THE UNIVERSITY OF MELBOURNE

Melbourne Veterinary School

# Veterinary Bioscience: Cardiovascular System
# Lecture 3: Electrical Activity of the heart

## VETS30014 / VETS90124

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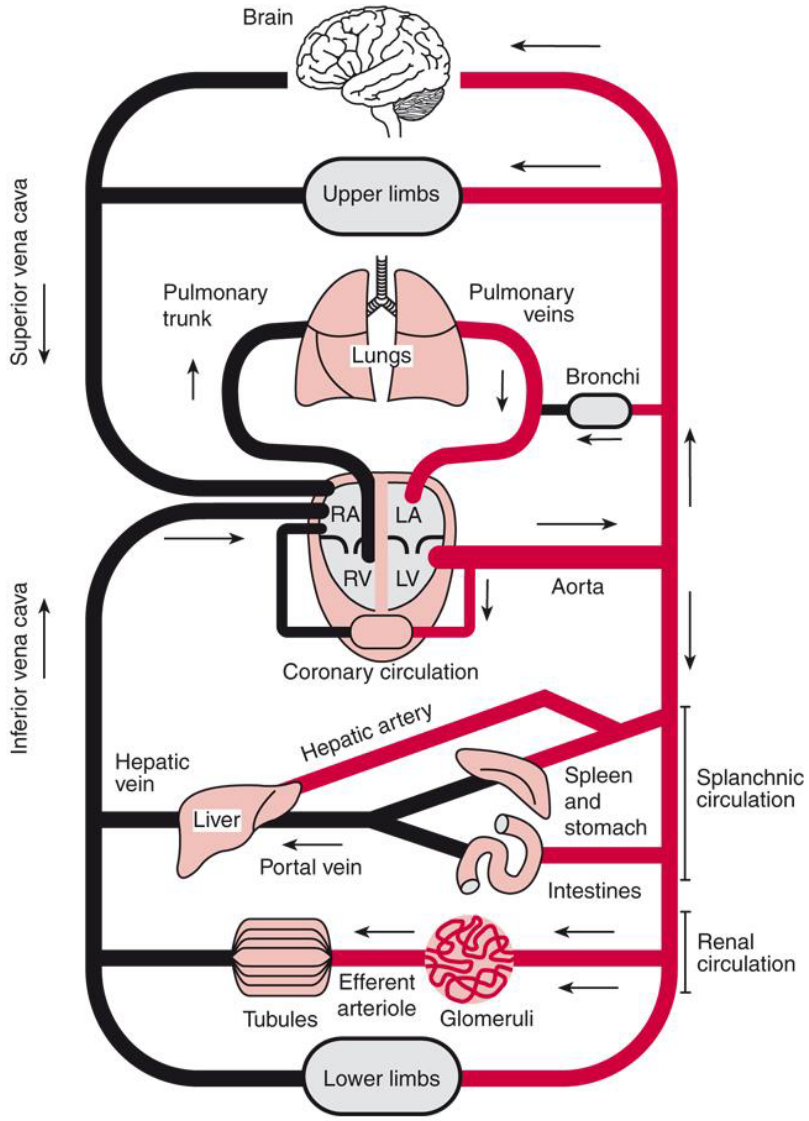
# Lecture 3: Intended learning outcomes

At the end of this lecture you should be able to:

- Describe how the resting membrane potential is created in cardiac myocytes.
- Explain the ionic changes that occur during action potentials in contractile cardiac myocytes and pacemaker cells, including a description of the differences between these
- Identify the refractory period of the cardiac cell electrical cycle, and explain the functional significance of this
- Describe the structural organisation of the pacemaker and conducting tissues of the heart and the normal pathway
of action potential conduction through the heart.
- Describe how cardiac sympathetic and parasympathetic nerves alter heart rate and conduction of cardiac action
potentials.

# Cardiovascular System

- The heart - the driving force
  *propels blood around the body*
- Arterial system
  *the distribution channels*
- The microcirculation
  *the exchange vessels*
- The venous system
  *the blood reservoirs, return blood to the heart*



# Lectures 3&4: How does a heart ‘beat’?

**Lecture 3:**

- Action potentials in cardiac myocytes: how are they generated and coordinated?
- Autorhymicity: how the heart ‘beats’
- Autonomic nervous system control of  HR

**Lecture 4:**

- Mechanical activity of the heart
- How the electrical activity links to mechanical activity
- Cardiac muscle cell performance (contractility)

# Electrical Activity of the Heart: how does the heart 'beat'?

- Contraction is triggered by action potentials (AP) sweeping across the cell membrane

- The heart beats rhythmically due to AP it generates itself – this property is called **'autorhythmicity'**

- Two specialised types of cells:
  1. *Contractile cardiac muscle cells*: do the mechanical work of pumping . They do not normally initiate their own AP

  2. *Autorhythmic ('pacemaker') cells:* specialised for initiating and conducting the AP that contract the contractile cardiac muscle cells. They do not contract.

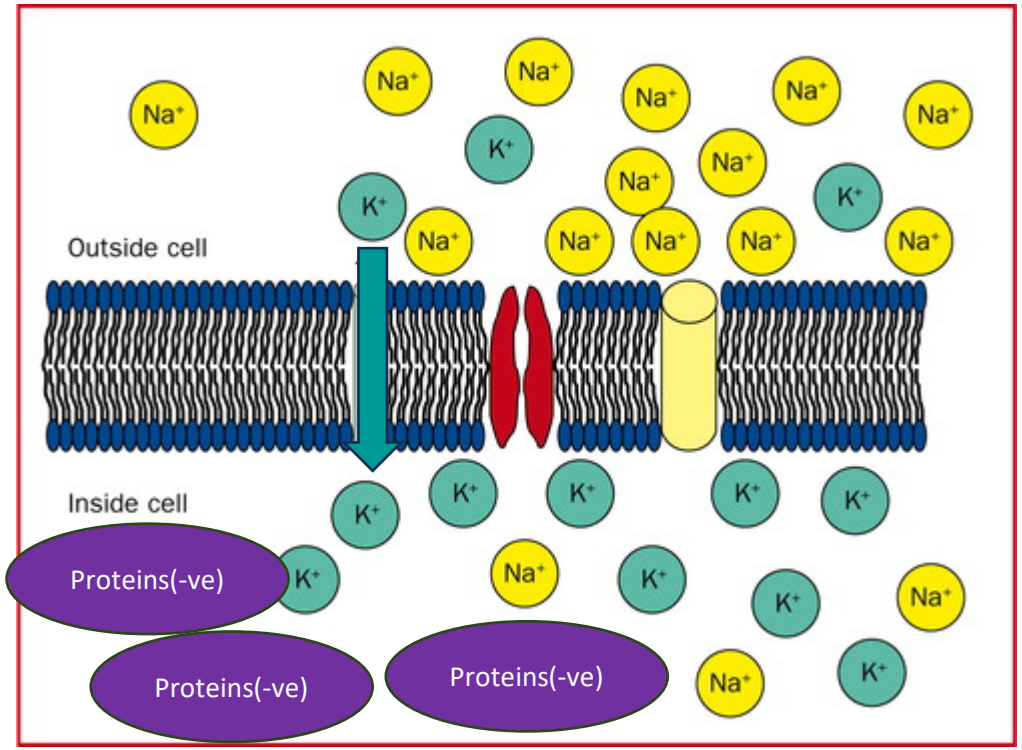
We will first look at action potentials in the *contractile cardiac muscle cells*

# Contractile Cardiomyocyte: resting potential

**Key idea:** *All cells have an electrical potential across their membranes, caused by separation of electrical charges across the membrane*

In cardiac muscle cells:

- Fixed proteins (negative charge) inside the cell
- Cell membrane permeable to $K^+$ ions - these move freely to balance change
- Balance of $K^+$ is controlled by opposing electrical and concentration gradients
- This creates the membrane potential (Nernst equation): - 90 mV

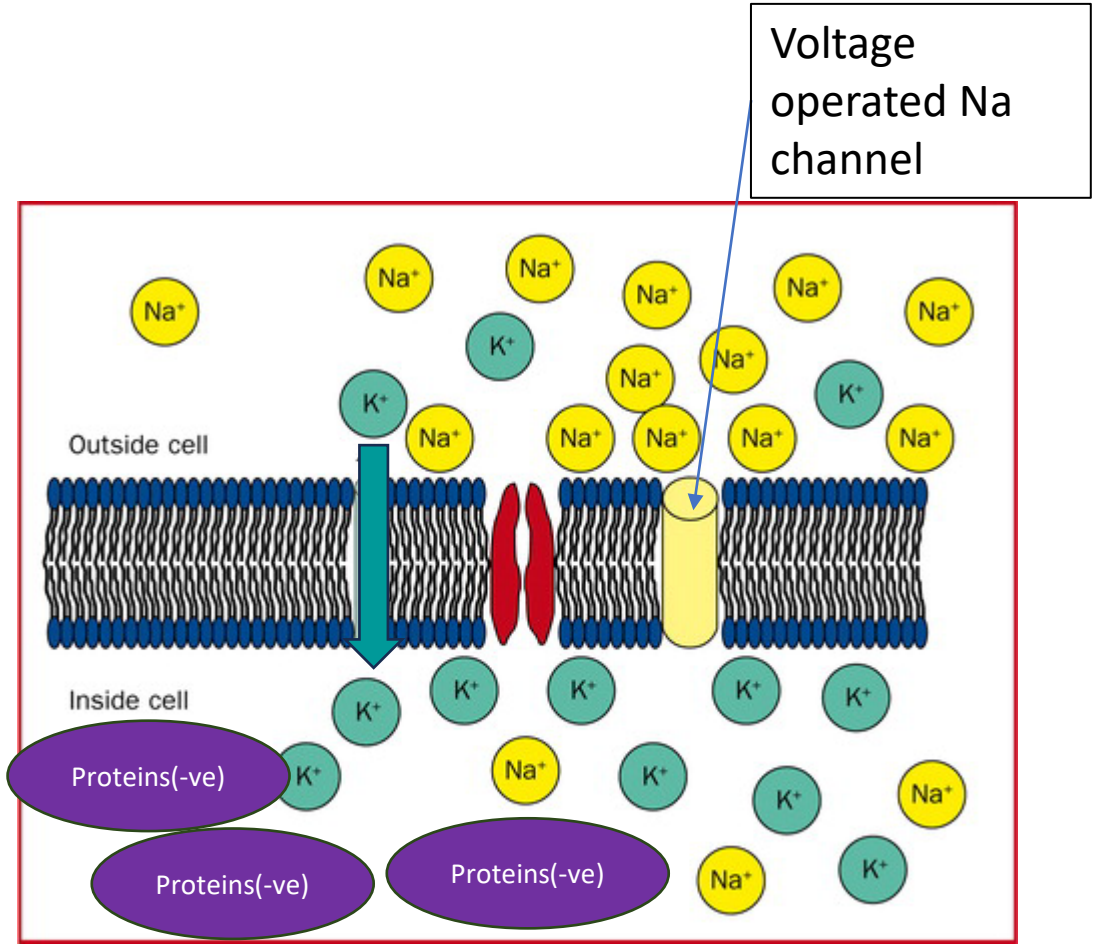



https://www.magonlinelibrary.com/doi/abs/10.12968/bjca.2015.10.3.140

**Resting membrane potential depends on differing $K^+$ concentrations across the membrane**

# Cardiomyocyte: resting potential

- Resting membrane potential dependent differing $K^+$ concentrations across the membrane
- Ion channels can be receptor or voltage-operated
- Voltage operated:
  - Controlled by changes in membrane potential
  - $Na^+$ channels involved in generation of AP
  - Once channel is open, ions enter passively down concentration gradient

