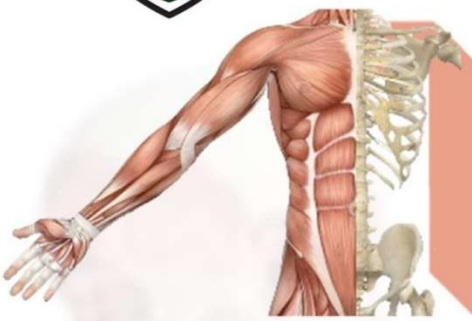

MSS

Musculoskeletal System

Doctor 2019 | Medicine | JU

NO.2

Physiology

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Grammatical correction	Areej Almanaseer
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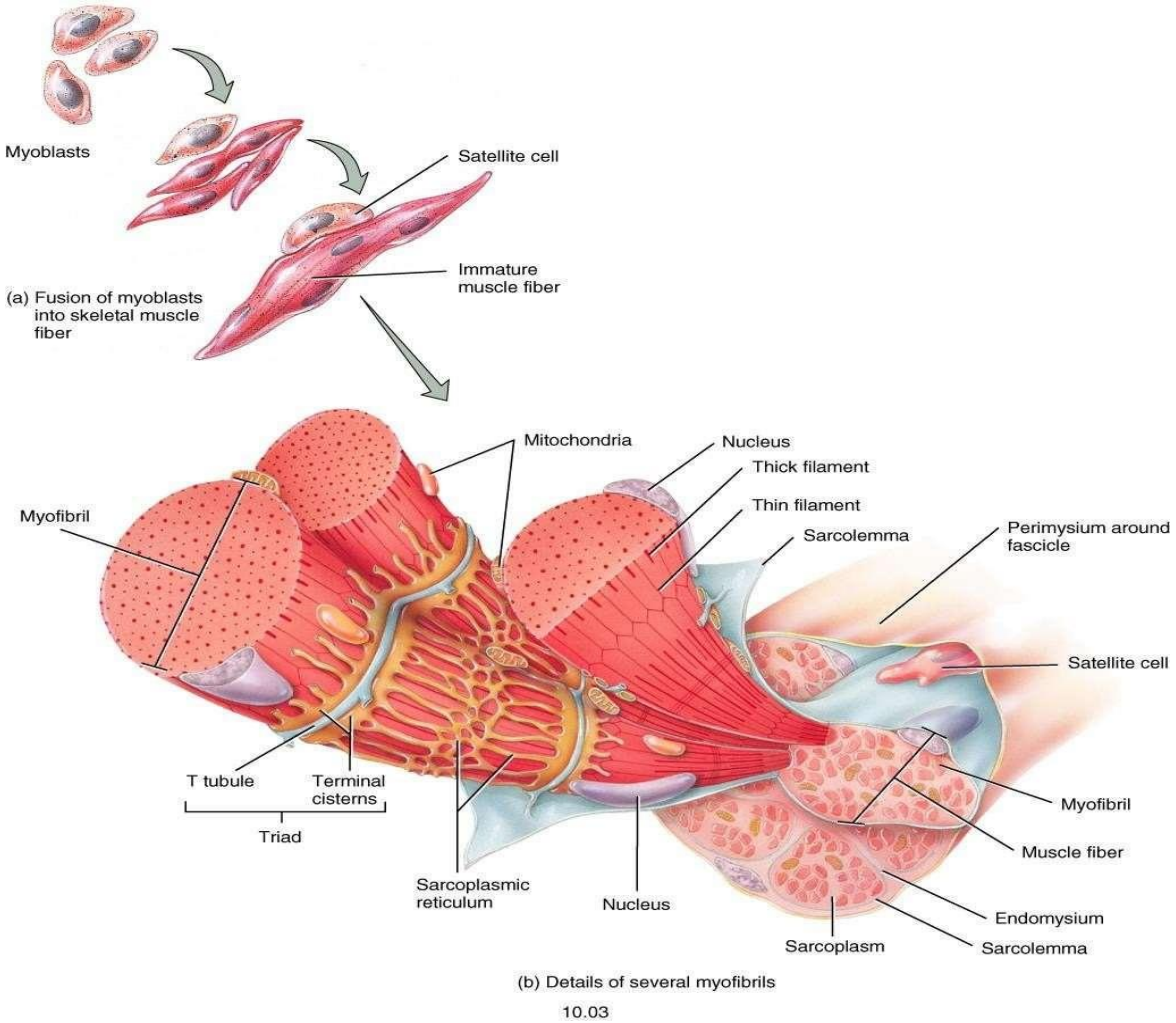
Muscle physiology

❖ **Reference book: Guyton, chapter 6,7 and 8**

0:0-10:0

- Briefly, types of muscles are: striated muscles (that includes skeletal muscle, cardiac muscle) and unstriated smooth muscle cells. They have different mechanisms of contraction and we will go through how these muscles are contracting and how we are getting the contraction of striated muscles. We are focusing on striated muscles more precisely for example, cardiac muscle is a striated muscle and we will see how it is contracting, we have different mechanisms for the contraction of cardiac muscle than in skeletal muscle.



