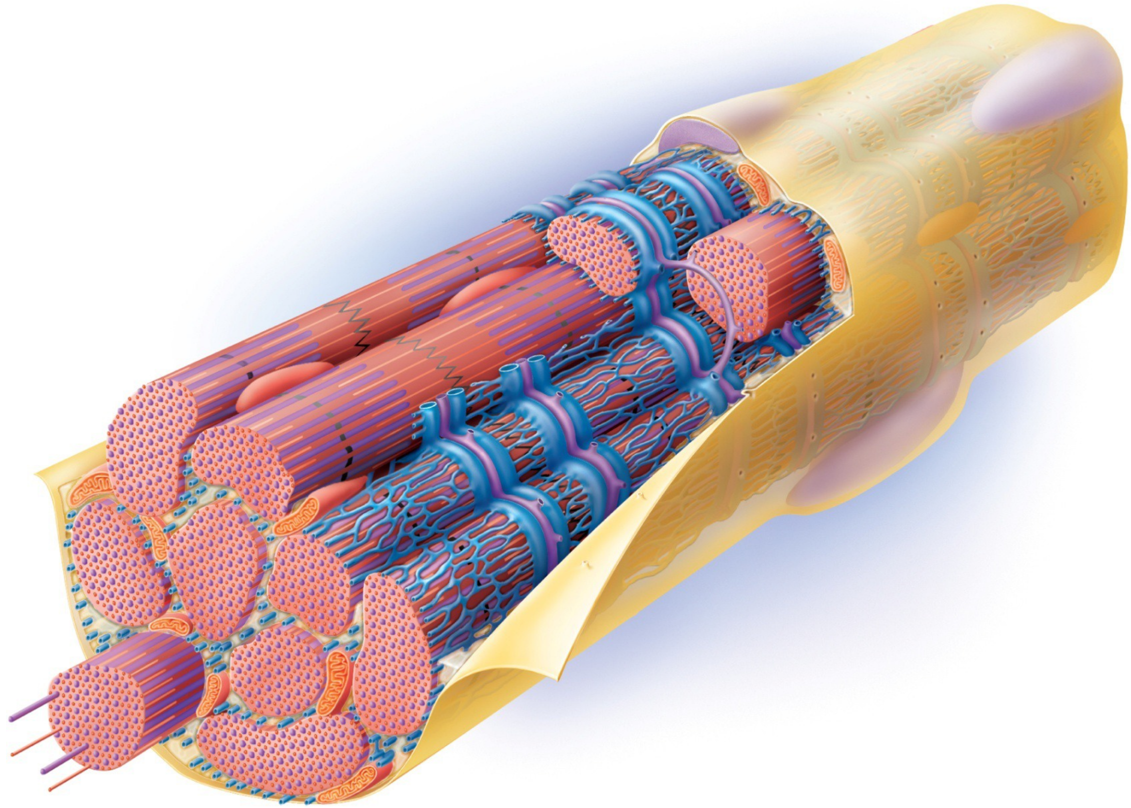
Chapter 11.1

Skeletal Muscle Structure and Function



Introduction to Muscle Physiology

- All muscle cells (skeletal, cardiac, and smooth) change chemical energy of ATP into mechanical energy of a muscle contraction

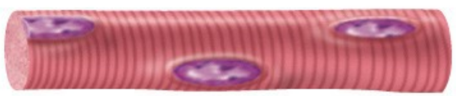
- Contraction occurs when a "muscle cell shortens".

  - How do skeletal muscle cells shorten?

  - How is a muscle contraction explained in molecular-biology?

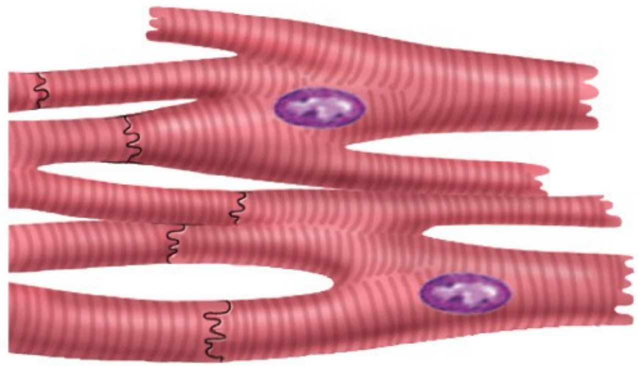
- *In this lecture we will focus on the structure and function of skeletal muscle cells. These are also called muscle fibers. // We will briefly define cardiac and smooth muscle function but cover the cardiac muscle in detail in Unit 3*

Skeletal muscle



- Voluntary
- Striated
- Multi-nucleated

Cardiac muscle

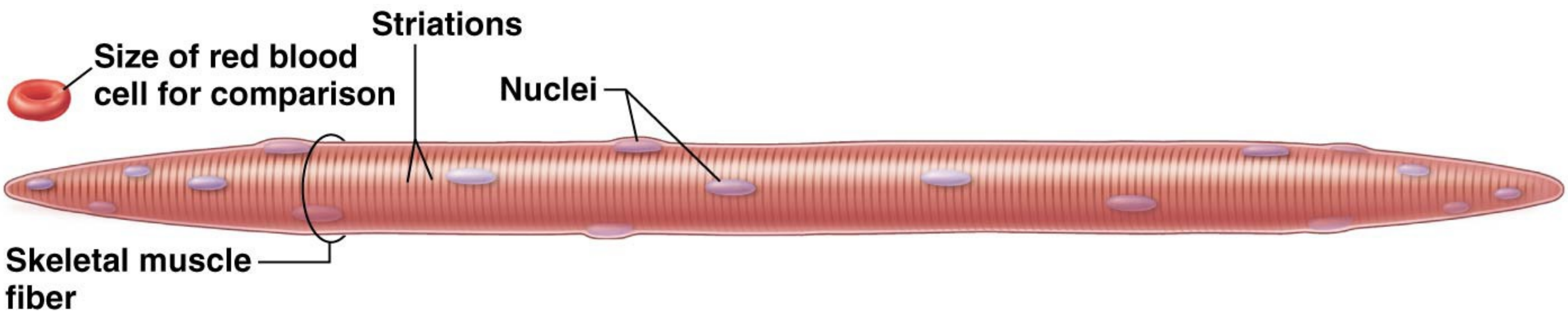


- Involuntary
- Striated
- One nucleus

Smooth muscle

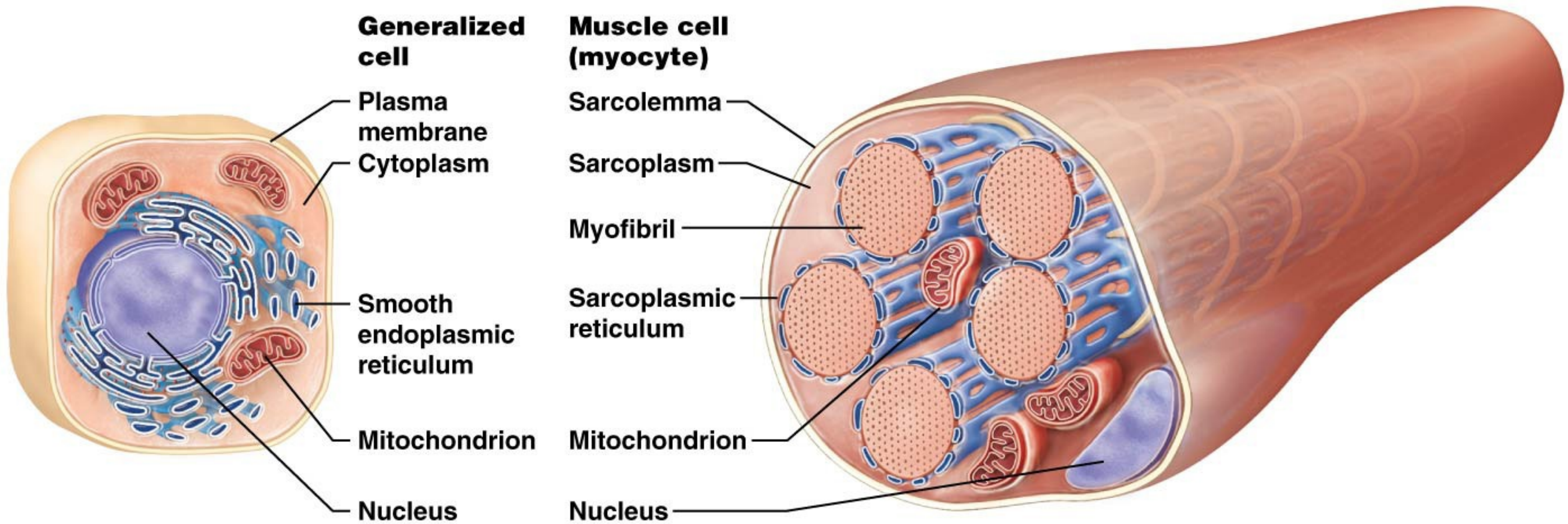
- Involuntary
- Non-striated
- One nucleus

Size and shape of a skeletal muscle fiber compared to a typical cell.



Why do we call a skeletal muscle cell a muscle fiber?

A generalized cell (left) compared with a generic muscle cell (right).

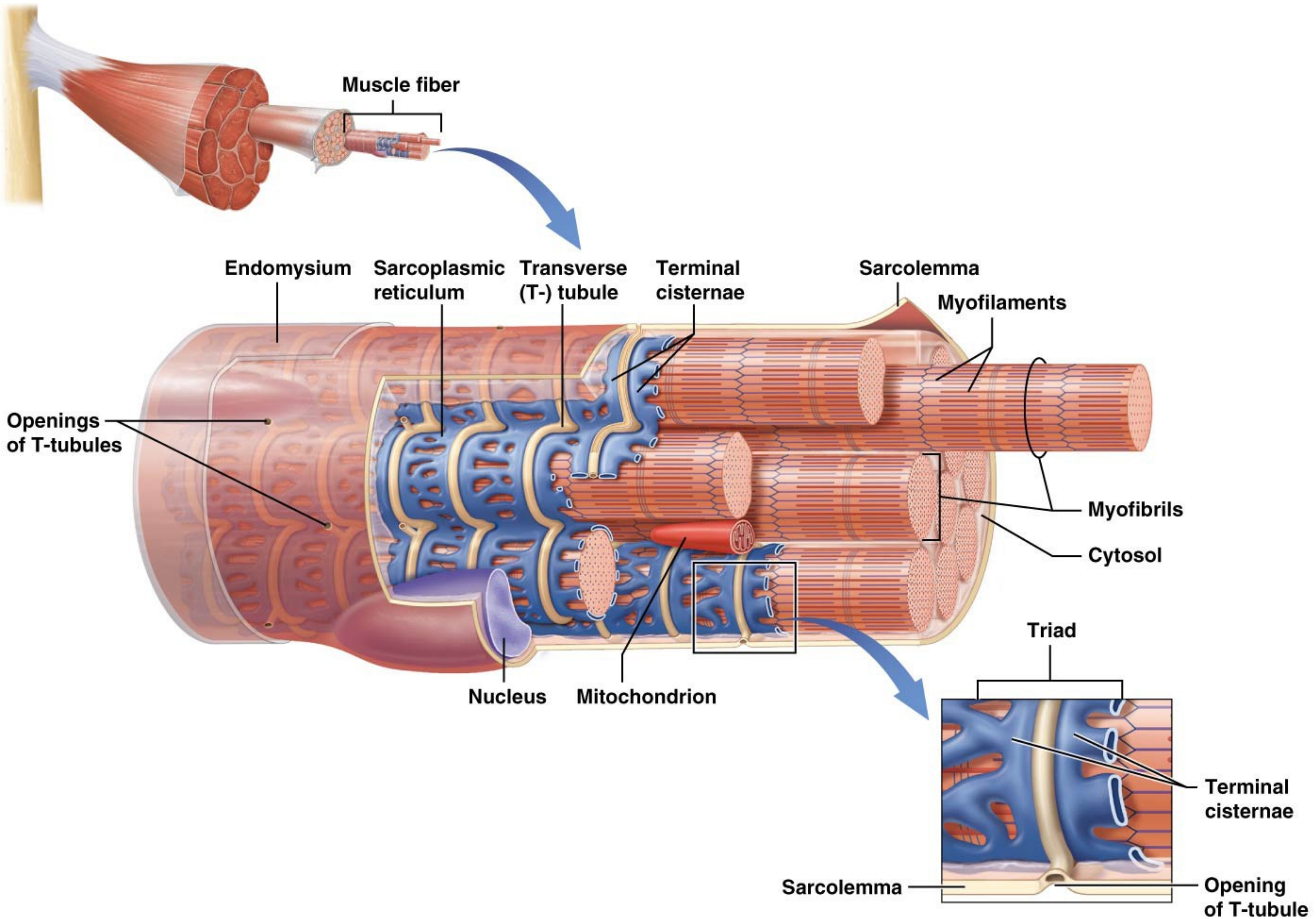


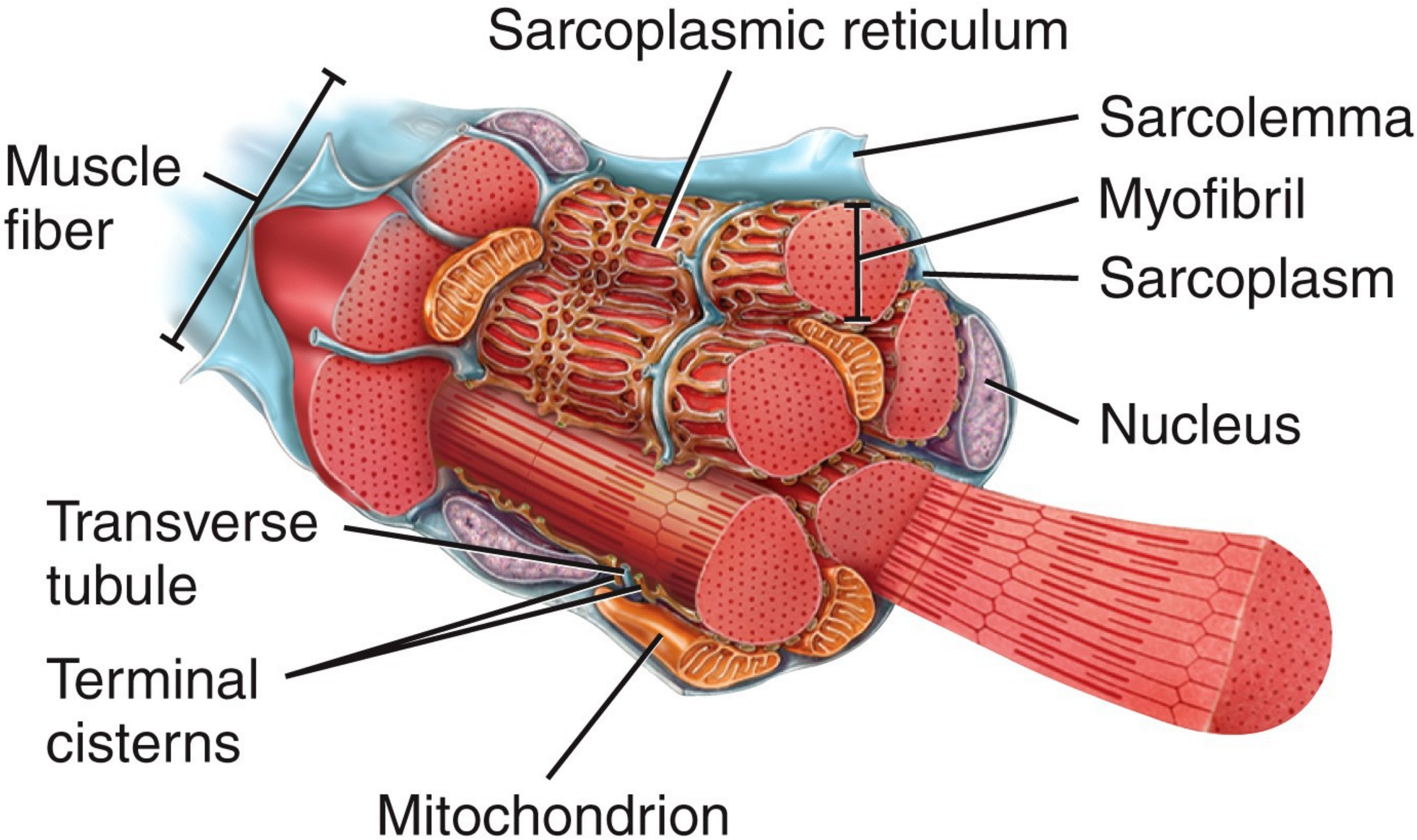
Note: skeletal muscle fibers are “multi-nucleated”

