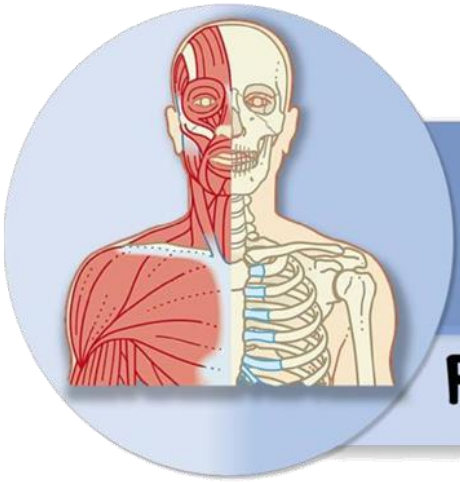

MSS system

Physiology

◉ Sheet ○ Slide

Number: 1

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Muscle physiology

As we already know we have 3 types of muscles:

1. Skeletal muscle
2. Cardiac muscle
3. Smooth muscle

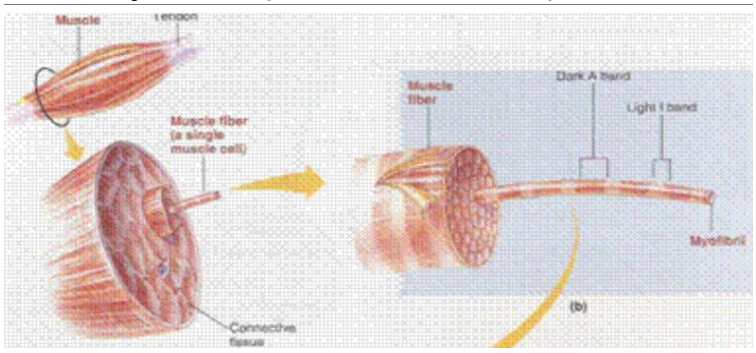
This lecture will discuss the skeletal muscle physiology, and as we took before the main characteristics of this muscle are:
Microscopic appearance: striated.
Innervation: somatic innervation (*voluntary)*

The skeletal muscle is composed of muscle fibers that are found parallel to each other and are striated due to a certain organization of contractile proteins at the level of that muscle.

There are some components of the muscle cell you should know:

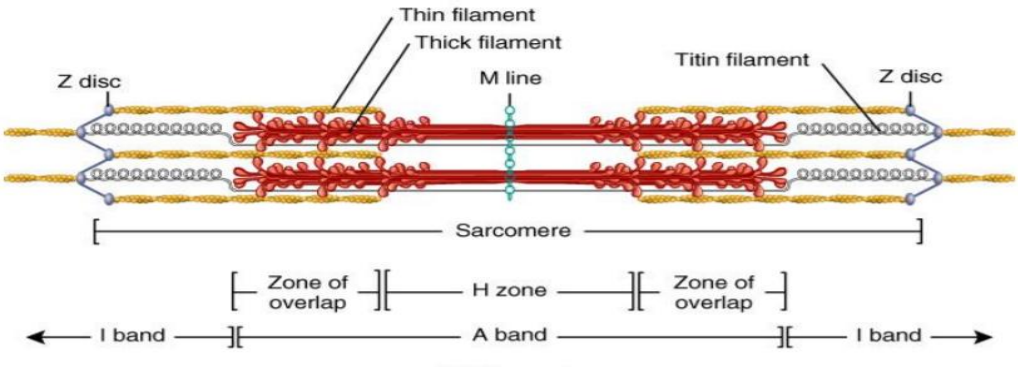
- Sarcolemma: membrane of muscle cell
- Sarcoplasmic reticulum: endoplasmic reticulum of muscle cell
- Sarcoplasm: cytosol of muscle cell

The organizations of these contractile proteins are found in a cylindrical-like structures called **myofibrils** (which are striated).



