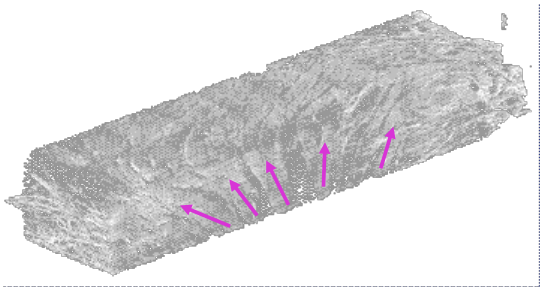
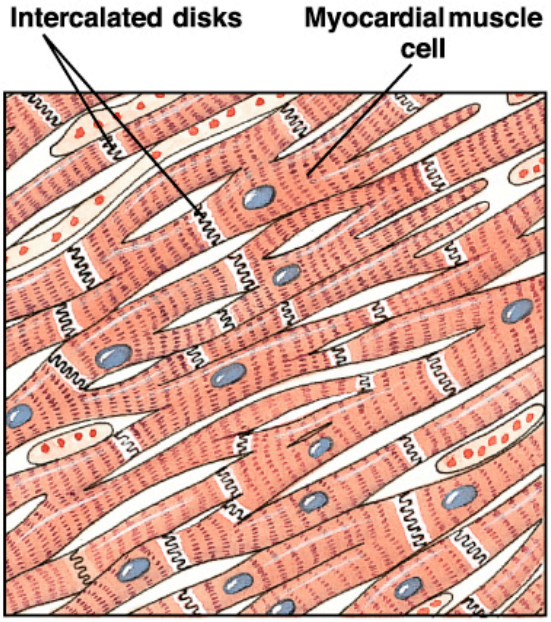
Electrophysiology of Cardiac Tissue

Structure

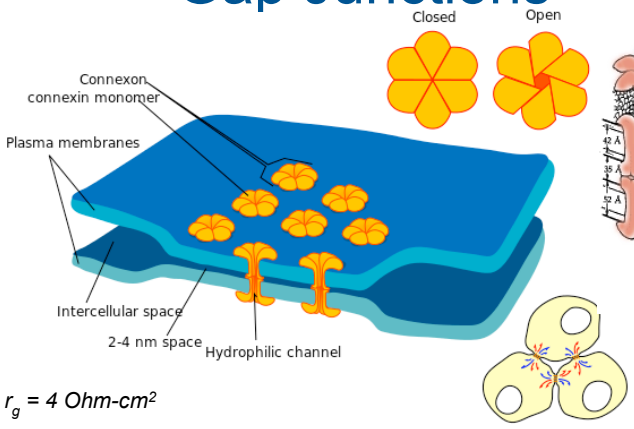
Cardiac Tissue

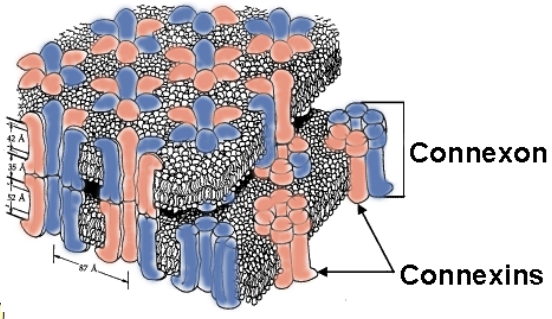
- Syncytium (to a point)
- Fibers
- Anisotropy
- Gap junctions





Gap Junctions

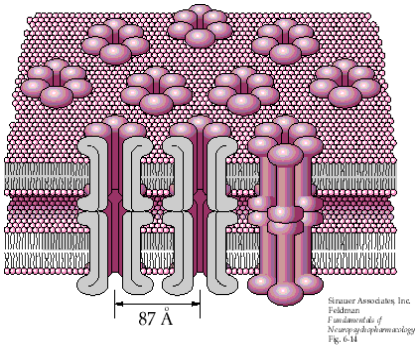


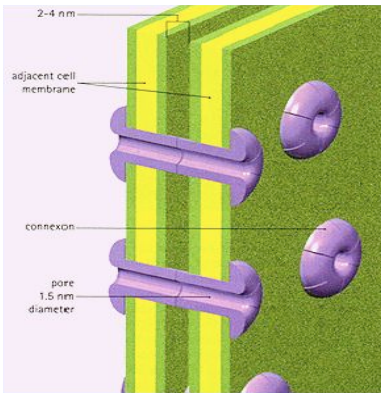


r_g = 4 Ohm-cm^2

r_m = 5000 Ohm-cm^2

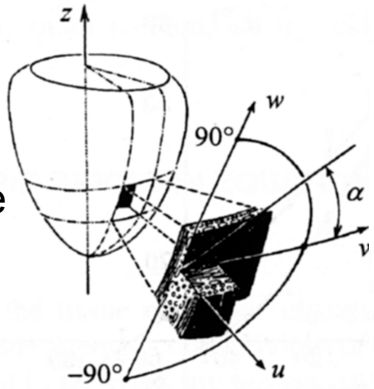
Pore size: 1.5 nm

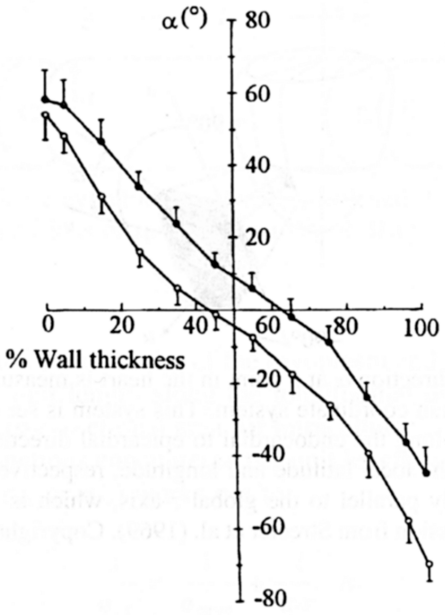




Myocardial Anisotropy

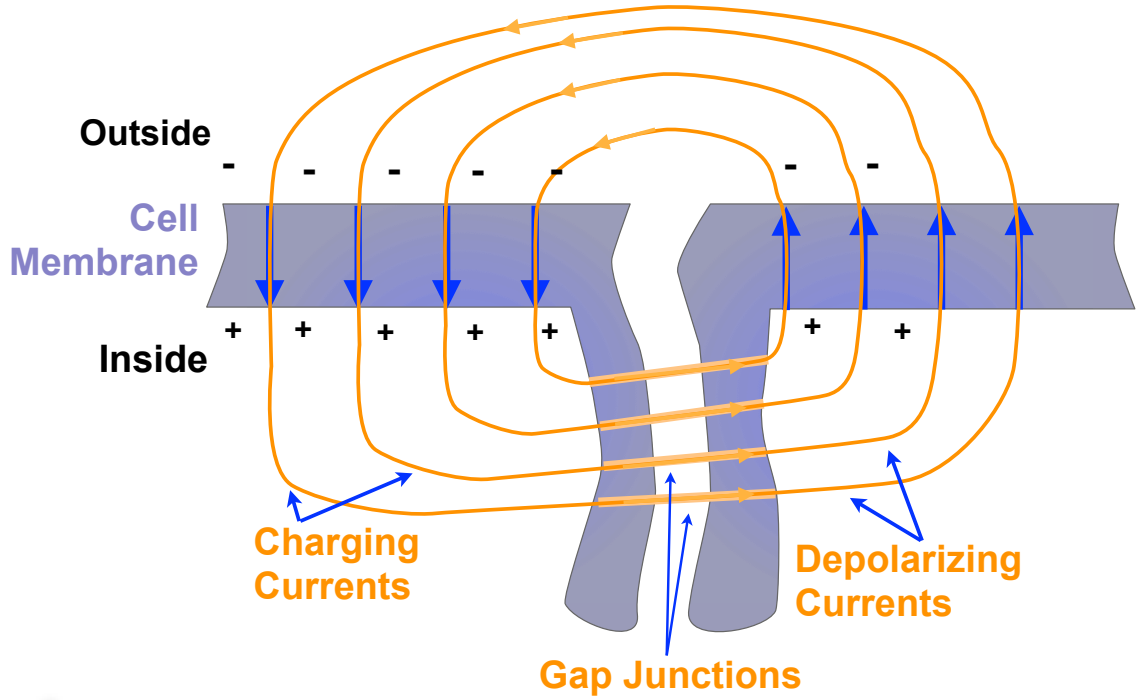
- In ventricles ranges from 90–180 degrees of rotation
- Rotation more rapid near ventricle walls
- Imbrication angle of 3--5 degrees



