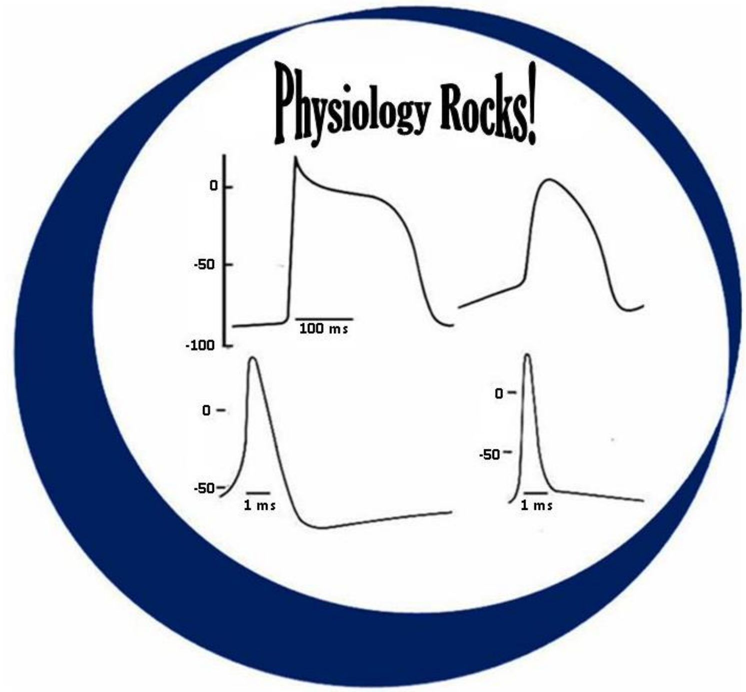
Lecture 1
Cardiac Electrical Activity



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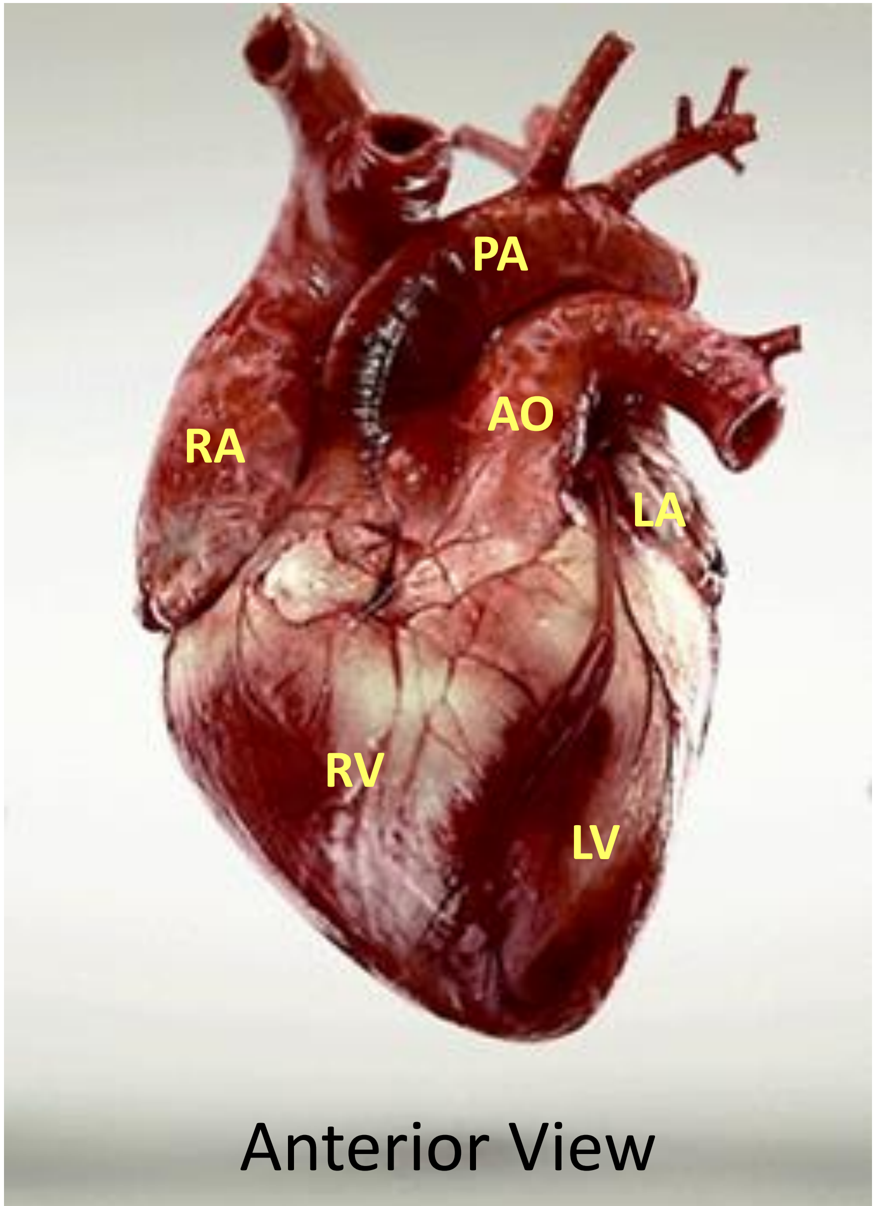
Topics

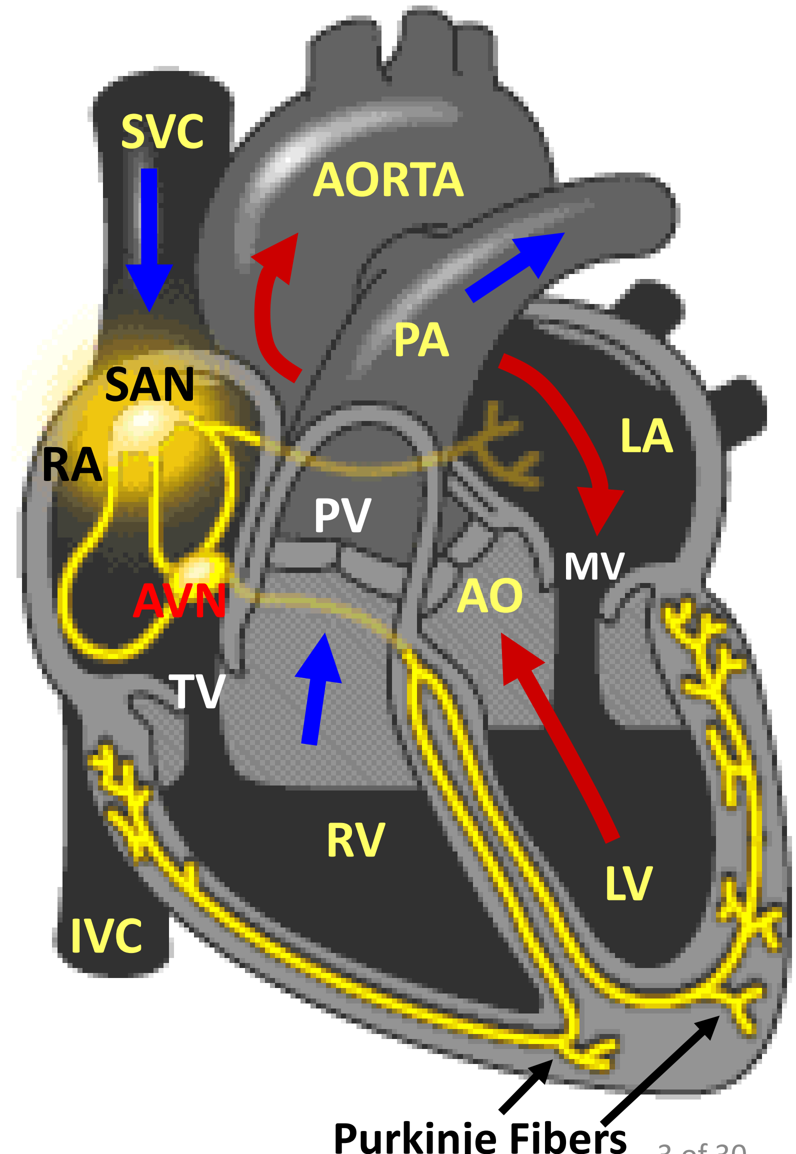
- Cardiac functional anatomy and function
- Cardiac electrical patterns and action potential timing
- Fast response action potential features
- Membrane ionic channels and currents
- Temporal aspects
- Action potential conduction patterns