The Sliding Filament Theory of Skeletal Muscle

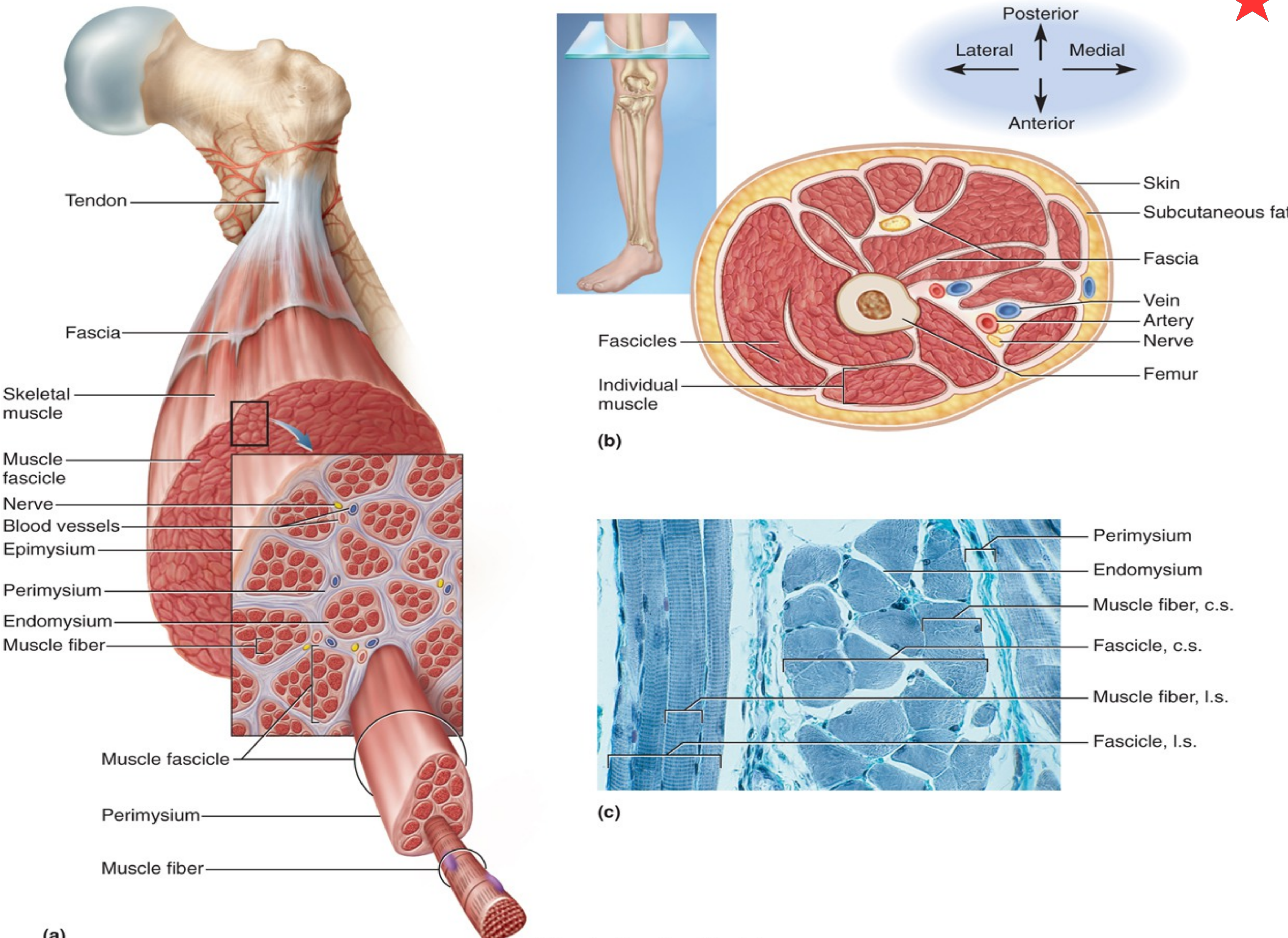
- In the early 1950s, a hypothesis to explain skeletal muscle function was to think of proteins folding like an accordion
- With the discovery of the electron microscope, scientist could “see” the thin and thick proteins inside the skeletal muscle.
- These proteins did not shorten during contraction (no accordion like action) – therefore
- Original hypothesis was wrong so …....
- New hypothesis was formulated suggesting muscle fiber shortened by the proteins sliding across each other.
- This hypothesis was proven to be “true” and is now called the sliding filament theory.

Structure of a skeletal muscle fiber.

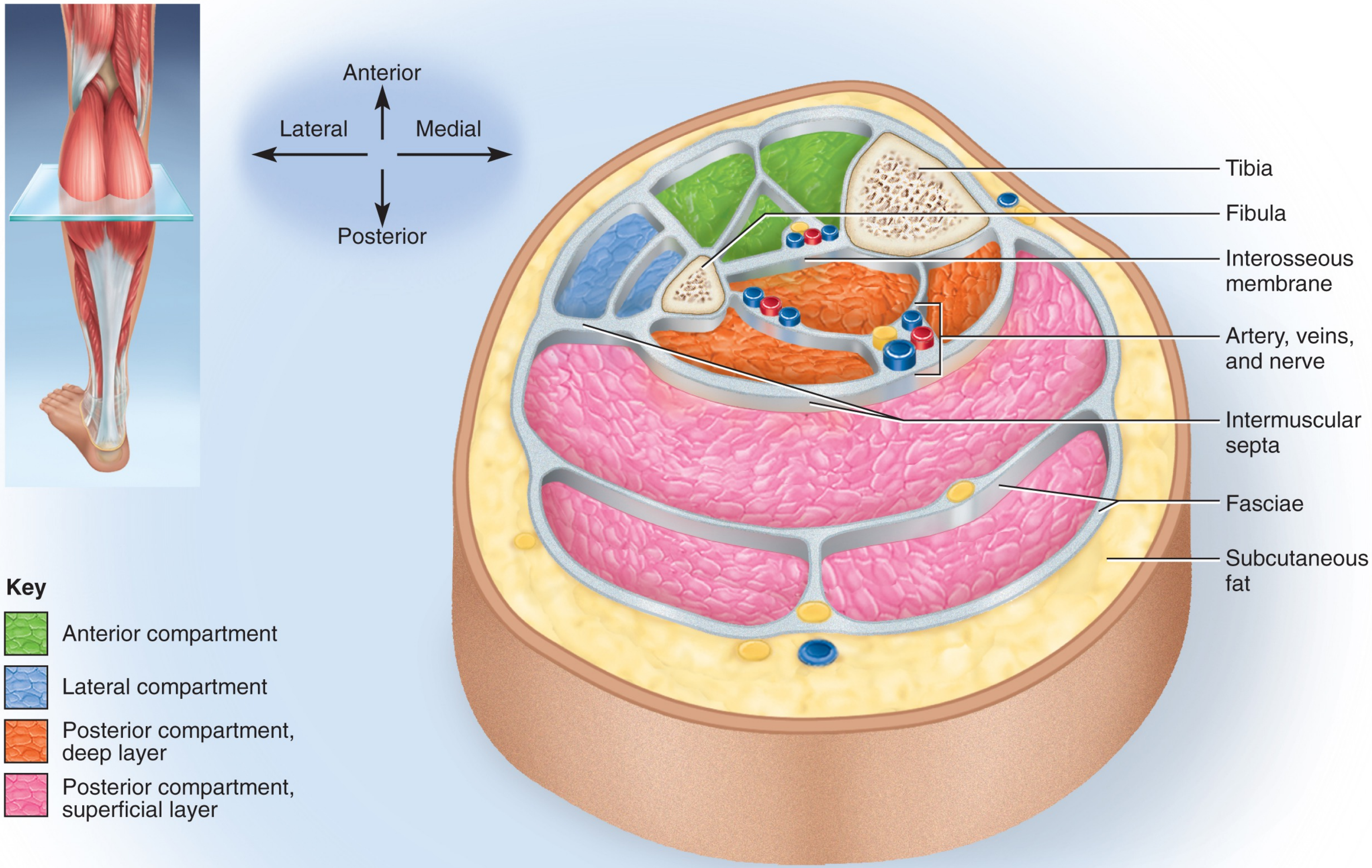




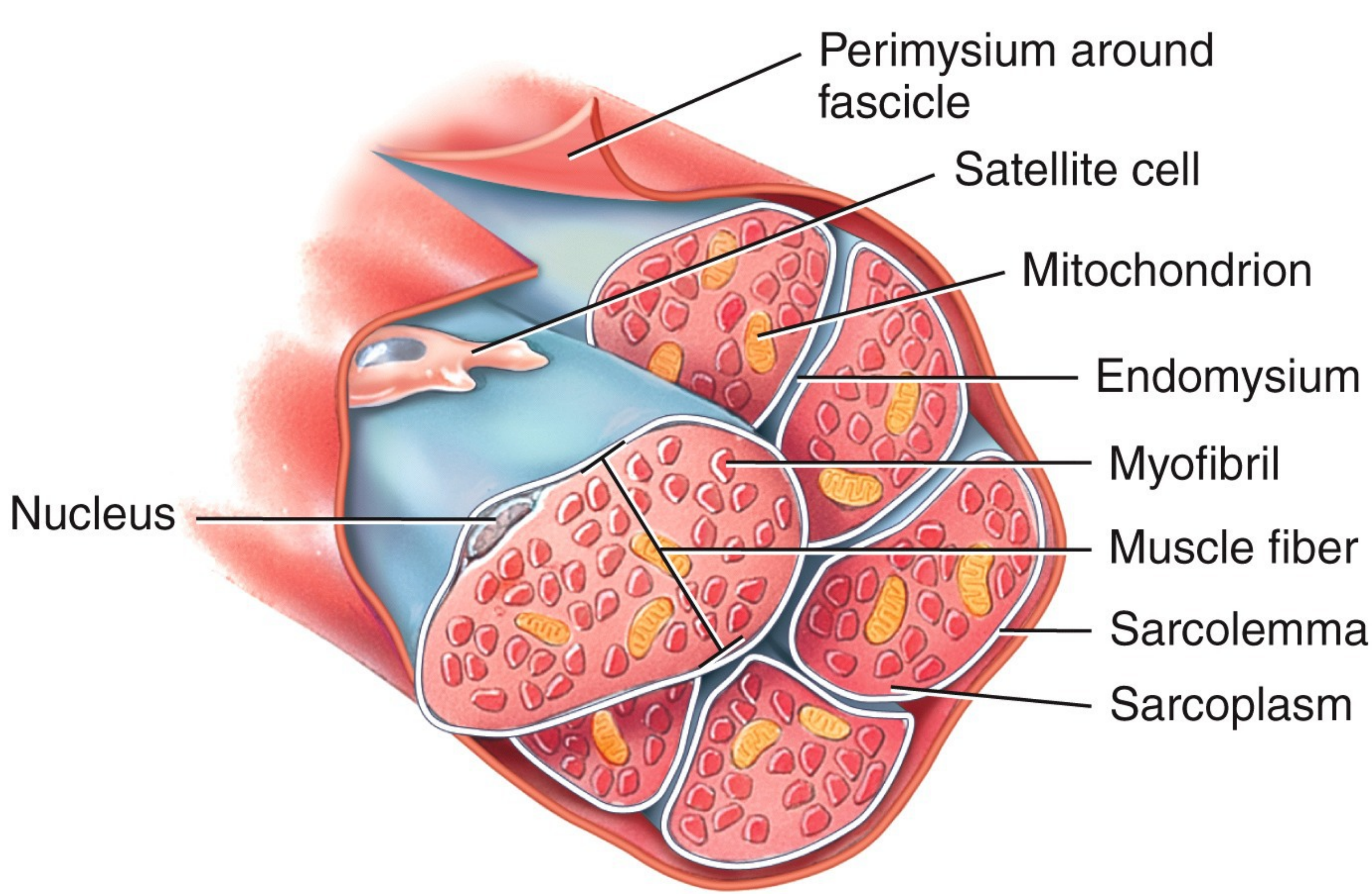
Muscle Fiber = Skeletal Muscle Cell



Tendon
Fascia
Skeletal muscle
Muscle fascicle
Nerve
Blood vessels
Epimysium
Perimysium
Endomysium
Muscle fiber
Muscle fascicle
Perimysium
Muscle fiber
(a)
Posterior
Lateral
Medial
Anterior
Skin
Subcutaneous fat
Fascia
Vein
Artery
Nerve
Femur
Fascicles
Individual muscle
(b)
Perimysium
Endomysium
Muscle fiber, c.s.
Fascicle, c.s.
Muscle fiber, l.s.
Fascicle, l.s.
(c)



What is compartment syndrome?



(b) Organization of a fascicle

- What type of CT is used to encapsulate the skeletal muscle organ?
- What type of CT is used to make tendons?
- What is the significance?