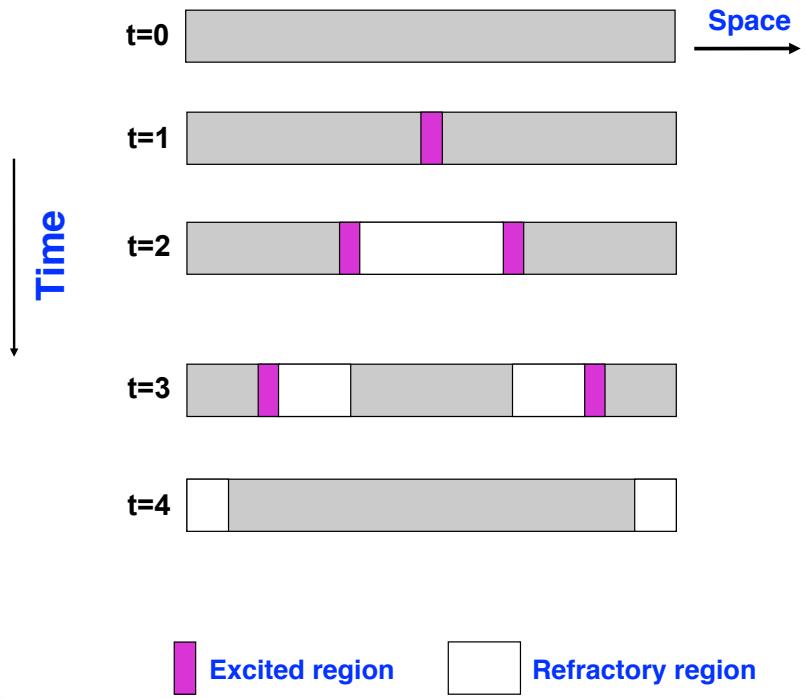


Theory/Mechanisms

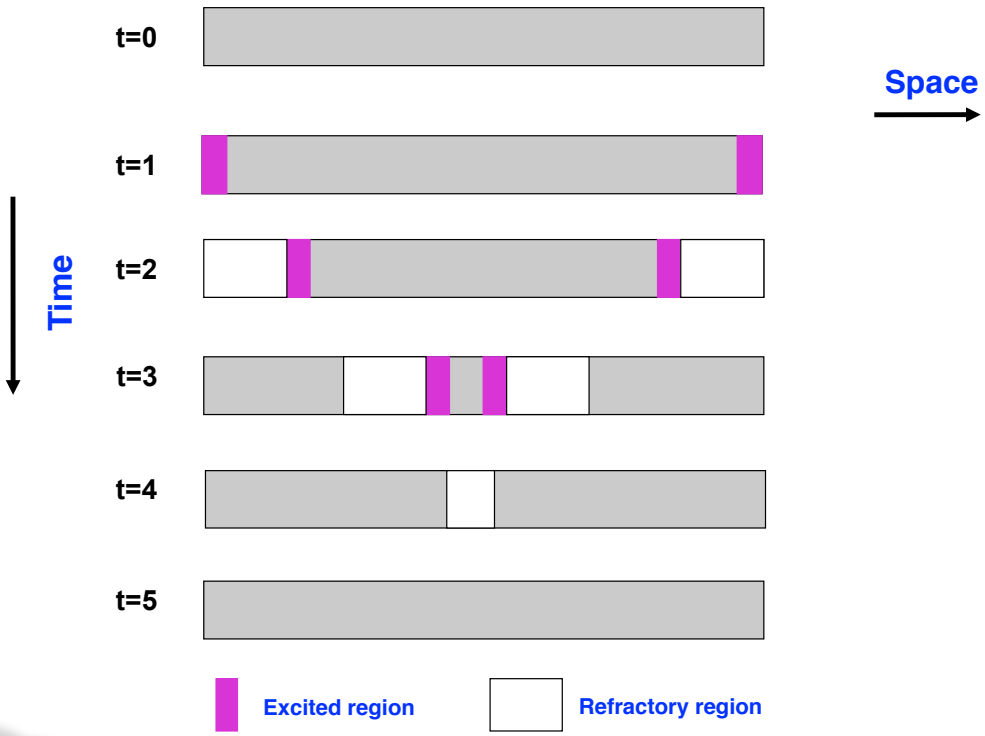
Local Circuit Currents



Propagation Example 1



Propagation Example 2 (collision)



Propagation Velocity

$$v = \sqrt{\frac{K D \, dV/dt}{R_i C_m}}$$

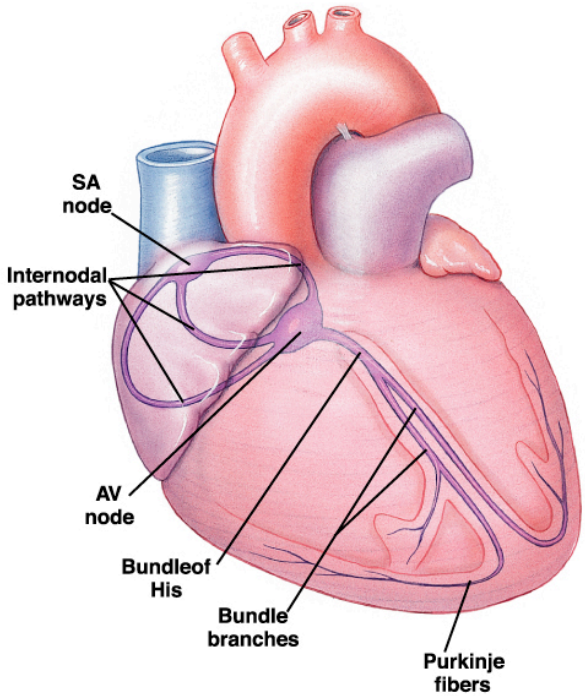
- K = constant
- D = diameter of fiber (or nerve axon)
- dV/dt = rate of rise of action potential
- R_i = intracellular resistivity
- C_m = membrane capacitance
- Approximate but qualitatively correct

Cardiac Propagation: Essential Summary

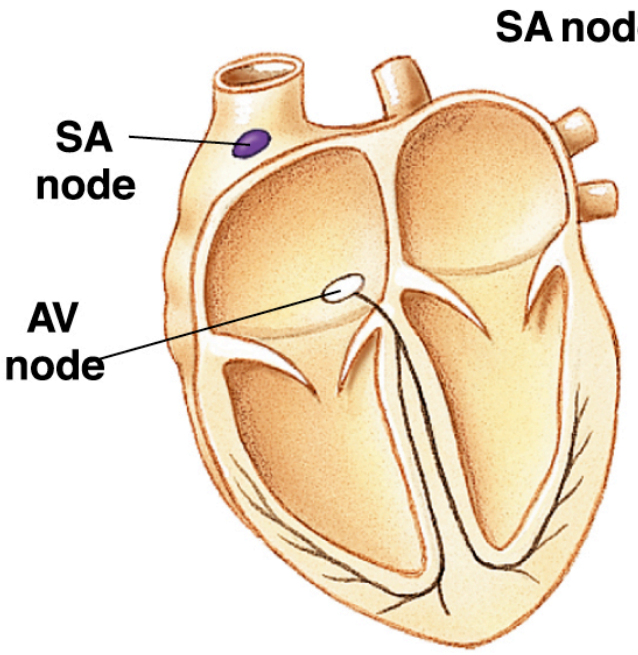
- Requires a network of connected, excitable cells
- Driven by an all-or-nothing phenomena
  - no superposition (unlike other waves)
  - collisions result in annihilation
  - amplitude does not diminish with distance
- Anisotropic due to preferential connections between cells
  - wavefronts are elliptical and not spherical
  - propagation depends on muscle structure (fiber orientation)
- Exhibits refractoriness
- Can be blocked

Electrophysiology of the Whole Heart

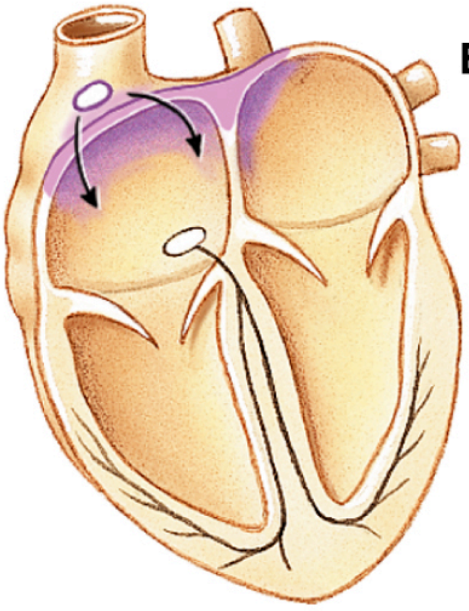
- Specialized Conduction system
  - sinoatrial (SA) Node
  - atrioventricular (AV) node
  - Purkinje system
- Pacemaker functions
  - SA Node
  - AV Node
  - Purkinje Fibers
- The Electrocardiogram (ECG)



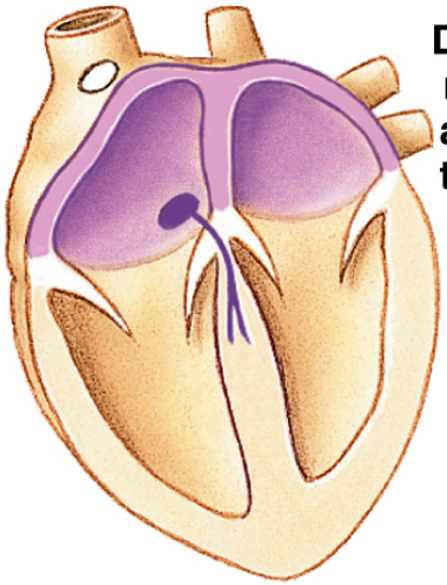
Cardiac Activation Sequence



Cardiac Activation Sequence

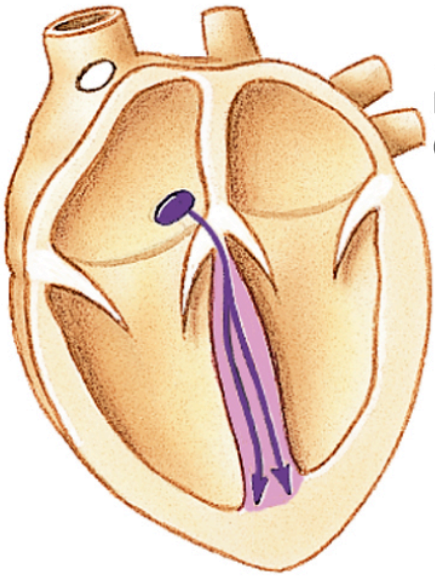


Cardiac Activation Sequence



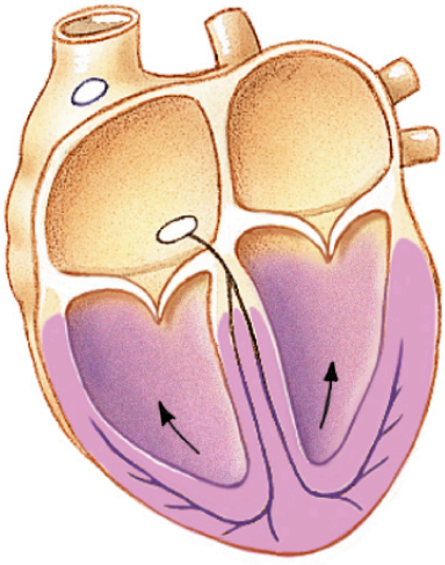
Depolarization spreads more slowly across atria. Conduction slows through AV node.

Cardiac Activation Sequence



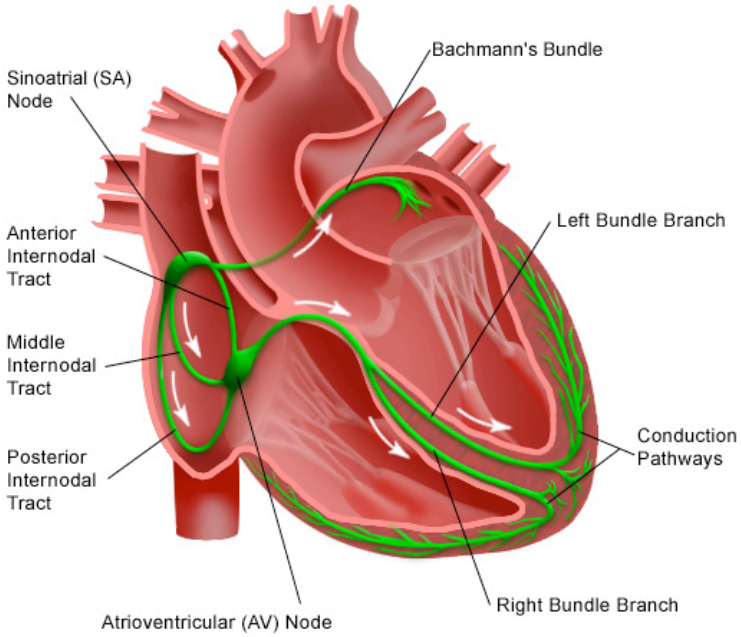
Depolarization moves rapidly though ventricular conducting system to the apex of the heart.