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

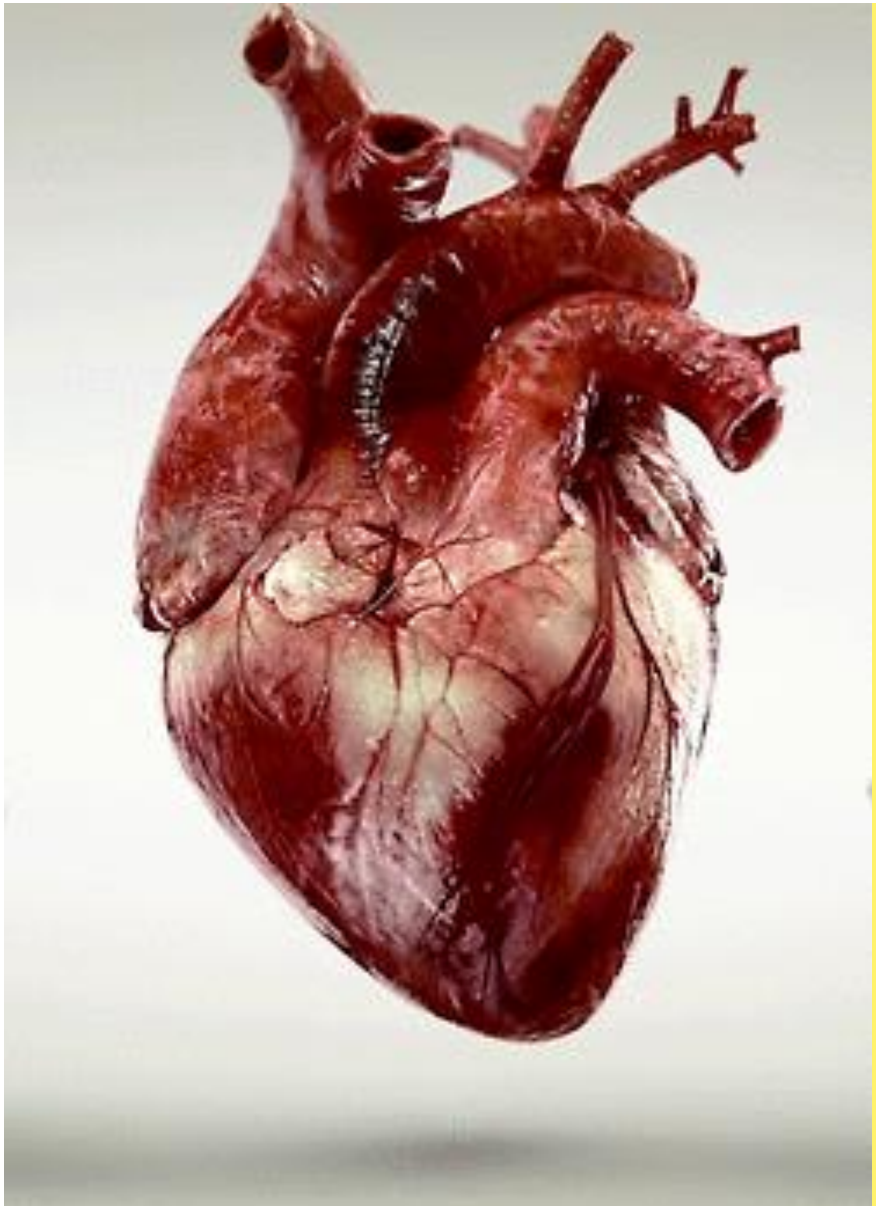
The Beating Heart: Functional Anatomy

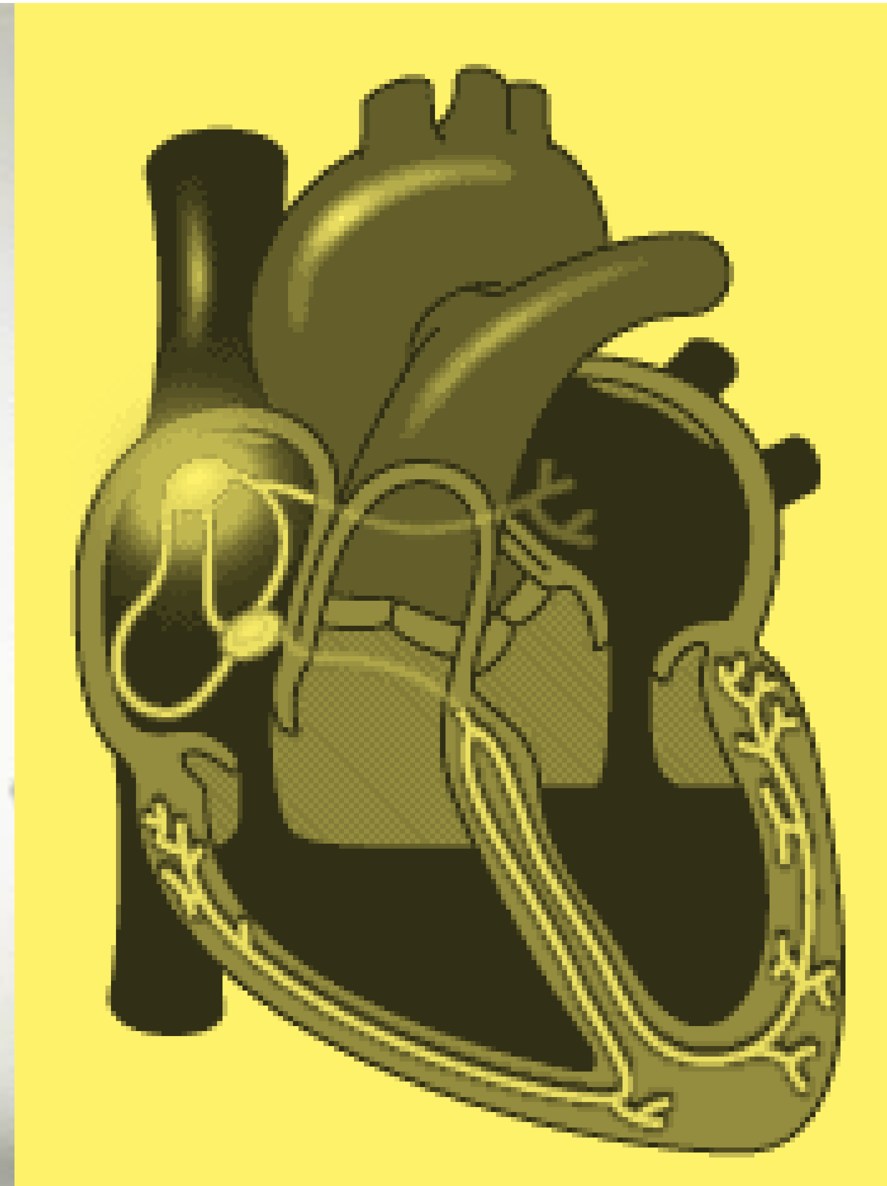


Anterior View



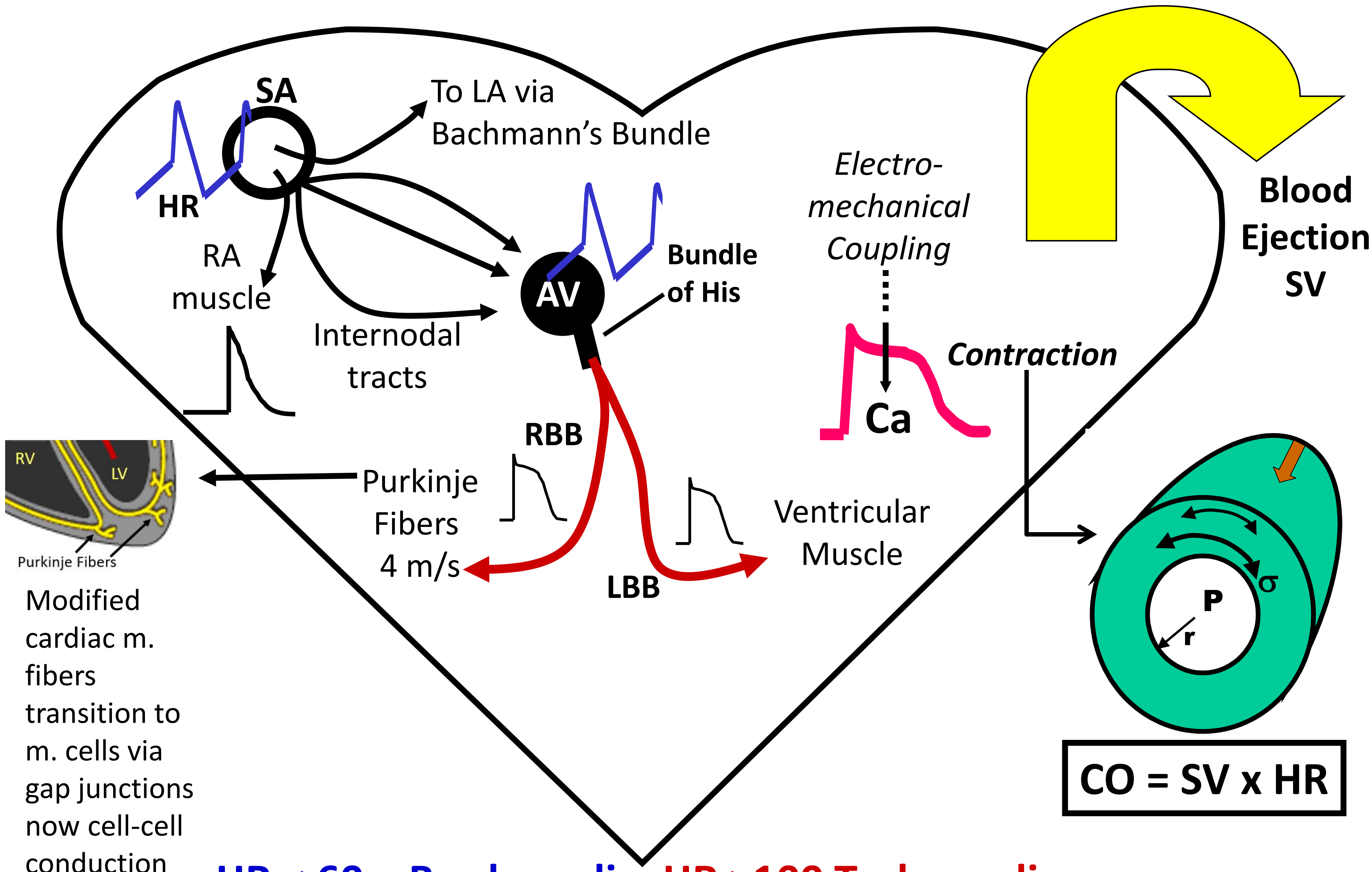
The Beating Heart: Functional ACTIONS





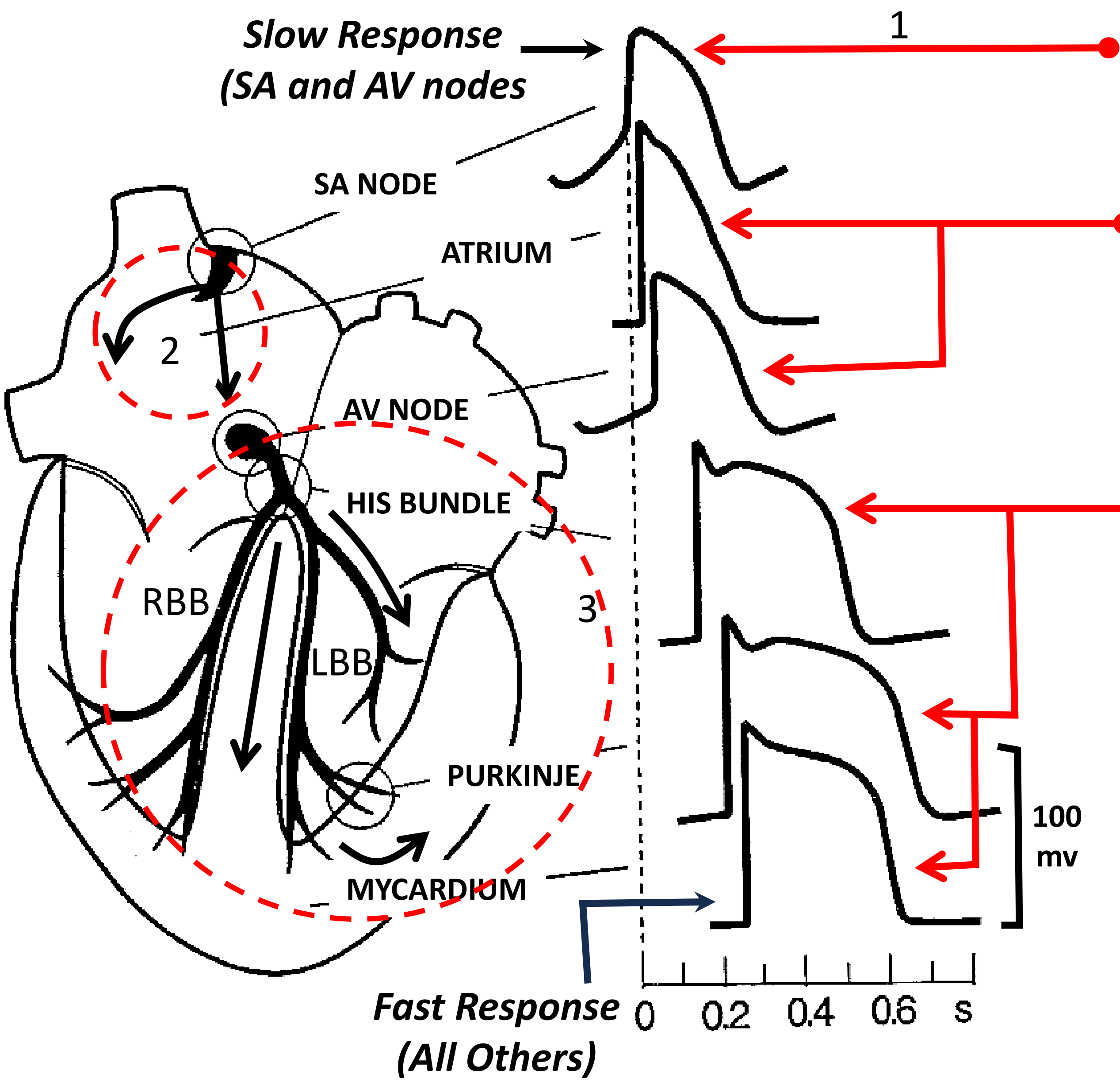
Cardiac Electrical Overview

Normal Cardiac Conduction Pathways and Effects



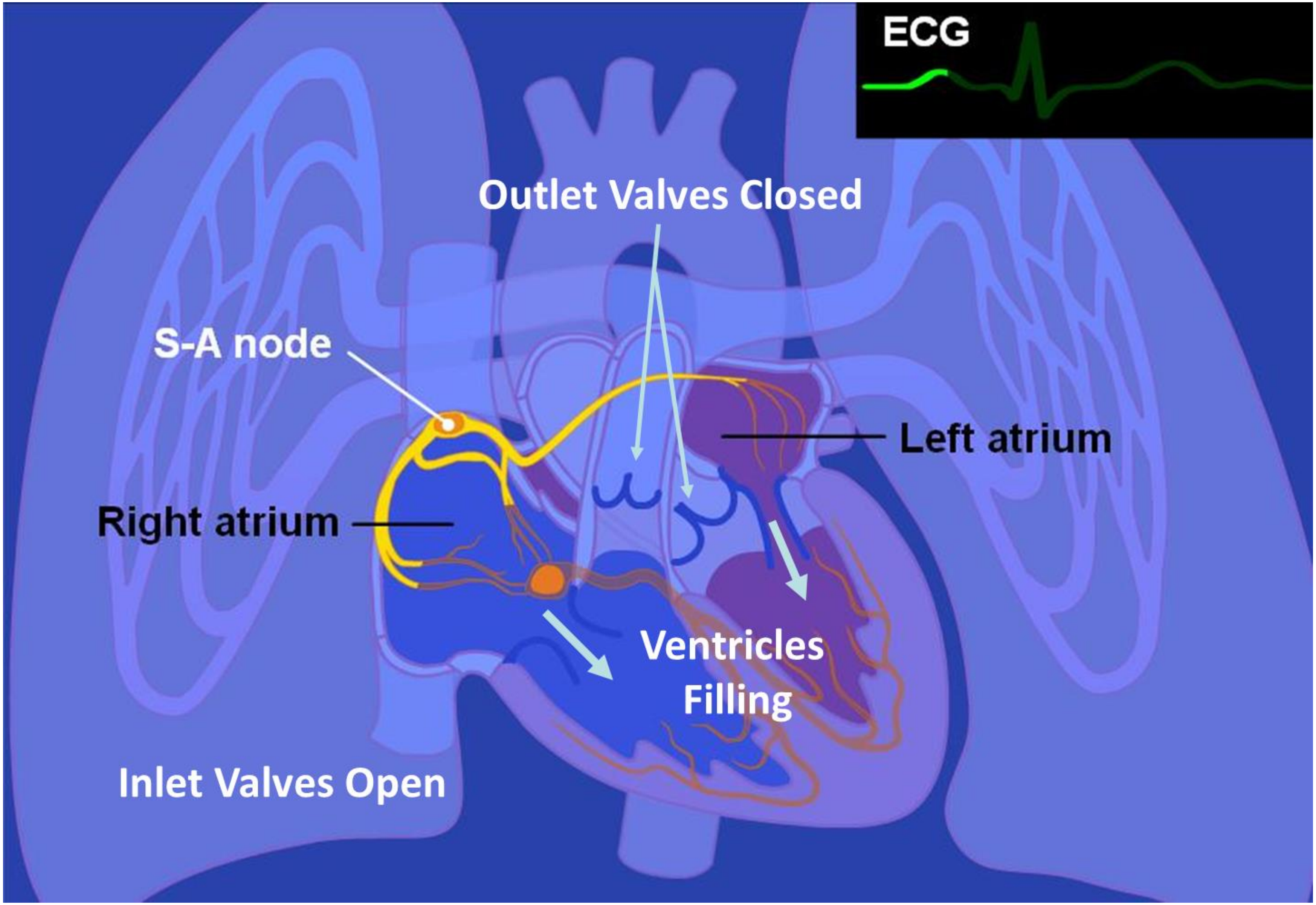
HR < 60 = Bradycardia; HR >100 Tachycardia

