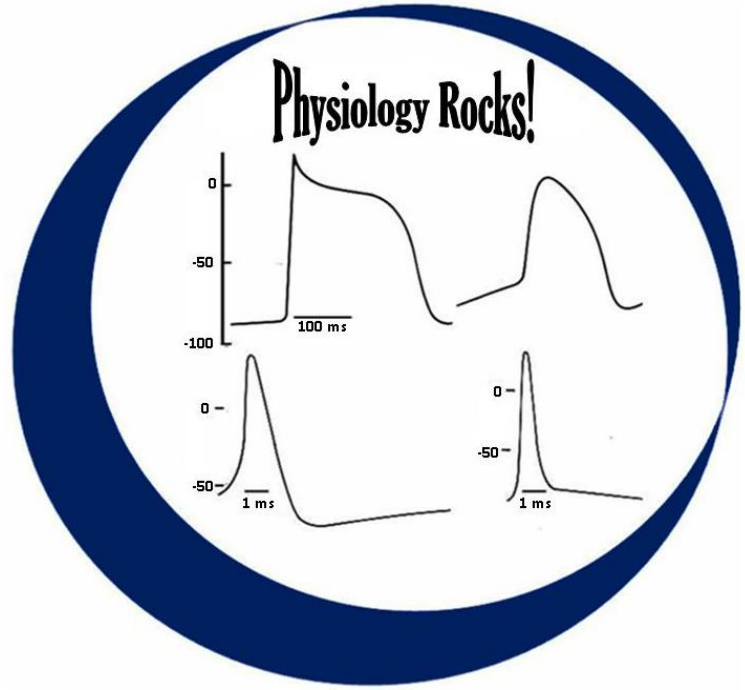
# Lecture 1
# Cardiac Electrical Activity

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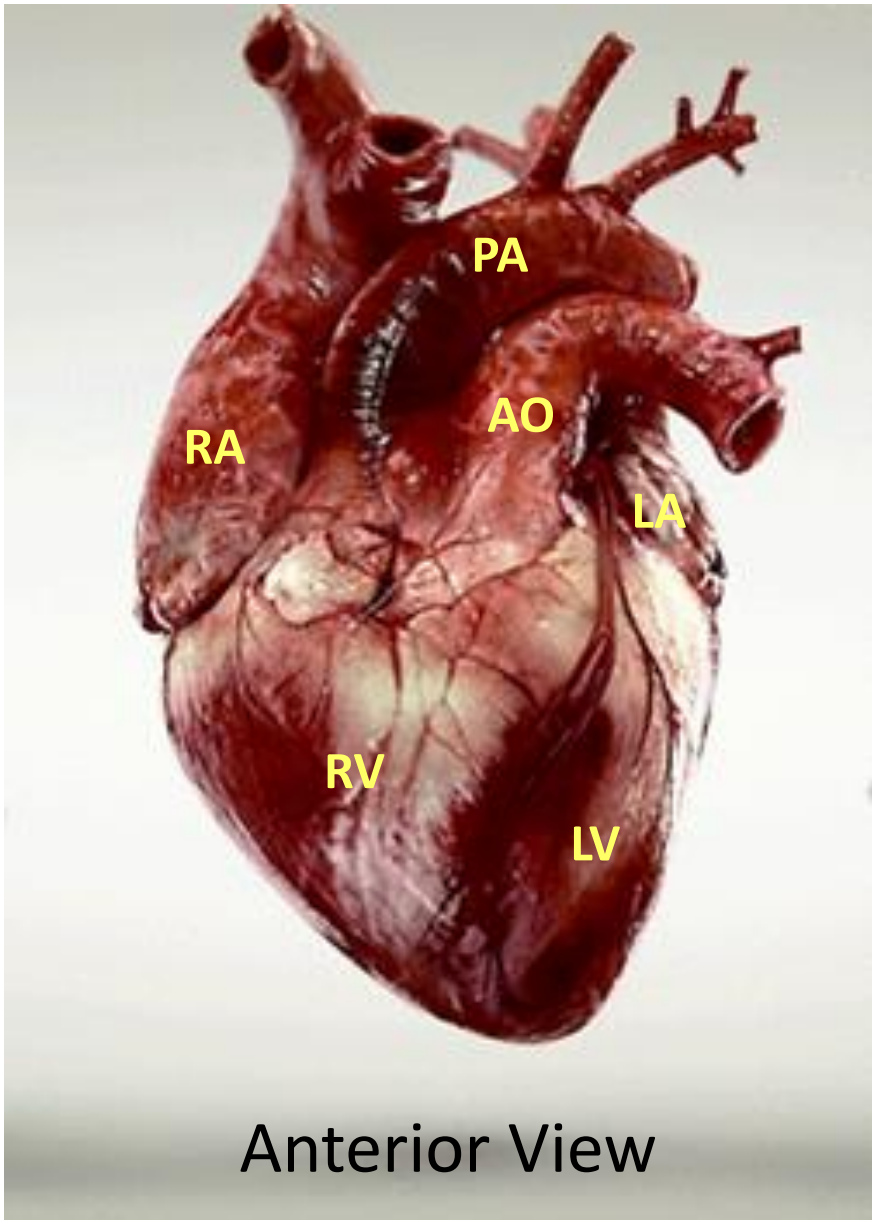
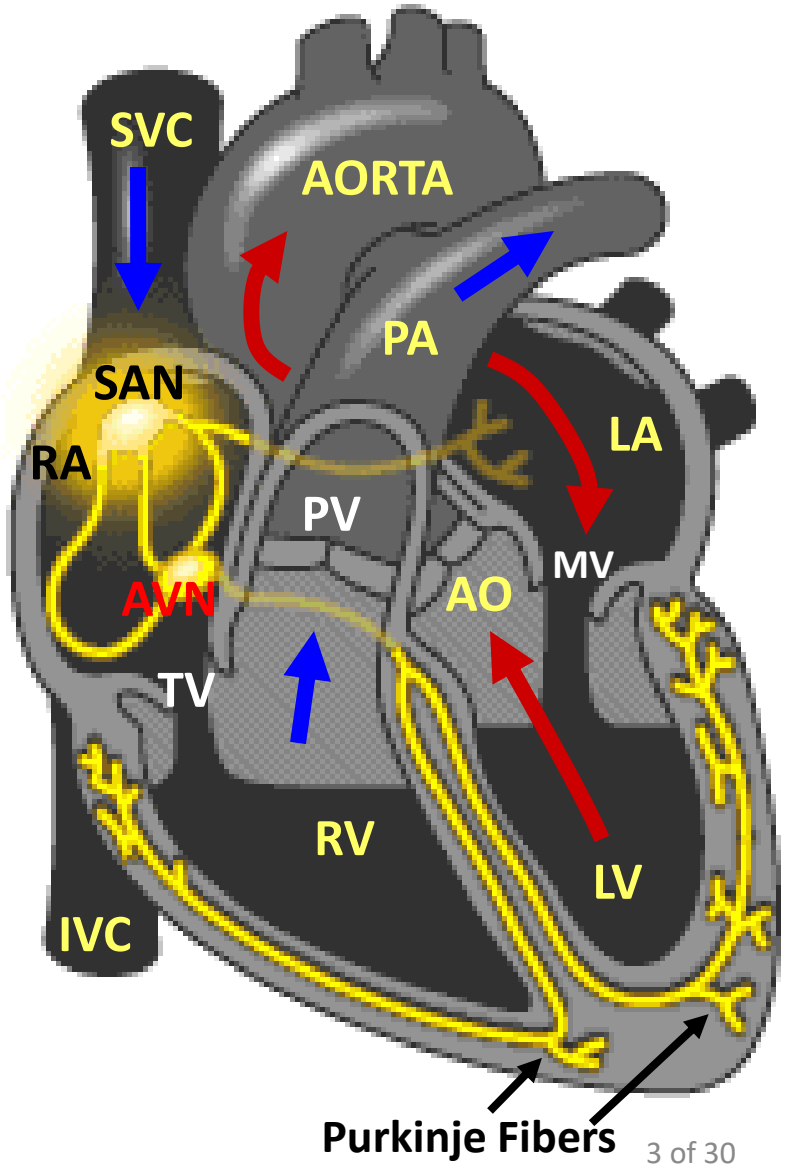
# Topics

- Cardiac functional anatomy and function
- Cardiac electrical patterns and action potential timing
- Fast response action potential features
- Membrane ionic channels and currents
- Temporal aspects
- Action potential conduction patterns

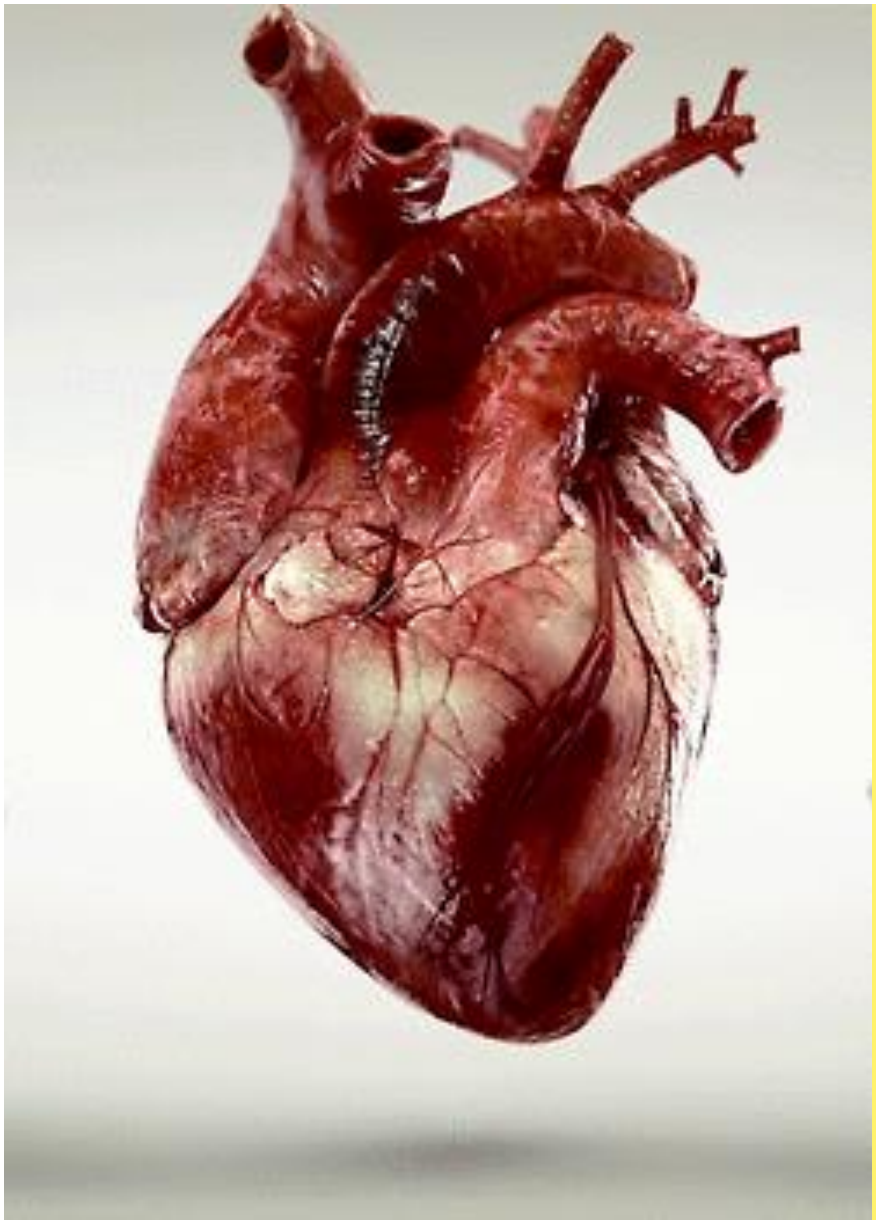
  1. Depolarization  2. Repolarization
- Conduction in relation to the EKG
- Refractory periods
- Interactive questions