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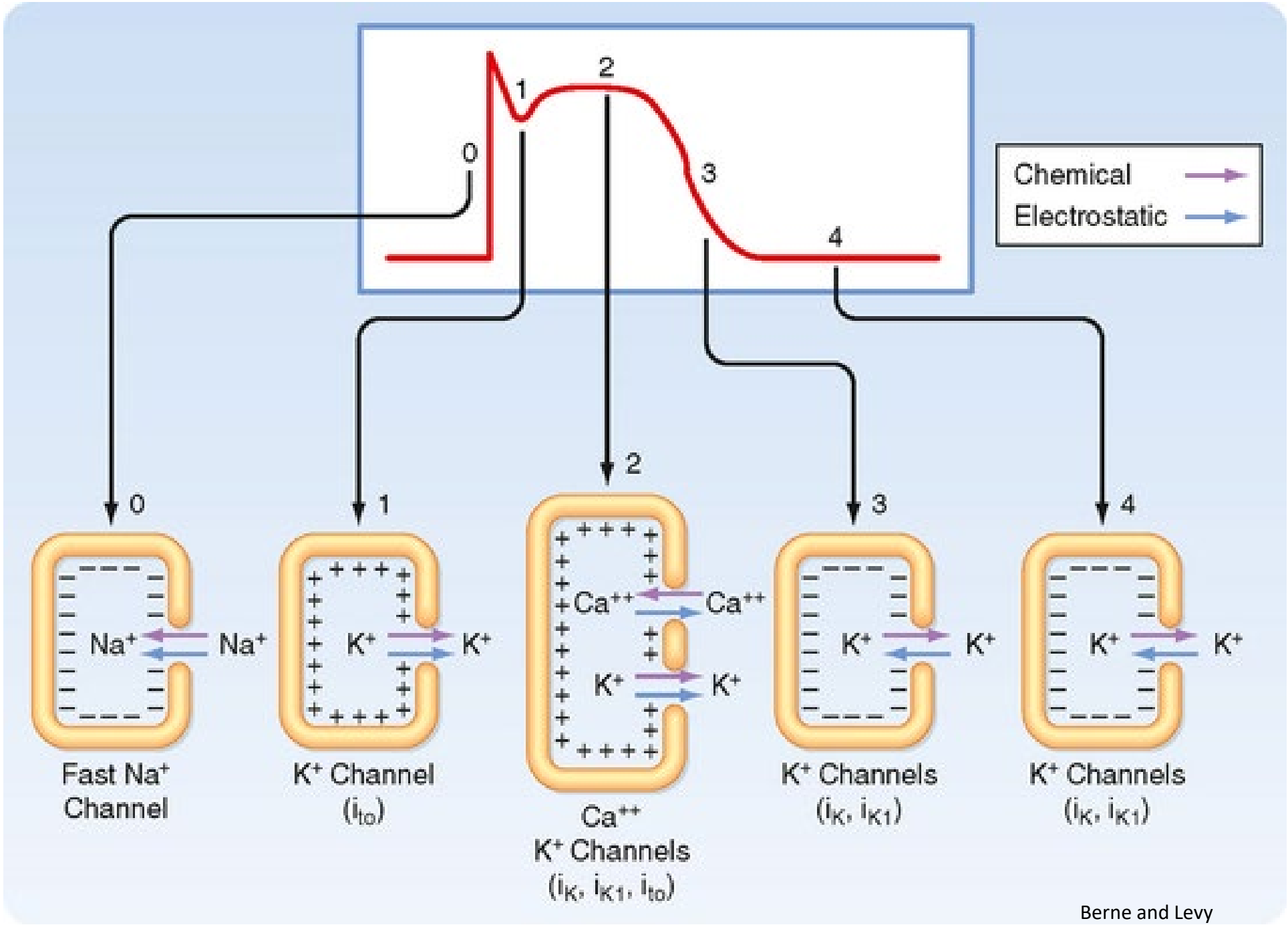


Berne and Levy

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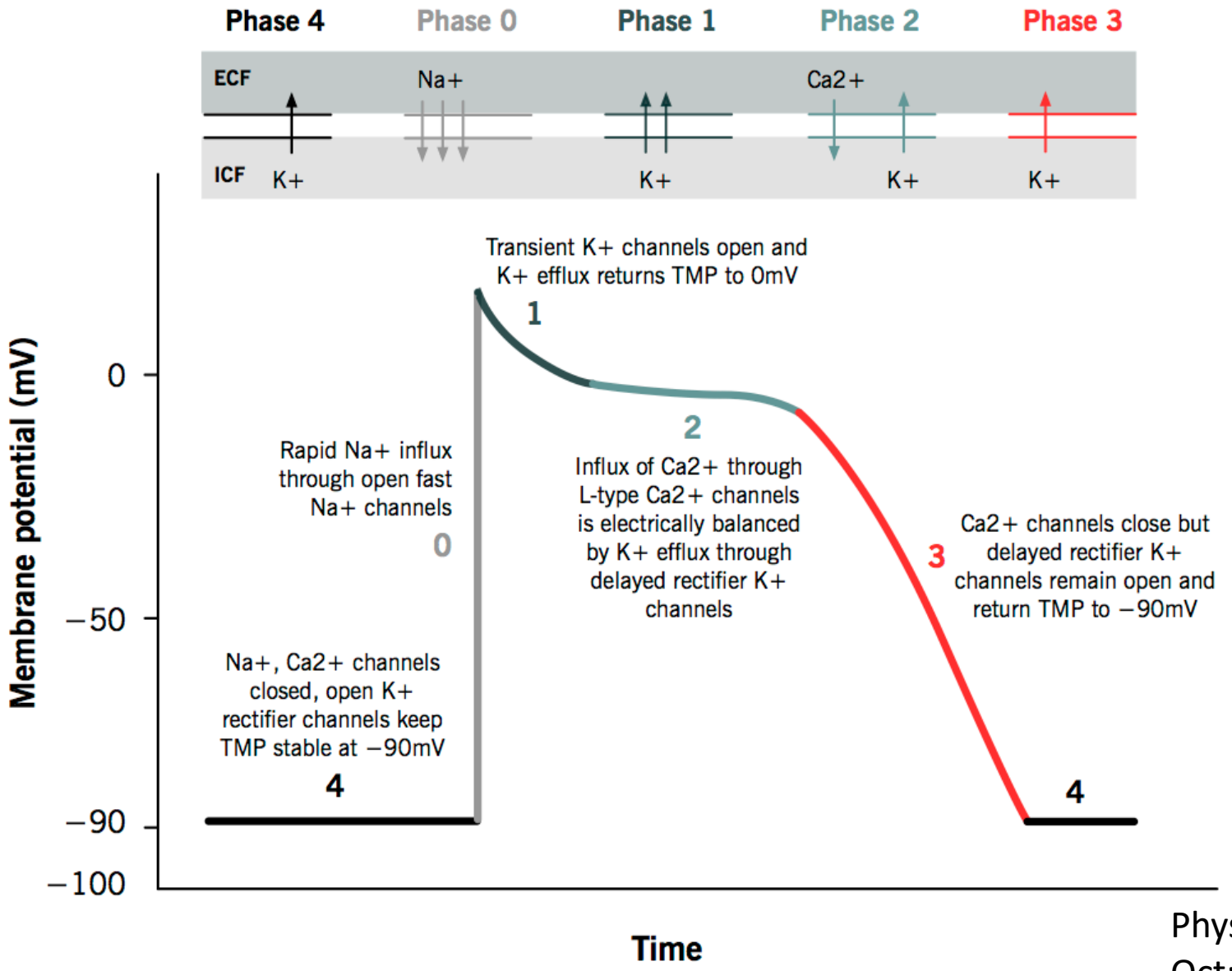
# Action potential of cardiac muscles

