PHOL 519
CARDIAC ARRHYTHMIA

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What is cardiac arrhythmia?

Cardiac Arrhythmia – an abnormal variation in the normal heart rate/rhythm

Cardiac Arrhythmias are caused by:

(1) abnormal impulse formation
(2) conduction disturbances (re-entry)

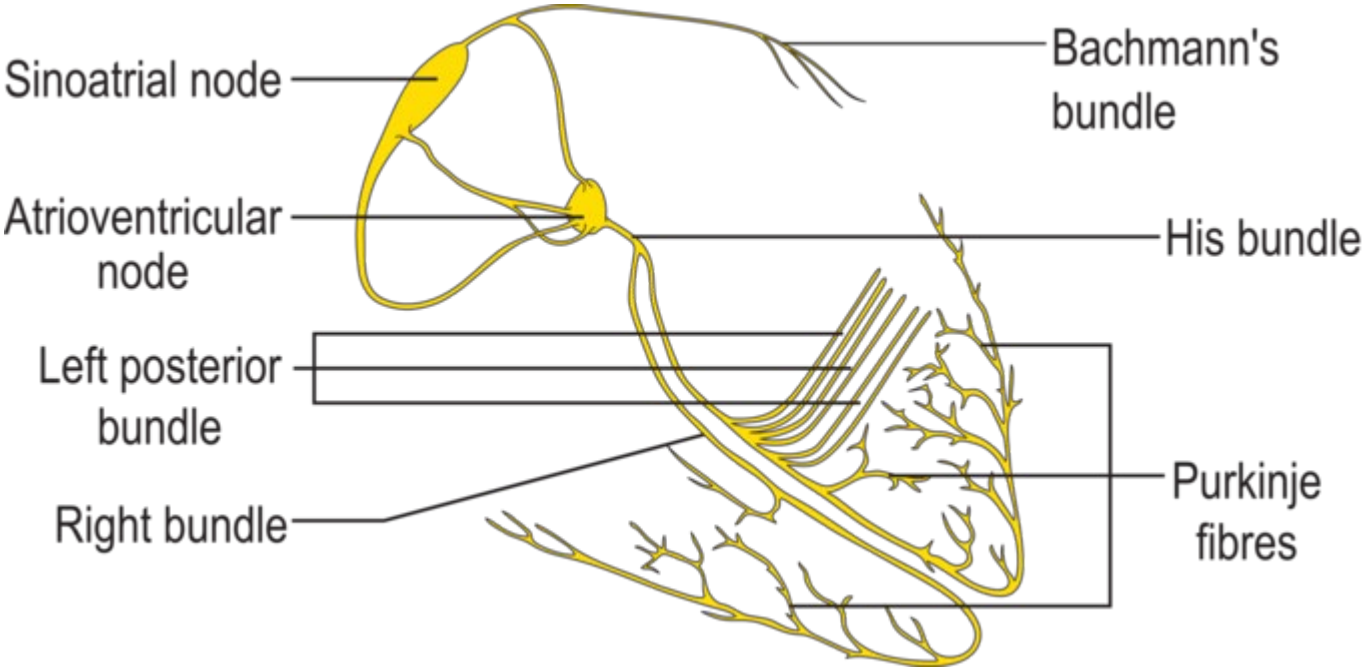
Cardiac Arrhythmia: Facts and Figures

- Arrhythmias are very common – most people will experience an abnormal heart rhythm sometime in their lives
- During a 24-hour period about 20% of healthy adults are likely to have frequent premature ventricular heartbeats
- Most arrhythmias are not life-threatening, but many are –
- In the US, 850,000 people are hospitalized for arrhythmia every year
- Atrial fibrillation is the most common sustained heart rhythm disorder
- >100,000 Americans have an implantable defibrillator

Two types of arrhythmias

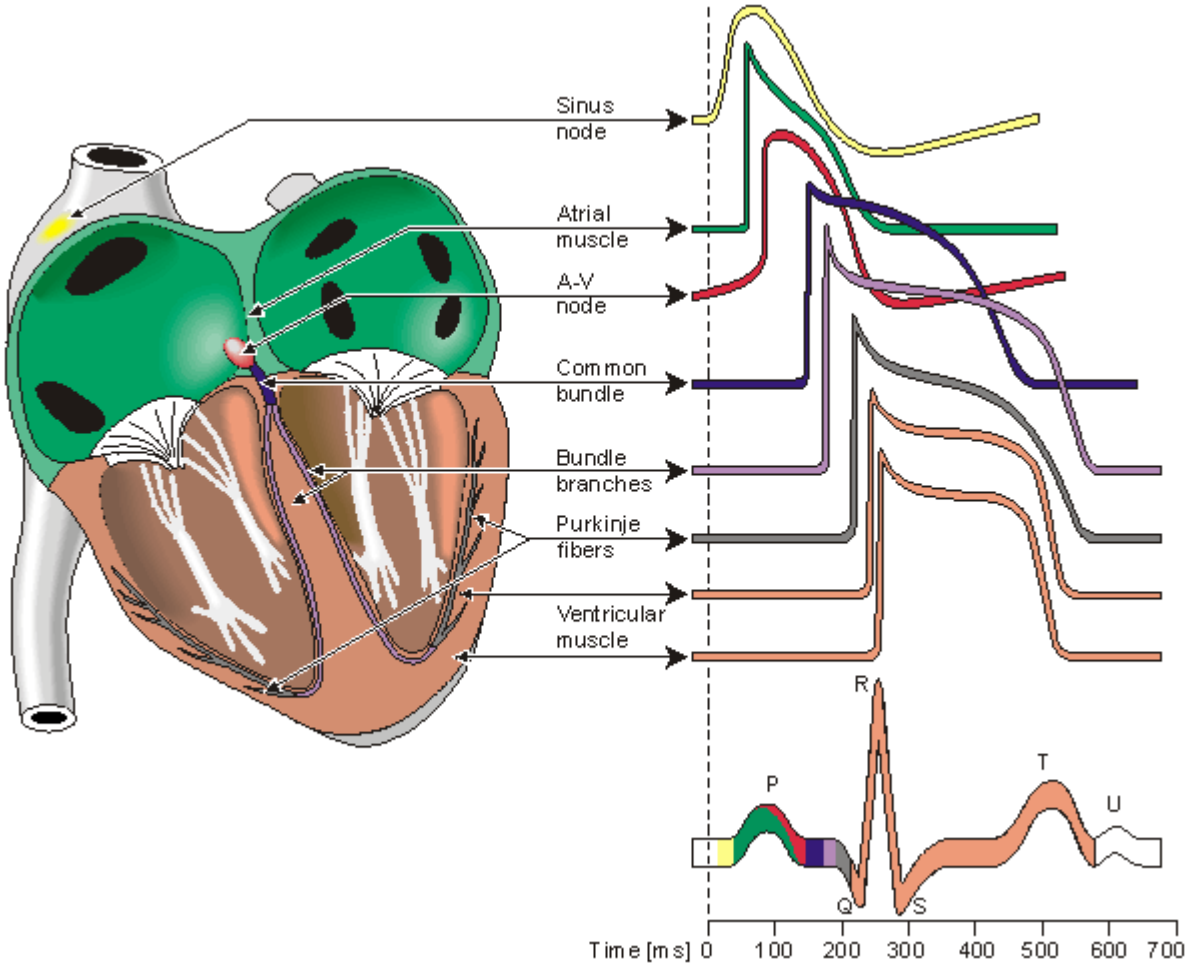
- Slow heart rhythms (usually atrial in origin)
  - Bradycardia: <60 bpm in sedentary adults
  - Heart ‘Blocks’ – conduction problem
  - Slow heart beat can occur due to dysfunction of either the SA node or AV node
  - Symptoms include fatigue, lightheadedness, dizziness, blackouts
  - May necessitate pacemaker to ‘normalize’ heart rate
- Fast heart rhythms (atrial or ventricular origin)
  - Tachycardia: >150 bpm
  - Atrial rhythms – SVT, Atrial flutter, atrial fibrillation – rarely life threatening
  - Ventricular rhythms – VT, ventricular fibrillation – life threatening!

