Gross, Microscopic, and Ultra Structure of Skeletal Muscles

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Learning Objectives

At the end of the lecture student should be able to:

- - Understand the gross anatomy of skeletal muscles
- - Describe the microscopic structure of muscle fibers
- - Explain the ultra-structure and molecular components
- - Relate muscle structure to function and movement

MUSCLE CELLS

- **are excitable cells.**
- **can transmit action potential along their cell membrane.**
- **convert chemical energy into a mechanical response**

Physiologic Properties of Muscle Cells

- **EXCITABILITY**
- **CONDUCTIVITY**
- **CONTRACTILITY**
- **ELASTICITY**
- **EXTENSIBILITY**
- **PLASTICITY (Adaptability)**
- **TETANUS**
- **FATIGUE**
- **TONE**

- ***1. <u>Excitability (Irritability)</u>***
- The ability to **respond to stimuli** (e.g., nerve impulses, electrical signals).
- Skeletal muscle fibers have **resting membrane potential** and **can generate action potentials** when stimulated by motor neurons.
- **2. *<u>Conductivity</u>***
- The ability to **transmit electrical impulses** along the muscle fiber.
- Action potentials spread from the **neuromuscular junction (NMJ)** across the **sarcolemma** and into **T-tubules**, leading to muscle contraction.

- ***3. <u>Contractility:</u>***
- The ability to **generate force and shorten** when stimulated.
- **Mechanism:**
  - Involves the **sliding filament theory** where **actin and myosin filaments** interact.
  - Requires **calcium (Ca^{2+}) release from the sarcoplasmic reticulum (SR)** and **ATP** for cross-bridge cycling.
- ***4. <u>Extensibility</u>***
- The ability to **be stretched without damage**.
- Allows muscles to accommodate different joint positions and return to resting length.

- ***5. <u>Elasticity</u>***
- The ability to **return to its original length** after stretching or contraction.
- Maintained by **elastic proteins** like **titin**.
- ***6. <u>Plasticity (Adaptability)</u>***
- Skeletal muscles can **adapt to different levels of use** (e.g., hypertrophy with training or atrophy with disuse).
- Involves **muscle fiber type transformation** based on activity demands.

- **7. *Tetany (Summation of Contractions*)**
- A muscle fiber can undergo **sustained contraction** if stimulated at high frequency, leading to **tetanic contraction**(important in force generation).
- **8. *Fatigue***
- The decline in **muscle force generation** due to **metabolic exhaustion, ion imbalances, or central nervous system fatigue**.

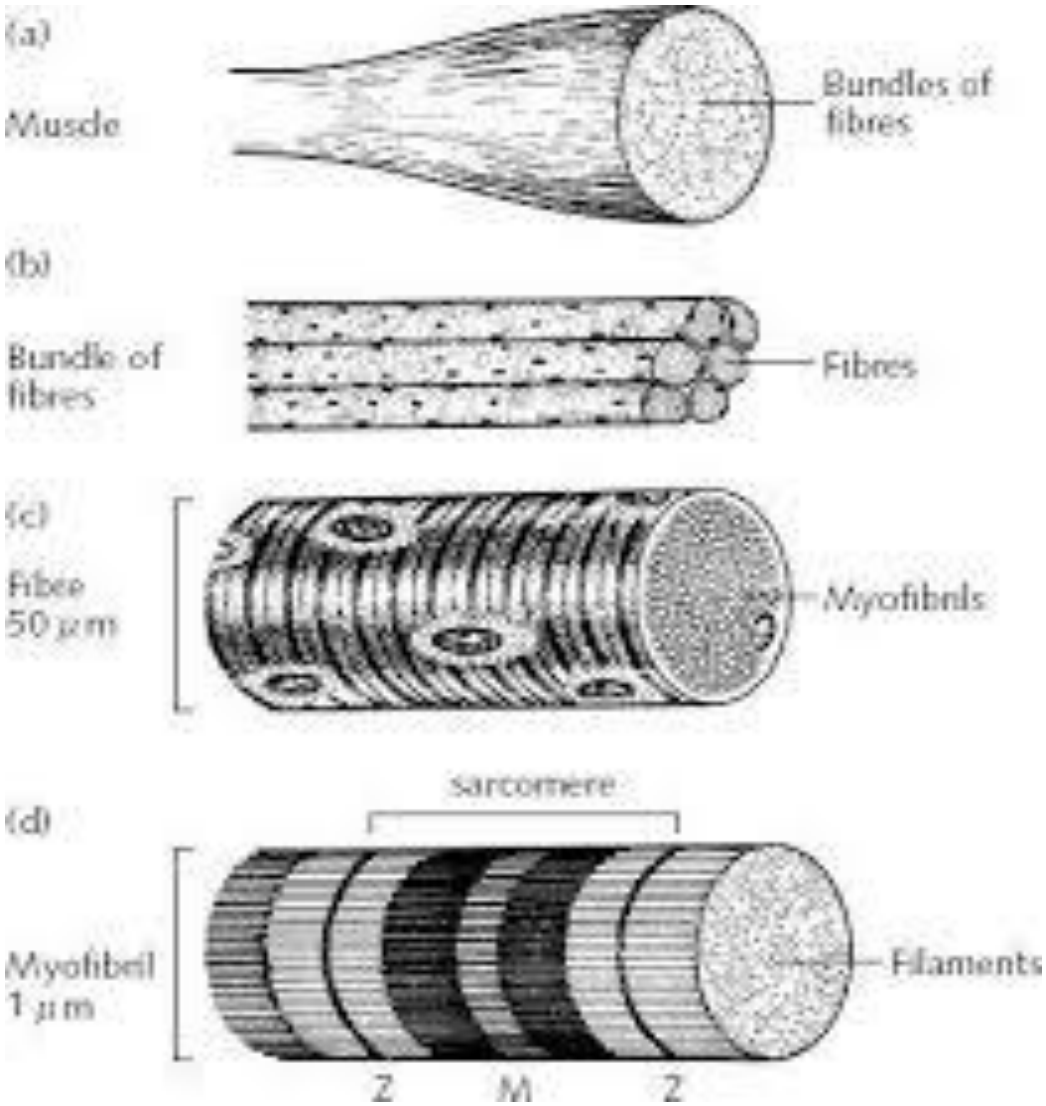
- **9. *<u>Tone (Tonus):</u>***
- Skeletal muscles maintain a **low level of continuous contraction** (muscle tone) even at rest.
- Maintained by **spinal reflexes** to prevent complete relaxation.

Primary Function

- **locomotion**
- **Posture**
- **Stabilization of joints**
- **Production of heat**

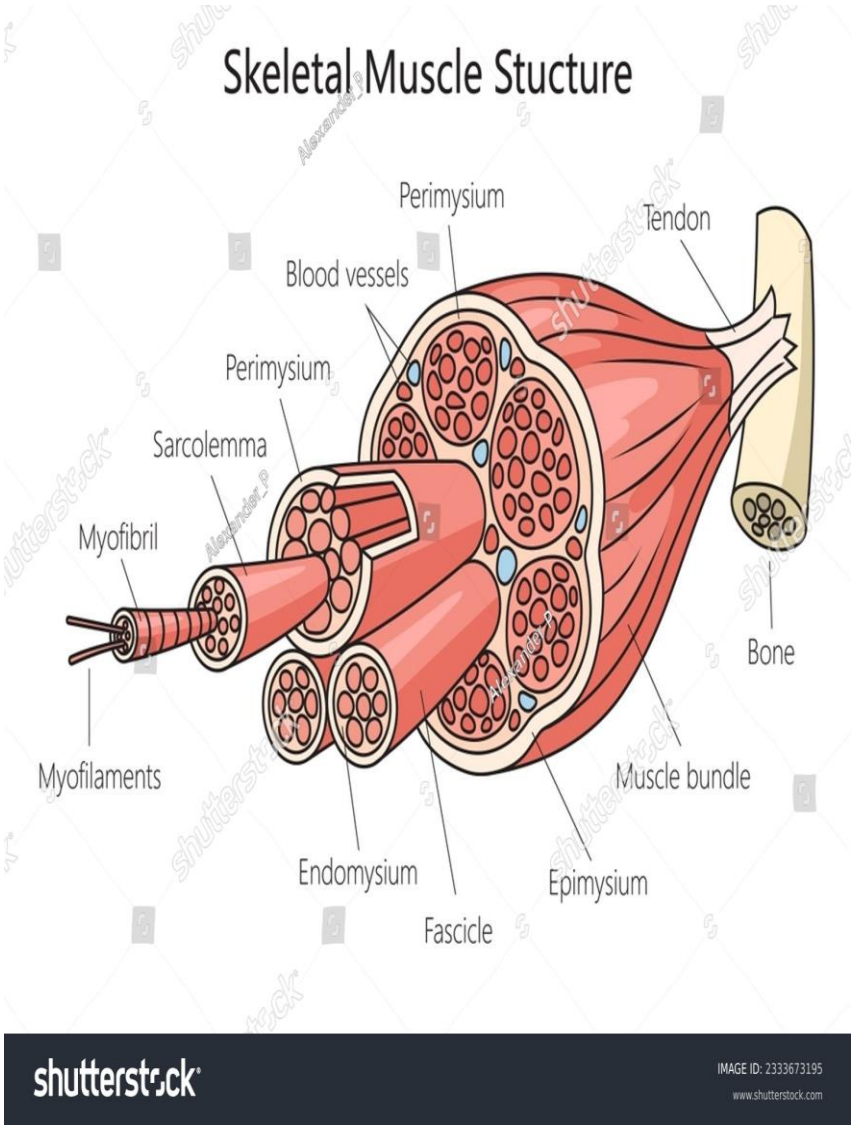
Gross Structure of Skeletal Muscle

- Skeletal muscles are composed of thousands of muscle fibers arranged in bundles and connected to bones via tendons.



Macroscopic Anatomy

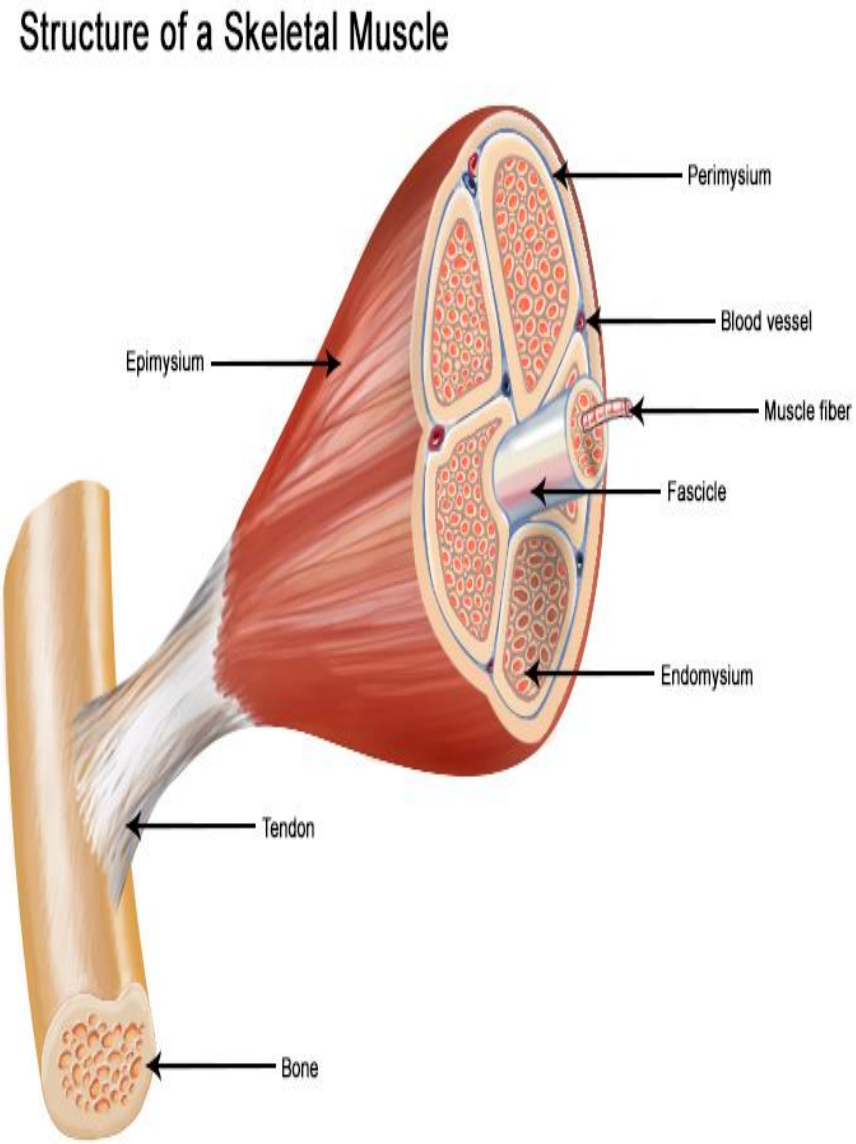
- Each muscle is made up of multiple bundles of muscle fibers known as **fascicles**.
- Surrounded by **connective tissues**, which provide support and transmit force.
- Skeletal muscles attach to bones via **tendons** or **aponeuroses**.