Grigoriy Ikonnikov and Eric Wong



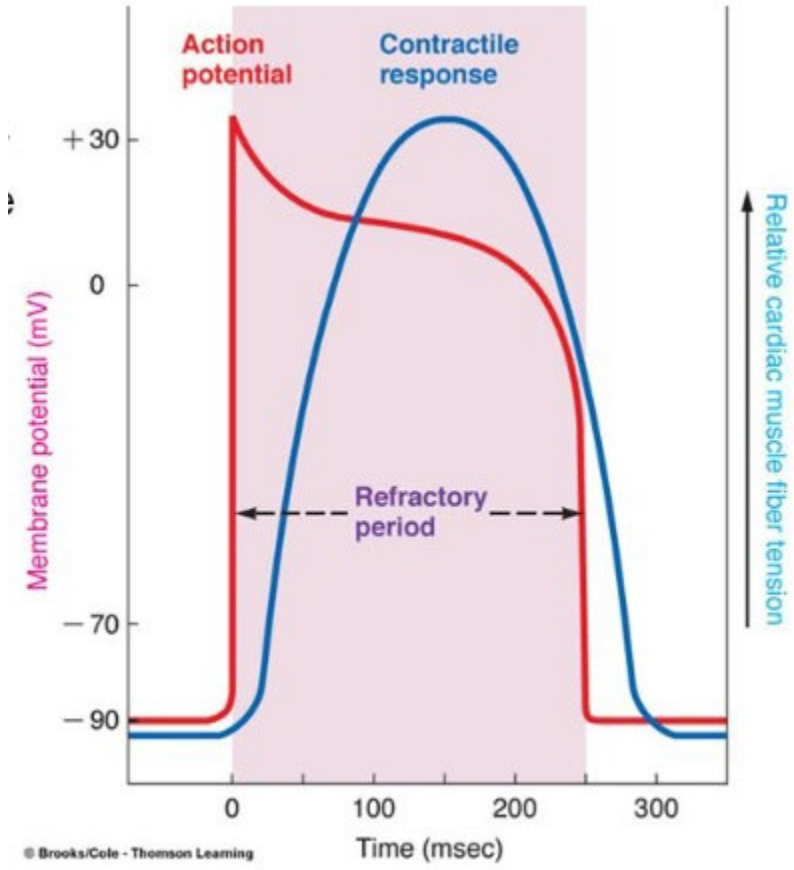

Physiol Rev. 2005 Oct;85(4):1205-53

# Refractory period: a special feature of cardiac myocytes

- AP are long – one AP per contraction
- Extended absolute refractory state

- Voltage-operated $Na^+$ channels inactivated at the end of Phase 0;

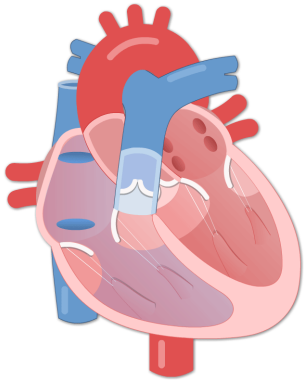
  → they cannot reactivate until membrane potential drops

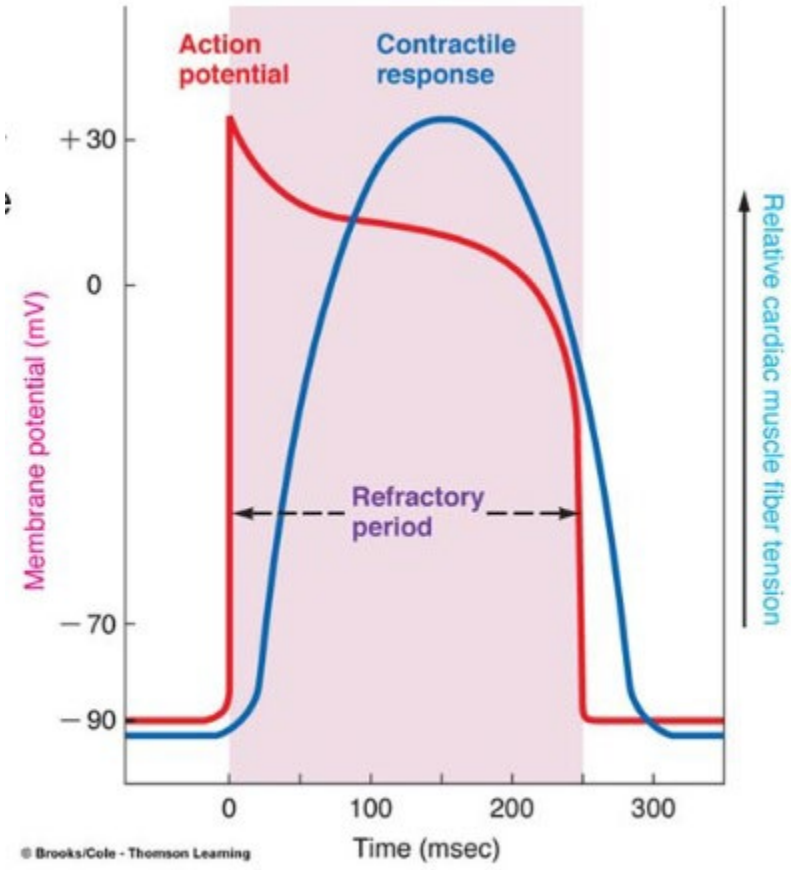


# Refractory period: a special feature of cardiac myocytes

Why is this important?

- Cardiac muscle cannot be restimulated until contraction is almost over
- Sustained maximal contraction '*tetanus*' cannot occur
- Pumping blood requires alternate phases of contraction (emptying) and relaxation (filling)





# Electrical Activity of the Heart: how does the heart 'beat'?

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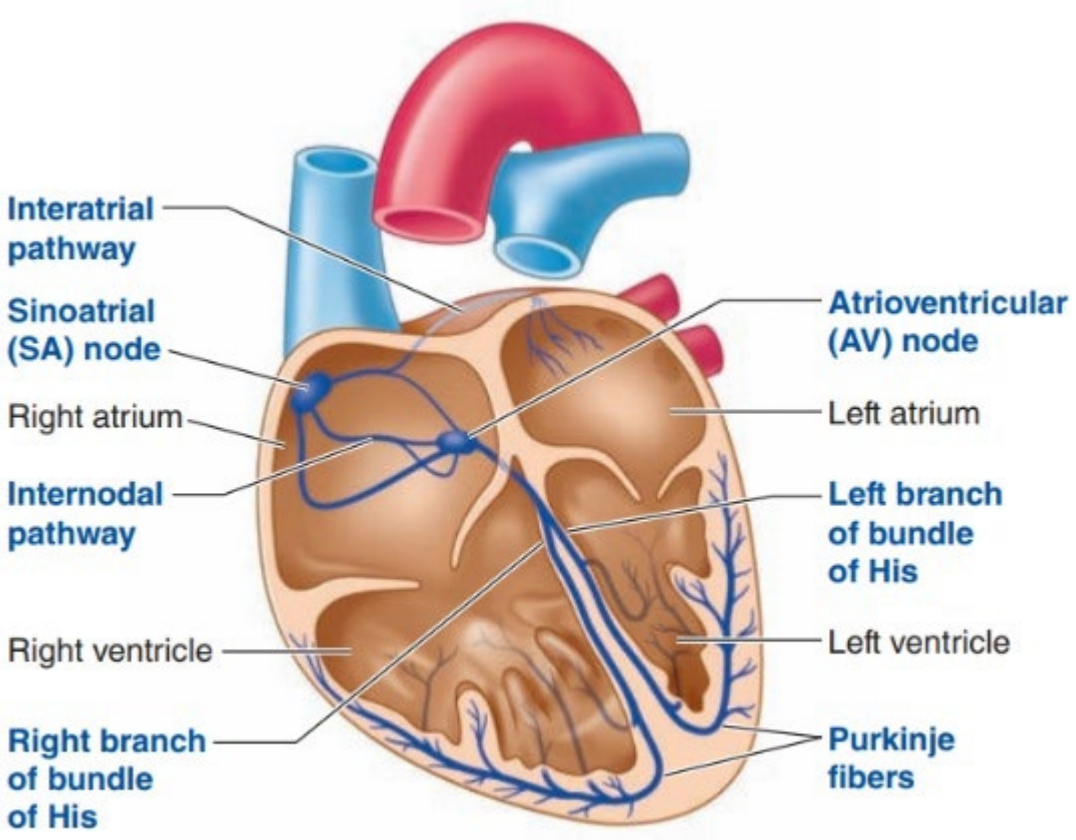
# Cardiac autorhythmic cells display pacemaker activity

- The heart contracts as a result of AP it generates itself
- This ‘autothythmicity’ is a function of specialised pacemaker cells
- They initiate AP that spread through the heart to trigger rhythmic beating (without nervous stimulation)



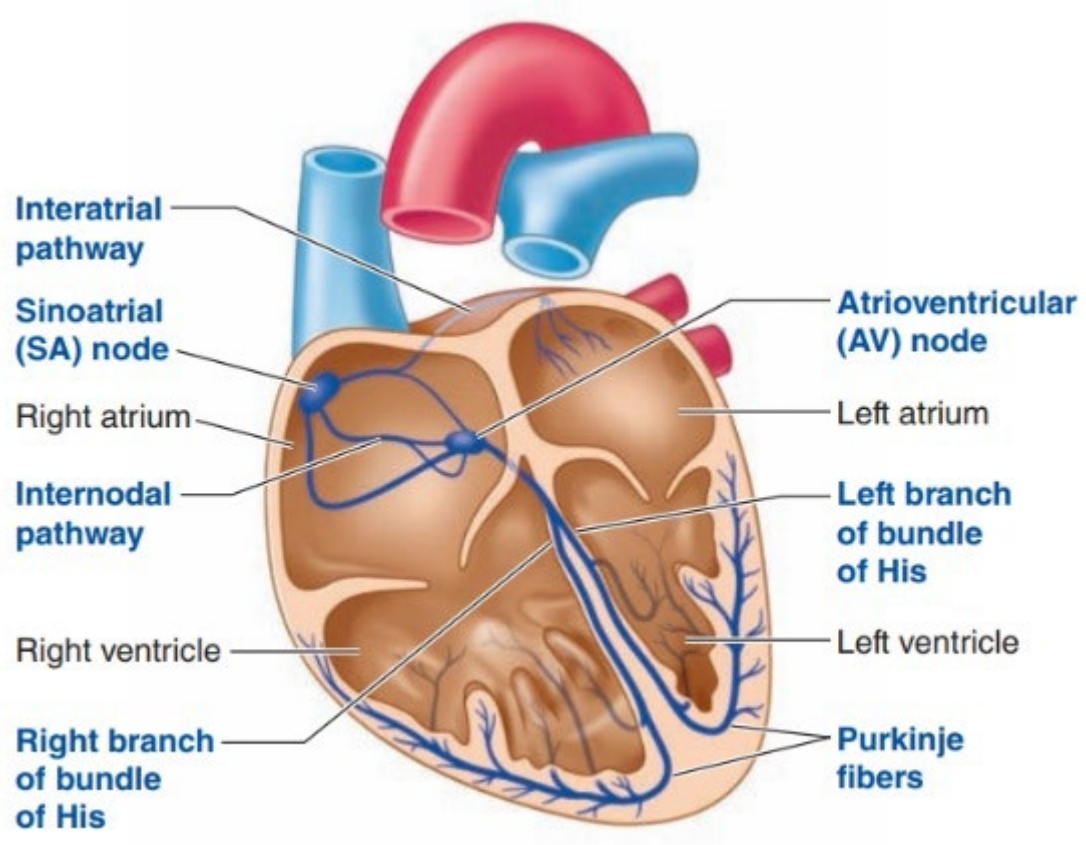

**(a)** Specialized conduction system of the heart

Sherwood 2015

# Cardiac autorhythmic cells display pacemaker activity

Autorhythmic ‘pacemaker’ cells are located in:

1. **Sinoatrial node (SA node)**: located in right atrial wall
2. **Atrioventricular node (AV node**): located at base of right atrium
3. **Bundle of His:** originates at the AV node, enters the IV septum, then divides into left and right bundle branches
4. **Purkinje fibres**: small terminal fibres that extend from bundle of His




(a) Specialized conduction system of the heart

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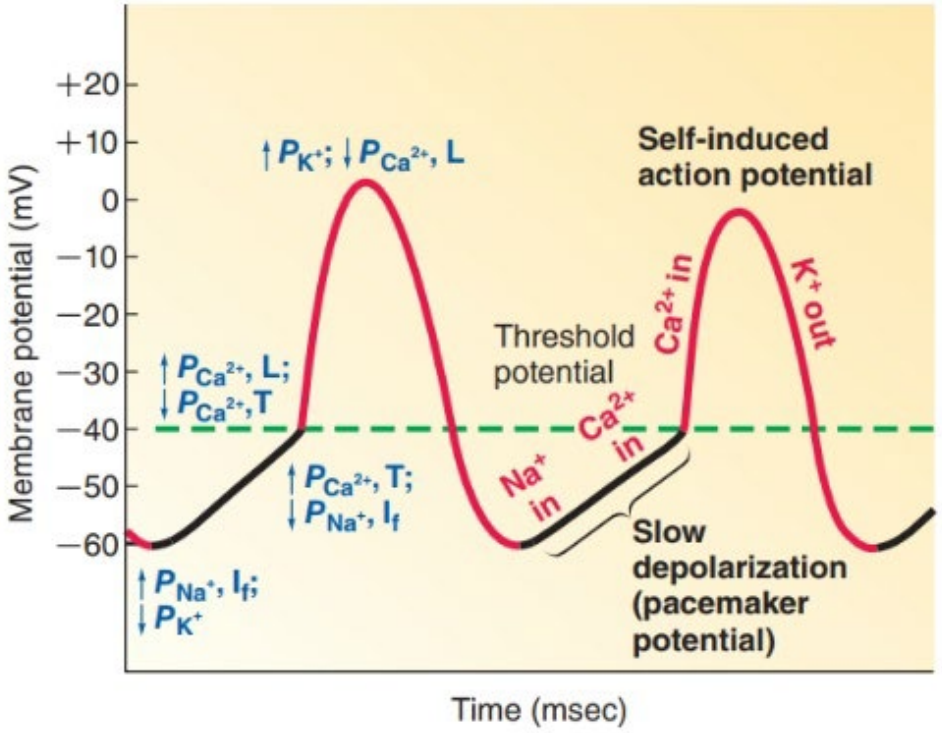
# Pacemaker cell action potentials

- Pacemaker cells do not have a constant ‘resting potential’
- Their membrane potential slowly depolarises (drifts) between action potentials

- Cyclically initiate Aps that are conducted through the heart to trigger rhythmic beating – with no nervous stimulation!

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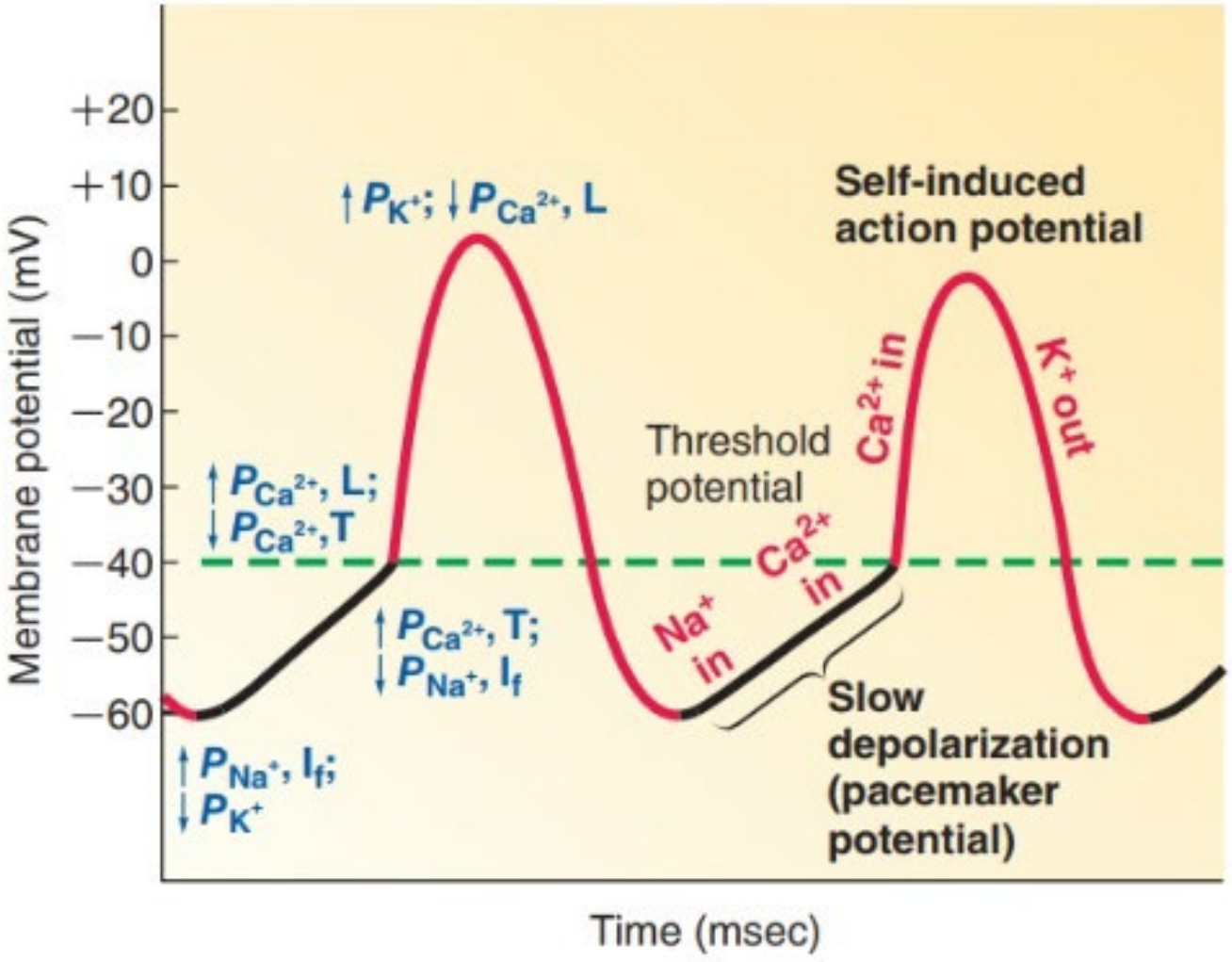
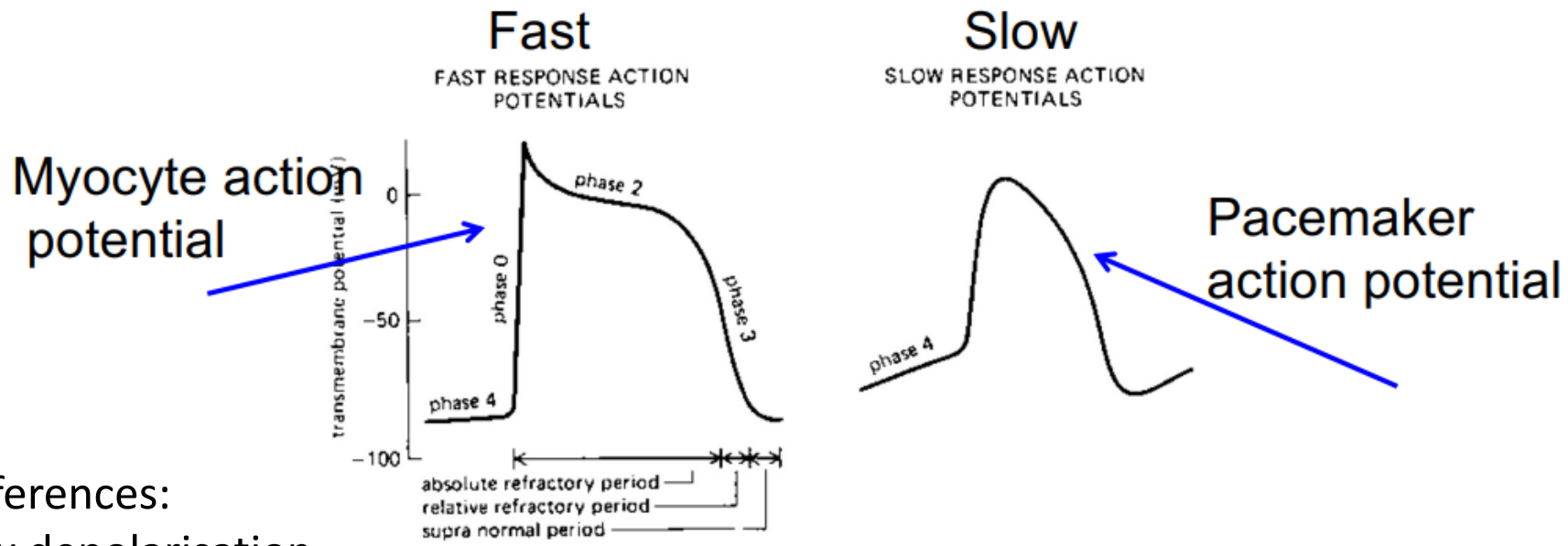
# Pacemaker cell action potentials



# ‘Fast’ and ‘Slow’ action potentials




Key differences:

- Slow depolarisation
- Shorter plateau
- Unstable resting potential
- No voltage-operated $Na^+$ channels
- Threshold for depolarisation is more positive (due to dependence on voltage operated $Ca^{2+}$ channels)
- Permeability to $K^+$ does not remain constant between APs

