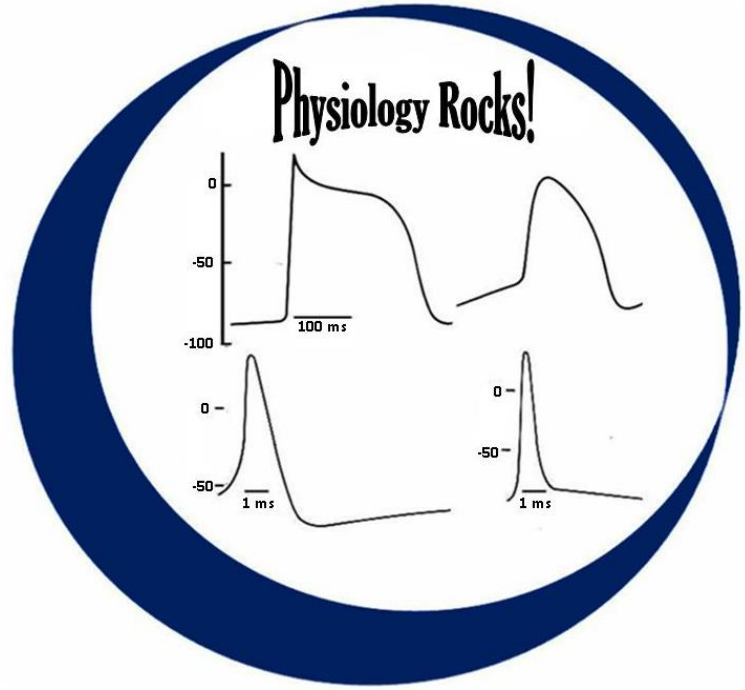
Lecture 2
Cardiac Electrical Activity 2



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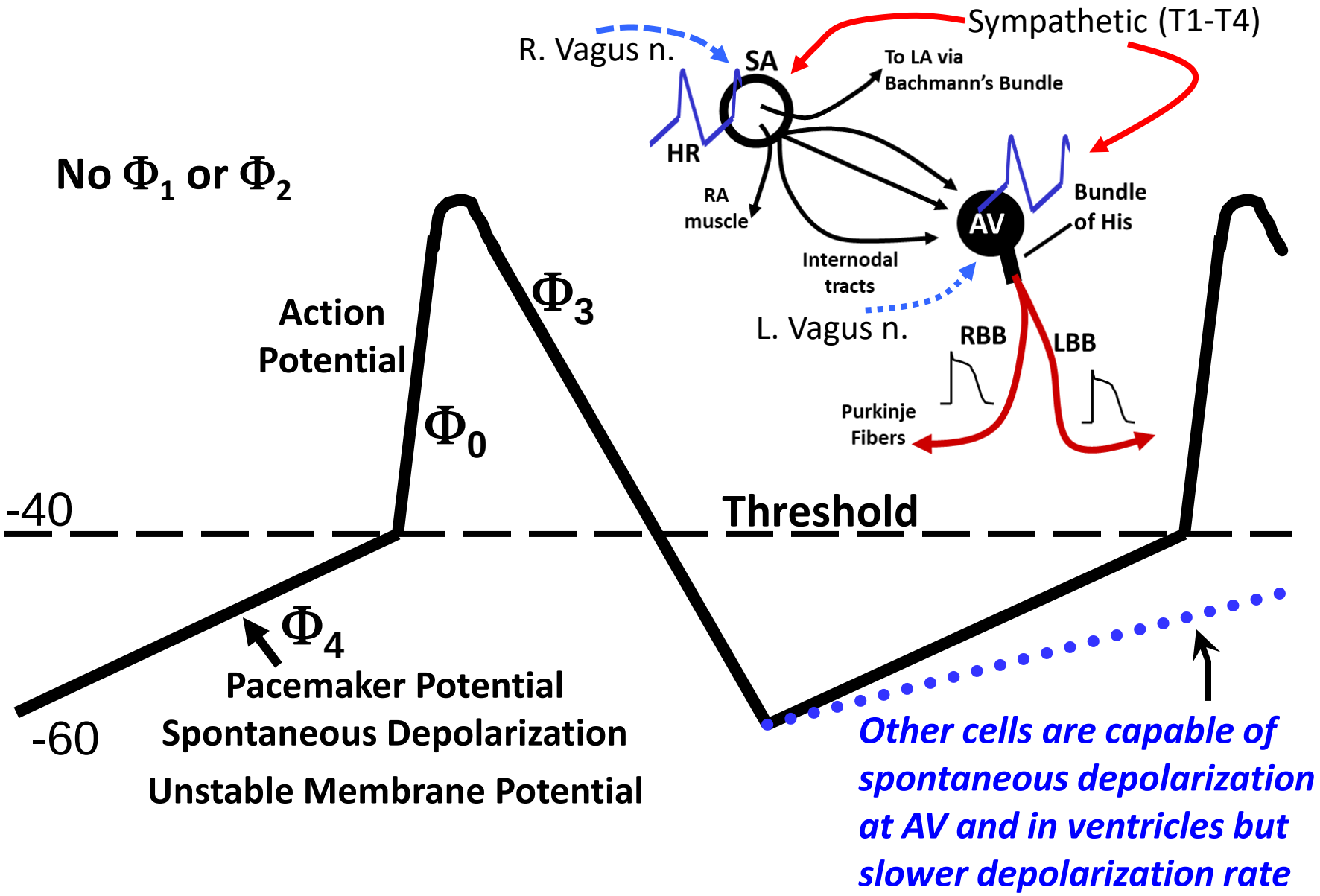
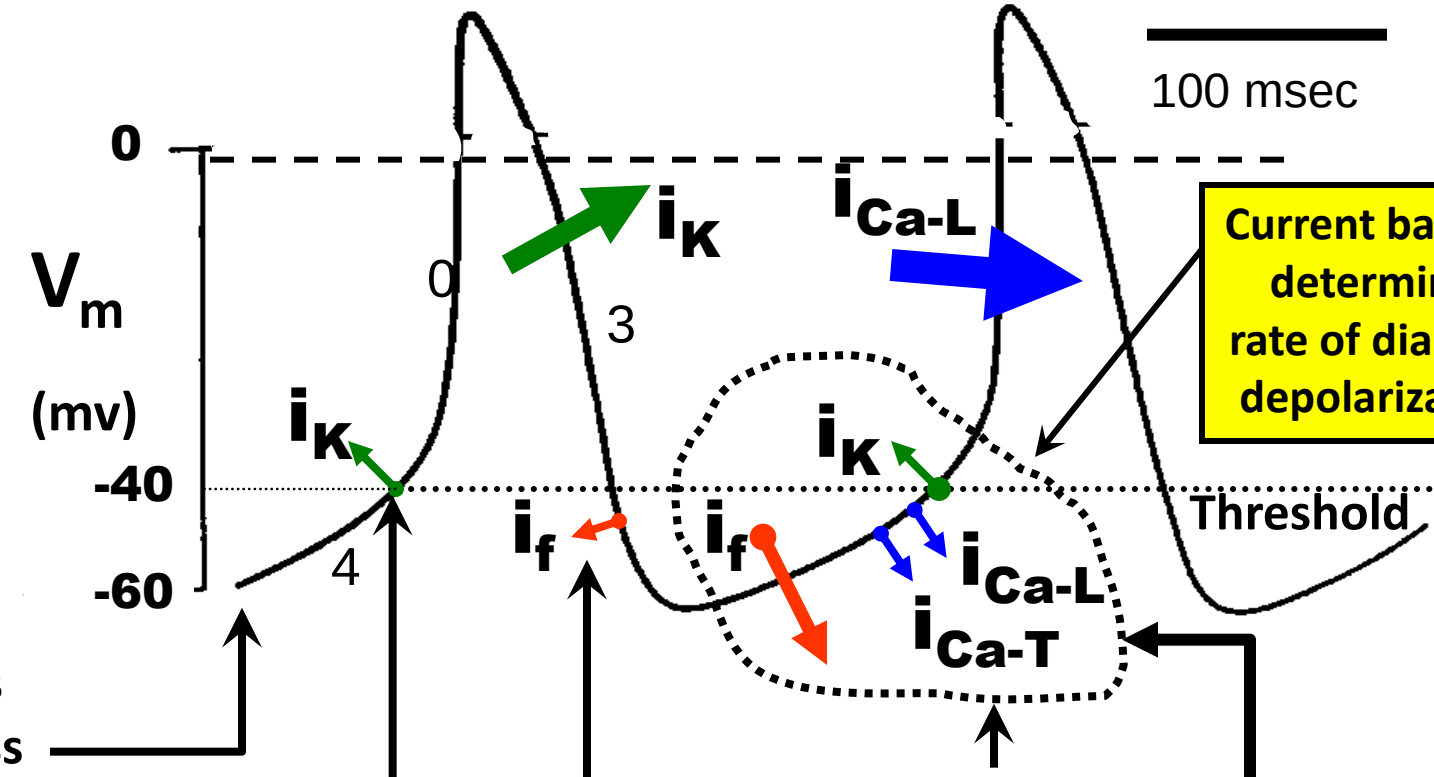
Topics

- Slow response action potentials overview
- Pacemaker ionic currents features and timing
- Vagal stimulation: Channels and function
- Sympathetic stimulation Channels and function
- Intrinsic heart rate concept
- Action potential conduction speed and determinants
- Detrimental conduction
- Hyperkalemia effects on fast and slow response action potentials
- Ectopic impulses and effects
- Reentry concept and effects
- Early and late afterdepolarizations

SA Node Cell "Slow-Response": Definitions/Patterns



Pacemaker Ionic Currents (Introduction)



Current balance determines rate of diastolic depolarization

Starts at Less negative potential so any Fast Na channels that might be present are inactivated