Cardiac Activation Sequence

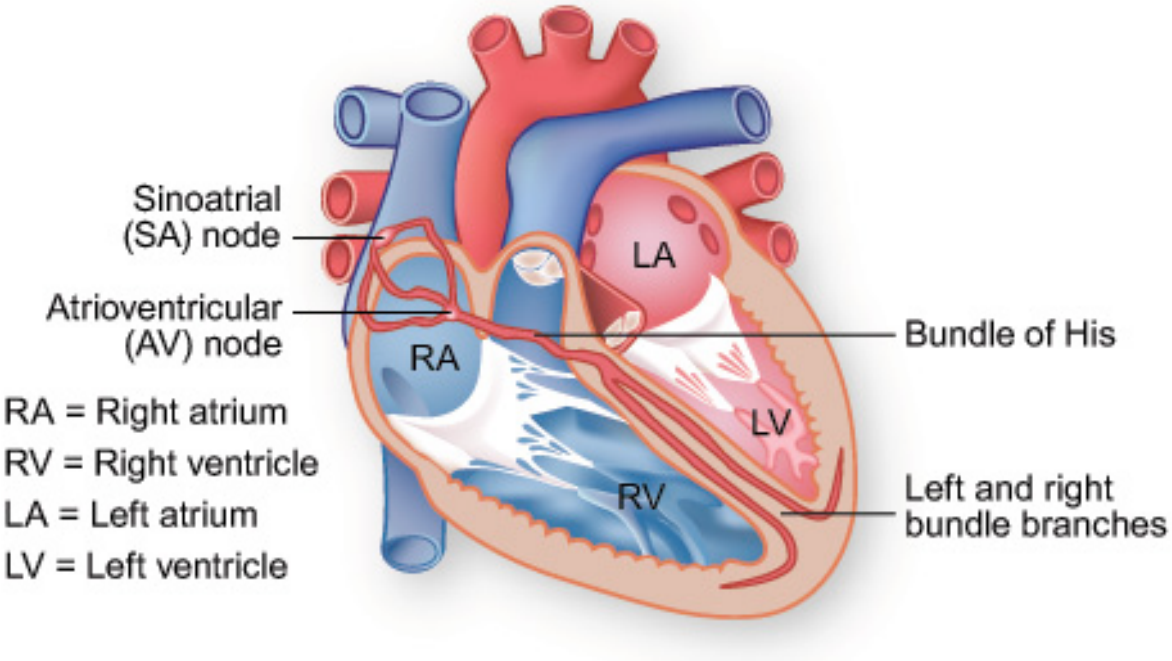


Depolarization wave spreads upward from the apex.

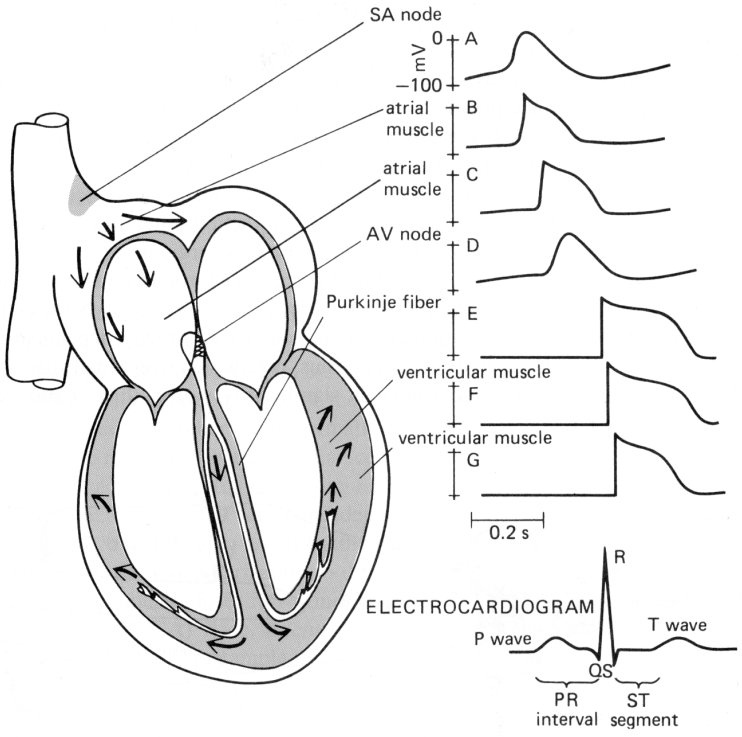
Cardiac Activation Sequence



Another View of Conduction System

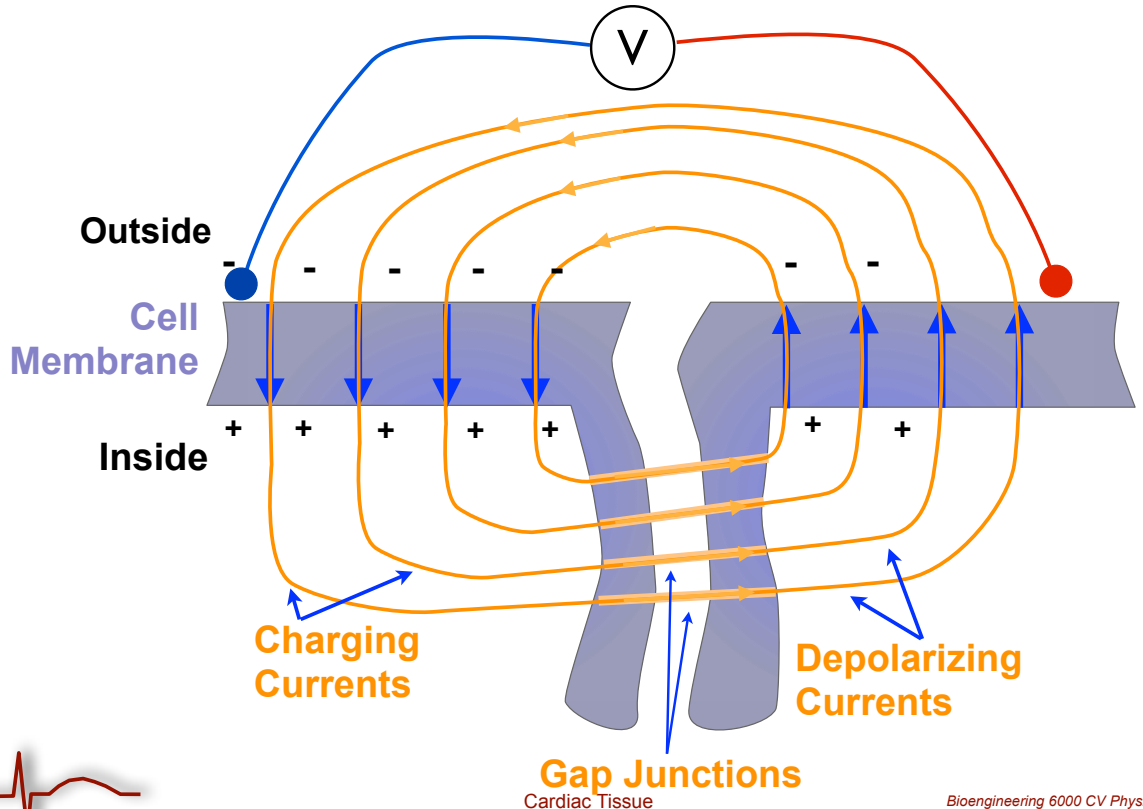


Cardiac Activation Sequence



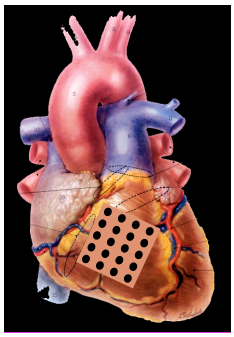
Measurement

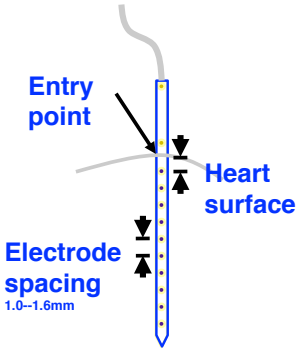
Extracellular Potentials

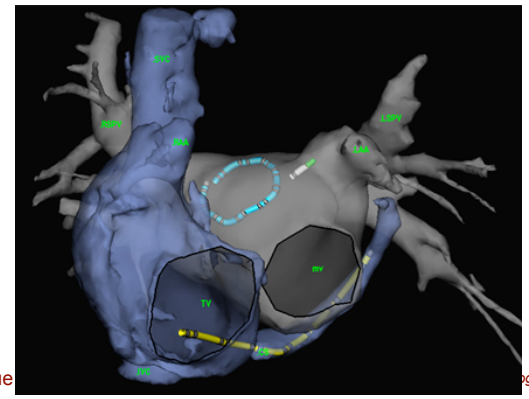


Measuring in Cardiac Tissue

- Electrodes
  - extracellular
  - unipolar versus bipolar
  - surface, volume, catheter
- Cardiac Mapping
  - multiple recording sites
  - isopotential maps
  - isochrone maps
- Applications
  - experimental
  - clinical

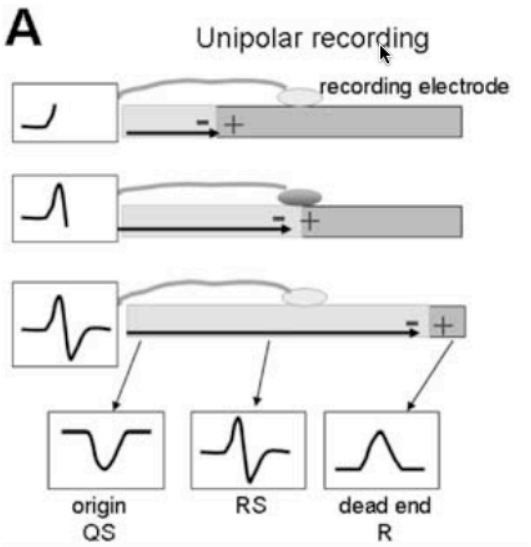






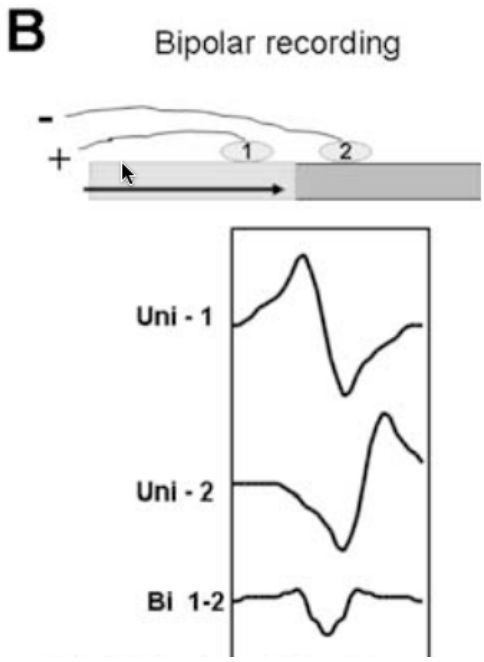
Unipolar vs. Bipolar

- Potential differences between a single electrode site and a remote reference.
- Features
  - Recording field is infinite and uniform in all directions, hence no directional sensitivity
  - Signals contain far field components and are sensitive to distant electrical activity.
  - Signal morphology indicates wavefront direction
  - Morphology depends on choice of reference