Cardiac Action Potential Patterns and Timing

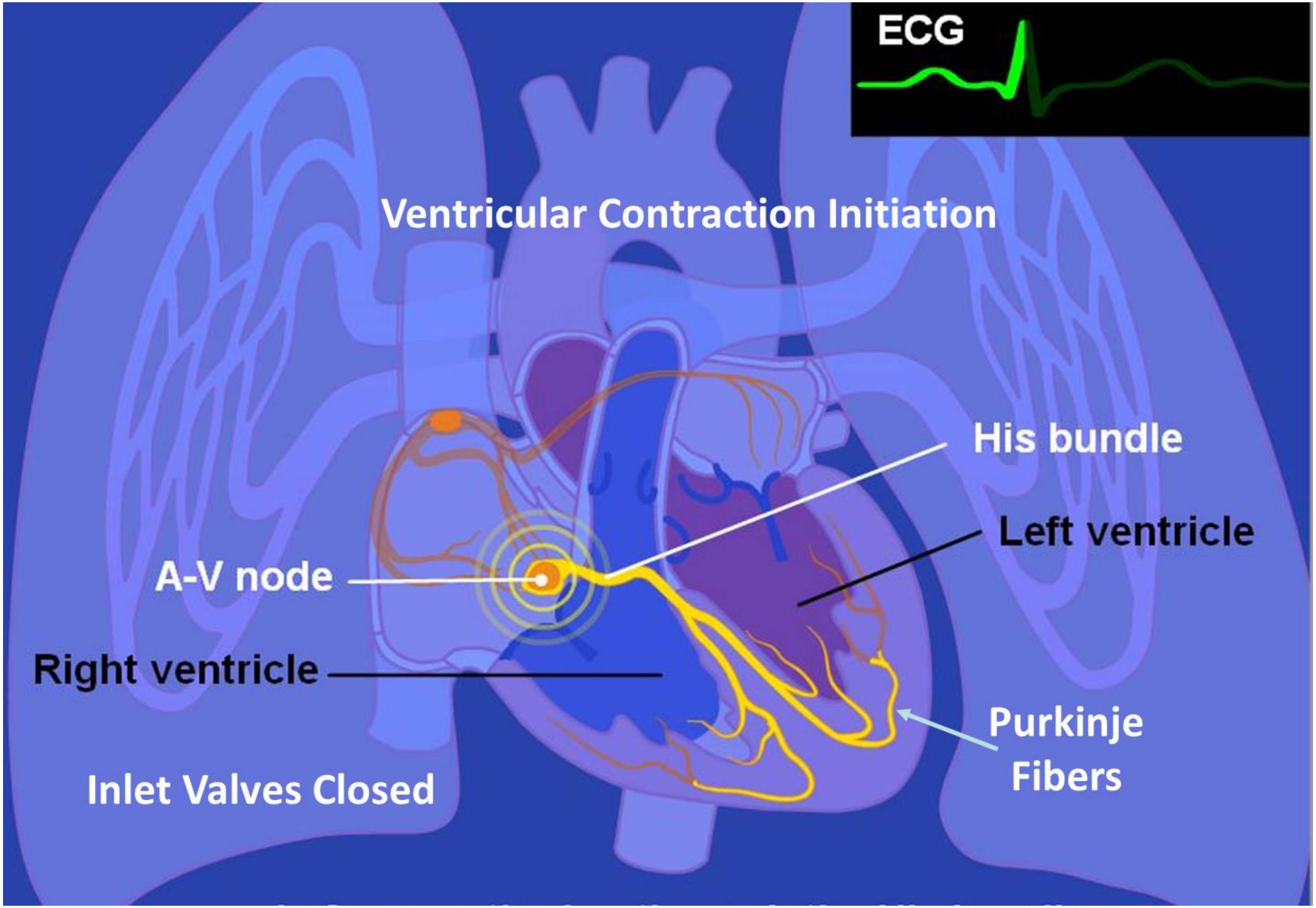


- (1) SAN depolarization is spontaneous
- (2) Action potential (AP) is transmitted to atria and AVN Atrial Contraction
- (3) After short delay AP exits the AVN; passes to His bundle then right bundle branch (RBB) and left bundle branches (LBB) ending in Purkinje fibers → highest AP conduction speed
- (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