Skeletal Muscle Cell = Muscle Fiber

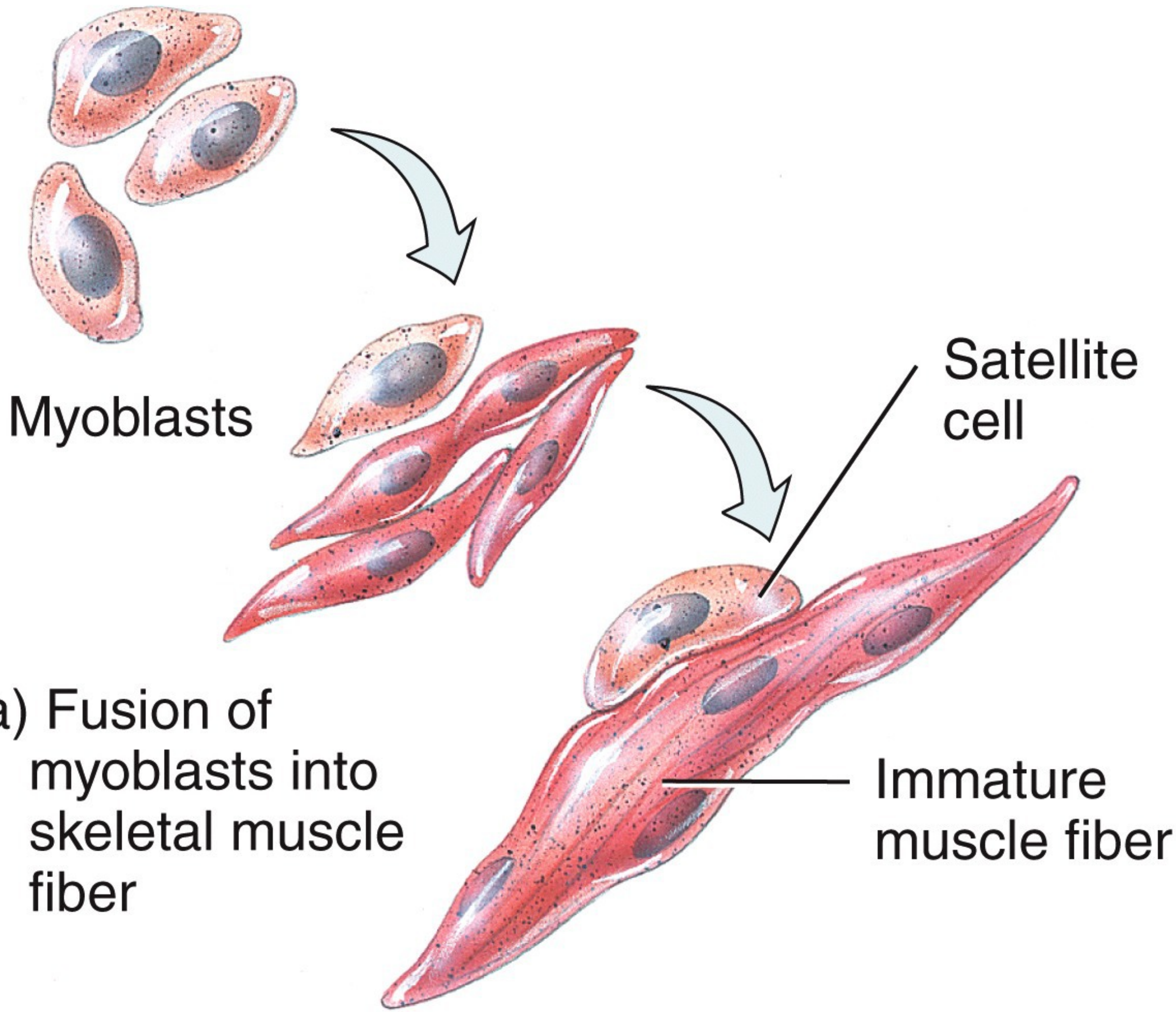
- Sarcolemma - plasma membrane of a muscle fiber
- Sarcoplasm - cytoplasm of a muscle fiber
  - glycogen – stored in abundance to provide local source of energy used at start of exercise
  - myoglobin – red pigment – small but local source of oxygen which is needed to produce ATP, used at start of exercise
- Myofibrils - long protein bundles that occupies the main portion of the sarcoplasm
- Multiple nuclei - flattened nuclei pressed against the inside of the sarcolemma

Skeletal Muscle Cell = Muscle Fiber

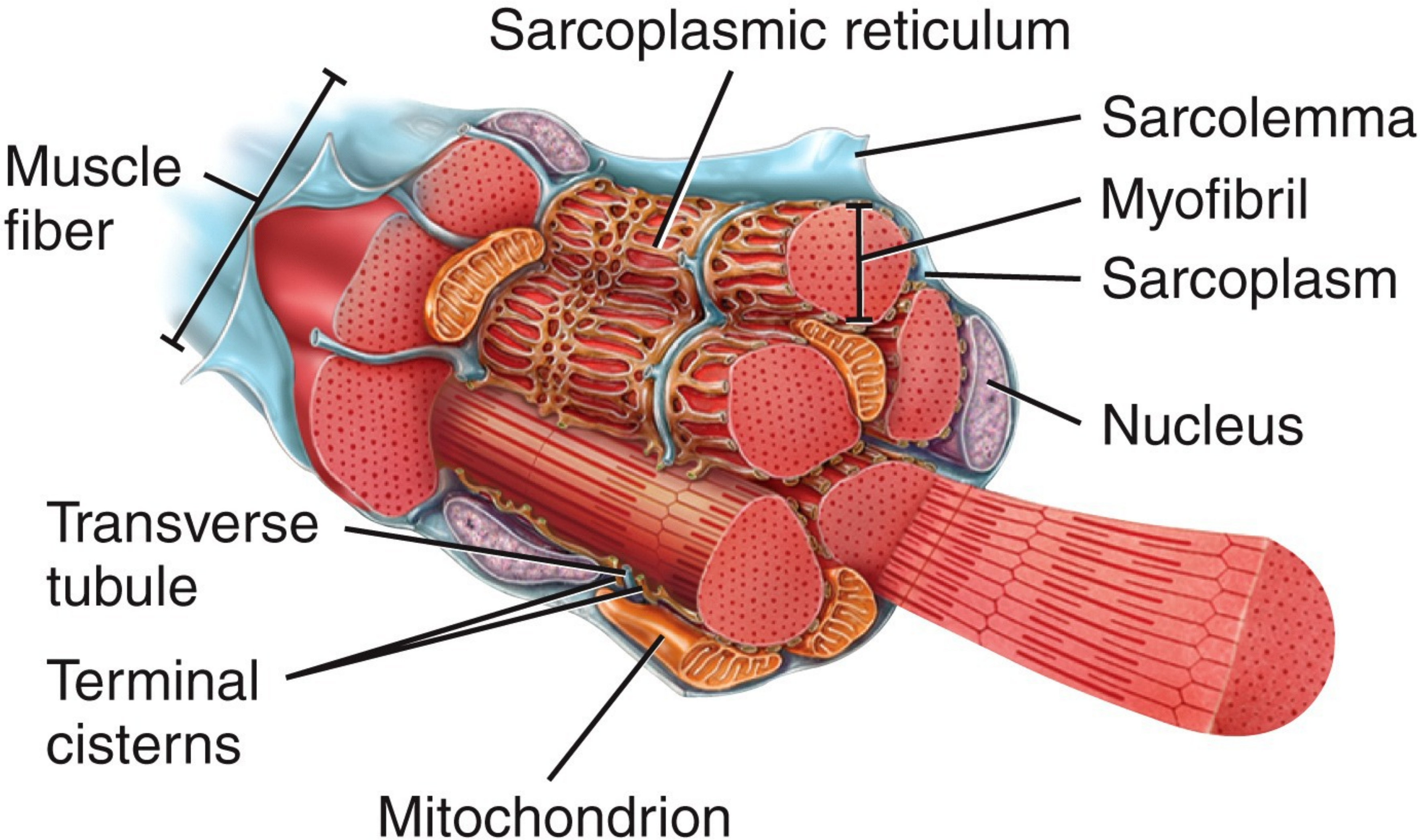
- Mitochondria // packed in spaces between myofibrils
- Sarcoplasmic reticulum (SR) // smooth ER that forms a network around each myofibril – calcium reservoir /// calcium activates the muscle contraction process
- Terminal cisternae // dilated end-sacs of SR which cross muscle fiber from one side to the other
- T tubules // tubular infoldings of the sarcolemma which penetrate through the cell and emerge on the other side
- Triad // a T tubule and two terminal cisterns

Skeletal Muscle Cell = Muscle Fiber

- Myoblasts // many stem cells in embryonic development fuse to form a muscle fiber – this is how the fiber becomes multinucleated
- Satellite cells – unspecialized myoblasts remaining between the muscle fiber and endomysium // may multiply and produce new muscle fibers to some degree
- Repair by fibrosis // Muscle fibers not able to undergo mitosis
  - Skeletal fibers are in G zero.
  - Unable to regenerate new functional cells /// severe damaged muscle fibers are replaced with scar tissue (fibrosis – fibroblast and connective tissue replace lost muscle fibers)



(a) Fusion of myoblasts into skeletal muscle fiber

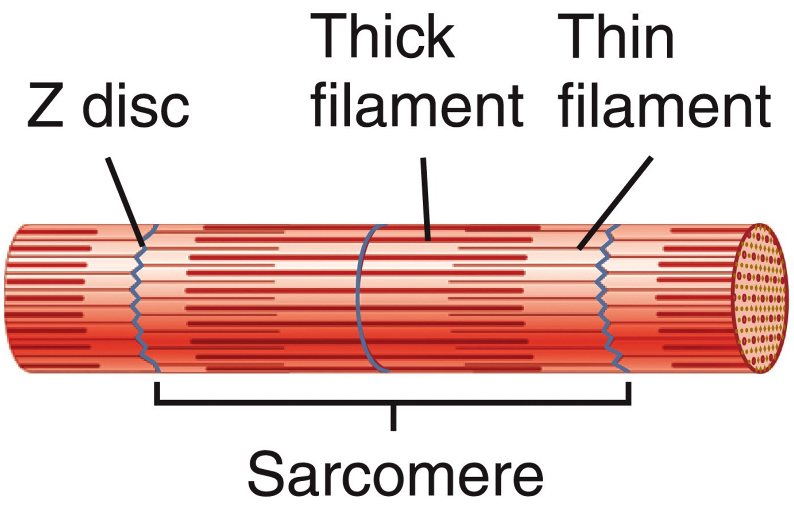

Sarcoplasmic reticulum
Muscle fiber
Sarcolemma
Myofibril
Sarcoplasm
Nucleus
Transverse tubule
Terminal cisterns
Mitochondrion

Sarcomeres

- **Sarcomere** = segment from Z disc to Z disc /// this is the functional contractile unit of a muscle fiber

- Muscle cells shorten because their individual sarcomeres shorten

  - Z disc (Z lines) are pulled closer together
  - thick and thin filaments slide past (over) each other



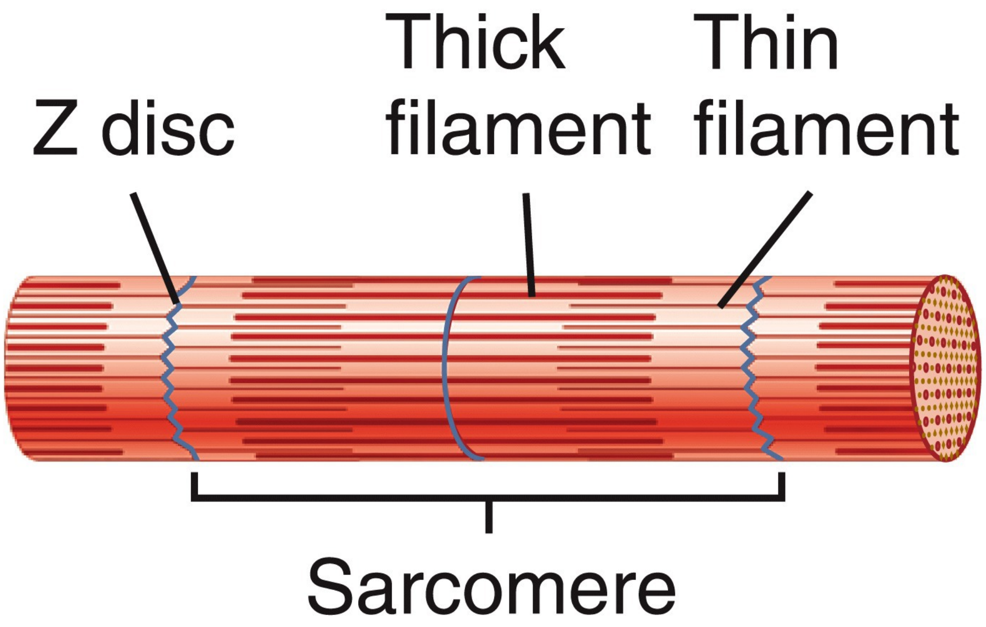
Three Classes of Proteins in the Sarcomere

★ ★

- **Contractile Proteins (#1)**

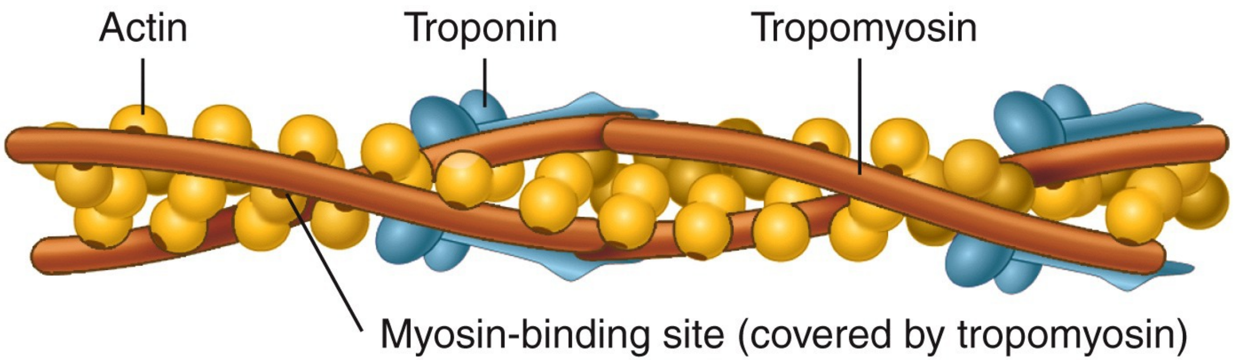
  – **Myosin = Thick Filament (ATP binding site and ATPase // also called the *motor protein*)**

  – **Actin = Thin Filament (interacts with myosin to form "cross bridge" between contractile proteins**



Three Classes of Proteins in the Sarcomere

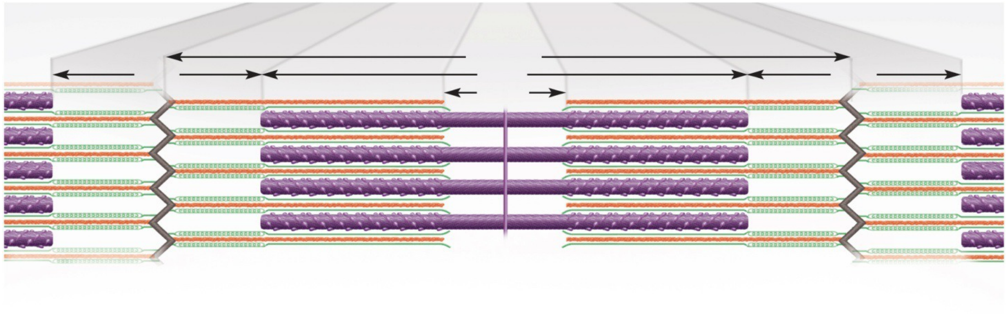
- **Regulatory Proteins (#2)**
  - **Tropomyosin (when muscle relaxed it blocks myosin binding site)**
  - **Troponin (when calcium binds to troponin, it will cause tromomyosin to move and expose myosin binding sites)**

