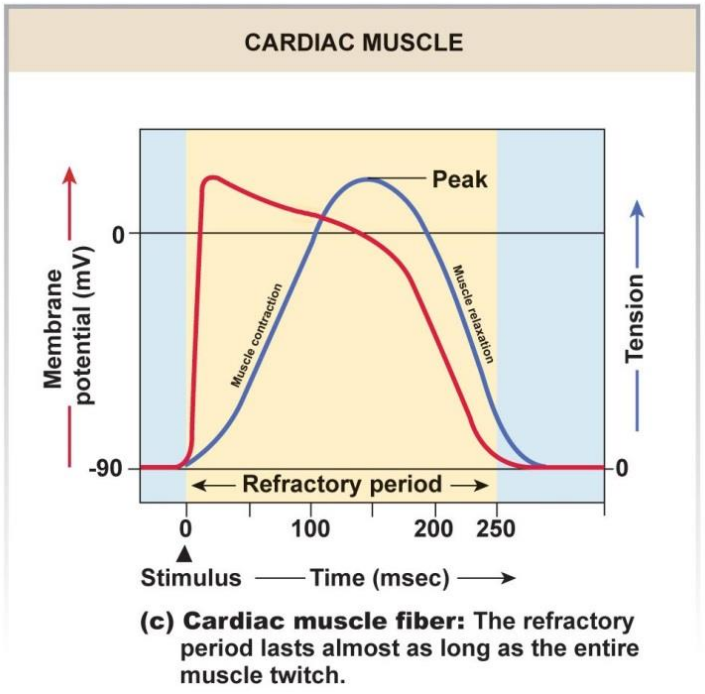
(a) Skeletal muscle fast-twitch fiber: The refractory period (yellow) is very short compared with the amount of time required for the development of tension.



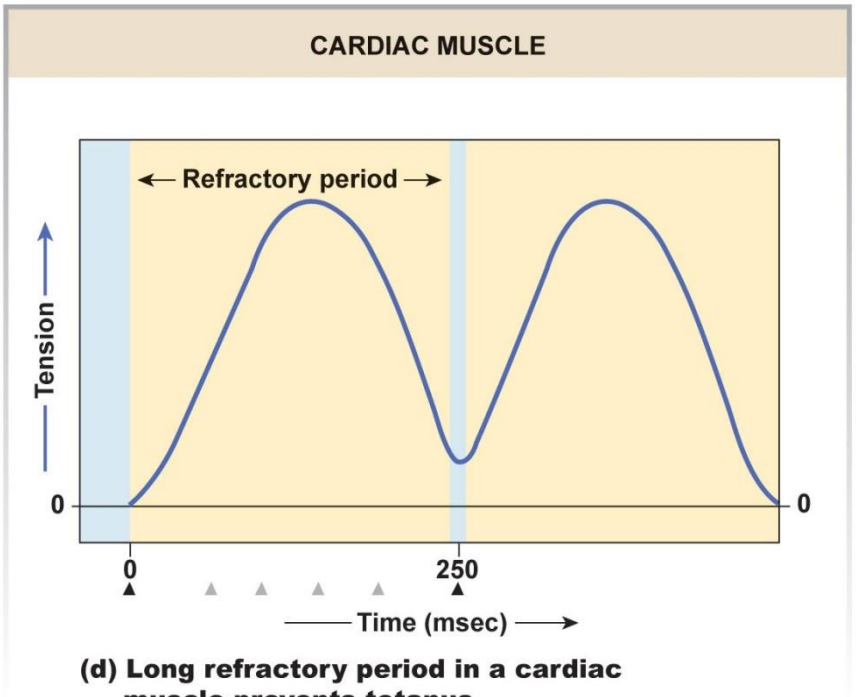
(c) Cardiac muscle fiber: The refractory period lasts almost as long as the entire muscle twitch.

Myocardial Physiology
Contractile Cells

- Plateau phase prevents summation due to the elongated refractory period
- No summation capacity = no tetanus
  - Which would be fatal



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



(d) **Long refractory period in a cardiac muscle prevents tetanus.**

Summary of Action Potentials

Skeletal Muscle vs Cardiac Muscle

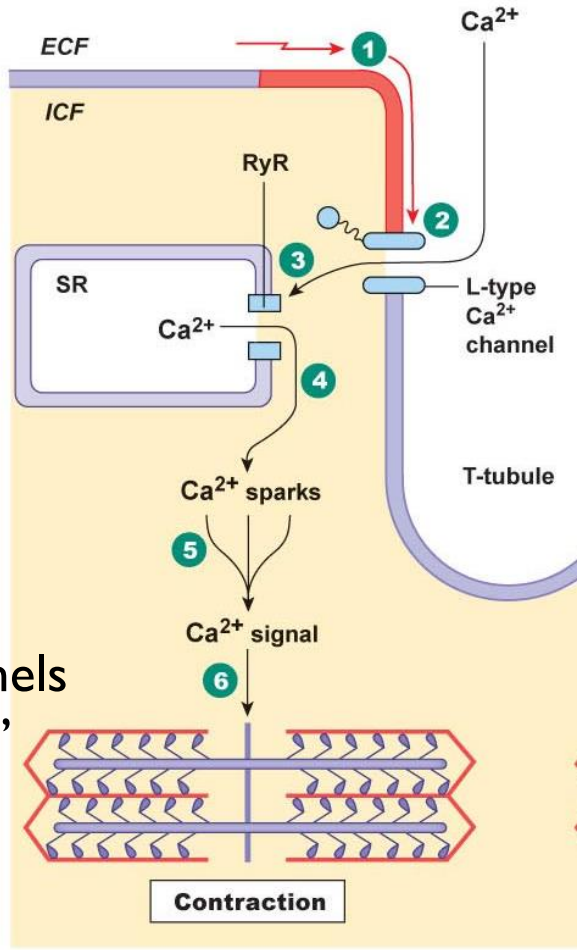
TABLE 14-3 Comparison of Action Potentials in Cardiac and Skeletal Muscle