Structure of the muscle:

- The whole muscle is composed of muscle cells which are also called muscle fibers as you see this is one muscle fiber here in this photo.

That muscle fiber has a striated appearance.that striated appearance is resulting from that creation that we are having in a cylindrical structures inside that muscle fibers which are called **myofibrils**

Myofibrils are found inside muscle fibers and they are cylindrically structured.

- You have to differentiate between myofibrils and myofibers (muscle fibers)
- The whole muscle fiber is called myofiber
- Myofibril have a striated appearance because of the organization of the contractile proteins inside it.
- We have two types of contractile proteins or filaments which are called: thick filaments and thin filaments which are forming the myofibril structure.
- A band: the viewing region where we have thick filaments with the portion of thin filaments that overlap on both ends on thick filaments and in the muscle appearance it appears as a dark region.
- And we have a lighter area that contains thin filaments which is called I band.

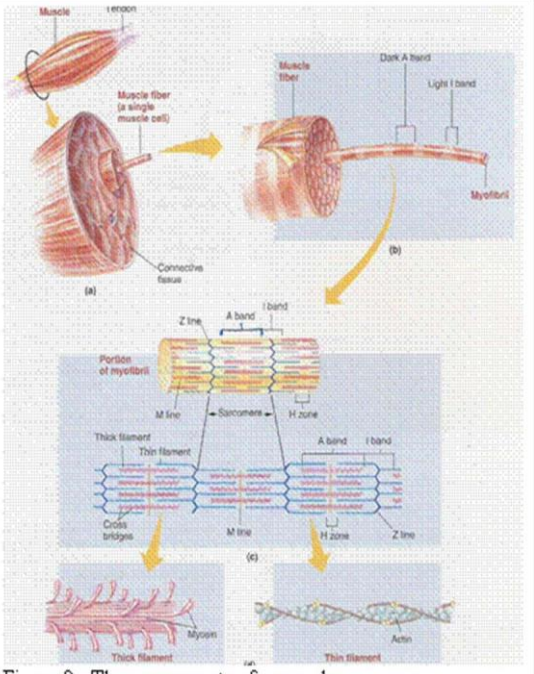
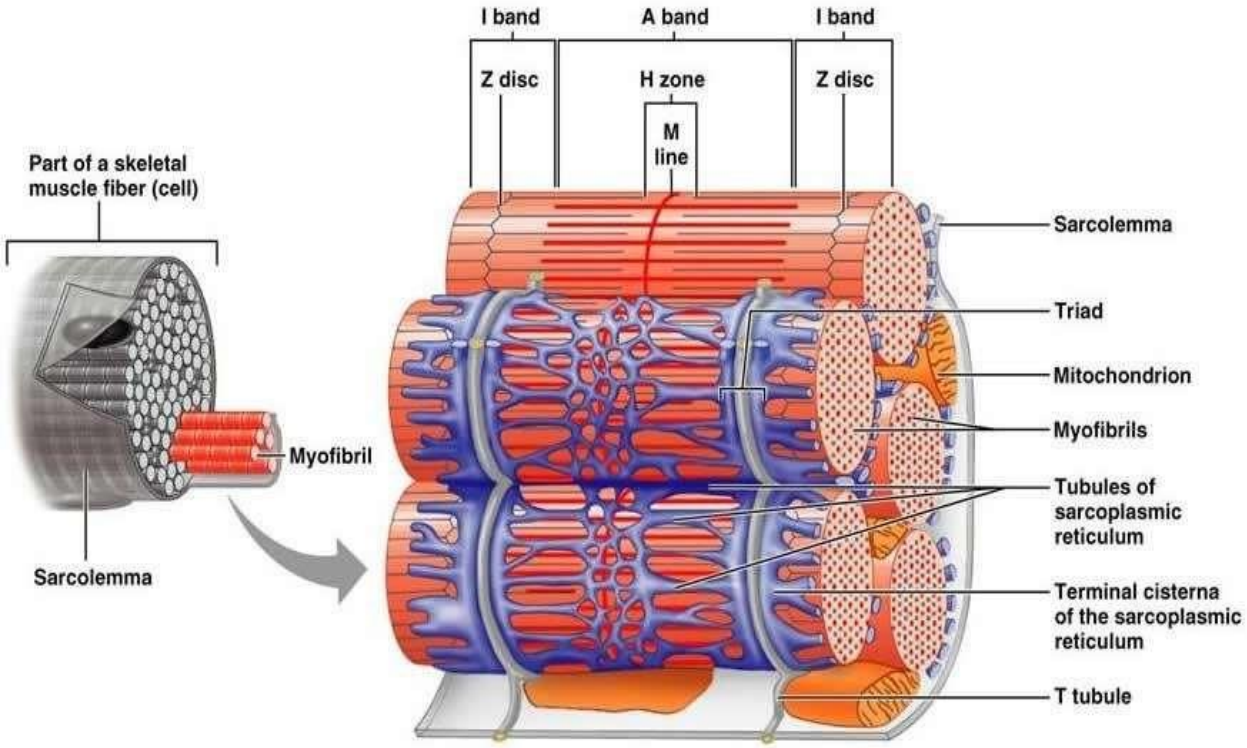