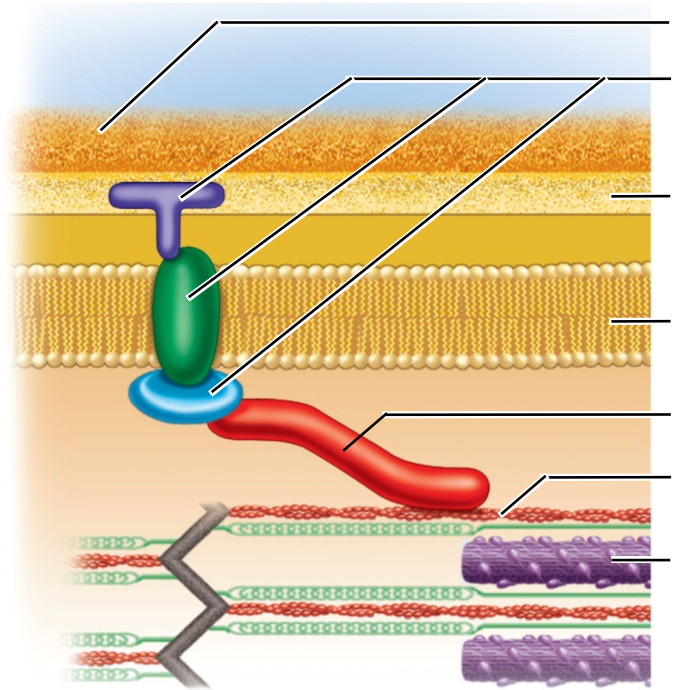


(b) Portion of a thin filament

Three Classes of Proteins in the Sarcomere

- **Structural Proteins (#3)**
  - Titin (know this)- elastic element to hold myosin centered between Z discs / the green filament in this illustration
  - Alpha-actinin
  - Myomesin
  - Nubulin
  - Dystrophin

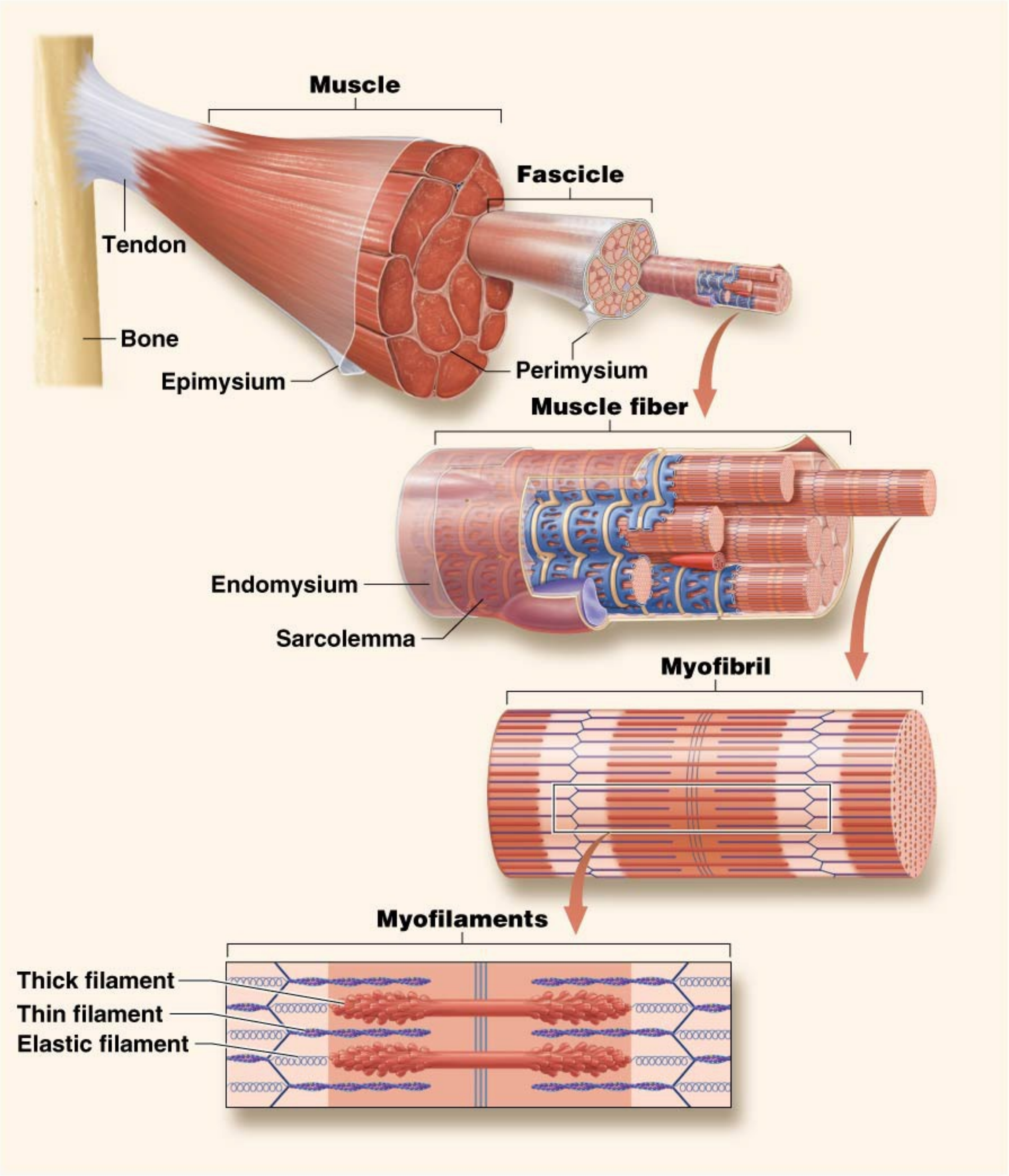




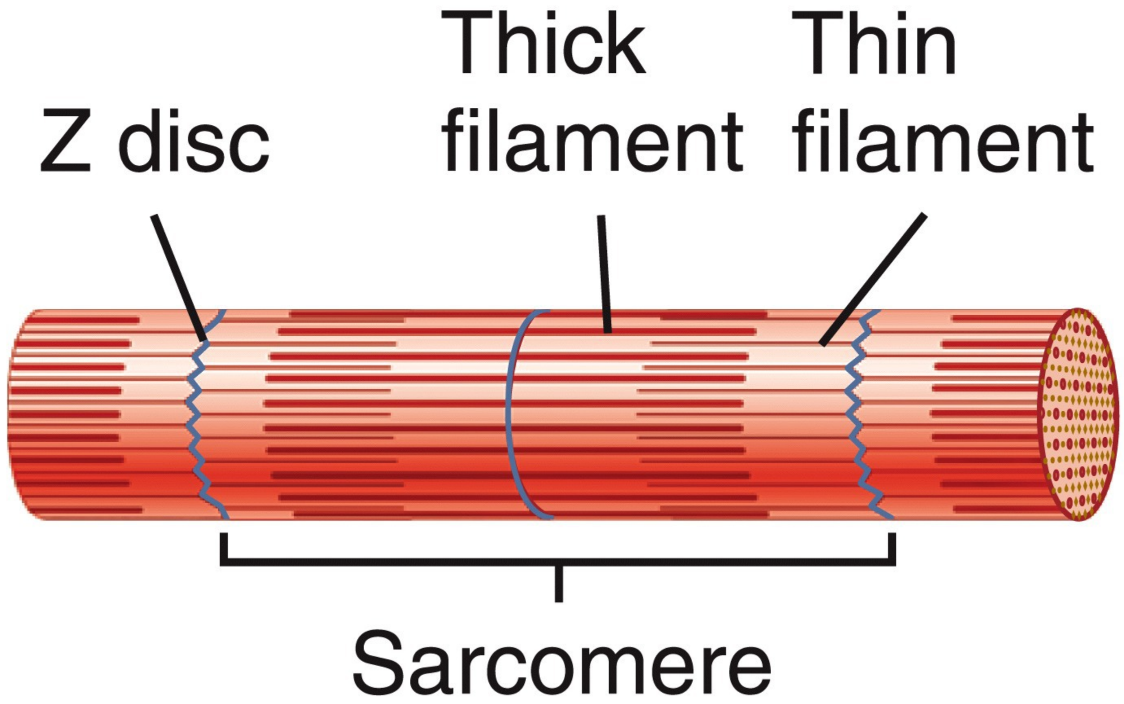
Sarcomeres

- Neither thick nor thin filaments change their length during conctraction
- Only the amount of overlap changes
- During contraction (i.e. shortening) – force generated by sarcomere is transferred from the myofibrils to the endomysium by way of linking proteins (e.g. dystrophin) - force transferred to connective tissue's (endomysium / perimysium / epimysium) of the muscle fiber and then to the tendons.
  - continuous and direct transfer of force through CT from endomysium surrounding one muscle fiber, to perimysium, , to epimysium, to tendon, to periosteum, to sharpe fibers, and ultimately into the bone matrix
    - this physical force is also used to influence bone remodeling
    - mechanical force regulates osteoblast (builds bone) and osteoclast (removes bone)

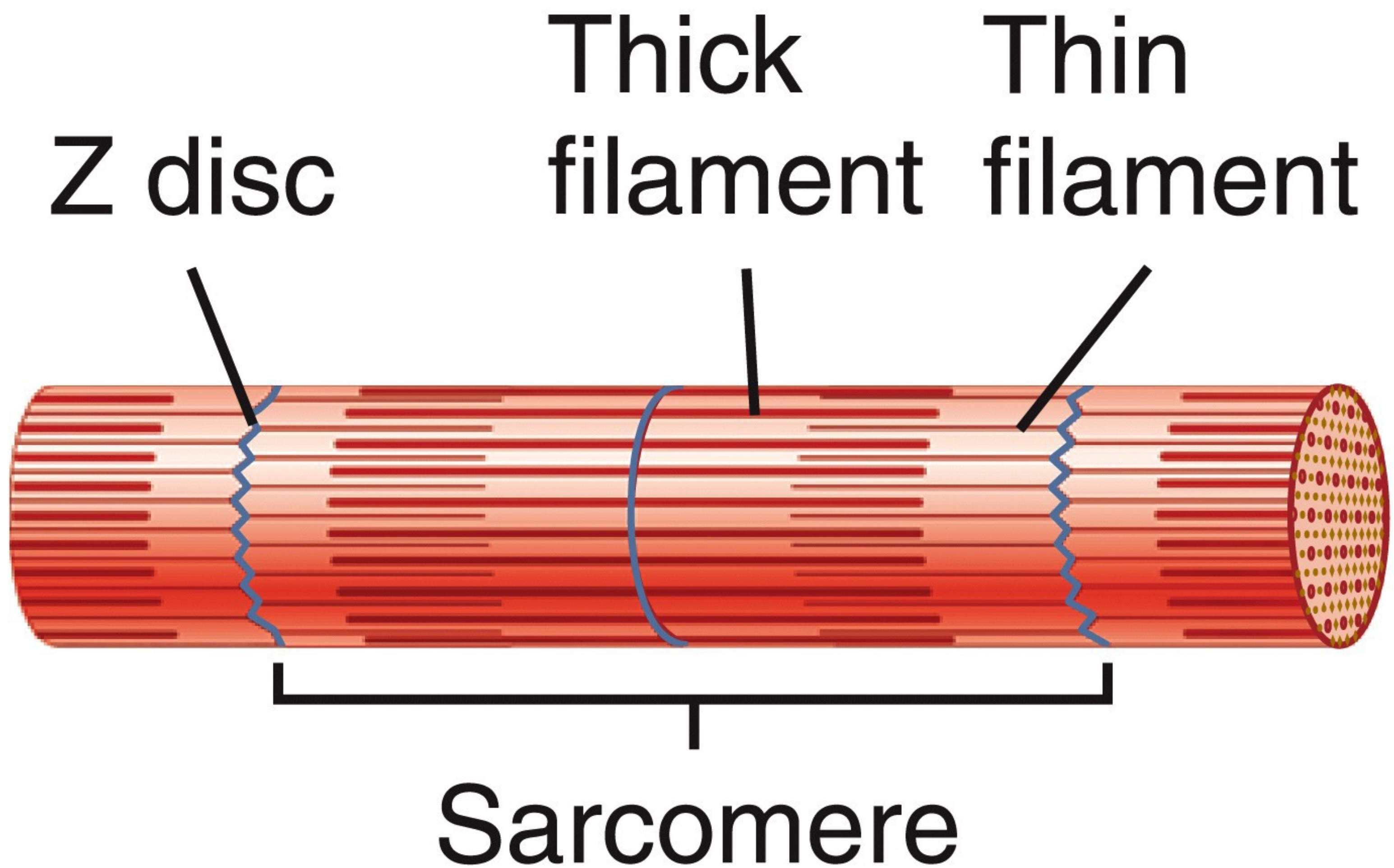
The Big Picture of Levels of Organization within a Skeletal Muscle



Striations, Sarcomeres, and the Sliding Filament Theory



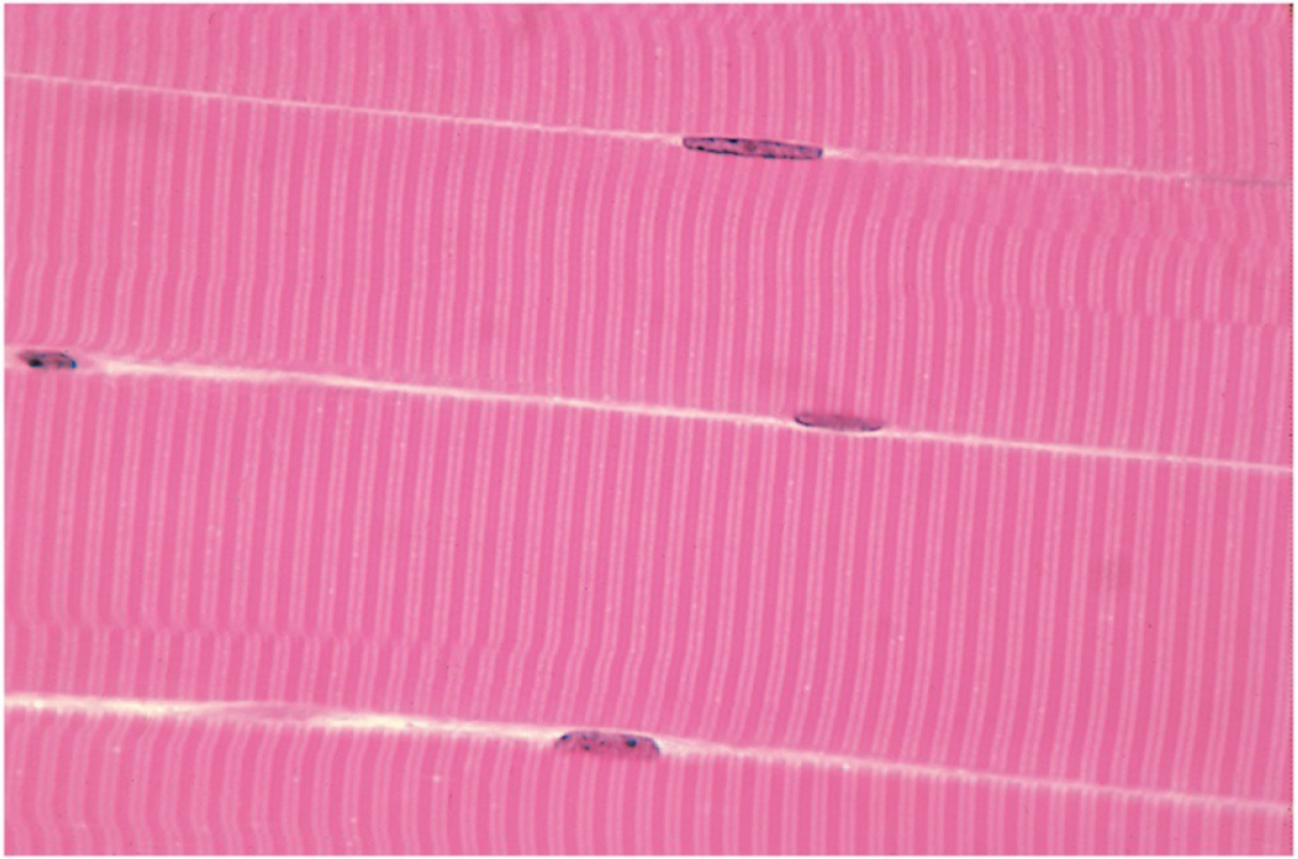
- ***<u>Sarcomere is the functional contractile unit of a muscle fiber</u>***
  - muscle shortens because protein fibers slide across each other
  - sarcomere shorten but the length of individual proteins do not shorten
  - pulls z discs closer to each other