Cardiac conduction system: His-Purkinje Network

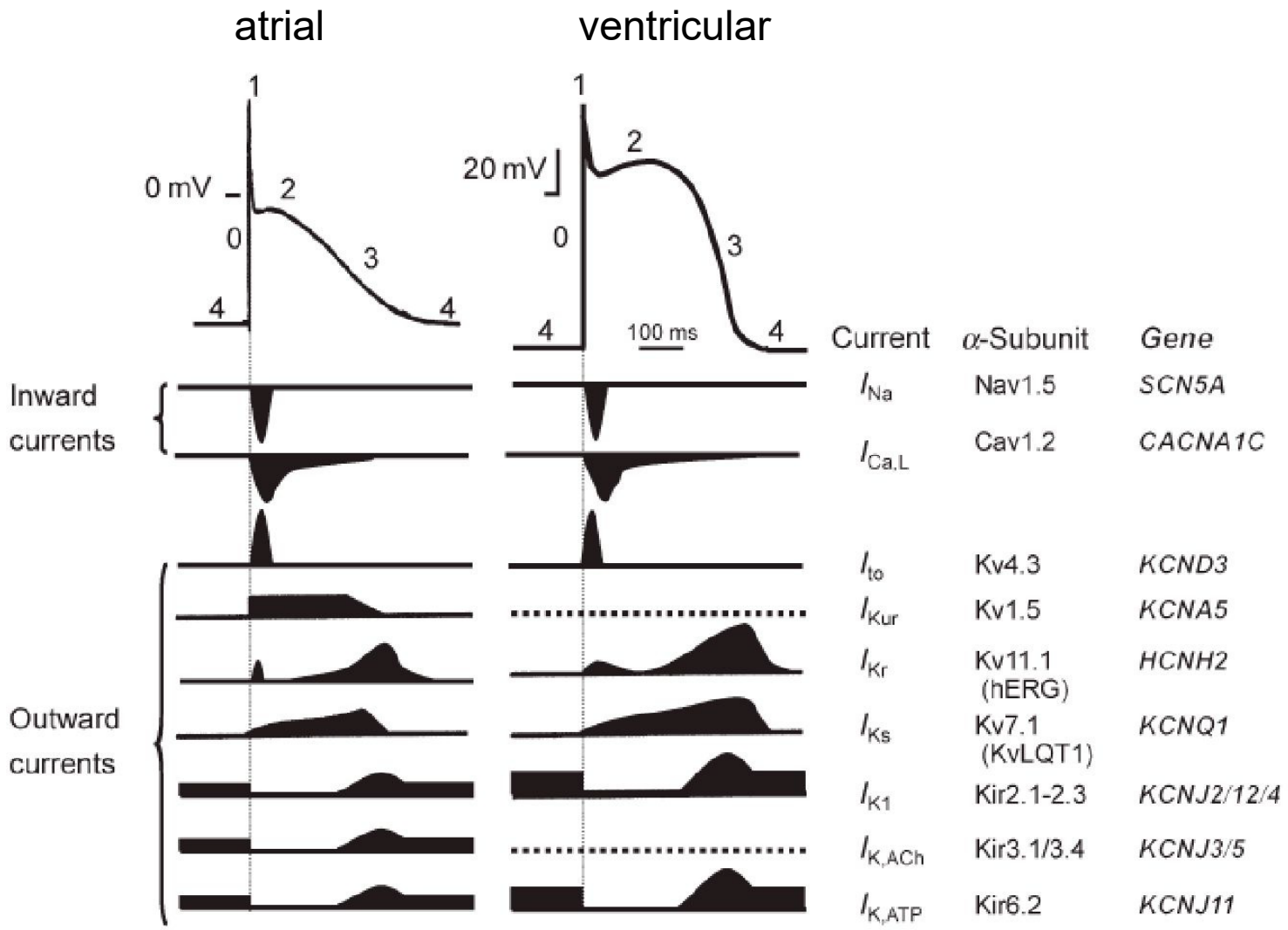


- Electrical activity originates in the SA node, pumps blood from atrium to ventricle
- AV node delays activity, allowing the ventricles to fill with blood
- Activity propagates via the His-Purkinje Network
- Purkinje fibers cause ventricular depolarization