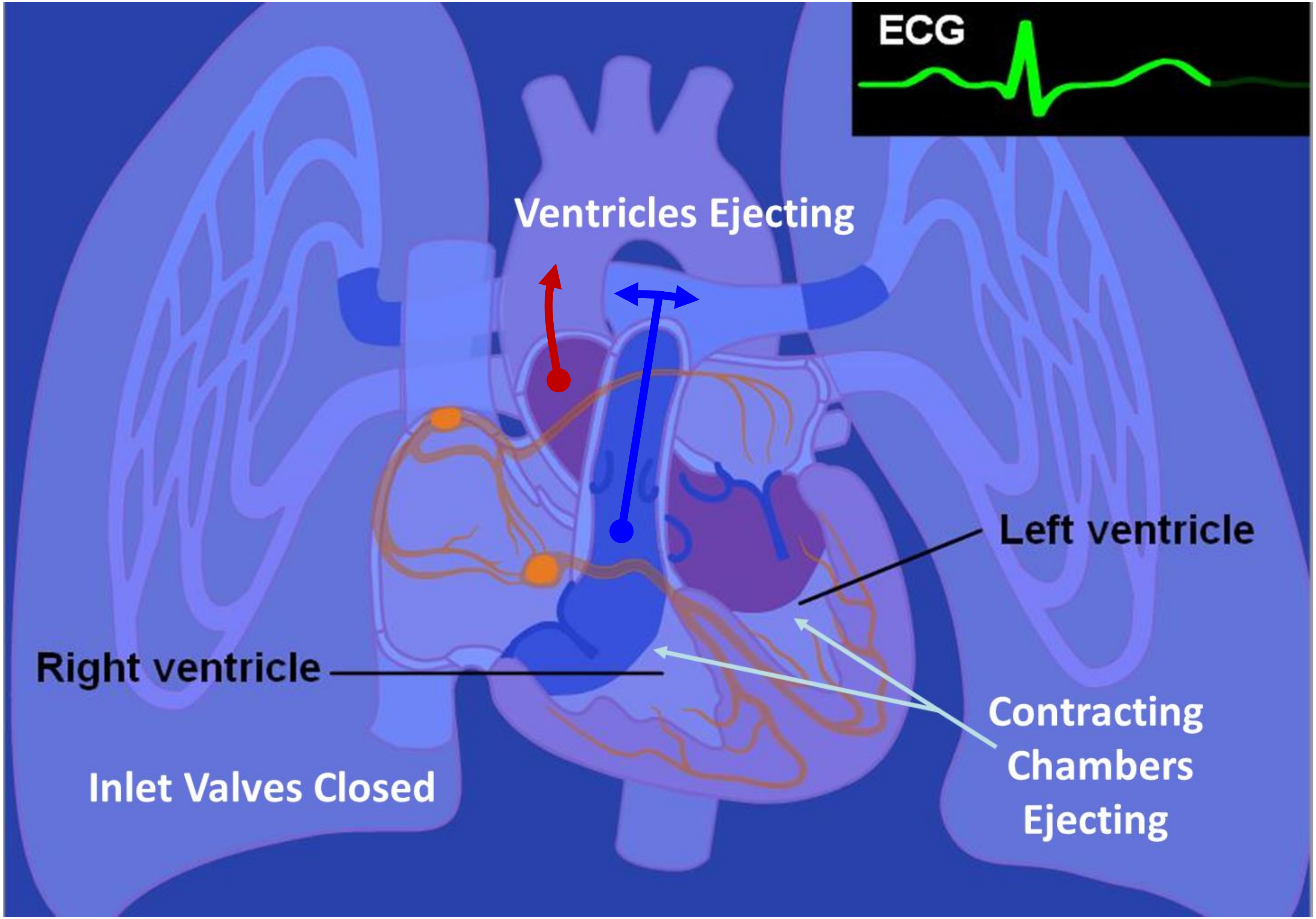
Electro-Mechanical Coupling



Electro-Mechanical Coupling

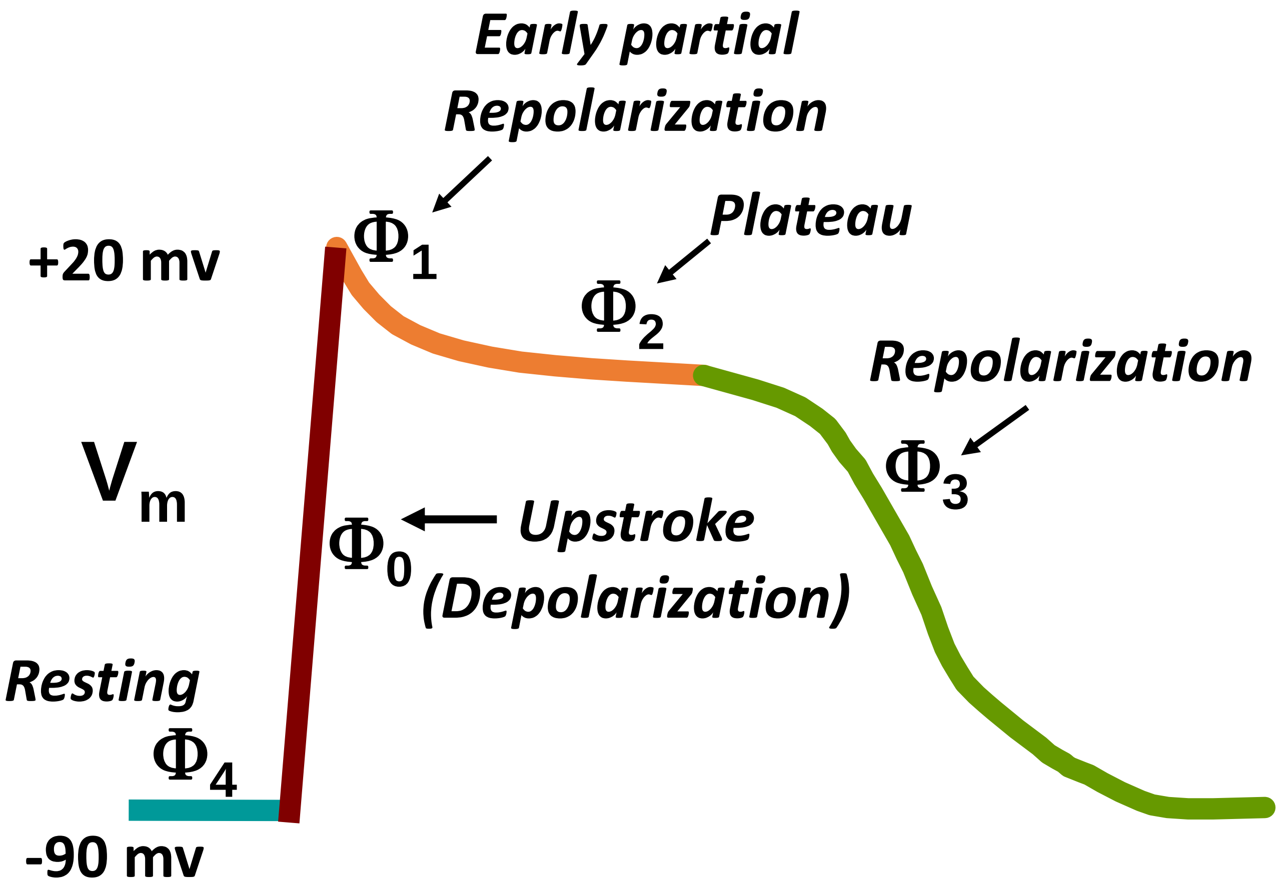


Electro-Mechanical Coupling



Closer Look at Action Potential Details

Fast Response Cardiac Action Potential: Definitions



Cardiac Ion Channels and Currents

Na^+

- Fast Response
  - I_{Na}
- Slow Response
  - $I_f = I_h$

Also, Pacemaker Current = I_h

Ca^{++}

- L (Long lasting)
- T (Transient)

K^+

- K_s
- K_r
- k_{ur}

"Delayed outward rectifier"
Slow-Rapid-Ultrarapid
Combined = I_K
Repolarization

- K_1
- K_{Ach}
- K_{ATP}

"Inward rectifier"