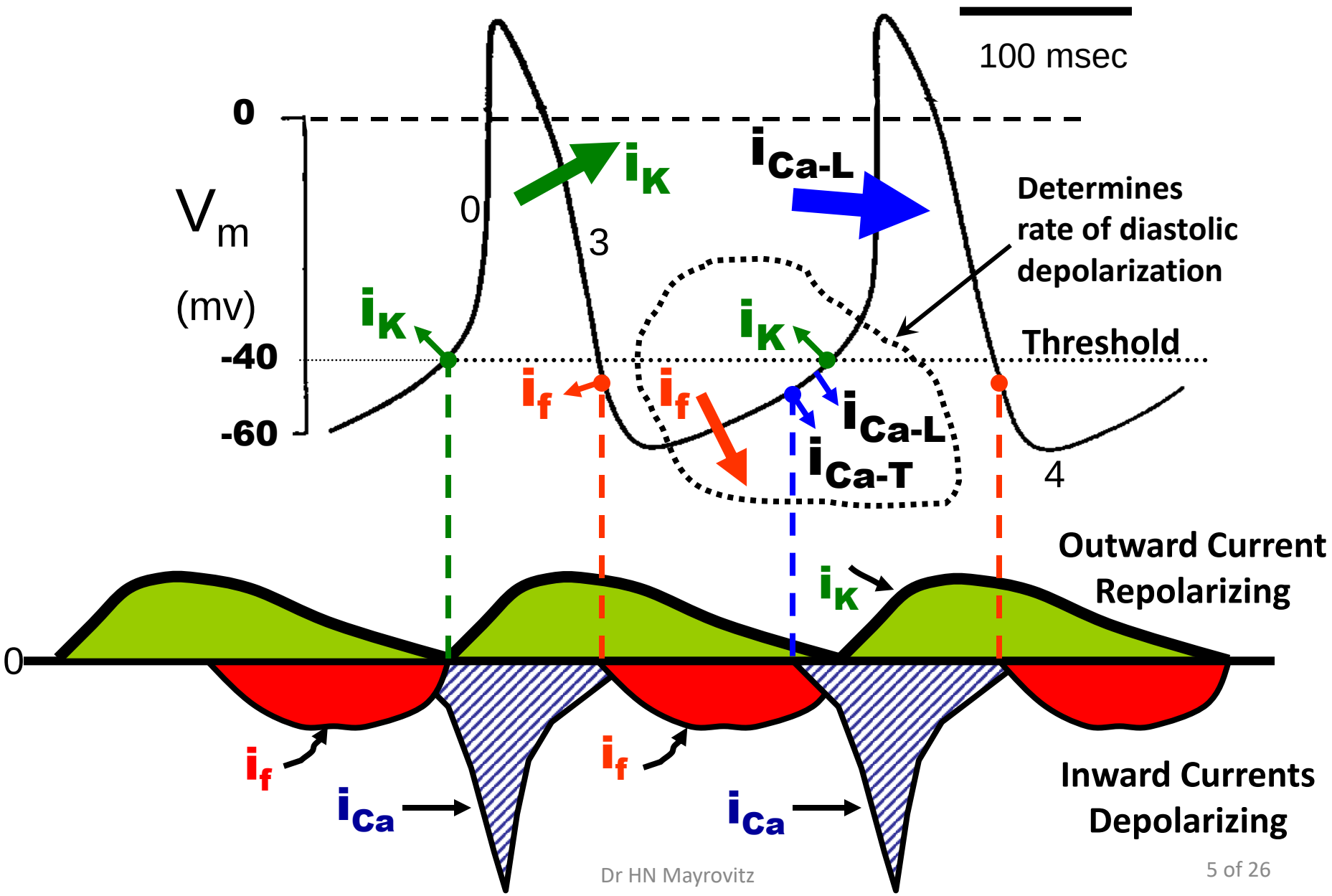
Outward I_K ~ fast response repolarizing K^+ Current 'Delayed Rectifier'

Inward I_f activated during repolarization Mainly inward Na^+ some K^+

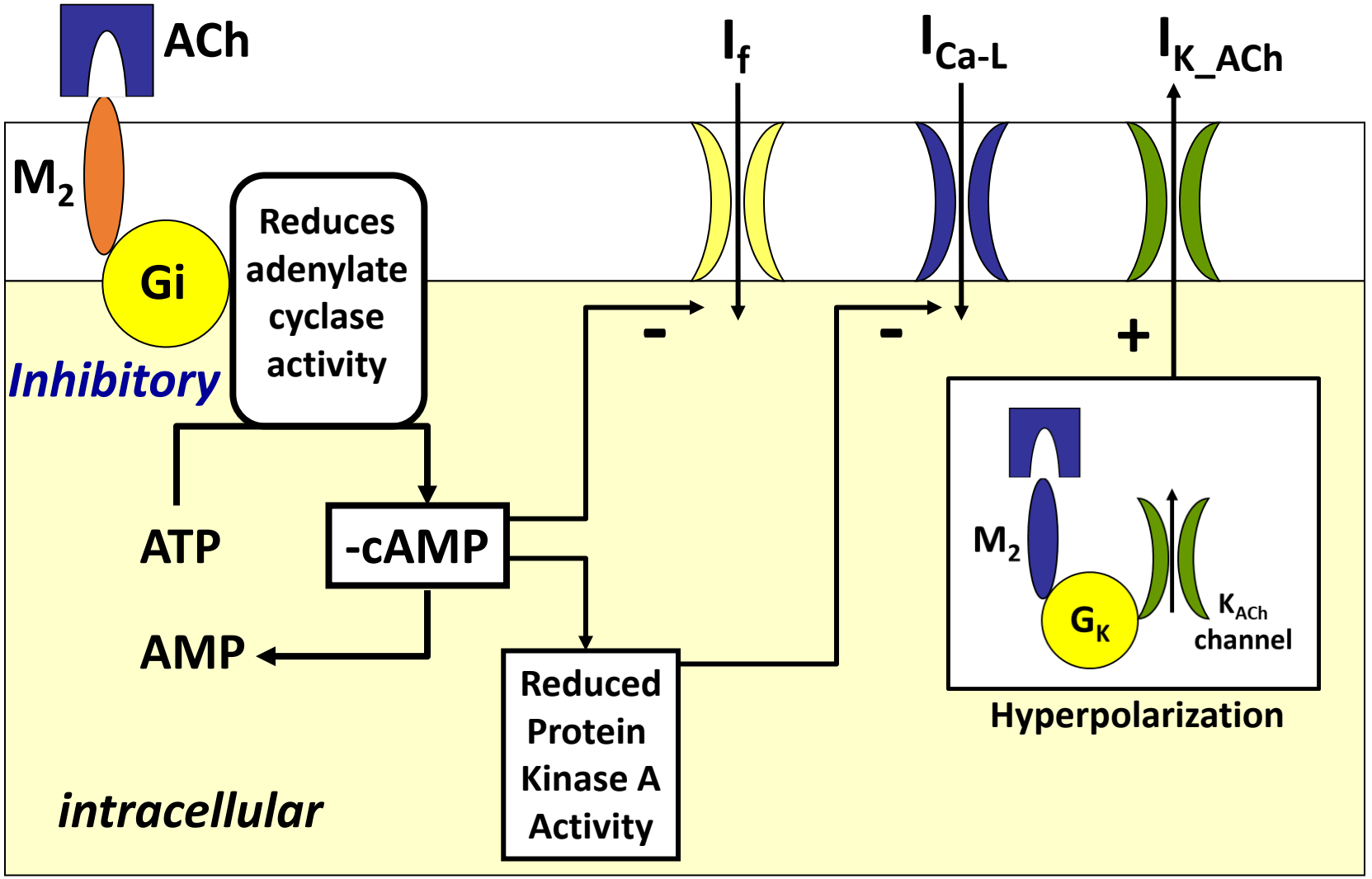
Ca^{++} channels are gated open with depolarization

If more outward I_k, then hyperpolarization causes the threshold to be achieved more slowly (+I_K out) → - HR
If more inward I_{ca} then threshold achieved more quickly (+I_{Ca} in) → + HR

Pacemaker Ionic Currents (Timing Patterns)