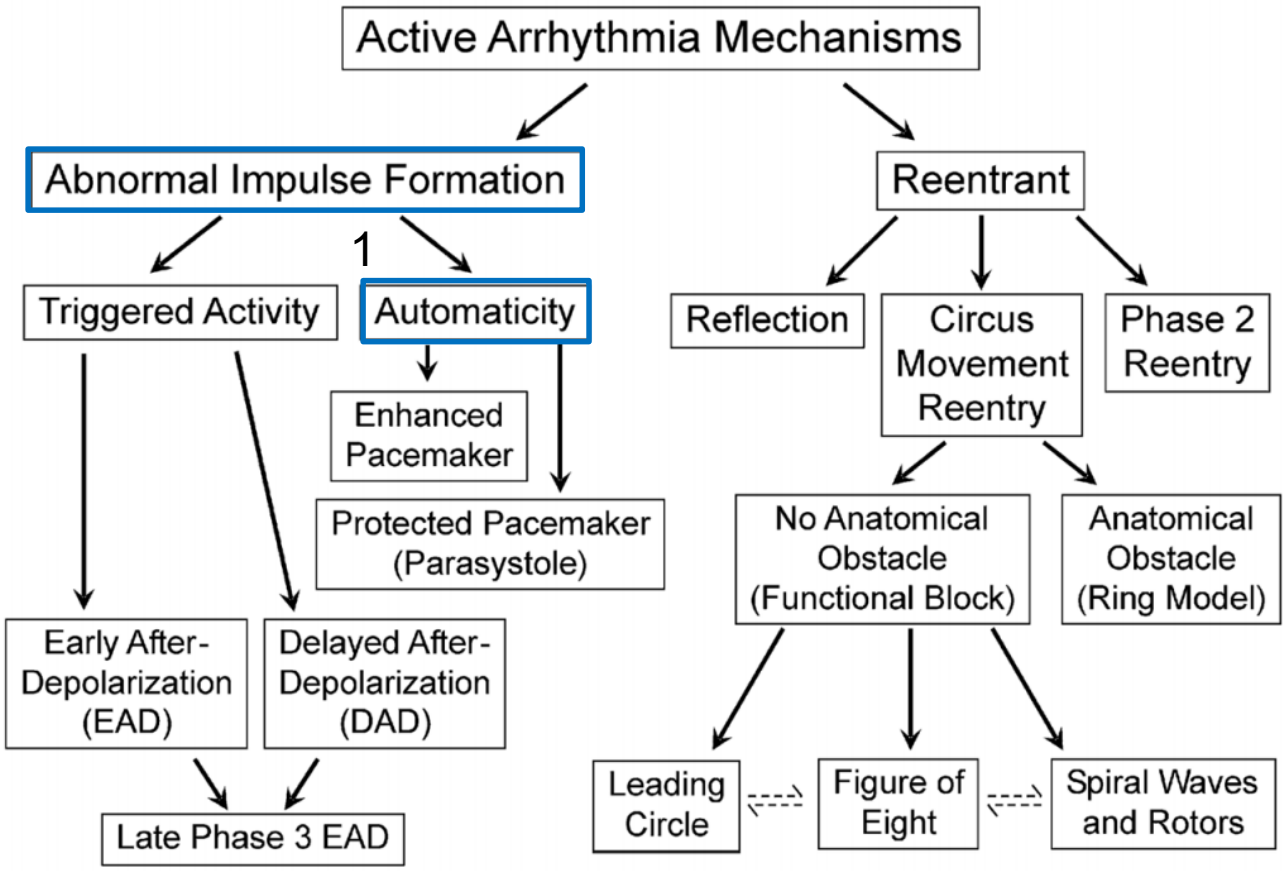
Propagation of the cardiac action potential



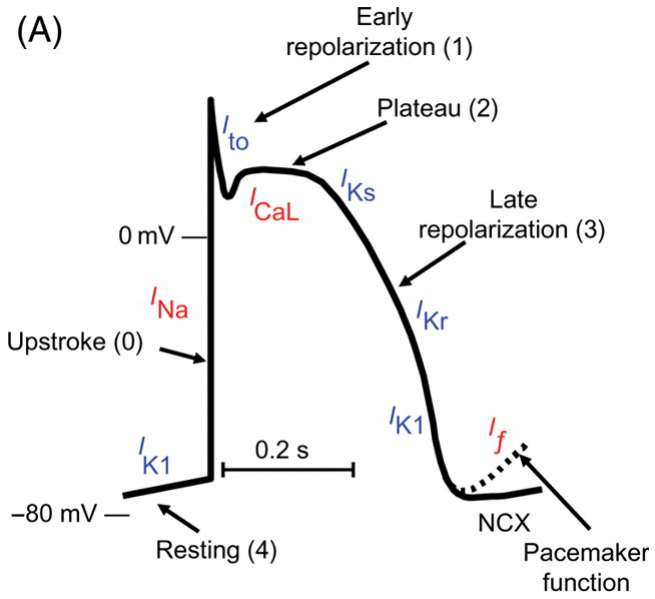
Cardiac action potential: ionic currents

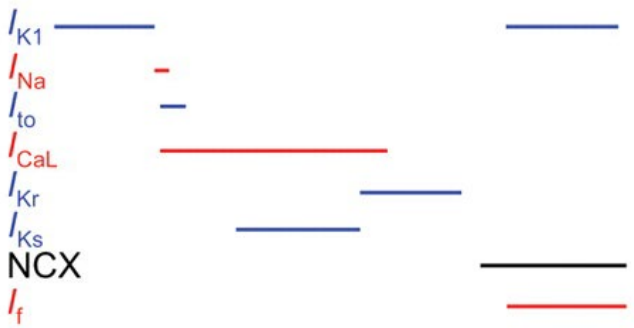


Arrhythmia Mechanisms



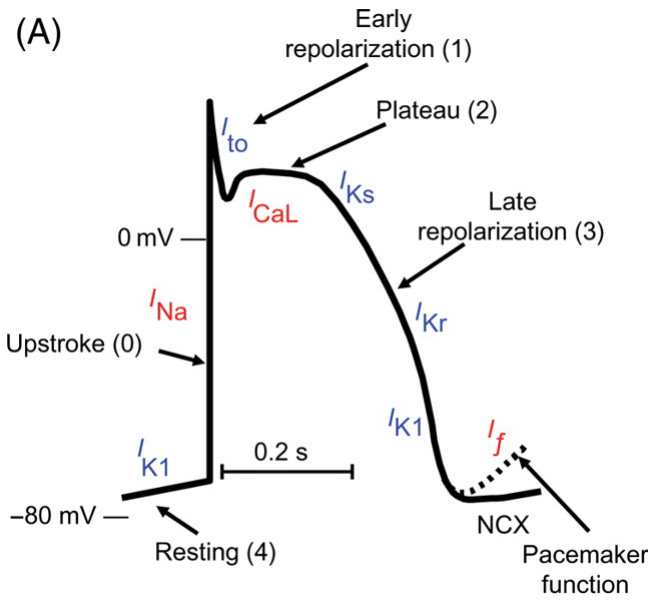
Voltage mechanism of cardiac rhythm: I_f