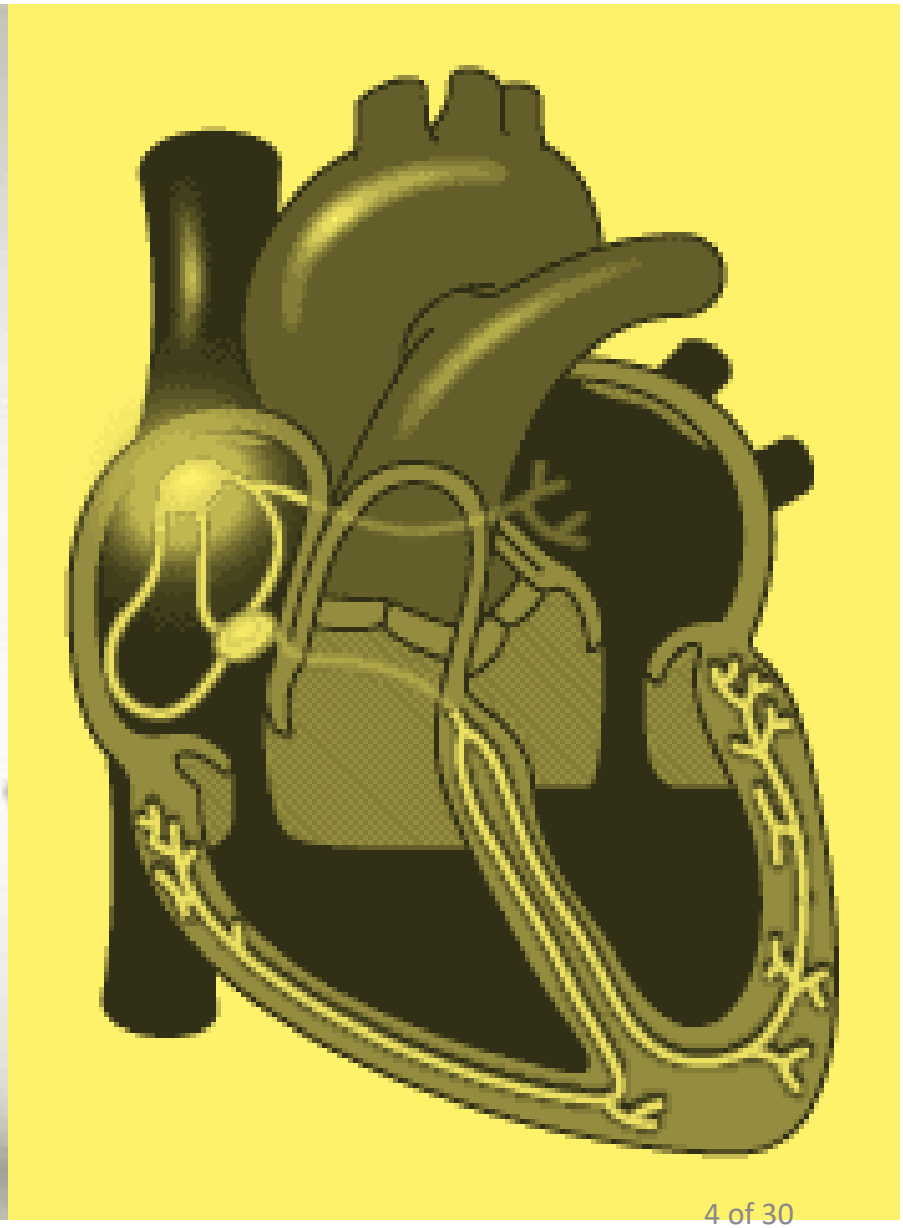
# The Beating Heart: Functional Anatomy



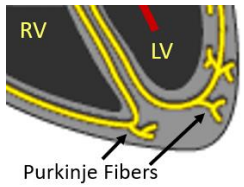
# The Beating Heart: Functional ACTIONS





# Cardiac Electrical Overview

# Normal Cardiac Conduction Pathways and Effects




Modified cardiac m. fibers transition to m. cells via gap junctions now cell-cell conduction