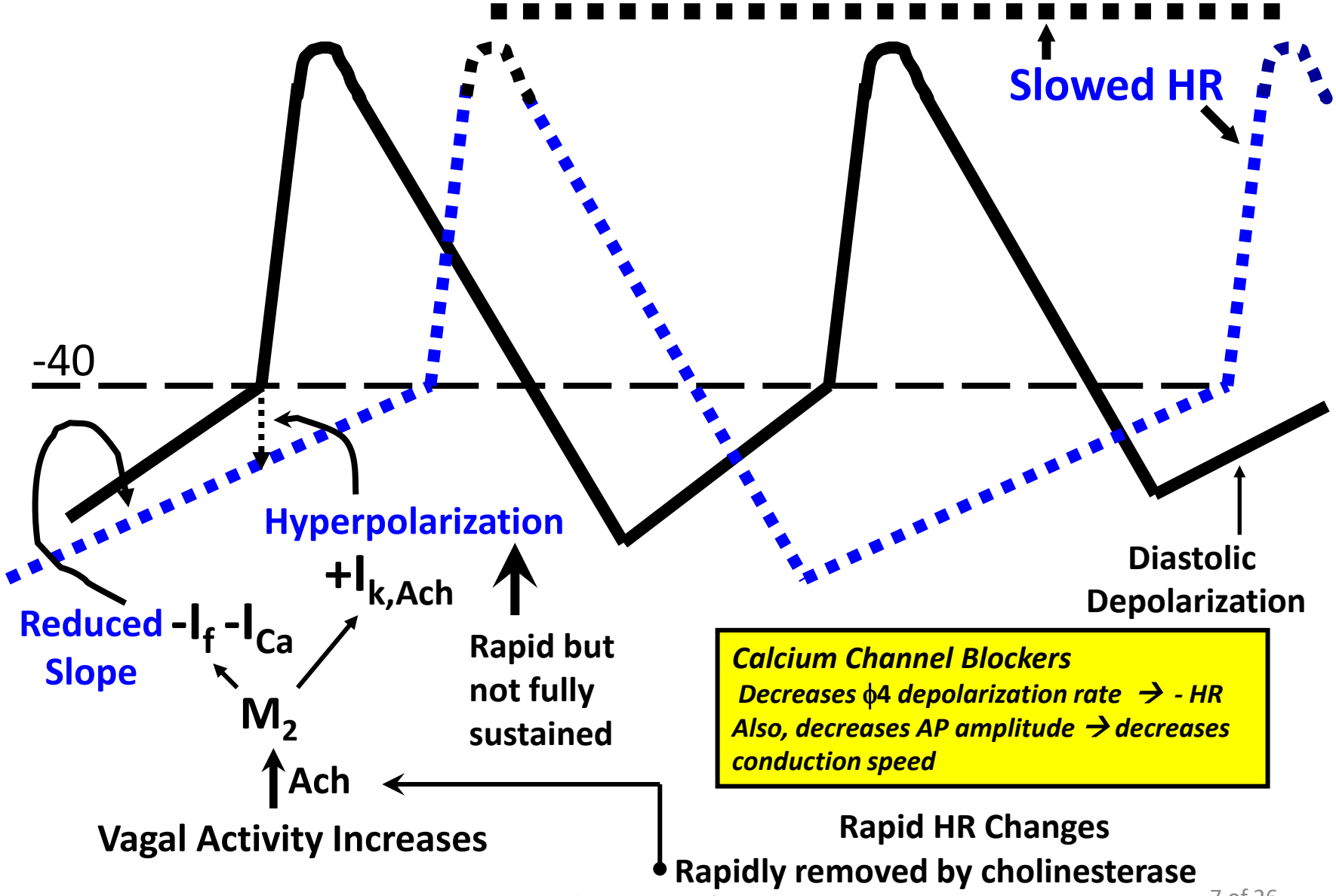


Channel Mechanisms: Vagal Stimulation

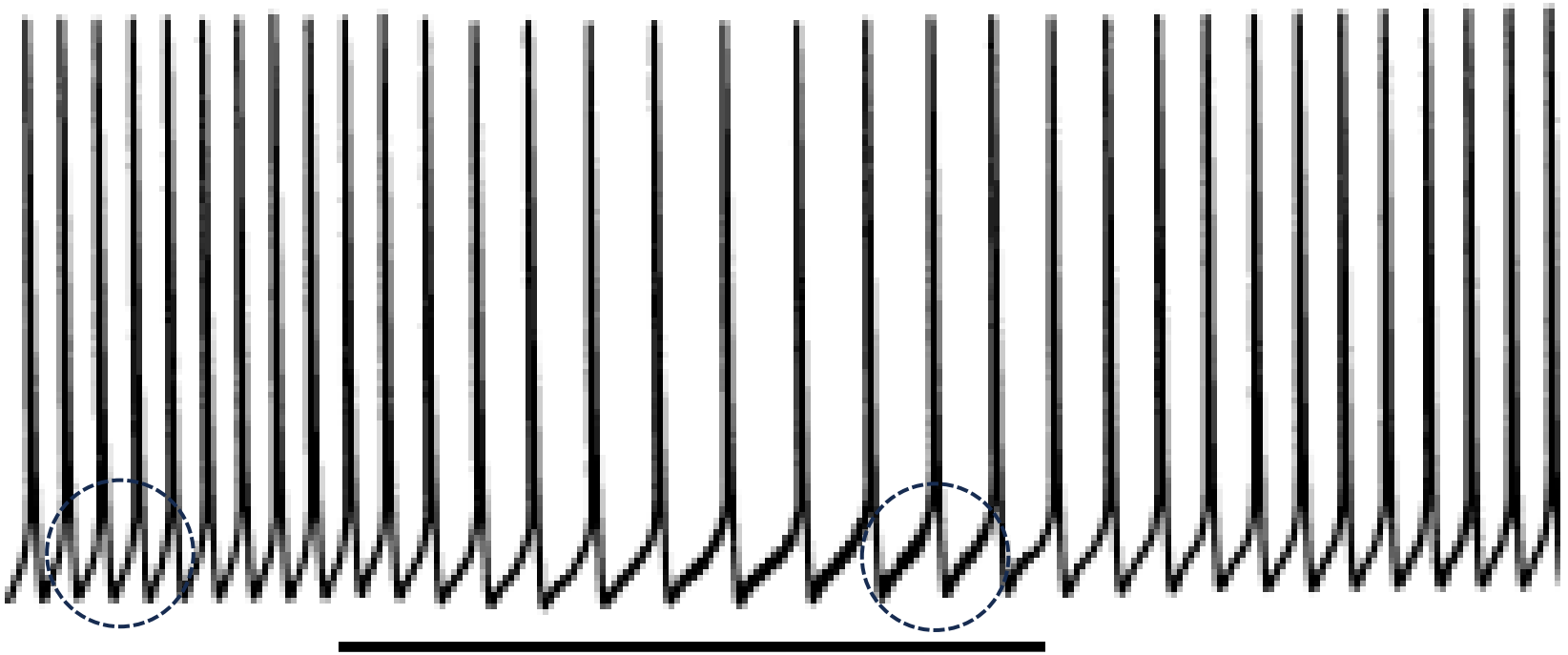


Net Effect: ($-I_f$, $-I_{ca-L}$ and $+I_{K\_Ach}$)
-Chronotropic -Dromotropic -small Inotropic

HR Changes: Vagal Activity



HR Changes: Vagal Activity

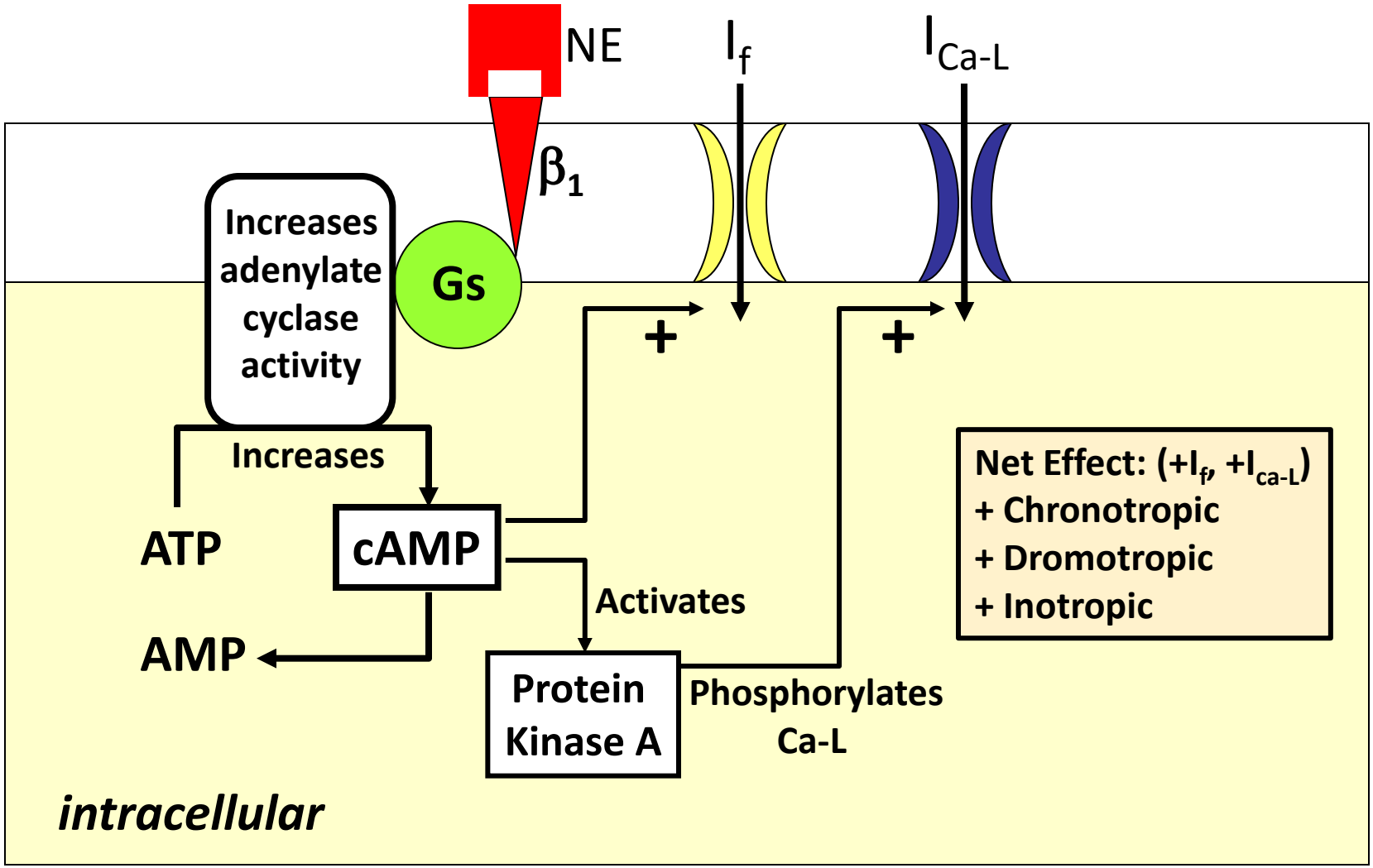


Vagal Stimulation (10s @ 10 Hz)

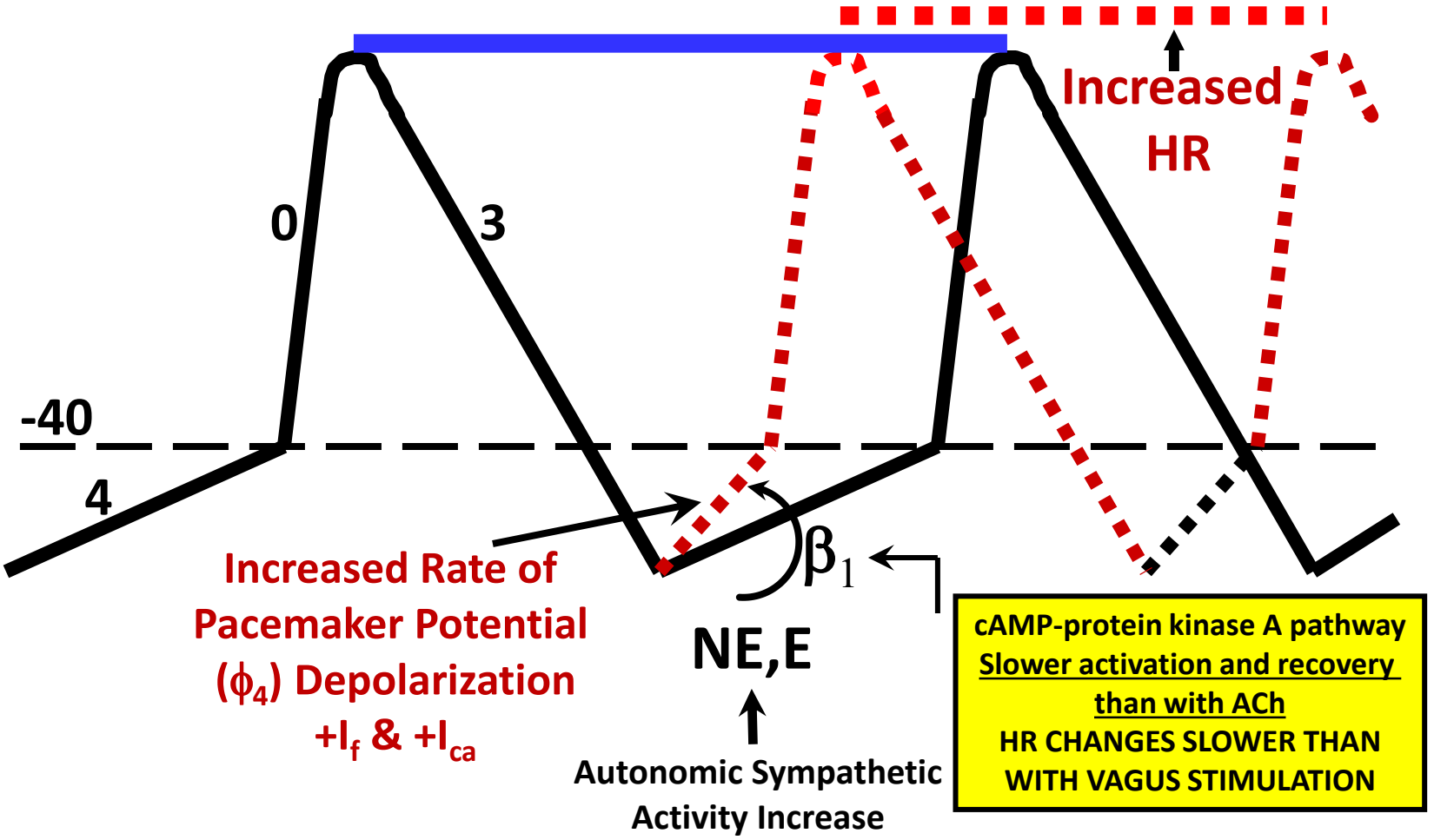
- **Reduced rate of diastolic depolarization**
- **Reduced heart rate**
- **Rapid recovery**

