THE UNIVERSITY OF MELBOURNE

Melbourne Veterinary School

Lecture 4, Week One
Mechanical Activity of the Heart
Semester Two 2023

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VETS30014 / VETS90124

Checkpoints for learning: lecture 3

1. In a resting cardiac myocyte the membrane is permeable to ___ ions.
2. At rest intracellular sodium concentration is higher/lower than extracellular concentration.
3. Selective movement of ions into the cell during stimulation occurs through _____ &_____ channels.
4. 'Fast' action potentials are typical of _____ heart tissue.
5. 'Slow' action potentials differ by having ……..

(Can you explain the ionic basis of these differences?)

6. During the absolute refractory period, sodium channels are _____ .
7. Stimulation of the sino-atrial node by parasympathetic nerves will increase/decrease heart rate.

This is due to a change in resting permeability to ___ ions, leading to _____ and _____ .

Lecture 4: Characteristics of cardiac cells
Mechanical activity of the heart

- Matching the structure to the task
  - the cardiac skeleton
  - specializations in cardiac muscle and cardiac histology
- Linking the electrical to the mechanical:
  - excitation- contraction coupling
- Cardiac muscle cell performance:
  - Length- tension relationships and
  - The Frank-Starling Law

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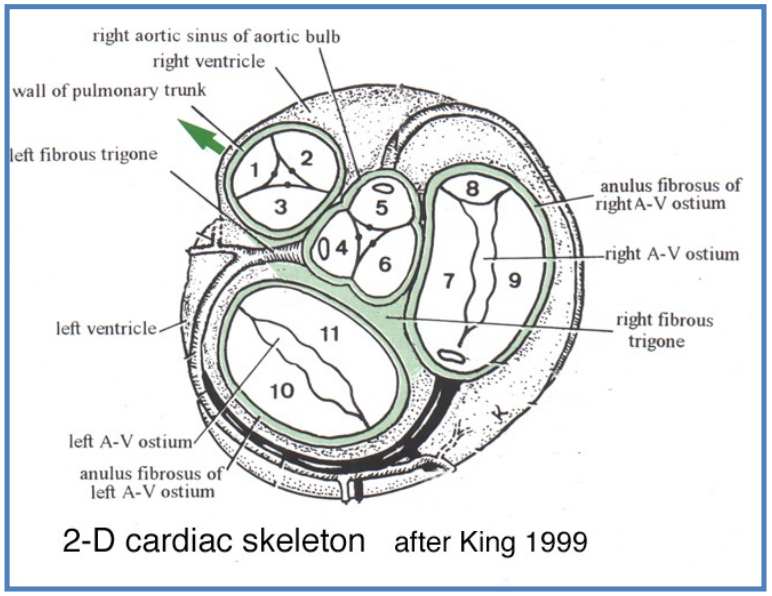
The Cardiac Skeleton

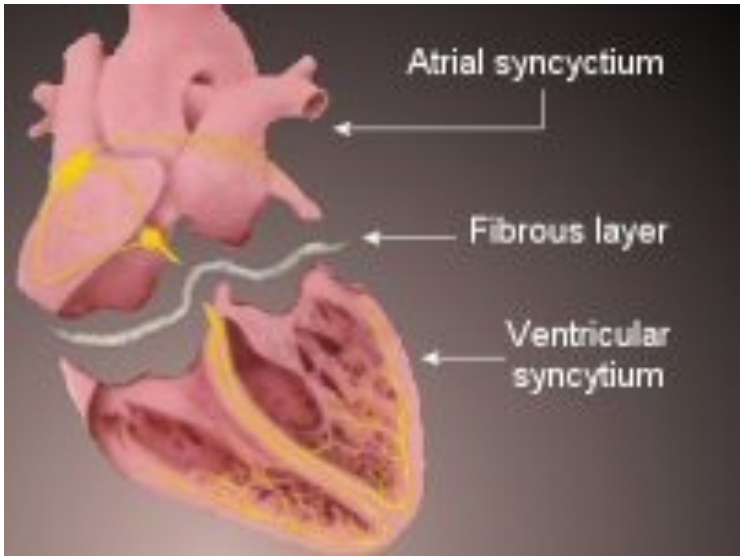
- In simple 2-D terms
- Fibrous plate with five holes:
  - One fibrous ring for each of -
    - Left A-V valve
    - Right A-V valve
    - Aortic semi-lunar valve
    - Pulmonic semi-lunar valve
    - The atrio-ventricular bundle



2-D cardiac skeleton after King 1999

Functions of Cardiac Skeleton

- ‘Electrophysiological discontinuity’
- Attachments for atrial and ventricular myocardium
- Strong yet flexible support for valvular openings



The Cardiac Skeleton

- Plate - 2 triangular areas - trigones
- Reinforced by cartilage or bone:
  - Ox - 2 bones
  - Sheep - 1 bone ('os cordis')
  - Cat, Dog, Pig, Horse - cartilage

The heart

Wall 3 layers

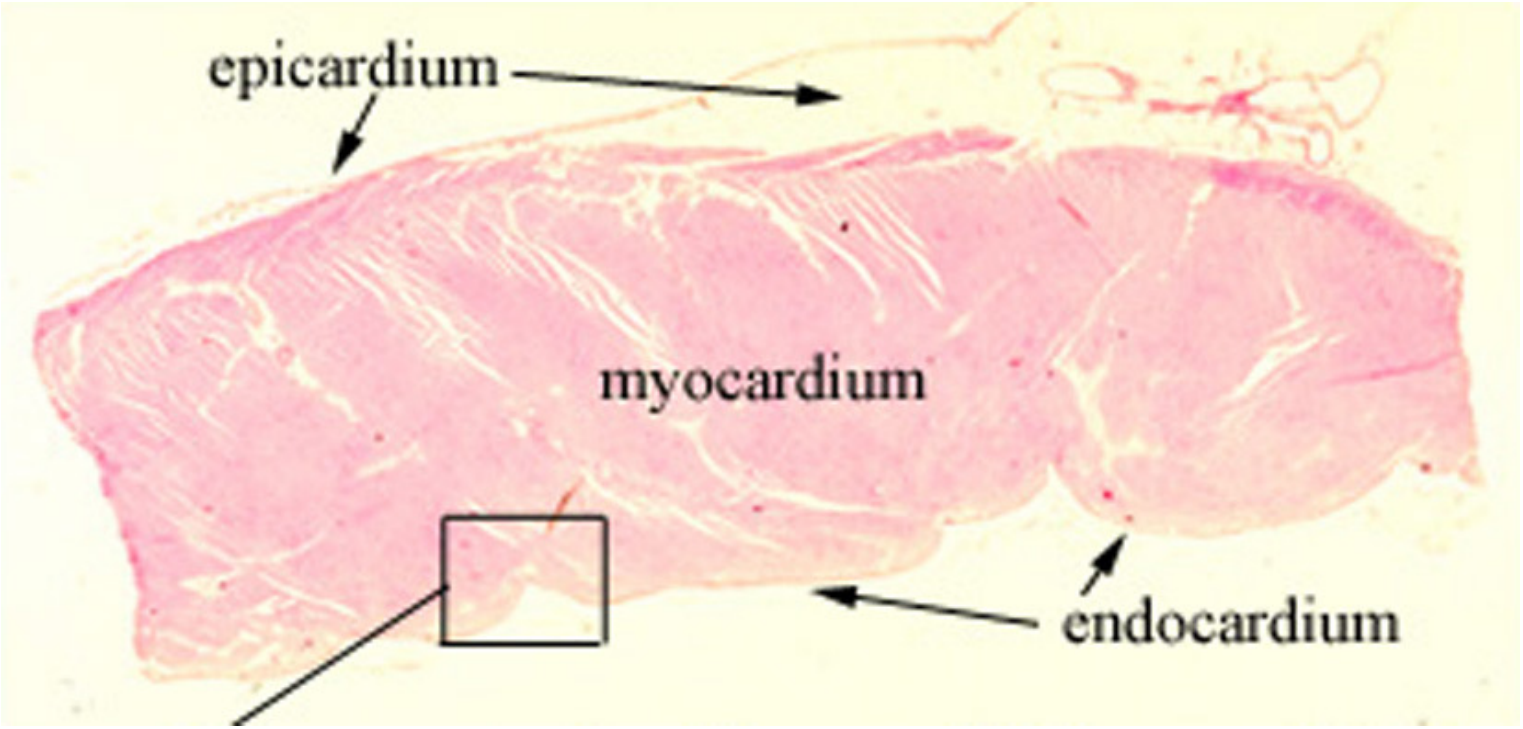
- Endocardium
  - Endothelium
  - Inner subendothelial layer
  - Outer subendothelial layer
- Myocardium
  - Bundles of cardiac muscle cells
- Epicardium
    - Mesothelial cells of visceral pericardium
    - Subepicardial connective tissue