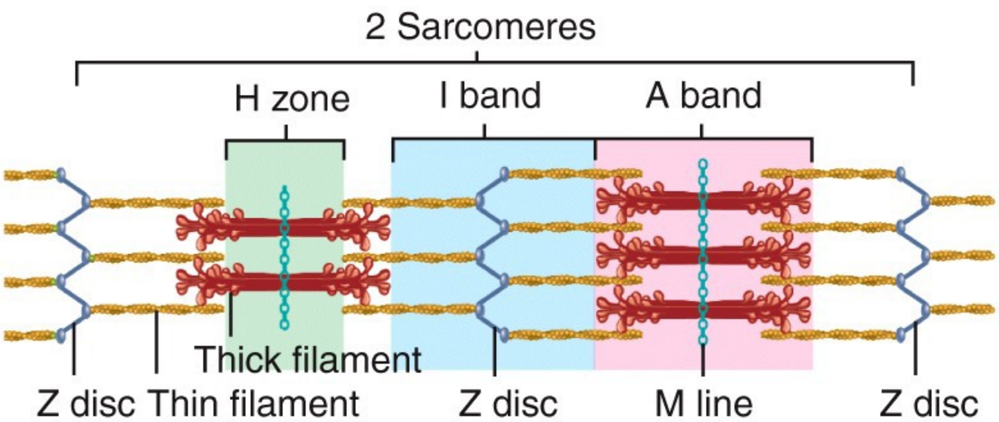
Thick filaments = myosin

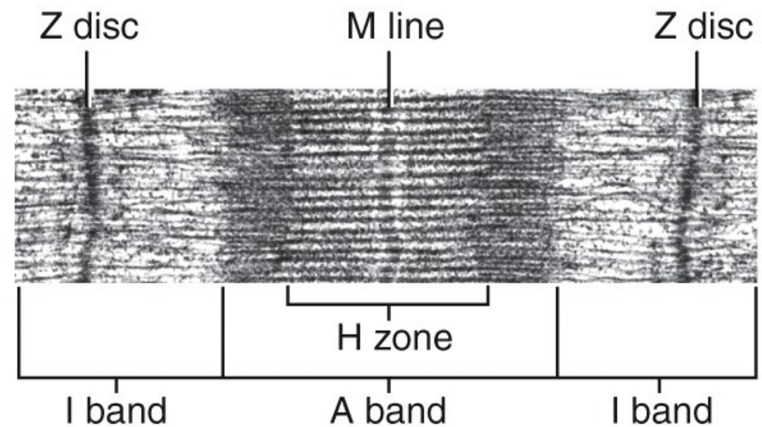
Thin filaments = actin

Striations of Skeletal Muscle

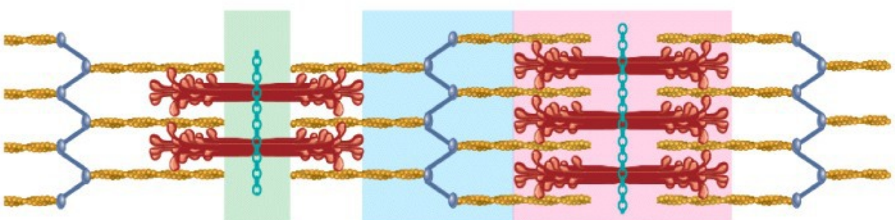


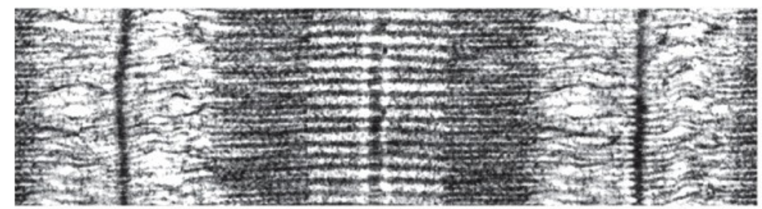
Alternating light and dark transverse bands of myofibrils // results from overlapping of contractile proteins within muscle fibers



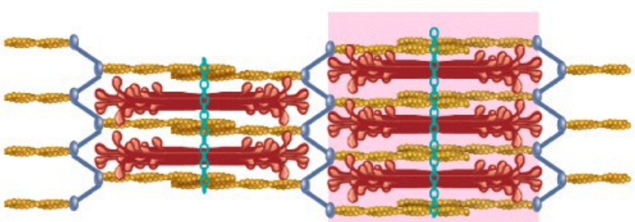


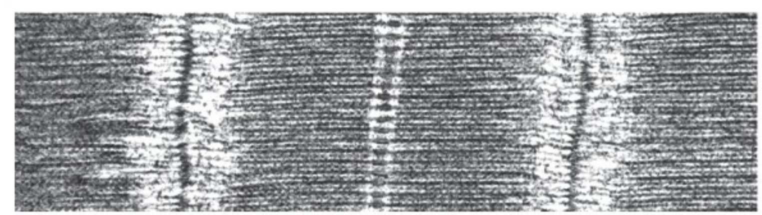
(a) Relaxed muscle





(b) Partially contracted muscle



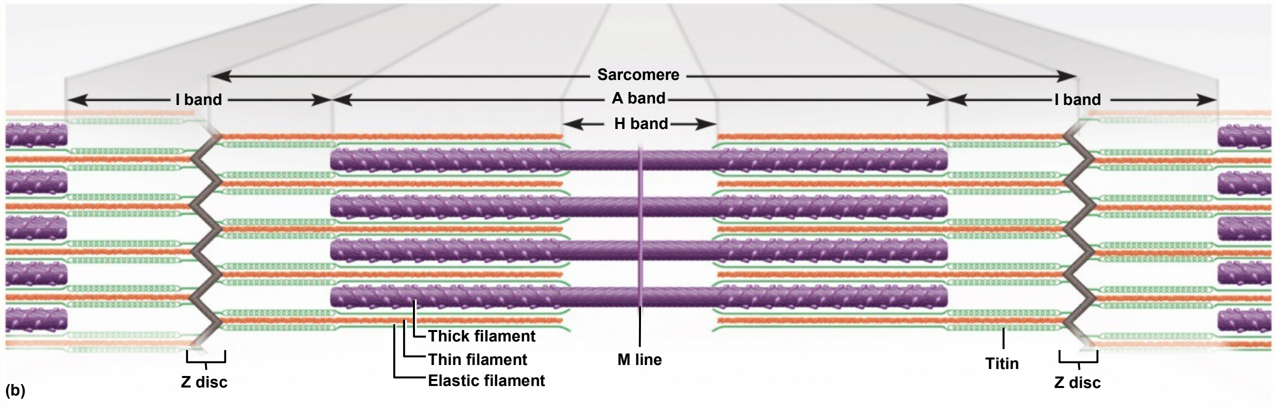


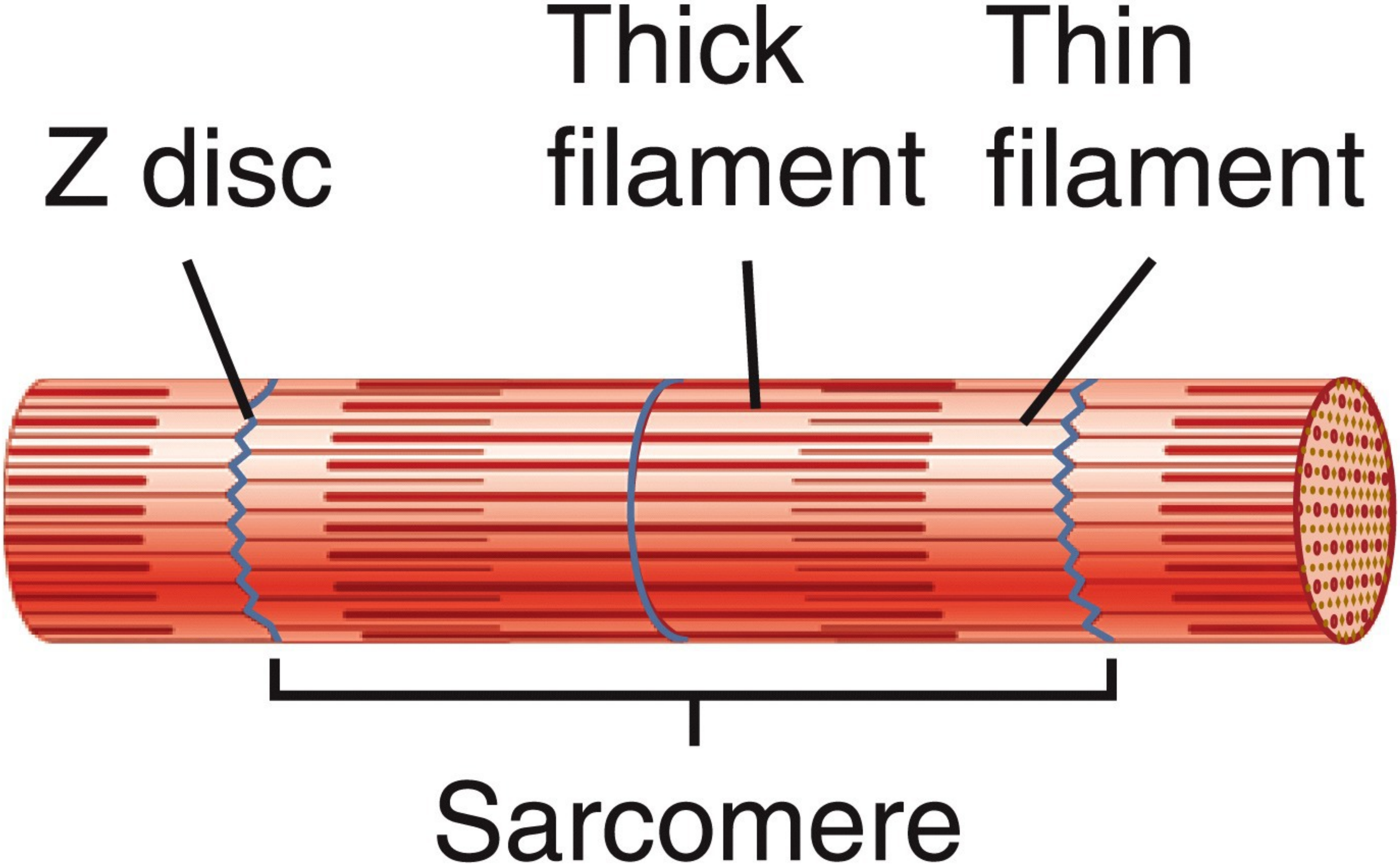
Courtesy Hiroyouki Sasaki, Yale E. Goldman and Clara Franzini-Armstrong

(c) Maximally contracted muscle

More About the Sarcomere

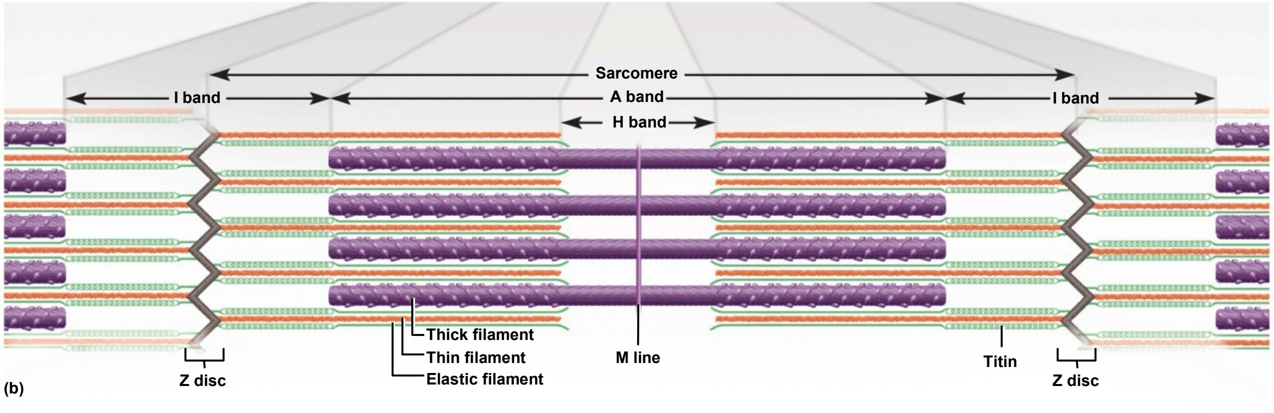
- **myosin** and **actin** are "contractile" proteins found in all cells (including non muscle cells) // e.g. actin in the peripheral protein of the cell's cytoskeleton
  - In non muscle cells these proteins function in cellular motility, mitosis, transport of intracellular material
- organized in a precise way in **skeletal** and **cardiac** muscle
- results in striated appearance / over-lapping of proteins




Thick filament
Thin filament
Z disc
Sarcomere

More About the Sarcomere

- A band – dark – A stands for anisotropic
  - part of A band where thick and thin filaments overlap is especially dark
  - H band in the middle of A band – just thick filaments
  - M line is in the middle of the H band
- I band – alternating lighter band – I stands for isotropic
  - the way the bands reflect polarized light

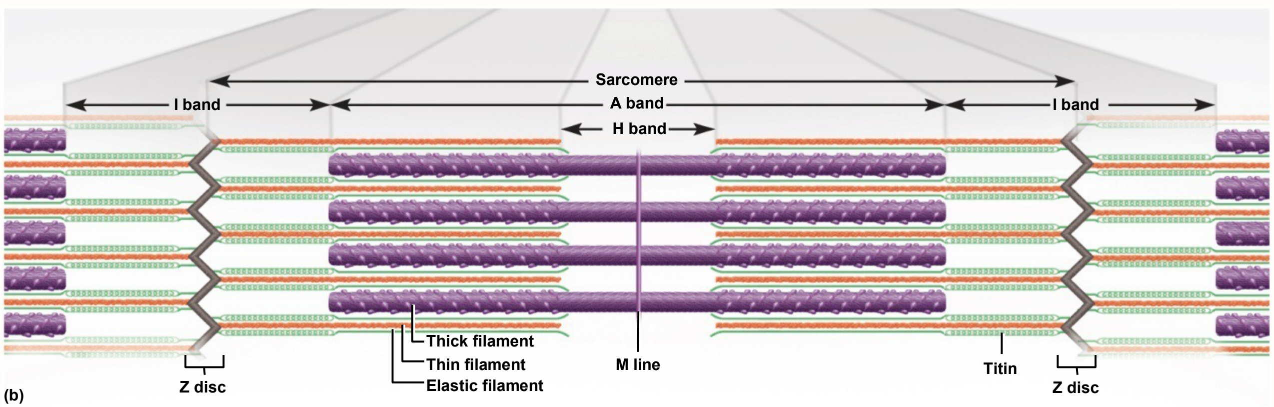


More About the Sarcomere

- z disc – provides anchorage for thin filaments and elastic filaments (titin)
  - bisects I band