SA

HR

To LA via Bachmann's Bundle

RA muscle

Internodal tracts

AV

Bundle of His

RBB

LBB

Purkinje Fibers 4 m/s

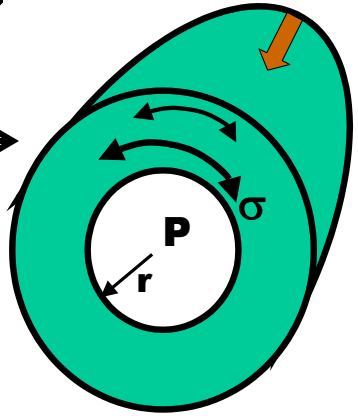
Ventricular Muscle

*Electro-mechanical Coupling*

Ca

***Contraction***

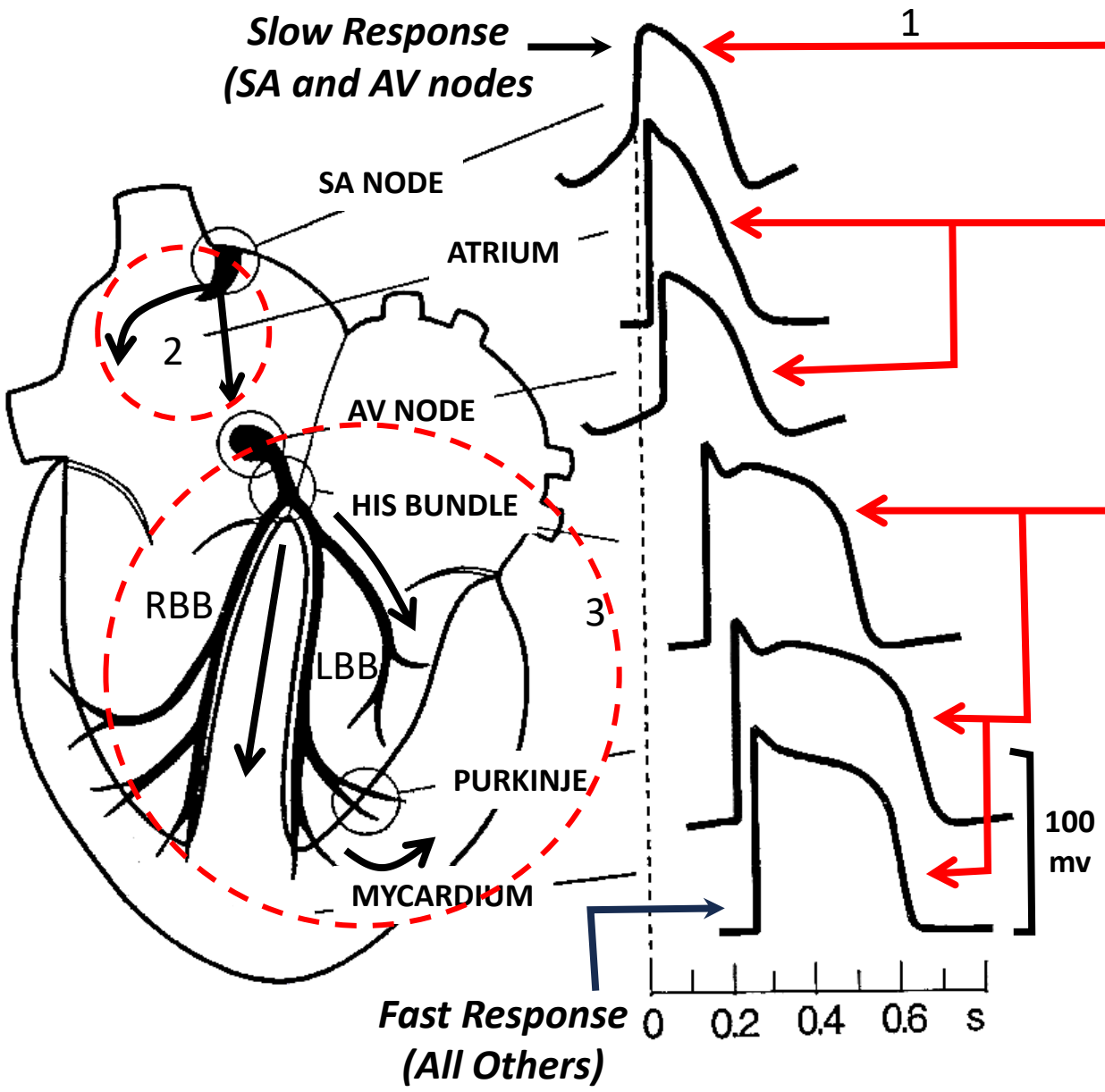
**Blood Ejection SV**




**CO = SV x HR**

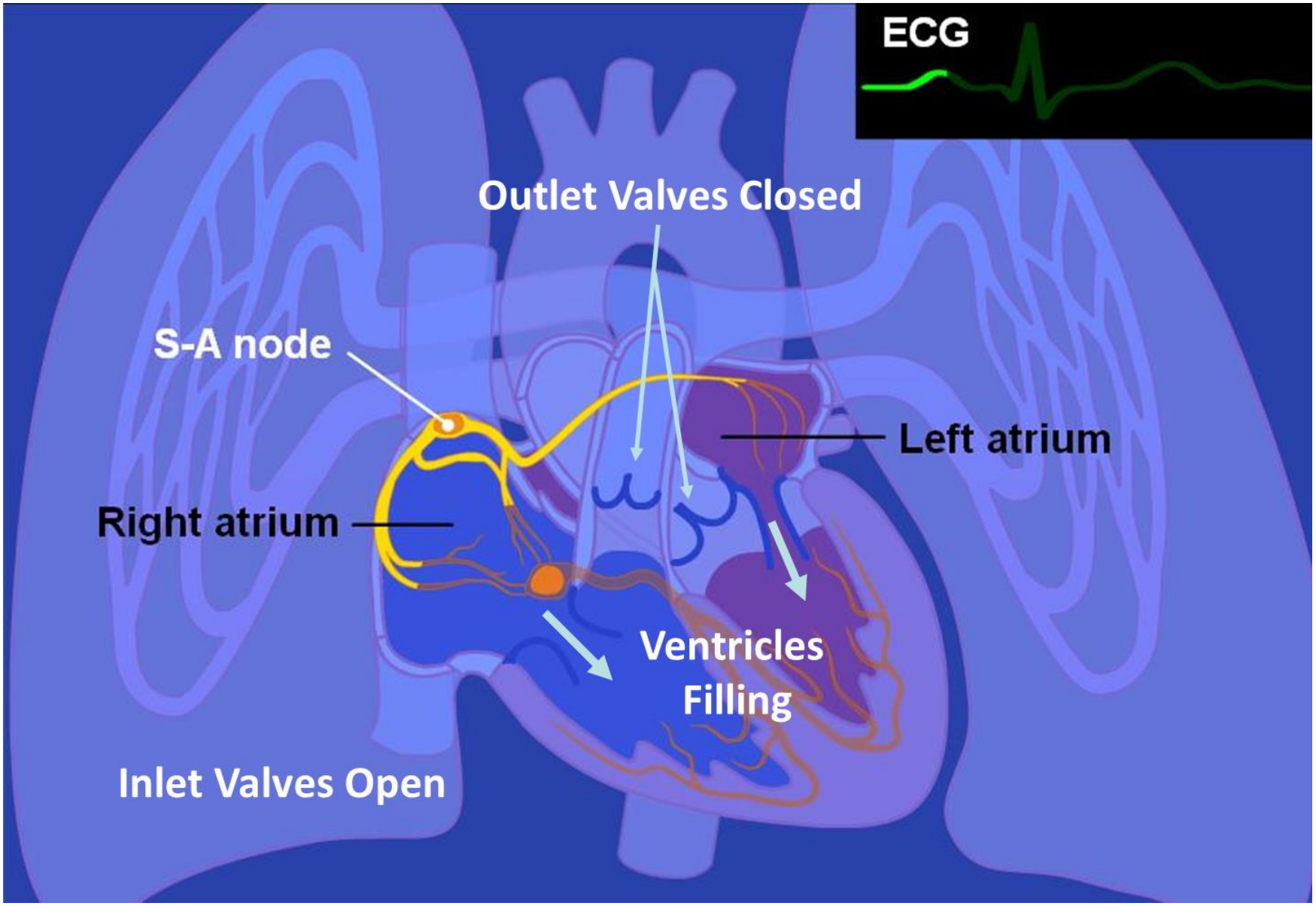
**HR < 60 = Bradycardia; HR >100 Tachycardia**

# Cardiac Action Potential Patterns and Timing

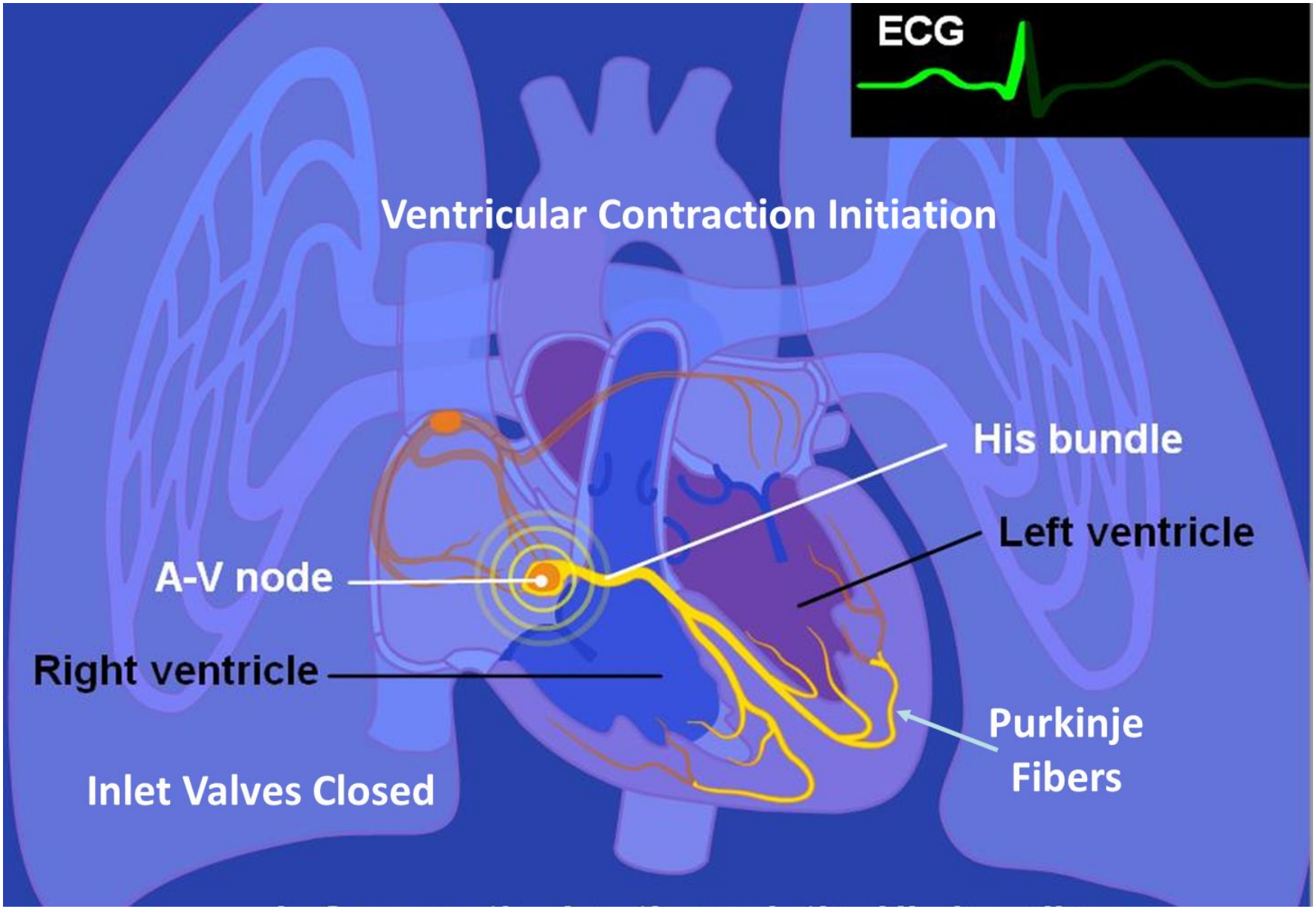



- (1) SAN depolarization is spontaneous
- (2) Action potential (AP) is transmitted to atria and AVN Atrial Contraction
- (3) After short delay AP exits the AVN; passes to His bundle then right bundle branch (RBB) and left bundle branches (LBB) ending in Purkinje fibers → highest AP conduction speed
- (4) Purkinje fiber APs excite the myocardium via electro-mechanical coupling with $Ca^{++}$ entry into the myocytes with contraction ensuing
- (5) SAN and AVN AP are slow response AP with all others known as fast response types