The heart…

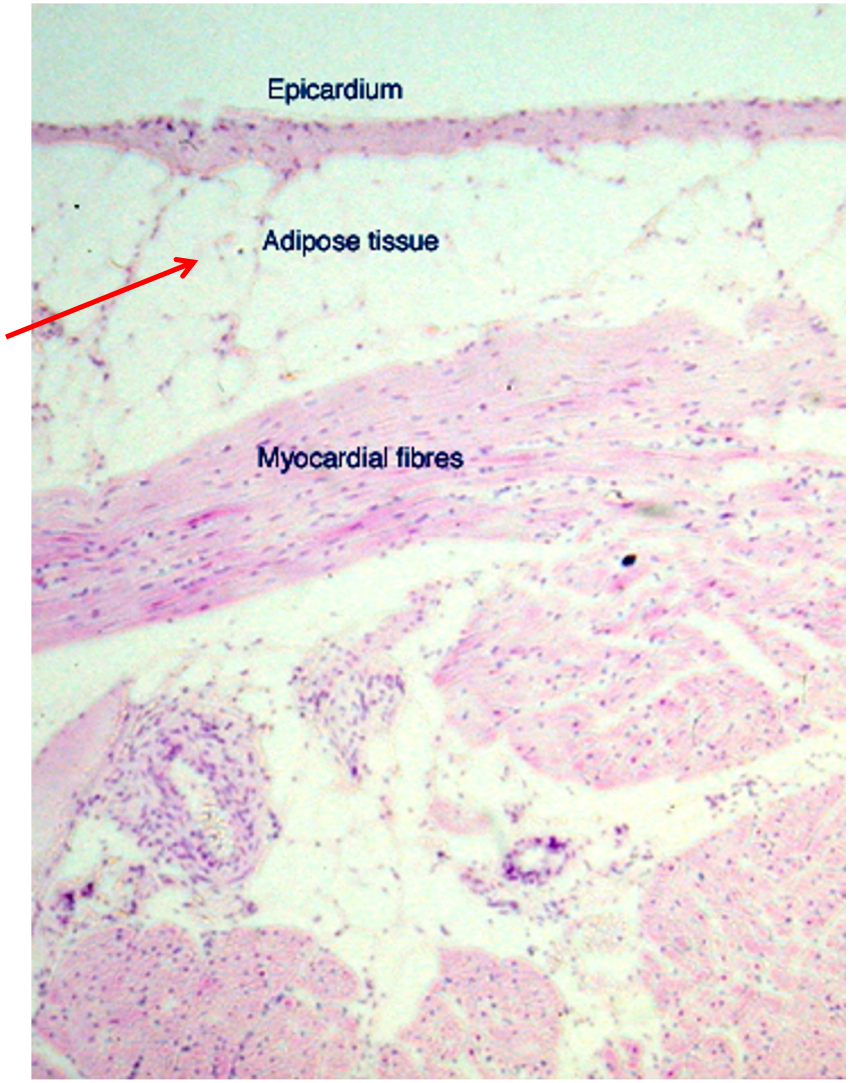
(some clues to finding your way around)

- Epi… “upon”/above
- Myo… muscle
- Endo…”within”

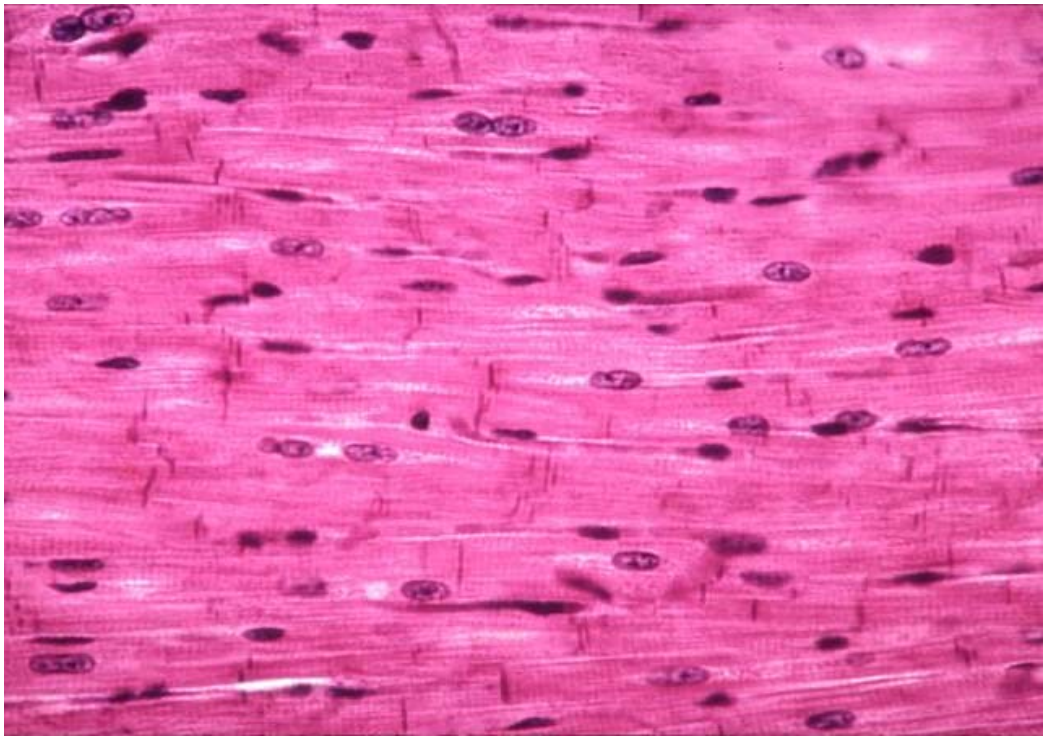
How can I tell outside from inside?