Connective Tissue Layers

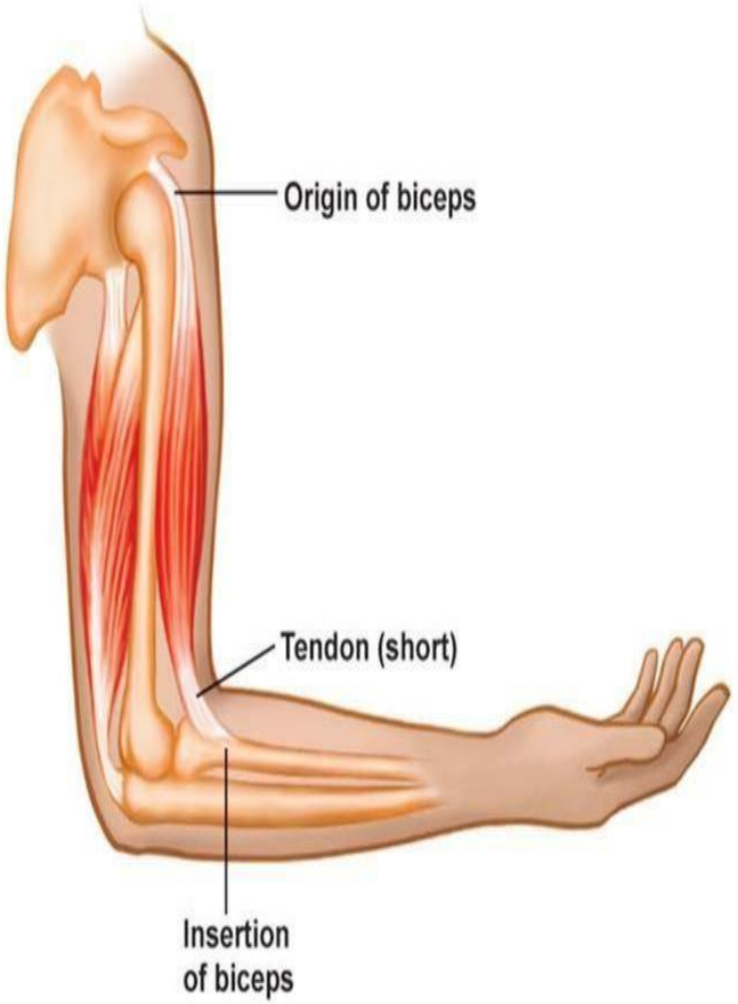
Skeletal muscles have three primary layers of connective tissue:

1. **Epimysium** – Outermost layer covering the entire muscle.
2. **Perimysium** – Surrounds each fascicle (group of muscle fibers).
3. **Endomysium** – Thin layer around individual muscle fibers.



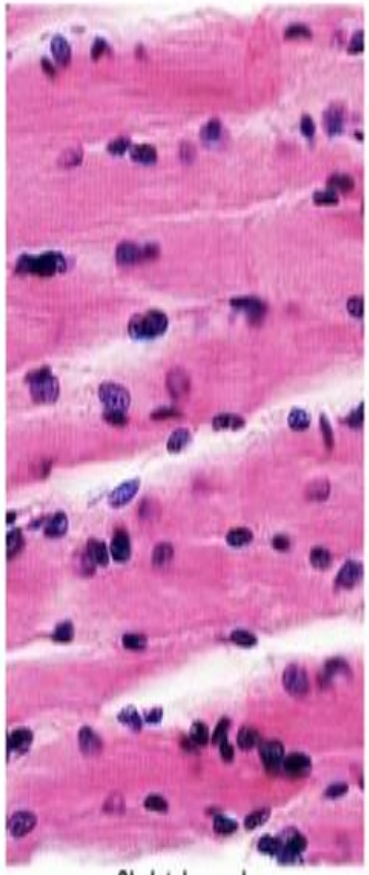
Muscle Attachments

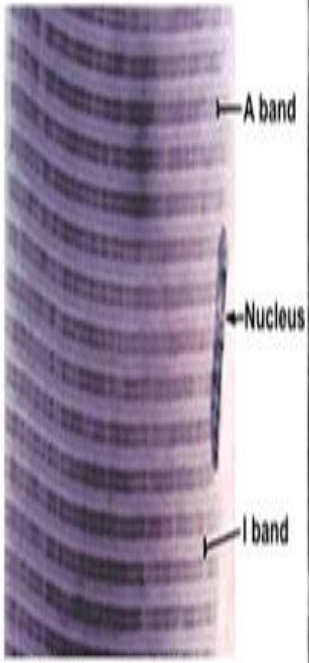
- **Tendons**: Fibrous connective tissue that connects muscle to bone.
- **Origin and Insertion**: The origin is the fixed attachment, while the insertion moves during contraction.



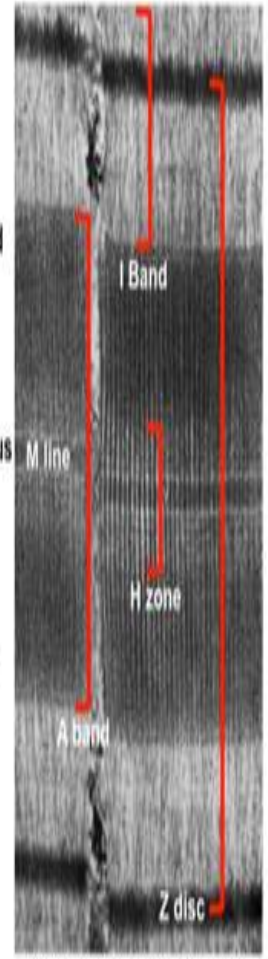
Microscopic Structure of Muscle

- At the microscopic level, skeletal muscle fibers are multinucleated cells composed of contractile units called **sarcomeres**.
- **Muscle Fibers and Sarcomeres**
- The basic functional unit of a muscle fiber is the **sarcomere**.
- Sarcomeres contain **actin (thin) and myosin (thick) filaments**, responsible for contraction.
- Arranged in a repeating pattern, giving skeletal muscles their **striated appearance**.