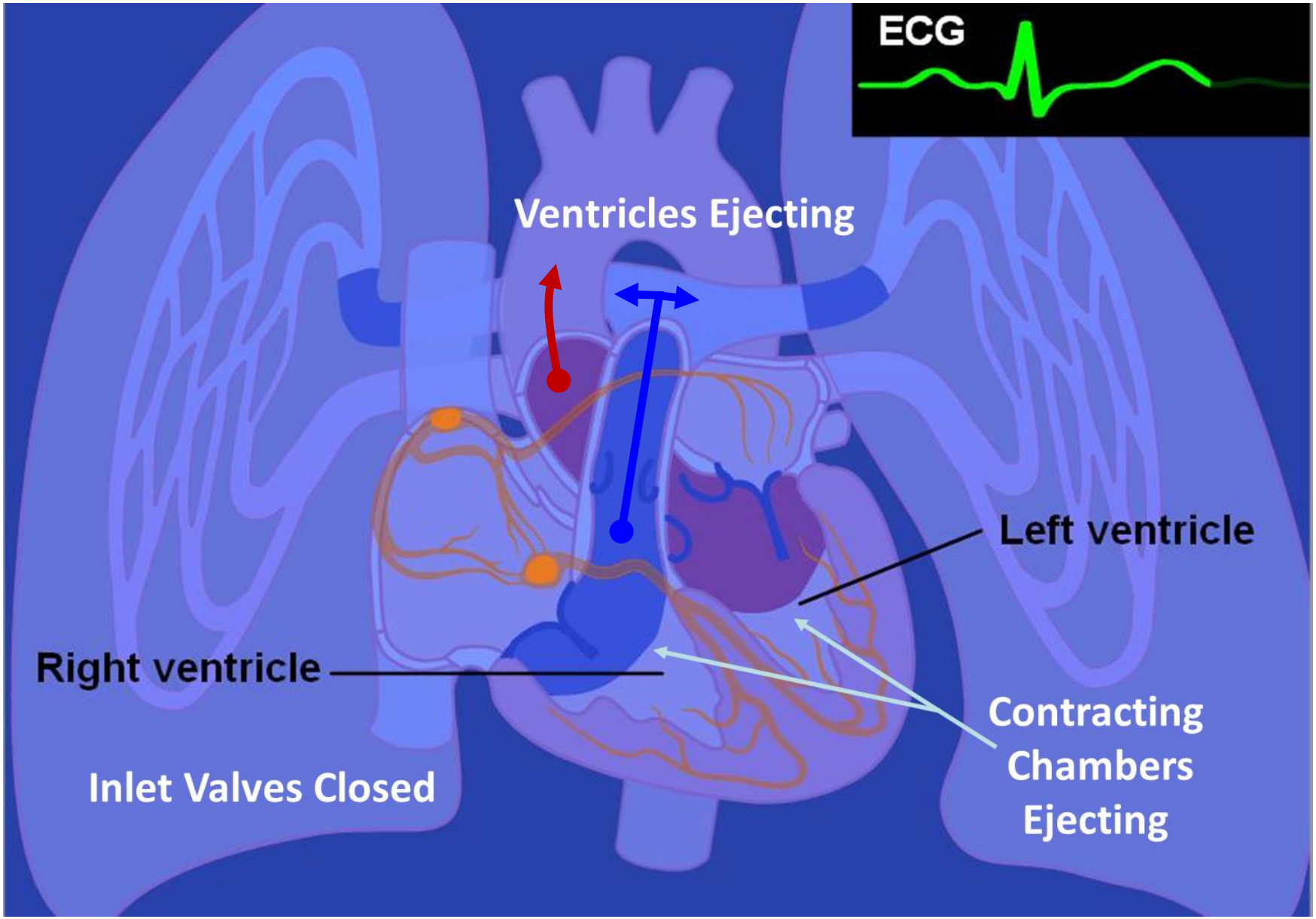
# Electro-Mechanical Coupling



# Electro-Mechanical Coupling

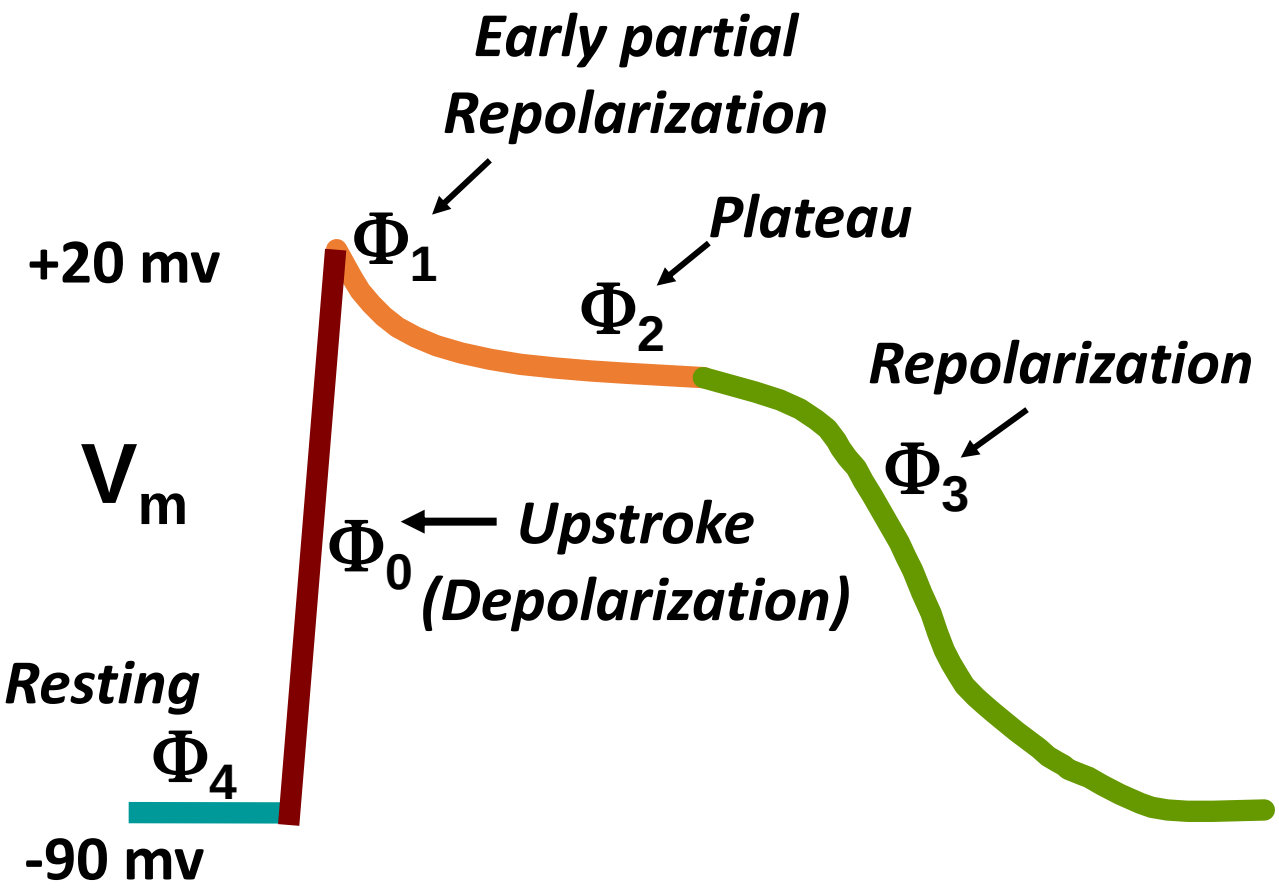


# Electro-Mechanical Coupling

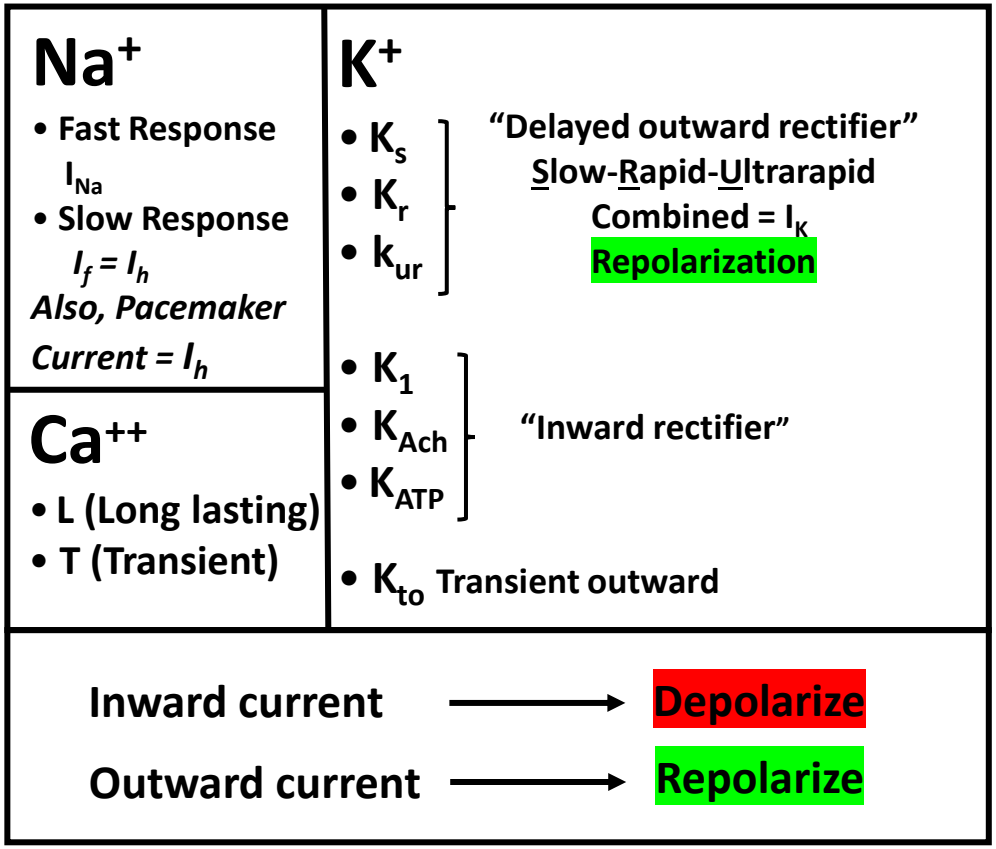


# Closer Look at Action Potential Details

# Fast Response Cardiac Action Potential: Definitions

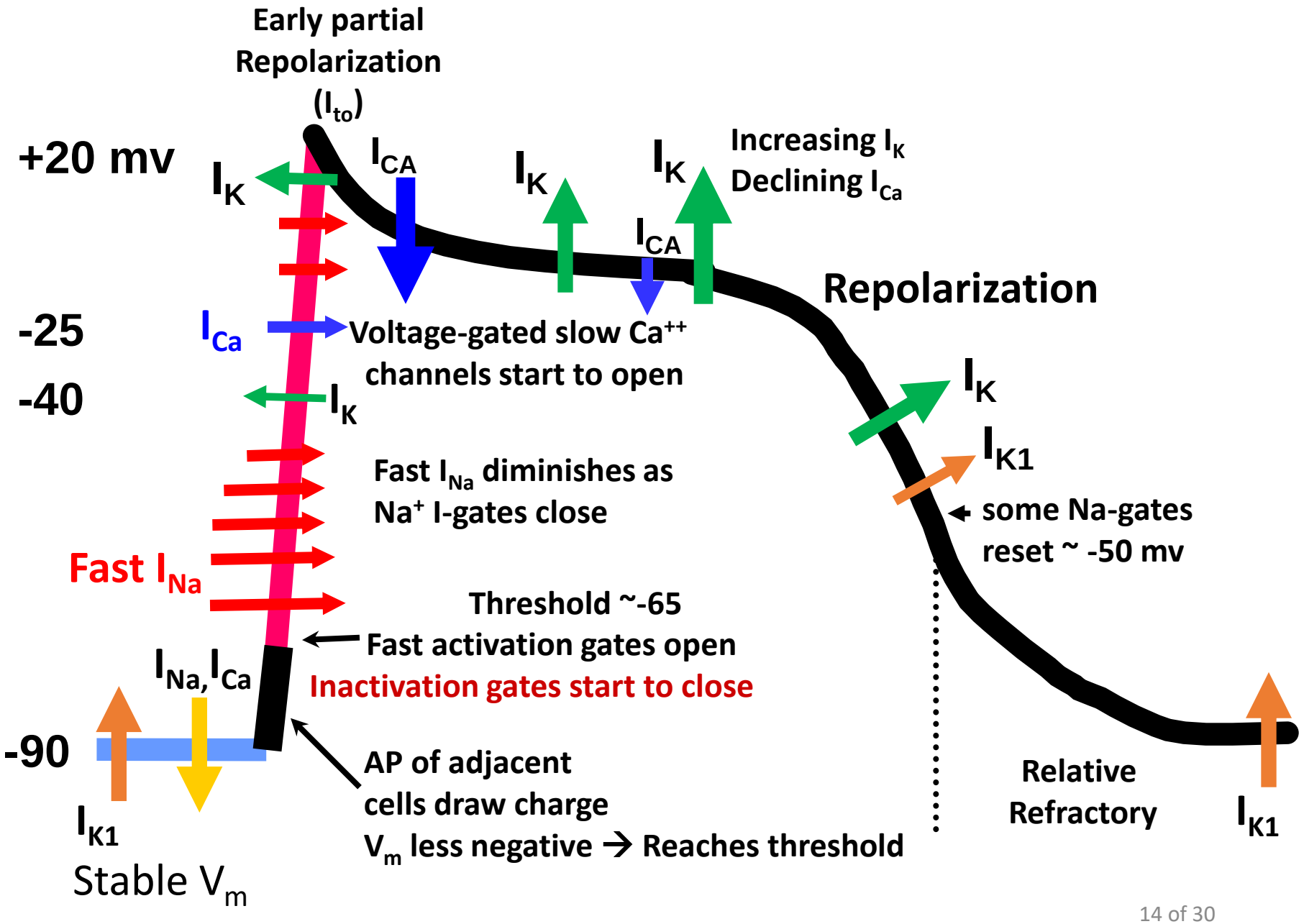


# Cardiac Ion Channels and Currents

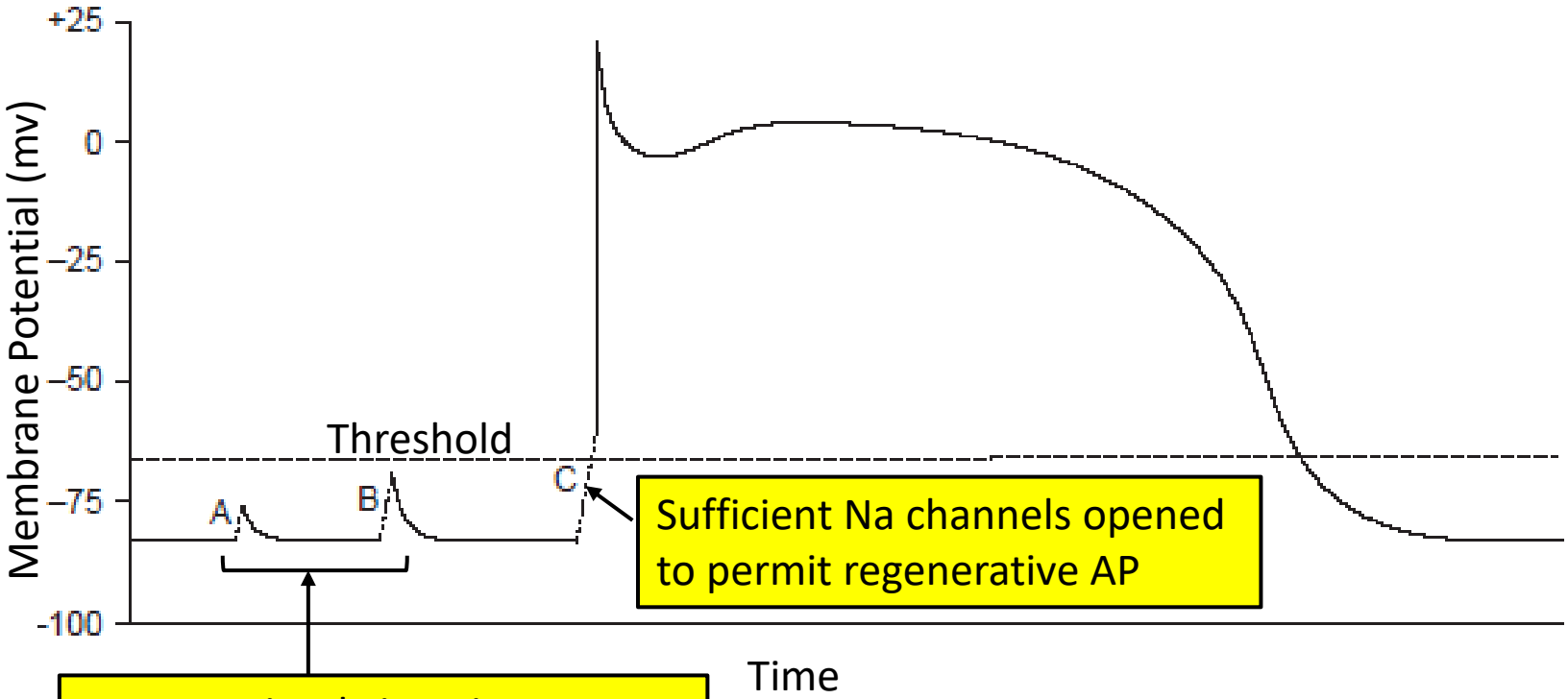



- **$I_f$**: Movement through HCN (Hyperpolarization-activated-cyclic nucleotide-gated channels
- Cyclic nucleotides (cAMP) binding lowers voltage threshold and activates near resting membrane potential
