

# Muscle



## Muscle: a specialized contractile machine

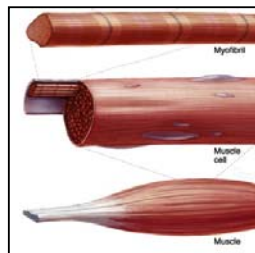


- Three types of muscle cells
  - Smooth muscle
  - Skeletal muscle
  - Cardiac muscle
- All use actin and myosin to generate unidirectional movement

## Anatomy of the skeletal muscle



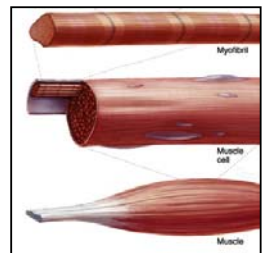
- A skeletal muscle is a parallel arrangement of muscle cells - **myofibers**
- A myofiber consists of multiple **myofibrils** also arranged in parallel



## Anatomy of the skeletal muscle



- In each myofibril actin and myosin are organized into a **linear** chain of highly ordered structures - sarcomeres



## Sarcomere

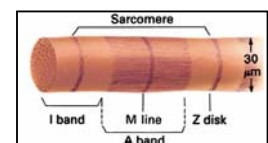


- Structural and functional unit of contraction
- 2mm long in resting state
- Contraction = shortening of the sarcomere
  - Each sarcomere shortens by 30%
- Every contraction is a binary event
- Graded contractions are achieved by varying number of activated muscle cells

## Sarcomere

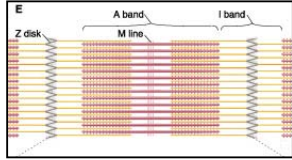


- A segment from one Z disk to the next
- Contains thin filaments (actin) and thick filaments (myosin II)
- Sarcomeres are lined up end to end



## Skeletal muscle – an array of actin and myosin

- I band - light band - thin filaments (actin)
- A band - dark band - thick filaments (myosin)
- Z disk is in the middle of I band (I band is made out of two light bands from neighboring sarcomeres)

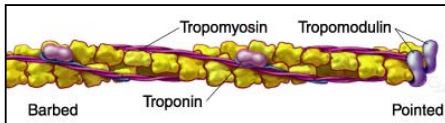


## Z disk

- Lattice of fibers
- Anchors barbed ends of actin filaments
- Cap Z and actinin  $\alpha$

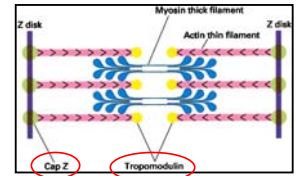
## Thin filaments

- Actin filaments + tropomyosin and troponin
- Barbed end associated with Z disk
- Pointed end near the center of sarcomere
- Both stabilized with actin capping proteins



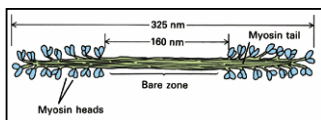
## Actin capping proteins stabilize actin filaments in the sarcomere

- Cap Z at the barbed end
- Tropomodulin at the pointed end
- Prevent depolymerization
- Actin is anchored at the Z disk



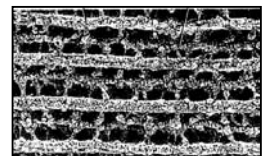
## Thick filaments

- Filaments of myosin II
- Tails of myosin II associate with each other
- Myosin heads are sticking out while tails form filaments
- Myosin is effectively anchored (can not move)



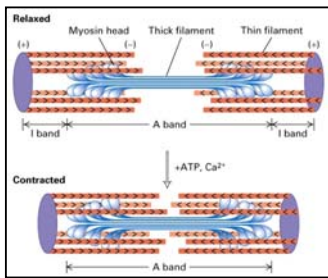
## Myosin II

- Filaments are bipolar
  - Heads at the distal tips
  - Tails in the center
- Heads of myosin form cross-bridges between filaments
- M line – tails without heads