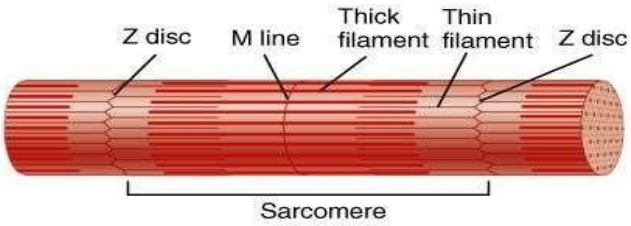
Figure 2. The components of a muscle.
Taken from Sherwood, 2004.

❖ Because of the organization of thick and thin filaments we get that striated appearance which appears in skeletal muscle.

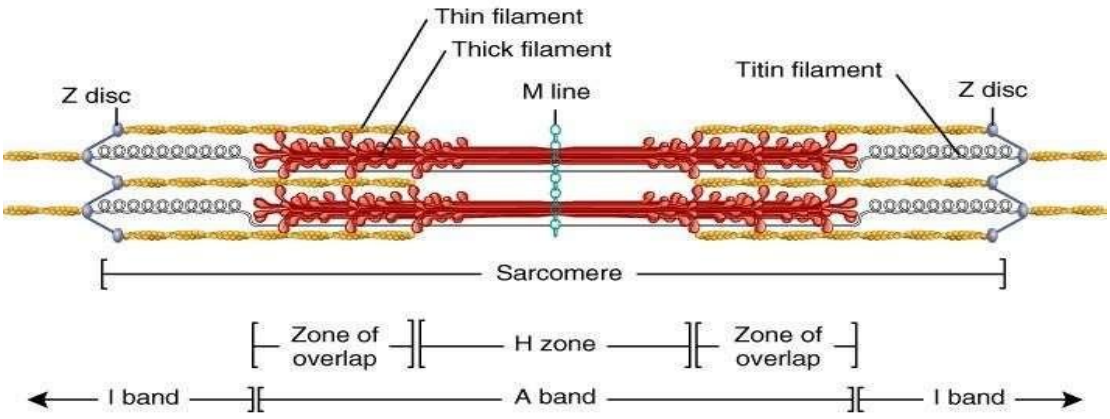


- Here we have thick filaments overlapped with some thin filaments, all that region which is corresponding to the dark region is called the **A band**
- We also have a region where we have only thin filaments with no overlap between the thin and thick filaments and appear as lighter region it is called the **I band.**
- In the middle of the I band we have a structure which is holding the thin filaments in both directions. It is called the **Z disc**
- The distance between the two z discs is called the sarcomere which is the contractile unit at the level of the muscle or at the level of myofibrils.
- In the middle of the sarcomere here we have a protein structure which is holding the thick filaments. It is called **M line** or **M disc**.
- The region in the middle of the A band where we have only thick filaments with no overlapping by the thin filaments is called the **H zone**.
- At the junction between the A band and the I band in skeletal we have another structure which is called the **transverse tubule**.
- Between the transverse tubules in both sides we have sacs of sarcoplasmic reticulum (the endoplasmic reticulum in the muscle level that stores calcium ions that are needed for the contraction of the muscle)

❖ To understand how the muscle is contracting. We are going to analyze these structures more and what happens by the contraction is finally an interaction between thick and thin Filaments this is representing the thick filaments.