# The sinoatrial node is the pacemaker of the heart

- Autorhythmic tissues exhibit different rates of depolarisation

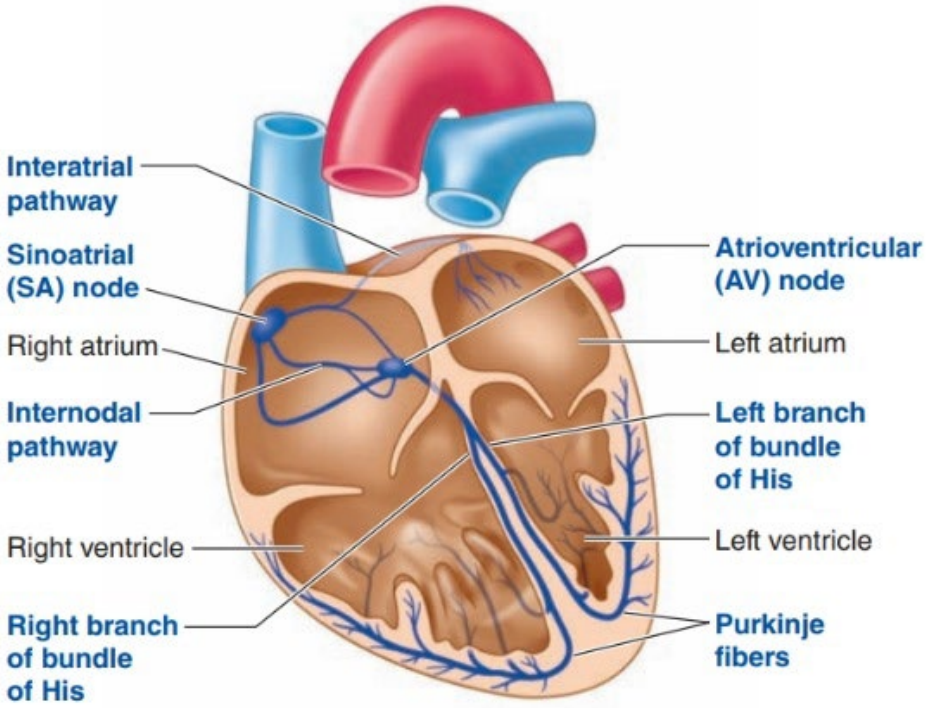
  **SA node > AV Node > Bundle of His > Purkinje Fibres**

- Tissues with faster rate of depolarisation generate action potentials more frequently

- Cells in the SA node have the fastest rate of AP initiation

- AP are transmitted through the conduction system and via gap junctions (more about these soon!) to the rest of the myocardium

- SA node is the pacemaker of the heart – the entire heart beats at the pace set by the SA node!




(a) Specialized conduction system of the heart

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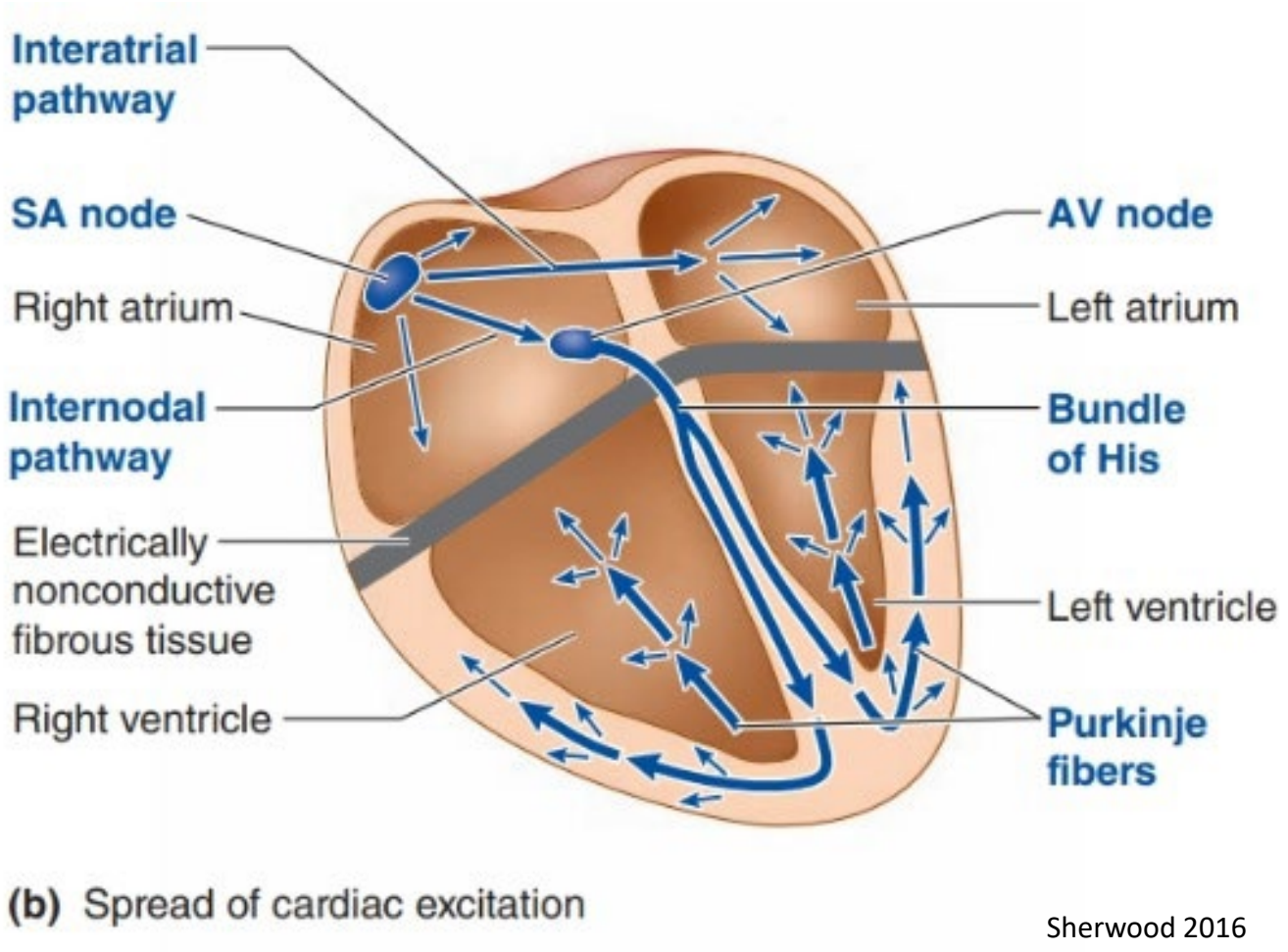


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The rate set by the SA node is called the **SINUS RHYTHM**

# Anatomy of the conducting system of the heart

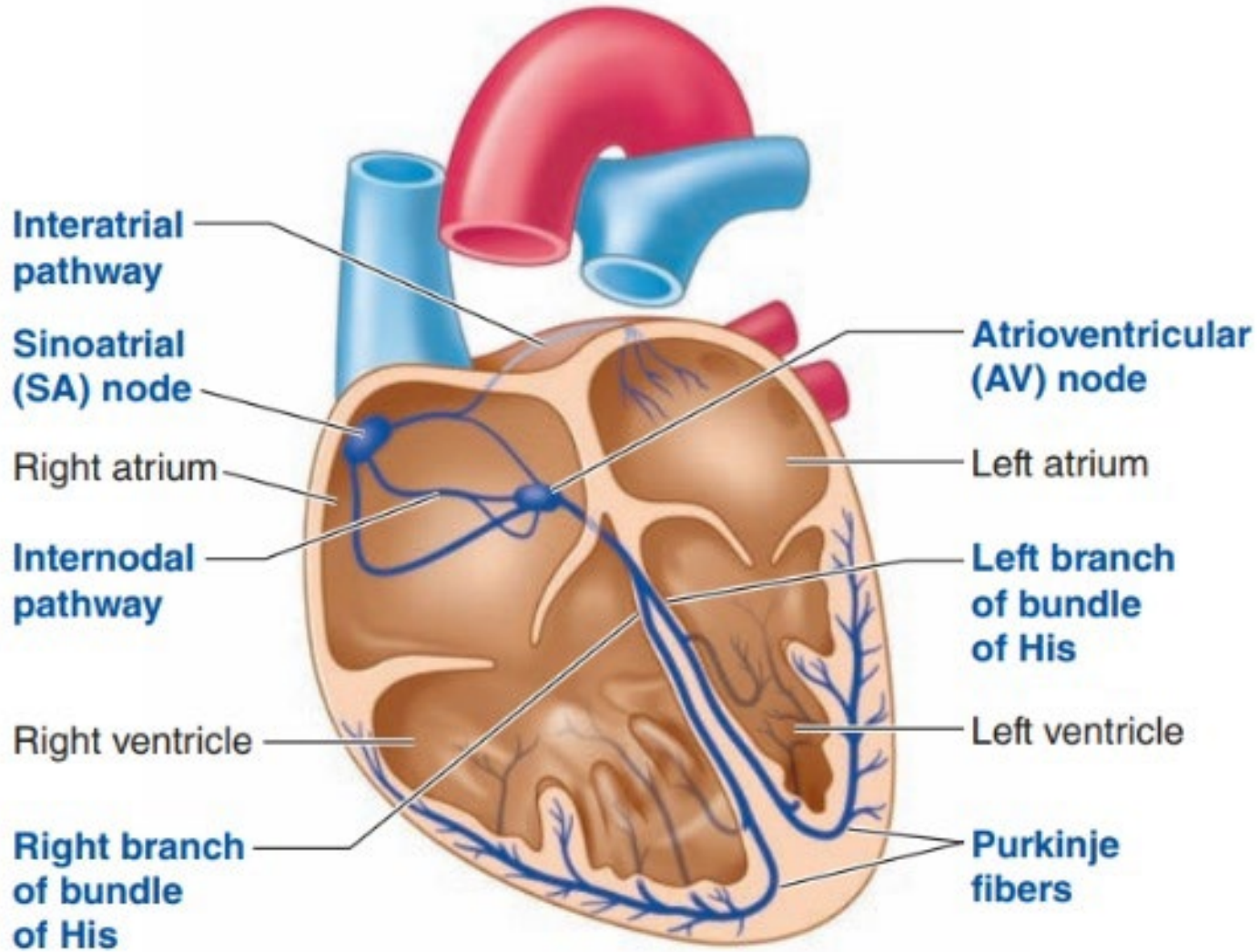
**1. Sinoatrial node (SA node**): in the right atrial wall