	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

Myocardial Physiology

Contractile Cells

- Initiation
  - Action potential via pacemaker cells to conduction fibers
- Excitation-Contraction Coupling
  1. Starts with CICR (Ca^{2+} induced Ca^{2+} release)
     - AP spreads along sarcolemma
     - T-tubules contain voltage gated L-type Ca^{2+} channels which open upon depolarization
     - Ca^{2+} entrance into myocardial cell and opens RyR (ryanodine receptors) Ca^{2+} release channels
     - Release of Ca^{2+} from SR causes a Ca^{2+} "spark"
     - Multiple sparks form a Ca^{2+} signal

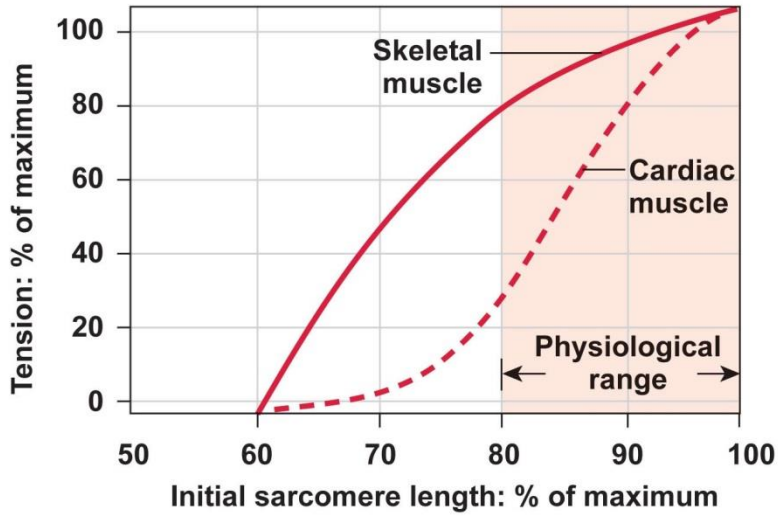


Spark Gif

Myocardial Physiology

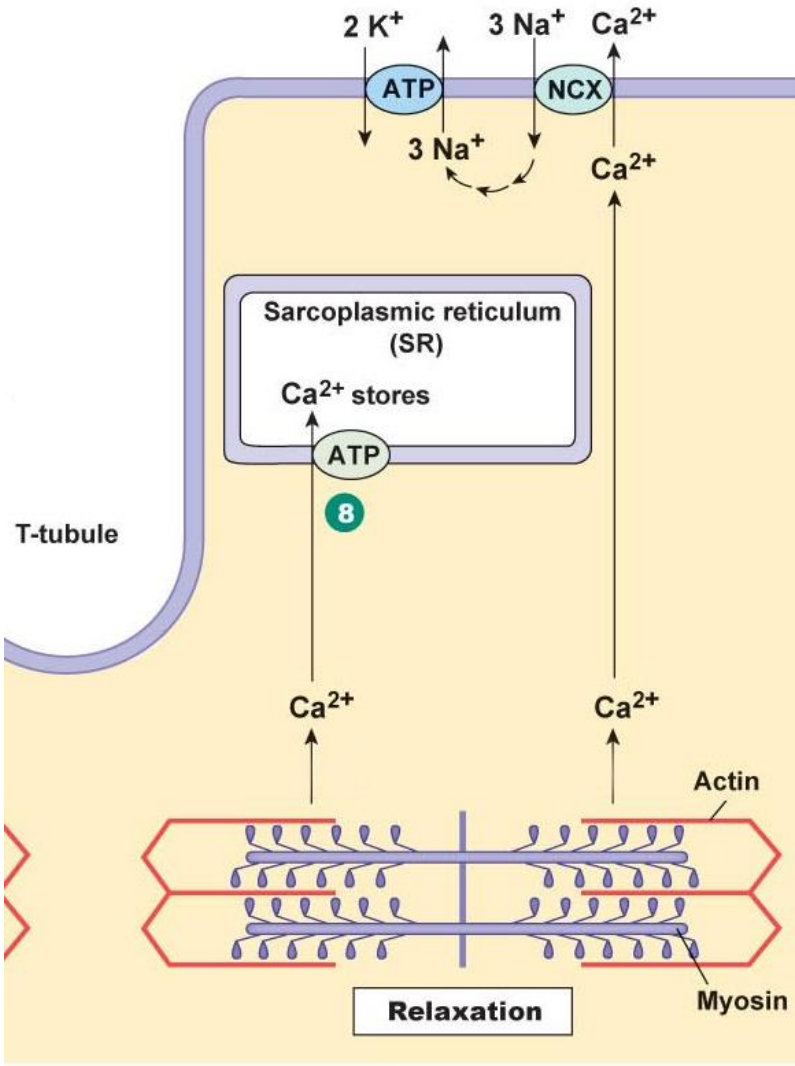
Contractile Cells

- Excitation-Contraction Coupling cont…
  2. Ca^{2+} signal (Ca^{2+} from SR and ECF) binds to troponin to initiate myosin head attachment to actin
- Contraction
  - Same as skeletal muscle, but…
  - Strength of contraction varies
    - Sarcomeres are not "all or none" as it is in skeletal muscle
      - The response is graded!
        - Low levels of cytosolic Ca^{2+} will not activate as many myosin/actin interactions and the opposite is true
    - Length tension relationships exist
      - Strongest contraction generated when stretched between 80 & 100% of maximum (physiological range)
      - What causes stretching?
        - The filling of chambers with blood



Myocardial Physiology
Contractile Cells

- Relaxation
  - Ca^{2+} is transported back into the SR and
  - Ca^{2+} is transported out of the cell by a facilitated Na^{+}/Ca^{2+} exchanger (NCX)
  - As ICF Ca^{2+} levels drop, interactions between myosin/actin are stopped
  - Sarcomere lengthens