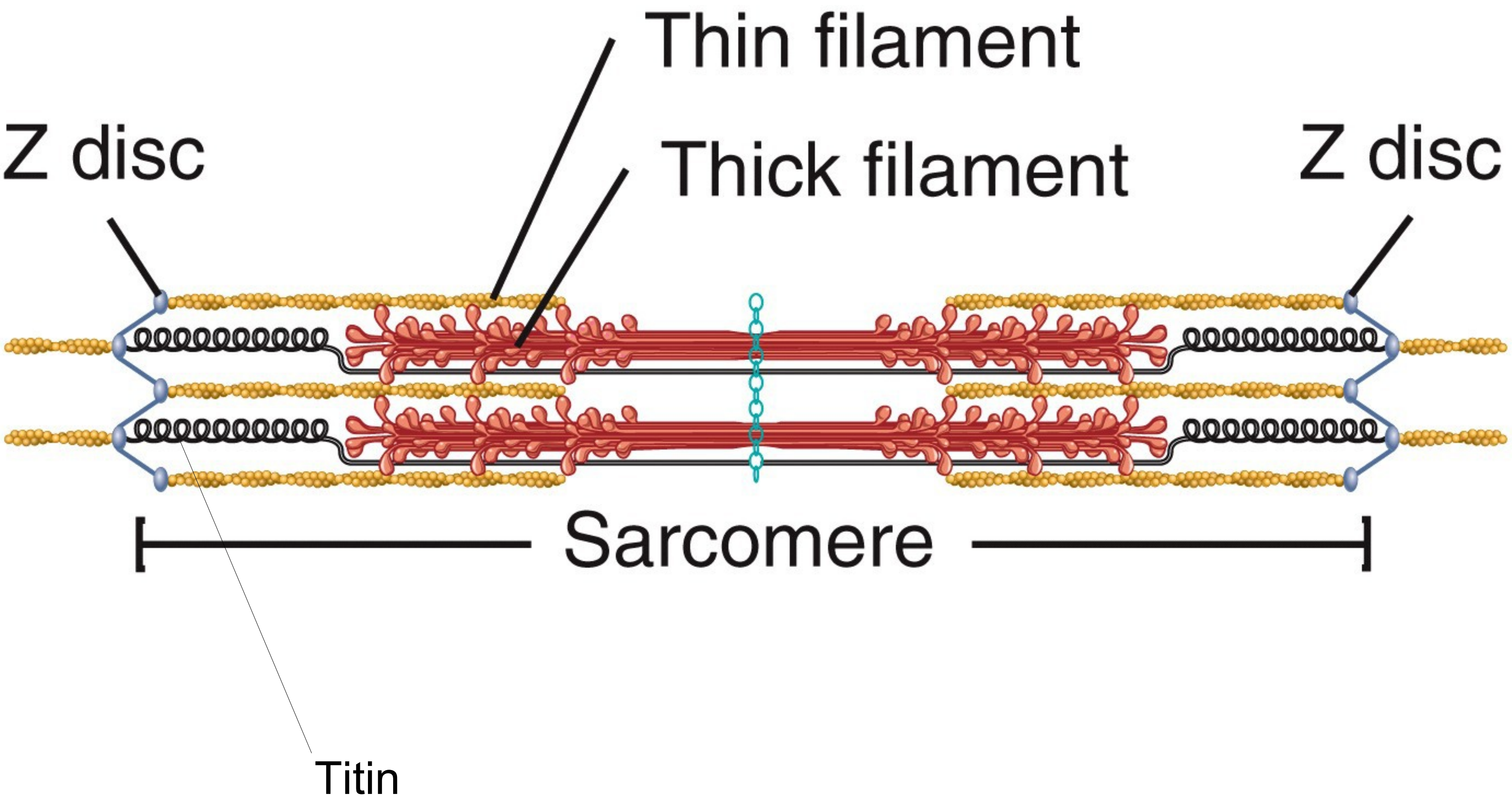
- sarcomere – the segment of the myofibril from one z disc to the next

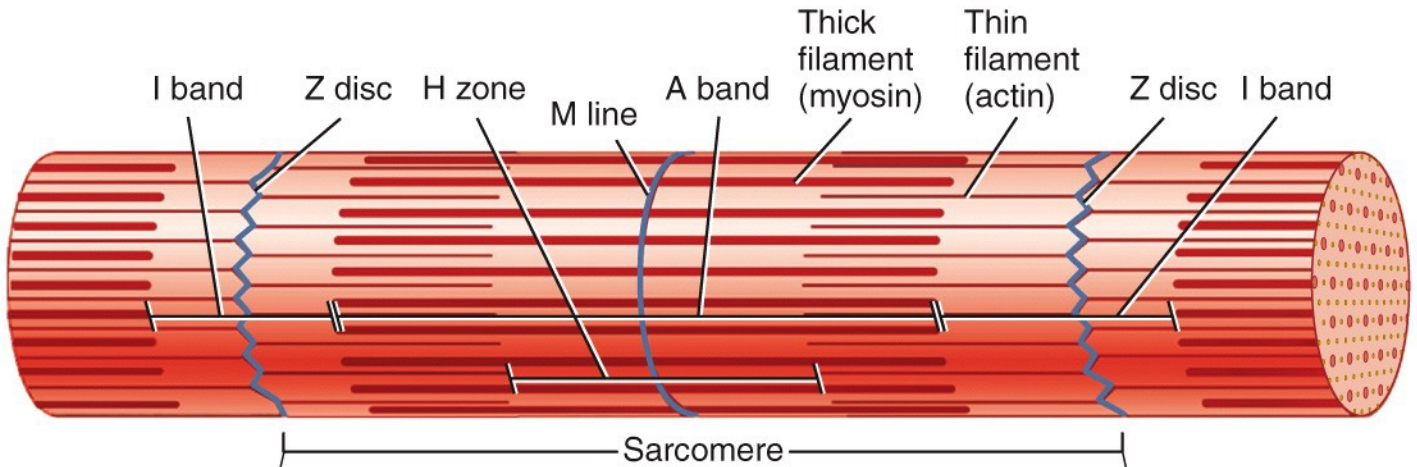
- The actin and myosin polymers do not change length during a muscle contraction!



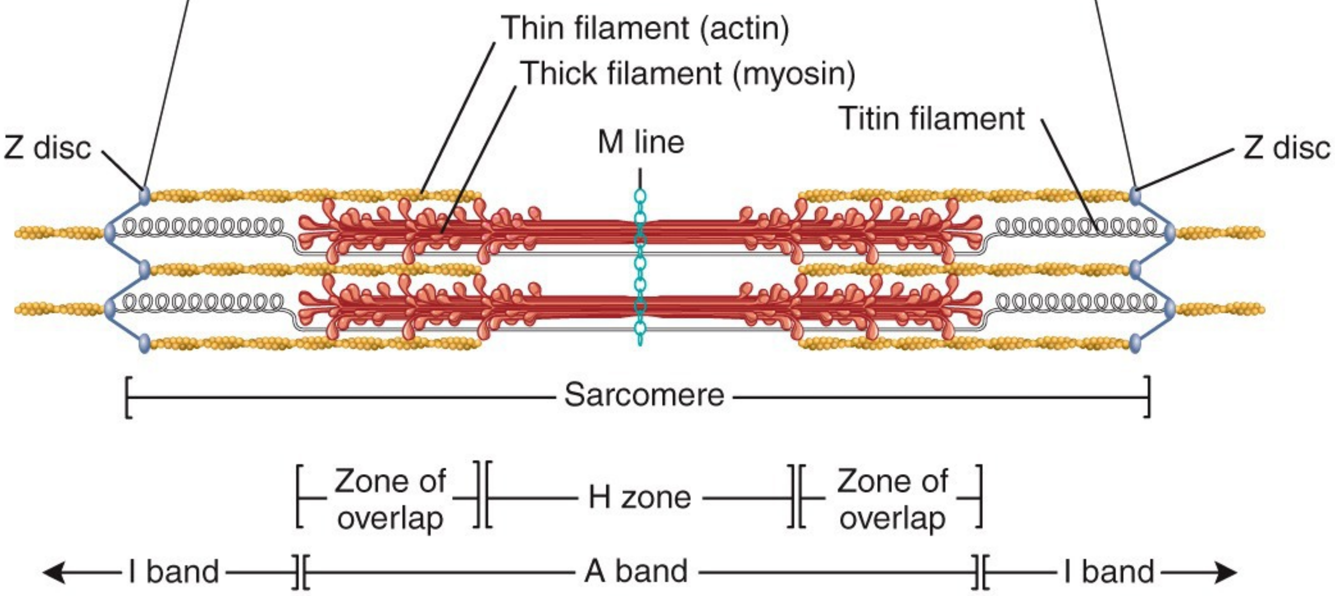
What structure is located in the middle of the light band?

What is tinin's function?
When a muscle contracts what happens to the Z discs?



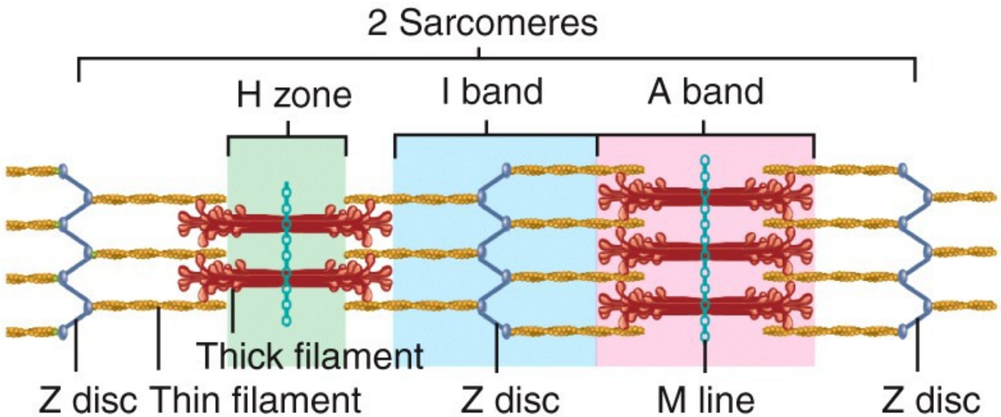


(a) Myofibril

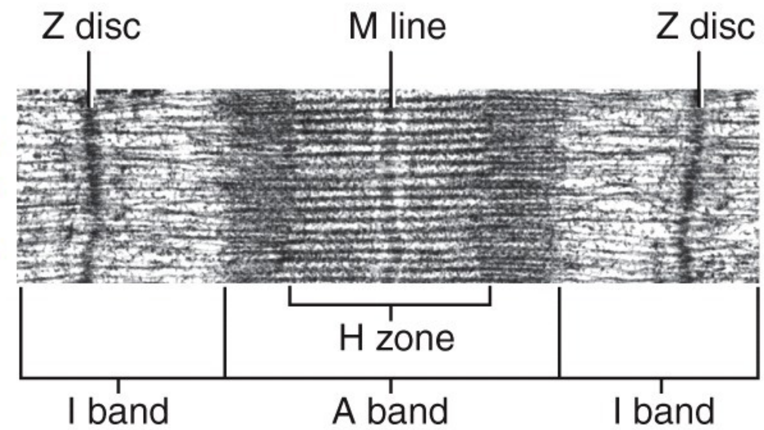


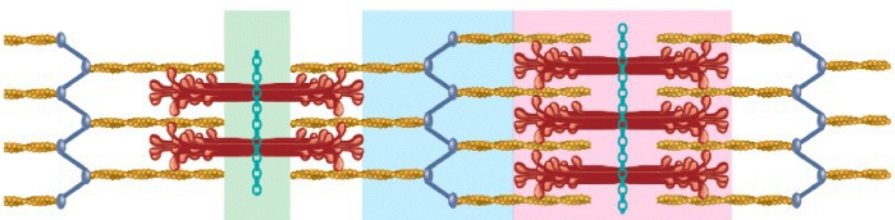
(b) Details of filaments and Z discs

What structure holds the thick filament between the Z discs?