- **Rectification**: Large change in channel conductance with membrane voltage **$g = f(V_m)$**
- **Outward Rectification**: Current flows more easily outward then inward
- **Inward Rectification**: Current flows more easily inward then outward (e.g. **$I_{K1}$**)
- **Current Direction**: Direction of ion movement

# Fast Response Ionic Currents: Descriptive Overview



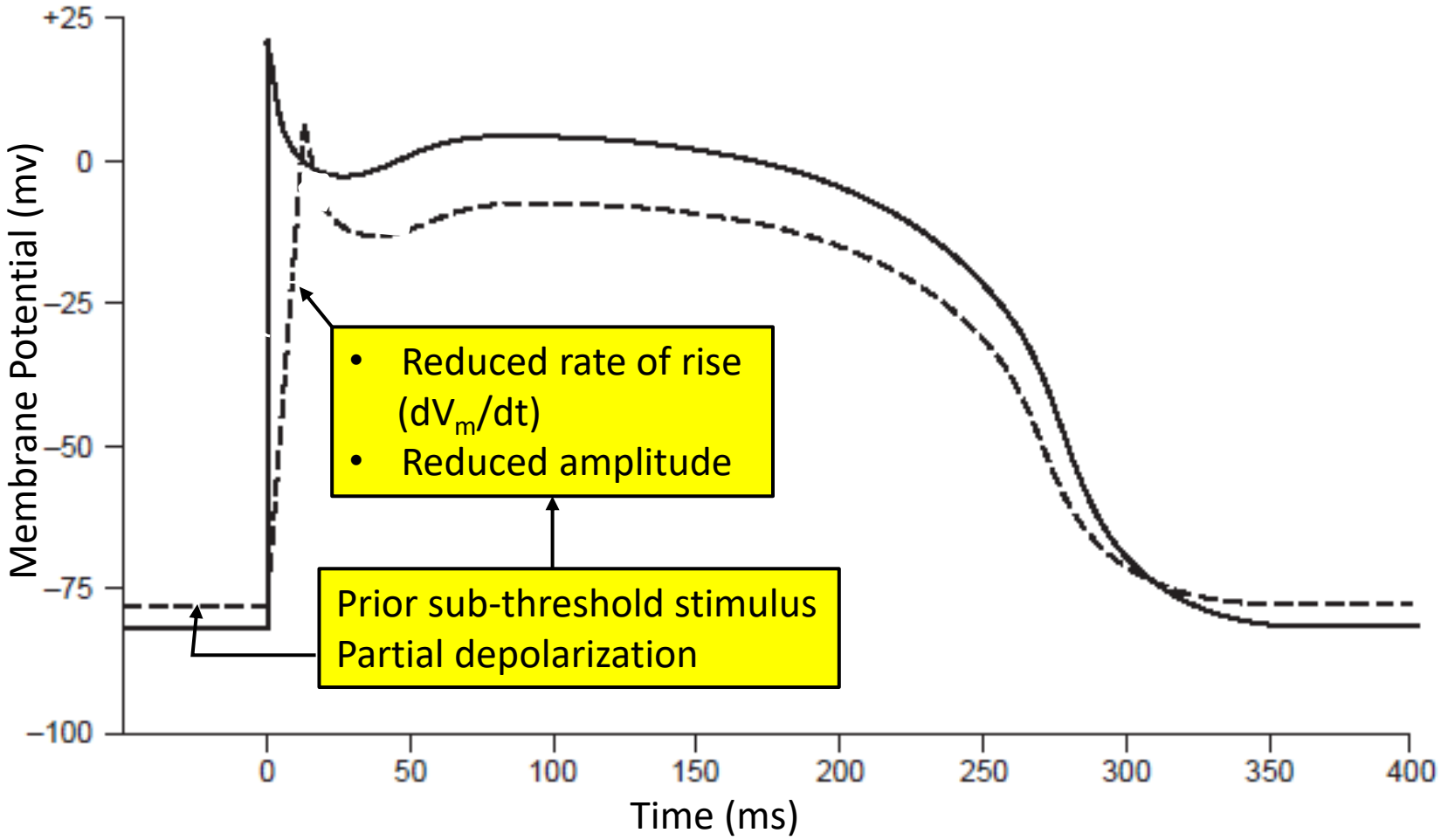
# Threshold



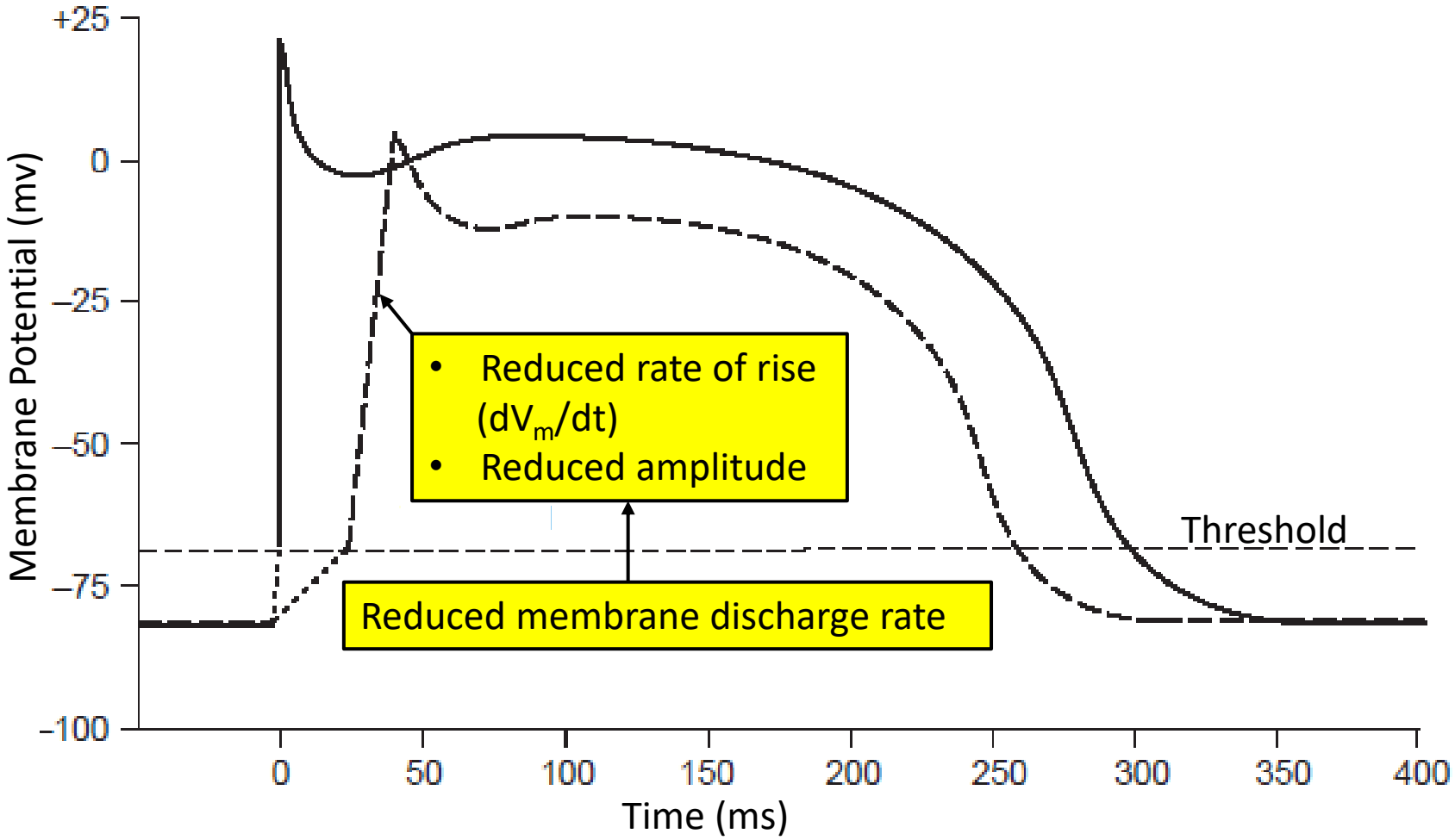

Sufficient Na channels opened to permit regenerative AP

May transiently inactivate some Na channels that will decrease depolarization rate and extent Of following APs