Campbell et al. J. Physiology, 1989; 414:57-68
Guinea-pig pacemaker cells

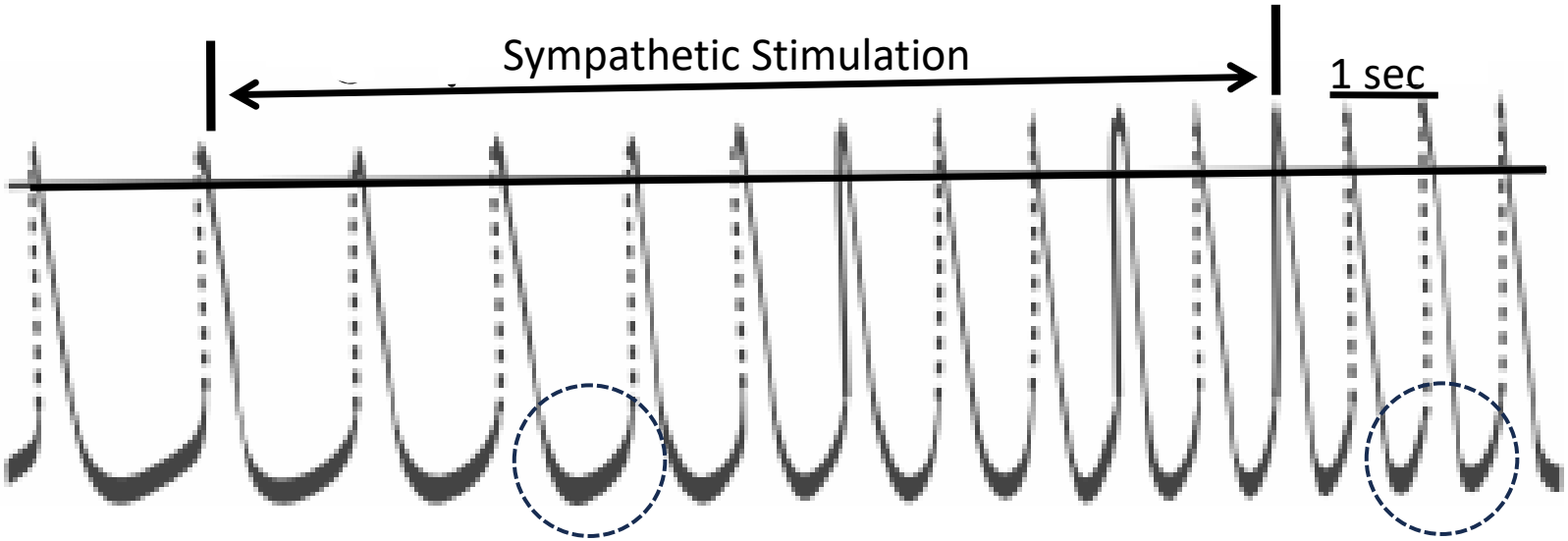
Channel Mechanisms: Sympathetic



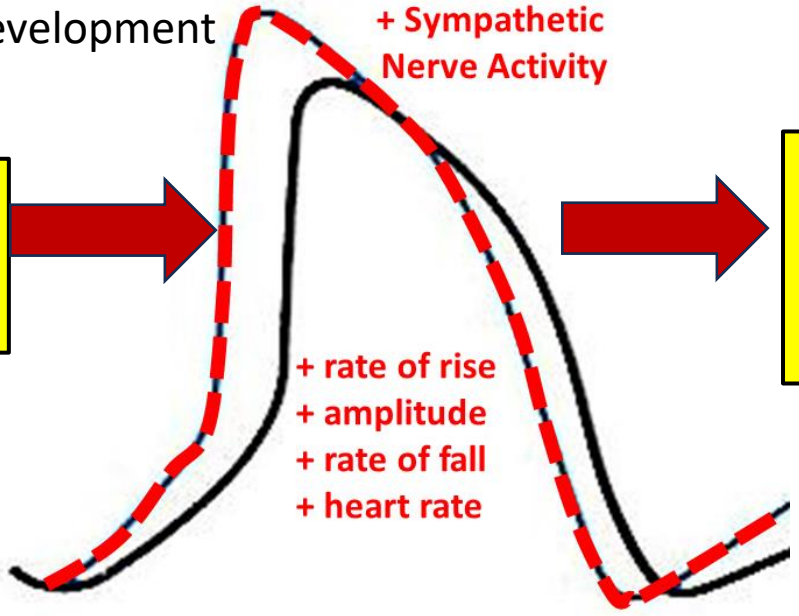
HR Changes: Sympathetic Activity



HR Changes: Sympathetic Activity

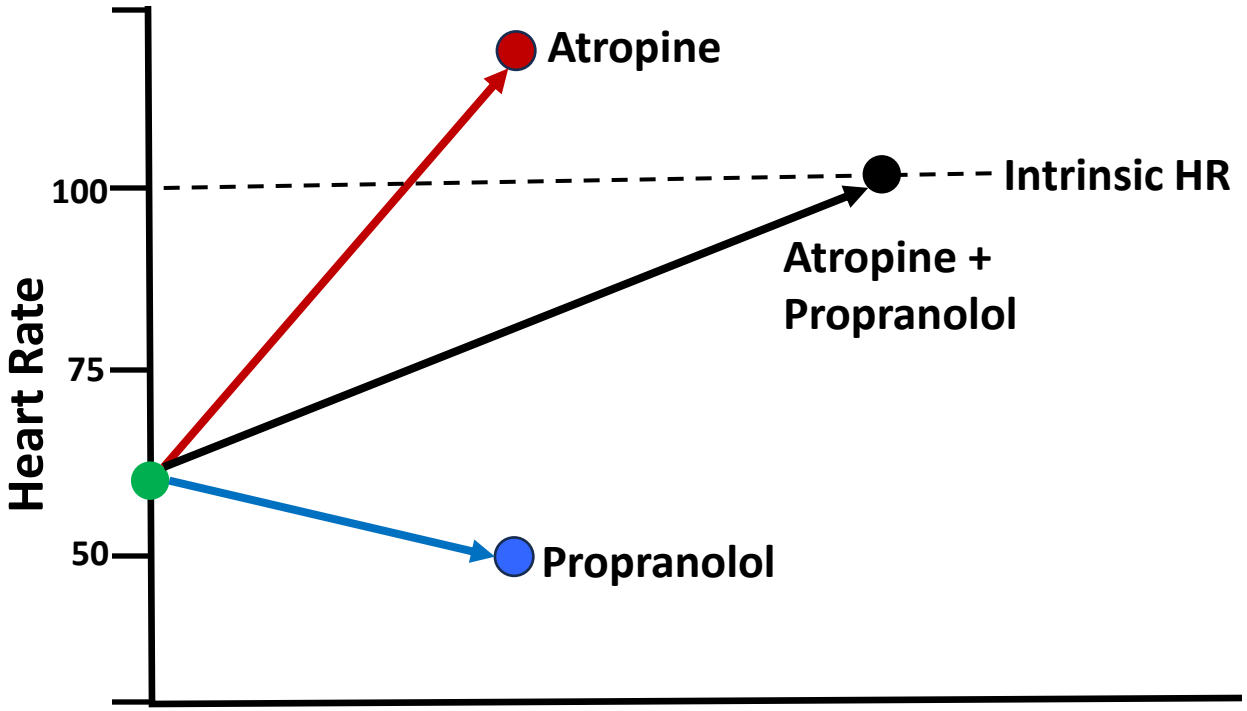


Overall impact of sympathetic stimulation of the SA node action potential



Increased HR and conduction speed

Intrinsic Heart Rate (HR)



What happens if:

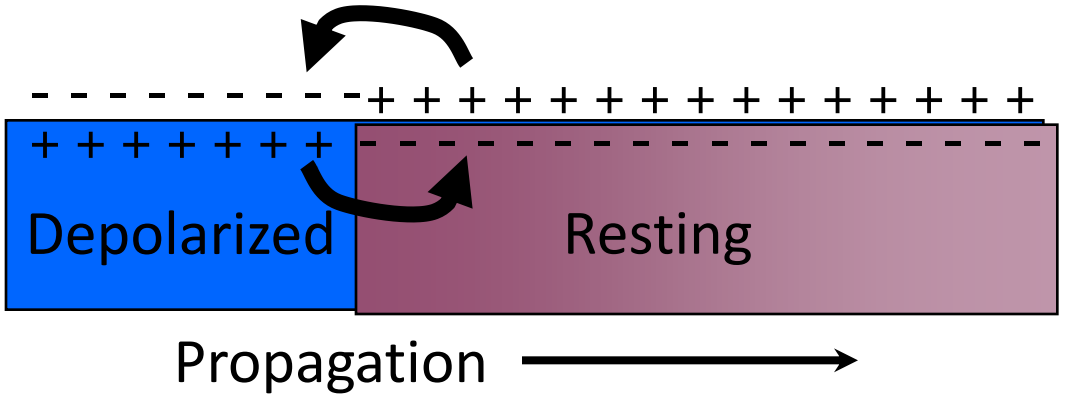
A person with a resting HR of 60 bpm is given a **muscarinic receptor blocker** (Atropine)

A person with a resting HR of 60 bpm is given a **β-adrenergic receptor blocker** (Propranolol)

A person with a resting HR of 60 bpm is given both drugs)