Adipose tissue is found under the epicardium



What's special about cardiac myocytes?

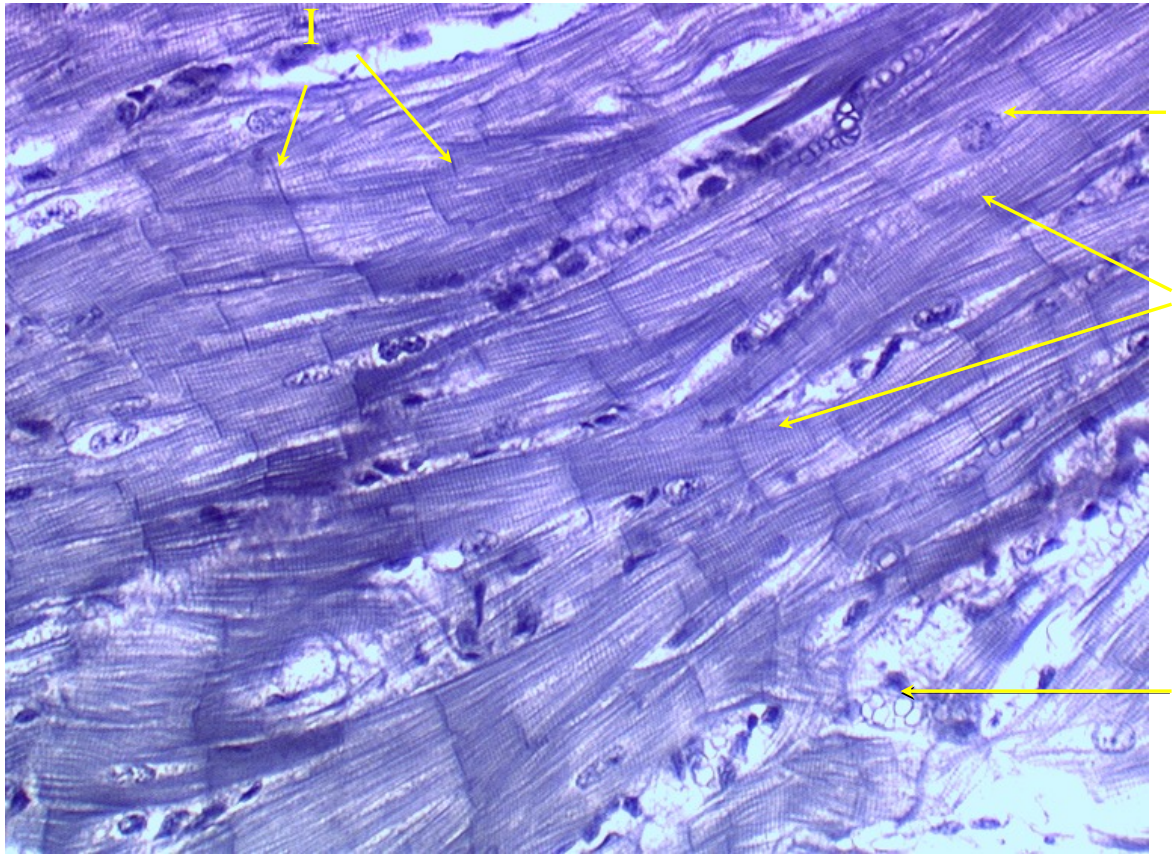


- Abundant mitochondria
- Dependent on aerobic respiration
  - No rest periods
  - No oxygen debt possible

Histology of Cardiac muscle

How does it differ from skeletal muscle?

Intercalated discs, central nuclei (usually one but sometimes two) with perinuclear space, branched fibres, good blood supply.