Skeletal muscle



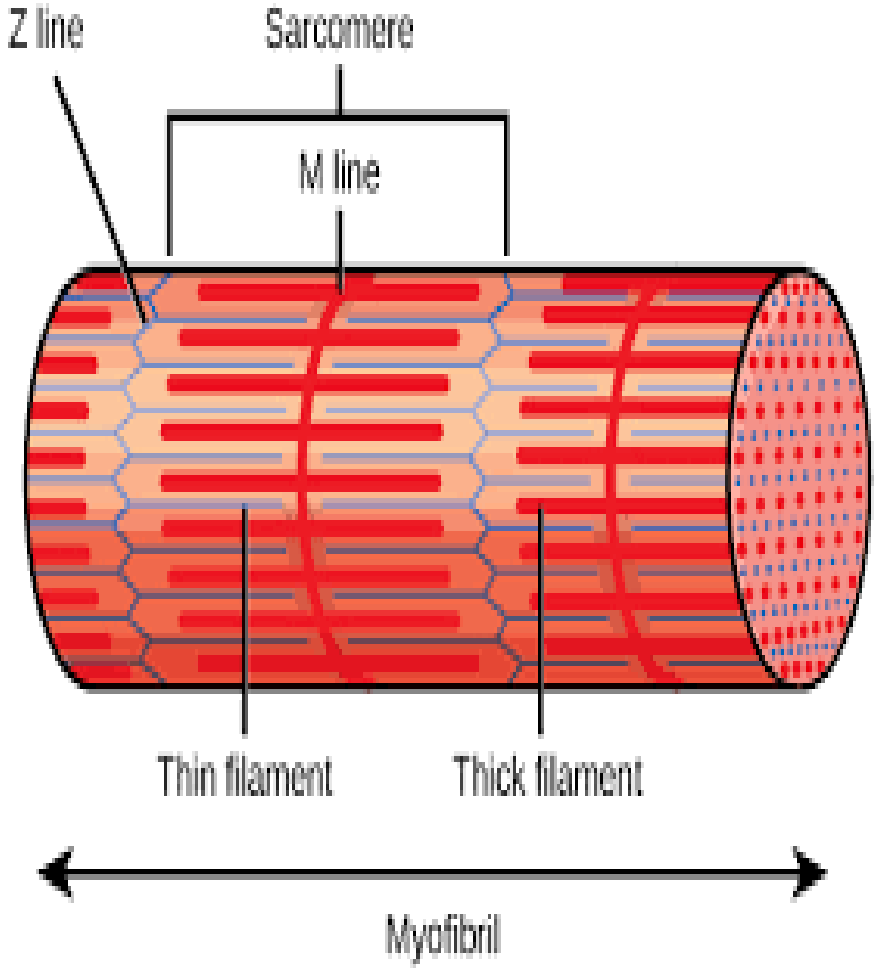
Skeletal muscle striations



Sarcomere = Z disc to Z disc

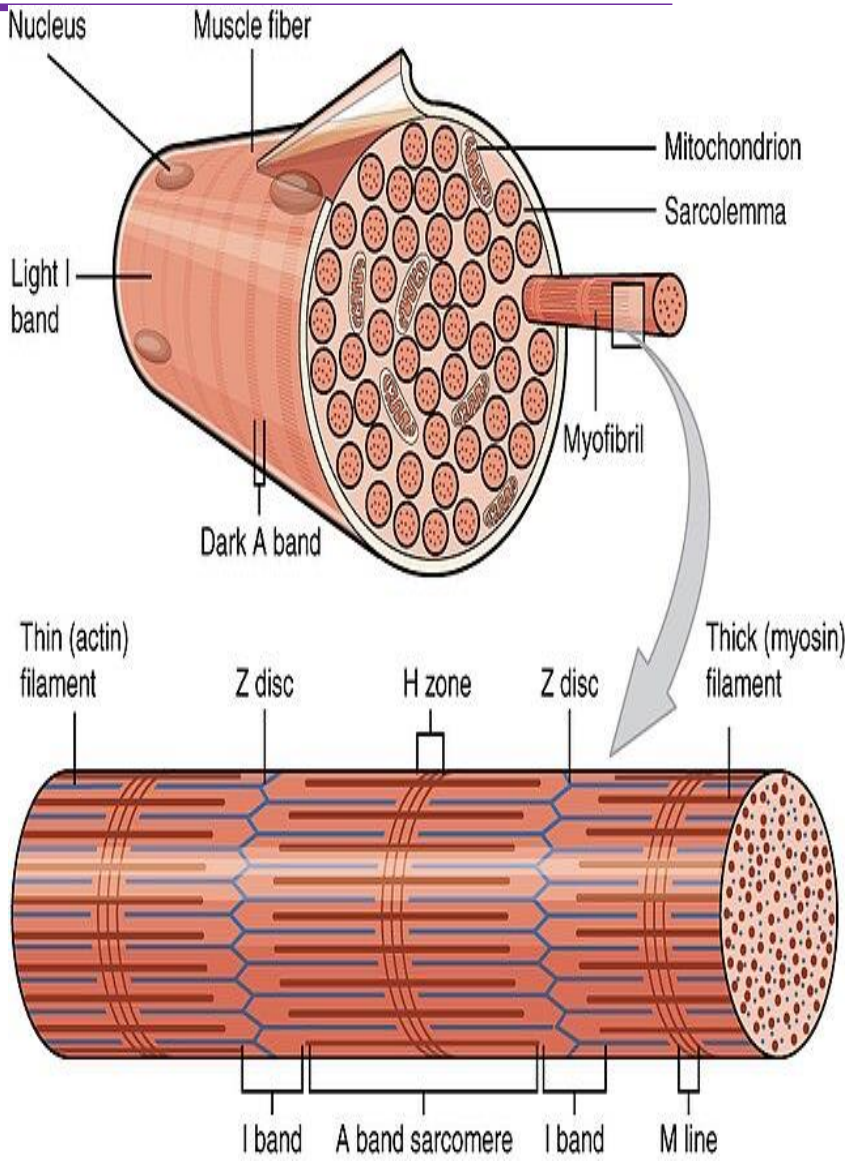
Muscle Fibers and Sarcomeres

- **Muscle Fiber (Myocyte):**Long, cylindrical, multinucleated cells.
- Sarcolemma: Plasma membrane of the muscle fiber.
- Sarcoplasm: Cytoplasm containing organelles and myofibrils
- **Sarcomere:** single contractile unit of muscle fiber is sarcomere



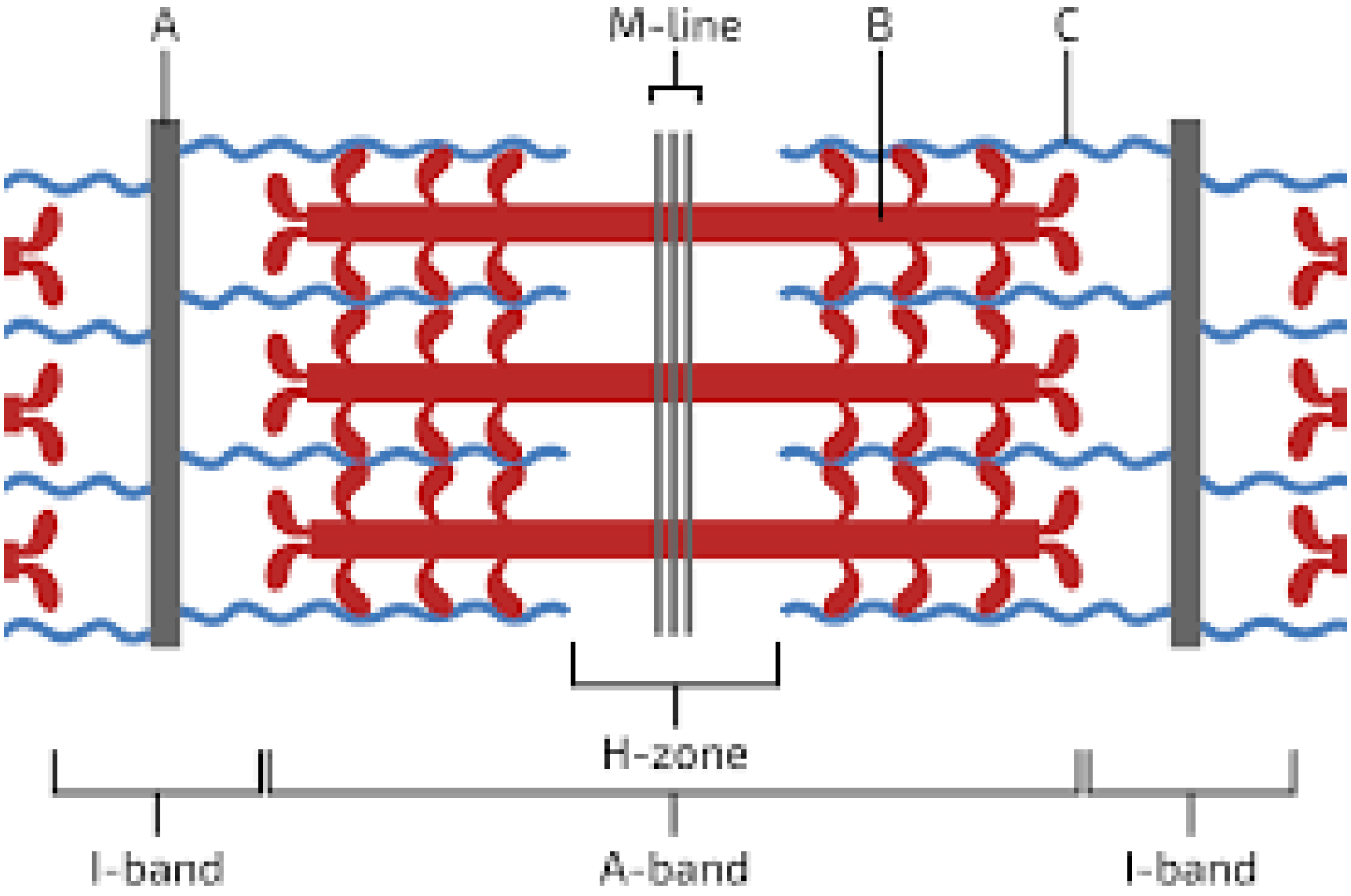
Histology of Skeletal Muscle

- **Myofibrils:** Thread-like structures running longitudinally through the fiber.
- Composed of repeating units called sarcomeres.

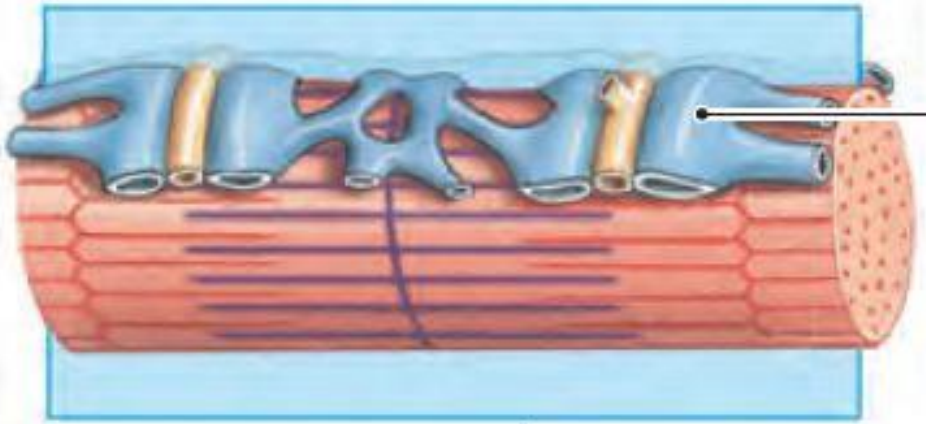


Microscopic structure :

- **Sarcomere:** The basic contractile unit of muscle fiber.
- **Bands and Lines:**
  - **Z-Line:** Defines the boundaries of a sarcomere.
  - **I-Band:** Light band containing thin (actin) filaments.
  - **A-Band:** Dark band where thick (myosin) and thin filaments overlap.
  - **H-Zone:** Central region of the A-Band with only thick filaments.
  - **M-Line:** Middle line anchoring thick filaments.


A
M-line
B
C
H-zone
I-band
A-band
I-band

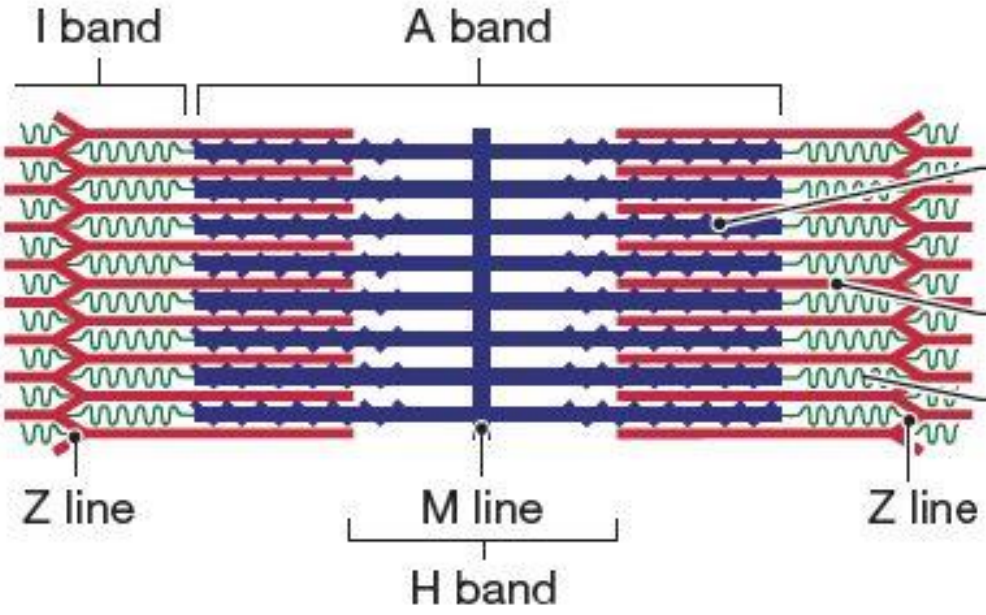
Myofibril



Surrounded by:
Sarcoplasmic reticulum

Consists of:
Sarcomeres
(Z line to Z line)