**2. Atrioventricular node (AV node):** located at base of right atrium

**3. Bundle of His:** originates at the AV node, enters the IV septum, then divides into left and right bundle branches

**4. Purkinje fibres:** small terminal fibres that extend from bundle of His

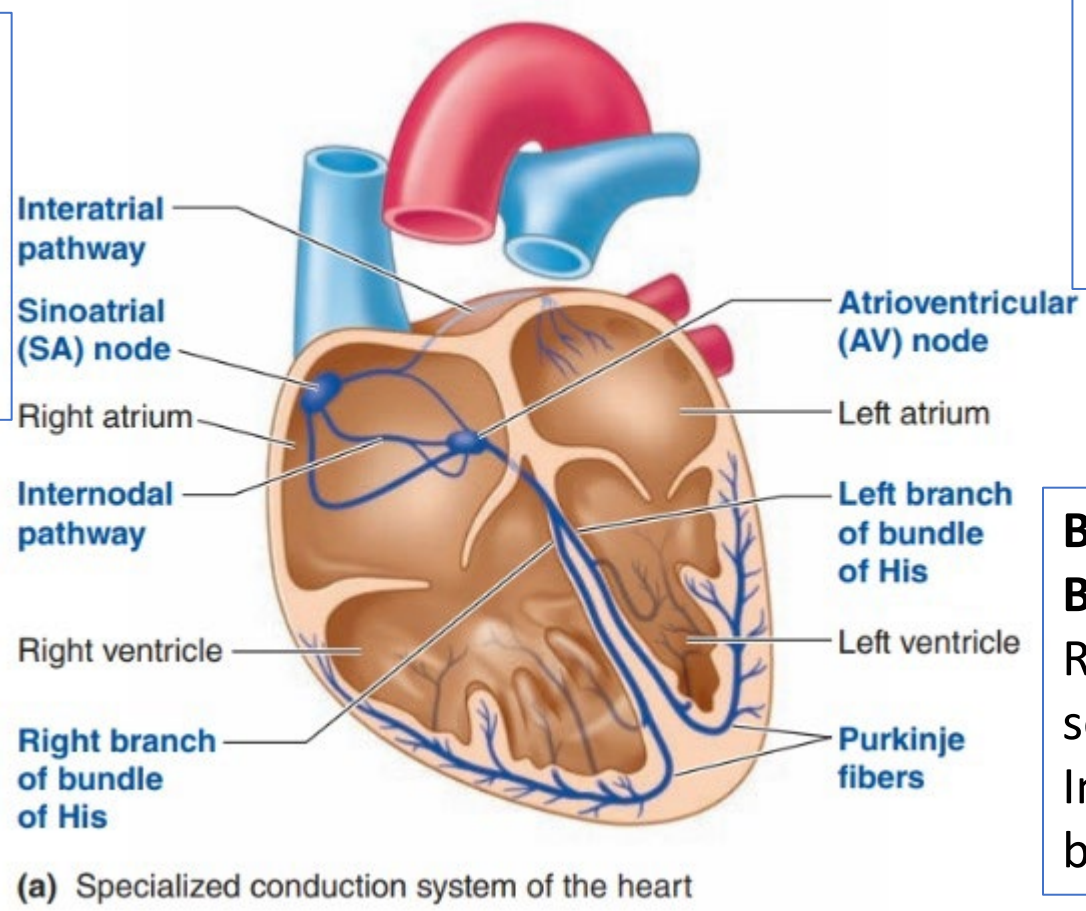
All are comprised of modified cardiac muscle cells




(a) Specialized conduction system of the heart

# Anatomy of the conducting system of the heart

**SA node**
- Lateral wall of RA
- Near junction of CrVC
- Mass of nodal myocytes
- Microscopic



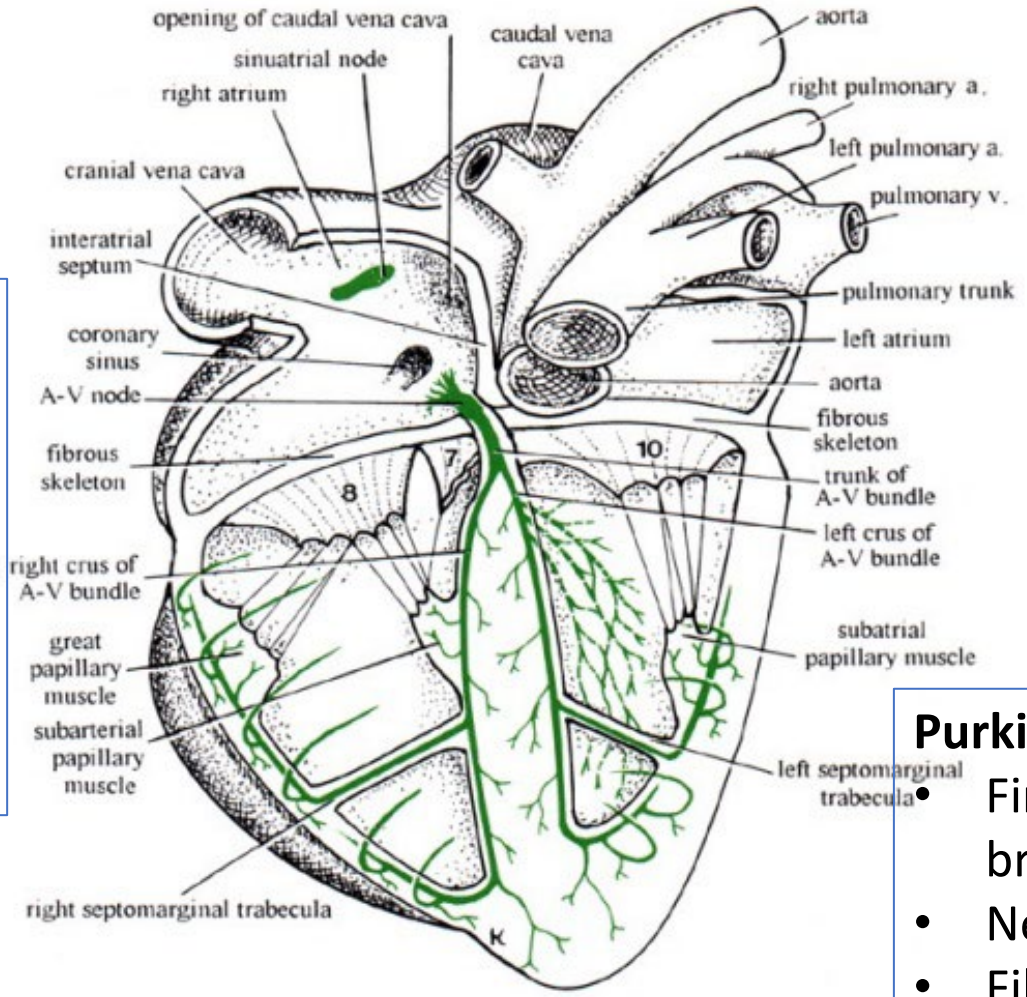
(a) Specialized conduction system of the heart

**AV node**
- Floor of RA , at junction of interatrial septum
- Microscopic

**Bundle of His/ Atrioventricular (AV) Bundle:**
Runs from AV node to dorsal IV septum
Immediately divides into R and L branches

**Right crus**
**(also called R bundle branch):**

- Runs to the apex in the subendocardium of the IV septum
- Branches to papillary muscles, outer wall of R ventricle




**Left crus (L bundle branch):**

- Subendocardial branches over surface of L ventricle
- Runs to the apex, up the outer wall of L ventricle
- Papillary muscles on outer wall

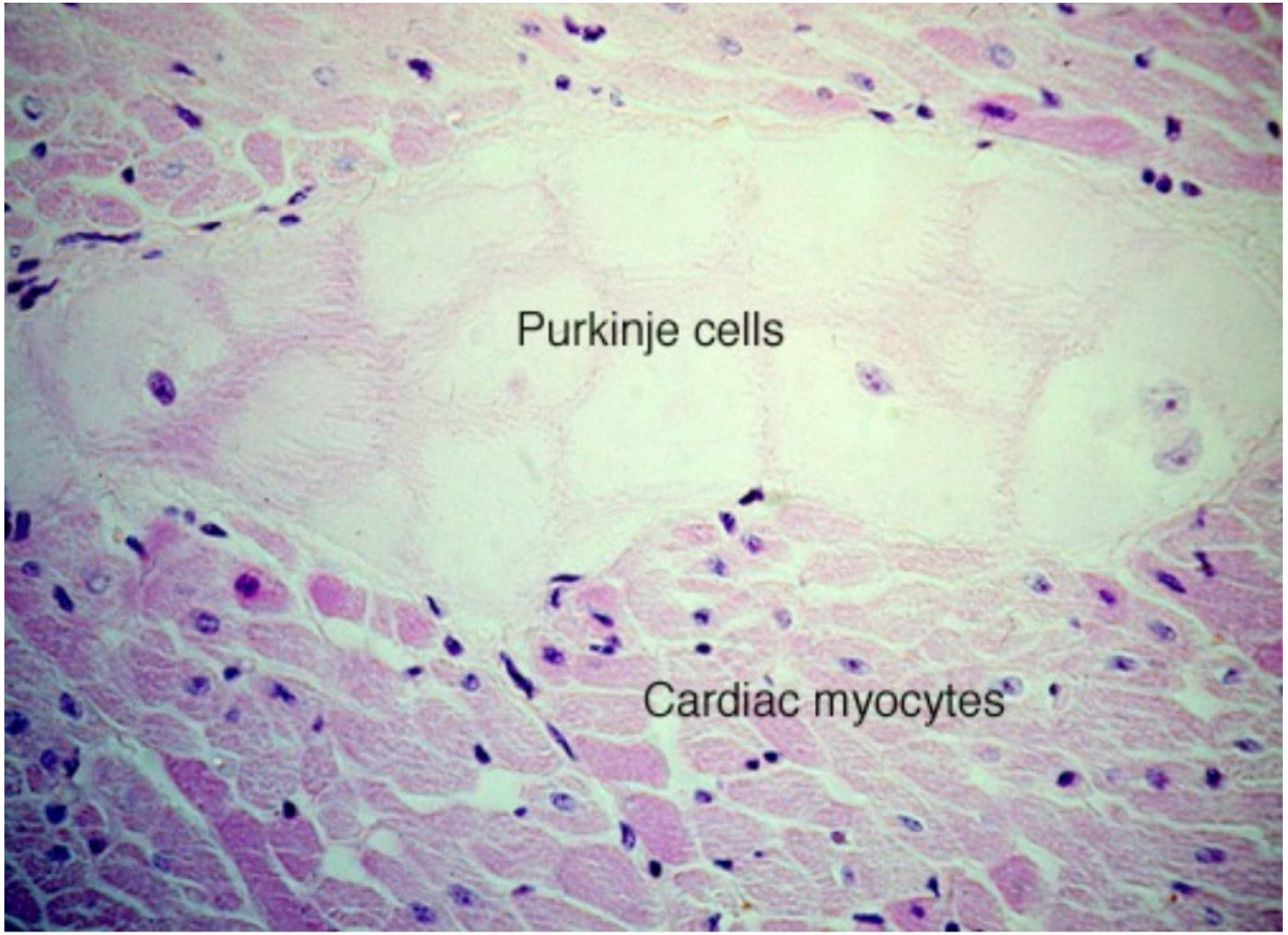
**Purkinje fibres:**

- Final extensions of R & L bundle branches
- Network of subendocardial fibres
- Fibre bundles enclosed in CT
- Fibres pass into cardiac muscle cells