# Partial Depolarization Effect on AP

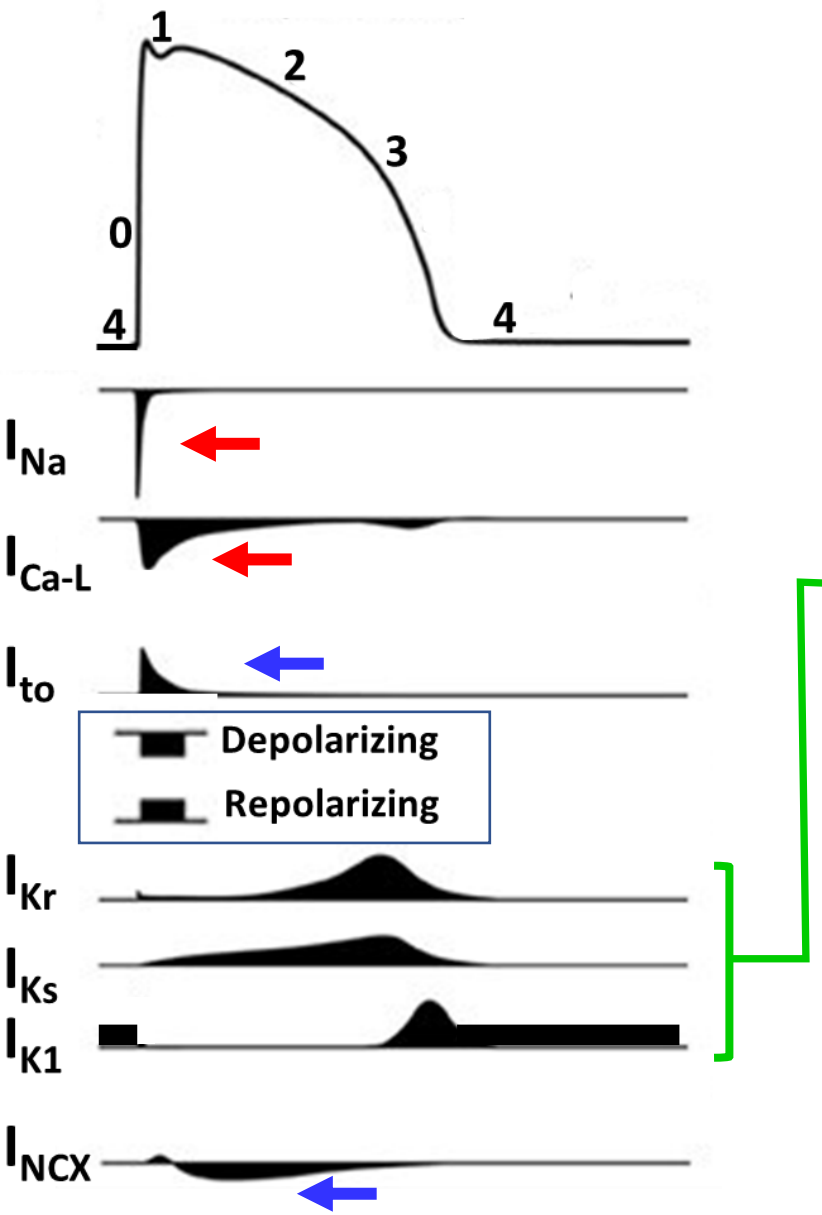


# Reduced Threshold Approach Rate Effects on AP



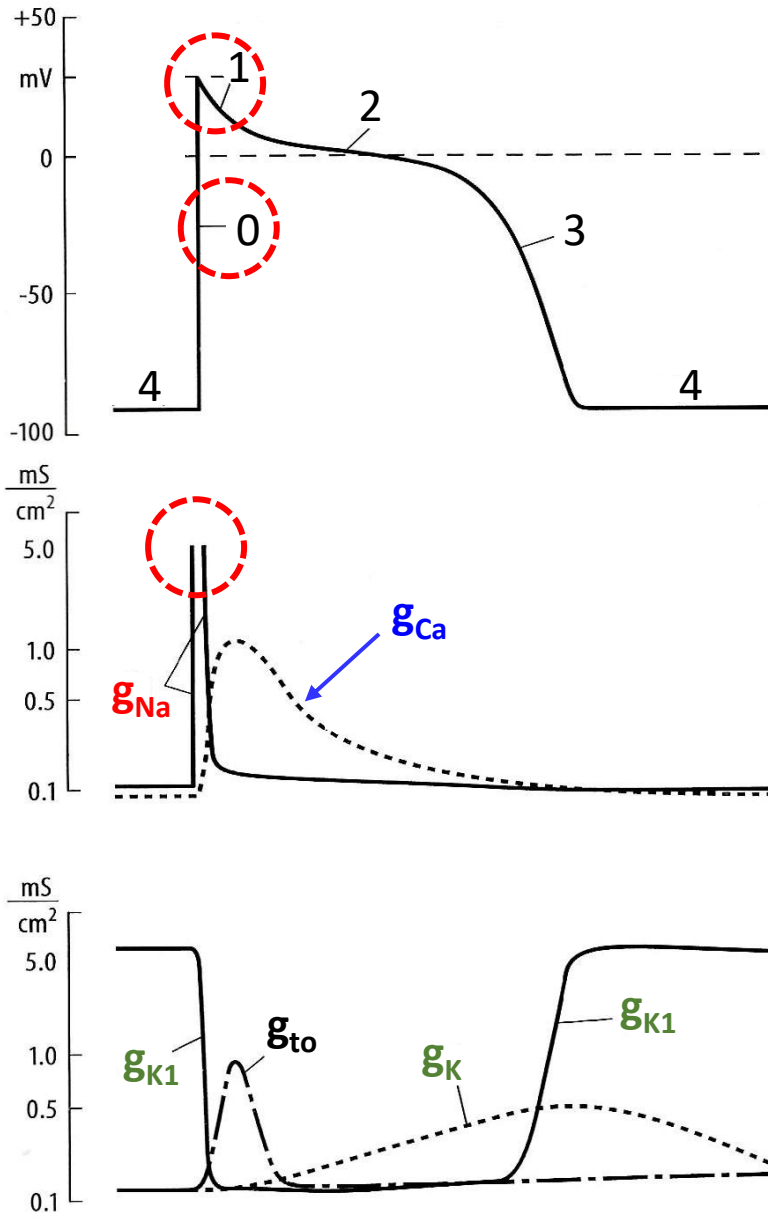
# Ionic Currents and Action Potentials

# Fast Action Potential: Ion Current Temporal Changes




- **Inward +ion flux depolarize; Outward +ion flux repolarize**
- Approximate time relations shown in diagram
- **$I_{Na}$ enters as fast Na gates open** due to AP depolarizing membrane to threshold. $I_{Na}$ ends as inactivation gates close.
- **$I_{Ca-L}$ is the long-lasting $Ca^{++}$ current** that starts during $\phi$0; it decreases progressively during $\phi$2.
- $I_{to}$ A substantial $\phi$1 is present in epicardial myocytes and Purkinje fibers. This *early partial repolarization* is due to a **transient outward $K^+$ current ($I_{to}$)**
- **Repolarization** is due to combined potassium currents consisting **of *rapidly acting delayed rectifier* ($I_{kr}$) and *slowly acting delayed rectifier* ( $I_{ks}$)** and ***reactivation* of $I_{k1}$.** Alterations in any of these effects action potential duration (**APD**) and QT interval.
- **$I_{K1}$** (***inward rectifying current***) together with depolarizing $Ca^{++}$ and $Na^+$ currents determine $\phi$4. $I_{K1}$ turns off with depolarization (- channel conductance) and reactivates during repolarization aiding repolarization.
- **$I_{NCX}$ [**$Na^+$-$Ca^{++}$ exchanger current **(3$Na^+$ for 1 $Ca^{++}$)].** Phase 0 rapid inward $I_{Na}$ causes transient reversal in NCX (inward flux of $Ca^{++}$ & efflux of $Na^+$). Then NCX **shifts back to forward** mode as internal $Ca^{++}$ accumulates due to $Ca^{++}$ entry via L-type channels and helps maintain $\phi$2 duration

# Fast Action Potential: Channel Conductance Changes



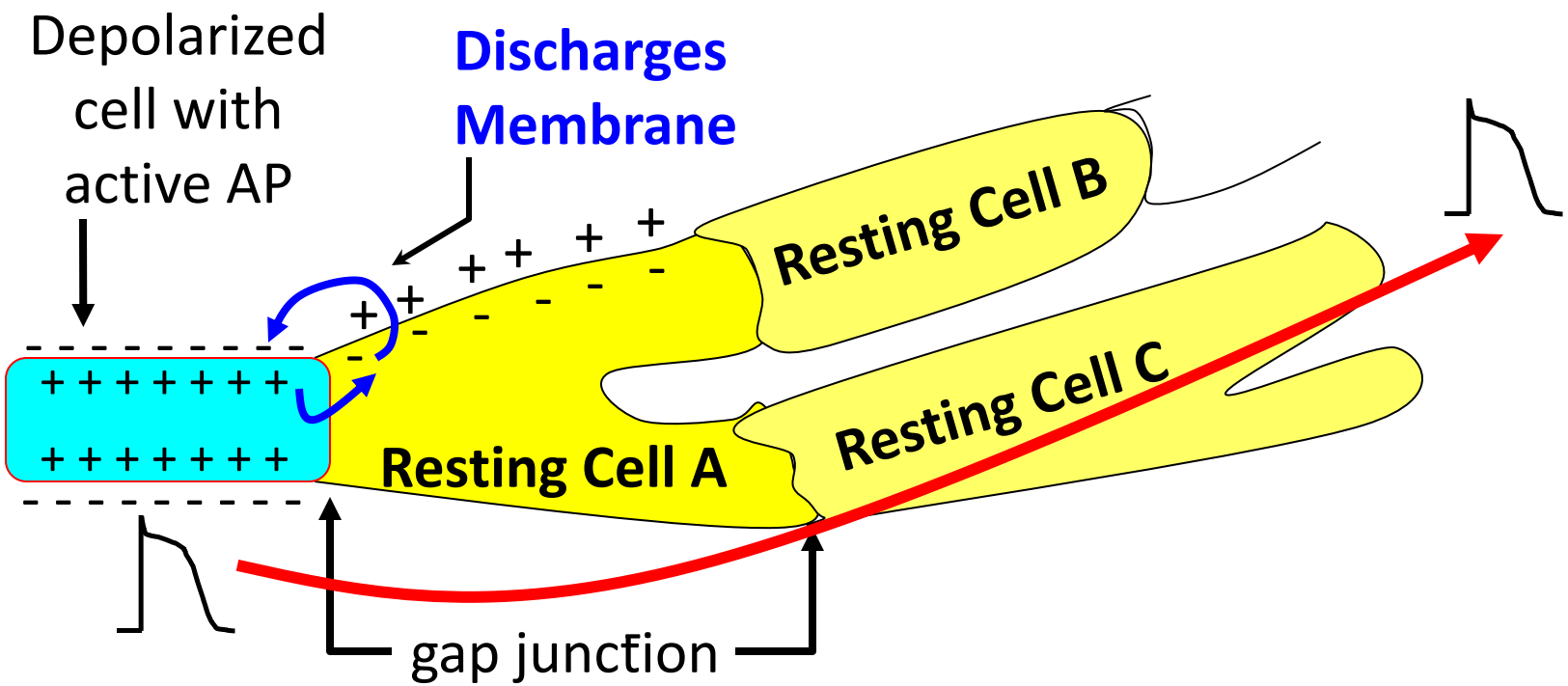

- Channel ion currents ($I_{CH}$) depend on both the electromotive chemical difference **($V_m$ - $E_i$)** and ion channel conductance ($g_i$) as **$I_{CH} = g_i \times (V_m - E_i)$**