Sarcomere



Contains:
Thick filaments
Thin filaments
Titin

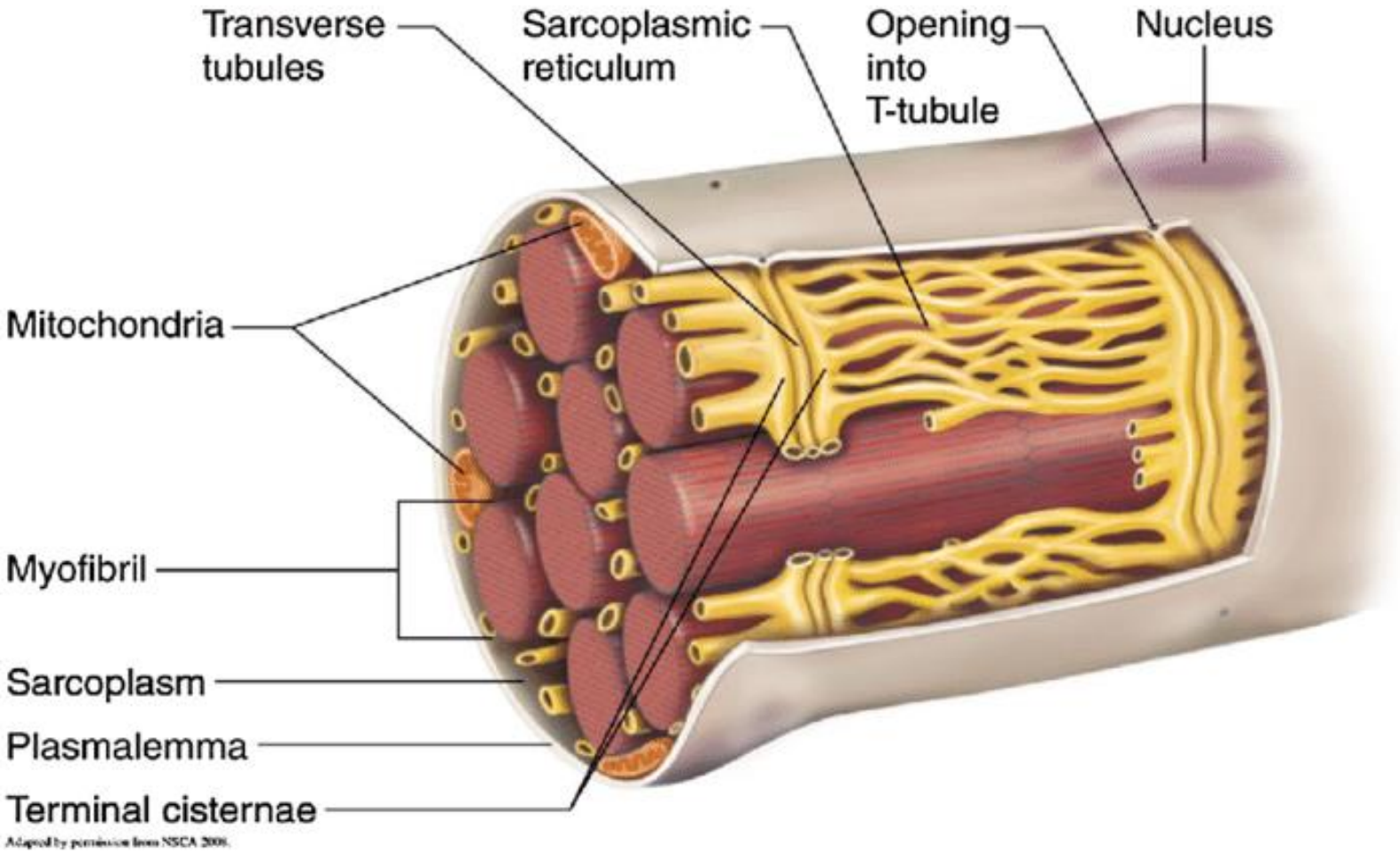
Actin and Myosin Filaments

- **Thick Filaments (Myosin):**Composed of myosin molecules with heads that form cross-bridges during contraction.
- **Thin Filaments (Actin):**Primarily actin, along with regulatory proteins troponin and tropomyosin.
- **Titin Filaments:**Elastic filaments that help maintain the alignment of thick and thin filaments.

Sarcoplasmic Reticulum and Mitochondria

- The sarcoplasmic reticulum (SR) is an organelle in muscle cells that regulates calcium levels and activates contraction. It's a specialized part of the endoplasmic reticulum.
- Mitochondria are the organelles that generate the energy (ATP) needed for muscle contraction

Sarcoplasmic Reticulum and Mitochondria



When the muscle fiber is contracted:

- The length of sarcomere is about 2micrometers.
- Actin filaments completely overlap the myosin filaments.
- The tips of Actin filament are just beginning to overlap each other .
- At this length the muscle is capable of generating its greatest force of contraction.

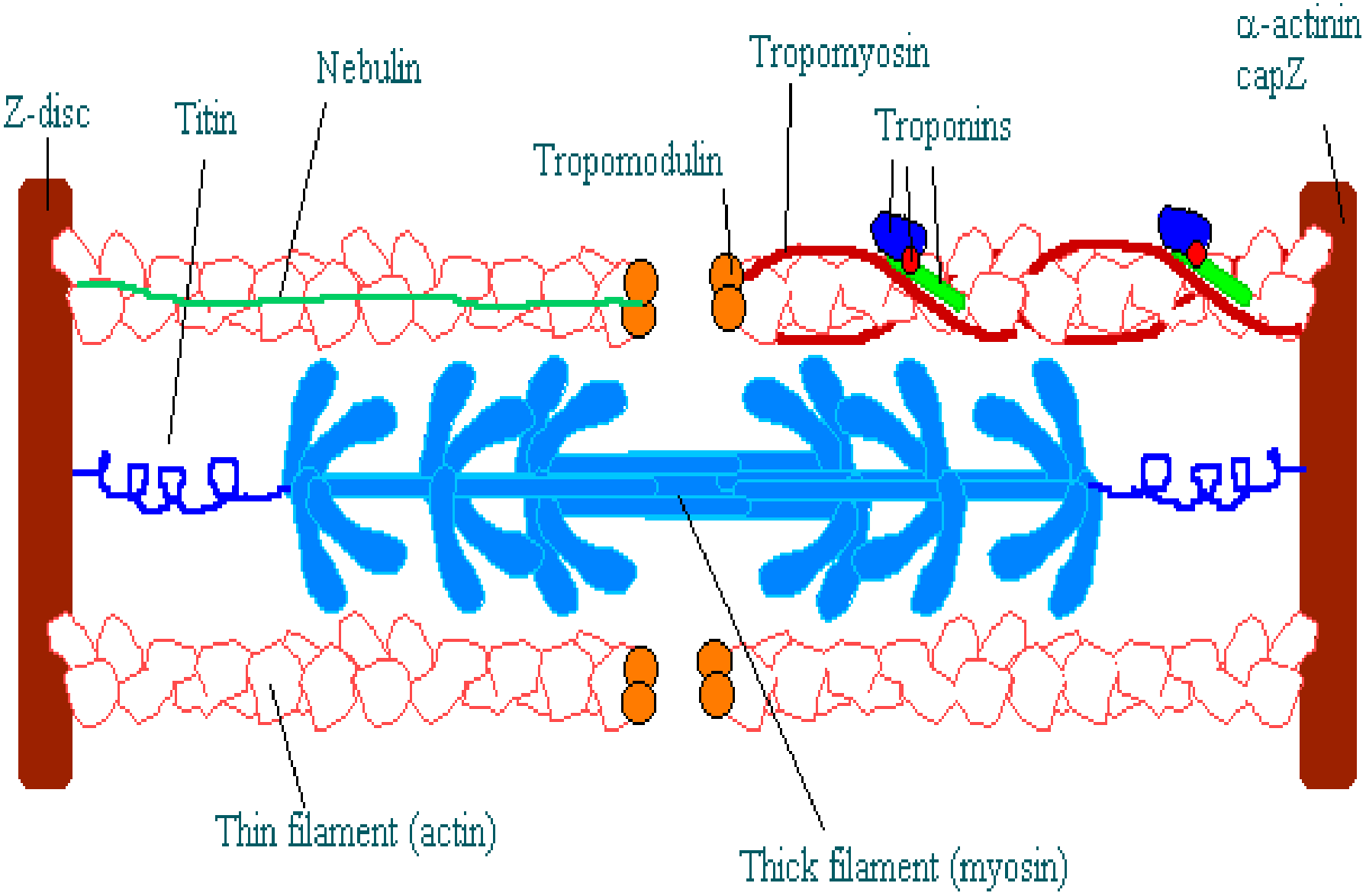
Titin filaments:

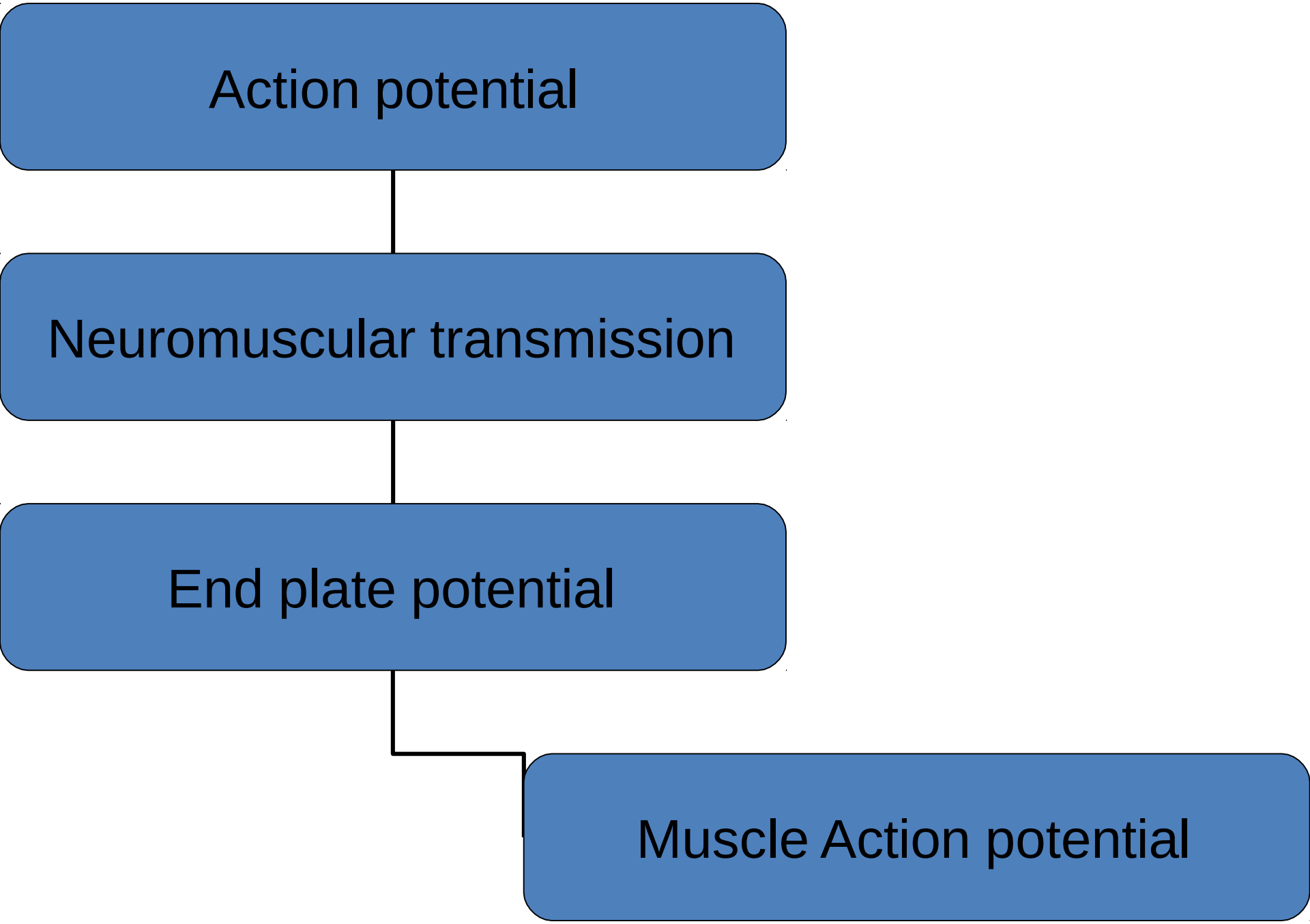
- The side by side relationship between actin & myosin filaments is maintained by ***TITIN***.
- MW 3 million, largest protein molecule.