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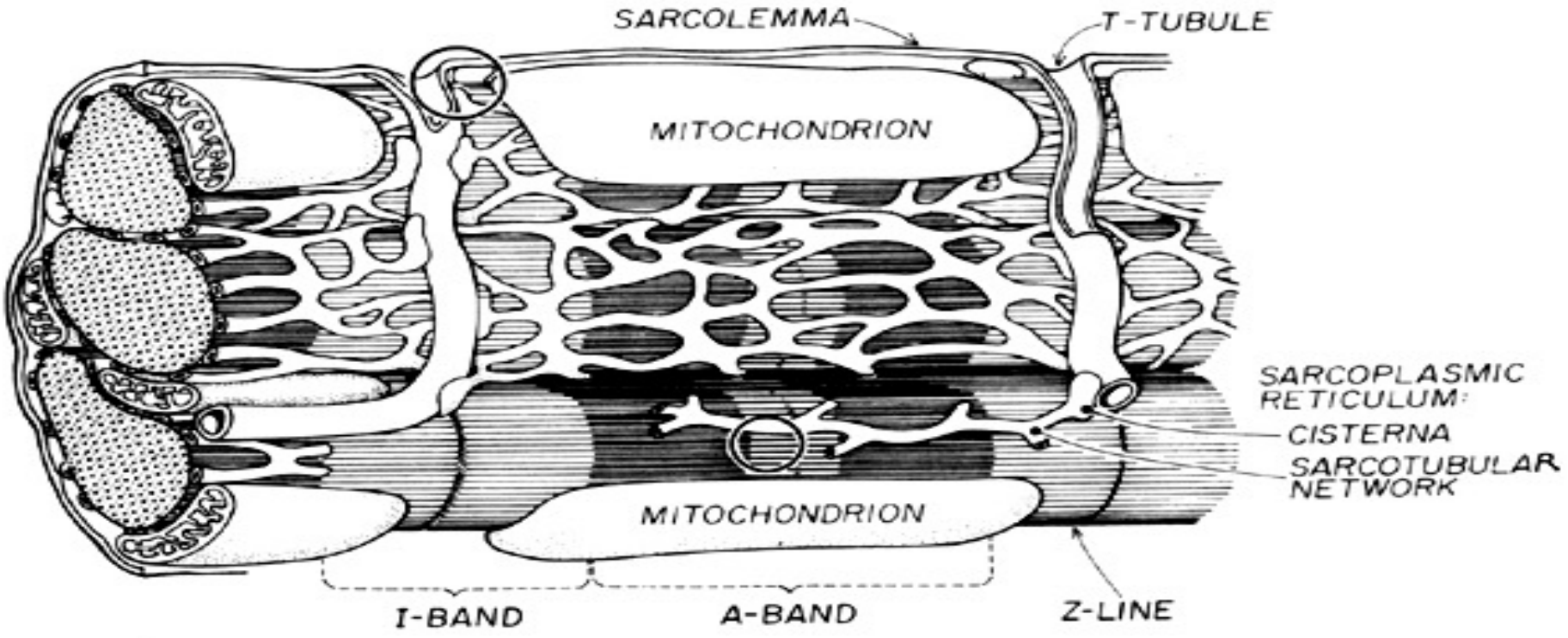
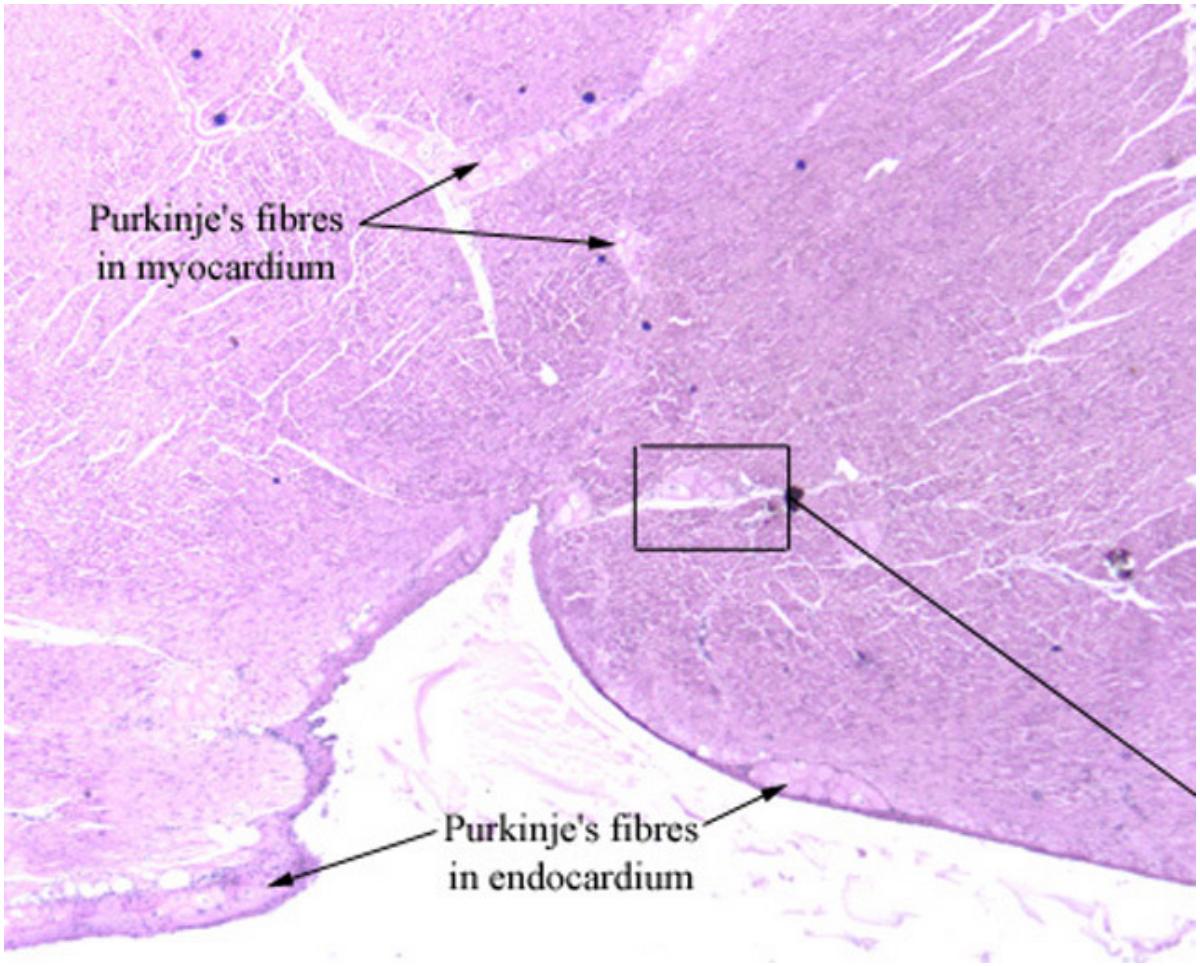


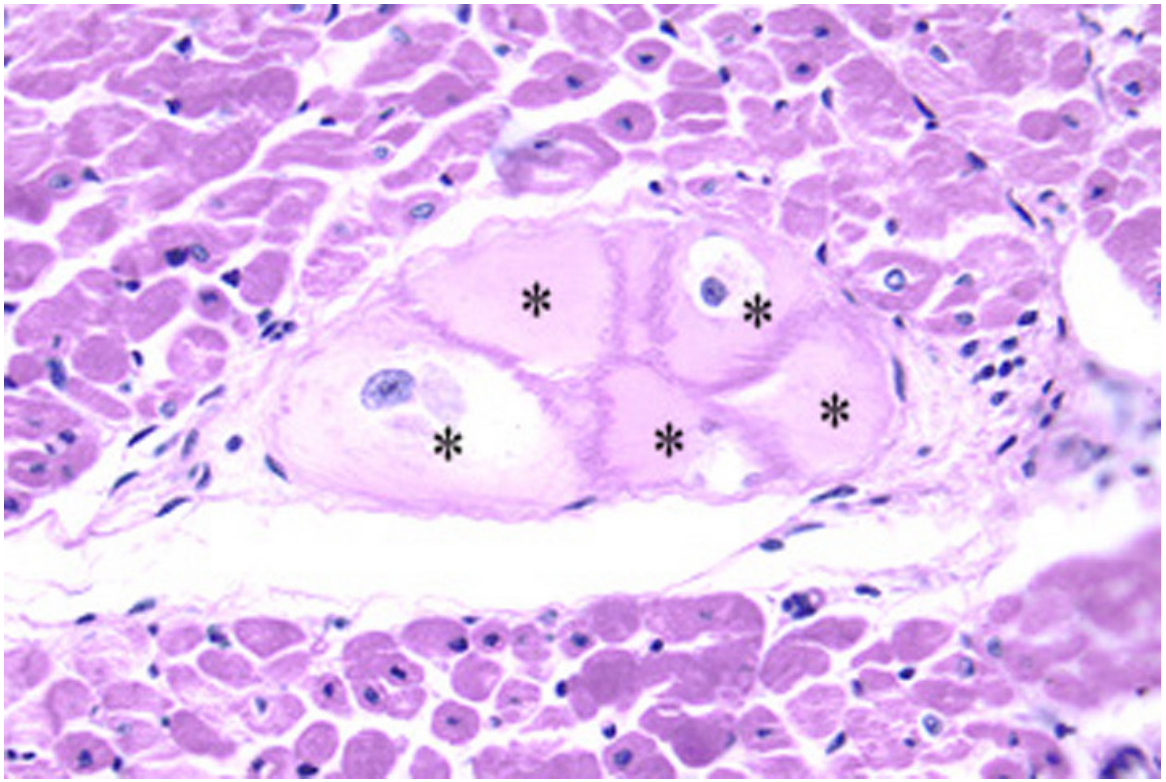
What's special about cardiac myocytes?