$E_i$ is the equilibrium potential for ion "i" e.g. $Na^+$

- (1) The large transient influx of $Na^+$ through the fast Na+ channels is due to the *large increase in $g_{Na}$ accompanying phase 0 depolarization*
- (2) The activation of and peaking of $Ca^{++}$ influx during phase 2 is due to the rise then fall in $g_{Ca}$
- (3) The early partial repolarization of phase 1 is due to the rise then fall of the conductance of the $K^+$ channel carrying this current
- (4) $I_{K1}$ turn off, then rise due to $g_{K1}$ decrease with depolarization and return during repolarization
- (5) Full repolarization due to increase in $g_K$ of the slow and rapid $K^+$ channels

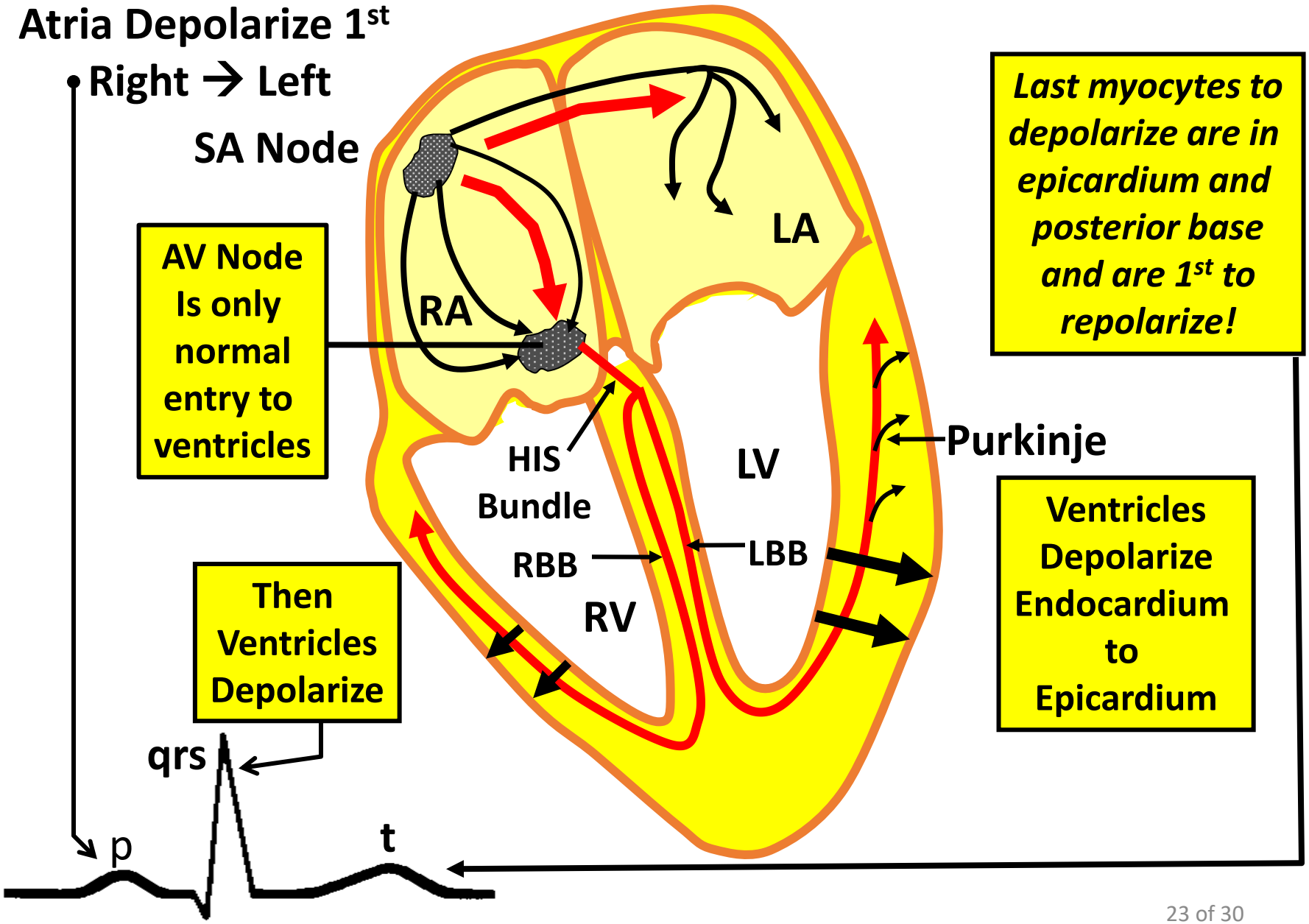
# Conduction Sequences Depolarization-Repolarization

# Conduction Process

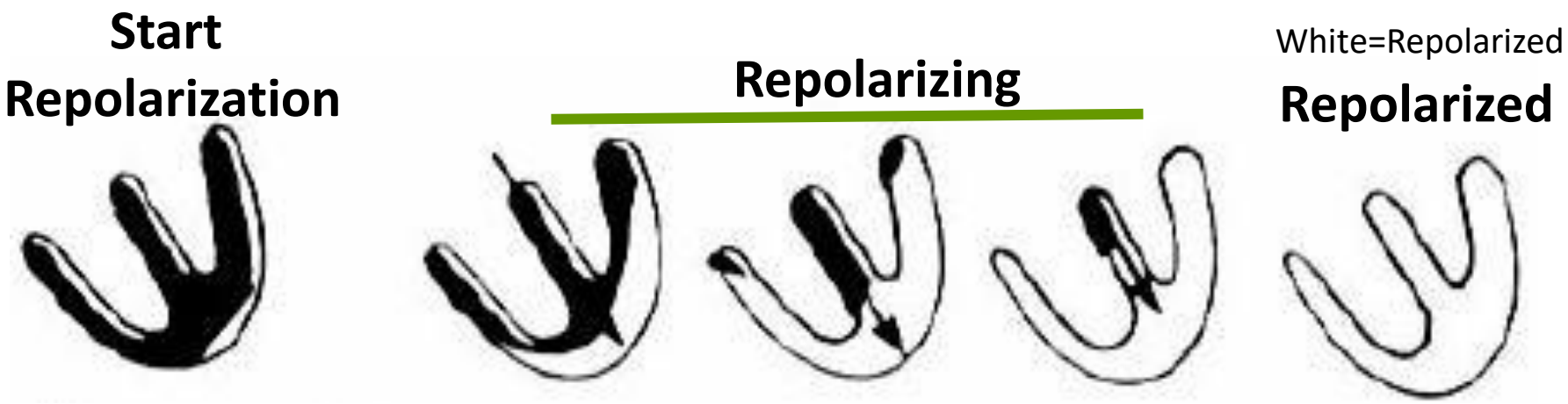



*When Cell A membrane reaches threshold it generates an AP that serves to discharge cells B & C bringing them to threshold resulting in conduction of an AP throughout*

# Depolarizing Sequence



# Repolarization Sequence



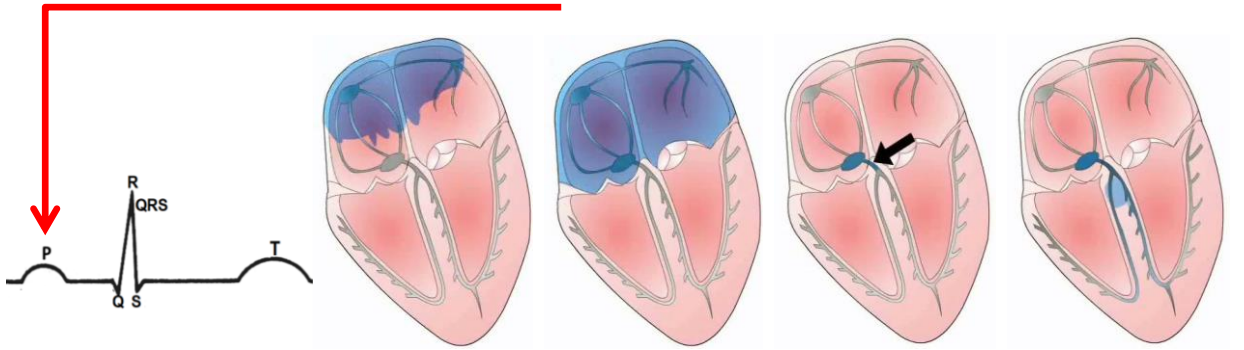

- Repolarization in reverse order to which myocytes depolarize
- Why?

→ Myocytes in epicardium & posterior base have shorter APD than AP in endocardium and apex

BECAUSE of :

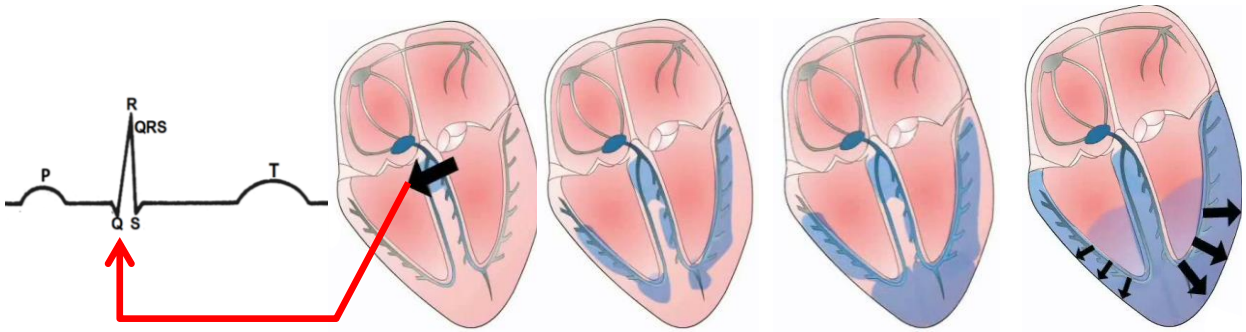
Different $K^+$ channel features → determinant of AP duration