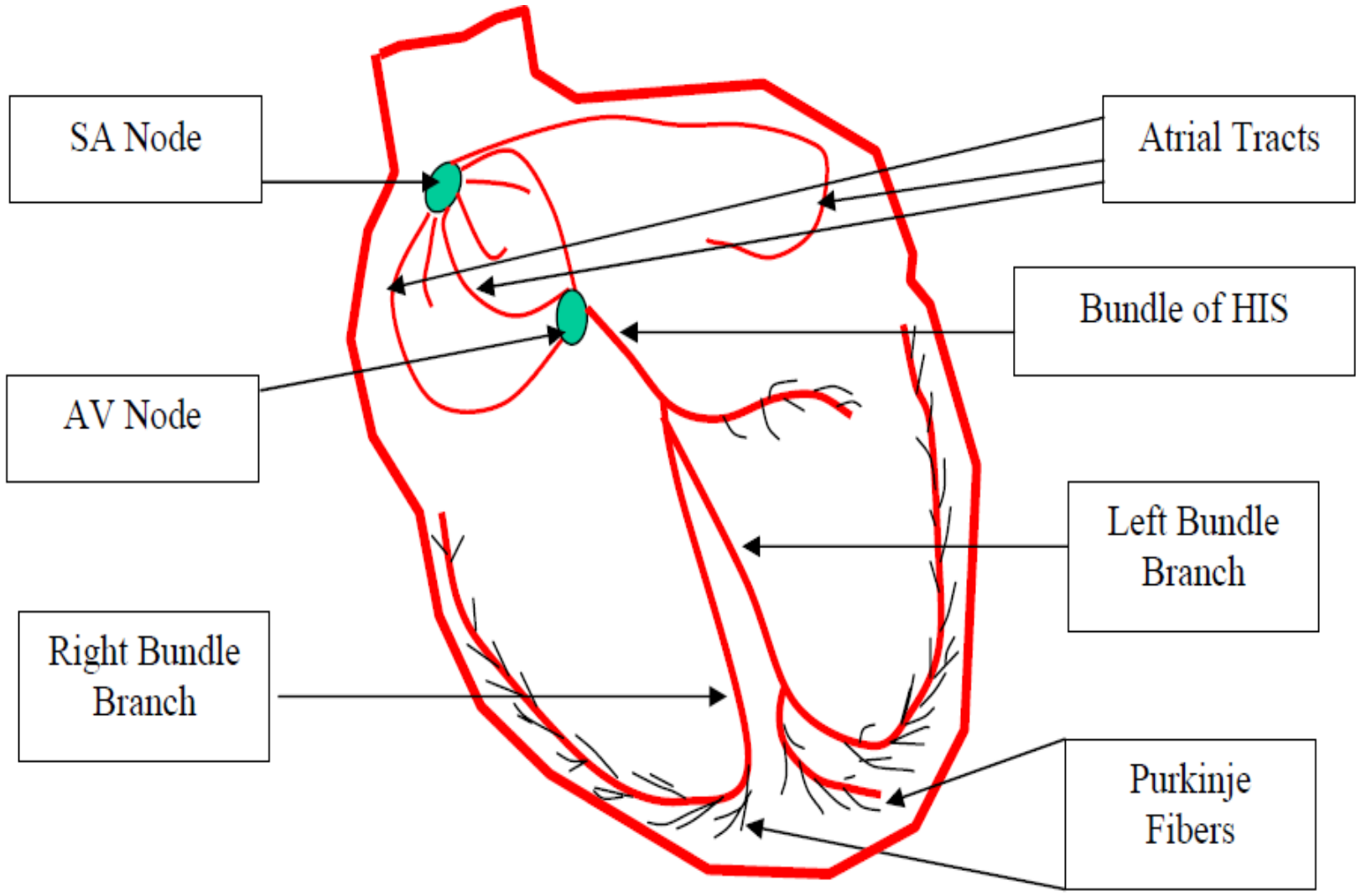


Cardiac Cycle

Coordinating the activity

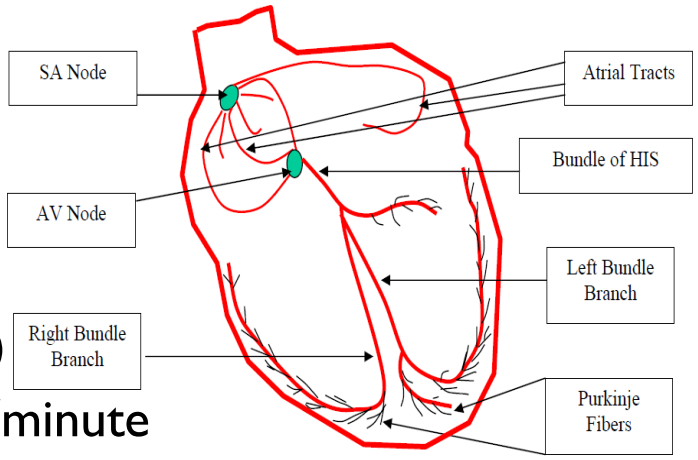
- Cardiac cycle is the sequence of events as blood enters the atria, leaves the ventricles and then starts over
- Synchronizing this is the Intrinsic Electrical Conduction System
- Influencing the rate (chronotropy & dromotropy) is done by the sympathetic and parasympathetic divisions of the ANS