- Intercalated discs:
  - Structurally attached at desmosomes
  - Electrically connected at gap junctions
- Cell membrane invaginations :T tubules
- Sarcoplasmic reticulum in apposition with T tubules

Also identifiable:
Purkinje Fibres: Specialised conducting cells



Purkinje fibres



- Matching the structure to the task
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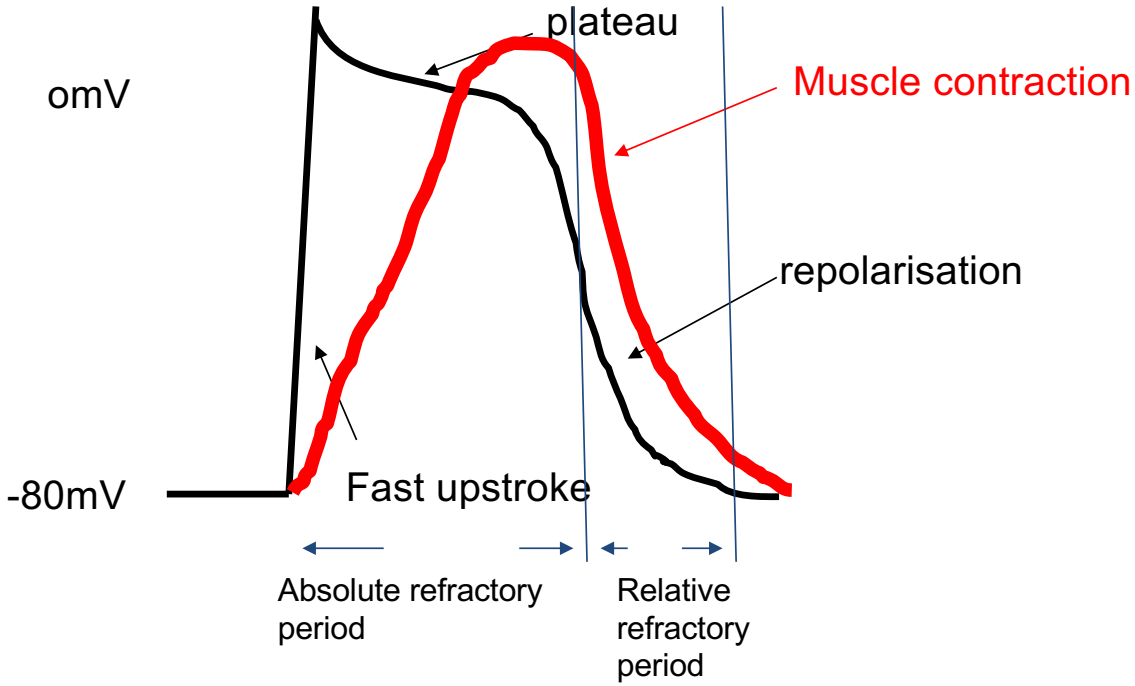
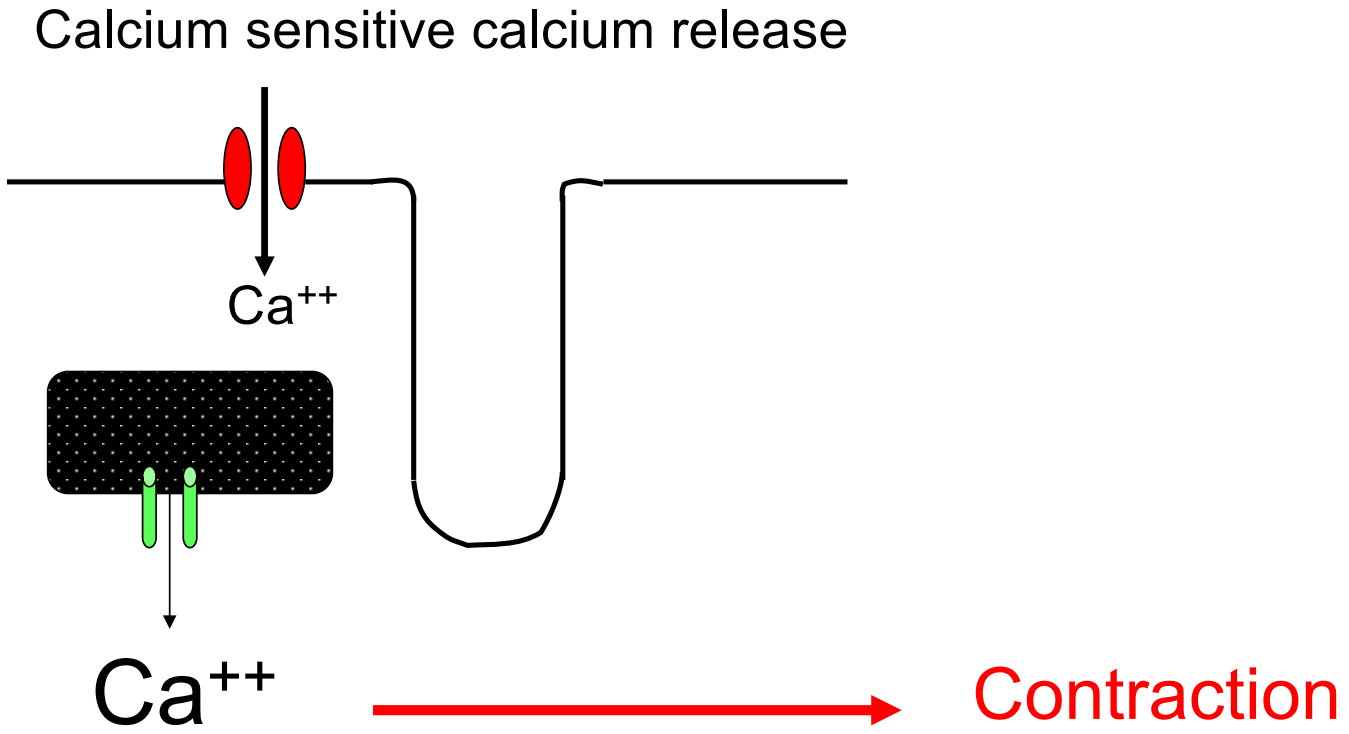
What links action potential and contraction ?