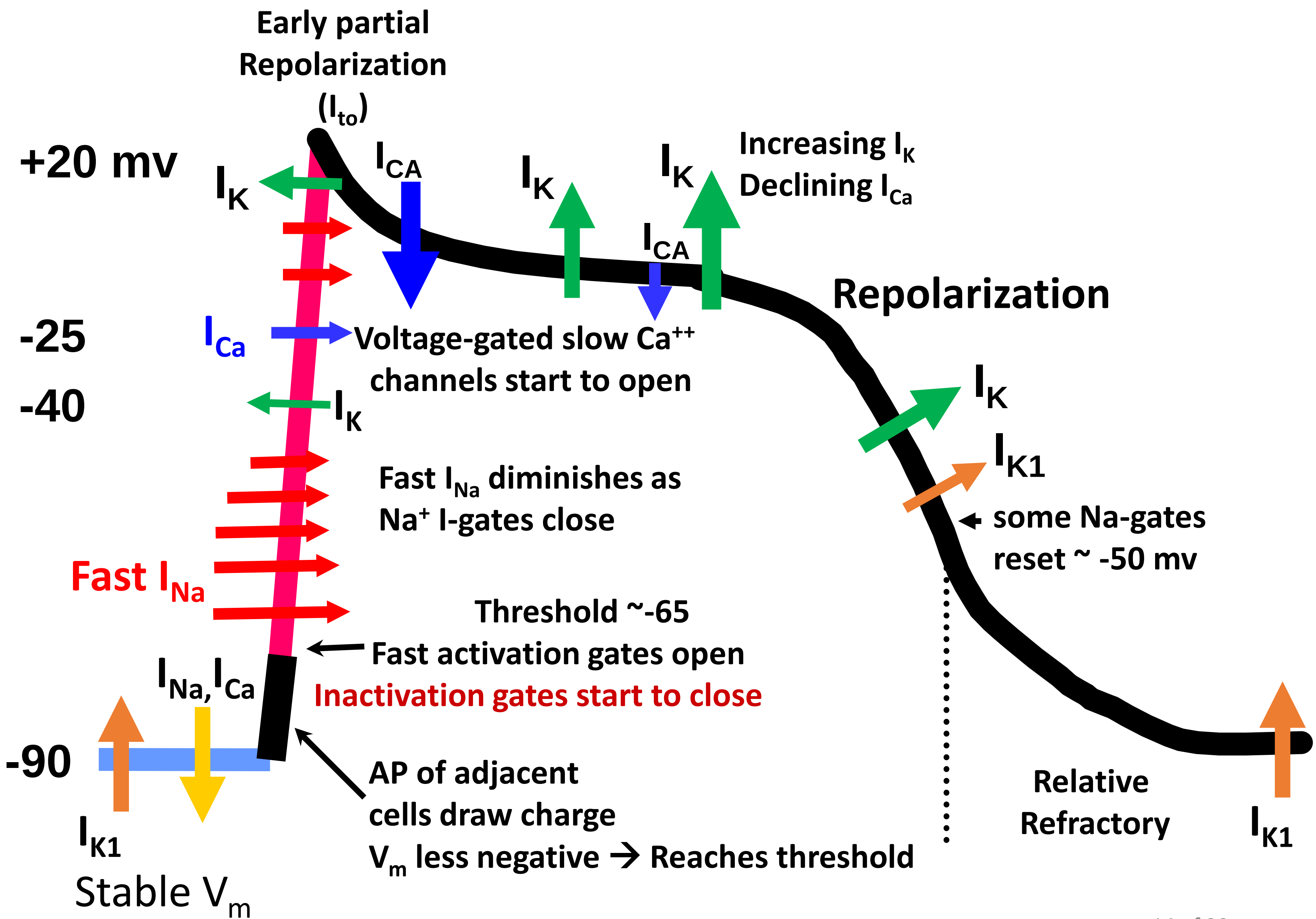
- K_{to} Transient outward

Inward current → Depolarize

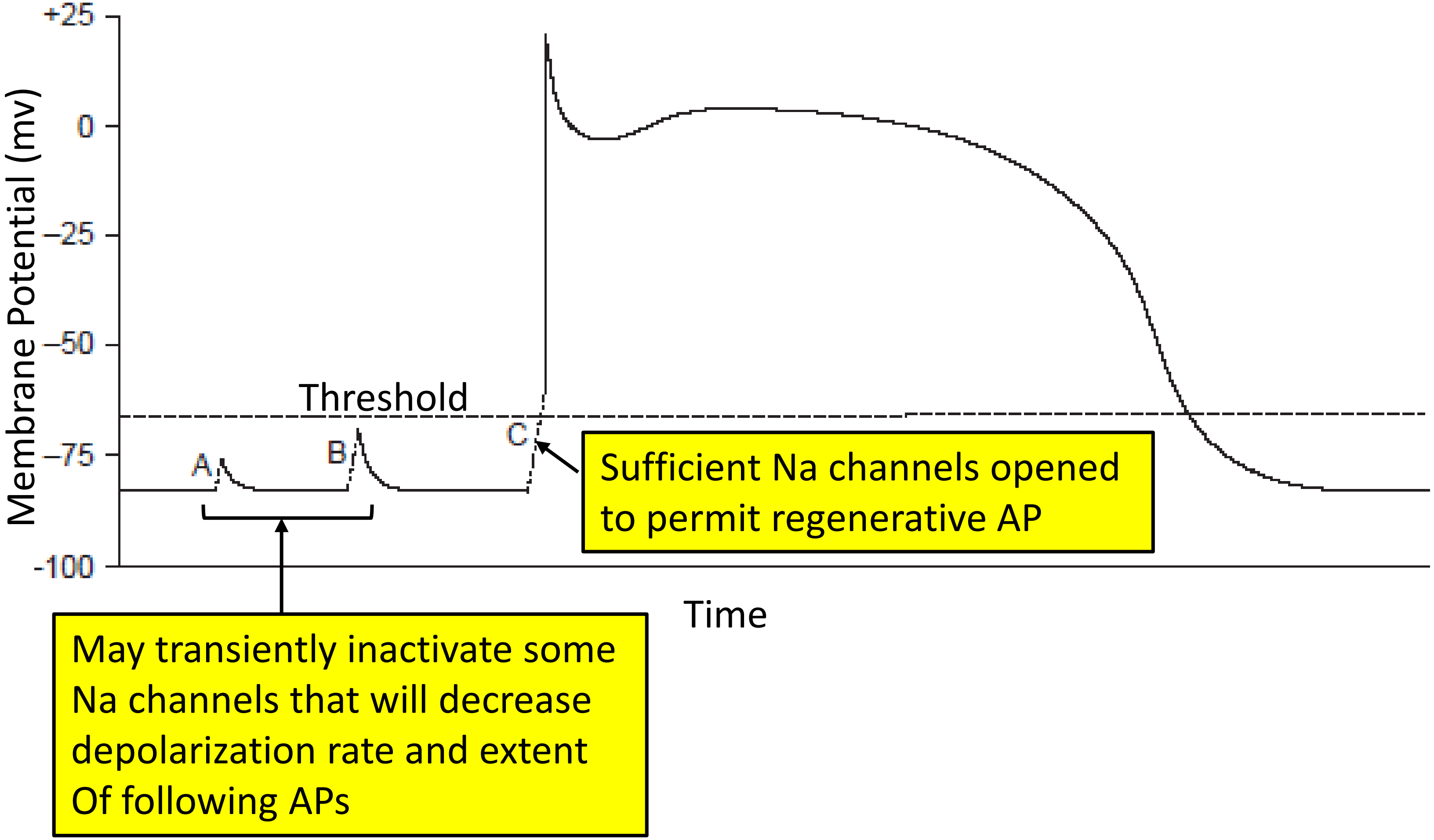
Outward current → Repolarize

- **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

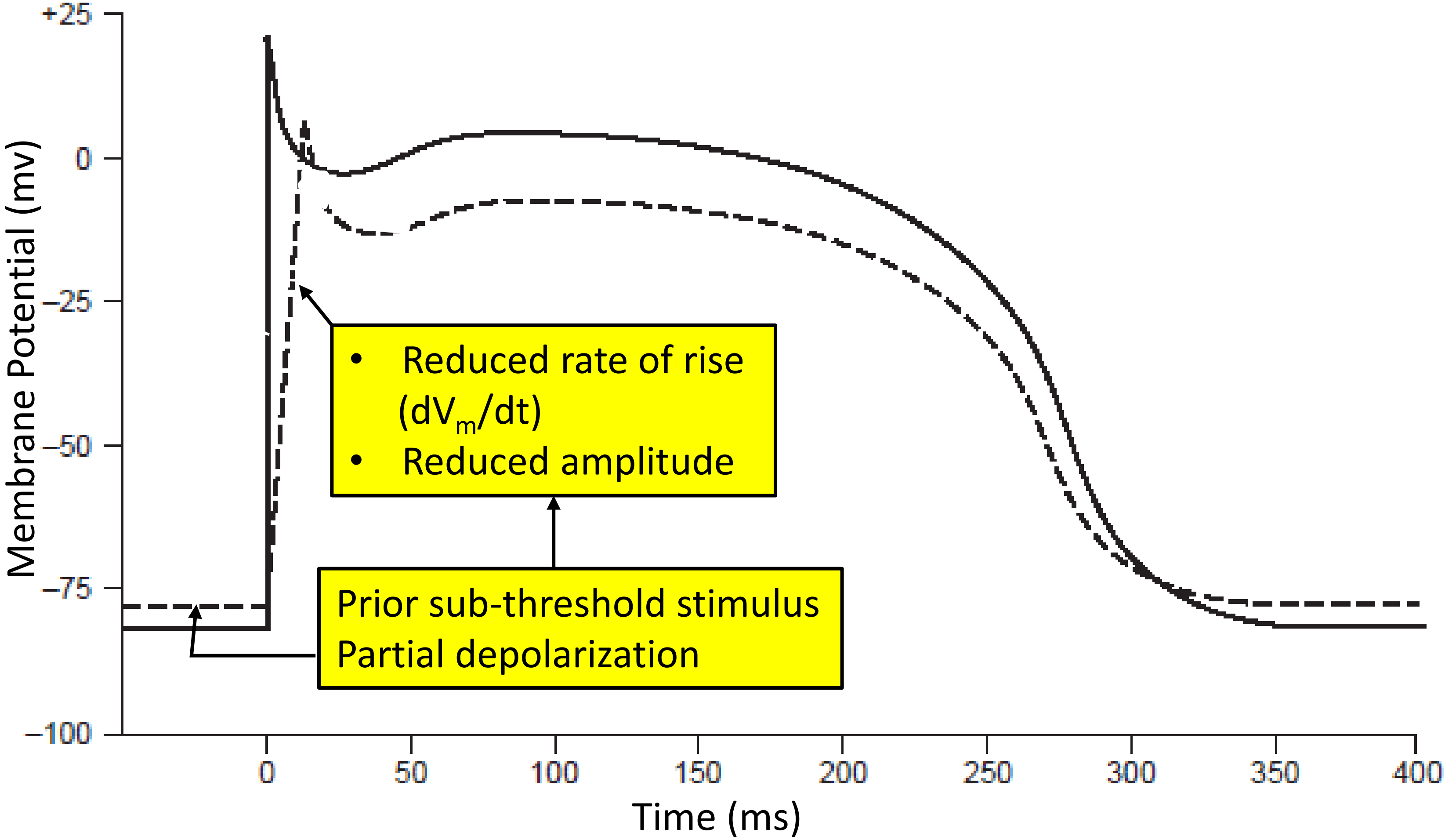
Fast Response Ionic Currents: Descriptive Overview



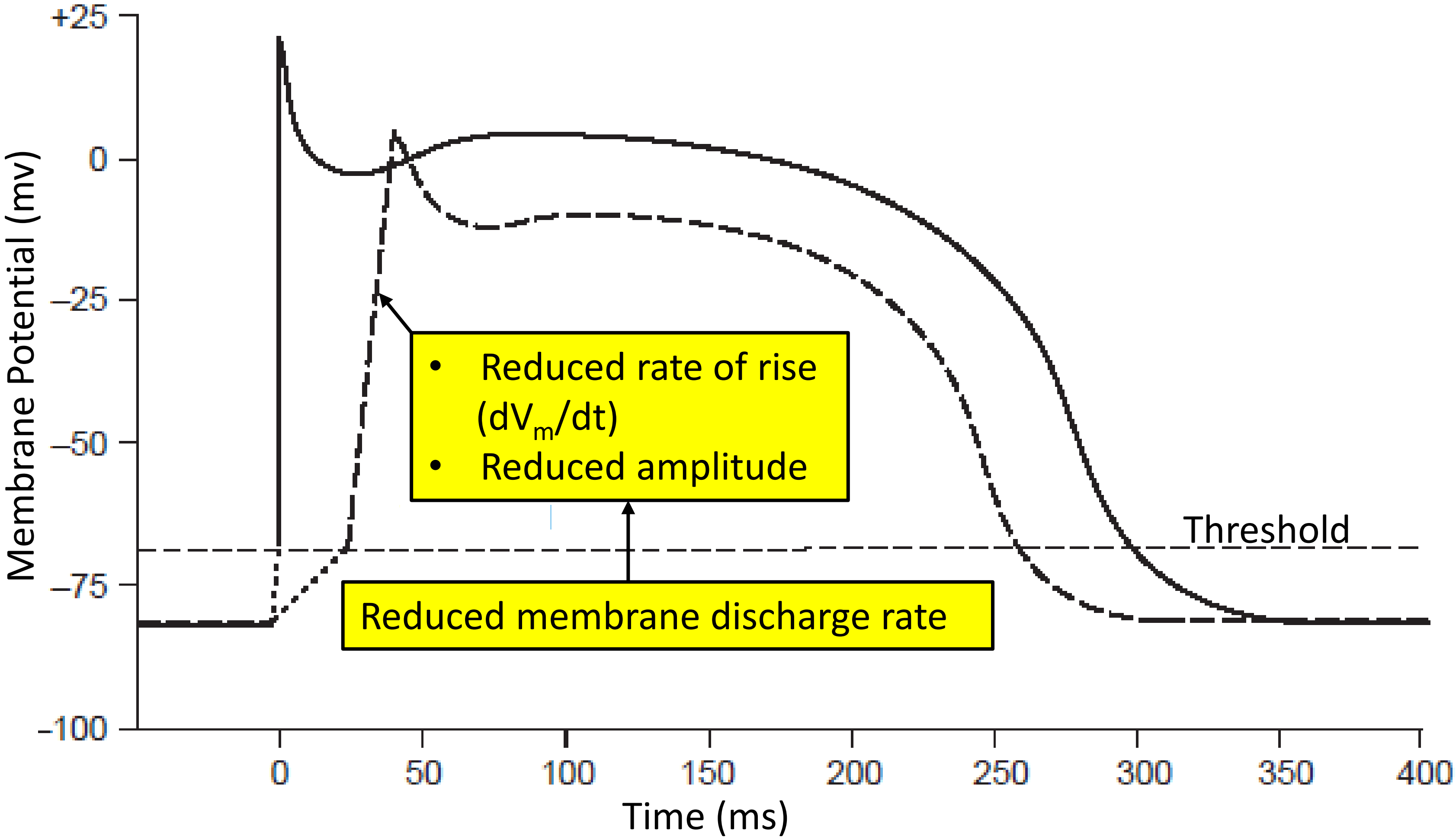
Threshold


+25
0
−25
−50
−75
-100
Membrane Potential (mv)
Threshold
A
B
C
Sufficient Na channels opened to permit regenerative AP
Time
May transiently inactivate some Na channels that will decrease depolarization rate and extent Of following APs