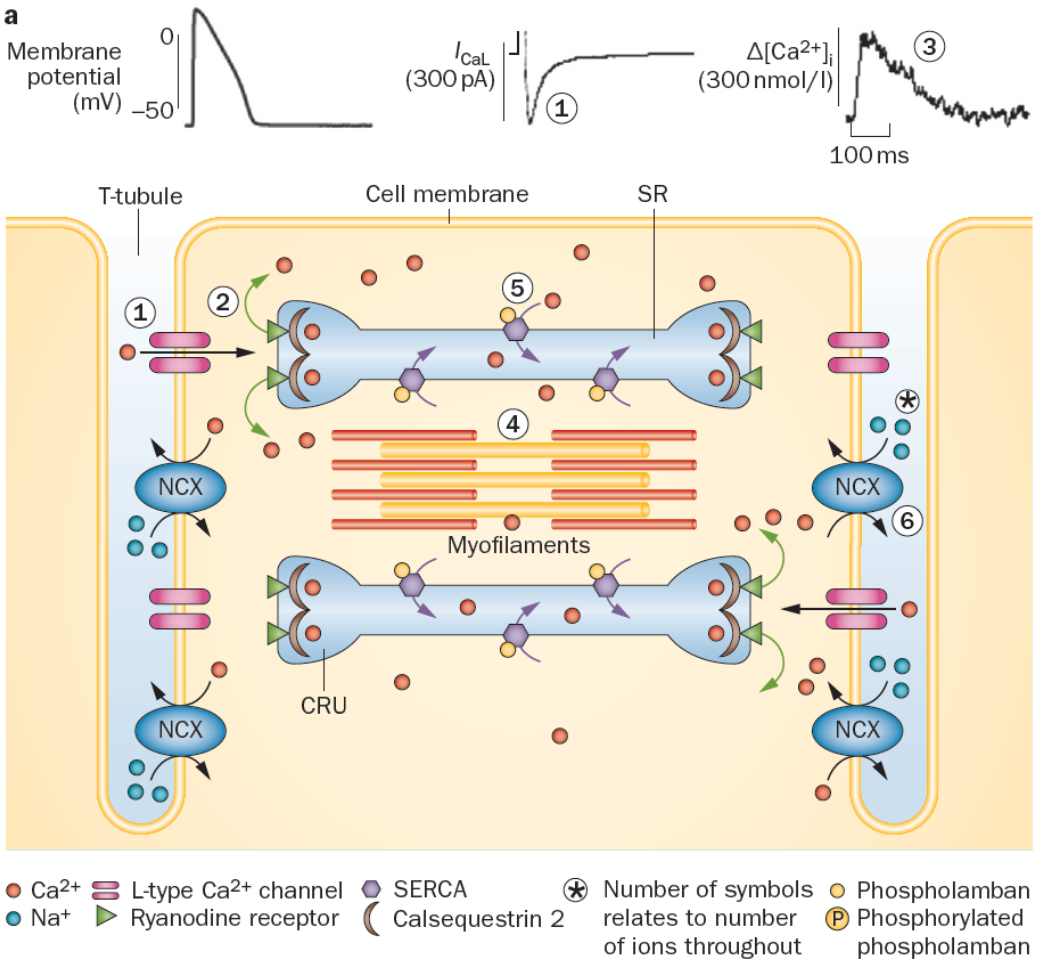
- Inward Na^+/Ca^{2+} and outward K^+ currents underlie the cardiac action potential
- Recurrent action potentials are caused by I_f, and thus hyperpolarization activated cation current generates rhythm