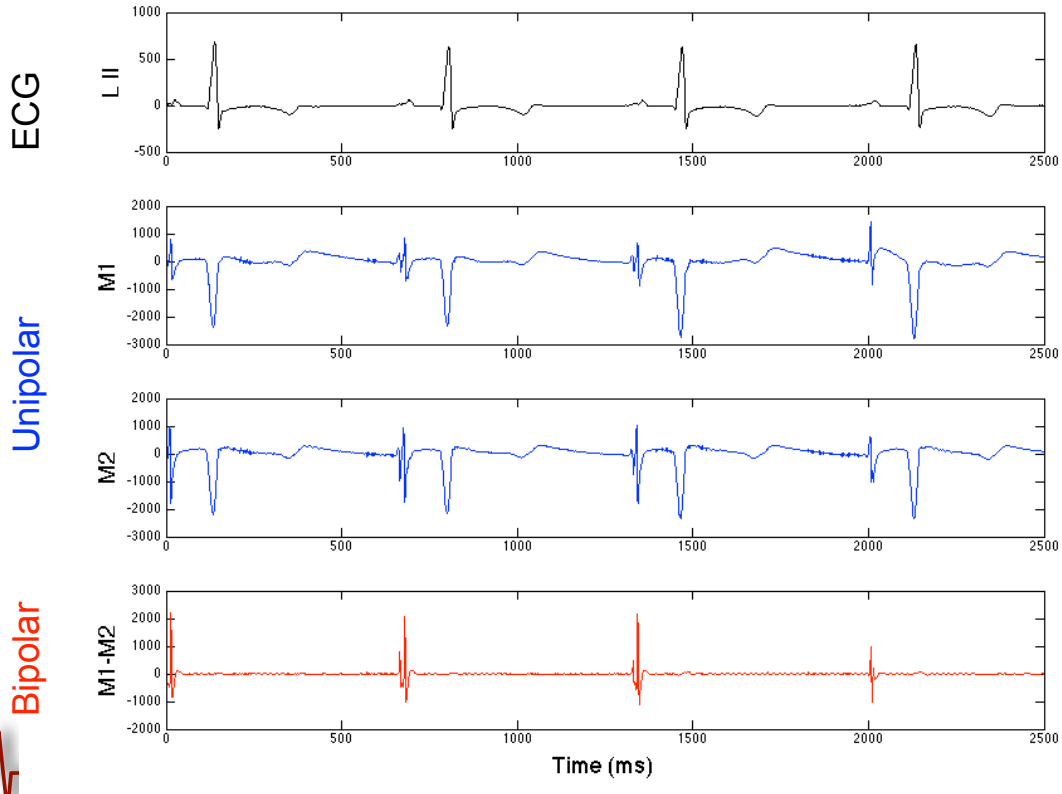


Unipolar vs. Bipolar

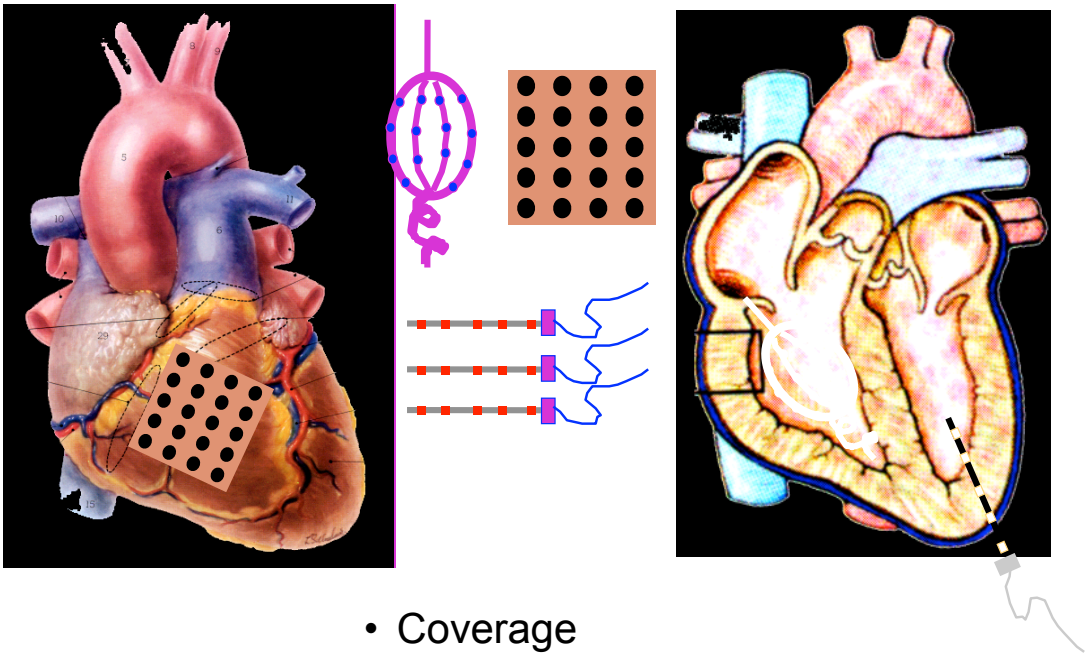
- Potential differences between two closely spaced electrodes.
- Features
  - Recording field falls off quickly, much less sensitive to distance activation fronts, hence recording of local events.
  - Method is sensitive to directional differences of the wavefront with respect to the axis of the bipole.
  - Morphology does not indicate wavefront direction



Electrogram Example

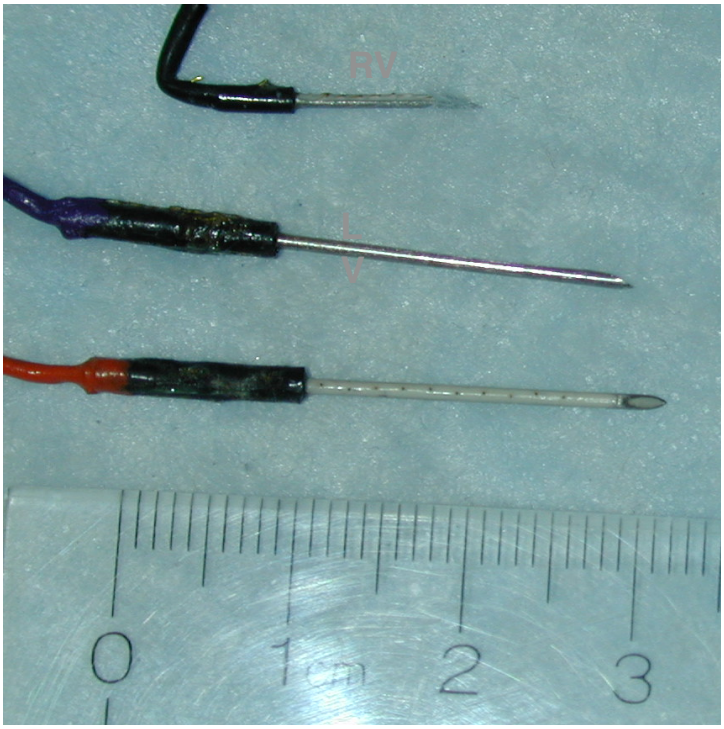


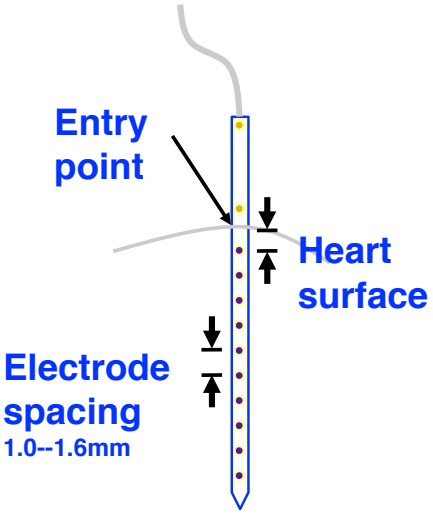
Cardiac Mapping



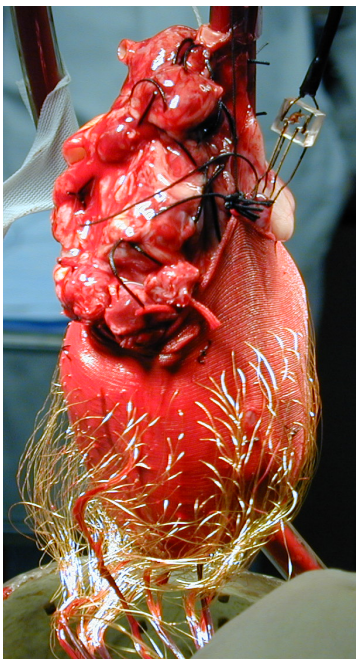
- Coverage
- Sampling Density
- Surface or volume

Cardiac Needle Electrodes





Cardiac Sock Electrodes



Activation Sequence: Human Heart

- Durrer et al., 1970
- Three sites of earliest activation
- Anisotropic conduction