# Conducting System Histology

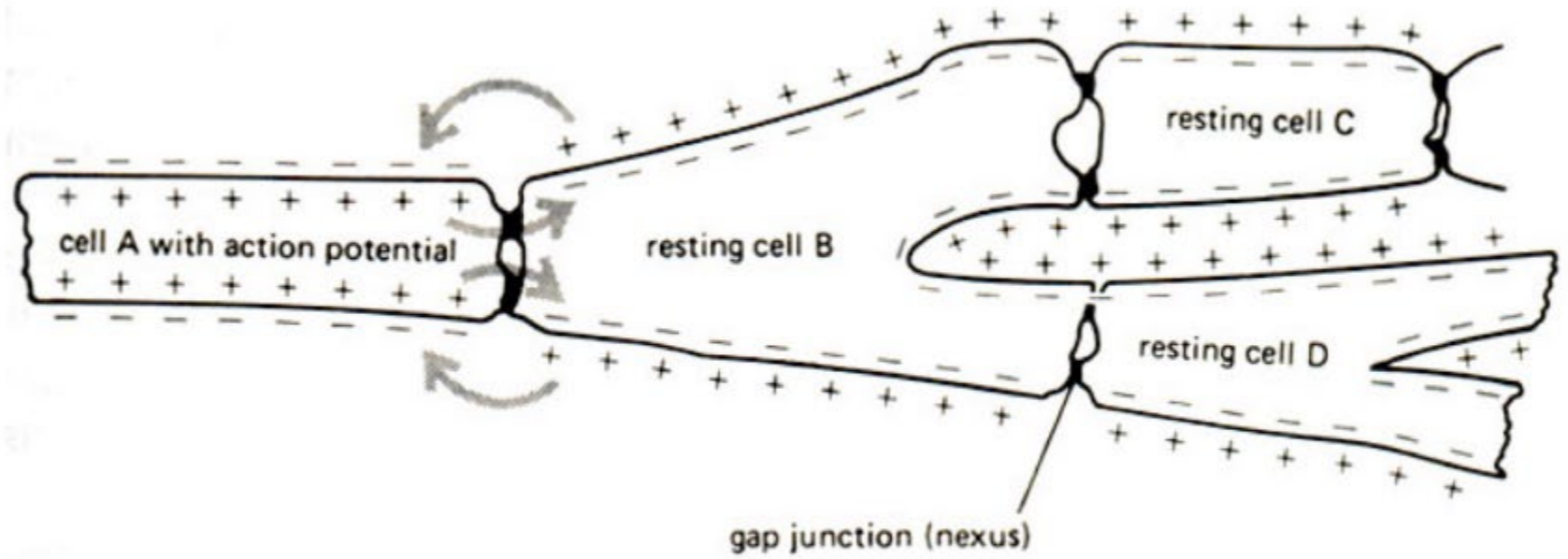
## Purkinje cells

- Specialised cardiac myocytes, not nerve cells
  - Large diameter
  - Pale central area (glycogen)
  - Marginalisation of myofibrils around periphery
  - Chains of Purkinje cells make Purkinje fibres



# Cardiac muscle fibres are connected by intercalated disks

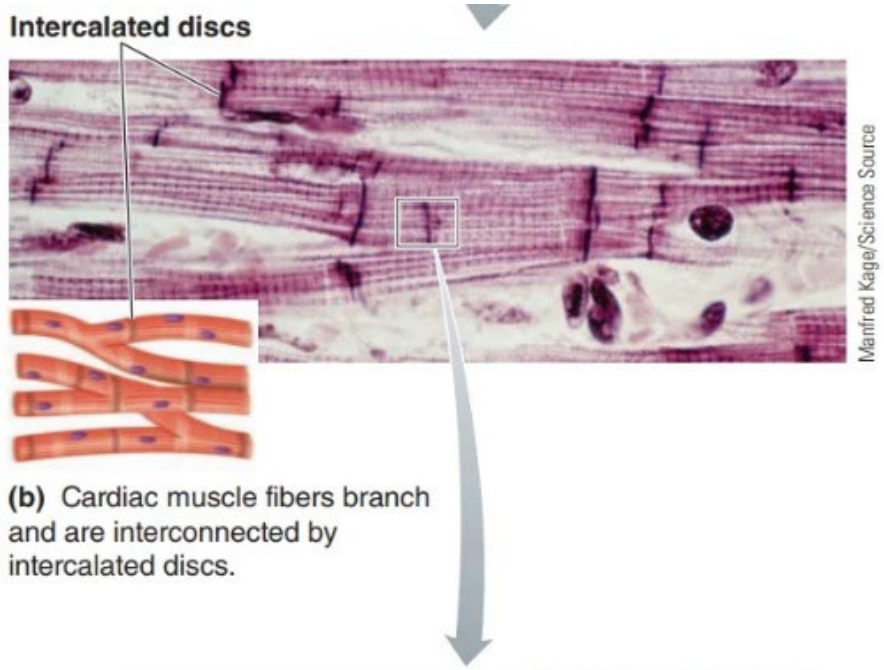
- Cardiac muscle cells are connected to form branching fibres
- Adjacent cells joined by intercalated discs




*Mohrman & Heller p31*

Within an intercalated disc, there are two types of membrane junctions:

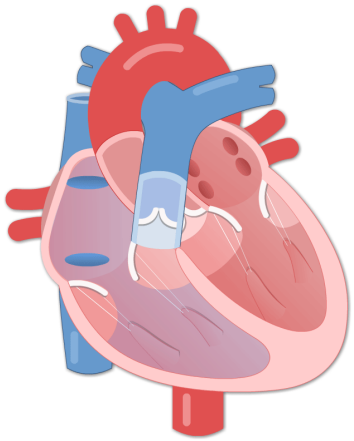
- **Desmosome** – mechanically holds cells together
- **Gap junction-** areas that allow action potentials to spread quickly between cells

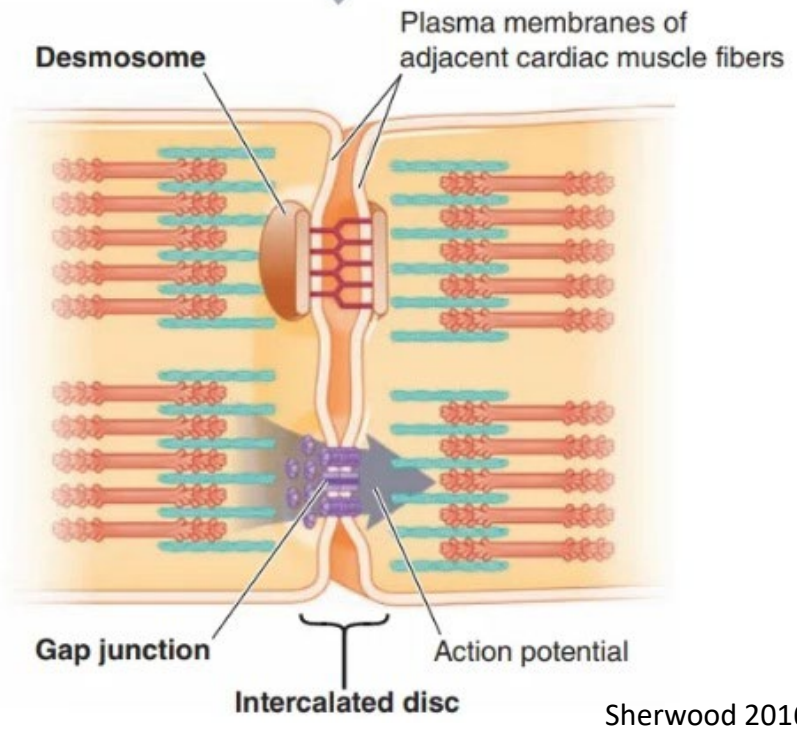



- Impulses generated in one part of the heart spread quickly across the heart

- Conduction velocity varies across the different tissues – slower through AV node