Congenital mutations altering Voltage Automaticity



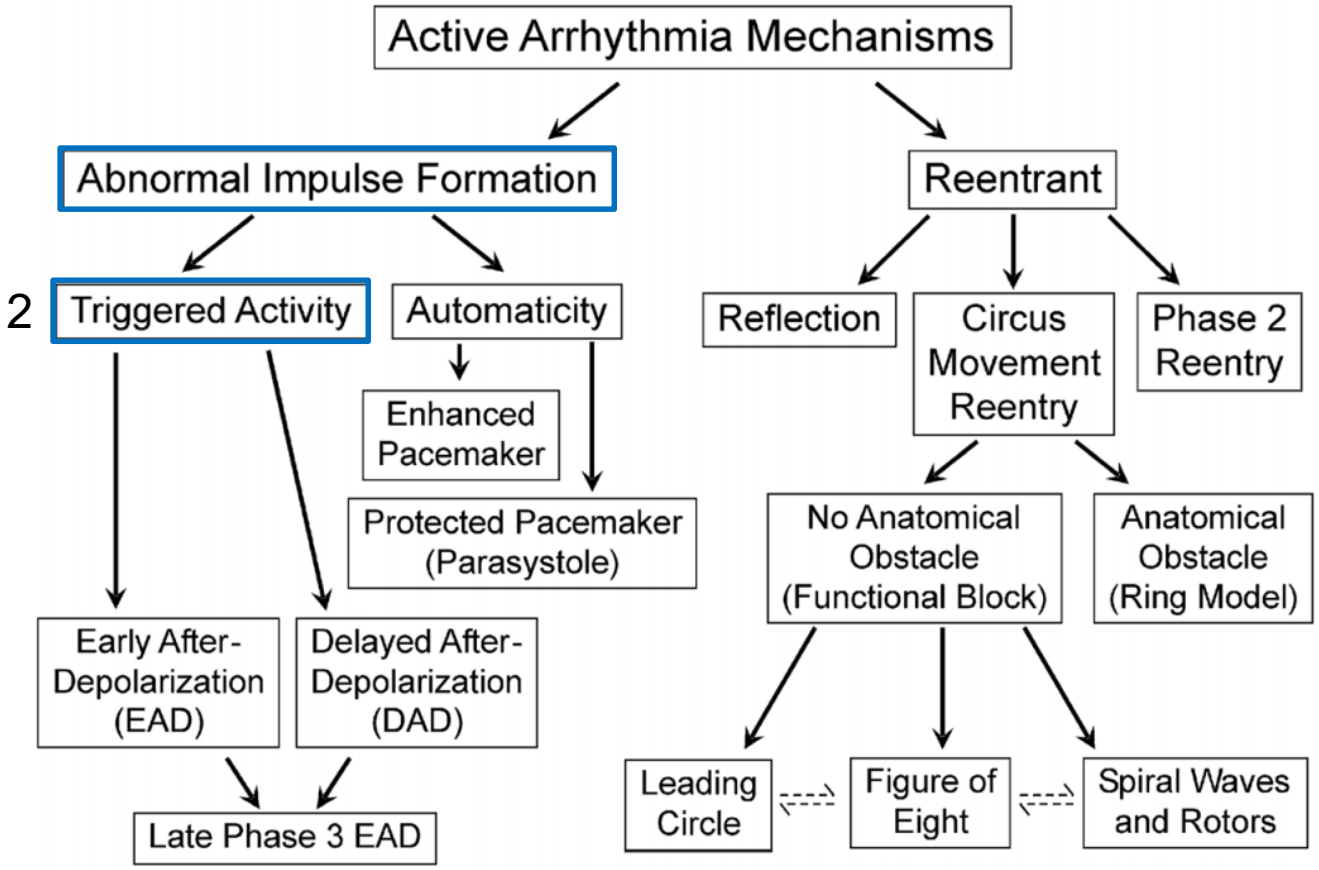
- *SCN5A* – depolarizing current (I_{Na})
- *KVLQT1* – repolarizing current (I_{Ks})
- *HCN4* – pacemaker current (I_f)

Ca^{2+} handling as a mechanism of rhythm generation

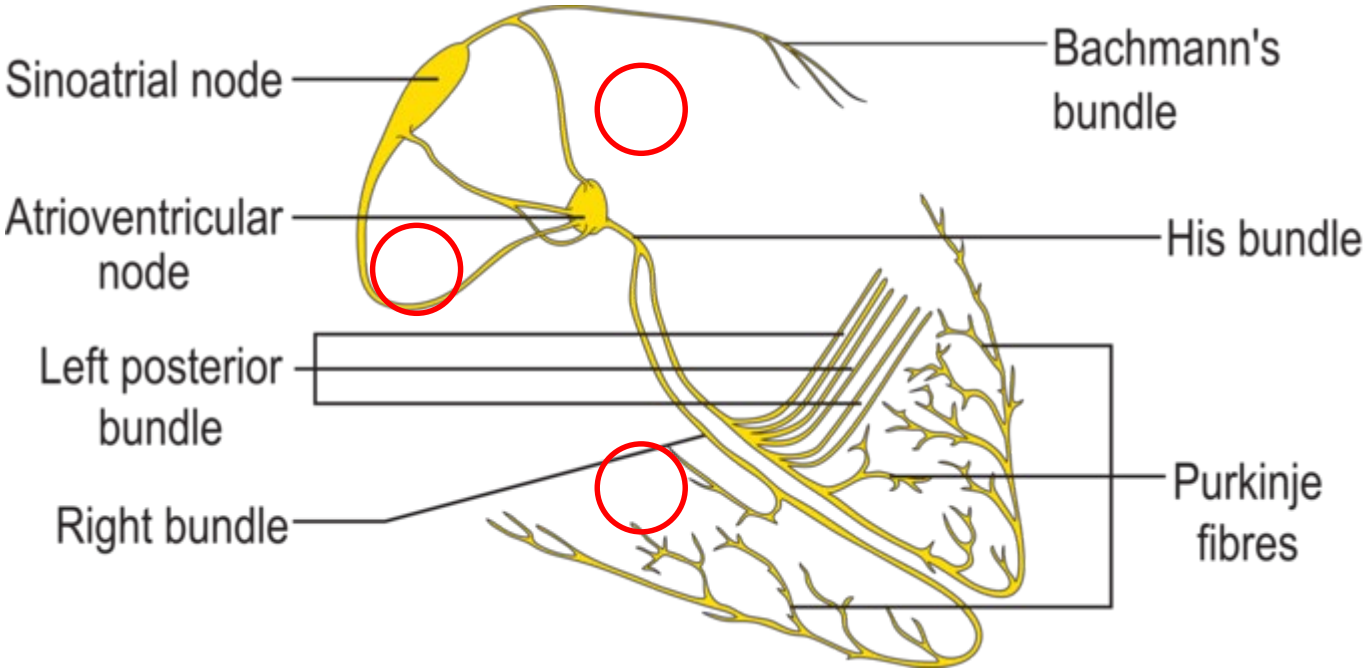


- *RYR2* – ryanodine receptor
- *CASQ2* – Ca^{2+} buffering protein in SR

Arrhythmia Mechanisms



Parasystole – protected pacemaker



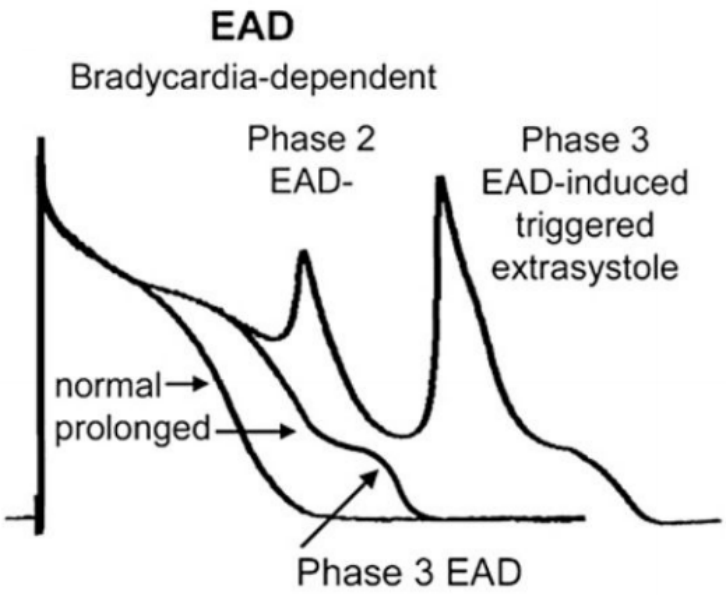
- SA node is dominant pacemaker because it is most excitable
- All other pacemakers ‘enslaved’ to SA node via reset by SA
- If a pacemaker is protected from impulse by SA due to ‘block’, then it can operate independently
- This is called **parasystole**