Electrical conduction pathway



Cardiac Cycle

Coordinating the activity

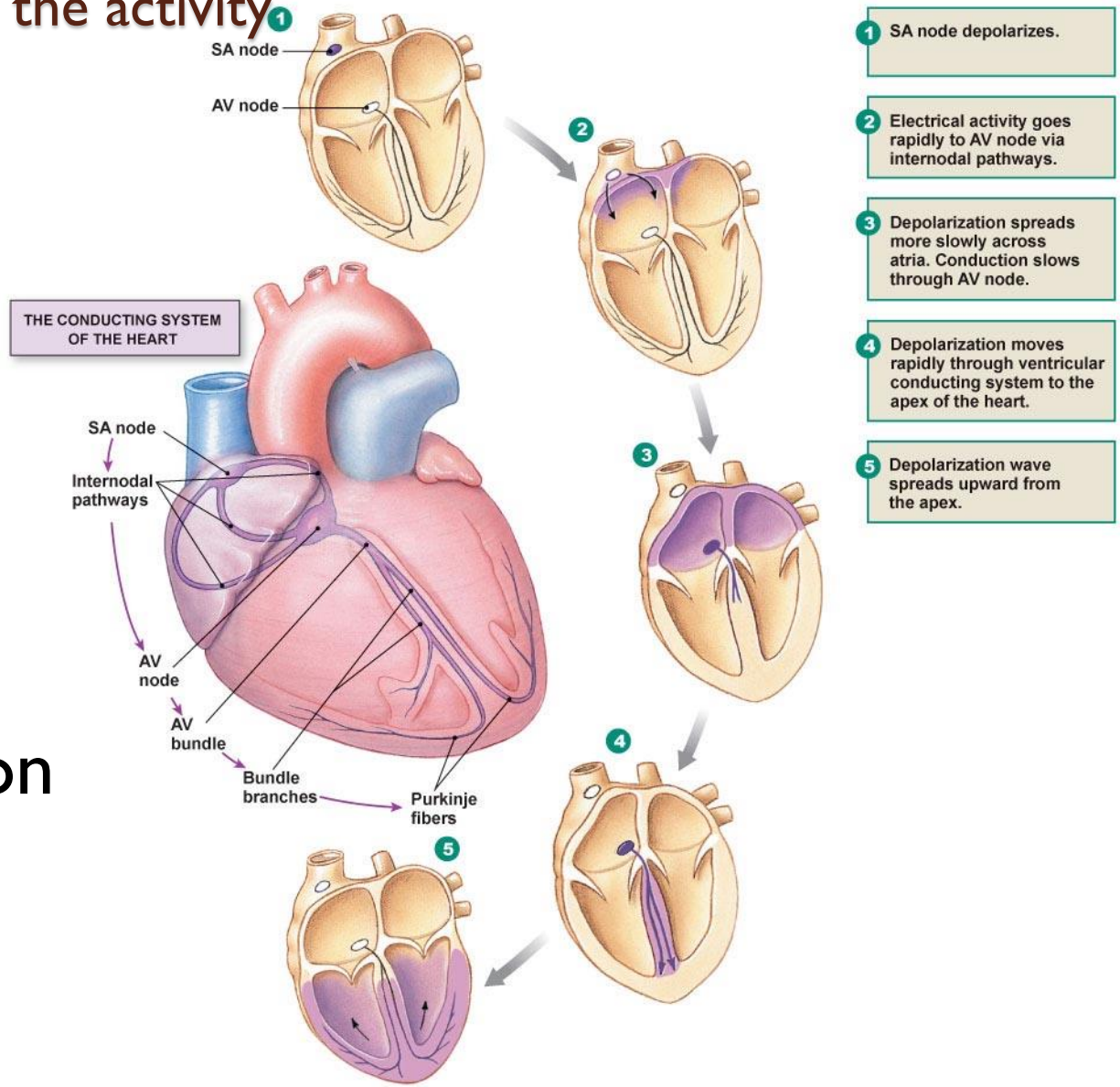


- Electrical Conduction Pathway
  - Initiated by the Sino-Atrial node (SA node) which is myogenic at 70-80 action potentials/minute
  - Depolarization is spread through the atria via gap junctions and internodal pathways to the Atrio-Ventricular node (AV node)
    - The fibrous connective tissue matrix of the heart prevents further spread of APs to the ventricles
    - A slight delay at the AV node occurs
      - Due to slower formation of action potentials
      - Allows further emptying of the atria
  - Action potentials travel down the Atrioventricular bundle (Bundle of His) which splits into left and right atrioventricular bundles (bundle branches) and then into the conduction myofibers (Purkinje cells)
    - Purkinje cells are larger in diameter & conduct impulse very rapidly
      - Causes the cells at the apex to contract nearly simultaneously
        - Good for ventricular ejection