(a) Myofibril



(b) Filaments

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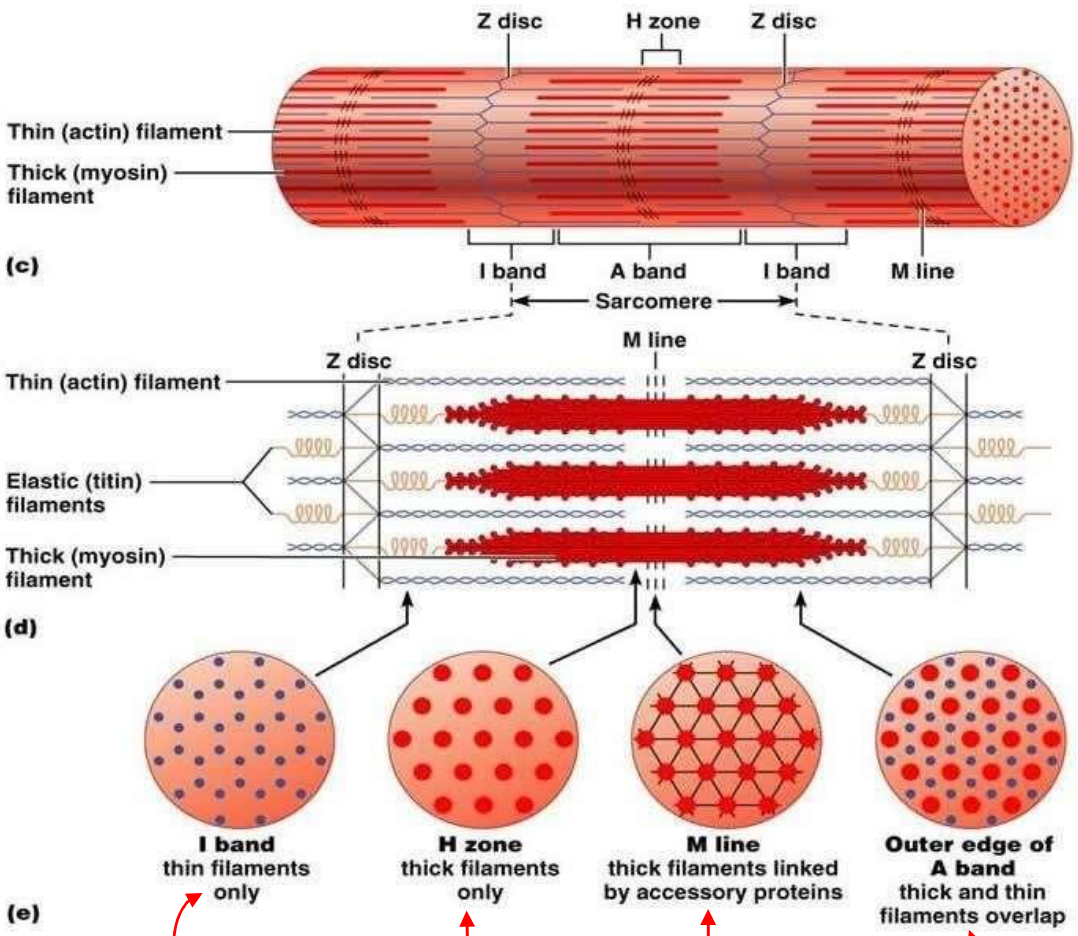
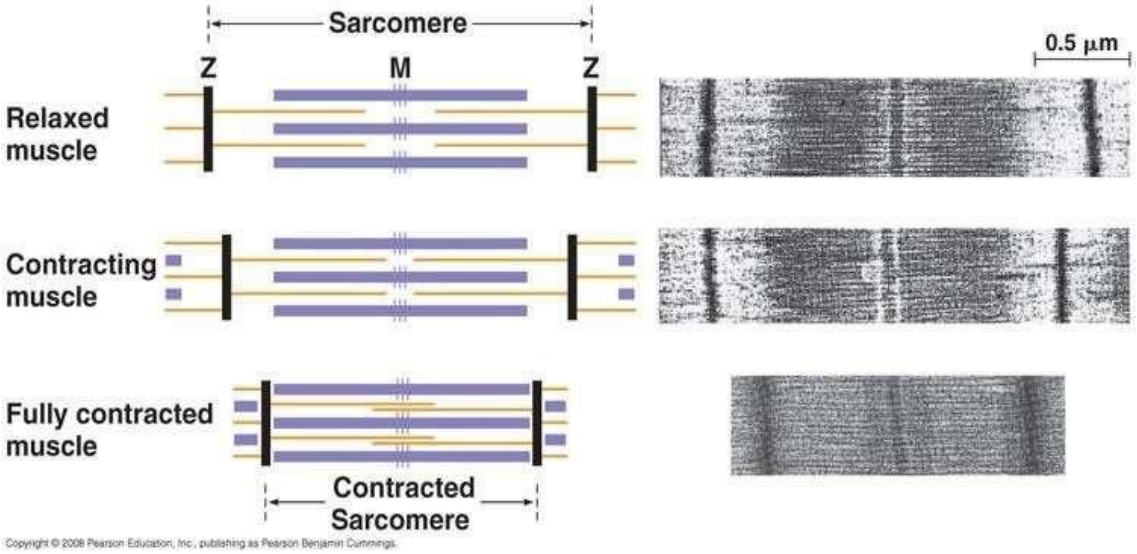


At this region here where we have no overlap, you will find only thin filaments.