Triggering of Arrhythmias

- A variety of extrinsic factors can trigger ‘afterdepolarizations’:
  - Injury
  - altered electrolytes – K^+, Ca^{2+}, Mg^{2+}
  - hypoxia – lung disease
  - acidosis
  - catecholamines – exercise, anxiety, CHF, hyperthyroidism
  - pharmacologics – caffeine, stimulants, antiarrhythmic
  - stretch – hypertrophy, valve disease
- Afterdepolarizations sometimes give rise to extrasystoles (ectopic action potentials) – these are arrhythmic events.

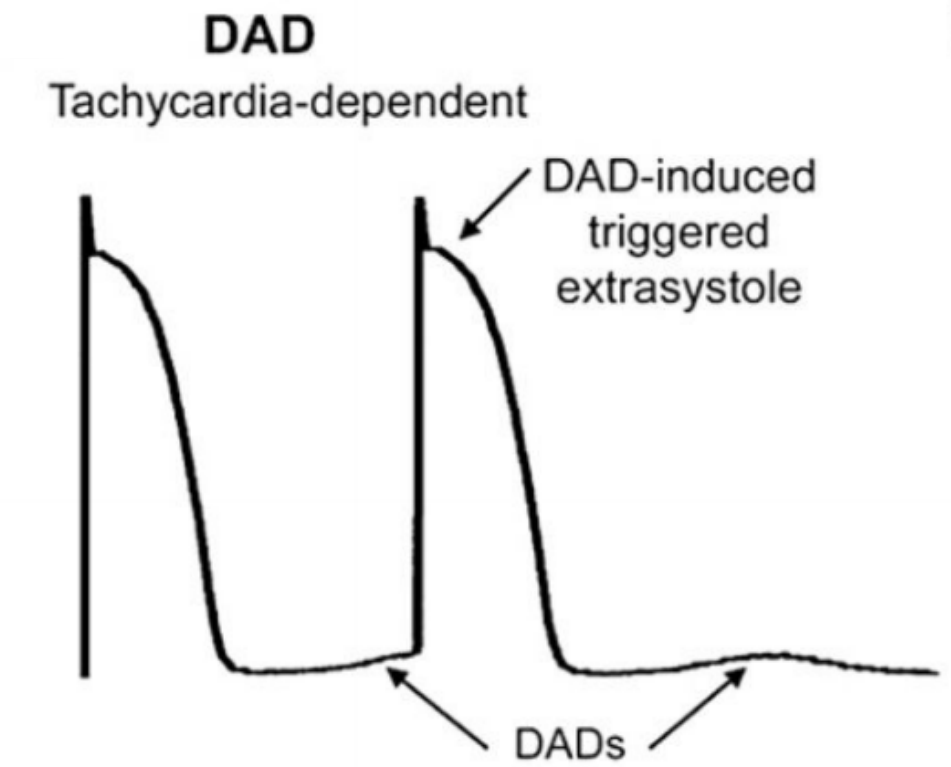
EADs

- Early After Depolarizations – lead to bradycardia during phase 2, or triggered extrasystole and tachycardia during late phase 3