Cardiac Cycle

Coordinating the activity

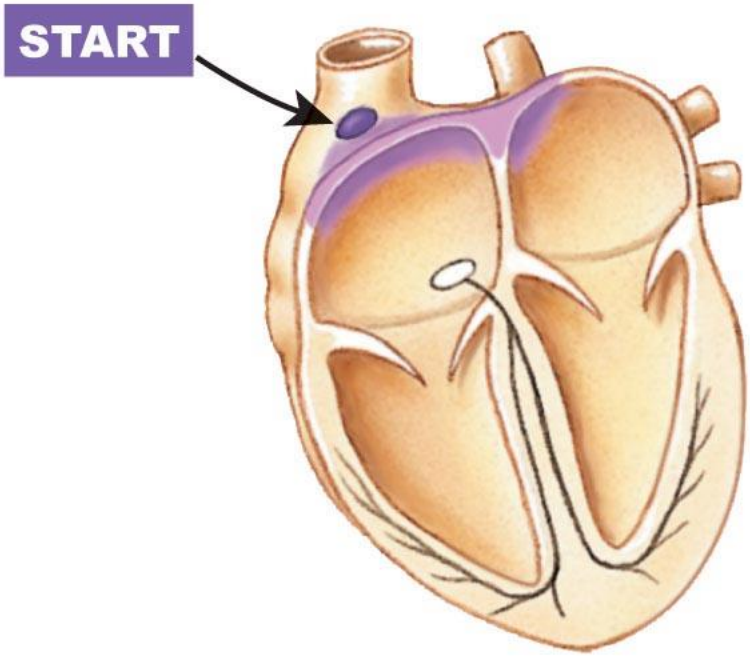
- Electrical Conduction Pathway

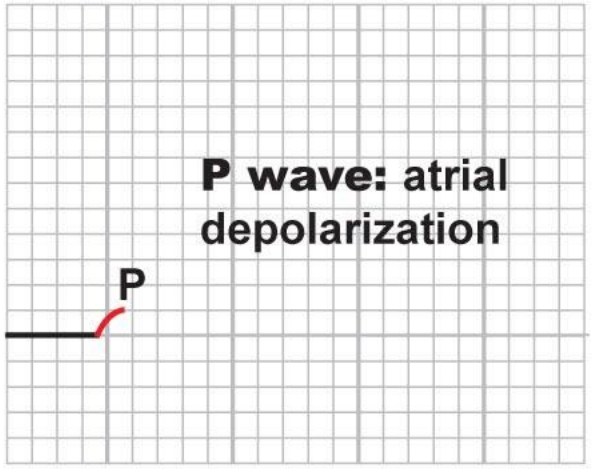


Cardiac Cycle
Coordinating the activity

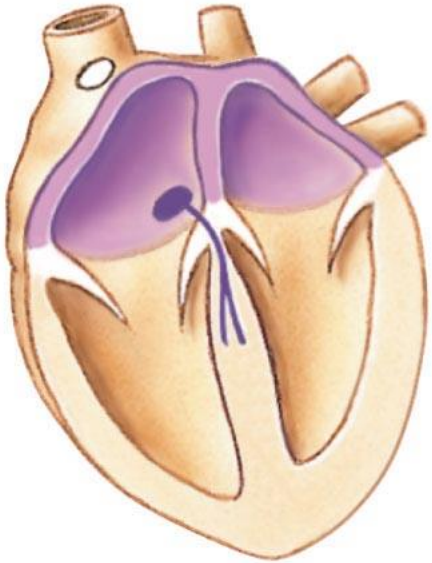
- The electrical system gives rise to electrical changes (depolarization/repolarization) that is transmitted through isotonic body fluids and is recordable
  - The ECG!
    - A recording of electrical activity
    - Can be mapped to the cardiac cycle

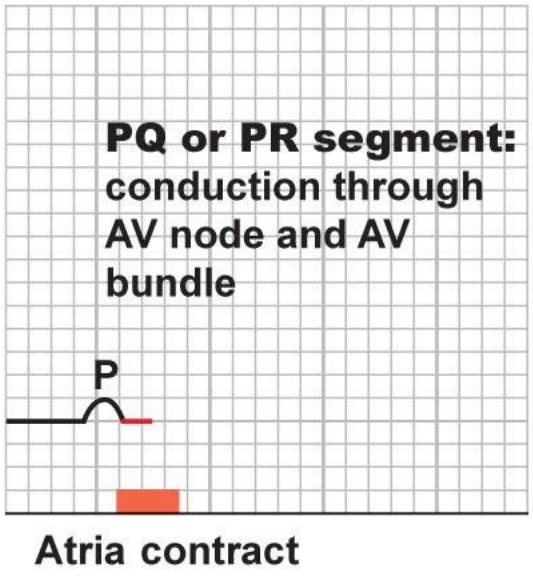
ELECTRICAL EVENTS OF THE CARDIAC CYCLE





ELECTRICAL EVENTS OF THE CARDIAC CYCLE





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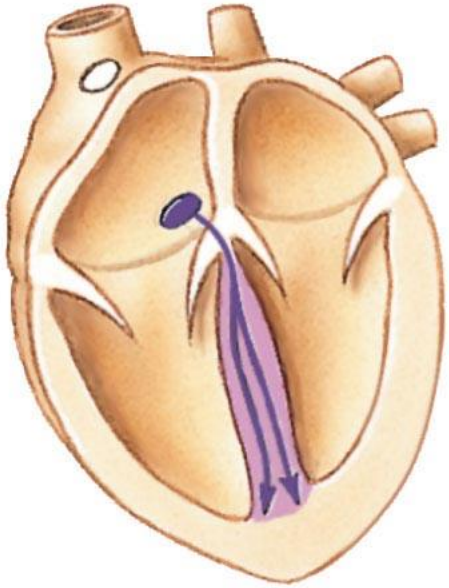

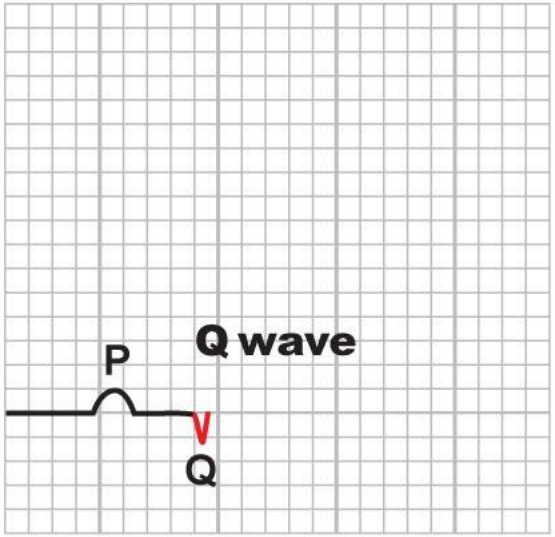

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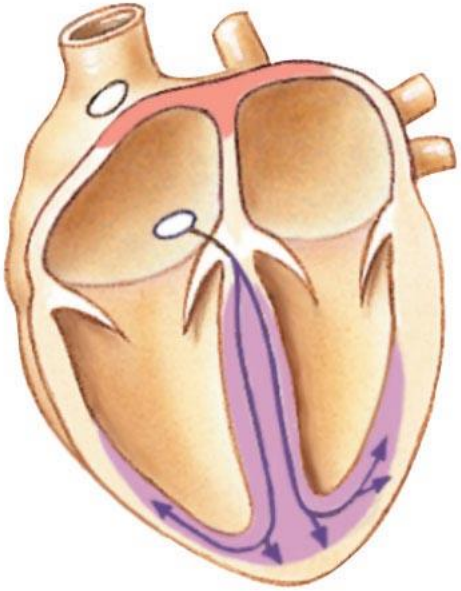