at the H zone you find only thick filaments

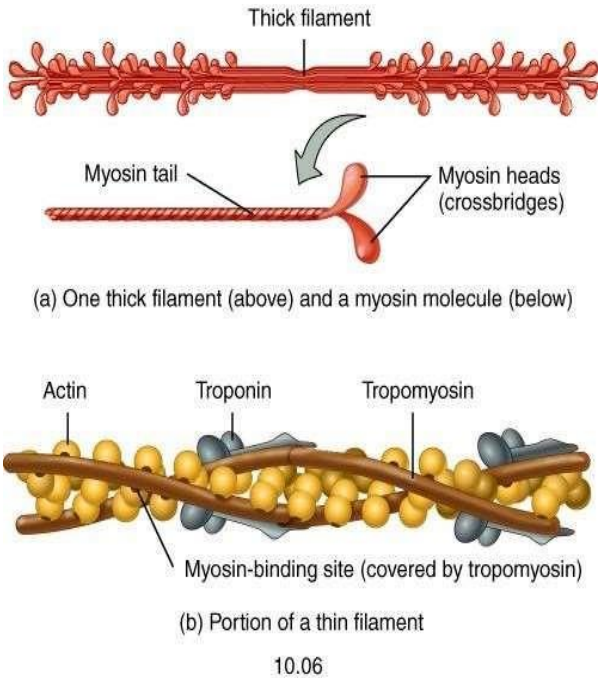
at the m line the protein structure which is holding the thick filaments is shown here.

at that region where thin and thick filaments overlap, each thick filament Is surrounded by 6 thin filaments and each thin filament is surrounded by 3 thick filaments So the ratio of thin filaments to thick filaments is about 2 to 1



- 10:00-16:00 We have interaction between thick and thin filaments during contraction and by that interaction we are getting shortened of the sarcomere. This is shown under the microscope when the muscle is relaxed and by stimulation we have the shortening of the sarcomere.

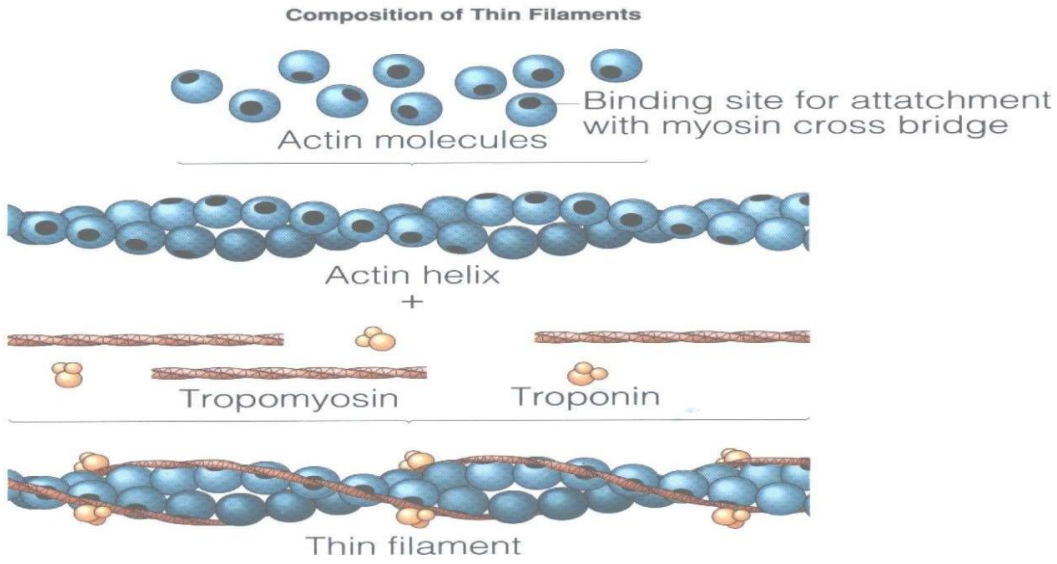
- **The structure of the thin and thick filaments:**
  The thick filaments are composed of myosin molecules and each myosin molecule has two parts: a tail and two heads (the tails form the backbone of the thick filaments and the heads protrude outside of the thick filaments) these heads are also called **cross bridges,** and by these heads we get the interaction between thick filaments and thin filaments.



  - Thin filaments are composed of actin molecules, these actin molecules are organized as a helix structure
  - The interaction occurs between thin filaments and the heads of myosin.

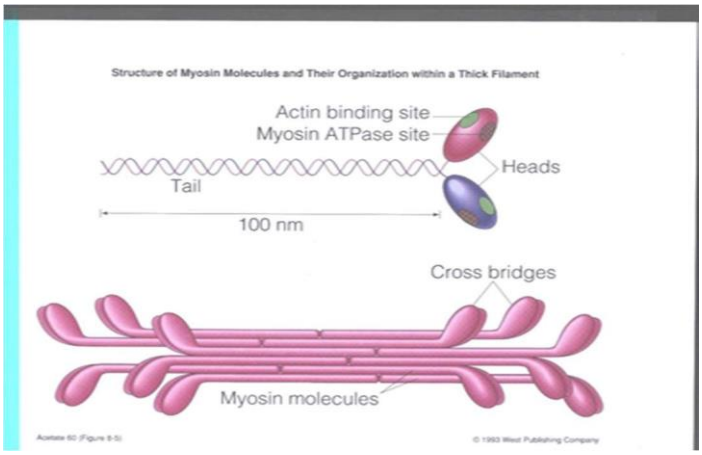
In addition to the helix structure of actin molecules we have other two regulatory proteins which forms the whole thin filaments which are called: tropomyosin (they cover the binding sites of myosin) and troponin