Conduction Speed: Determinants

1. Local ion currents depolarize membrane



2. If threshold reached (~-65 mv) for fast; (~-40 mv) for slow → AP (Phase 0) results

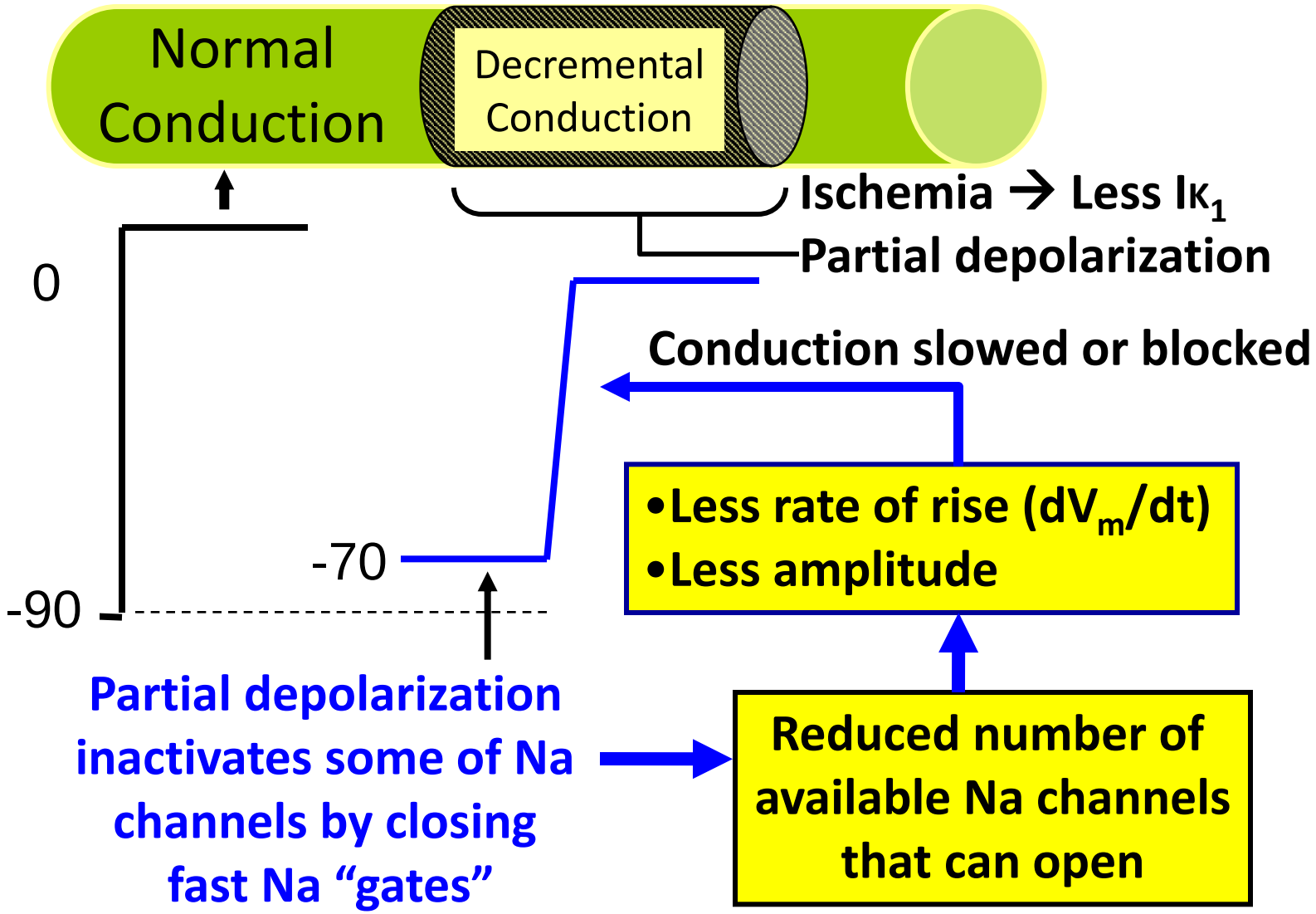
3. Impulse conduction speed depends on:

AP amplitude: If Less = Slower speed

Rate of rise: If Less = Slower speed

Threshold: If More = Slower speed

Decremental Conduction Example

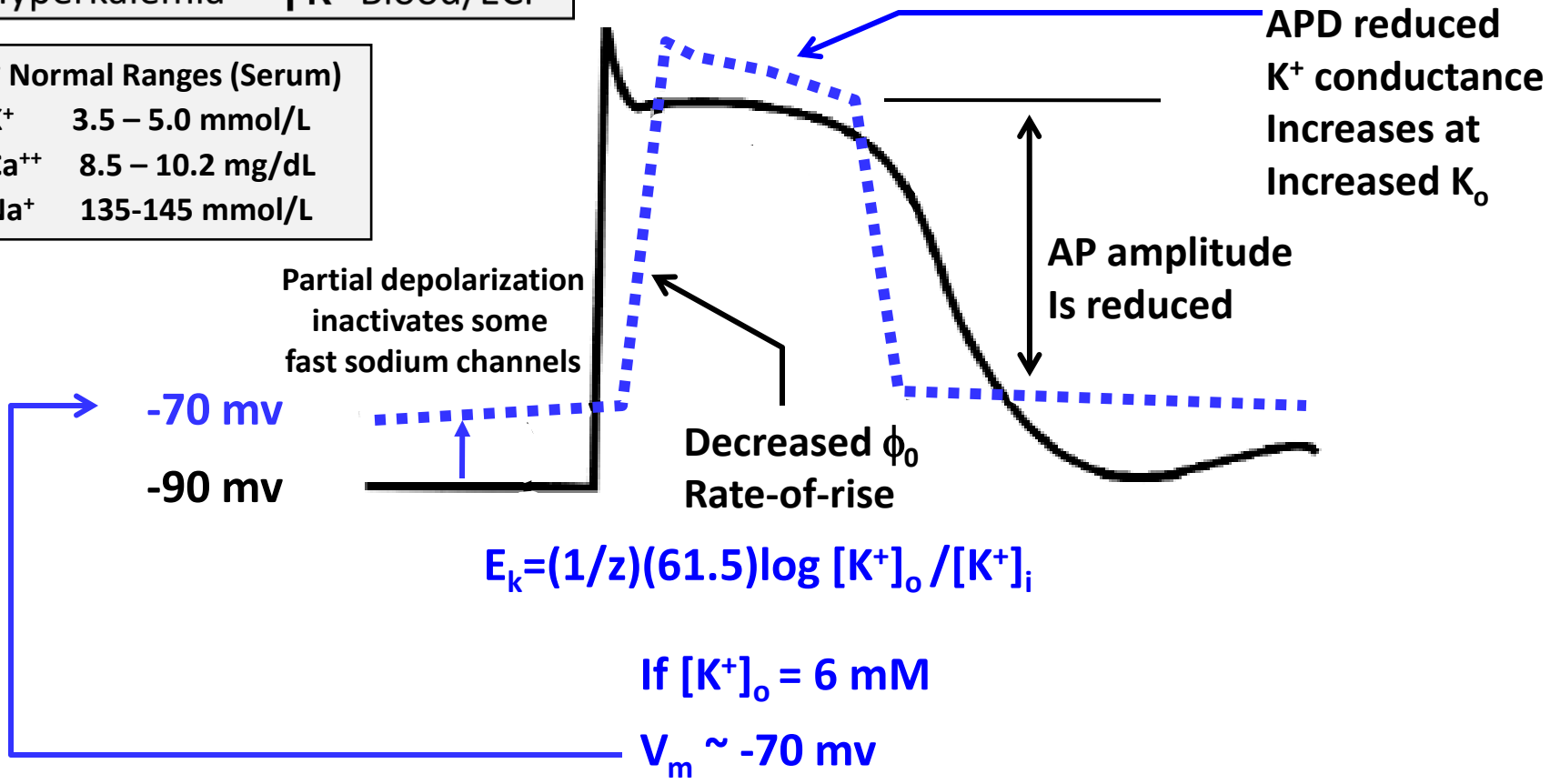


Hyperkalemia: Fast Response Effects

Hyperkalemia = ↑K^+ Blood/ECF

~ Normal Ranges (Serum)