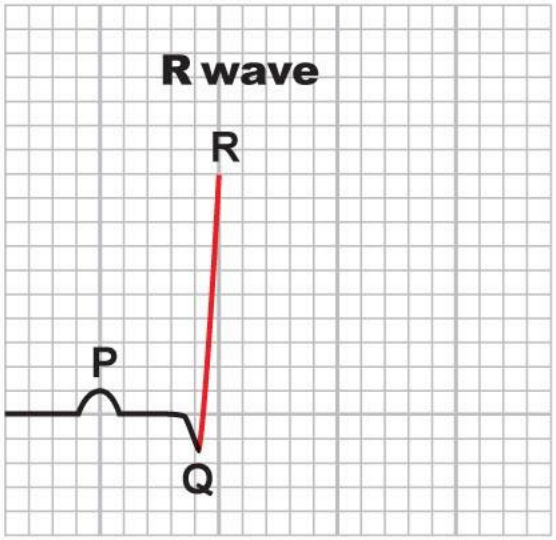

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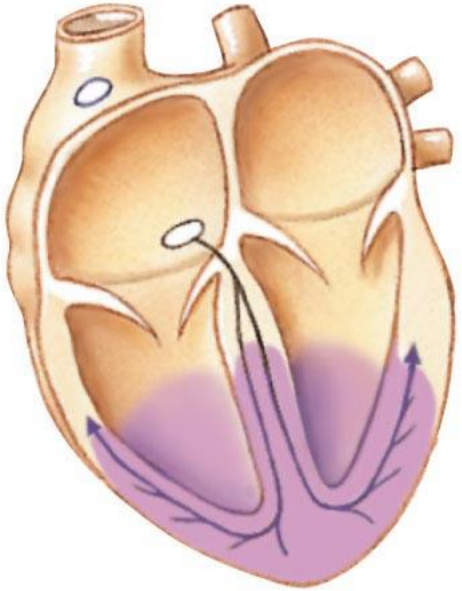
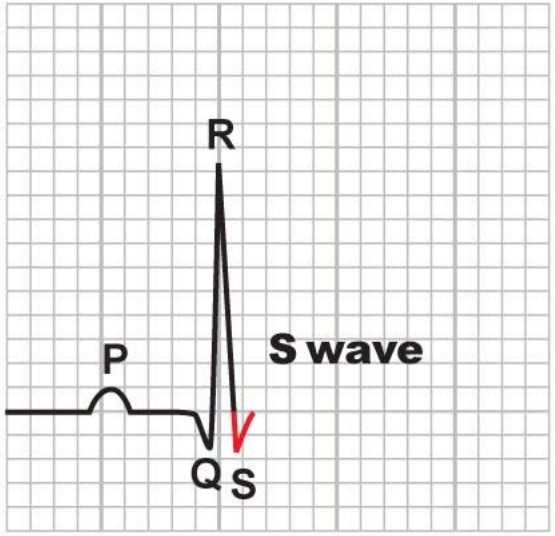
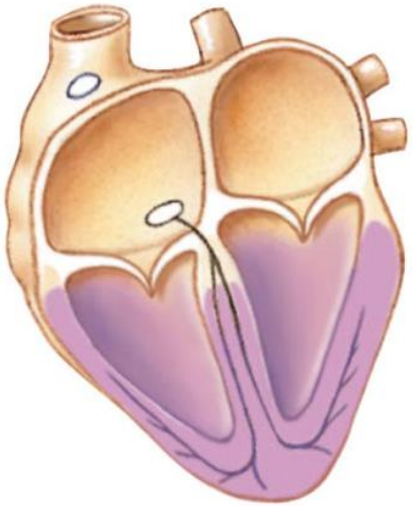
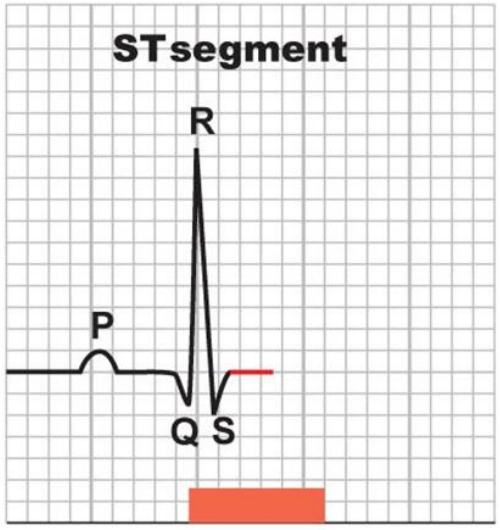