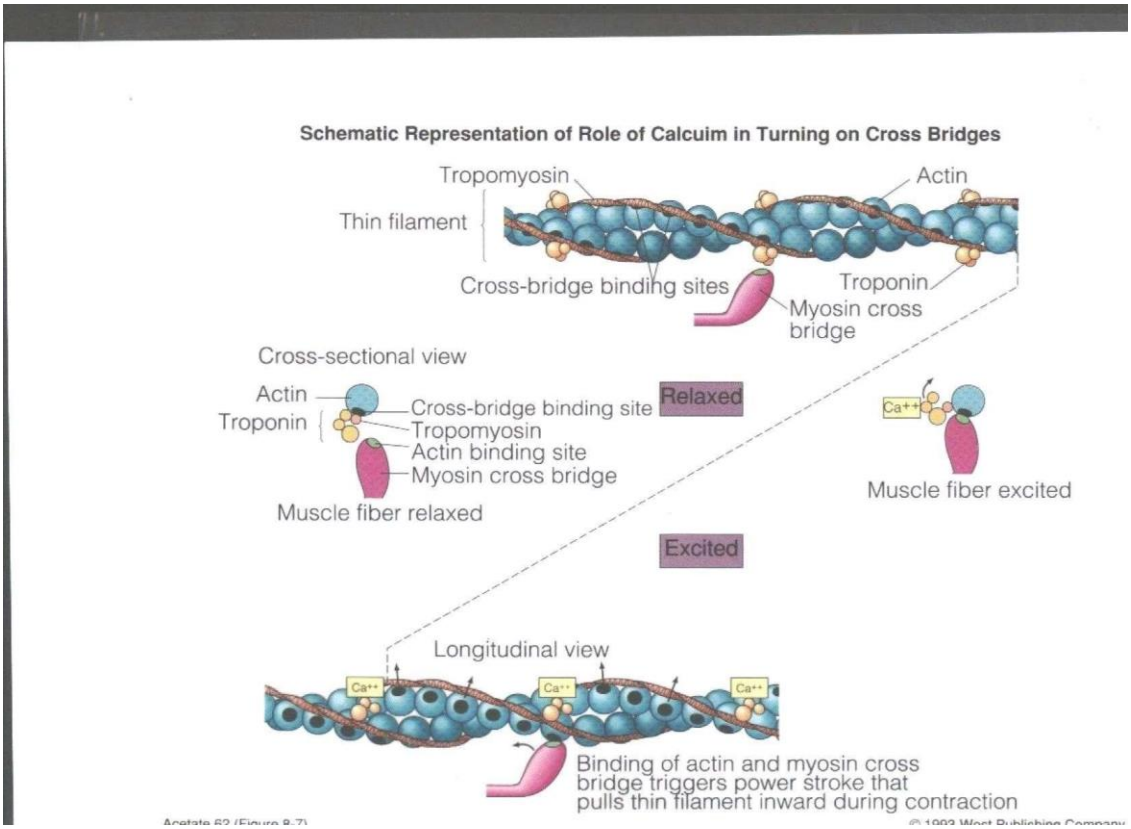
Troponin is a complex structure of 3 subunits, which plays a role in controlling muscle contraction. One subunit has affinity for actin (troponin I) and binds the T and C subunit, the other has affinity for tropomyosin (troponin T), and the third has affinity for Ca++ (troponin C).



We said that each myosin molecule have two heads and one tail. The heads of myosin have two sites one is called **actin binding site** and this binding site will interact with the site over actin molecules to get the contractile process, we have another site which is called **myosin ATPase site** and it has the power to split the ATP and to phosphorelate the other head.

The structure of myosin molecules filaments:





- As you see here, we have binding sites for actin molecules and over actin molecules we have binding sites for myosin, but the binding site for myosin over the thin filaments or over the actin molecule is covered now with tropomyosin.
- How the interaction is taking place? Simply once we had increased calcium concentration, we have that calcium binding to troponin c and once we have that calcium binding to troponin c, we have a displacement of tropomyosin away from the binding sites over actin. Once you have that displacement of tropomyosine away from binding sites over actin, you can have the interactions between the heads and the binding sites over actin, so in that way we have the interaction between the thick and thin filaments. once you have that interaction you will have the head tilting.

Min 16:00

How do the muscles contract?

-by having interactions between the heads of myosin and the binding sites of actin

The heads (of the thick filaments) move towards the center and pull the thin filaments towards the center of the sarcomeres, thus shortening the sarcomeres and shortening the muscles.