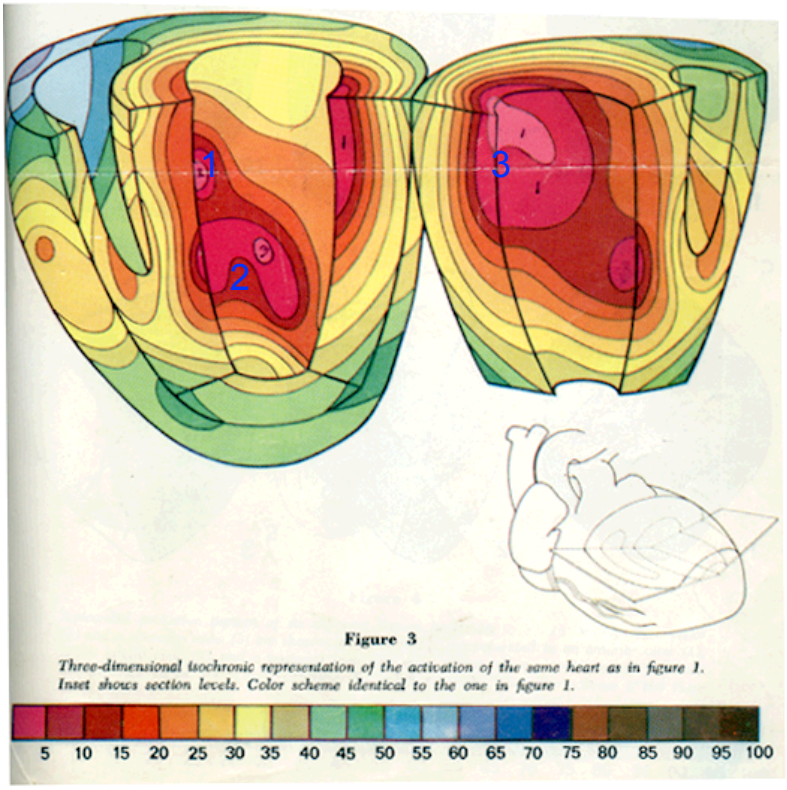


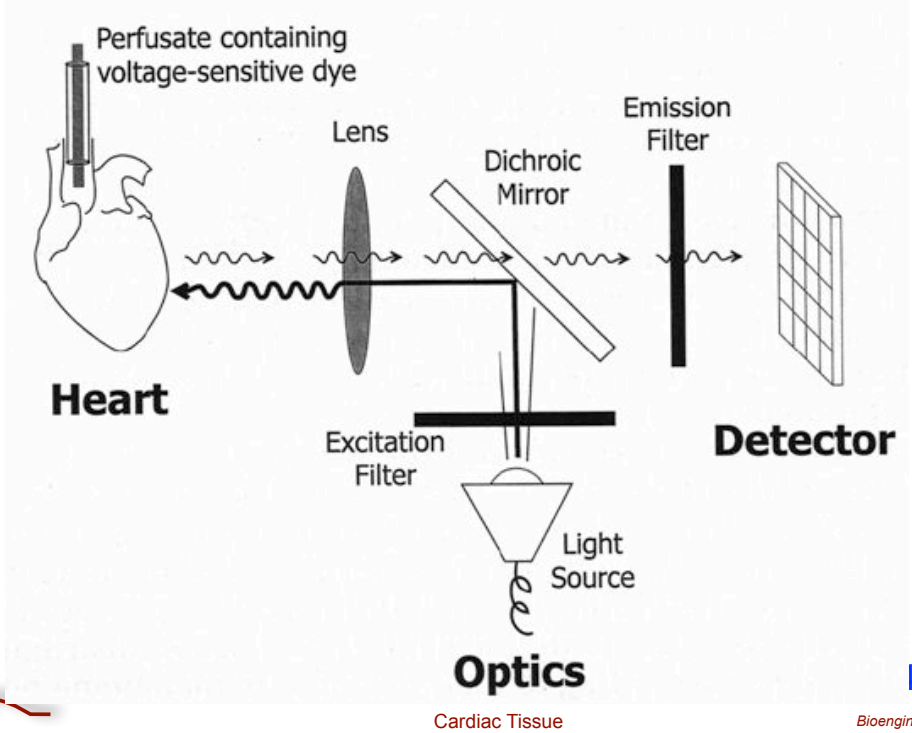
Figure 3

Three-dimensional isochronic representation of the activation of the same heart as in figure 1. Inset shows section levels. Color scheme identical to the one in figure 1.

Optical Mapping

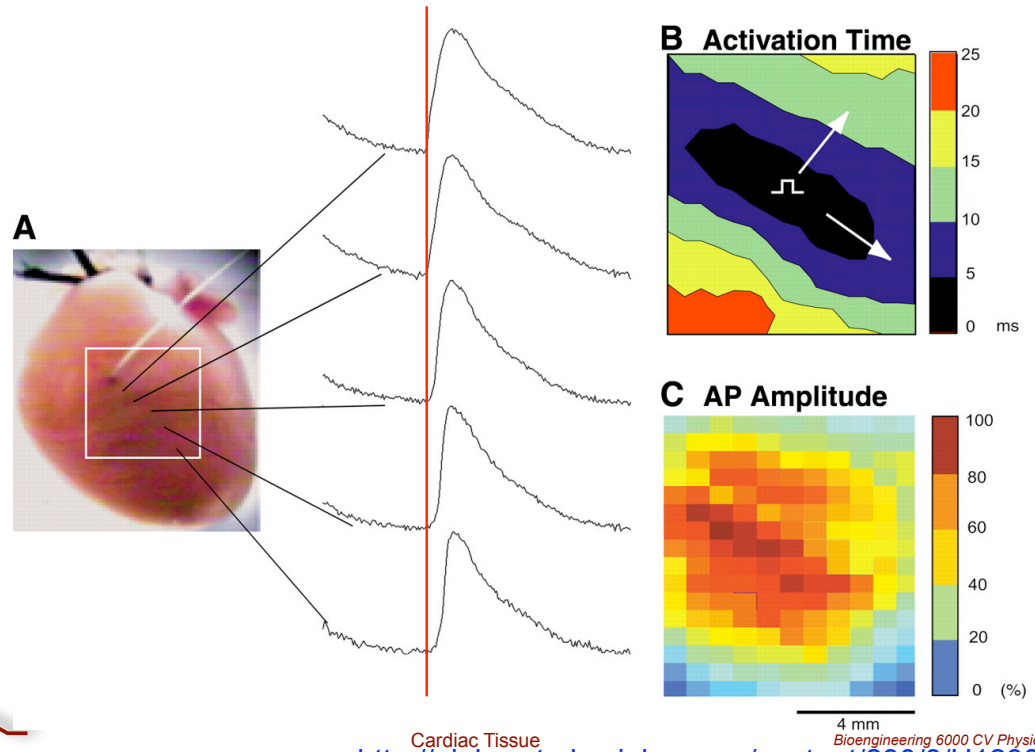
- Fluorescent Dyes
  - voltage sensitive
  - calcium sensitive
  - pH sensitive
- Confocal microscopy
- Multiple sensors
  - photodiodes
  - CCD cameras
- Advantages
  - no impalement or contact
  - can measure membrane potential
- Disadvantages
  - measures relative change so calibration a challenge
  - motion artifacts

Optical Mapping Setup



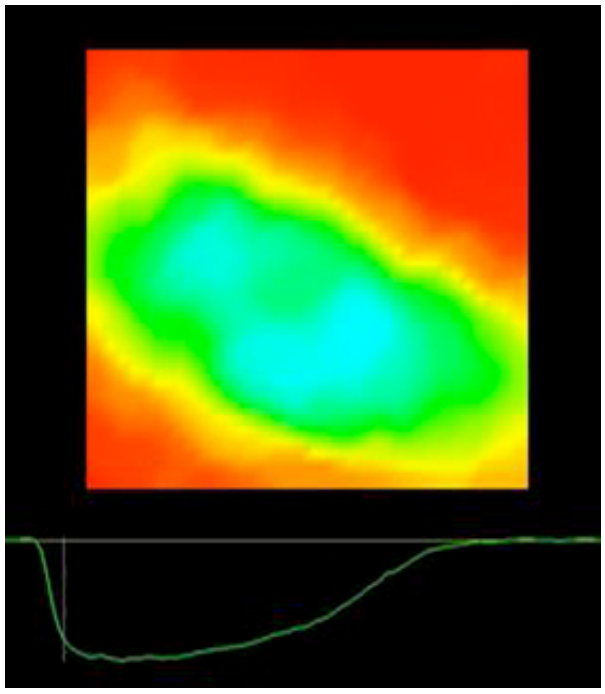
l2/1/wu.htm

Optical Imaging Example (Rat)

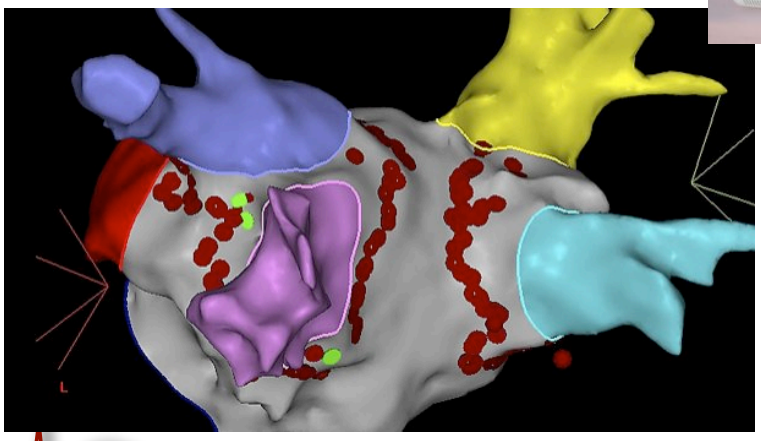


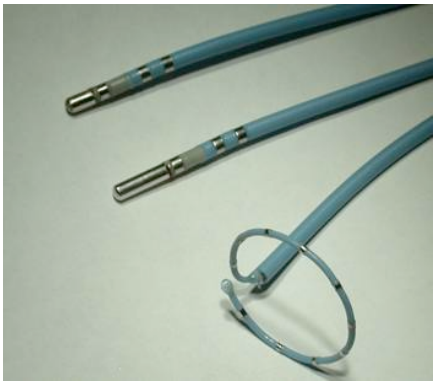
http://ajpheart.physiology.org/content/290/3/H1298