Partial Depolarization Effect on AP

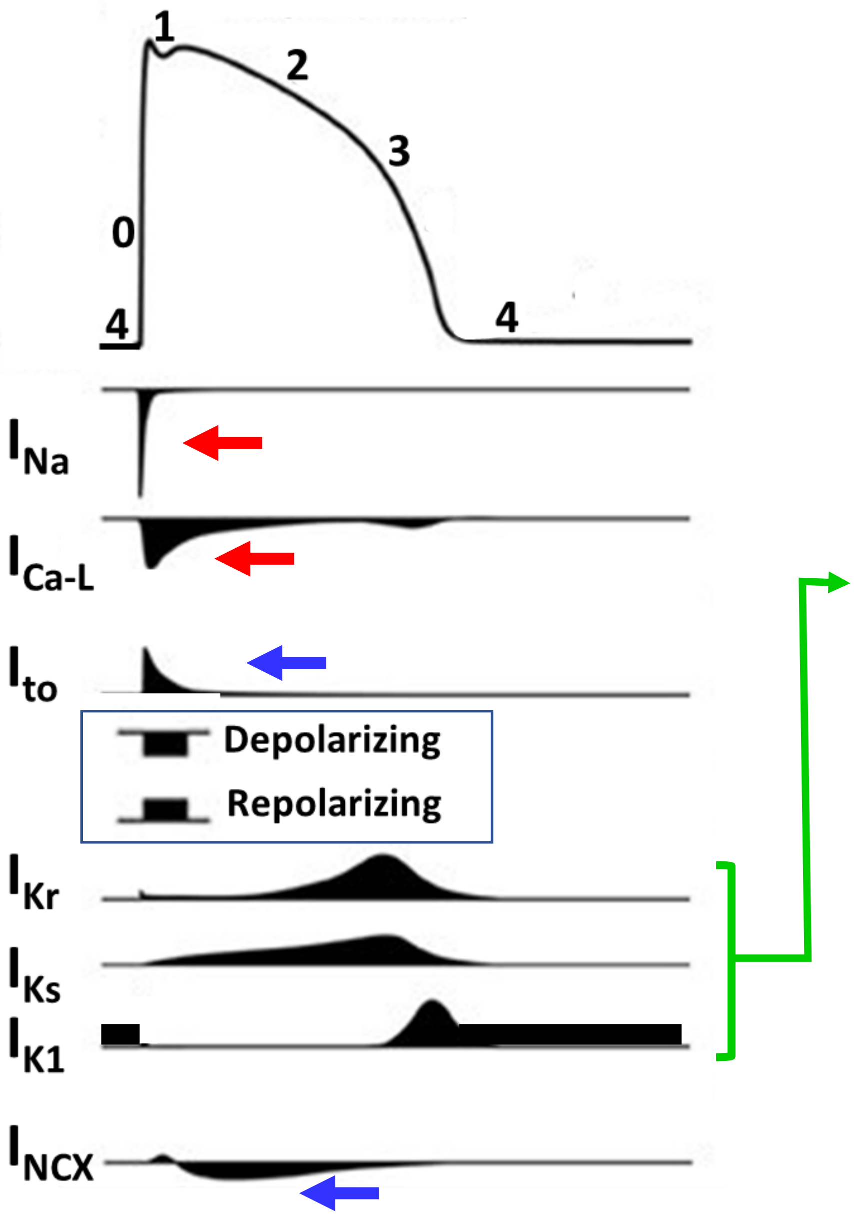


Reduced Threshold Approach Rate Effects on AP



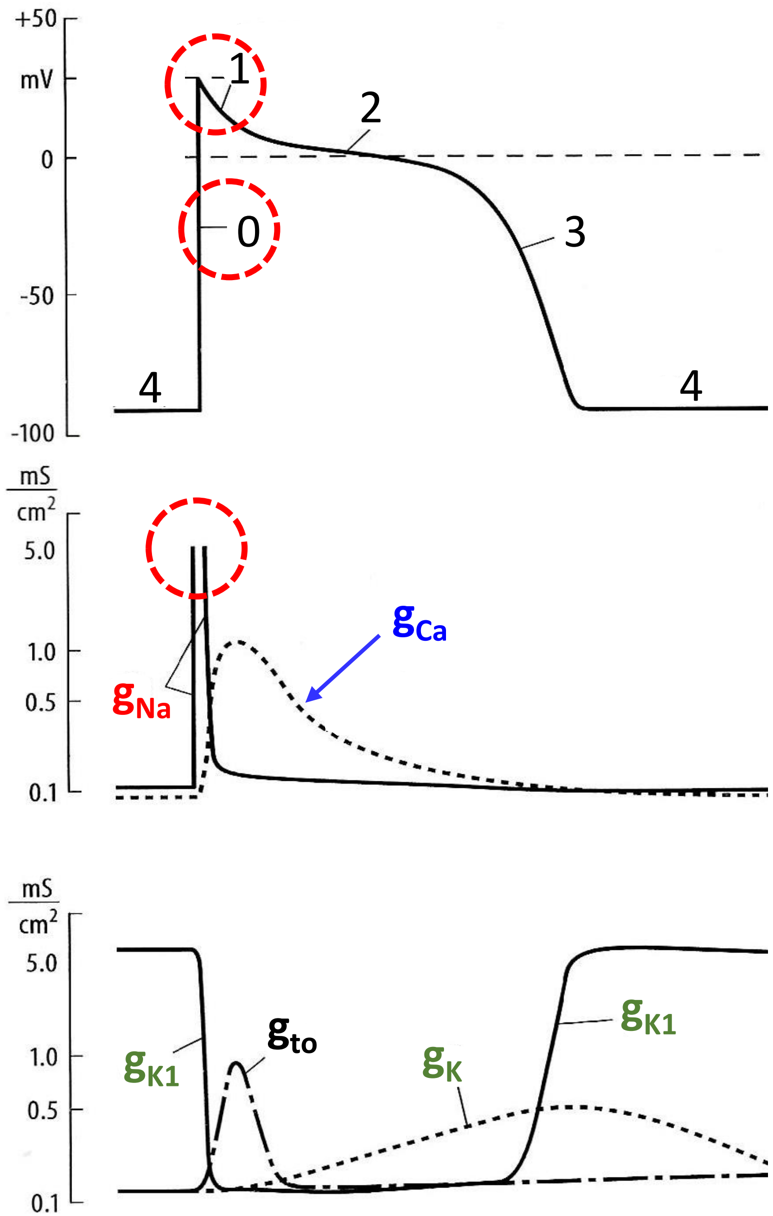
Ionic Currents and Action Potentials

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 ϕ0; it decreases progressively during ϕ2.
- I_{to} A substantial ϕ1 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 ϕ4. I_{K1} turns off with depolarization (- channel conductance) and reactivates during repolarization aiding repolarization.
- **I_{NCX}** [Na^+-Ca^{++} exchanger current **(3Na^+ 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 ϕ2 duration

Fast Action Potential: Channel Conductance Changes



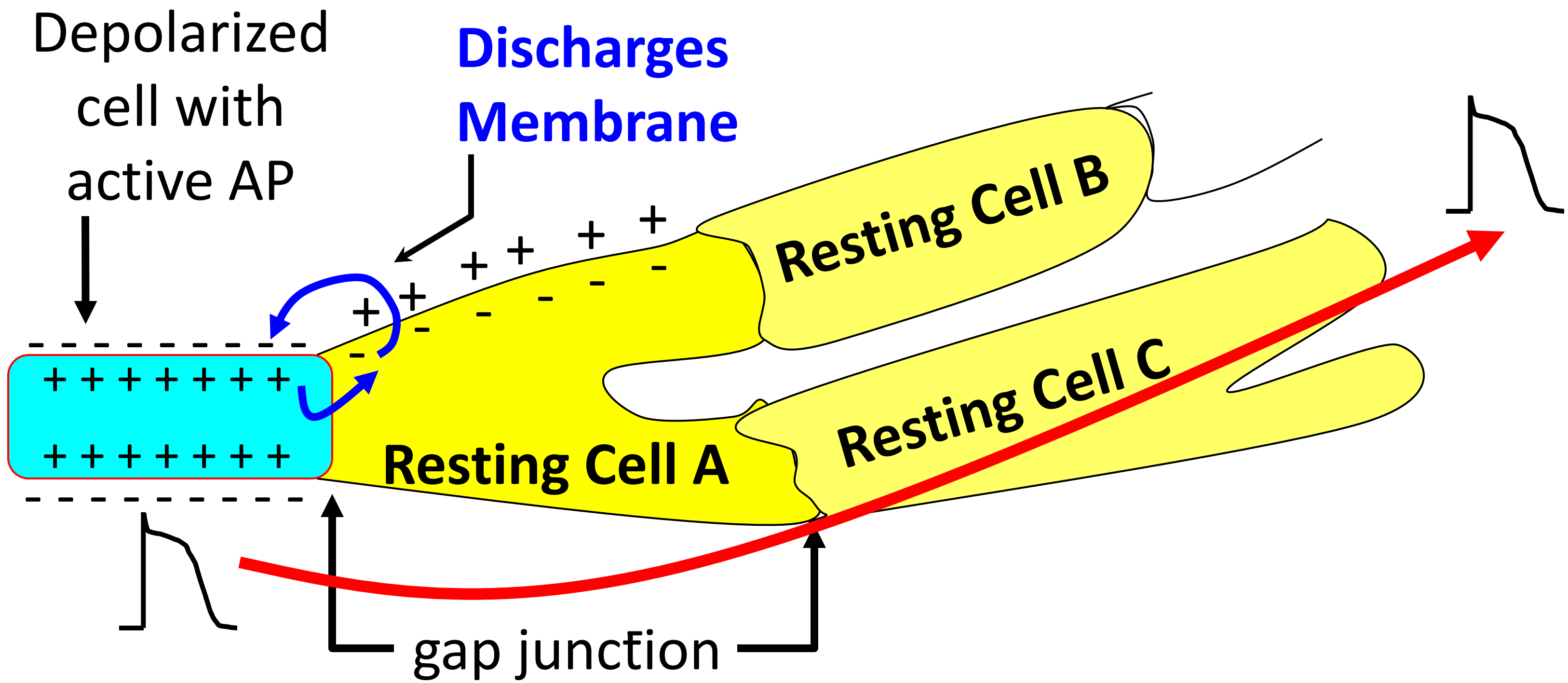
- Channel ion currents (I_{CH}) depend on both the electromotive chemical difference **(V_m - E_i)** and ion channel conductance (g_i) as **$I_{CH} = g_i \times (V_m - E_i)$**