-This process results in **decreasing in the length of the sarcomeres**, with **NO CHANGE in the length of the (A band)** because the A band is corresponding to the length of thick filaments and we are not shortening the thick filaments. We are just getting sliding of the the thin filaments over thick filaments towards the center of the sarcomers

We also get **shortening of the I band & the H zone** which has NO overlap between thin & thick filaments.

- ✓ The bending of myosin head towards the center when binding is called the **power stroke.**
- ✓ This process is achieved only when you have a **high concentration of calcium (ca^{2+})**

• The Role of Calcium Ions:

♣ The contraction of skeletal muscles involves the binding of myosin heads to actin molecules on the myosin binding site. This interaction happens only in the presence of large amounts of calcium ions.

♣ Under the condition of low Ca+2 concentration, the troponin-tropomyosin complex physically covers the binding site on actin and prevents the interaction between the myosin heads and actin.

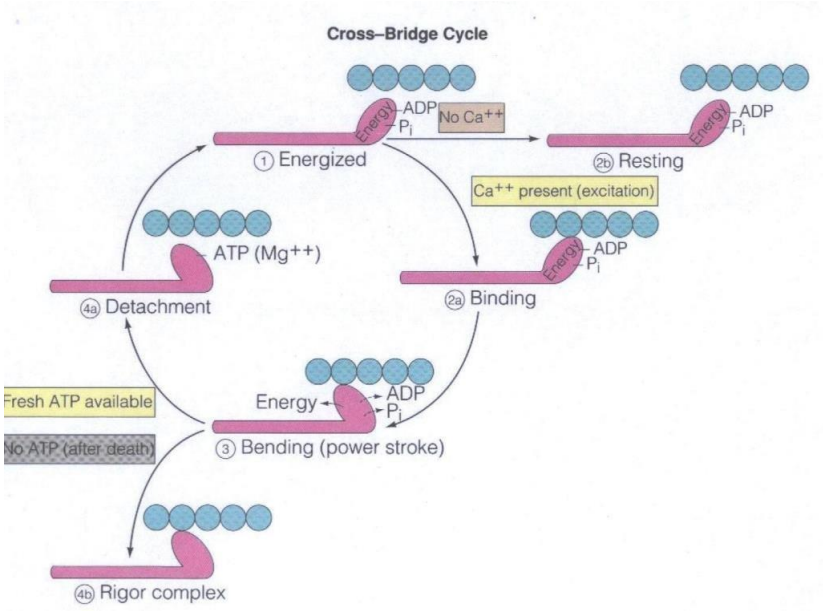
♣ **The presence of high Ca+2 concentration inhibits the effect of troponin-tropomyosin complex.** The exact mechanism of this inhibition is not known, but it is suggested that 4 Ca+2 bind to one molecule of troponin C which produces conformational changes that results in the displacement of tropomyosin away from the active sites on thin filaments.

♣ This action uncovers the active sites of the actin, thus allowing these active sites to attract the myosin cross-bridge heads and cause contraction to proceed.

The process of contraction is followed by **DETACHMENT**, so how this detachment is taking place?

By **dephosphorylating** the myosin head (by replacing the ATP with a new ADP), thus the affinity between the two binding sites is much decreased, and the ATP here is consumed.

*When the heads are **phosphorylated** we have a high affinity between the heads and the binding sites of the actin molecules.



About the picture:

- **Interaction of the Activated Actin Filaments and the Myosin Heads:**

♣ Prior to attachment, the myosin head is **energized** by splitting an ATP molecule at its ATP-ase site. **Mg^{2+} is required in this process for the attachment of the ATP molecule to the ATP-ase site.**

NOTE: for <u>each myosin head one ATP molecule is needed.</u>

♣ The attachment of a head to an active site causes the head to bend toward the arm and to drag the actin filament along with it. This bending of the head is called the **power stroke.**

♣ Immediately after bending, the head releases ADP and Pi from their site. The head then automatically breaks away from the active site by consuming another ATP molecule.

♣ Following detachment, the head of myosin is reenergized by splitting another ATP molecule and returns to its extended direction. It then binds with a new active site farther down along the actin filament; the head then bends again to cause a new power stroke, and the actin filaments move another step.