## Walking myosin pulls actin filaments together

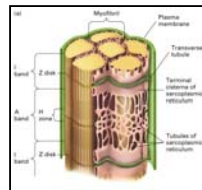


## Muscle contraction

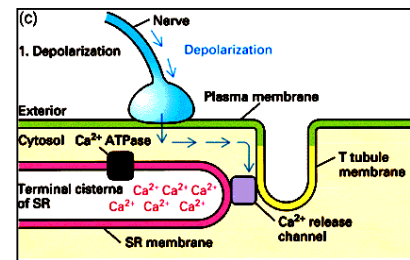
- Triggered by a rise in cytosolic  $\text{Ca}^{2+}$  concentration
  - Depolarization of muscle cell
  - $\text{Ca}^{2+}$  release of from sarcoplasmic reticulum
- Contraction
- $\text{Ca}^{2+}$  recovery by  $\text{Ca}^{2+}$  ATPases ends contraction

## Triads

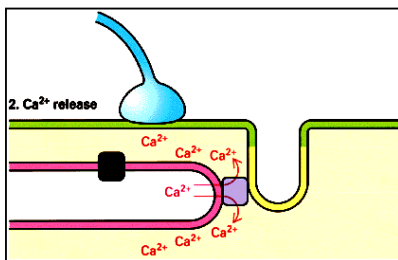
- Functional structures
- Bring depolarization in the immediate proximity of SR
- T (transverse) tubules - invaginations of plasma membrane



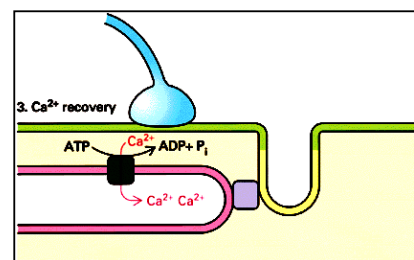
## A rise in cytosolic $\text{Ca}^{2+}$ triggers muscle contraction



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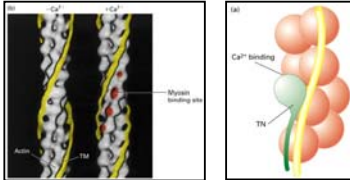


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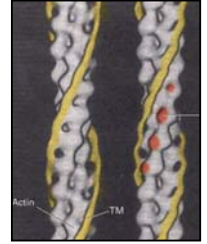
## Regulation of skeletal muscle function

- Actin-binding proteins tropomyosin and troponin are  $\text{Ca}^{2+}$  dependent



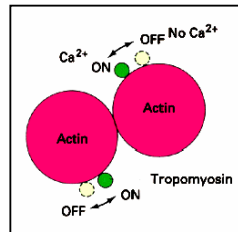
## Tropomyosin (TM)

- Ropelike molecule
- Forms a chain along actin
- Each molecule binds to seven actin monomers
- In high  $\text{Ca}^{2+}$  the shift of TM exposes myosin binding sites



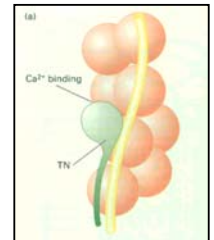
## Regulation of thin filaments by tropomyosin

- On and off states are  $\text{Ca}^{2+}$  dependent
- Myosin can bind but can not walk on actin filaments
- $\text{Ca}^{2+}$  binding exposes myosin binding sites



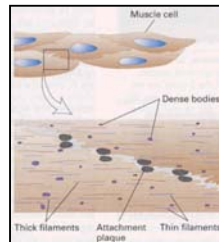
## Troponin

- Three subunits - T, I, C
- C is a calcium binding subunit
- Similar in sequence to calmodulin
- Forms a regulatory complex on actin filaments



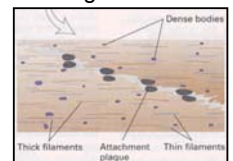
## Smooth muscle

- Elongated
- Spindle-shaped cells
- Mononuclear
- Slower increase in intracellular  $\text{Ca}^{2+}$  levels (no triads)
- Slower contraction



## Smooth muscle

- Actin and myosin filaments loosely arranged in bundles
- Filaments are attached to dense bodies in the cytosol = Z disks
- And to the plasma membrane through attachment plaques
- Both are rich in  $\alpha$ -actinin
- Vinculin binds actin to adhesion plaques



## Regulation of contraction in smooth muscle



- $\text{Ca}^{2+}$ - dependent
- Smooth muscle contain tropomyosin but no troponin
- Pathway of on-off employs caldesmon
  - Binds to actin at low  $\text{Ca}^{2+}$
  - Restricts the ability of myosin to bind to actin

## Cardiac muscle



- Thick and thin filaments like skeletal muscle organized in sarcomeres
- Have more mitochondria
- Larger T tubules
- Same mechanism of contraction