(ie excitation- contraction coupling)



It’s all about calcium



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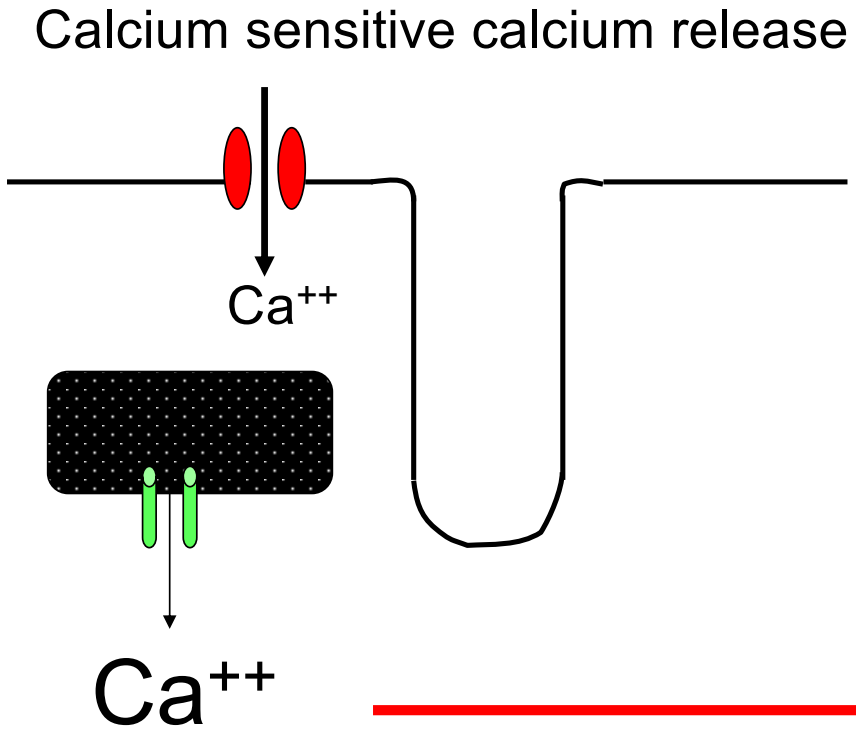


20% of the rise in intracellular Ca enters cell through VO channels

80% of the rise in intracellular Ca contributed by release from sarcoplasmic reticulum

Contraction

Excitation- contraction coupling

Action potential conducted across myocyte membrane and down T tubule leads to:

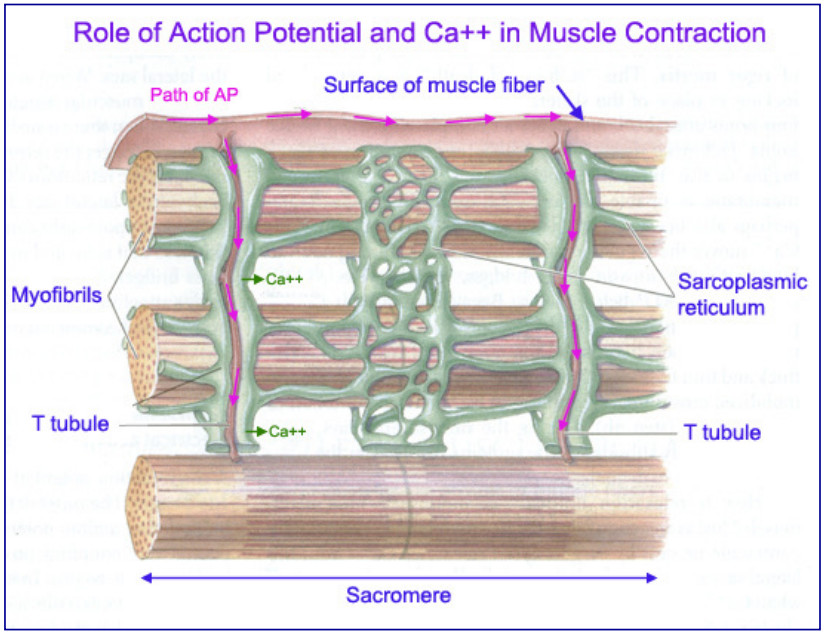
- Opening of VO Ca channels
- Entry of Ca to cell
- Increase in intracellular Ca that:

Stimulates release of Ca from sarcoplasmic reticulum (Ca sensitive release channels- ryanodine receptor channels) that:

Initiates contraction

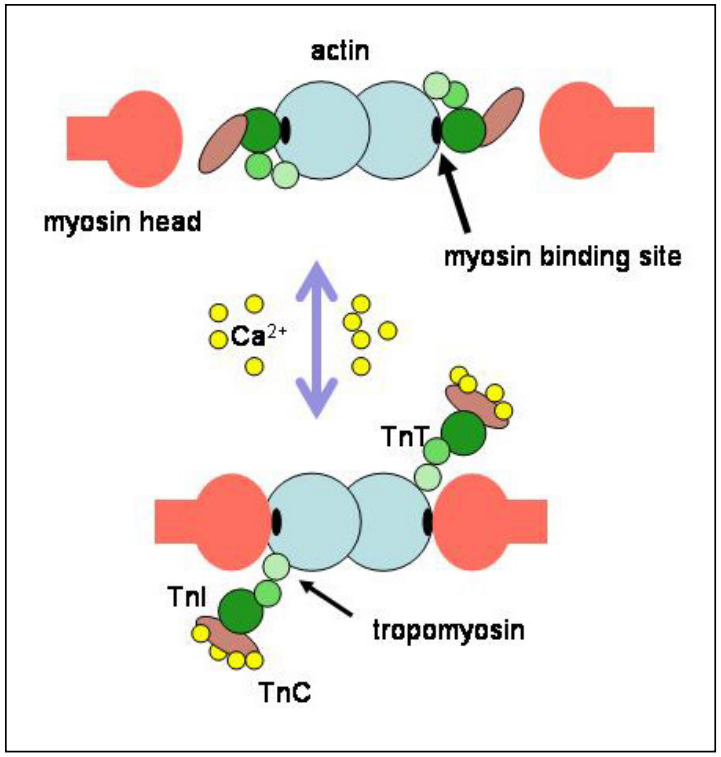
The Action Potential and Calcium

- Excitation- Contraction Coupling



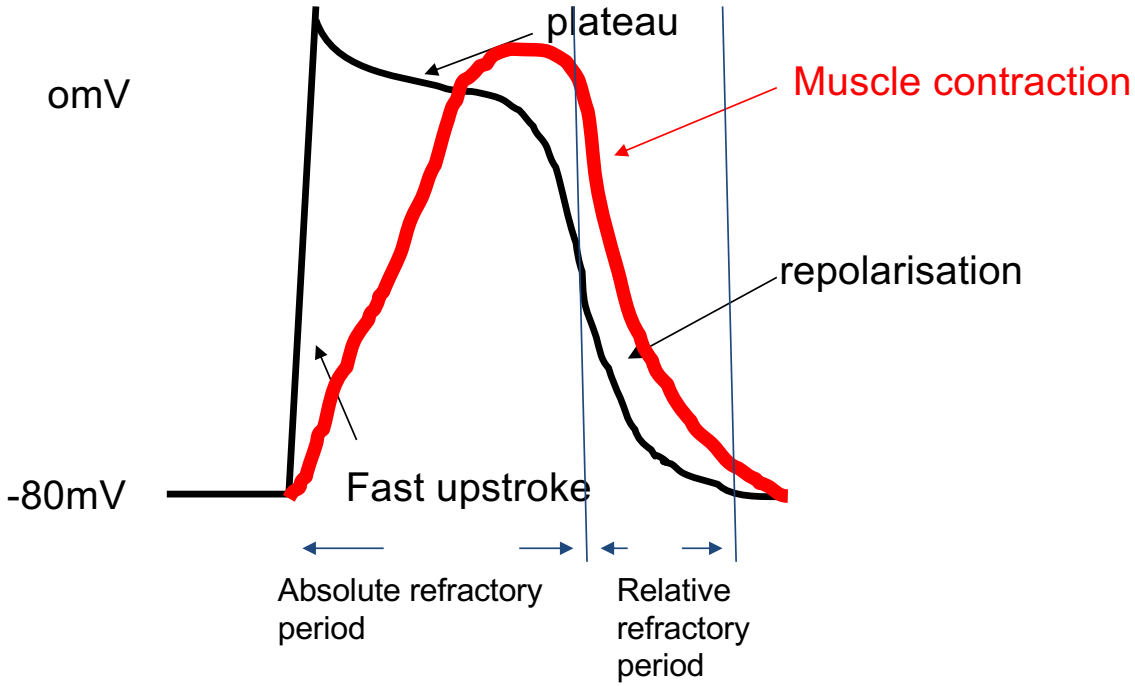
http://www.colorado.edu/intphys/Class/IPHY3730/image/figure9-2.jpg

Generation of tension



- Regulatory protein complex
  - Tropomyosin
  - Troponin
  - Prevent interaction between actin and myosin
- Calcium switch
  - Increased intracellular calcium
  - Ca causes tropomyosin to move aside
  - Myosin-actin cross bridges form
- --> Contraction (power stroke)
- Energy (ATP) supplied by ATP bound to myosin

Ca release from SR contributes to the plateau phase of the AP, and hence to the refractory period



Relaxation

- Active pumps return Ca to :
  - Sarcoplasmic reticulum
  - Extracellular fluid (less important)
- Calcium exchanged for extracellular Na
- Intracellular Calcium concentration falls
- Myocyte relaxes

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Generation of Tension

- The amount of Ca^{++} release (and hence force of contraction) depends on how much Ca^{++} is stored in the sarcoplasmic reticulum and the number of release channels activated.

- Tension generated is directly related to intracellular calcium levels.

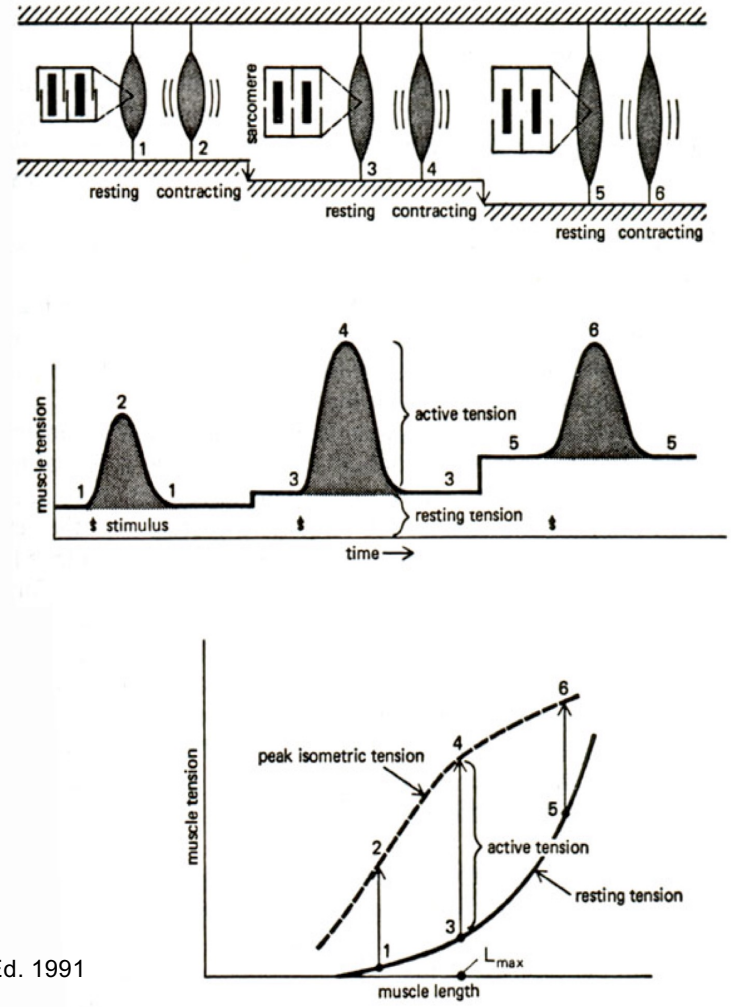
- Tension generated also depends on the length of the myocyte prior to contraction

Contraction in Cardiac muscle

- Isotonic contraction: activating an unrestrained muscle causes it to shorten without force development, as it has nothing to develop force against. Under these conditions a muscle shortens with maximal velocity.

- Isometric contraction: the muscle develops force at a fixed length- a measure of the muscle's maximum ability to develop tension (eg cardiac contraction before valves open)

Understanding length tension relationships



Mohrman DE & Heller LJ.
Cardiovascular Physiology. 3rd Ed. 1991

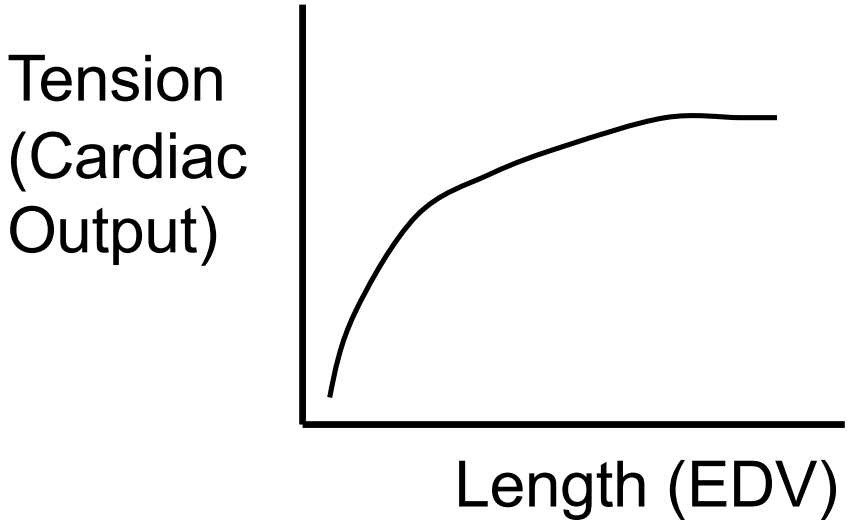
Effect of cell length

- Cell length determines overlap of thick and thin filaments
- Length of relaxed cells is determined by amount of blood in the ventricle

Optimal and normal cell length

- At a certain length overlap between thick and thin filaments is optimal and for a given rise in Ca will result in maximal tension
- Normal cell length is less than maximal

Length tension relationship



Contractility defined….