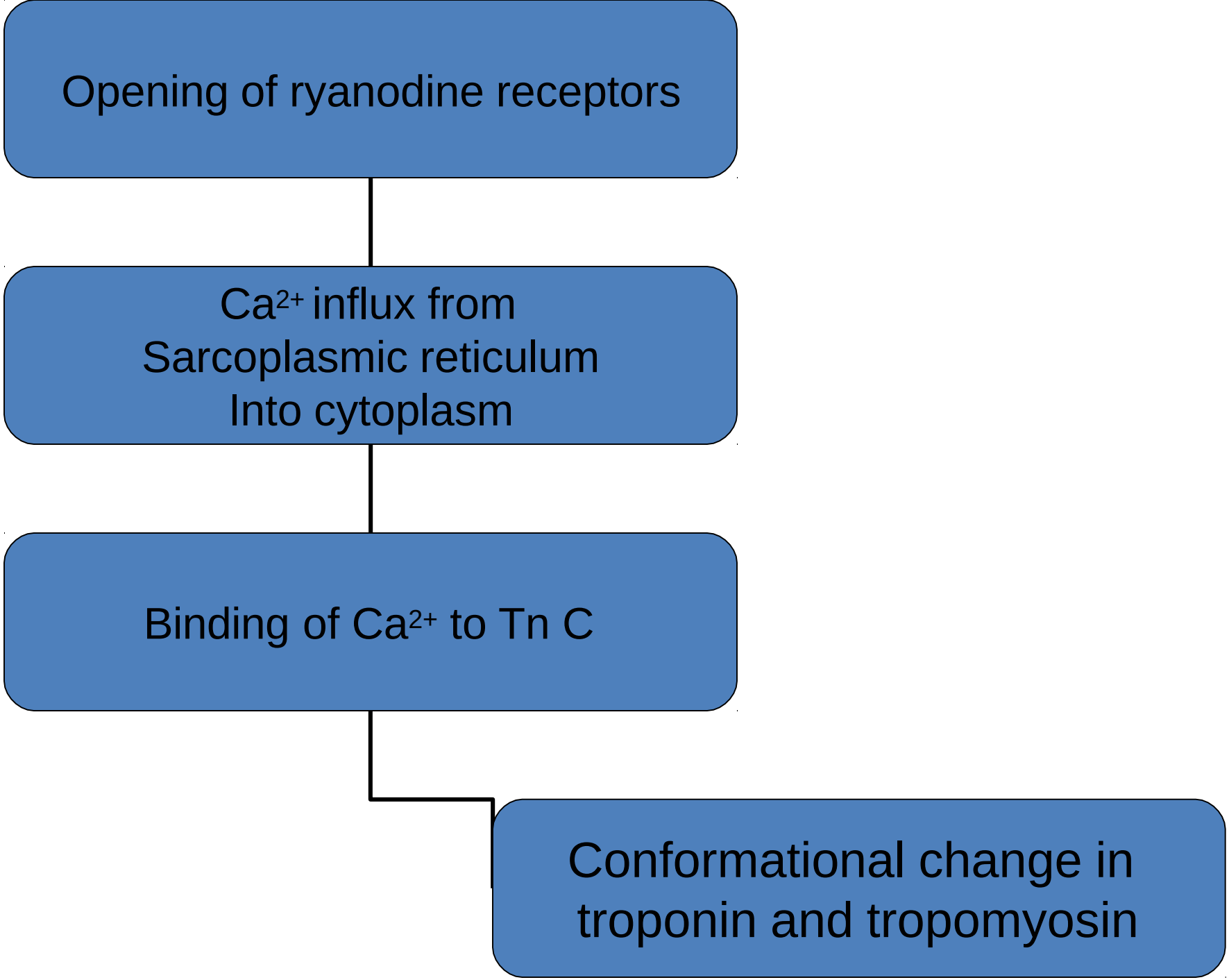
- It is ***Filamentous*** & ***Springy***.

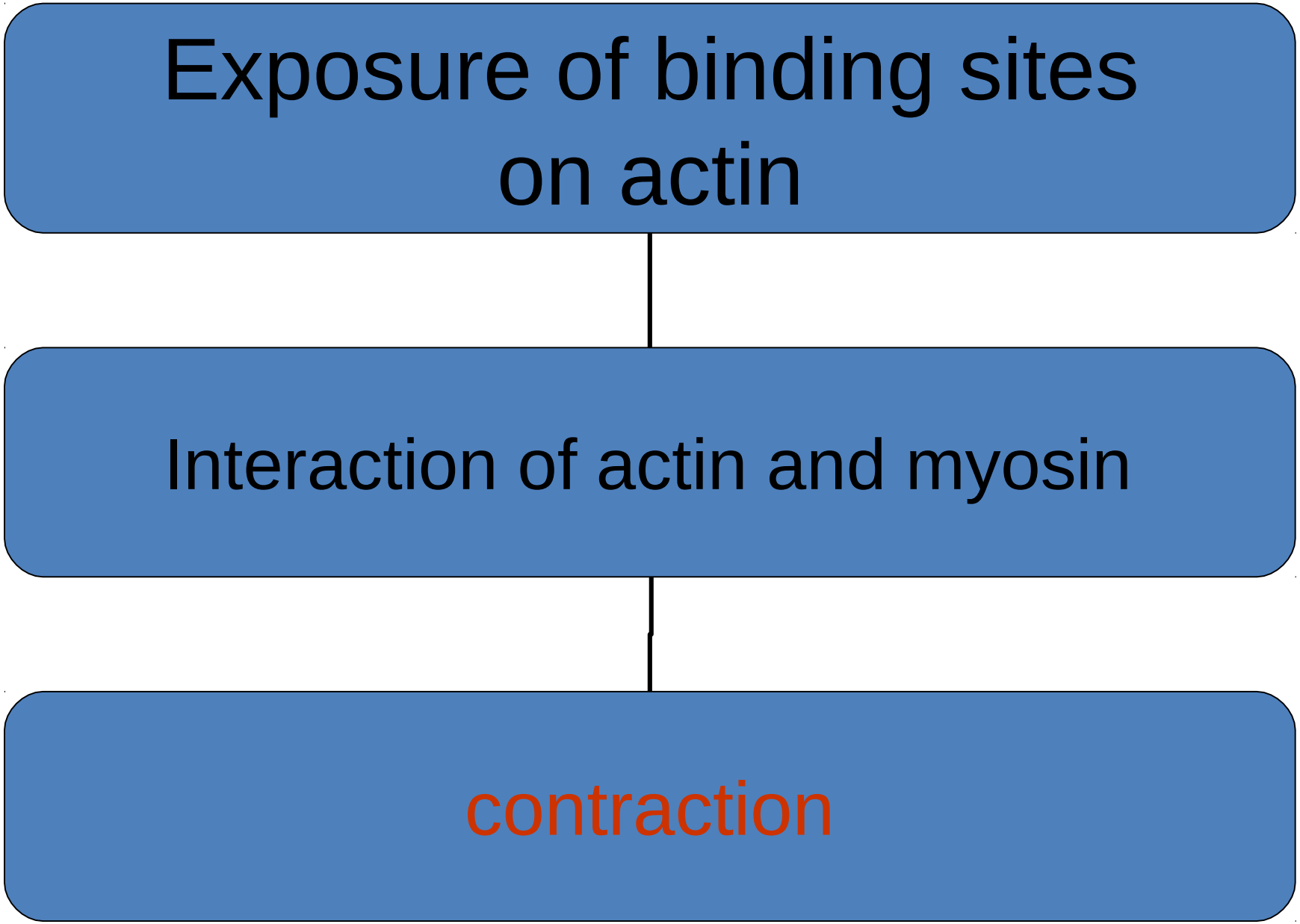
- One end is attached to the ***Z-Disc***. Acting as a spring, changing length as the sarcomere contracts & relaxes.

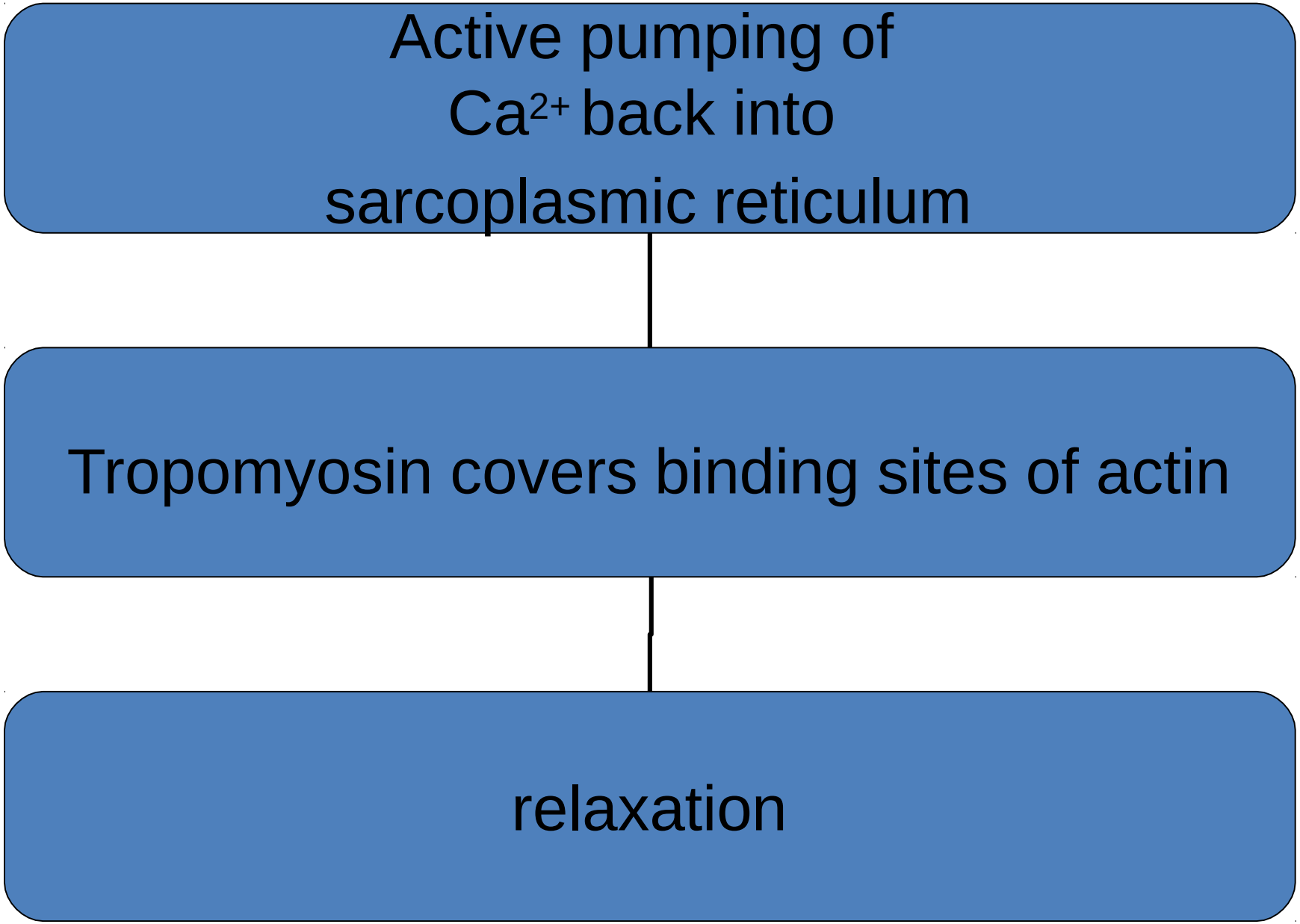
- Other end tethers it to the myosin thick filament.