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

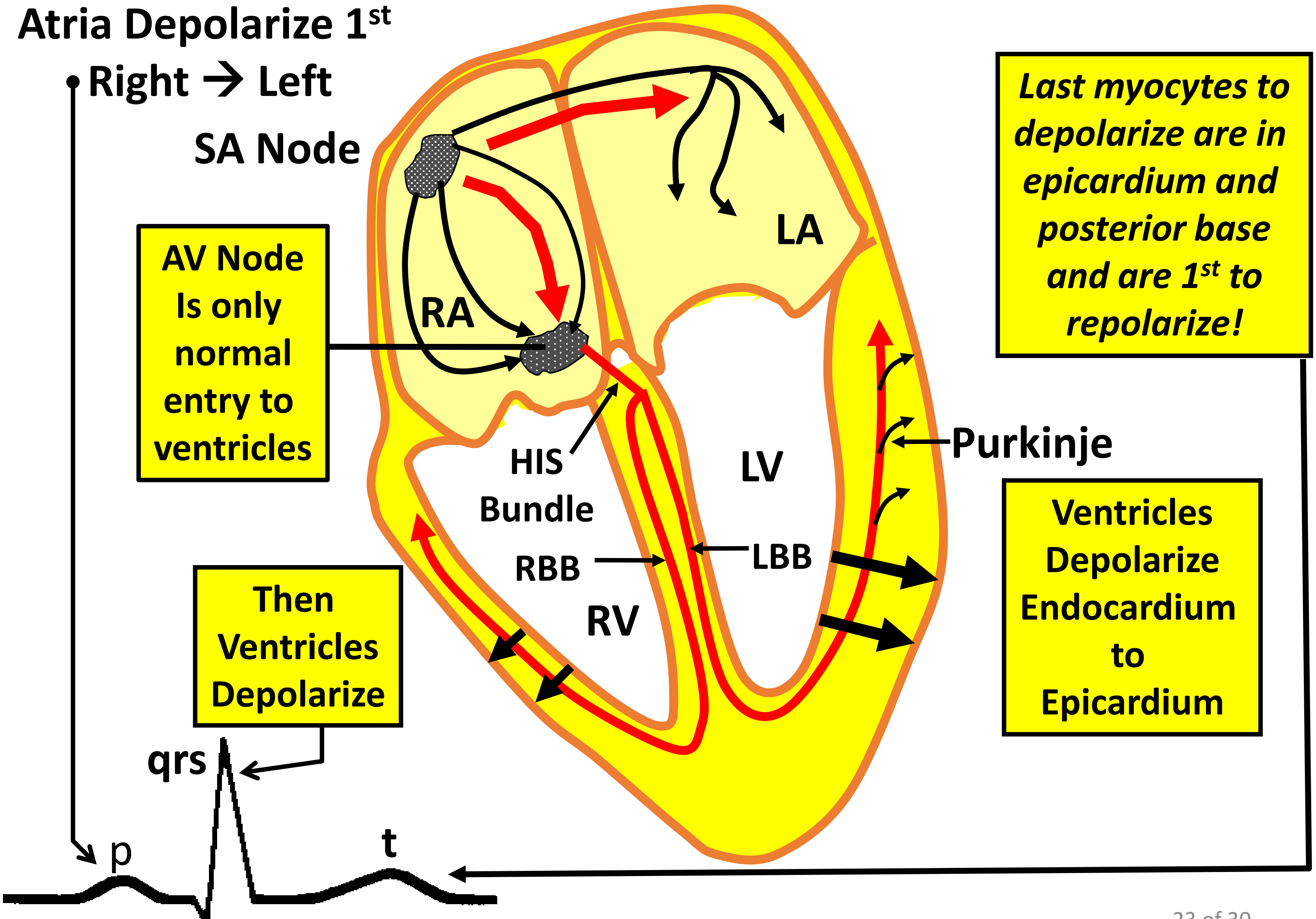
Conduction Sequences
Depolarization-Repolarization

Conduction Process



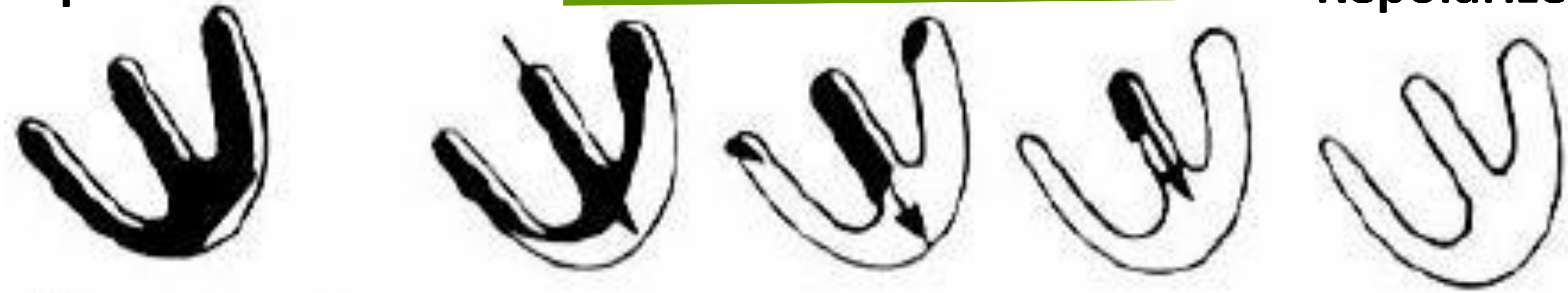
When Cell A membrane reaches threshold it generates an AP that serves to discharge cells B & C bringing them to threshold resulting in conduction of an AP throughout

Depolarizing Sequence



Repolarization Sequence

Start Repolarization | **Repolarizing** | White=Repolarized **Repolarized**



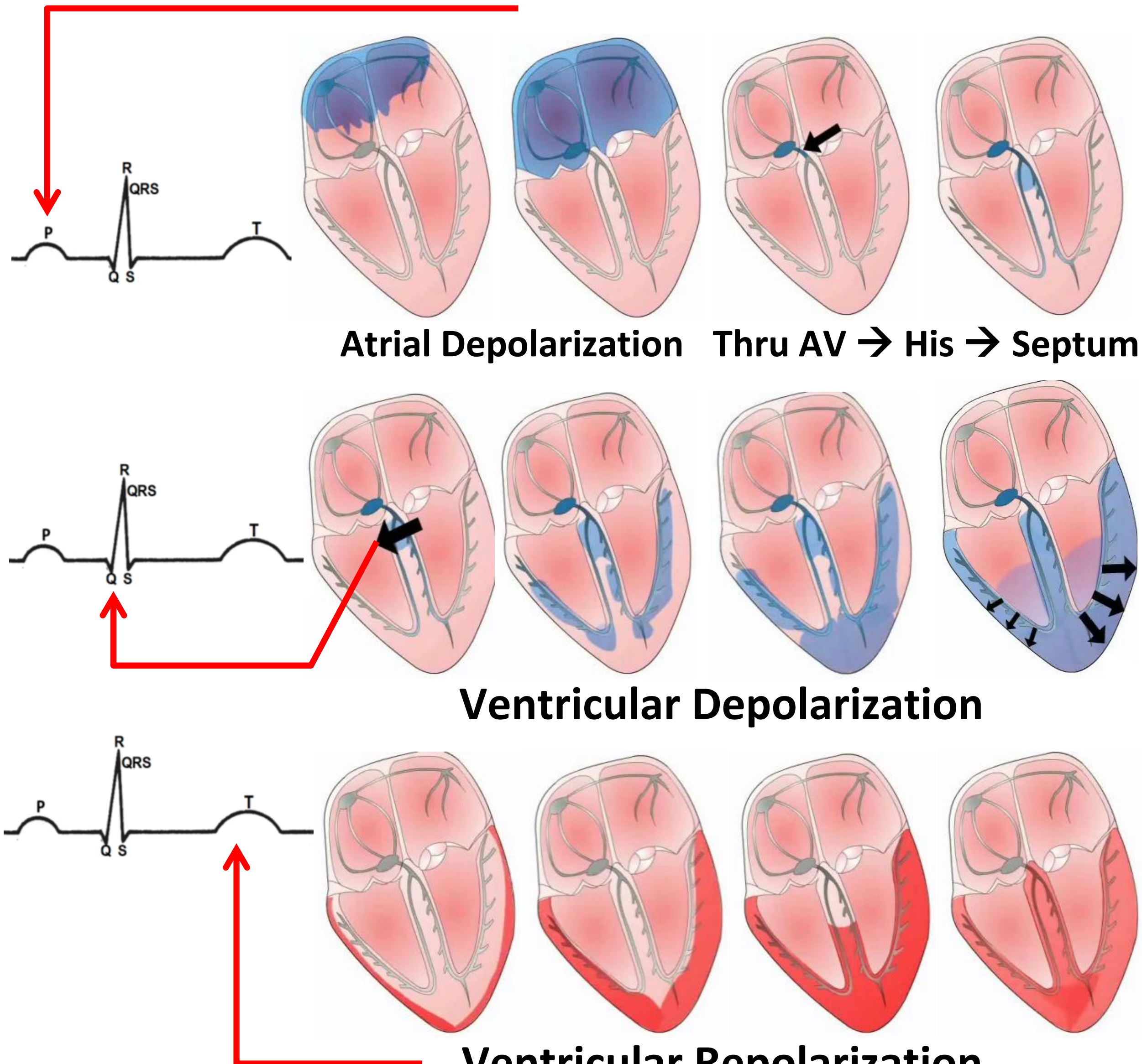
- Repolarization in reverse order to which myocytes depolarize
- Why?