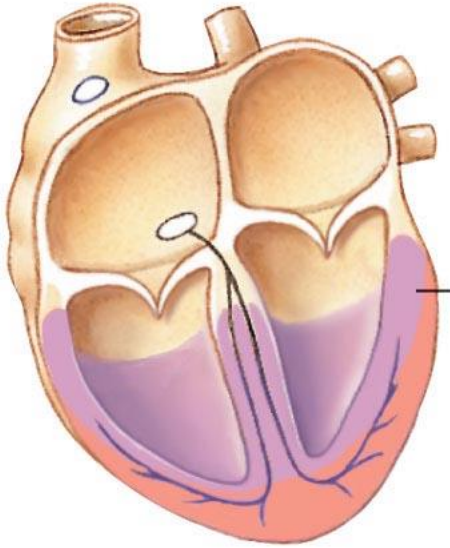
ELECTRICAL EVENTS
OF THE
CARDIAC CYCLE

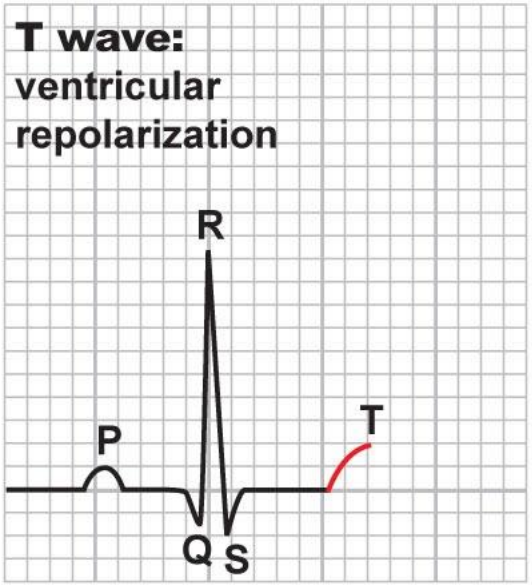




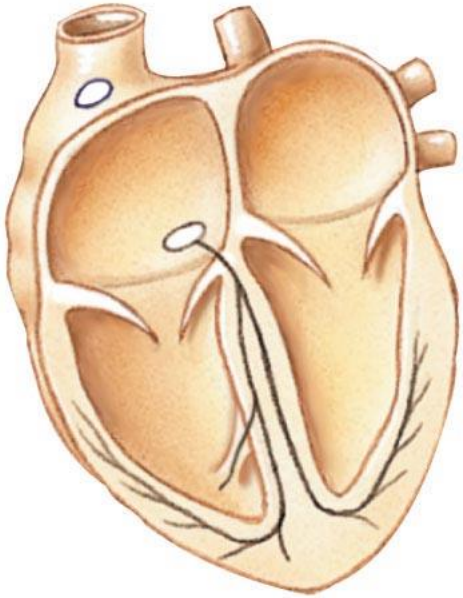
Ventricles contract

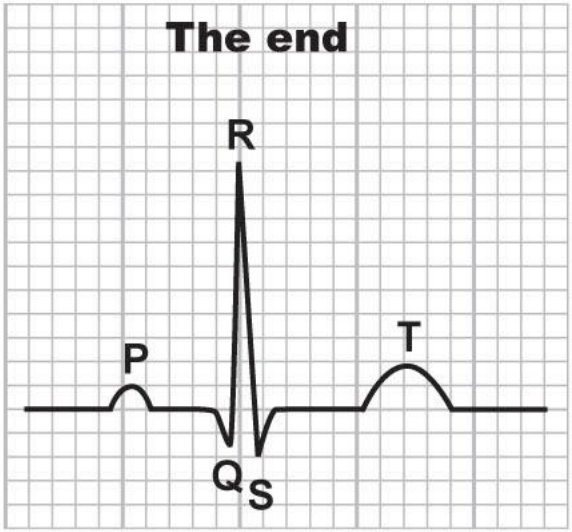
ELECTRICAL EVENTS OF THE CARDIAC CYCLE





ELECTRICAL EVENTS OF THE CARDIAC CYCLE





Cardiac Cycle

Phases

- Systole = period of contraction
- Diastole = period of relaxation
- Cardiac Cycle is alternating periods of systole and diastole
- Phases of the cardiac cycle

1. Rest
   - Both atria and ventricles in diastole
   - Blood is filling both atria and ventricles due to low pressure conditions
2. Atrial Systole
   - Completes ventricular filling
3. Isovolumetric Ventricular Contraction
   - Increased pressure in the ventricles causes the AV valves to close… why?
     - Creates the first heart sound (lub)
   - Atria go back to diastole
   - No blood flow as semilunar valves are closed as well