Example: Spread of Activation



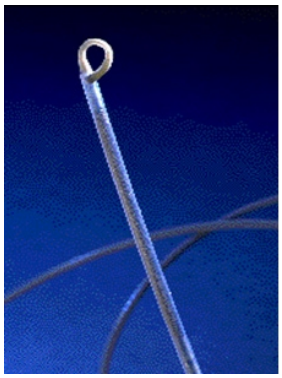
Clinical Mapping

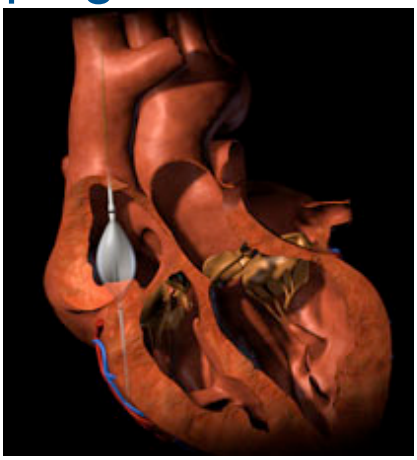


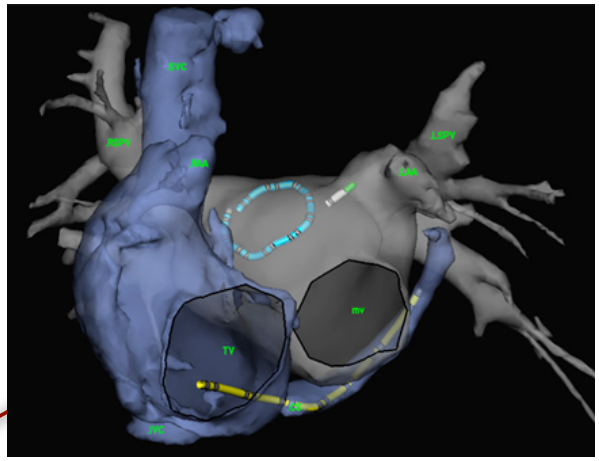


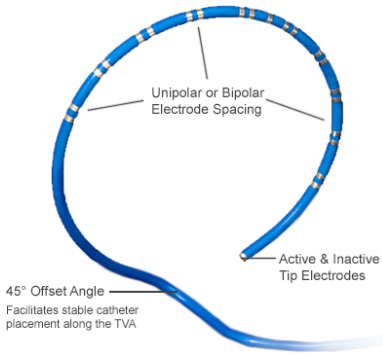
Cardiac Tissue

Clinical Mapping







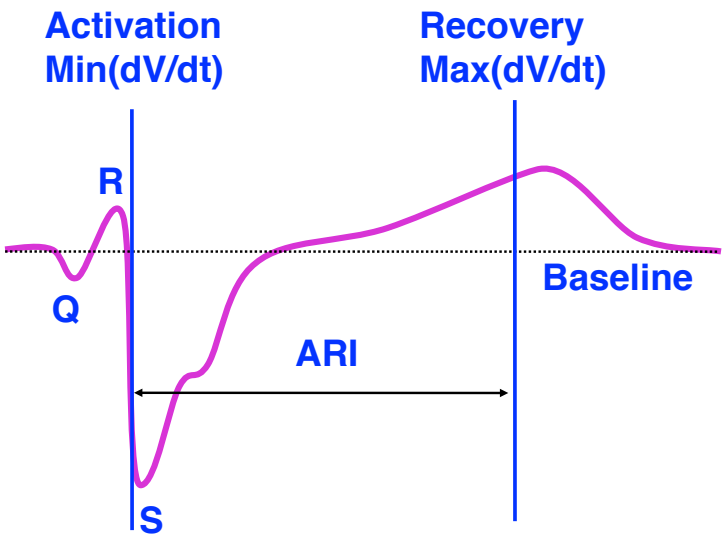


Signal Processing of Cardiac Data

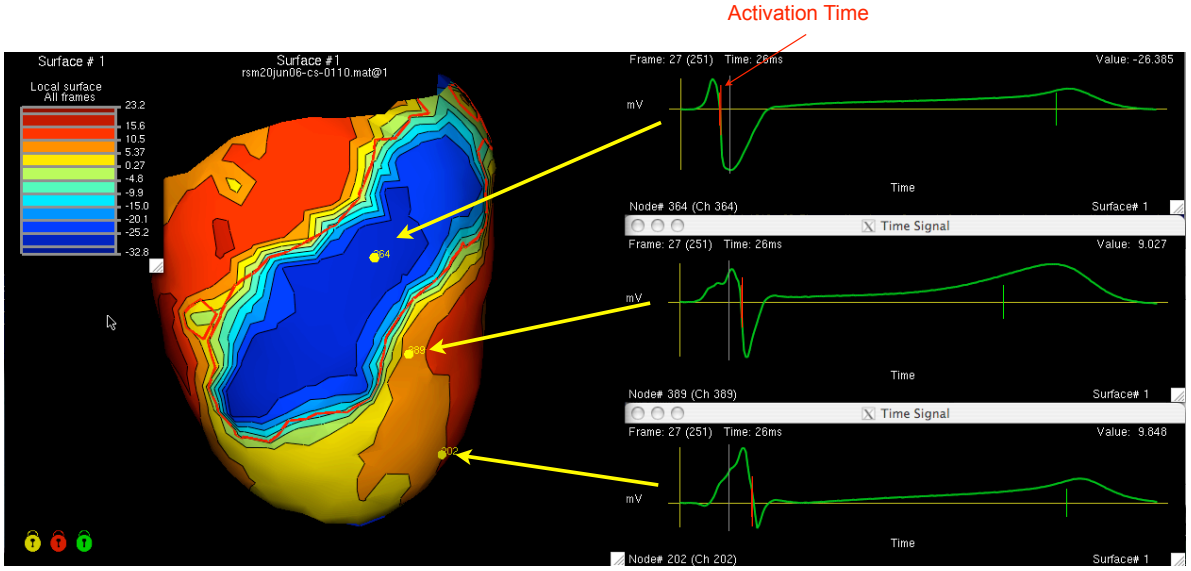
- Signal conditioning
  - Filtering
  - Baseline correction
- Feature extraction
  - Beat identification
  - Morphological measurements
- Visualization
  - Space and time preserving
  - Overlays, interaction, feature presentation

Signal Processing of Cardiac Data

Example



Interpreting Electrograms

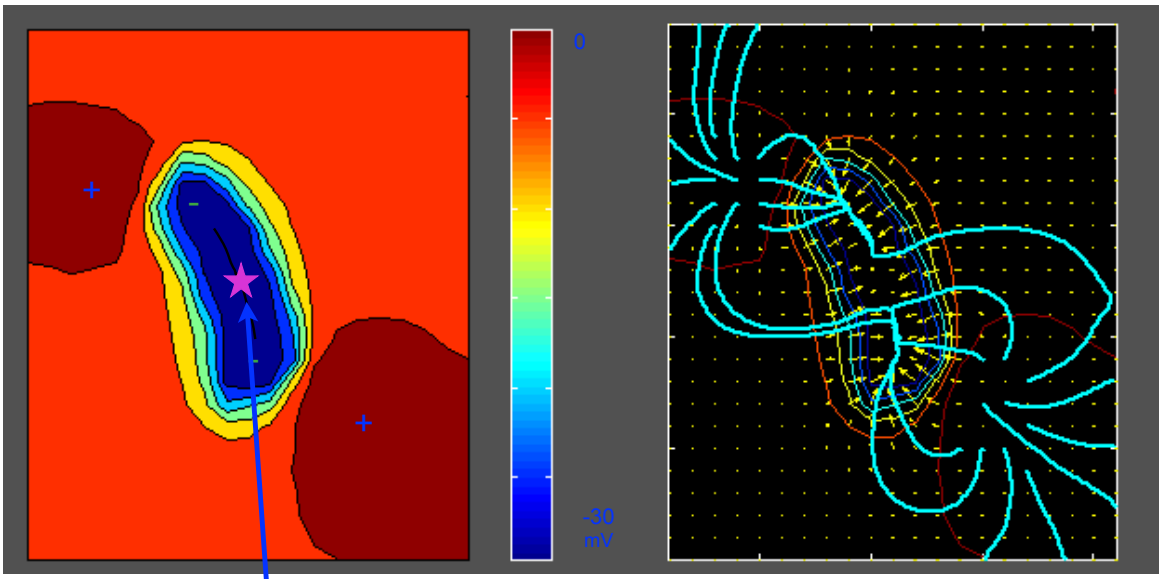


- Wavefront approaching = positive potentials
- Wavefront passing = rapid downward deflection
- Wavefront receding = negative potentials

Roles of Tissue Anisotropy

Voltage

Voltage + Current

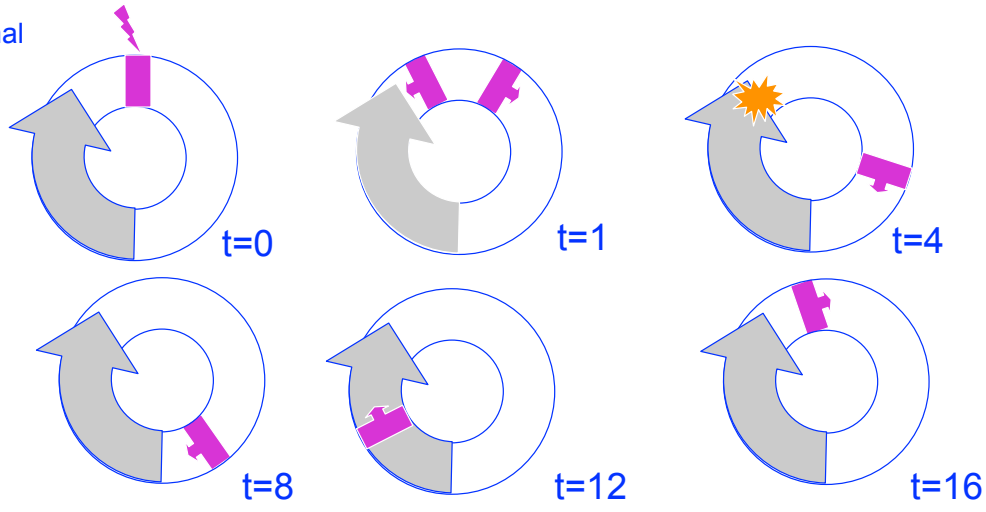


Site of stimulation

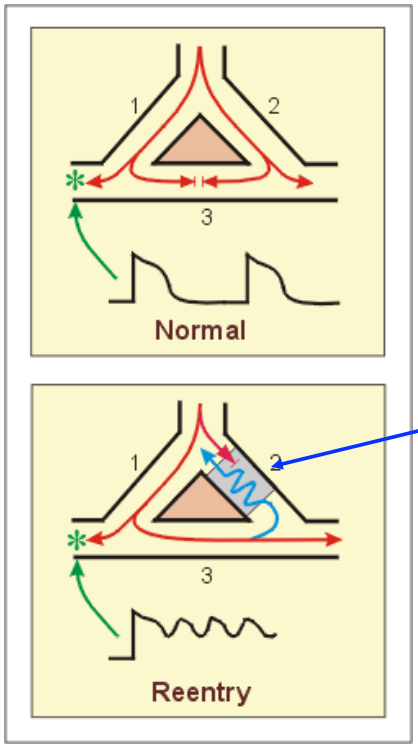
Arrhythmia Mechanisms

Reentry

Unidirectional Block

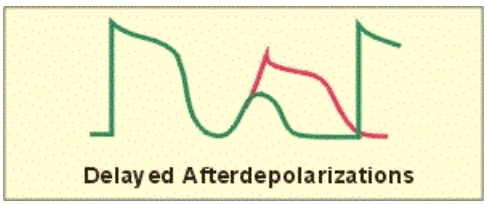


Reentry in the heart



Unidirectional Block (slow conduction)

Extrasystole (Premature Beat)



- Cellular origins
  - Abnormal Ca^{++} handling, ion concentrations, etc

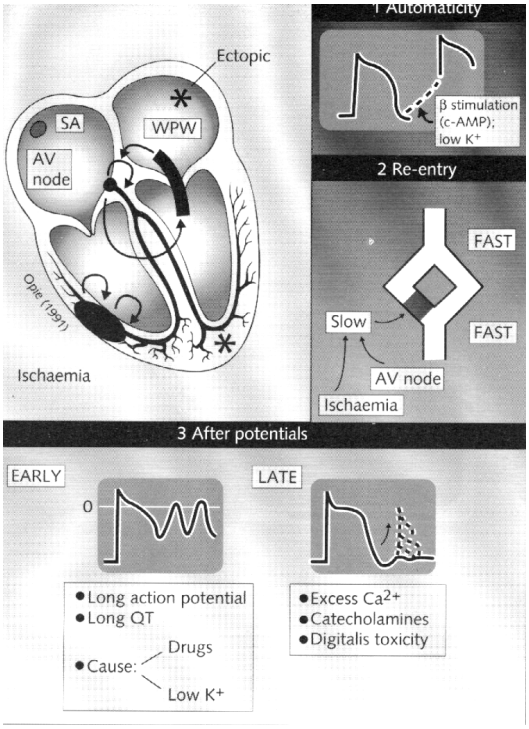
- Whole heart consequences
  - Extra beat, followed by compensatory pause

Reentry = Substrate + Stimulus

- Arrhythmogenic factors
  - slow conduction velocity
  - short refractory period
  - long, looping pathway
- Initiation
  - premature beat (extrasystole)
  - unidirectional block