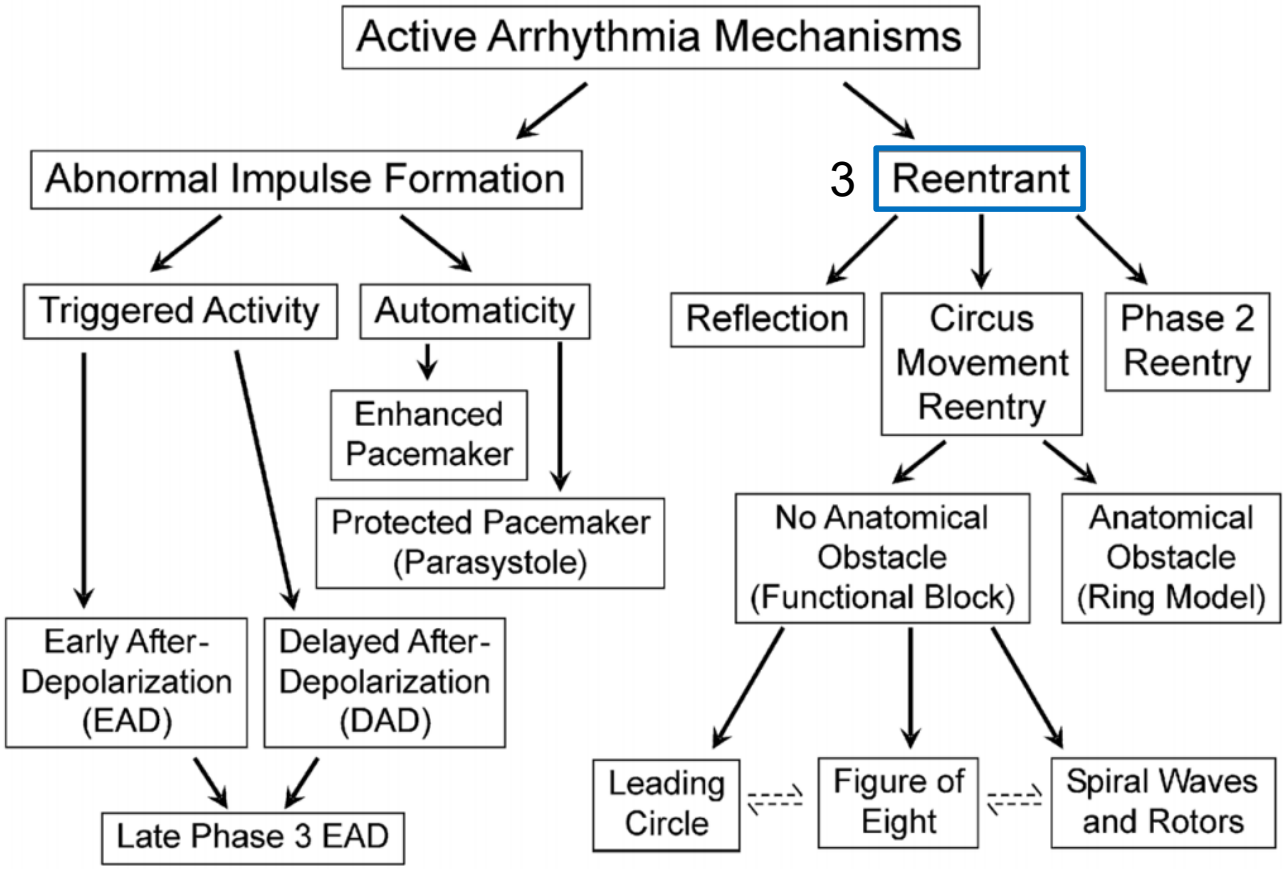


DADs

- Delayed After Depolarizations – lead to tachycardia, DADs can lead to triggered AP
- Often result from abnormal accumulation of cytosolic Ca2+