Z-disc
Titin
Nebulin
Tropomodulin
Tropomyosin
Troponins
α-actinin
capZ
Thin filament (actin)
Thick filament (myosin)


Action potential
Neuromuscular transmission
End plate potential
Muscle Action potential


Opening of ryanodine receptors
Ca^{2+} influx from
Sarcoplasmic reticulum
Into cytoplasm
Binding of Ca^{2+} to Tn C
Conformational change in
troponin and tropomyosin

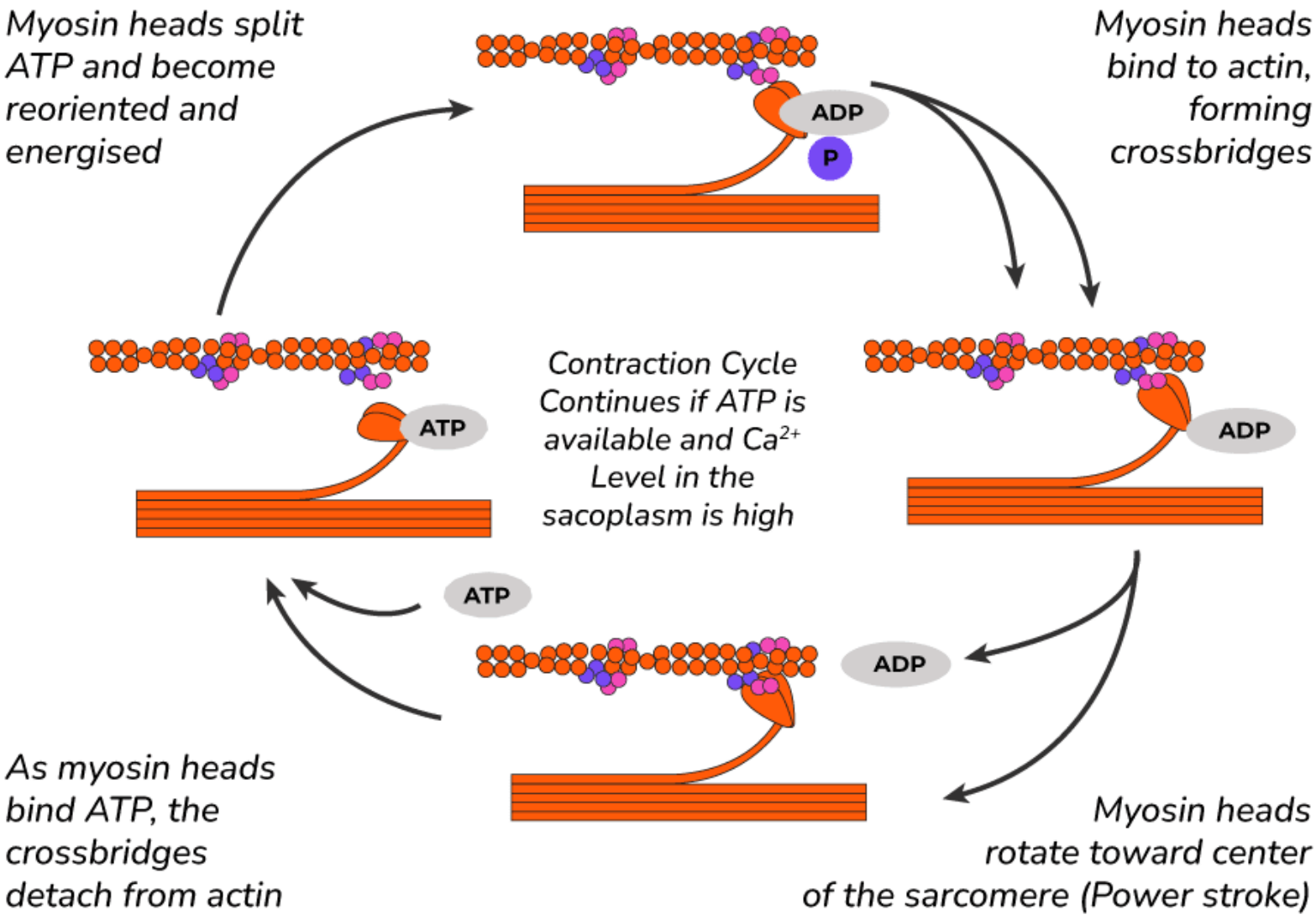

Exposure of binding sites on actin
Interaction of actin and myosin
contraction


Active pumping of
Ca^{2+} back into
sarcoplasmic reticulum
Tropomyosin covers binding sites of actin
relaxation

Sliding Filament Theory

- Filament sliding occurs by cyclic attachment and detachment of myosin on actin filaments. Contraction occurs when the myosin pulls the actin filament towards the centre of the A band, detaches from actin and creates a force (stroke) to bind to the next actin molecule.

Sliding Filament Theory

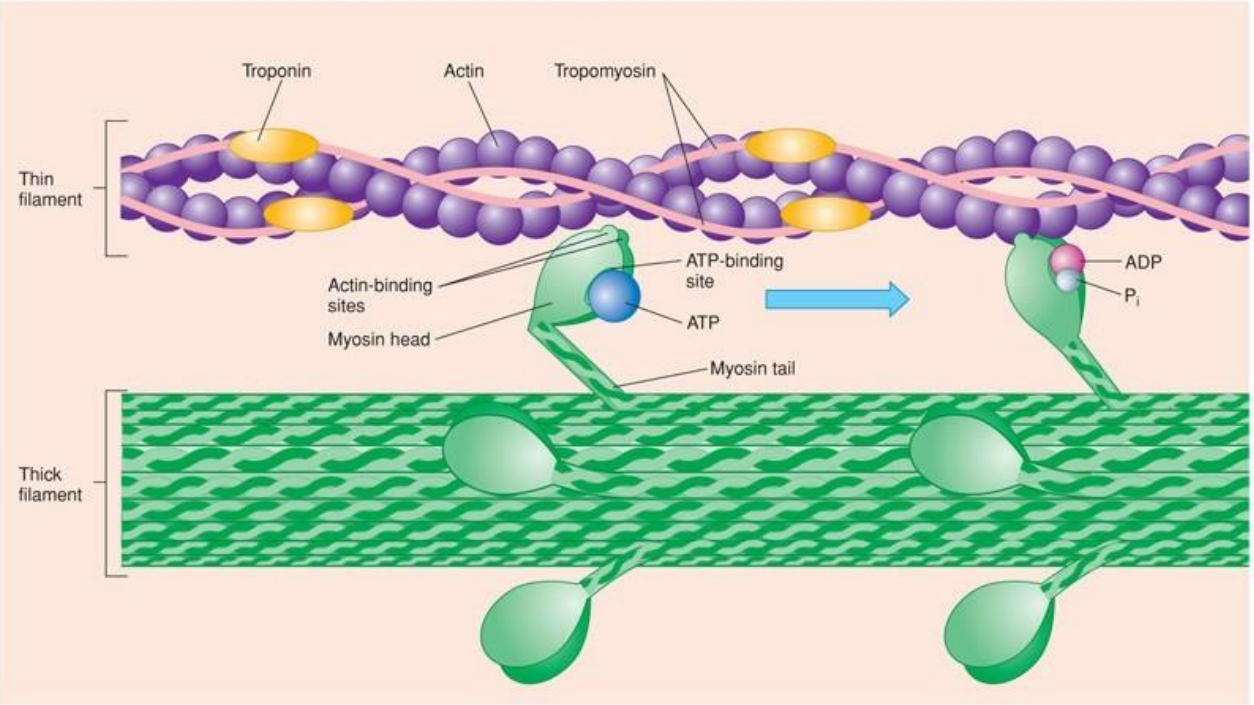


Molecular Mechanisms of Contraction

- Key steps involved in muscle contraction:
- **Cross-Bridge Formation:** Myosin heads attach to binding sites on actin filaments.
- **Power Stroke:** Myosin heads pivot, pulling actin filaments toward the center of the sarcomere.
- **Detachment:** ATP binds to myosin heads, causing them to release from actin.
- **Reactivation:** Hydrolysis of ATP repositions the myosin heads, preparing them for another cycle.

Cross Bridges

- Are formed by heads of myosin molecules that extend toward and interact with actin
- Sliding of filaments is produced by actions of cross bridges
  - Each myosin head contains an ATP-binding site which functions as an ATPase



ULTRASTRUCTURE

Myosin- thick-

- Myosin filament made of around 200 molecules of myosin

- ***Myosin molecule***

➢ composed of 6 polypeptide chains

➢ **2 heavy chains** (MW-200,000 each) and **4 light chains** (MW-20,000 each),form **Tail**

➢ One end of each chain forms globular polypeptide structure called **Myosin head**

➢ **4 light chains** are also a part of Myosin head. They help control the function of head.

➢ **Arm** Part of the boy of each molecule hangs to the site along with the head.

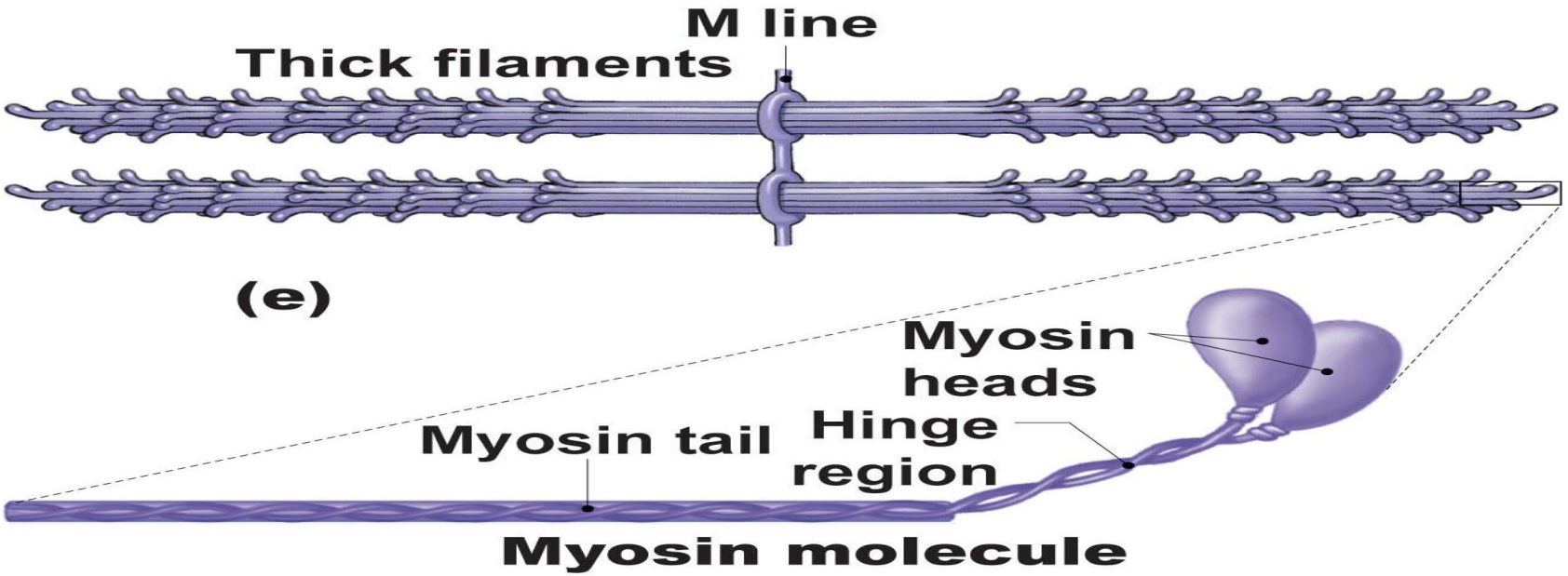
➢ **Arm and head** form **cross-bridge**