- The amount of tension that can be developed at any given stretch of cardiac muscle
- Contractility can be adjusted- physiologically and pathologically
- Inotropes are agents (physiological or pharmacological) that alter contractility

Contractility defined….

- Contractility is increased by an increase in intracellular calcium concentration
- Intracellular calcium can be modulated by
  - Receptor Operated Ca channels on cell membrane
  - Ryanodine channels on SR
- Modulation can be
  - Physiological (Noradrenaline, adrenaline at B receptor)
  - Pharmacological (inotropic drugs)

Length tension relationships: the Frank Starling relationship

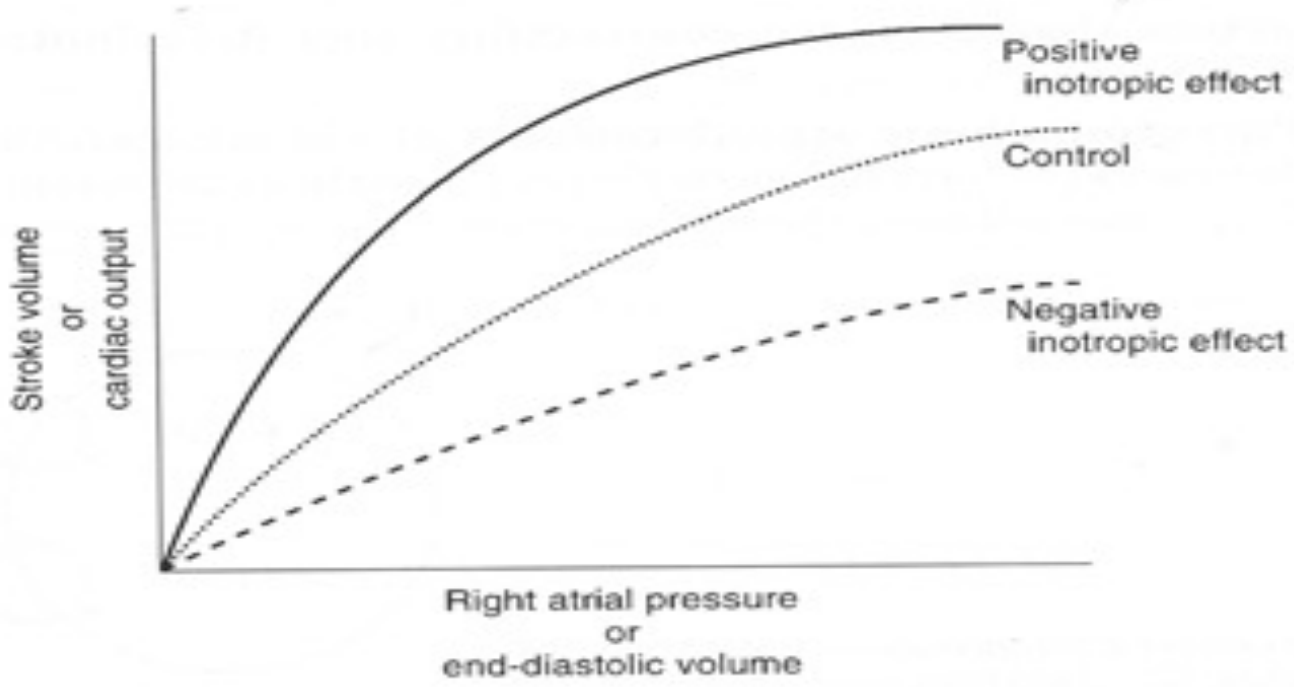
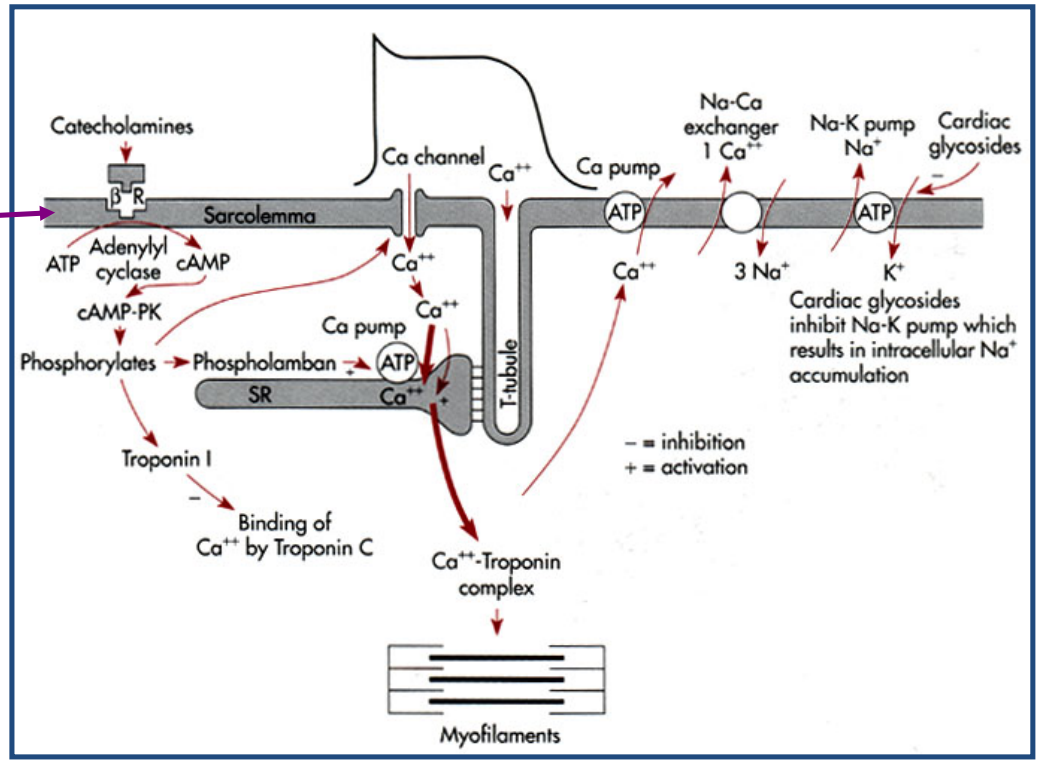


Figure 3-8. Frank-Starling relationship and the effect of positive and negative inotropic agents.

Increasing contractility…

what are positive inotropes?



- A role for the receptor operated calcium channel!

Summary

- Matching structure to the task
  - The cardiac skeleton
  - Cardiac histology
  - The cardiac myocyte
    - intercalated disks
    - T tubules
    - sarcoplasmic reticulum
- Excitation- contraction coupling
    - it's all about calcium:
    - membrane receptors and intracellular stores
- Cardiac muscle cell performance
    - the concept of contractility-- calcium and stretch
    - inotropy and modifiers of contractility