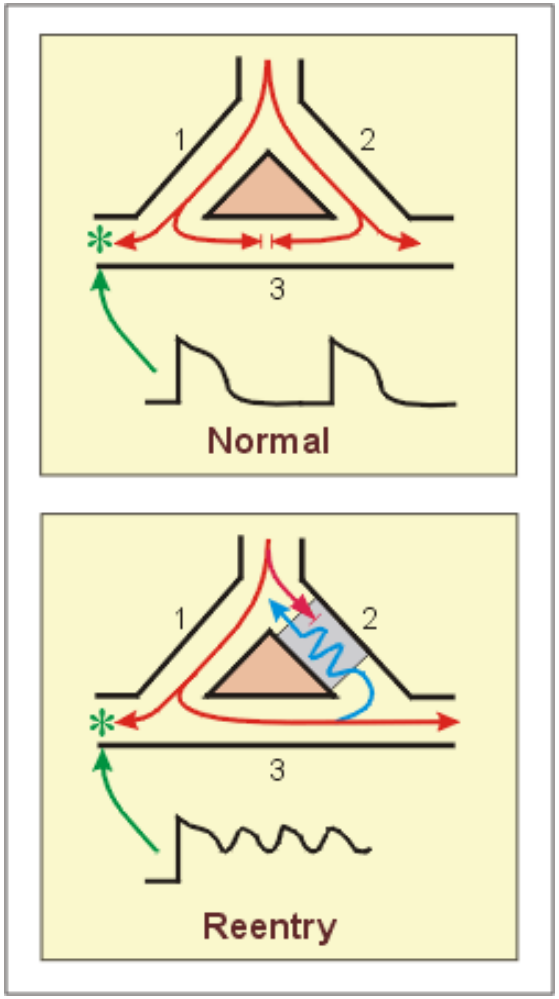


Classification of Arrhythmias

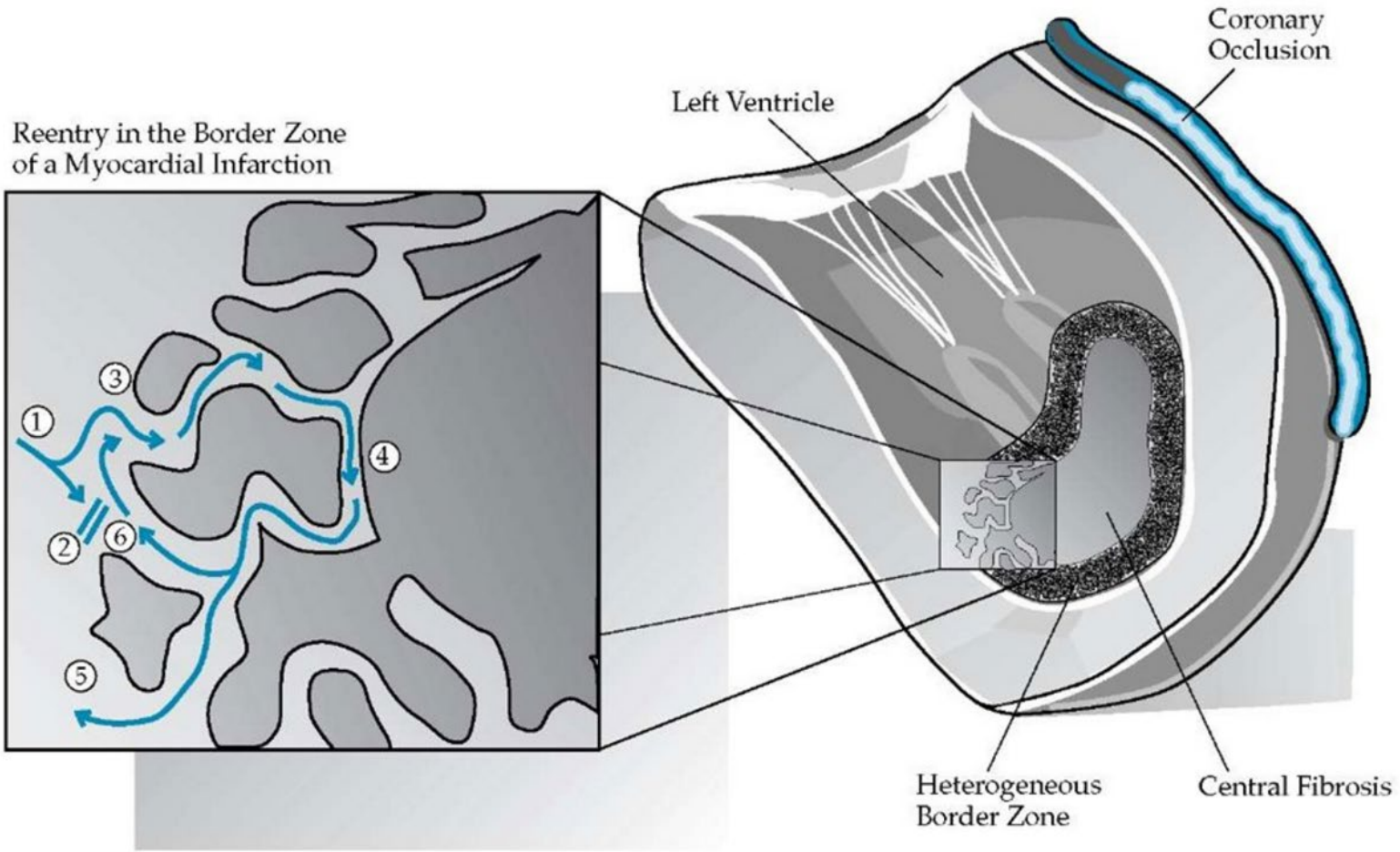


Re-entry: A fundamental mechanism of cardiac arrhythmia

- Branch 2 has unidirectional block, so impulses can travel retrograde (3 to 2) but not orthograde
- AP will travel down branch 1 and then retrogradely down branch 2.
- When AP exits the block on the proximal side, if it finds the tissue excitable then it will continue by **reentry** down branch 1
- Timing is critical – tissue can be in non-excitable state
- Re-entry can cause tachyarrhythmia

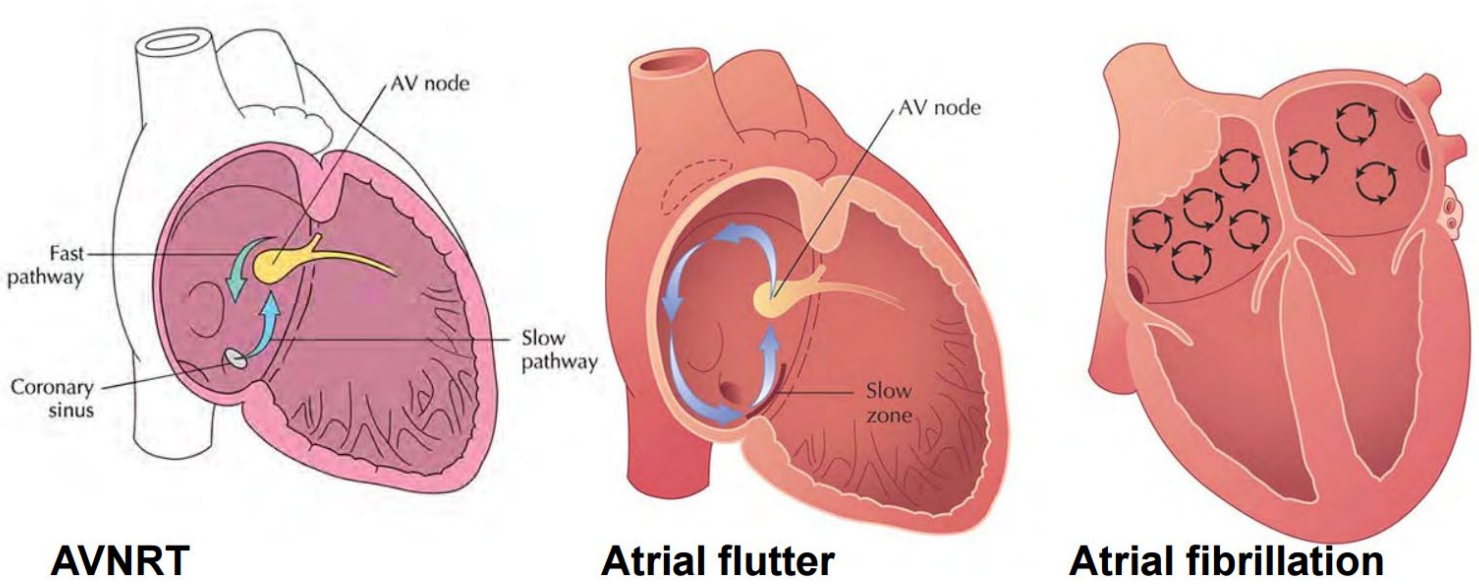


Re-entry is problem after Myocardial Infarction (MI)



Atrial Reentry

- Re-entry can cause different modes of atrial tachycardia
- Vagal maneuvers may allow termination of SVTs (Ach)
- Catheter ablation can sometimes be used to remove tissue causing re-entry – but only if the cause of the unidirectional block is identified



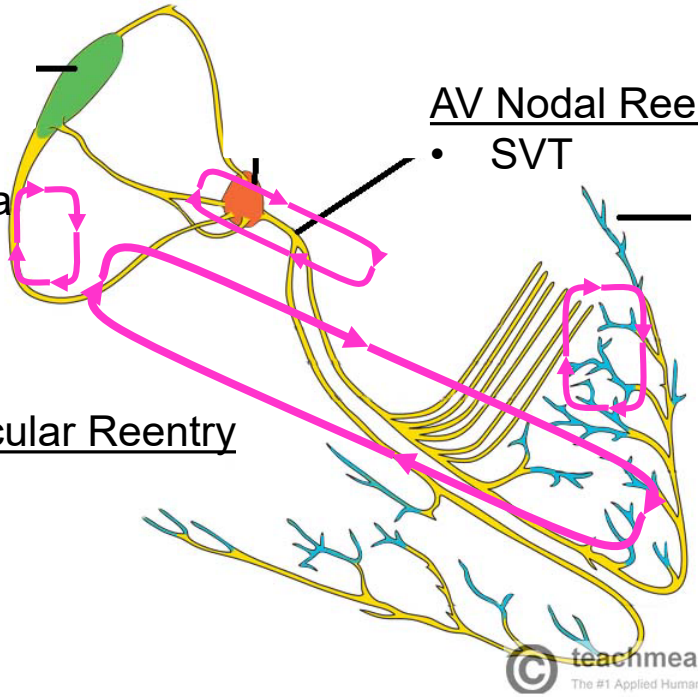
Other modes of Reentry

<u>Atrial Reentry</u>
- Atrial tachycardia
- Atrial fibrillation
- Atrial flutter

<u>AV Nodal Reentry</u>
- SVT

<u>Atrio-Ventricular Reentry</u>
- WPW
- SVT

<u>Ventricular Reentry</u>
- Ventricular Fibrillation (V-Fib)
- Life threatening
- Treated with a defibrillator



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