Clinical Arrhythmias

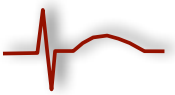
- Mechanisms
  - automaticity
  - reentry
- Substrate
  - necrotic tissue
  - unidirectional block
  - accessory pathway
- Stimulus
  - extrasystoles
  - afterdpolarizations



Treatment of Arrhythmias

Treatment of Cardiac Arrhythmias: Drugs

- Reduce excitability (Na blockers, reduce dV/dt of AP); Class I
- Reduce sensitivity to sympathetic stimulation (beta blockers); Class II
- Prolong repolarization (K channels blockers); Class III
- Block Ca-channels and thus reduce excitability (mostly in SA and AV nodes) ; Class IV

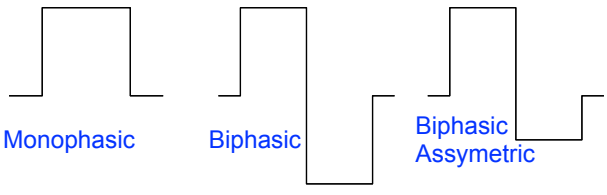


Treatment of Cardiac Arrhythmias: Devices and Interventions

- Defibrillators
  - External
  - Implantable (90,000 per year)
- Interventions
  - Invasive surgery: cutting, cryoablation
  - Catheter ablation: RF pulses, laser

External Cardiac Defibrillation

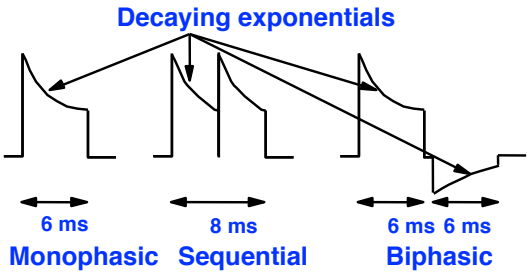
- Goals:
  - depolarize all cells
  - couple efficiently
  - minimize energy requirements through titration (25-400 J)
- Waveforms

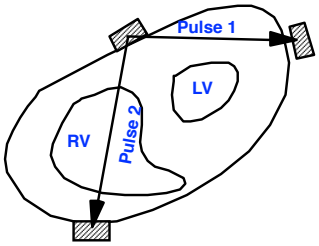


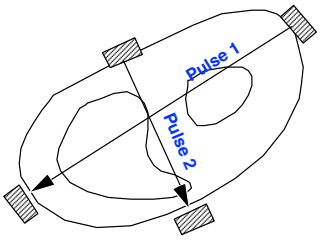
	Minimum	Typical	Maximum
Energie [J]	50	150	360
Voltage [V]	1100	1800	3000
Current [A]	22	36	60
Duration [ms]	3	5	8

Implantable Cardioverter Defibrillators

- Waveforms
  - Amplitude
  - Shape
  - Polarity
- Electrodes
  - Location
  - Number
  - Sequence

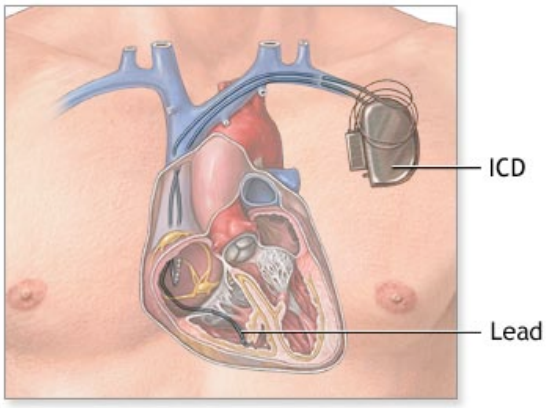


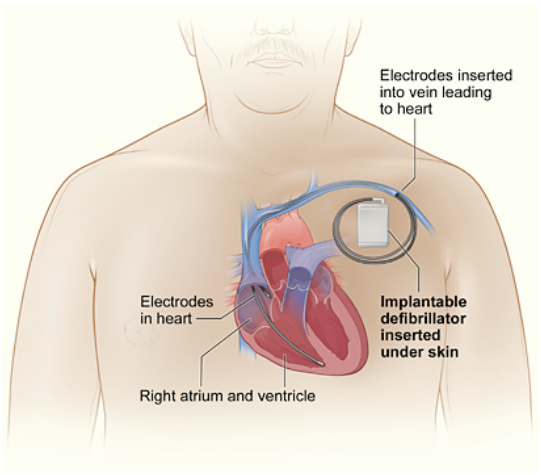




	Minimum	Typical	Maximum
Energie [J]	10	30	70
Voltage [V]	500	850	27
Current [A]	10	17	60
Duration [ms]	3	5	8

Implantable Cardiac Defibrillators (ICD)

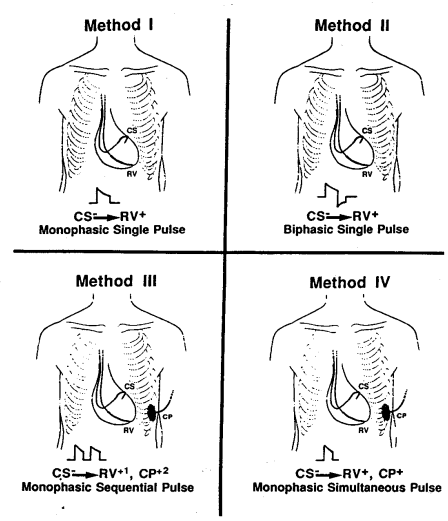


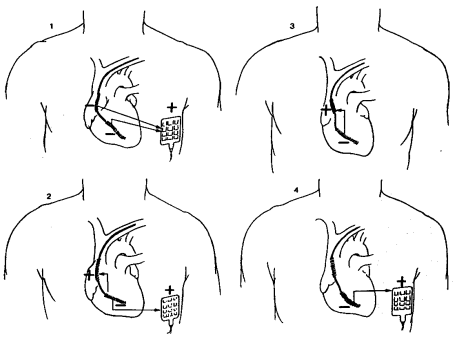


68,000 adult cases annually in the US (2004)

Implantable Cardioverter Defibrillators (ICDs)

- Electrode placement
  - surgical
  - by catheter
  - subcutaneous patch
- Shock protocol
  - monophasic
  - biphasic
  - sequential



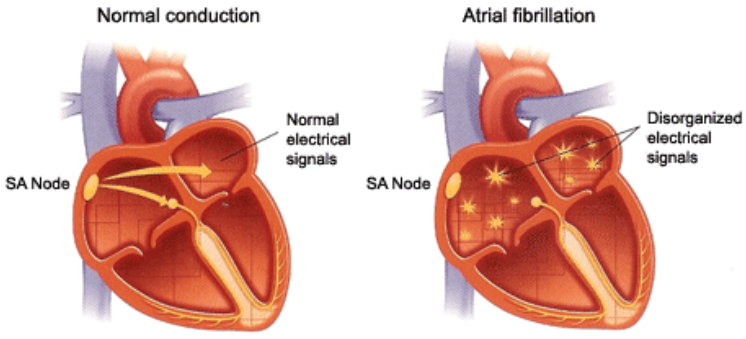


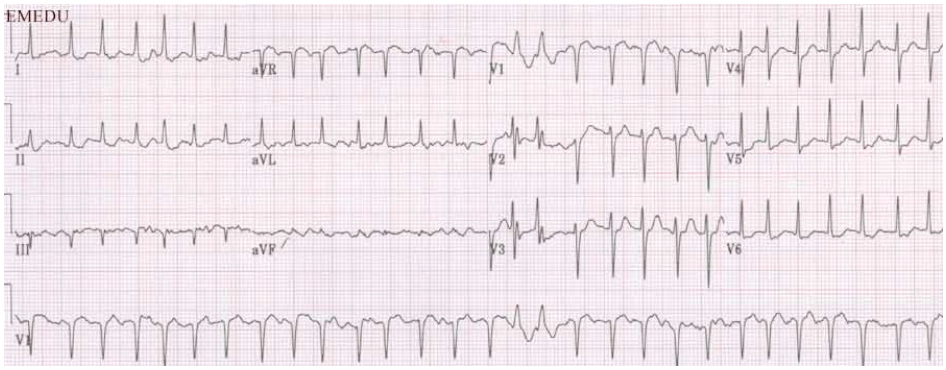
Clinical Example: Atrial Fibrillation

Atrial Fibrillation Background

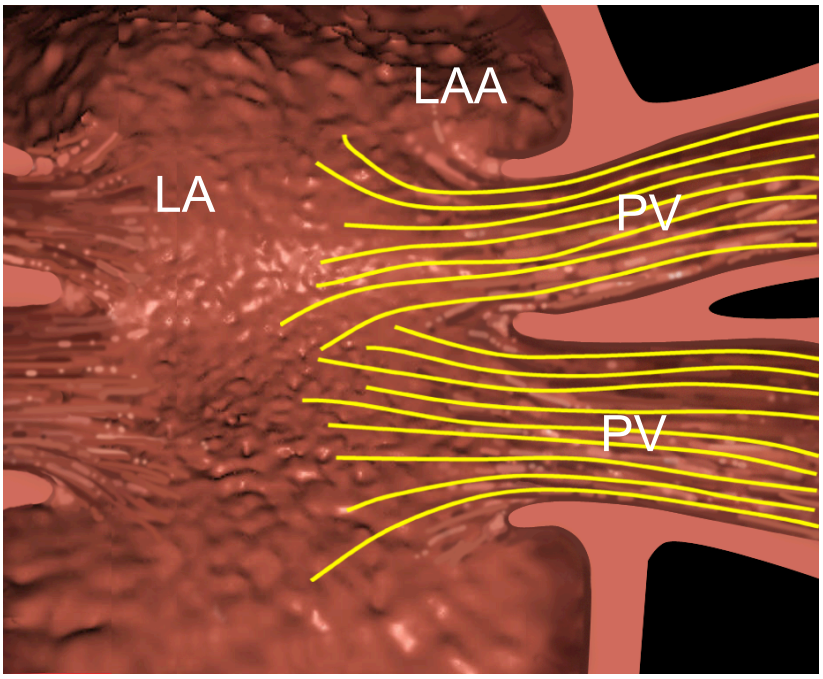
- Most common arrhythmia: 5% in > 65 years of age, 9% > 80 years
- Most common causes: ischemic heart disease, hypertension, mitral stenosis, congestive heart failure
- Presence of AF doubles mortality, increases risk of stroke by factor 2-7
- Once a heart is in AF, it becomes harder and harder to stop ("AF begets AF")
- Treatment by drugs (antiarrhythmics and anticoagulents) and ablation therapy.