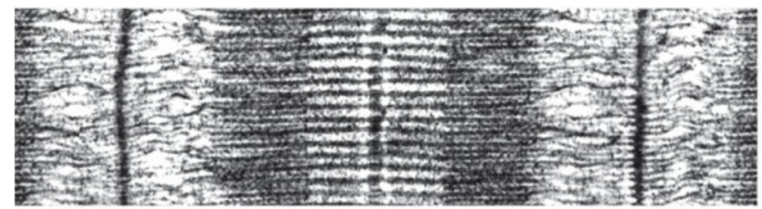


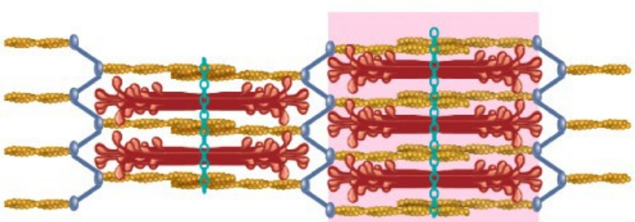
(a) Relaxed muscle



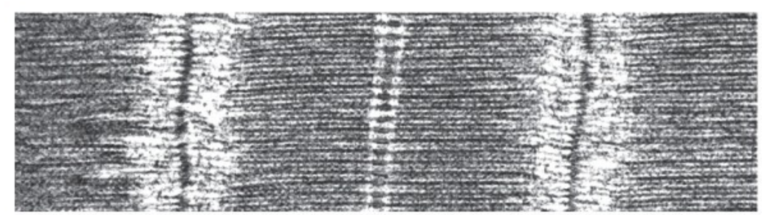


(b) Partially contracted muscle

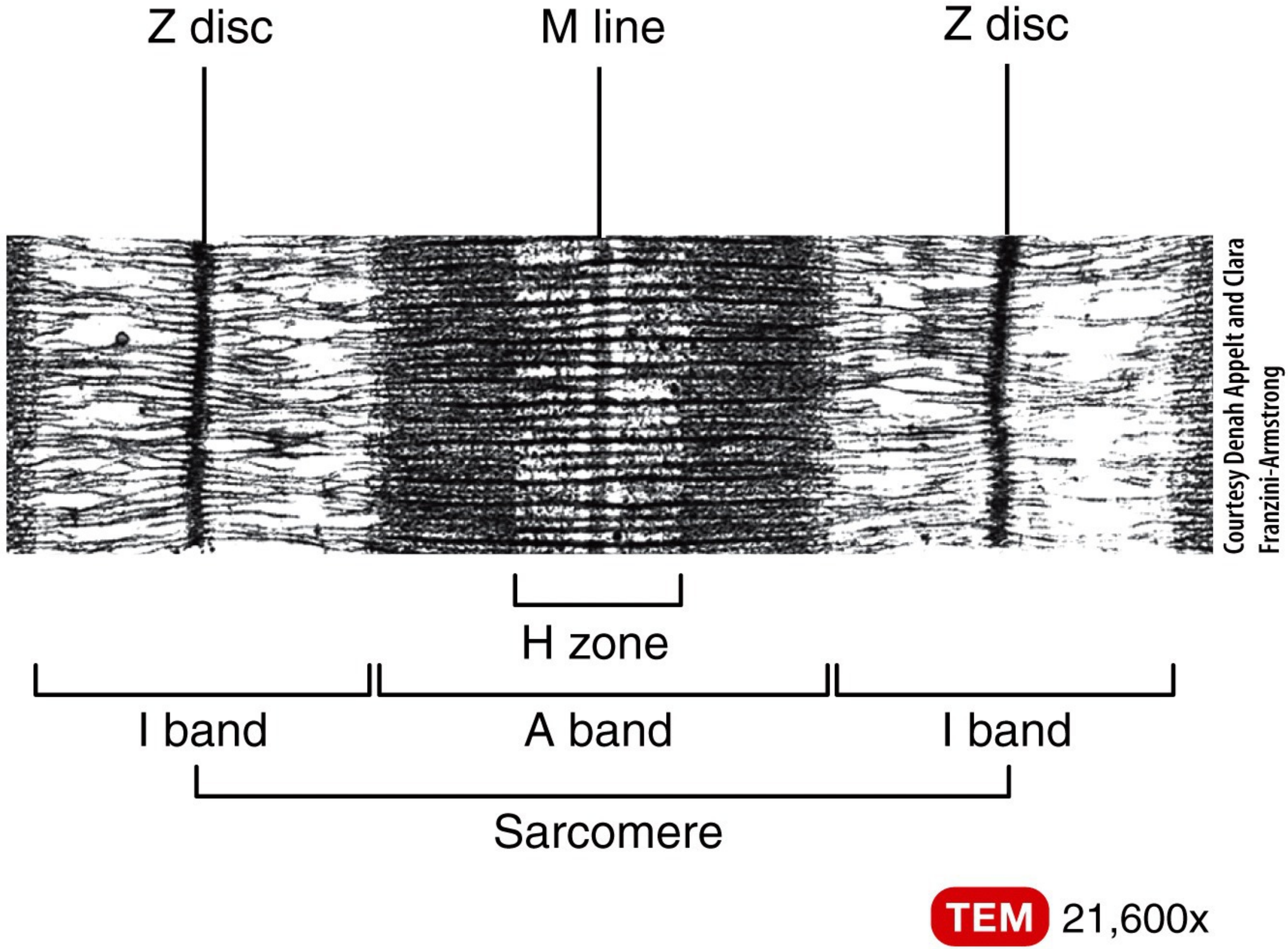




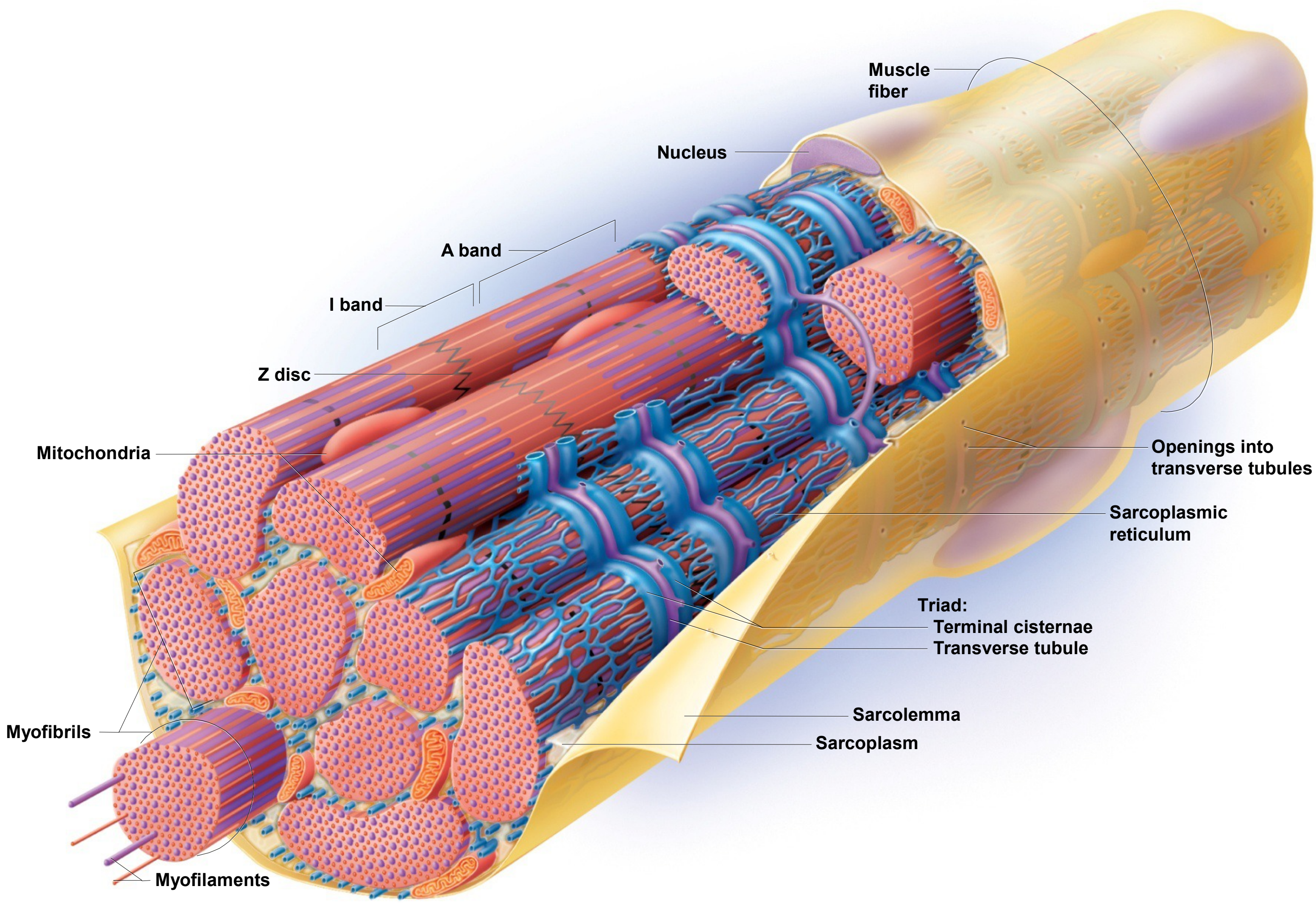
(c) Maximally contracted muscle



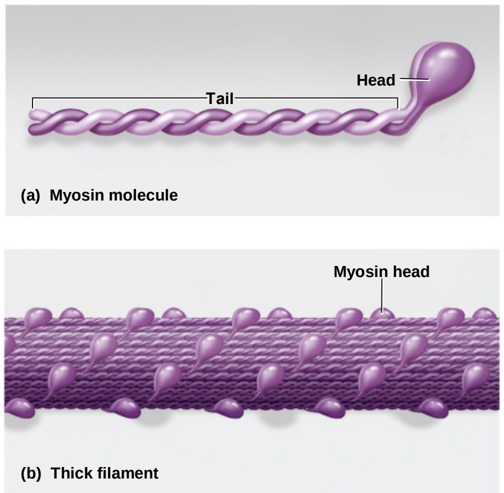
Courtesy Hiroyouki Sasaki, Yale E. Goldman and Clara Franzini-Armstrong


Z disc
M line
Z disc
Courtesy Denah Appelt and Clara Franzini-Armstrong
H zone
I band
A band
I band
Sarcomere
TEM 21,600x

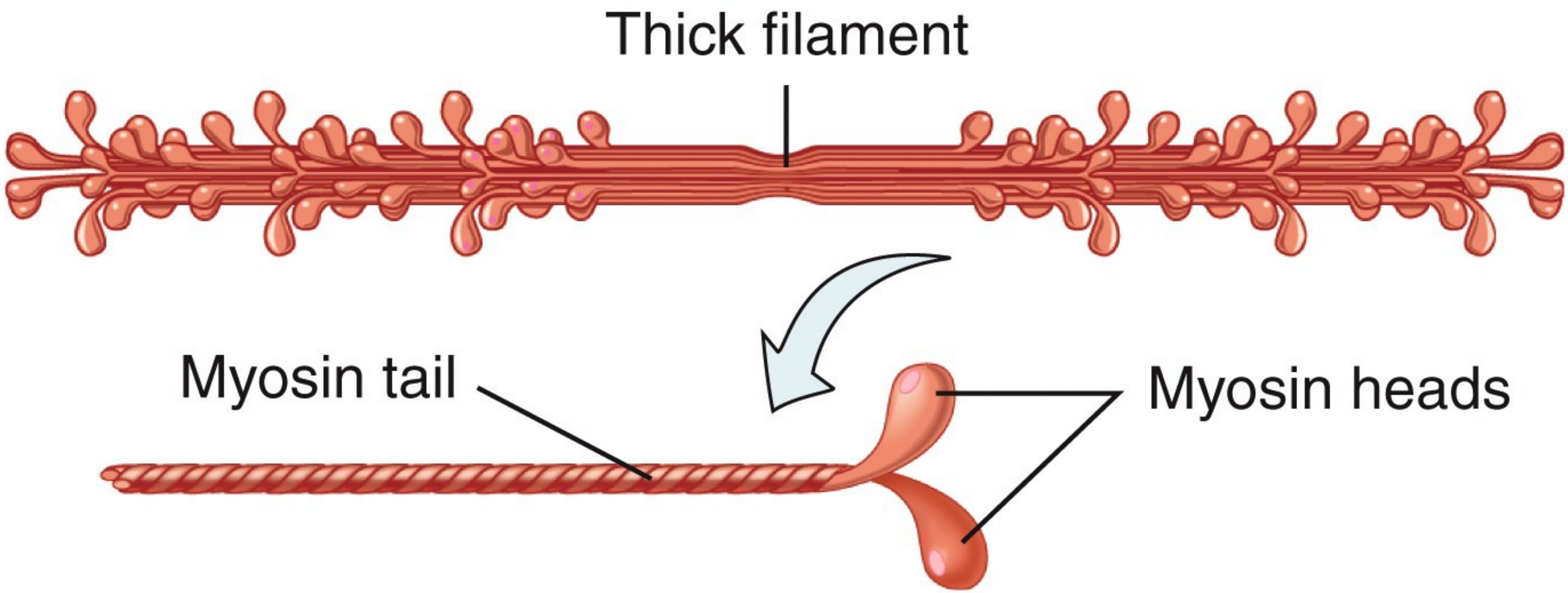
Structure of a Skeletal Muscle Fiber



Thick Myofilaments



- Constructed of hundreds of myosin molecules all nested together
  - One myosin molecule is shaped like a golf club
    - two chains intertwined to form a shaft-like tail
    - double globular head
  - heads directed outward in a helical array around the bundle
    - heads on one half of the thick filament angle to the left
    - heads on the other half angle to the right
    - bare zone with no heads in the middle



(a) A thick filament and a myosin molecule

How are the myosin heads “hinged” to the myosin tail?

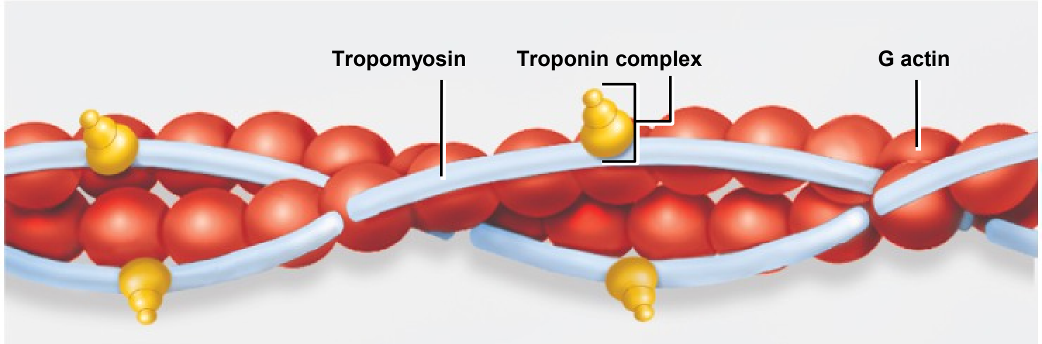
Is the thick filament length changed as the myosin head flex?

Thin Myofilaments

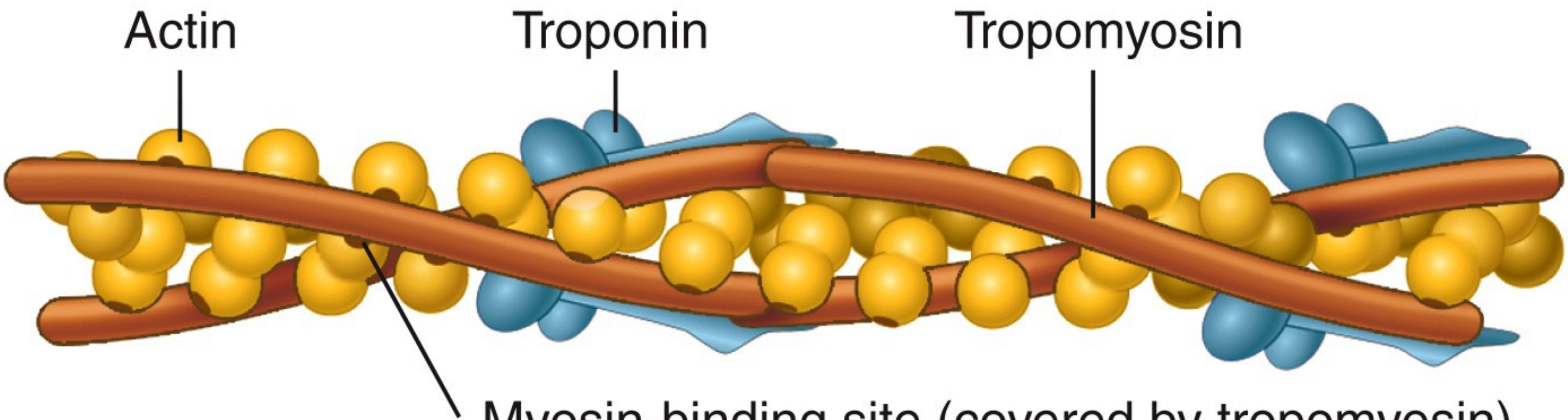
- fibrous (F) actin - two intertwined strands
  - string of globular (G) actin subunits each with an active site that can bind to head of myosin molecule

- tropomyosin molecules /// each blocking 6 or 7 active sites on G actin subunits (regulatory protein)

- troponin molecule - small, calcium-binding protein on each tropomyosin molecule (regulatory protein)



(c) Thin filament



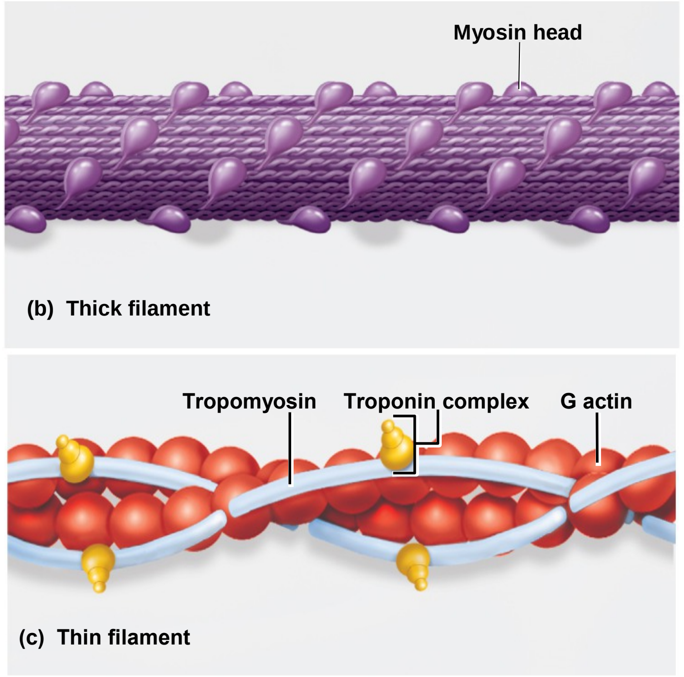
(b) Portion of a thin filament

Why are troponin and tropomyosin called regulatory proteins?