→ 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

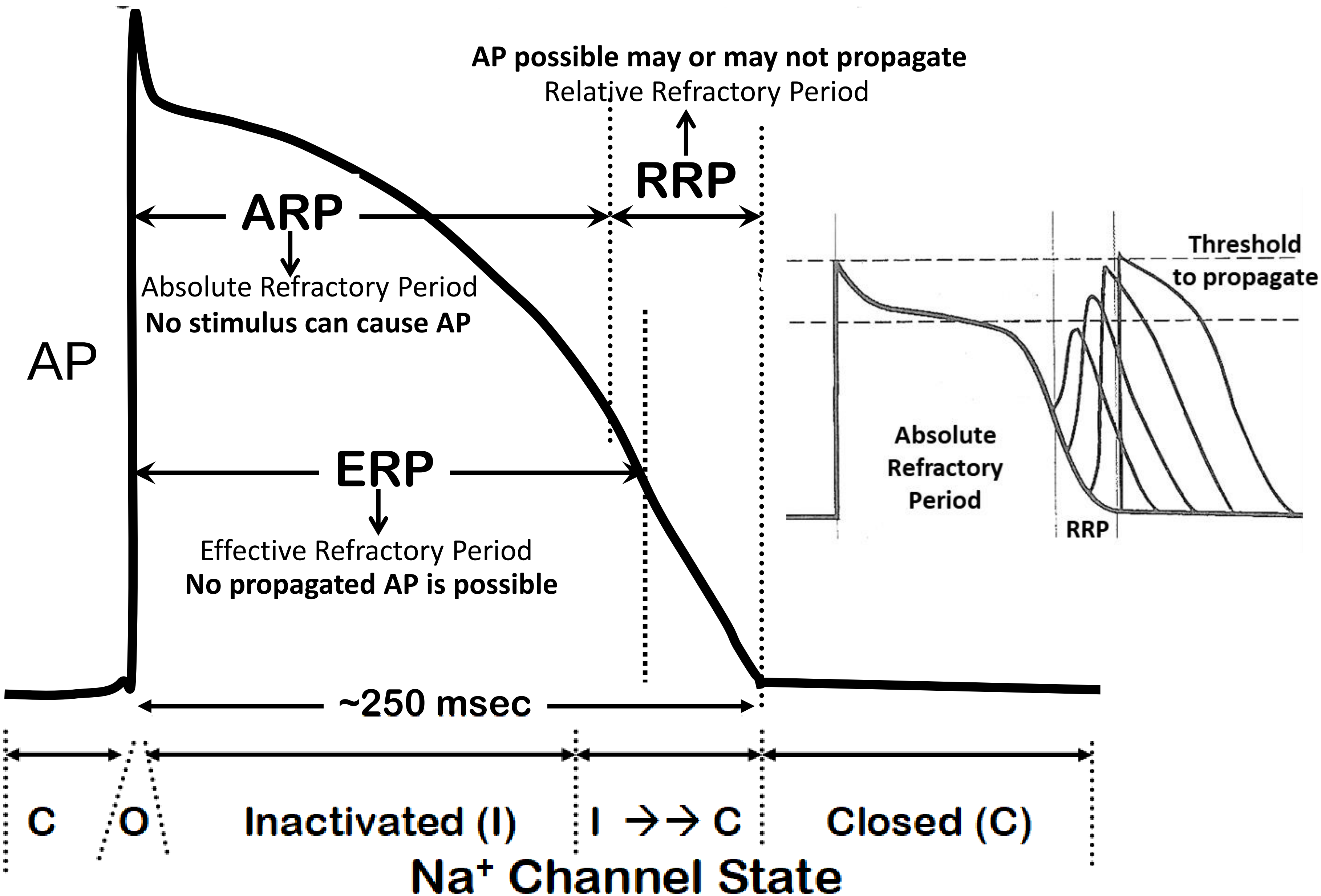


Depolarization is a “conduction” Process

Repolarization is a “Timing” Process

Refractory Periods

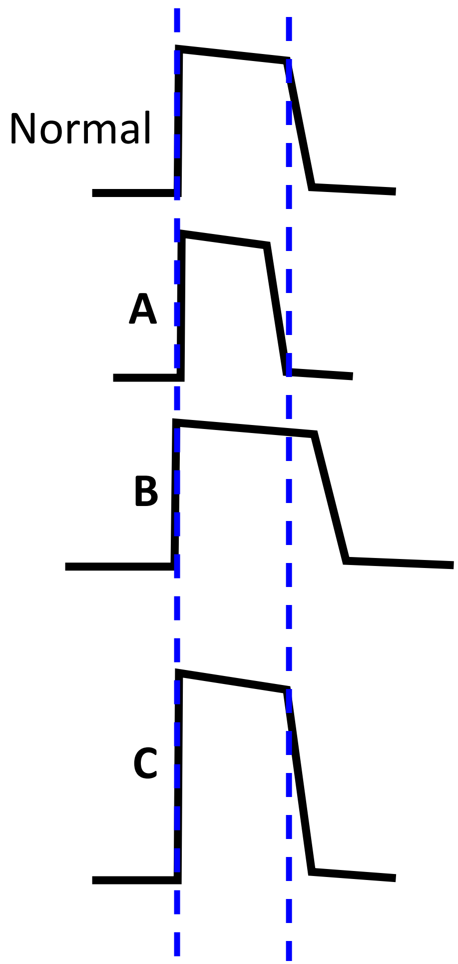
Refractory Periods and Na^+ Channel States



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

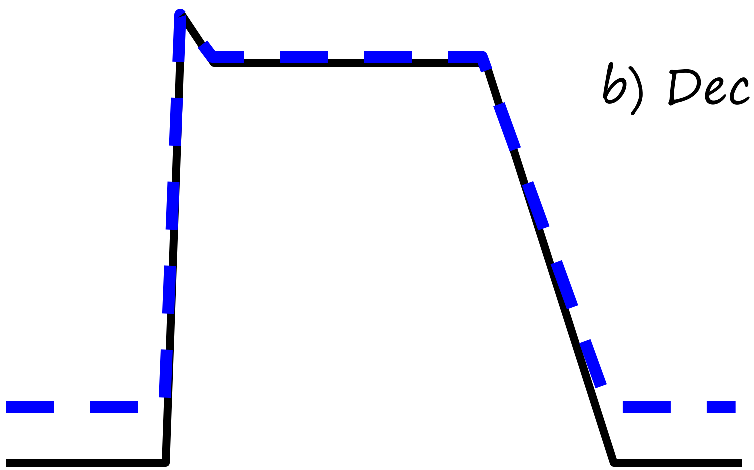


Interactive Question

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

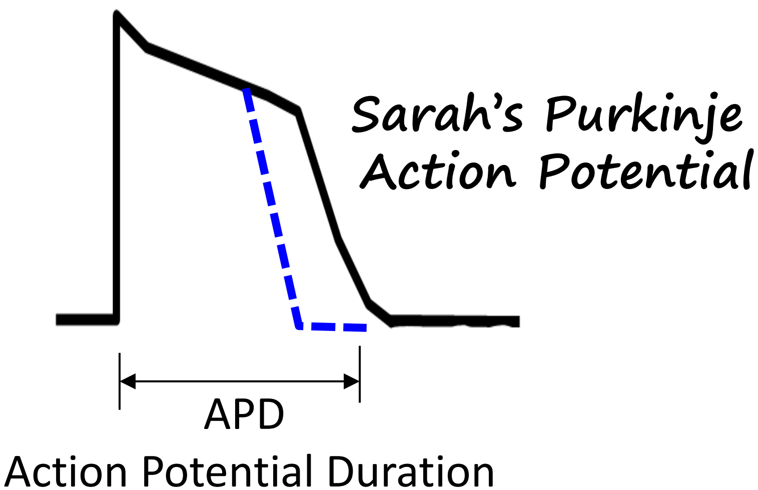
b) Decreased external sodium– hyponatremia



Normal reference values

Na^+ blood 135-145 mEq/L

K^+ blood 3.5 – 5.0 mEq/L



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

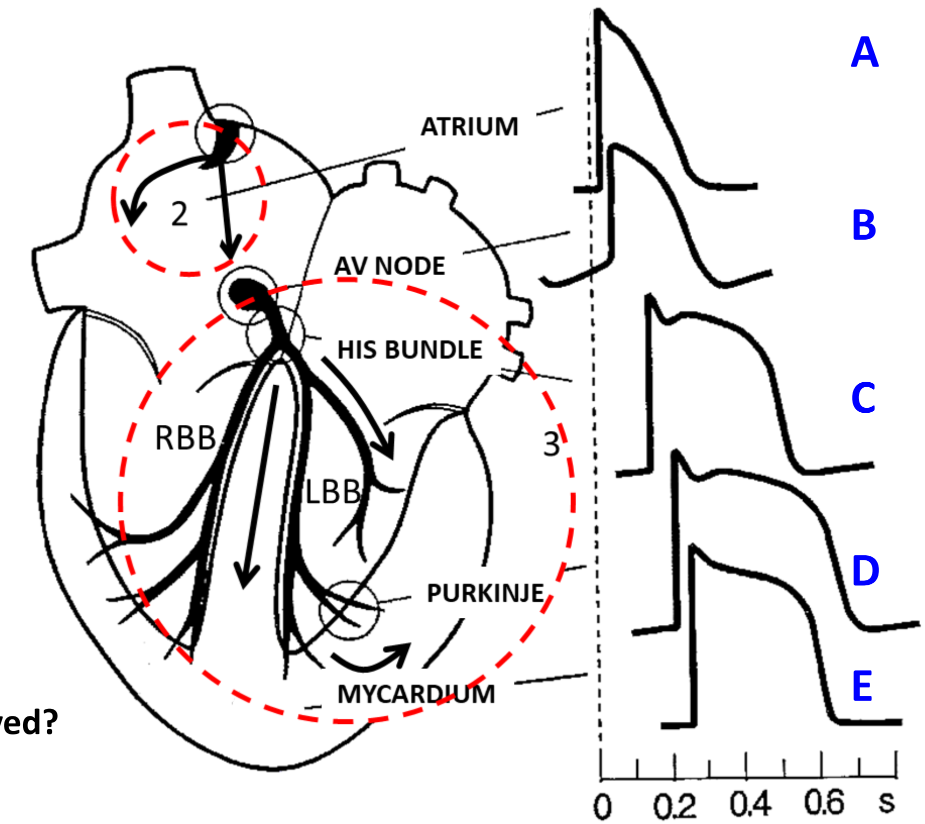
C. Essentially no change

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