K^+	3.5 – 5.0 mmol/L
Ca^{++}	8.5 – 10.2 mg/dL
Na^+	135-145 mmol/L



$$E_k=(1/z)(61.5)\log [K^+]_o/[K^+]_i$$

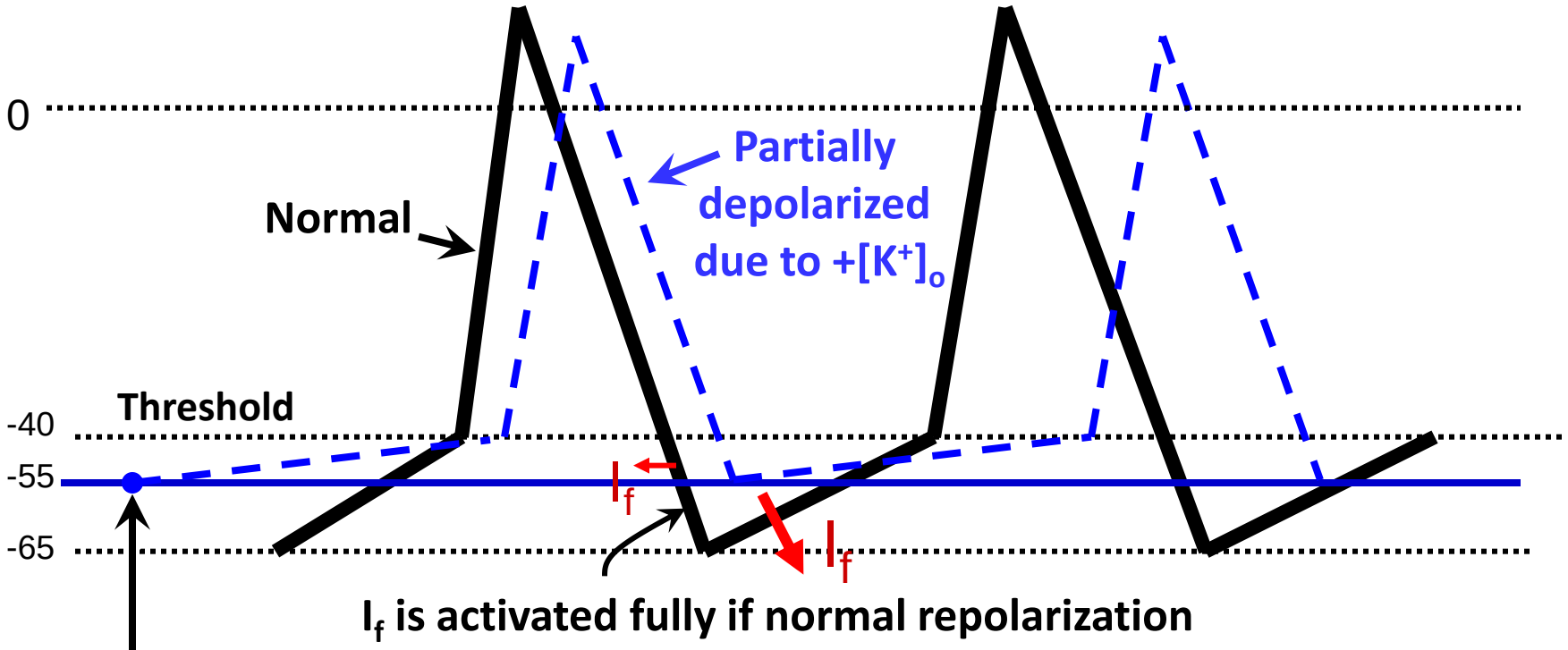
If $[K^+]_o$ = 6 mM

V_m ~ -70 mv

↓ amplitude, rate of rise → slowed conduction → •Arrhythmias •Heart Block

↑ excitability → Ectopic APs

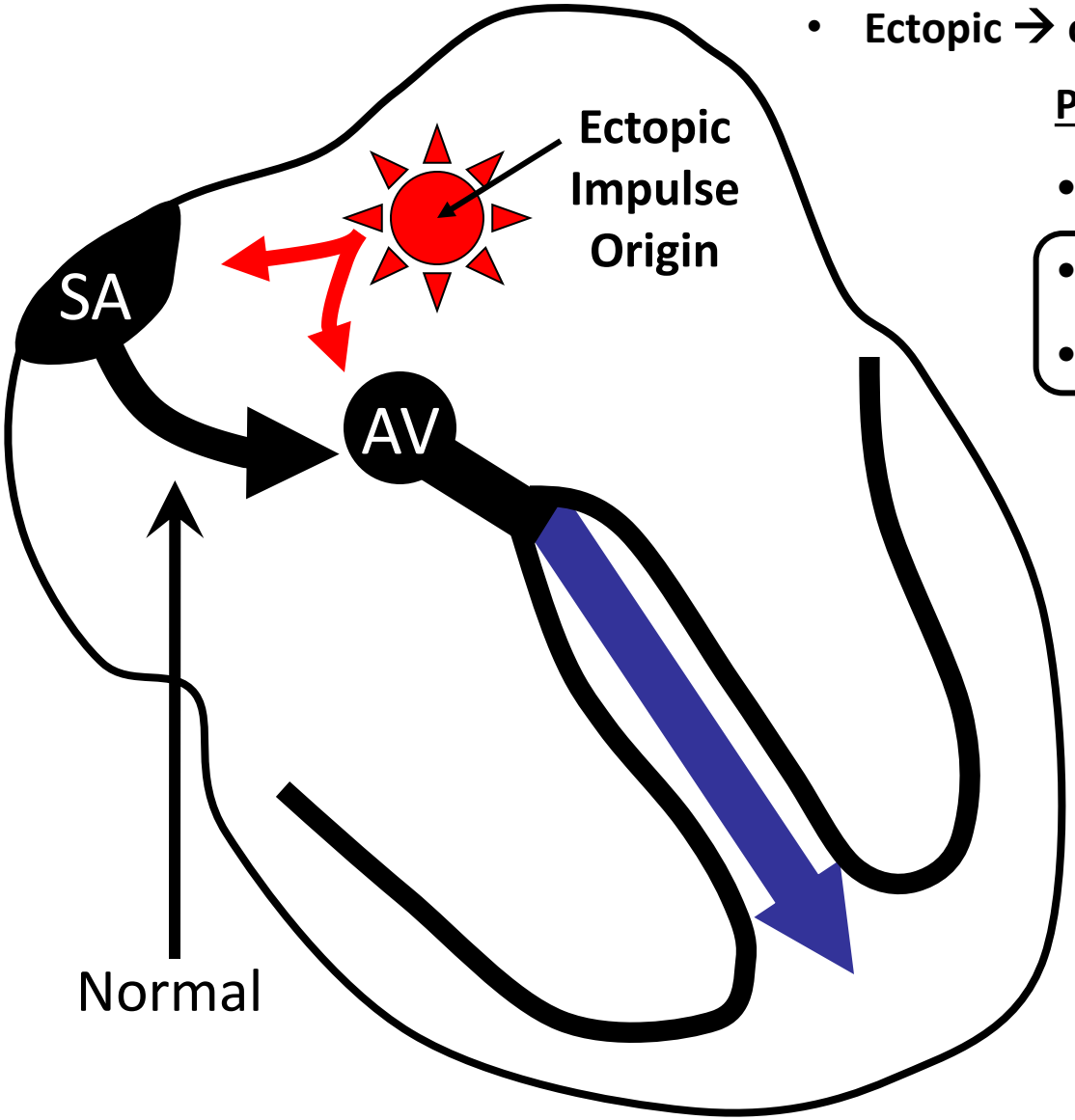
Hyperkalemia: Slow Response Effects



- If membrane partially depolarized due to hyperkalemia, full I_f activation does not occur!
- Rate of spontaneous depolarization less = reduced HR!

- If membrane doesn't repolarize to at least -50 mv
- Then no I_f and no action potential!
- No pacemaker action!

Ectopic Foci and Impulses: Overview



- **Ectopic → originating at other than normal site**

Possible Causes of Ectopic Activity

- *Increased Excitability*
  - *Depressed pacemaker*
  - *SA-to-ectopic path blocked*

→ Removes ectopic site suppression

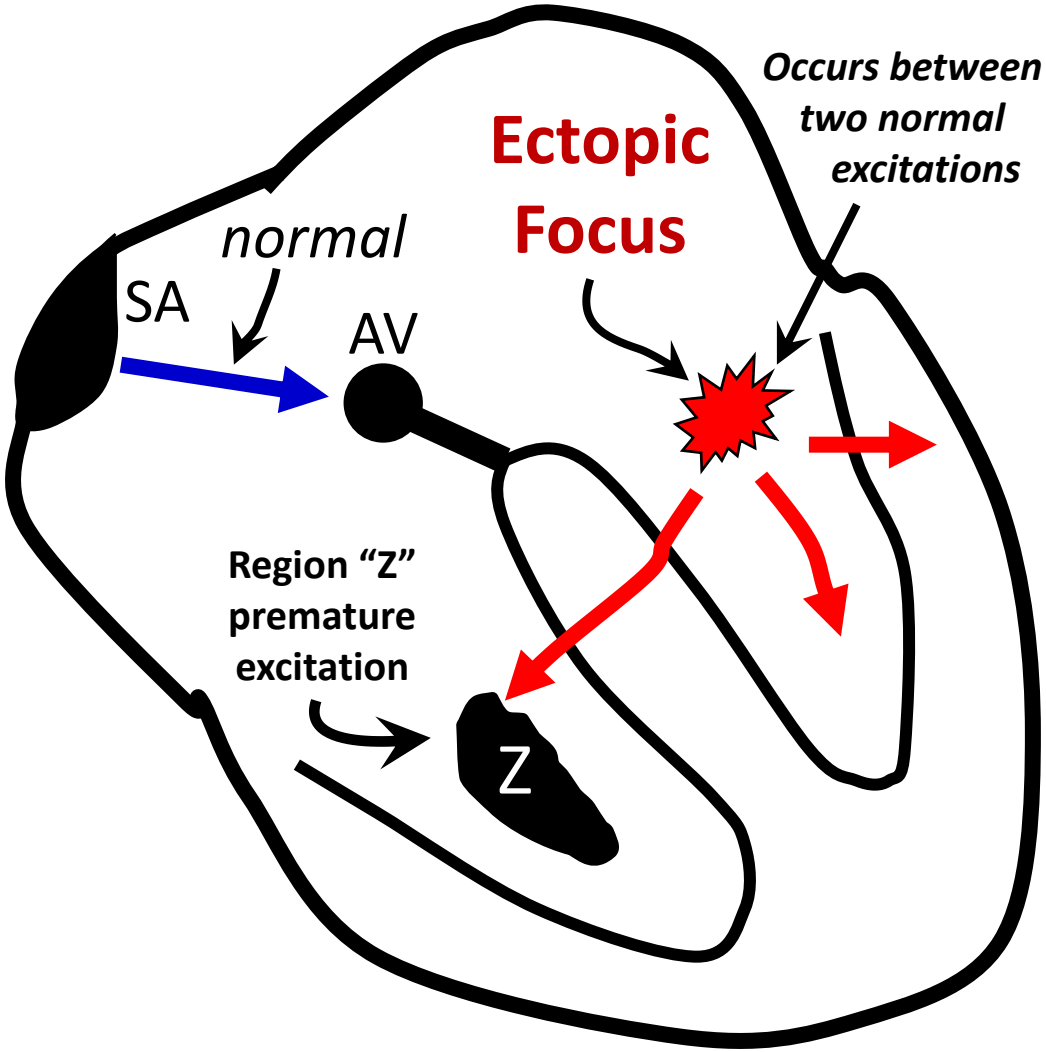
Possible Effects

Variable: Depends on:

Timing of arrival of ectopic Impulse

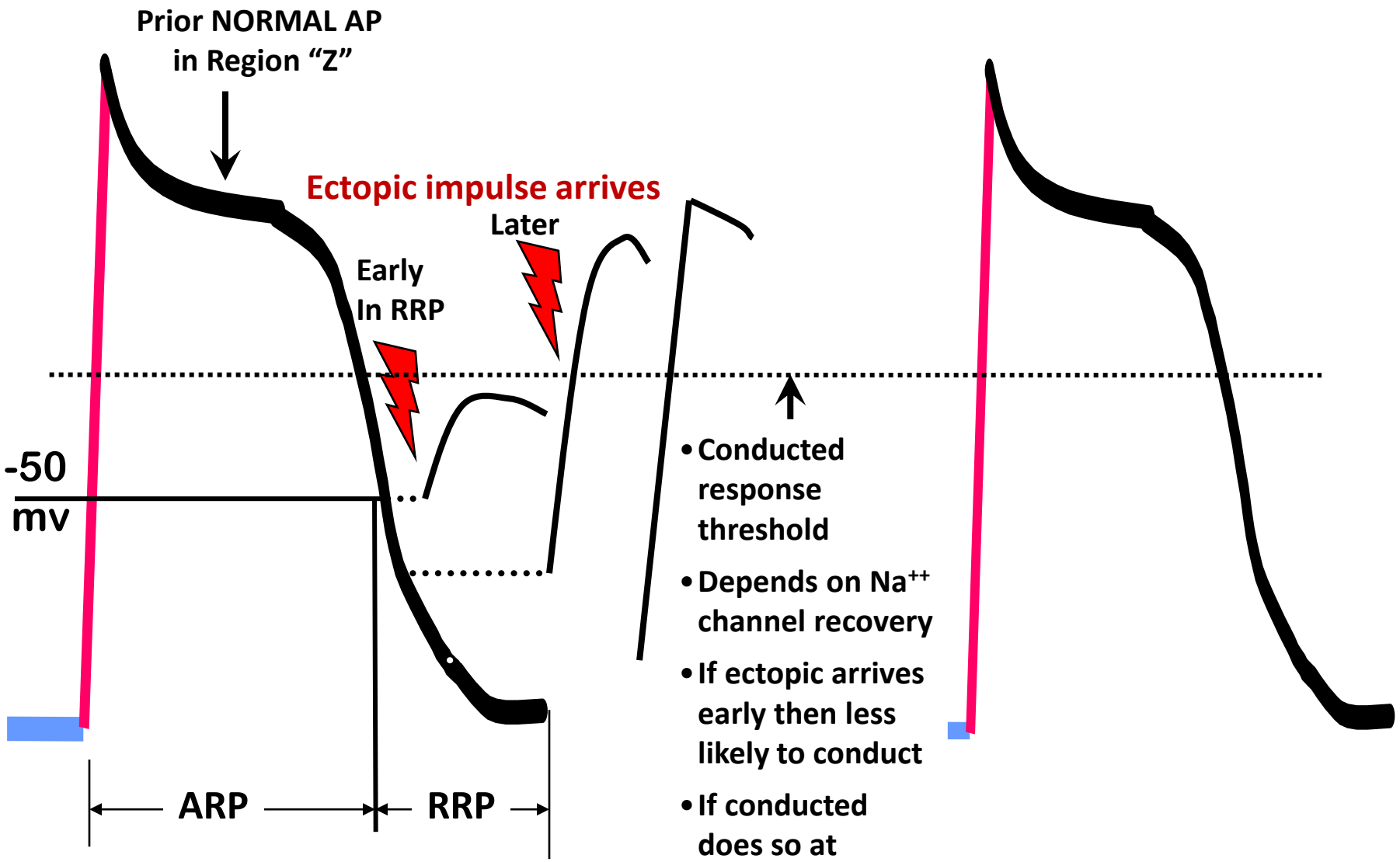
at other excitable cardiac sites

Premature Excitation by Ectopic Impulses



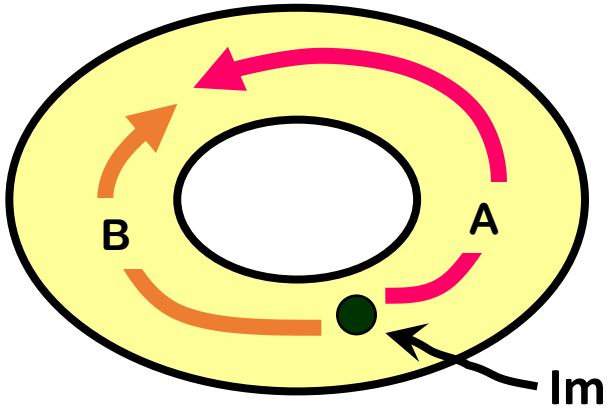
- Normal excitation starts at SAN
- If ectopic impulse occurs between two normal SAN impulses then it may trigger an event at a distant site if that distant site is not in a refractory state
- The figure shows a region "Z" that receives this ectopic impulse
- The question – what is the effect of this premature excitation?
- Is action potential **propagated**?

Premature Excitation → Reduced conduction speed



Reentry Concept

Ring of uniformly excitable tissue stimulated at the black dot

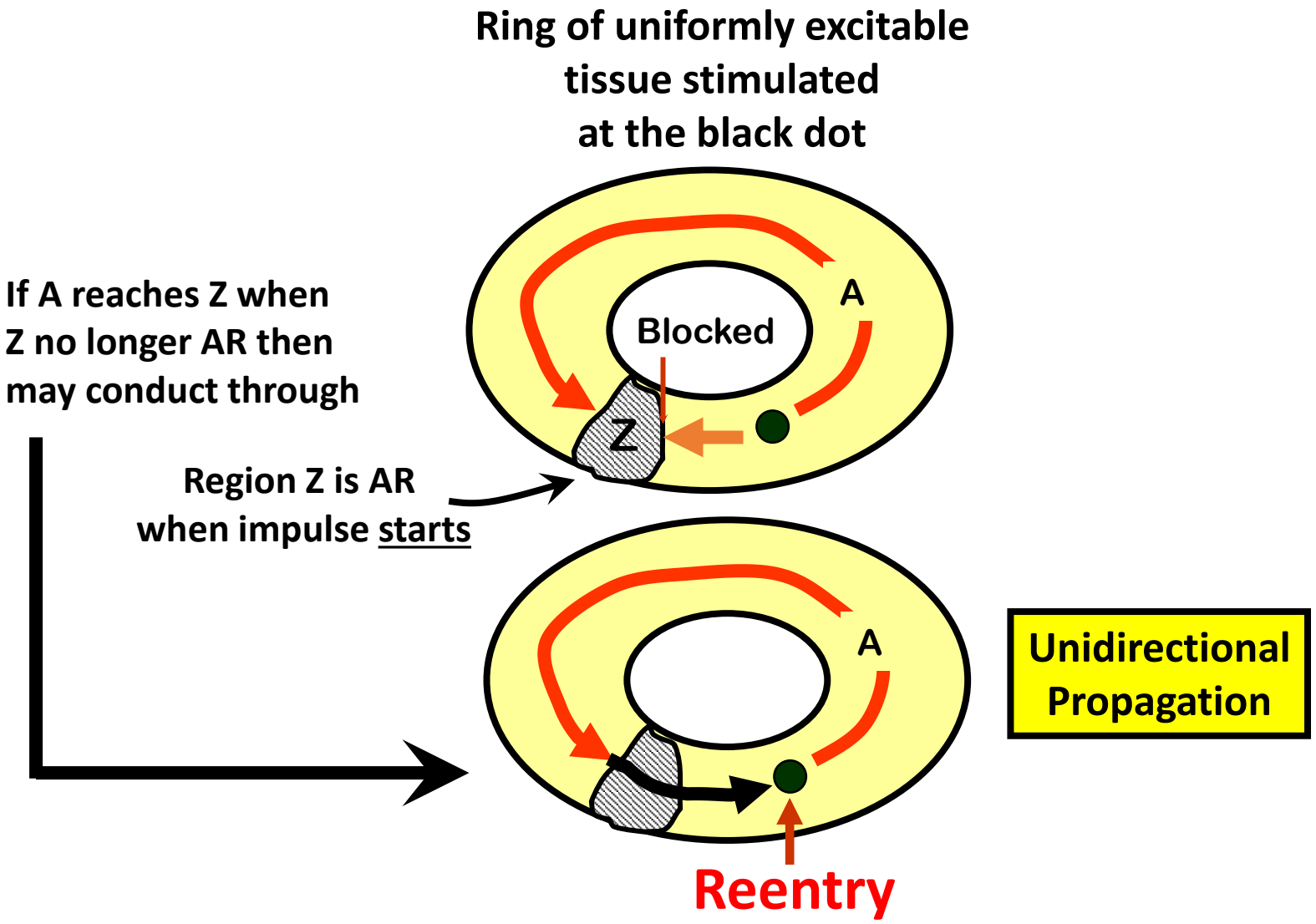


Bidirectional Propagation

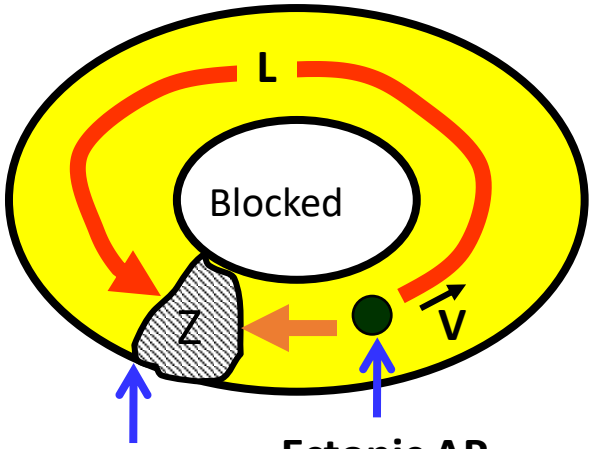
Impulse Starts Here

Impulses extinguish each other because pathways A and B are ABSOLUTELY REFRACTORY when A gets to B and B gets to A

Reentry Concept



Factors Tending to Promote Re-entry



Z initially refractory
Starts to repolarize @ T = 0
End of ARP at T = T_R

- Assume region Z was previously depolarized by a prior AP
- Z starts to repolarize at the instant that an ectopic impulse fires
- The ectopic impulse takes a time T to arrive at region Z
- During time T, Z is repolarizing
- The time for Z to become relatively refractory is denoted as T_R
- If $T < T_R$ then Z still absolutely refractory when impulse arrives
- If $T > T_R$ then impulse may reenter