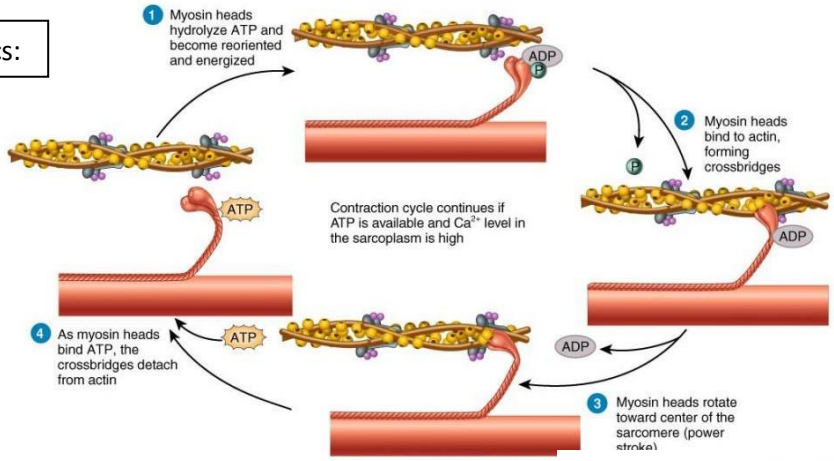
♣ The heads of the cross-bridges bend back and forth and step by step walk along the actin filaments pulling the ends of the two active filaments toward the center of the myosin filaments. This cycle continues as long as there is high concentration of calcium ions.

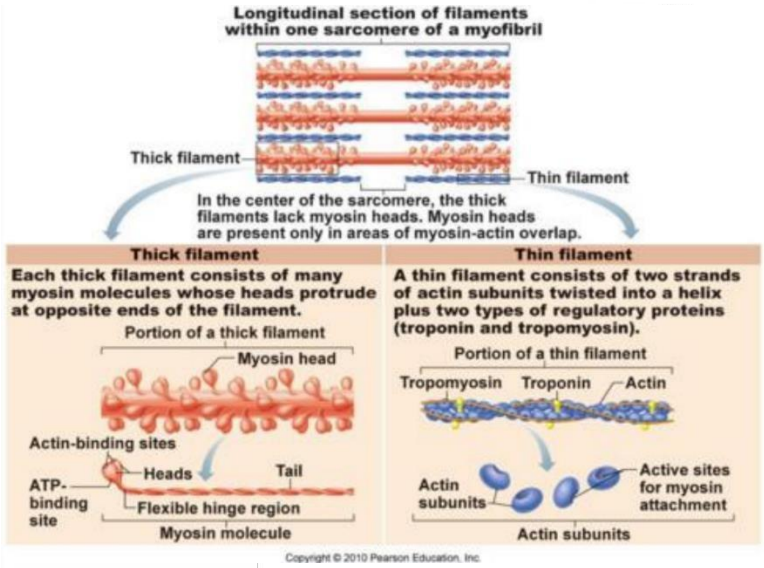
♣ This mechanism results in more overlap between thick and thin filaments by pulling thin filaments inside. This theory is known as "**sliding theory**" or "**walk-along**" theory.

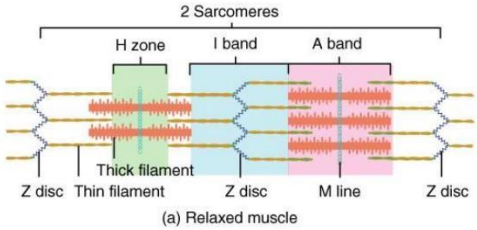
♣ According to this theory, after many cycles of (binding, power stroke, detachment, then binding again), a shortening of the sarcomere will be induced in the muscle by sliding thin filaments toward the sarcomere center.

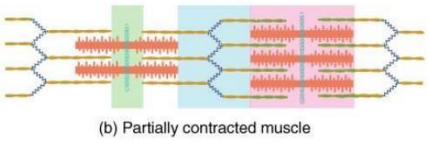
♣ Note! ATP is necessary for the detachment of cross bridges from actin. Inadequate supplies of ATP cause muscle stiff because of the inability of cross bridges to detach from actin after bending. This phenomenon is called **rigor mortis**(تصلب العضلات) ; it is defined as stiffness of skeletal muscles after 3-4 hours of death.

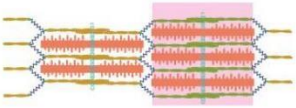
Another helpful pics:











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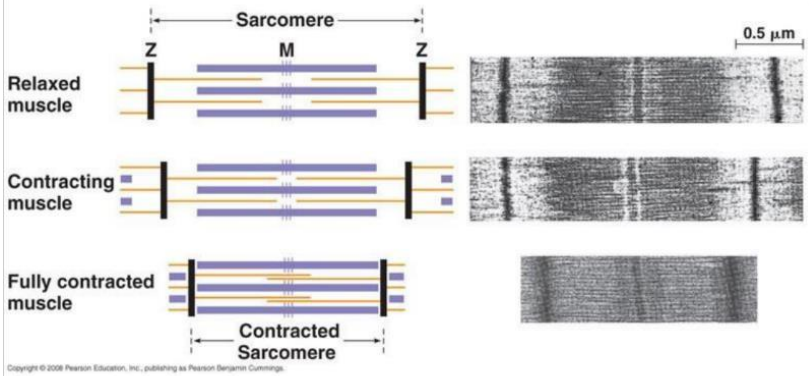

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Wish you the BEST