# Depolarization-Repolarization-EKG Relationship

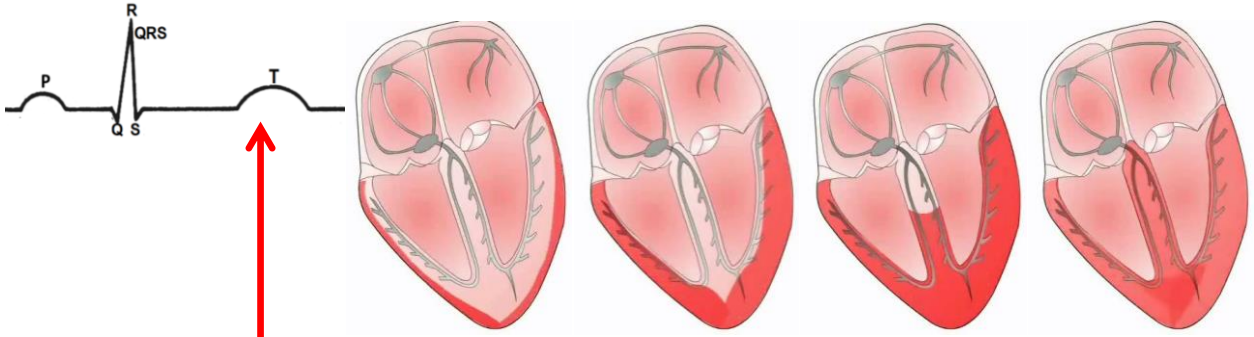



Atrial Depolarization Thru AV → His → Septum

Depolarization is a "conduction" Process




Ventricular Depolarization

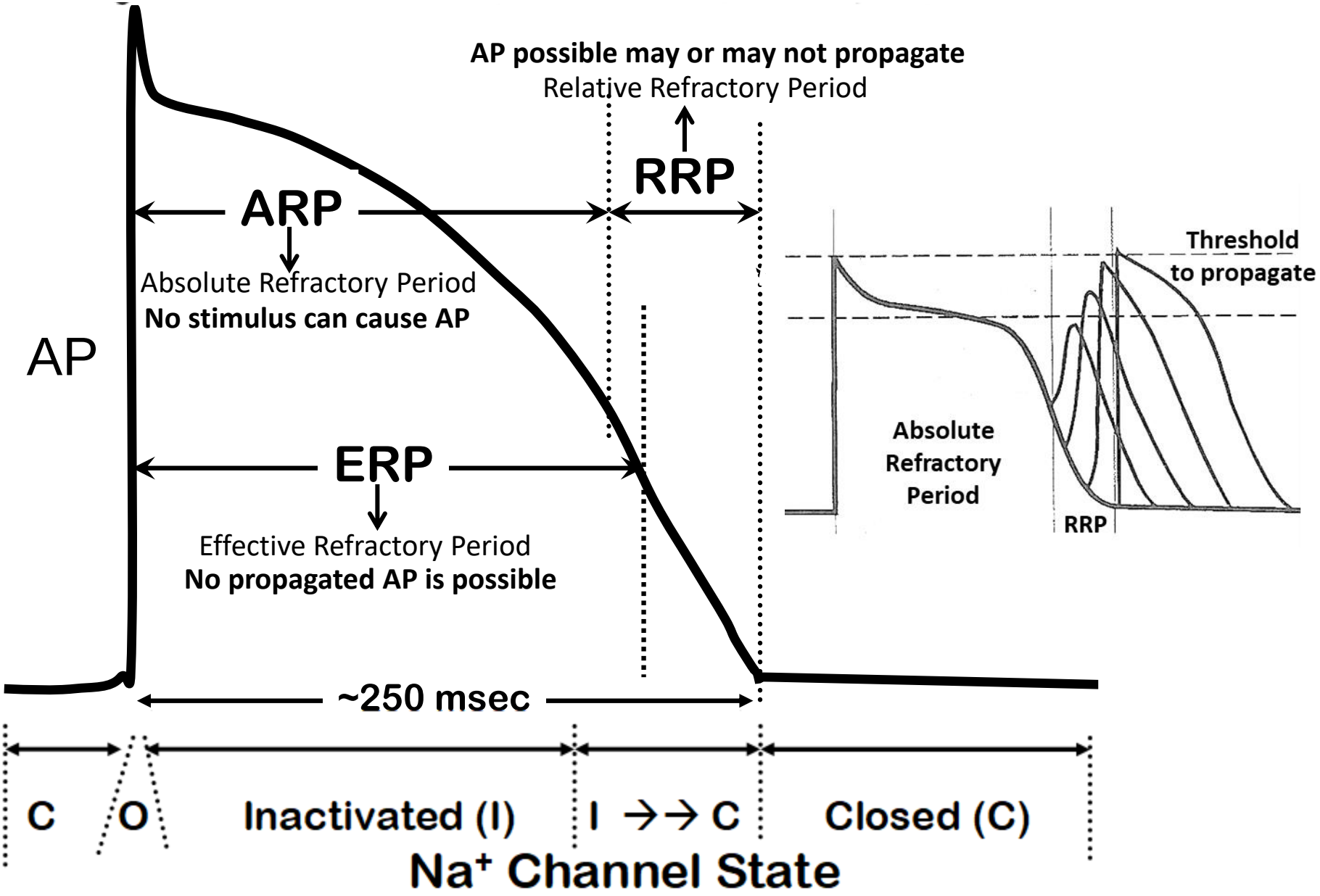



Ventricular Repolarization

Repolarization is a "Timing" Process

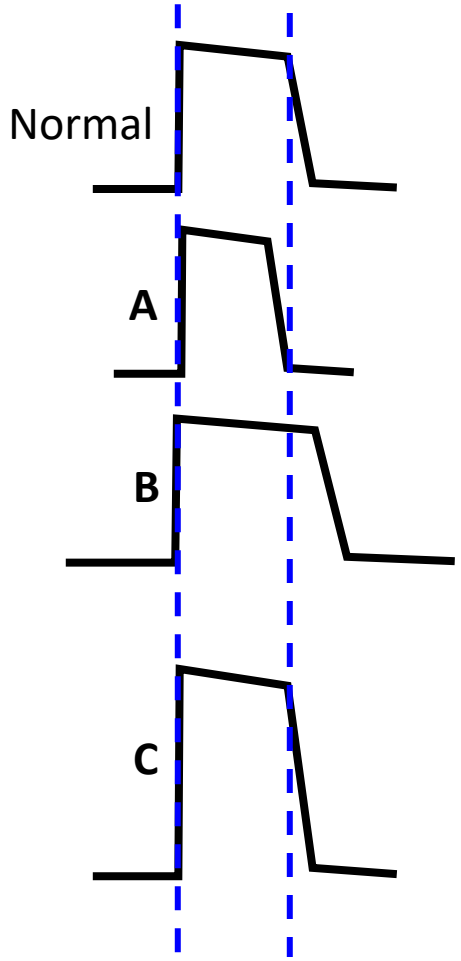
# Refractory Periods

# Refractory Periods and $Na^+$ Channel States



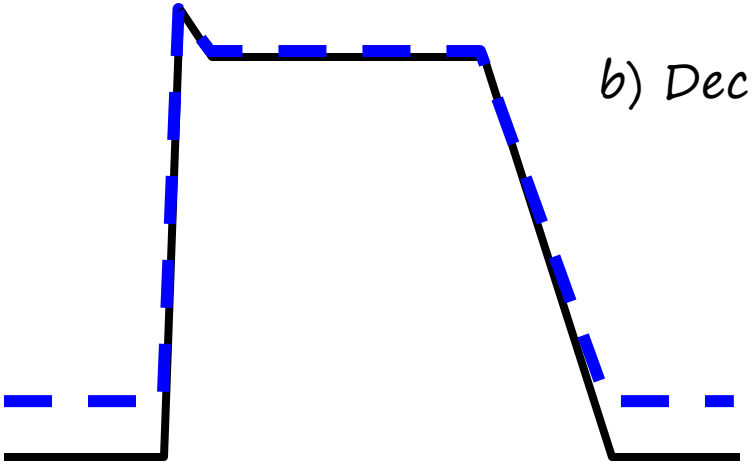
# Interactive Question

*Bob has been experiencing an irregular heart rhythm. He has been prescribed an antiarrhythmic drug (Amiodarone) that is a partial $I_{Kr}$ channel blocker. Which of the following (A, B or C) shows the most likely effect of the drug? 20s*



# Interactive Question

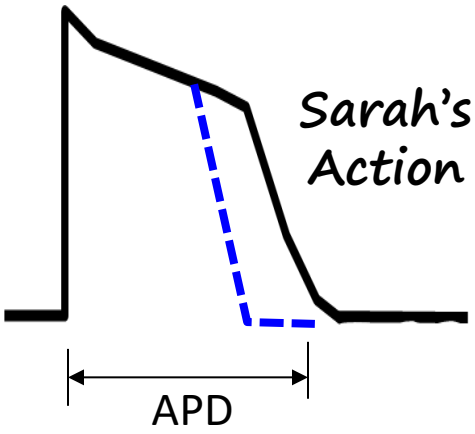
*Considering only the phase 4 effects, which blood concentration change could cause the change indicated by the blue dashed Purkinje action potential? 30 sec!*



a) Increased external potassium – **hyperkalemia**

b) Decreased external sodium- **hyponatremia**

| Normal reference values |
| --- |
| $Na^+$ blood 135-145 mEq/L |
| $K^+$ blood 3.5 – 5.0 mEq/L |




Action Potential Duration

What do you think would happen to Sarah's APD if she took a cardiac calcium channel blocking agent?
→ 15 sec!

A. Increase

B. Decrease

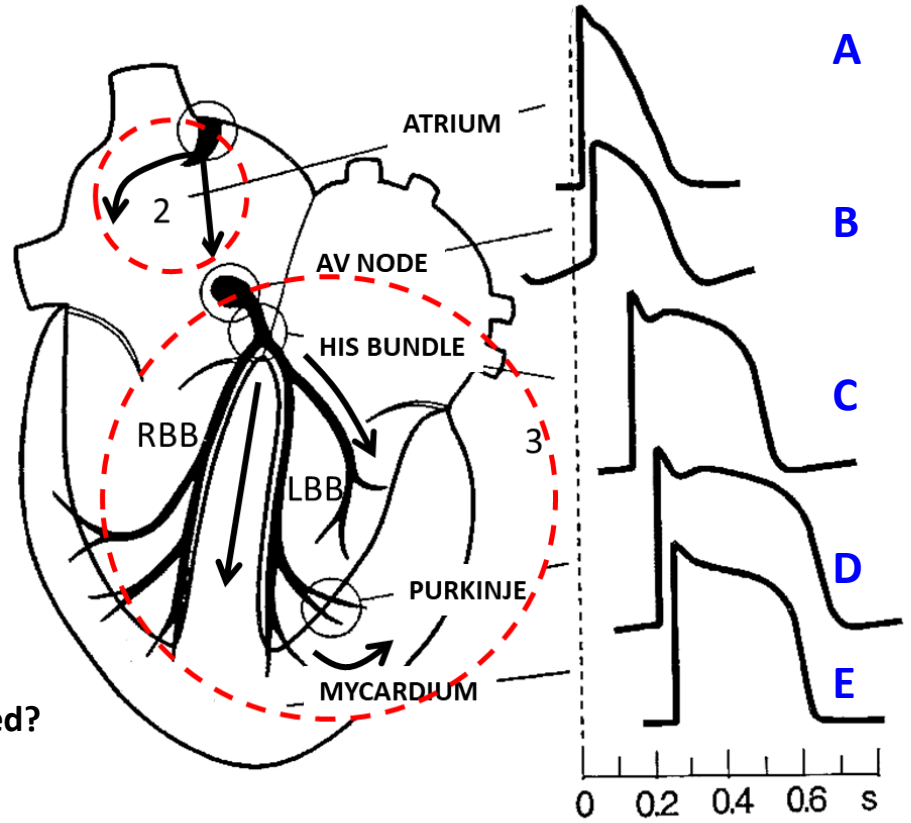
C. Essentially no change

D. Insufficient to determine

# Interactive Question

**EKG 1. Normal**

**EKG 2. Not Normal**




**If EKG 2 is observed, which AP would not be observed?**

**A**
**B**
**C**
**D**
**E**

# End CV Physiology Lecture 1