If $T < T_R$: Snuffed

If $T > T_R$: Reentry

- **Decreased V**
- **Increased L**
- **Decreased T_R**

T_R is decreased

↑ I_K ↓ I_{ca}

Reduced APD

+L if atria enlarge

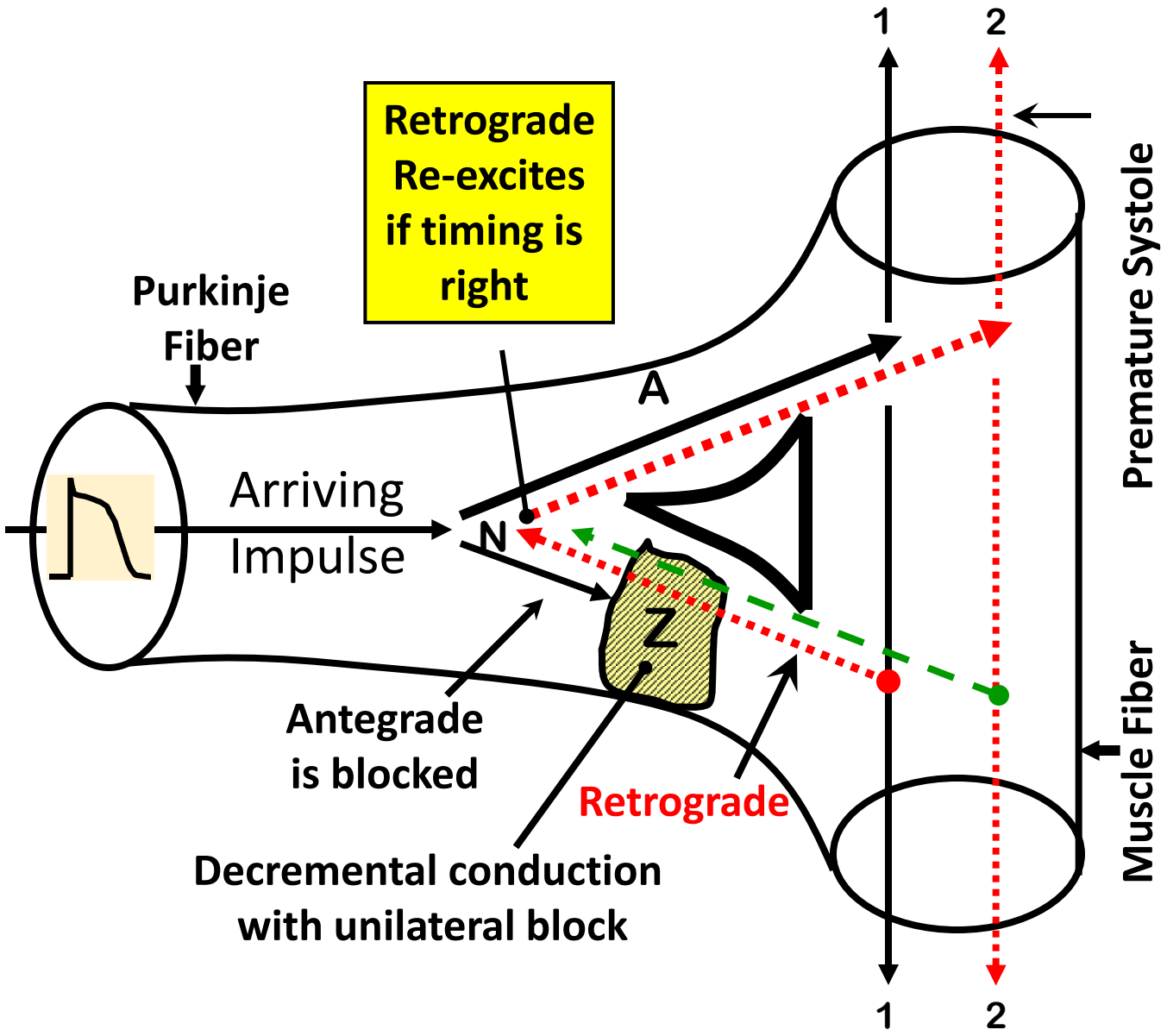
→ + T → Reentry

V decreased (+T) by

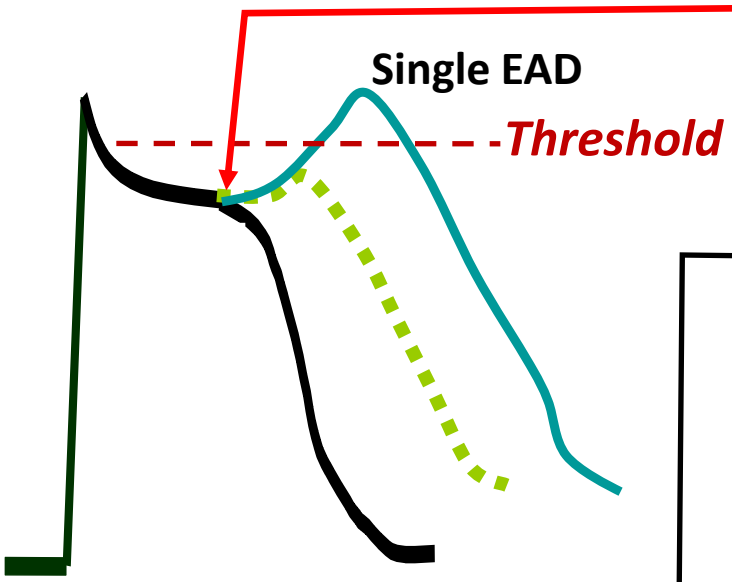
- Tissue Fibrosis
- ↓ I_{Na}
  - ↓ dV_m/dt
  - ↓ AP amp

All these changes favor reentry

Reentrant Induced Arrhythmia



Early Afterdepolarizations (EAD)



Abnormal spontaneous depolarization
During late ϕ2 or during ϕ3

↓ **Due to**

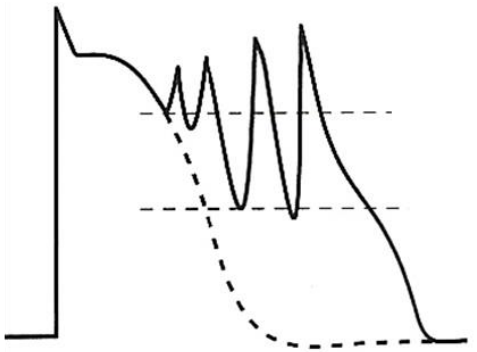
Reactivation of Ca^{++} channels (late ϕ2)
Reactivation of Na^{++} channels (ϕ3)

↓

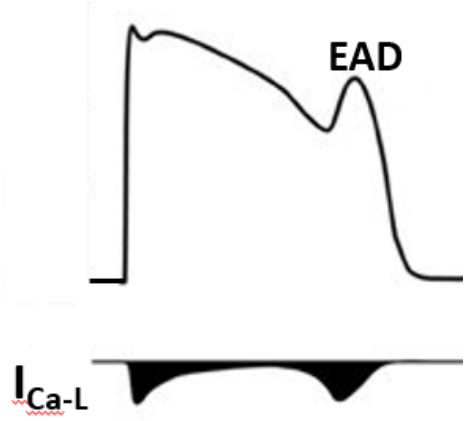
If Threshold Reached

↓

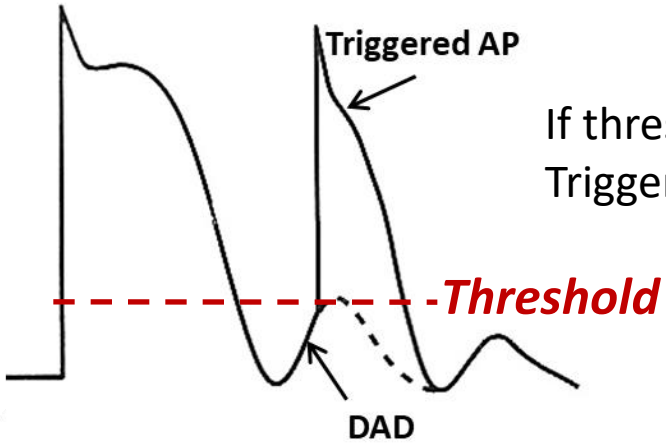
Single EAD → Extra Systole
Multiple EAD → Tachyarrhythmia



- **Re-activated I_{CA-L}**
- **Facilitated if prolonged APD**

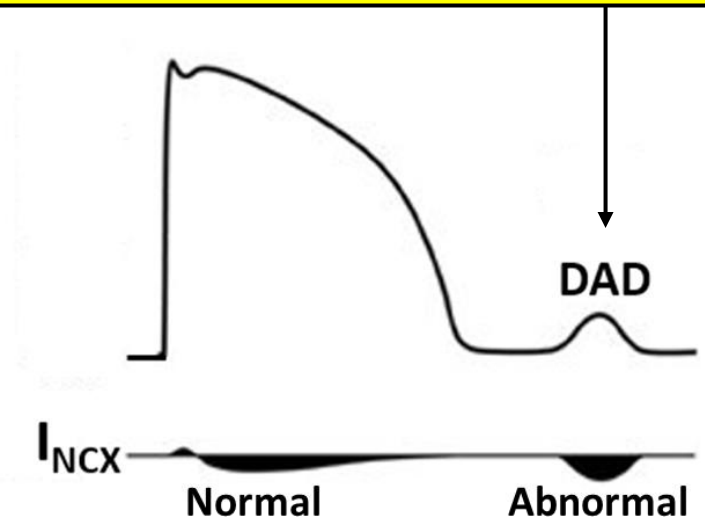


Delayed Afterdepolarization (DAD)

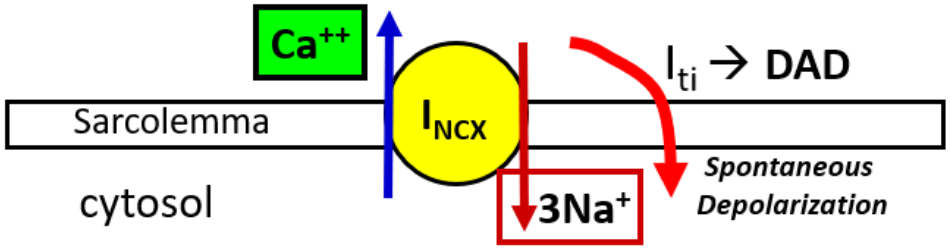


If threshold exceeded results in a Triggered action potential (AP)

DAD occurs after full repolarization (ϕ4)

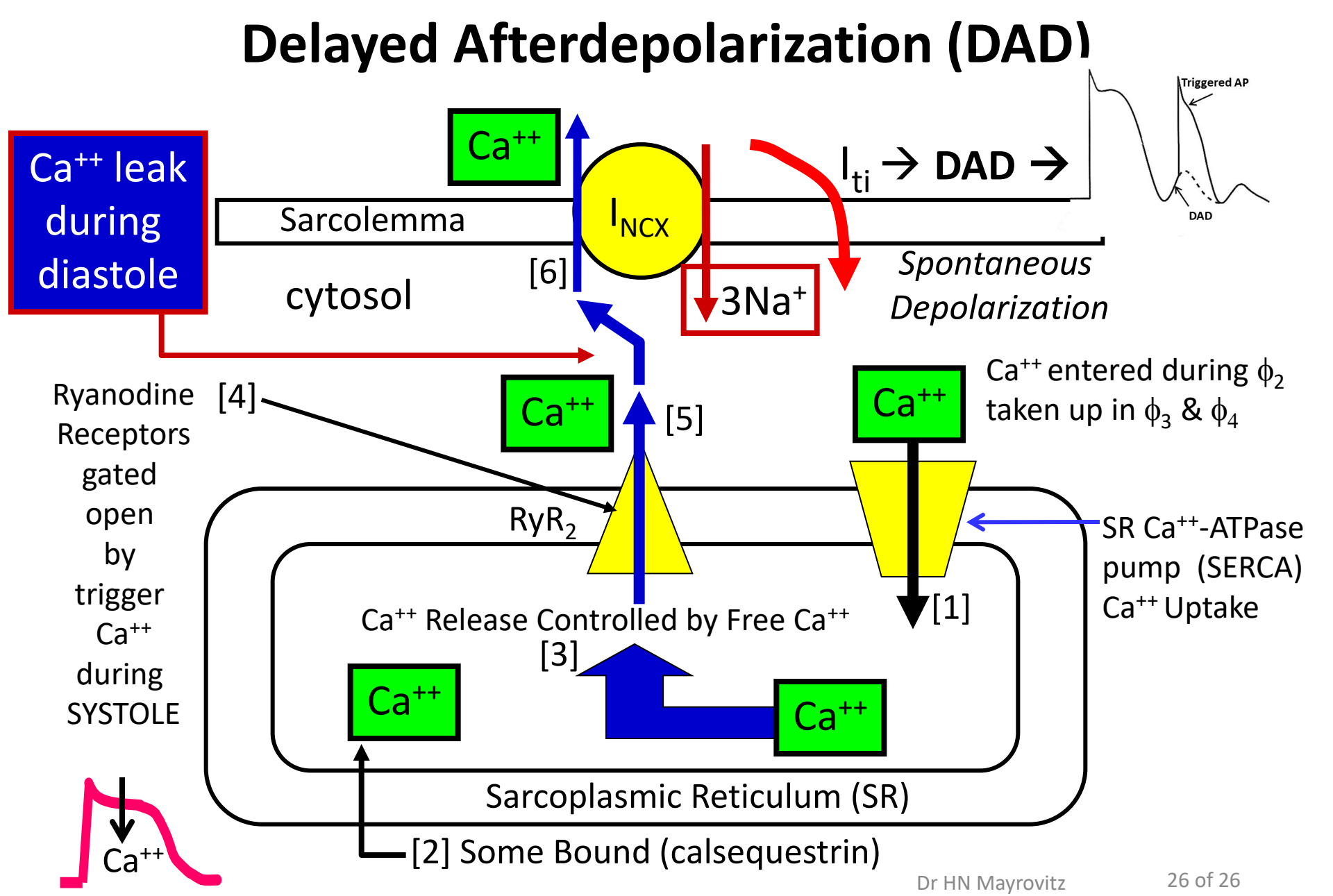


Due to transient Na^+ inward current triggered by Ca^{++} increase acting on Ca^{++}- Na^+ exchanger



Increased intracellular Ca^{++} favors DAD occurrence

Delayed Afterdepolarization (DAD)



If too much free Ca^{++} then abnormal Ca^{++} leak during ϕ_3-ϕ_4

End CV Physiology Lecture 2