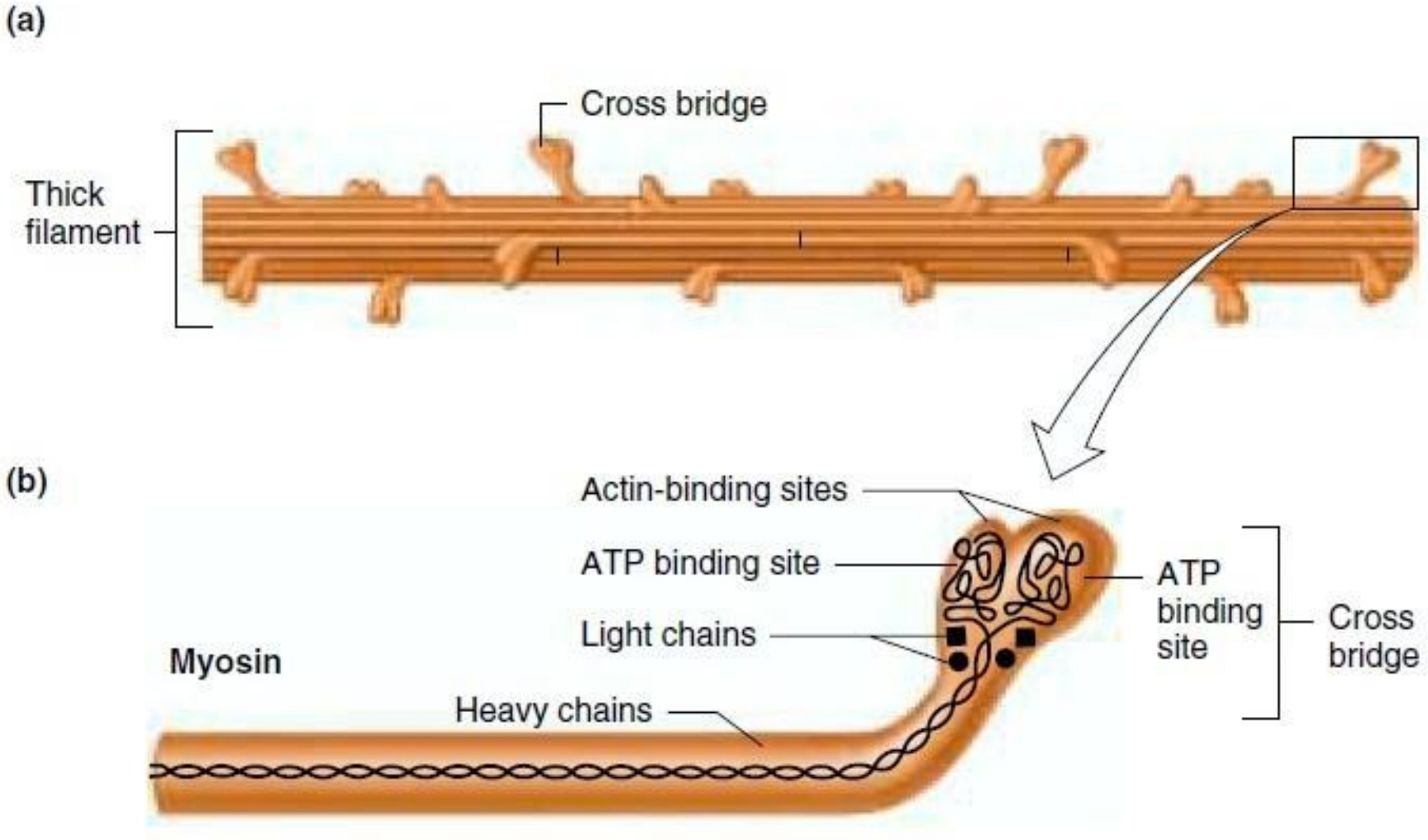
➢ **Hinges :** cross bridge is flexible at two points.

- ***ATPase Activity of Myosin Head***

- ***Cleaves ATP in contraction mechanism***

MYOSIN FILAMENT




(a)
Cross bridge
Thick filament
(b)
Actin-binding sites
ATP binding site
Light chains
Myosin
Heavy chains
ATP binding site
Cross bridge

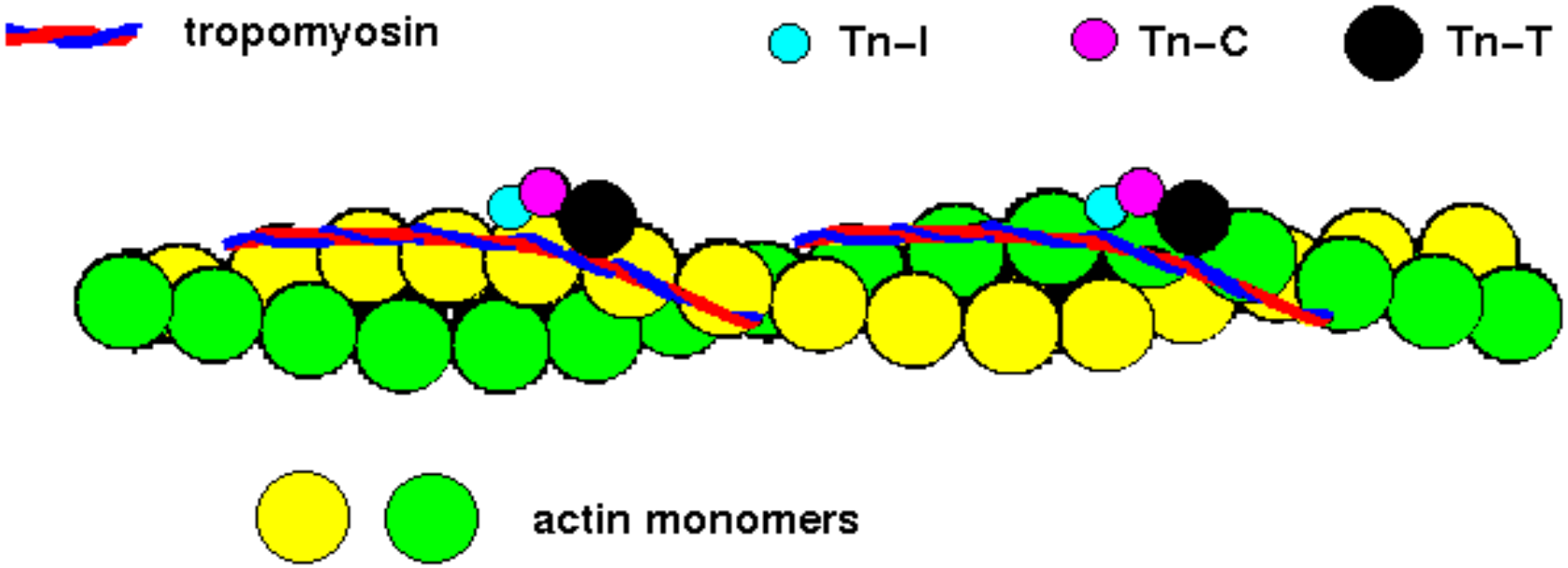
- ***Actin filament-*** 7nm wide and 1.0µm long

  Extend on both sides of z-lines

  F-actin forms a double helix

  Made up of 300 F-actin molecules (MW 42,000)

  F-actin has active sites ADP molecules for interaction with myosin heads

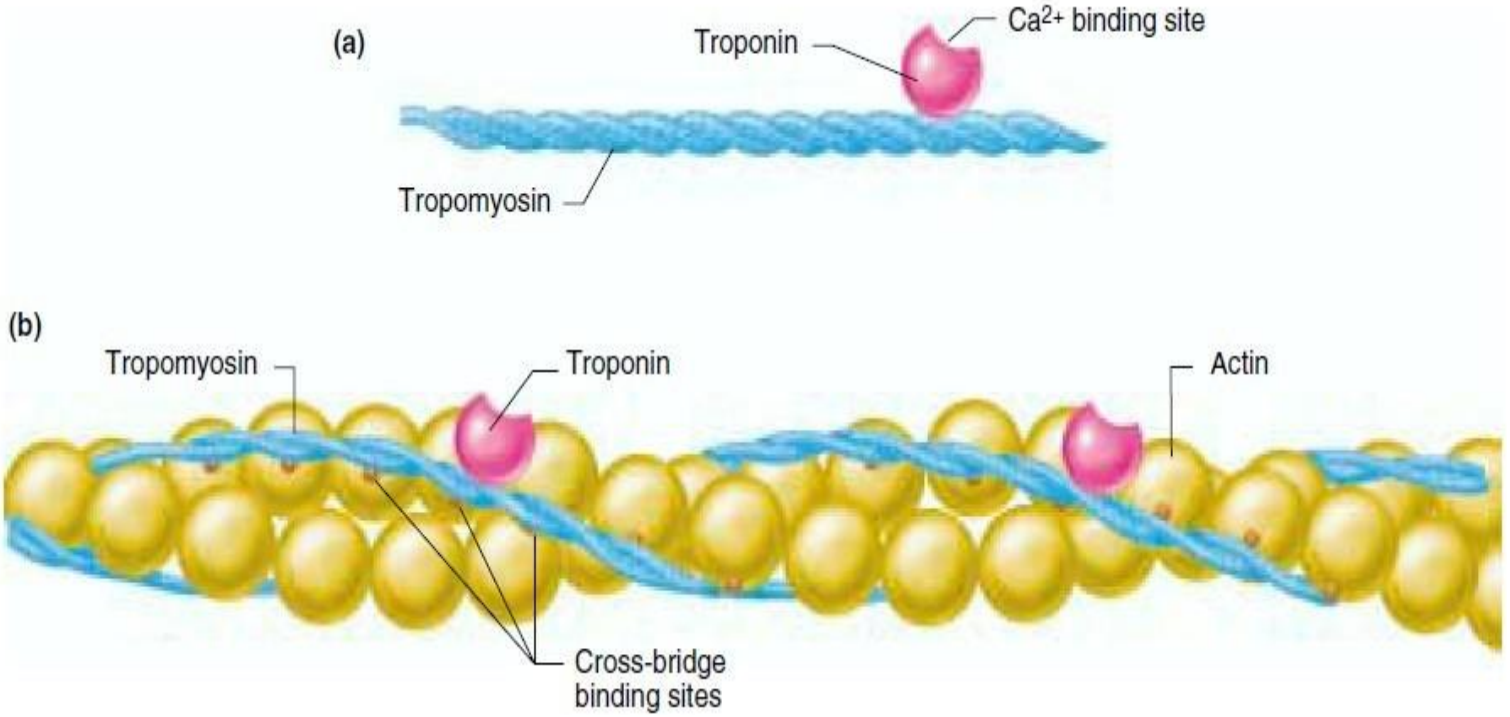


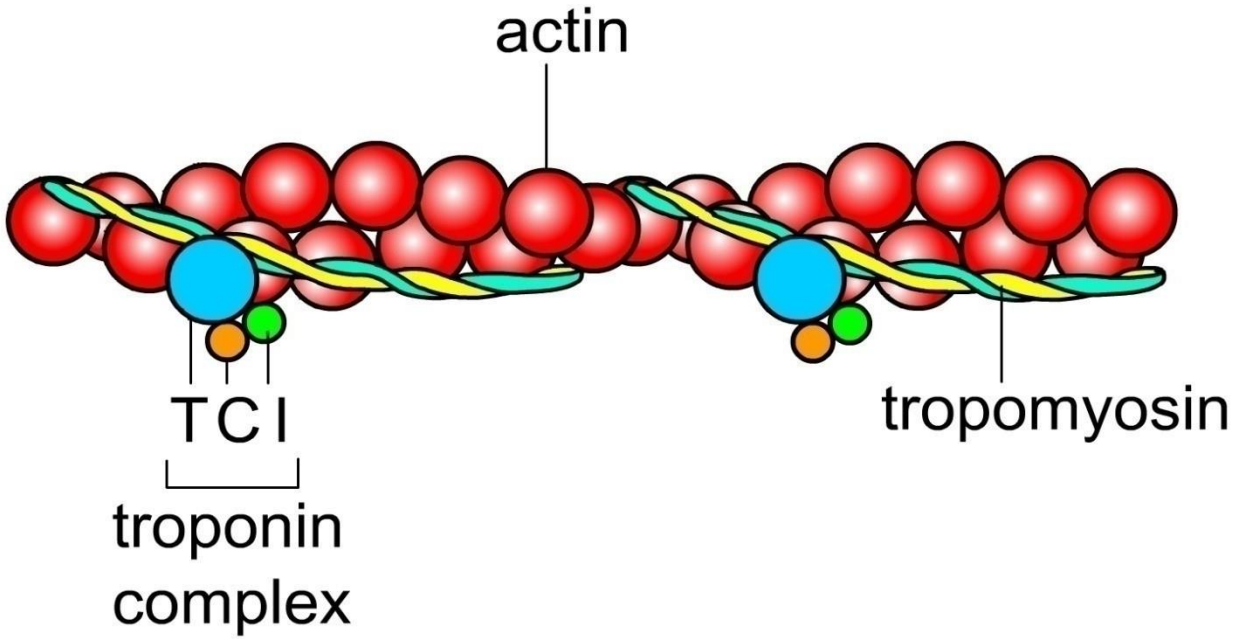
- ***Tropomyosin-*** 40nm length and MW of 70,000.