Cardiac Cycle

Phases

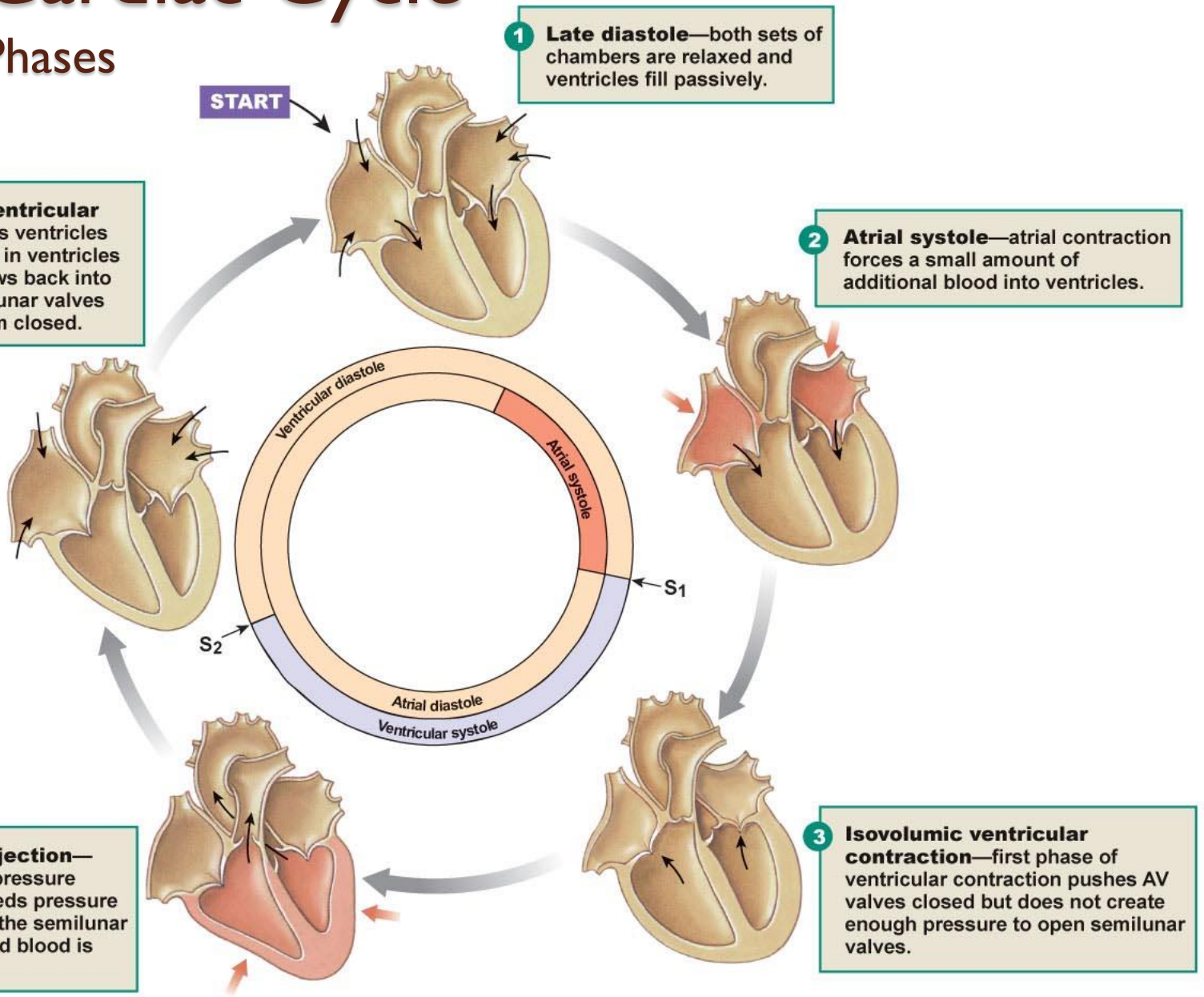
- Phases of the cardiac cycle

4. Ventricular Ejection
   - Intraventricular pressure overcomes aortic pressure
     - Semilunar valves open
     - Blood is ejected
5. Isovolumetric Ventricular Relaxation
   - Intraventricular pressure drops below aortic pressure
     - Semilunar valves close = second heart sound (dup)
   - Pressure still hasn't dropped enough to open AV valves so volume remains same (isovolumetric)

Back to Atrial & Ventricular Diastole

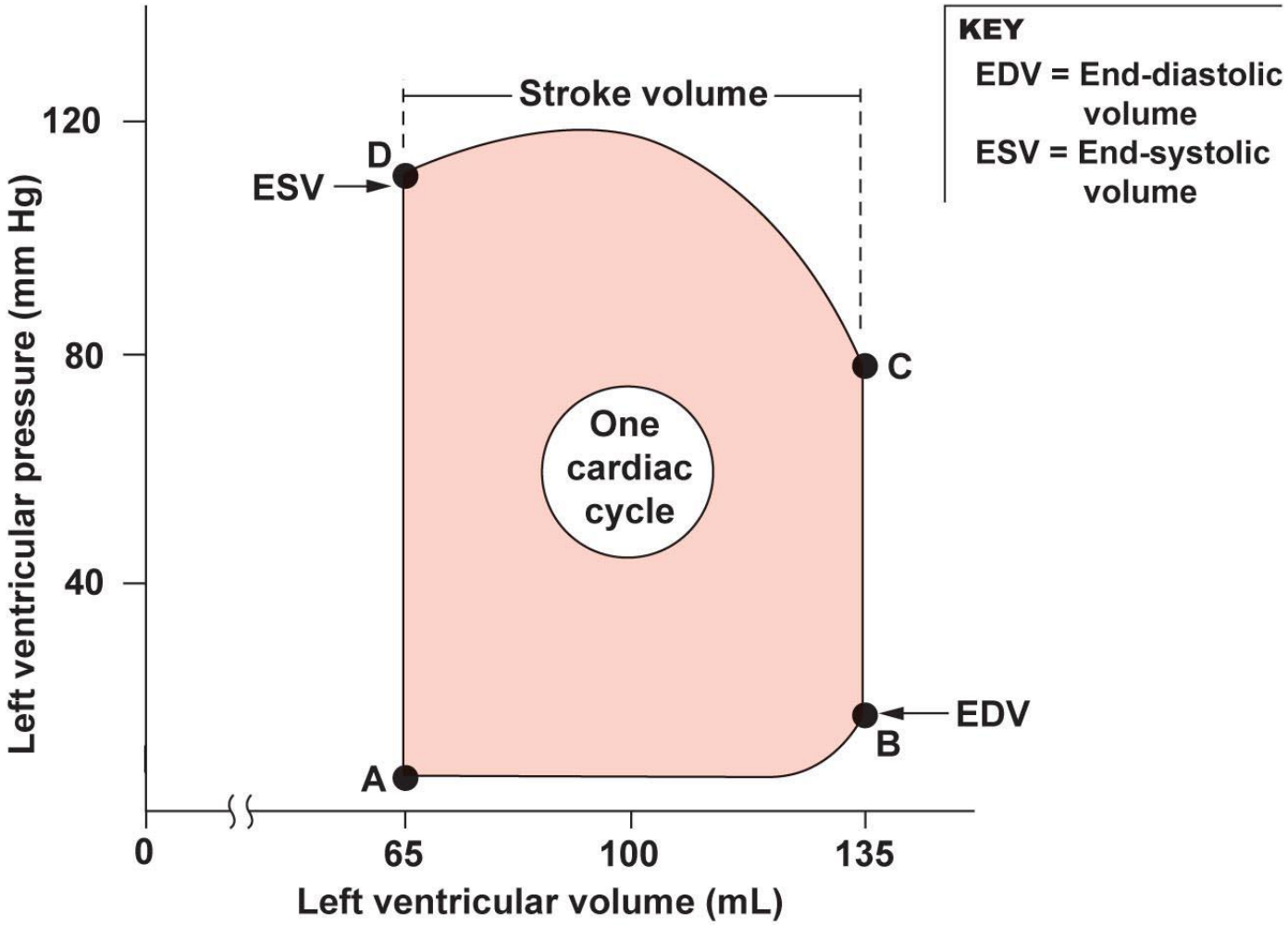
Cardiac Cycle

Phases



Cardiac Cycle

Blood Volumes & Pressure



Cardiac Cycle

Putting it all together!