**All the cells contract or none do – no 'half-hearted' contraction!!**



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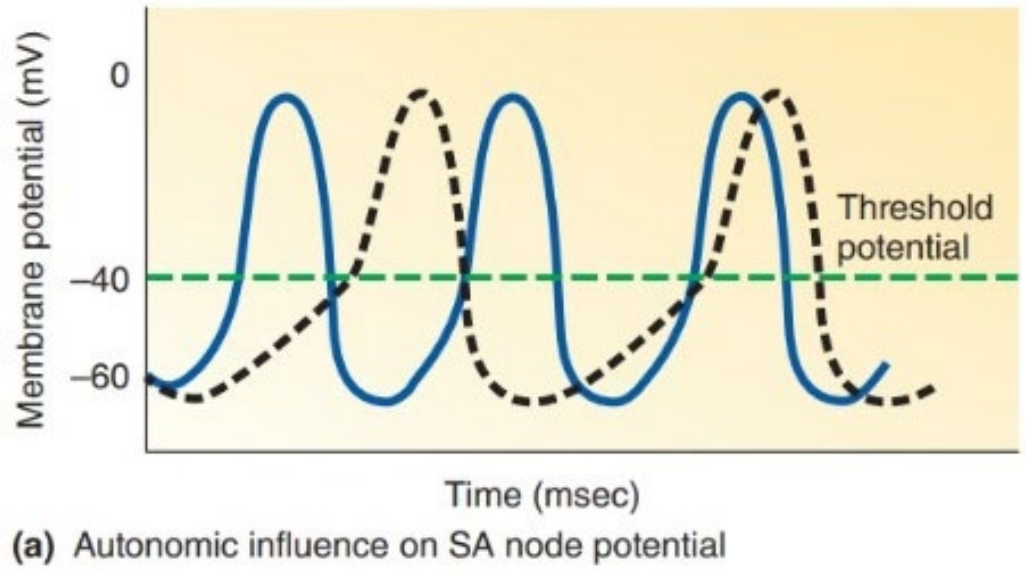
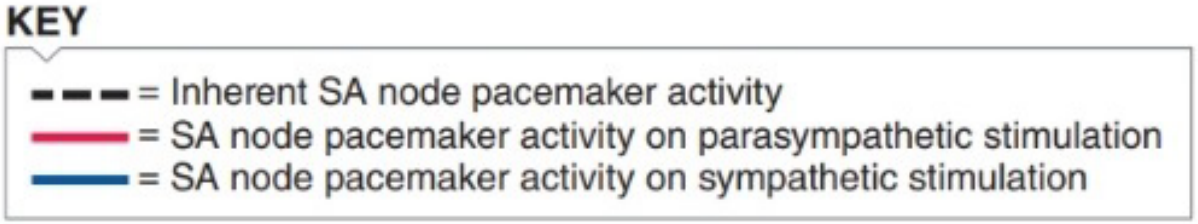
# Control of heart rate

- SA node depolarises independently
- Heart rate is influenced by neural and hormonal factors
- Heart is innovated by both divisions of the autonomic nervous system
    - Sympathetic stimulation will ↑HR
    - Parasympathetic stimulation (vagus nerve) will ↓HR
- Circulating adrenaline (hormonal factor) also increases HR

# Effect of sympathetic stimulation



(a) Autonomic influence on SA node potential

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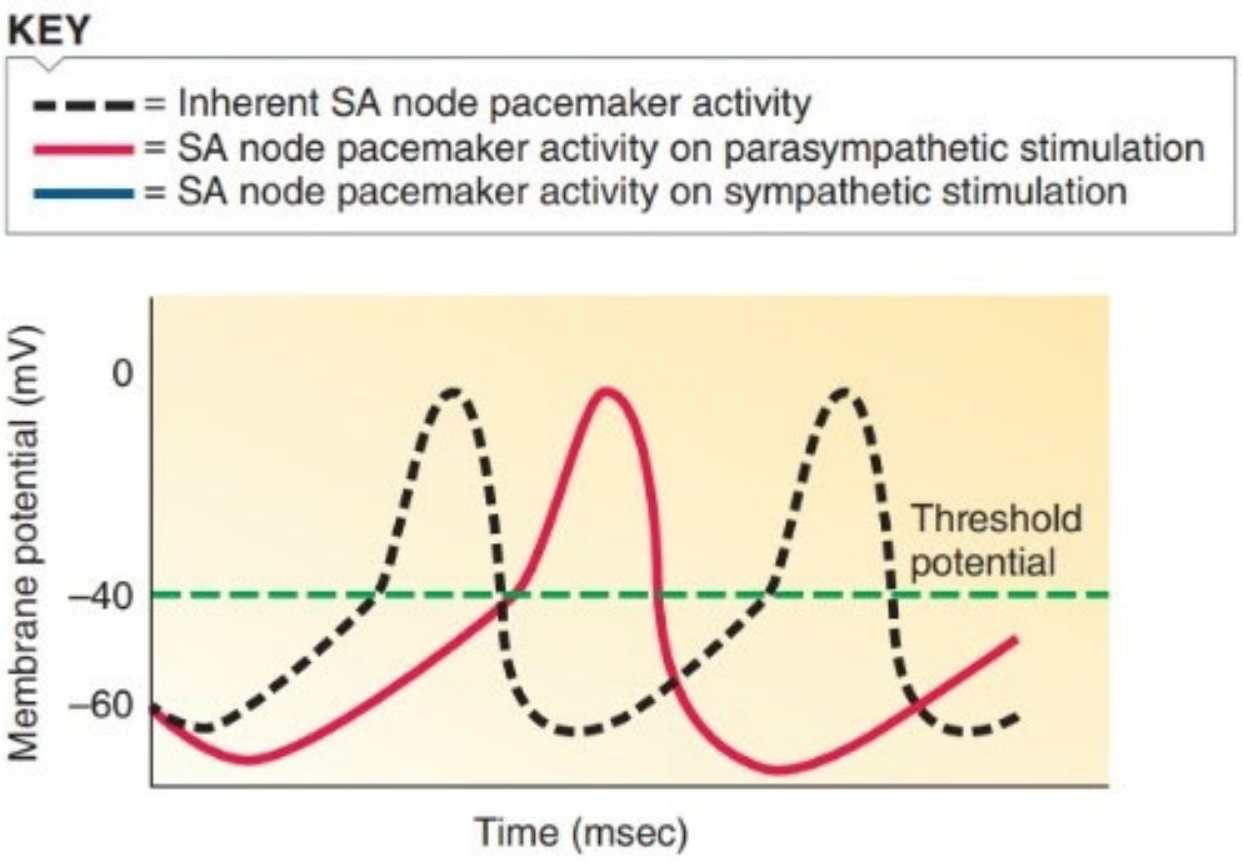
- Increased rate of depolarisation in SA node → ↓time to reach threshold
- Increases inwards movement of $Na^+$ and $Ca^{2+}$
- Also increases contractile strength; so both HR and force of contraction increase
- Sympathetic activity dominates during exercise or during emergency situations

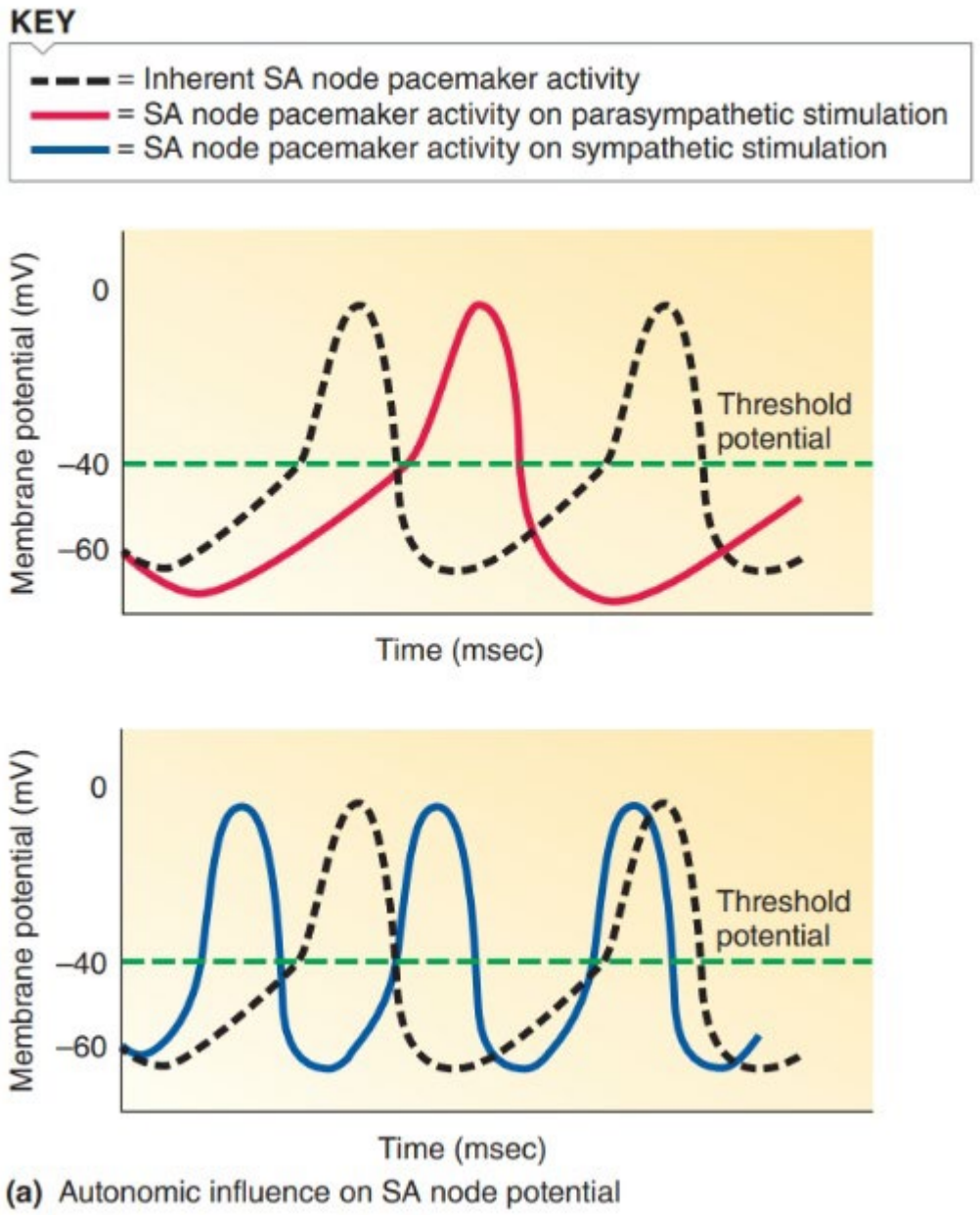
# Effect of parasympathetic stimulation




- Parasympathetic stimulation ↑ permeability to $K^+$ in the SA node – ↑ $K^+$ leaving the cell – longer time to reach threshold
- Mediated by ACh-regulated $K^+$ channels
- Parasympathetic action dominates at rest

- HR determined by the balance of sympathetic & parasympathetic effects
- At rest, parasympathetic is dominant
- Activity of these two branches of the autonomic nervous system is controlled at the CV control centre in the brainstem

- Note: adrenaline (hormone secreted by the adrenal gland) also increases heart rate – this reinforces the effect of the sympathetic nervous system on the heart



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