Calcium binds to what molecule?

After calcium binds to a regulatory protein, what happens?

Regulatory VS Contractile Proteins

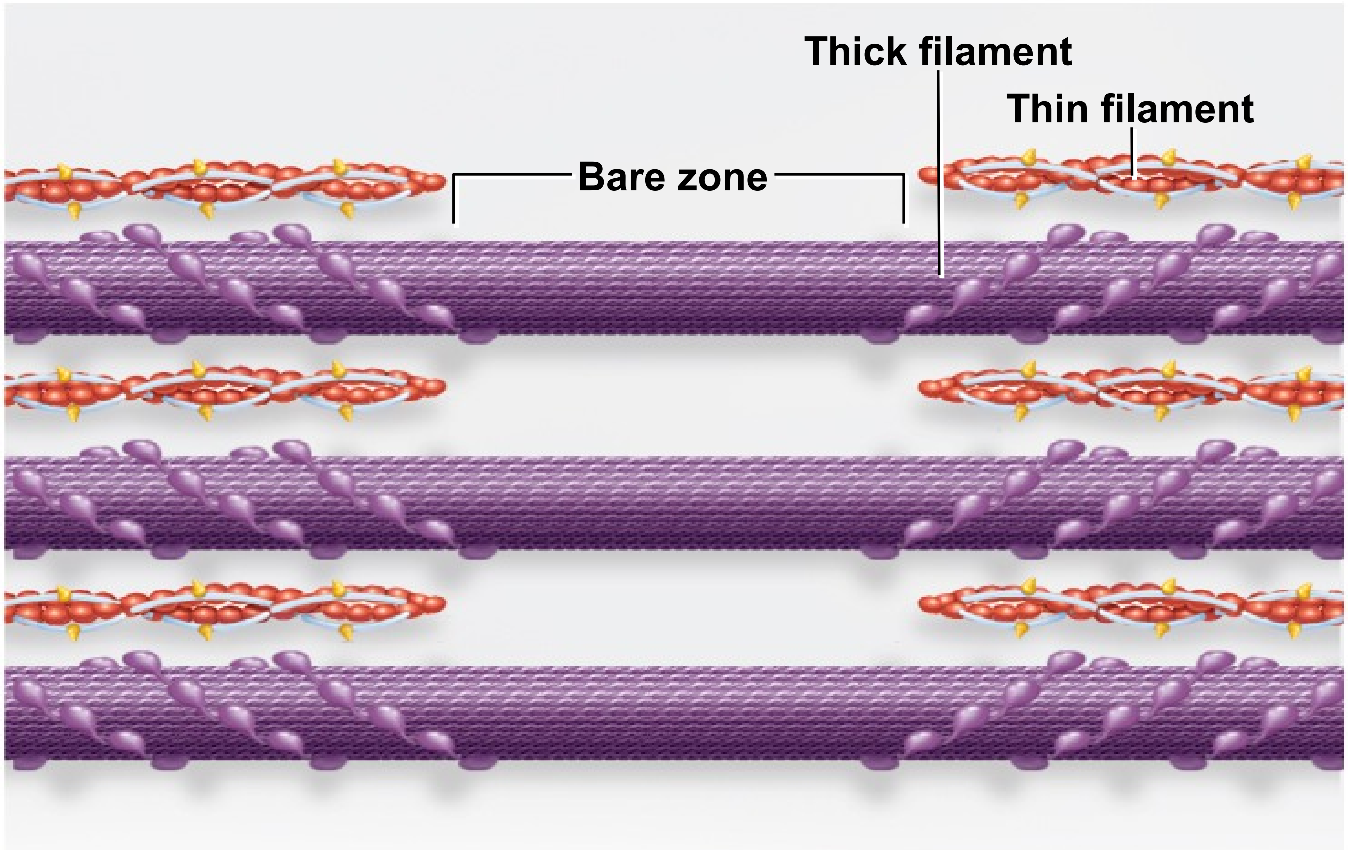


- Contractile proteins – myosin (motor protein) and actin (myosin pulls on actin to bring Z-discs together)

- Regulatory proteins - tropomyosin and troponin

  – like a switch that determine when the fiber can contract and when it cannot
  – contraction activated by release of calcium into sarcoplasm and its binding to troponin,
  – troponin changes shape and moves tropomyosin off the active sites on actin

Overlap of Thick and Thin Filaments

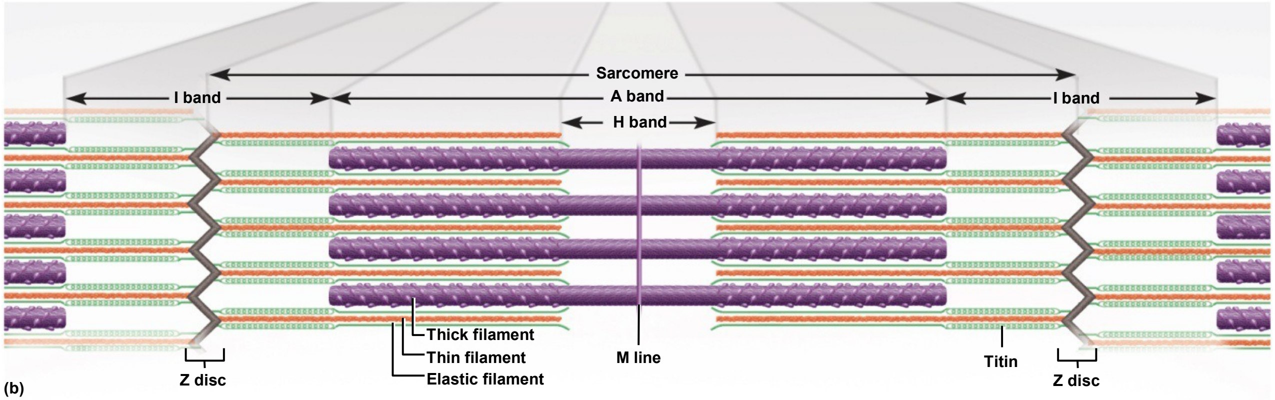


Portion of a sarcomere showing the overlap of thick and thin filaments

- What molecule is the regulatory protein?
- What molecule is the contractile protein?

Elastic Myofilaments

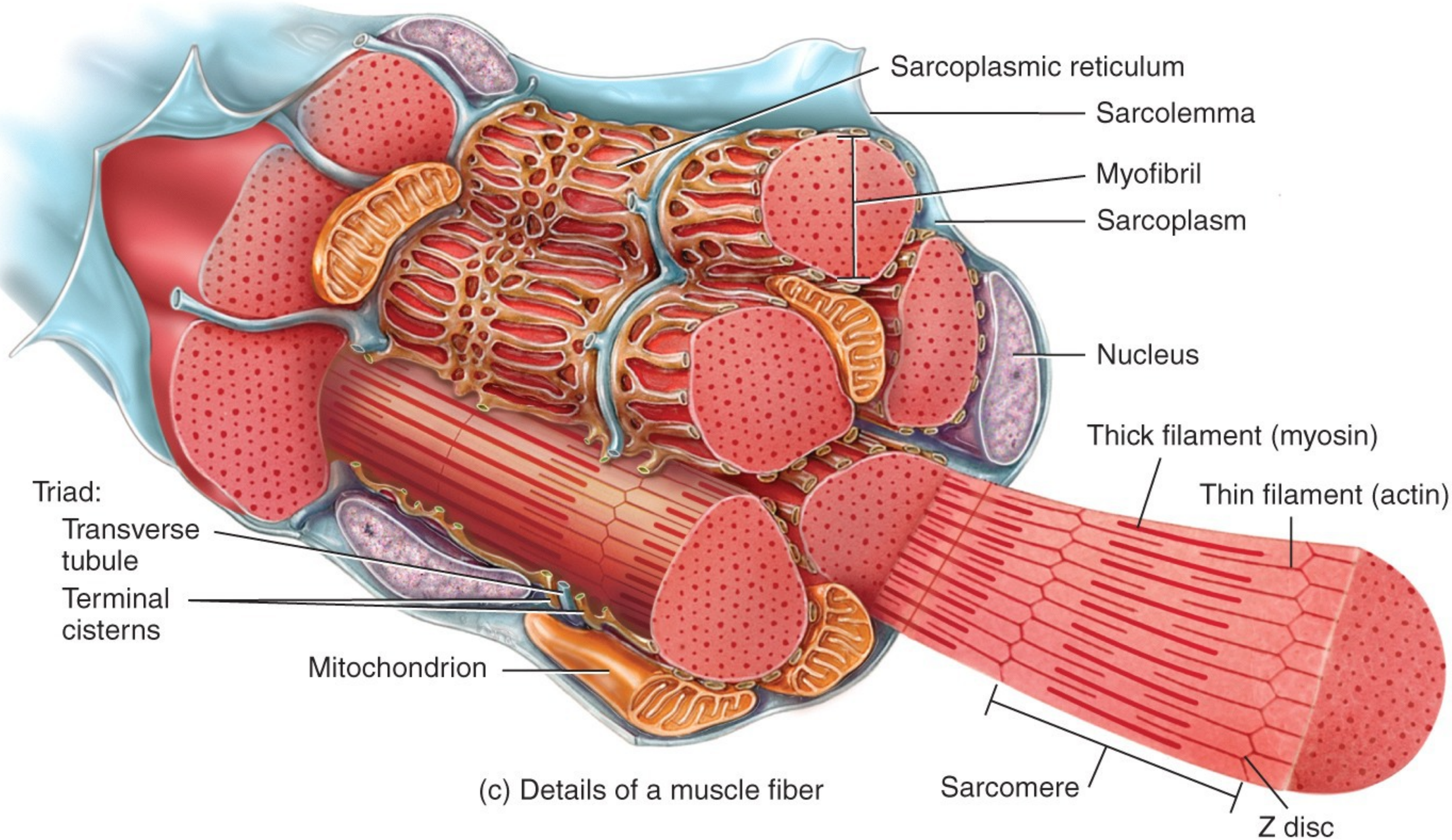
- **Titin (connectin)**
  - huge springy protein
  - flank each thick filament and anchor it to the Z disc
  - helps stabilize the thick filament
  - center myosin between actin (i.e. the thin filaments)
  - prevents over stretching



In this illustration the green fibers are the titin elastic elements

Titin hold myosin in the center of the sarcomere.

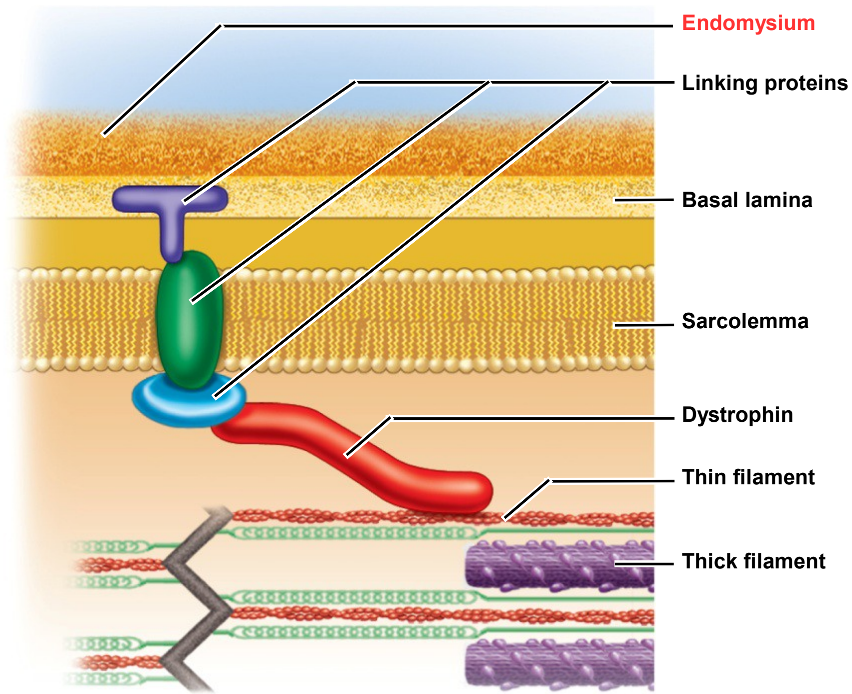
Different illustration will show this relationship in different forms but the function is the same, titin holds myosin in the center of the sarcomere.



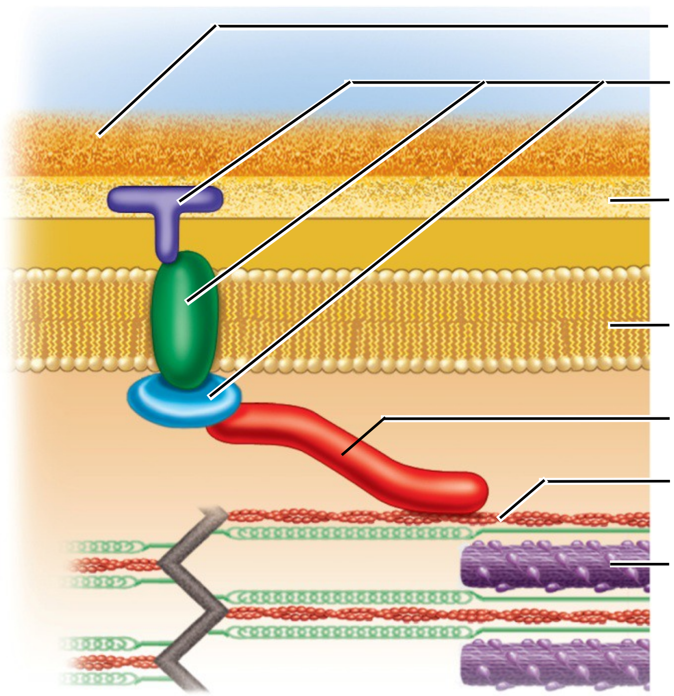
(c) Details of a muscle fiber

Sarcomere Linking Proteins

- Connect contractile proteins to endomysium (i.e. connective tissue surrounding muscle fiber)
- Series of proteins (seven or more)
- Associated with thick or thin filaments
  - anchor the myofilaments
  - regulate length of myofilaments
  - alignment of myofilaments for maximum effectiveness



Sarcomere Linking Proteins



See article aout new gene therapy cure for muscular dystrophy!

Dystrophin

- most clinically important
- links actin in outermost myofilaments to transmembrane proteins
- eventually links to fibrous endomysium surrounding the entire muscle cell
- transfers forces of muscle contraction to connective tissue around muscle cell
- genetic defects in dystrophin produce the disabling disease called muscular dystrophy