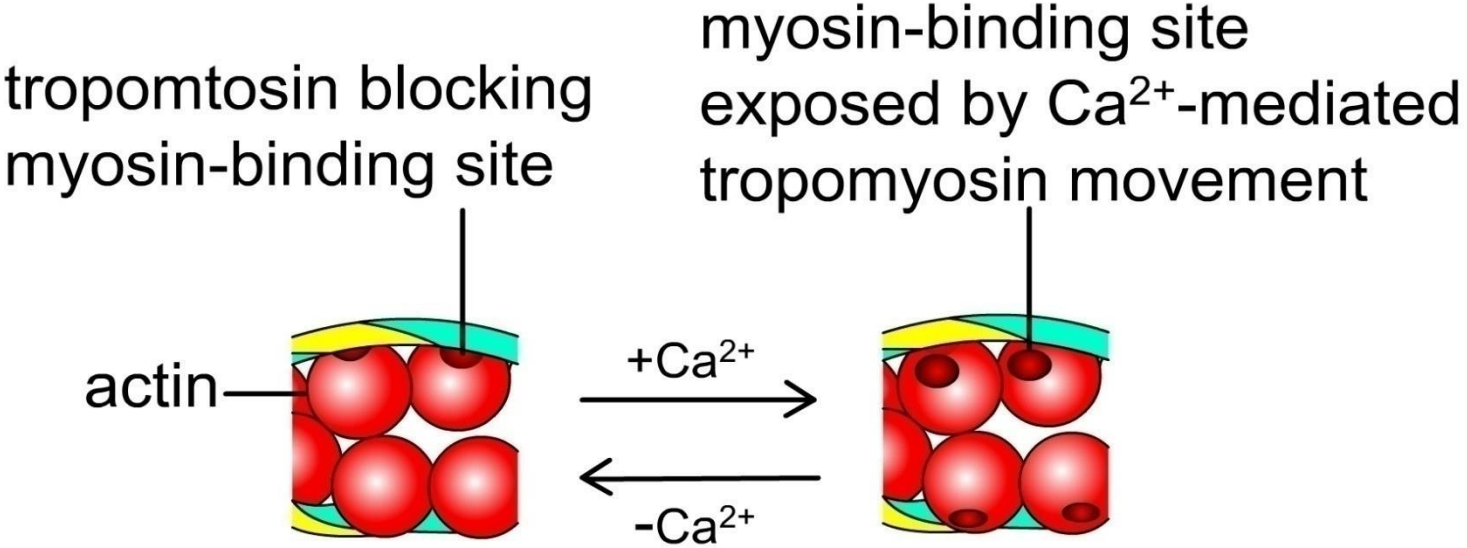
  Wrapped around F actin helix & covers active sites in resting phase.

  As a result of this attraction b/w Actin & Myosin cannot occur to cause contraction.

- ***Troponin-*** made of 3 protein subunits
- Troponin I----- strong affinity for ACTIN
- Troponin T---- strong affinity for TROPOMYOSIN
- Troponin C---- strong affinity for CALCIUM IONS


(a)
Troponin
Ca^{2+} binding site
Tropomyosin
(b)
Tropomyosin
Troponin
Actin
Cross-bridge
binding sites


actin
T C I
troponin
complex
tropomyosin


tropomtosin blocking
myosin-binding site
myosin-binding site
exposed by Ca2+-mediated
tropomyosin movement
actin
+Ca2+
-Ca2+

	RED MUSCLE	WHITE MUSCLE
	Type I fibers are more Smaller fibers	Type II fibers are more Larger fibers
	Myoglobin content is high. So, it is red	Myoglobin content is less. So, it is pale
	Sarcoplasmic reticulum is less extensive	Sarcoplasmic reticulum is more extensive
	Blood vessels are more extensive	Blood vessels are less extensive
	Mitochondria are more in number	Mitochondria are less in number
	Response is slow with long latent period	Response is rapid with short latent period
	Contraction is less powerful	Contraction is more powerful
	This muscle is involved in prolonged and continued activity as it undergoes sustained contraction i.e. Soleus muscle	This muscle is not involved in prolonged and continued activity as it relaxes immediately i.e. Anterior tibialis muscle
	Fatigue occurs slowly	Fatigue occurs quickly
	Depends upon cellular respiration for ATP production(oxidative metabolism is Primary)	Depends upon glycolysis for ATP production (oxidative metabolism is Secondary)

RIGOR MORTIS

Definition:

It is one of the recognizable signs of death in which several hours after death, all the muscles of the body go into a state of irreversible rigidity and contracture called *Rigor Mortis*. The body then becomes difficult to move or manipulate.

On Microscopy:

Continuous Actin-Myosin interaction.

Cause:

After death, cellular respiration in organisms ceases to occur, depleting the corpse (dead body) of oxygen used in the making of adenosine triphosphate (ATP).

Unlike in normal muscle contraction, after death as ATP is **NOT** available, the body is unable to complete the contraction cycle and release the coupling b/w actin and myosin. We know that a new molecule of ATP is required to interact with the myosin molecule to cause relaxation at the end of a power stroke. When it is not available, relaxation cannot take place and thus, there is a state of continuous muscular contraction.

Mechanism:

1. Absence of ATP→ No reuptake of Ca^{2+} into the SR as Ca^{2+} uptake also requires ATP-dependant Ca^{2+} pump → Ca^{2+} level of sarcoplasm ↑ →continued binding of Ca^{2+} to Troponin C →Abnormal, rigid and uninterrupted contraction.
2. No ATP →No relaxation a new molecule of ATP must attach to the myosin head for detachment of actin- myosin interaction →thus, when NO ATP is present, then myosin heads cannot detach themselves from actin.

Time Taken:

In humans, it commences after about three to four hours after death,

reaches maximum stiffness after 12 hours and gradually dissipates until approximately 48 to 60 hours (three days) after death.

Warm conditions can speed up the process of rigor mortis.

When does Rigor Mortis end:

when contractile proteins of the muscle like other body tissues undergo autolysis caused by enzymes released by lysosomes.

- **Q1:** Which connective tissue layer surrounds an individual muscle fiber?
  A) Epimysium
  B) Perimysium
  C) Endomysium
  D) Sarcolemma

- Answer: C) Endomysium

- **Q2:** Tendons primarily connect skeletal muscles to:
  A) Nerves
  B) Bones
  C) Blood vessels
  D) Ligaments

- Answer: B) Bones

- **Q3:** The fundamental contractile unit of skeletal muscle is the:
  A) Myofilament
  B) Myofibril
  C) Sarcomere
  D) Sarcolemma

- Answer: C) Sarcomere

- **Q4:** Which protein forms the thick filaments in skeletal muscle?
  A) Actin
  B) Troponin
  C) Tropomyosin
  D) Myosin

- Answer: D) Myosin

- **Q5:** What is the function of the sarcolemma?
  A) Stores calcium
  B) Transmits action potentials
  C) Produces ATP
  D) Regulates protein synthesis

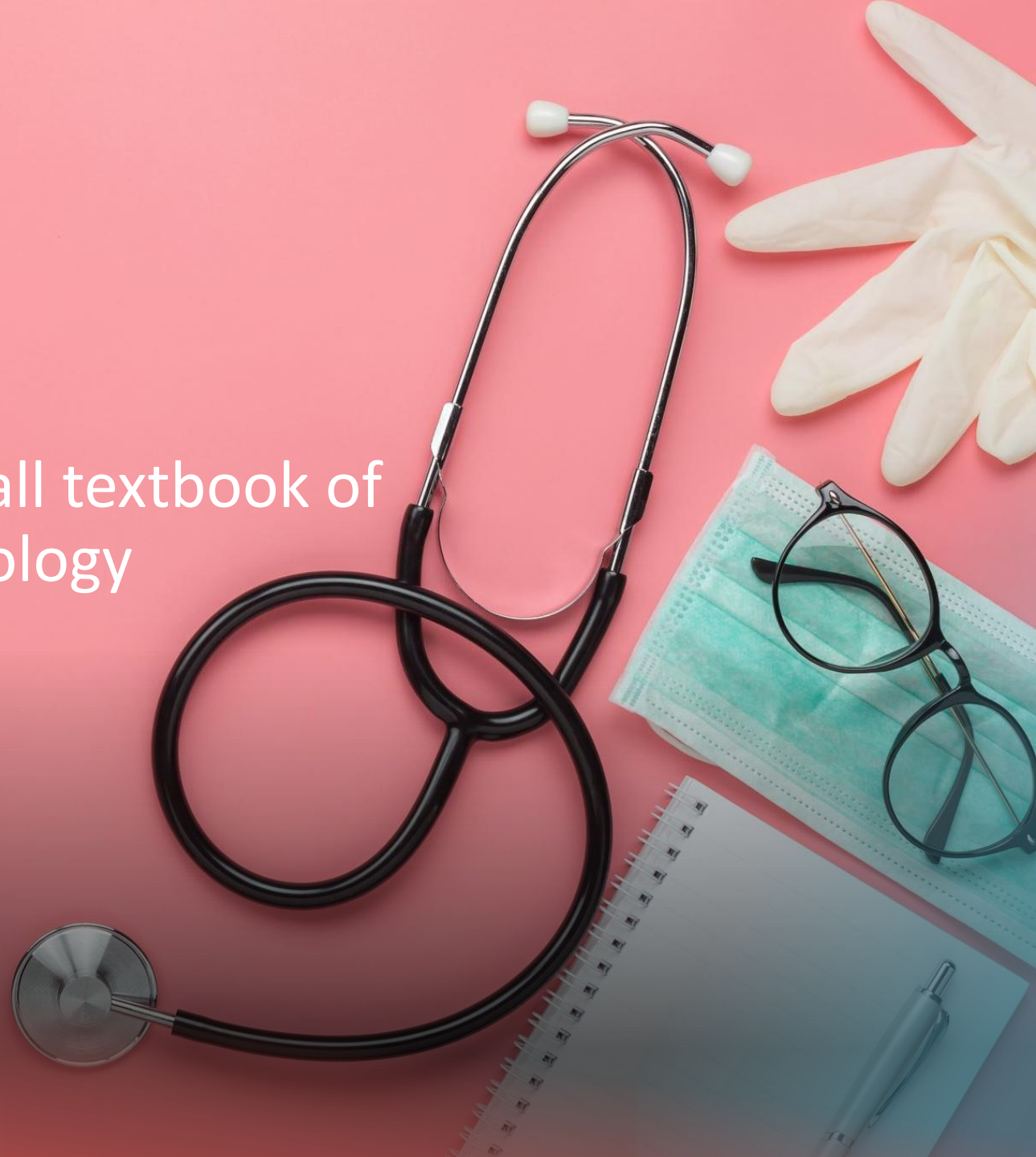
- Answer: B) Transmits action potentials

- **Q6:** The Z-disc of a sarcomere serves to:
  A) Attach thick filaments
  B) Anchor thin filaments
  C) Store calcium
  D) Generate ATP

- Answer: B) Anchor thin filaments

References:

- Guyton and hall textbook of medical physiology
- Sherwood
- Costanzo
- jaypee



Thank you