Mechanistic Background

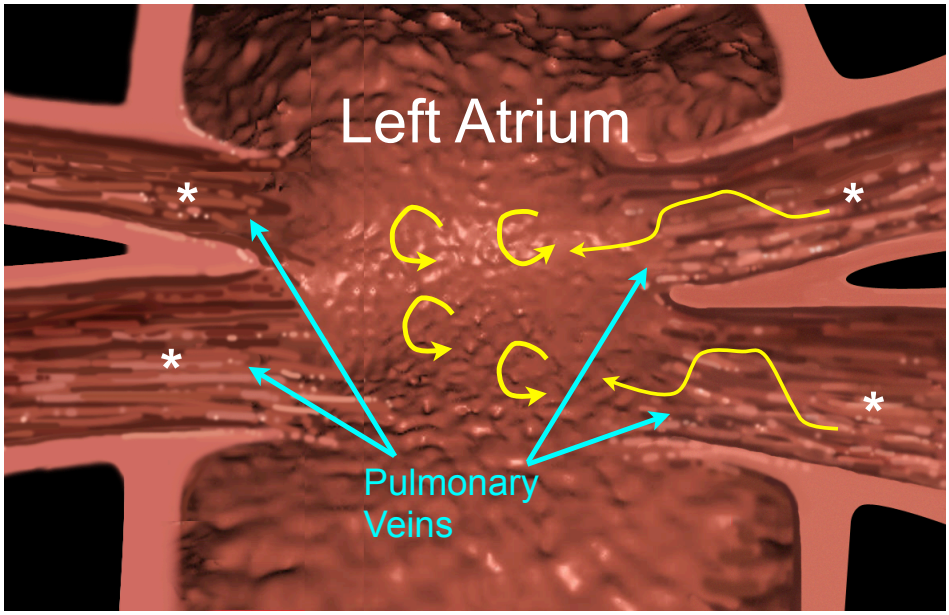




Substrate: Extension of PV muscle sleeves



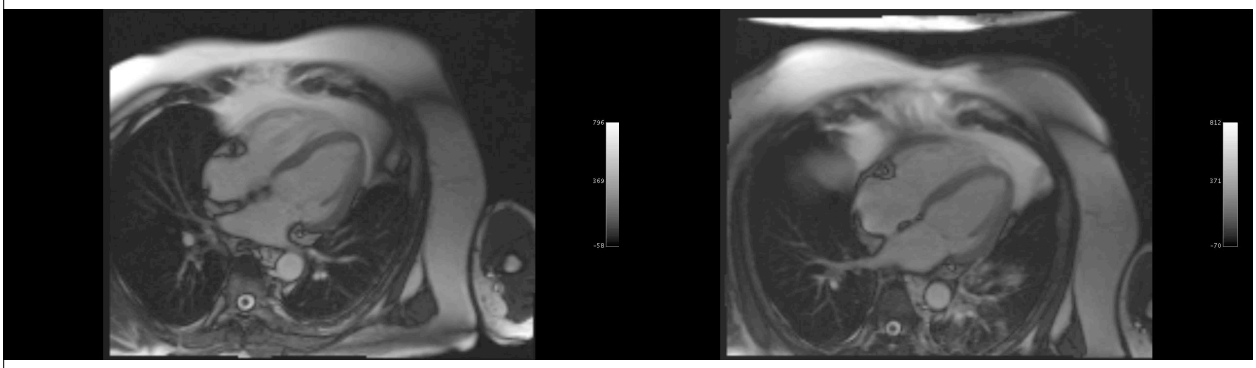
Mechanisms of Afib



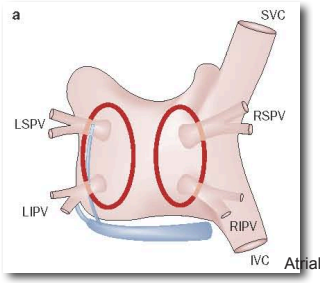
What is Afib?

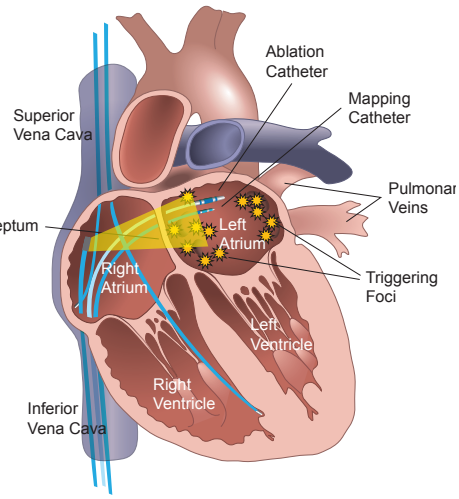
Normal Contraction

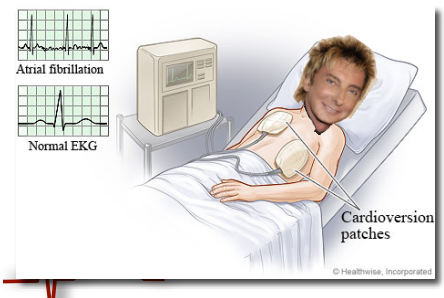
Atrial Fibrillation

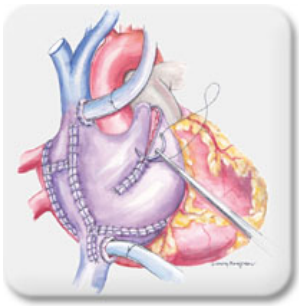


Effective Treatment of AF Eventually Involves Intervention



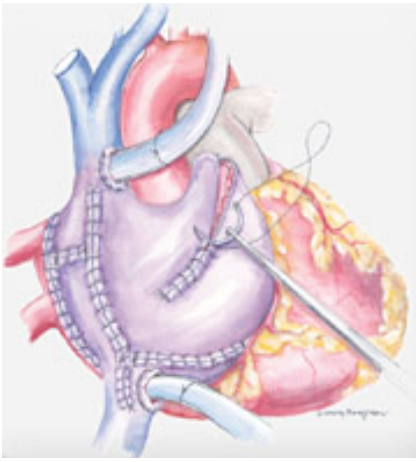


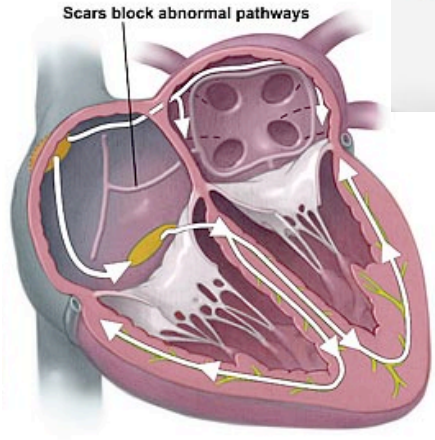




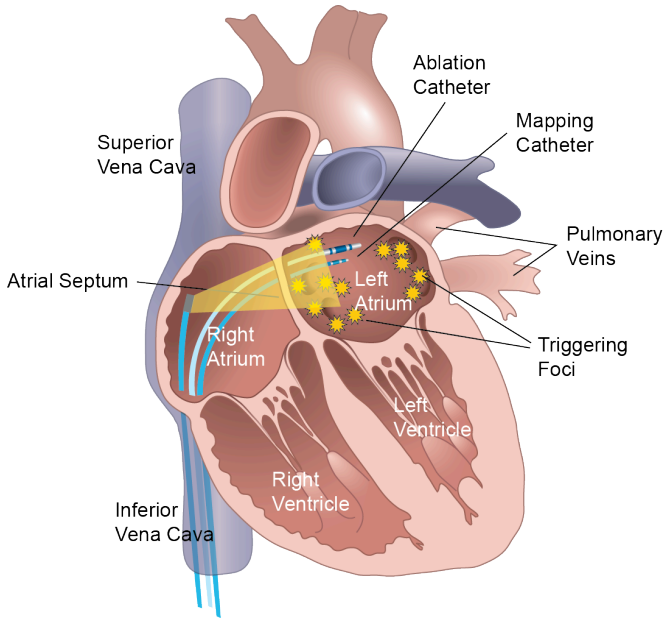
Treating AF

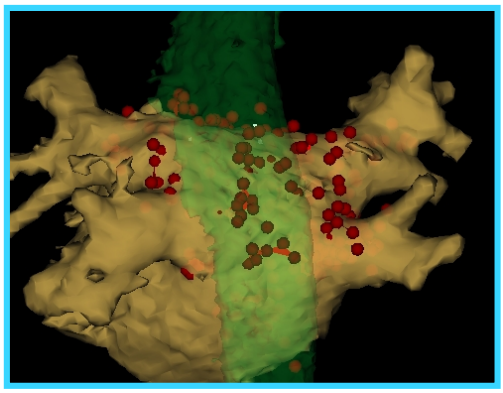
- Drugs + Defibrillation
  - Antiarrhythmics
  - Anticoagulants
  - Side effects
  - Life long burden
- Intervention
  - Maze procedure
  - Ablation



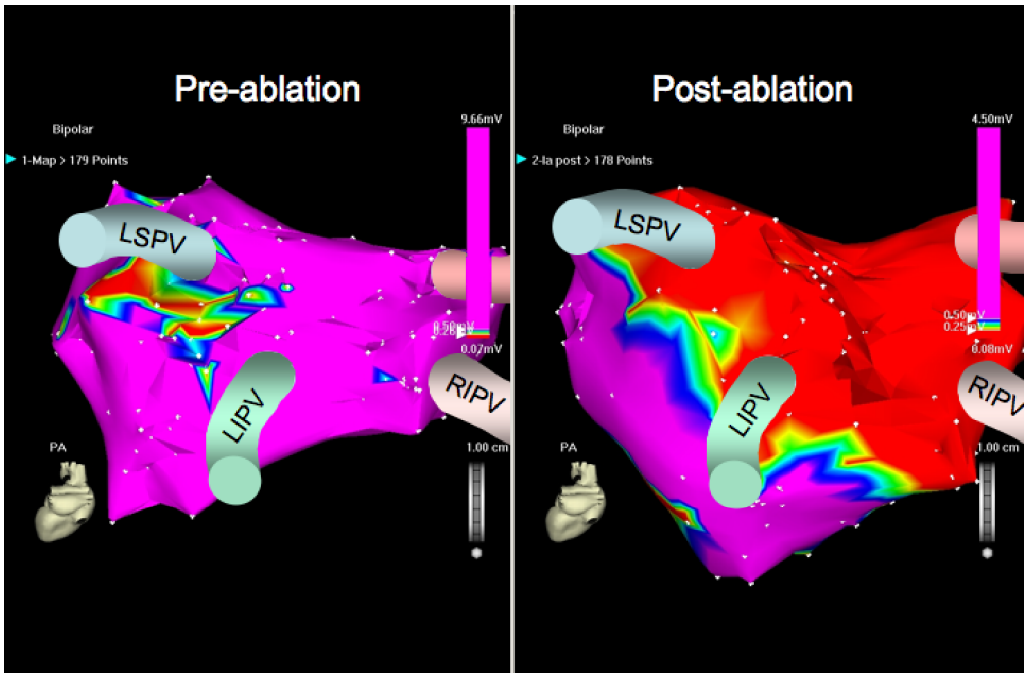


Ablation: Pulmonary Veins and Posterior Wall





Before and After Ablation



Segerson et al.

Summary

- Propagation of excitation in cardiac tissue
- Conduction system in the heart
- Activation sequence
- Cardiac Mapping
- Arrhythmias

Arrhythmia Video