The myofibril is made up of dark and light regions, whereas the dark regions correspond to thick filaments with overlapping of thin filaments on both ends and the light region is where thin filaments only are found, with the dark region knows as the **A band** while the light region as the **I band**.

The following figure represents a detailed structure of the myofibril filaments:



- The I band and A band have been discussed
- Z disc holds thin filaments together and is found in the middle of I band.
- Sarcomere: the distance between two Z discs **It represents the functional unit in skeletal muscle contraction.
- Zone of overlap is the region containing thin and thick filaments
- H zone is the region containing only thick filaments
- M line is a protein structure holding thick filaments

So how does the contraction of the muscle occur?

- By interaction of thick and thin filaments that result in pulling thin filaments <u>inward</u> toward the center of the sarcomere reducing the length of the sarcomere.

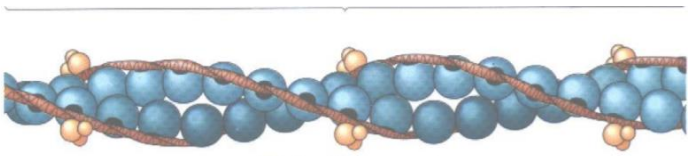
To understand how this contraction works, we must know the structure of thin and thick filaments.

Thin filaments composition:

1) Actin protein molecules polymerize in an alpha helix structure (double stranded) to form the backbone. Each actin molecule has a site that can interact with myosin (myosin binding site)
   The backbone has other regulatory proteins called tropomyosin and troponins.
2) Troponins is composed of 3 subunits:

- Troponin T (bound to tropomyosin)
- Troponin C (has affinity for Ca^{2+})
- Troponin I (it's the intermediate that links troponins T&C, and binds to actin)

3) Tropomyosin which wraps around the actin backbone and prevents the interaction between actin and myosin <u>in resting state</u>.

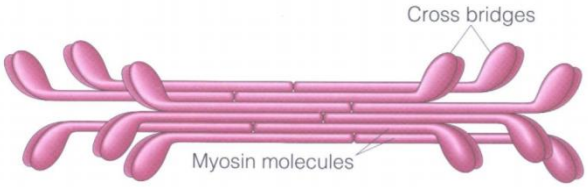


The figure above shows the actin backbone in the resting phase due to the tropomyosin covering the myosin binding sites preventing the interaction of thick and thin filaments; therefore, preventing the contraction of the muscle.

Thick filaments composition:

The thick filament is made up of several hundreds of myosin molecules held together in a specific arrangement. Each myosin molecule is made up of two identical subunits. Each has a globular head that projects out to one end and a tail that is intertwined with the tail of the other molecule. So, the tails make an alpha helix structure forming the backbone of the molecule, while the heads are projected towards the outside to form cross bridges as shown.

Cross bridges= The heads + portions of tail that are protruding from thick filaments.



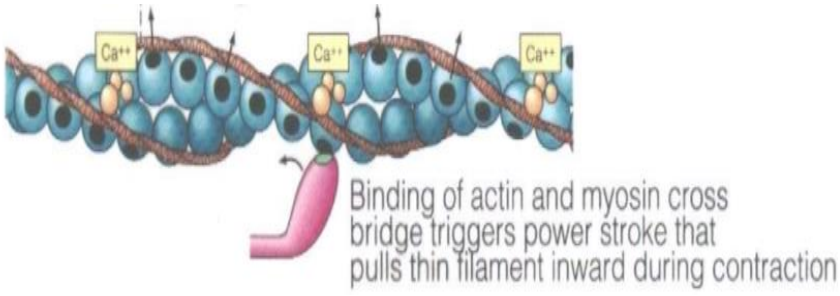
Each head has two binding sites:

1. Actin binding site which interacts with thin filaments.
2. Myosin ATP-ase site which acts like an enzyme that splits ATP to phosphorylate the head to interact with actin molecules.

Now in the resting state, there is no interaction between cross bridges and thin filaments due to tropomyosin blocking the active sites. So how does this interaction occur?

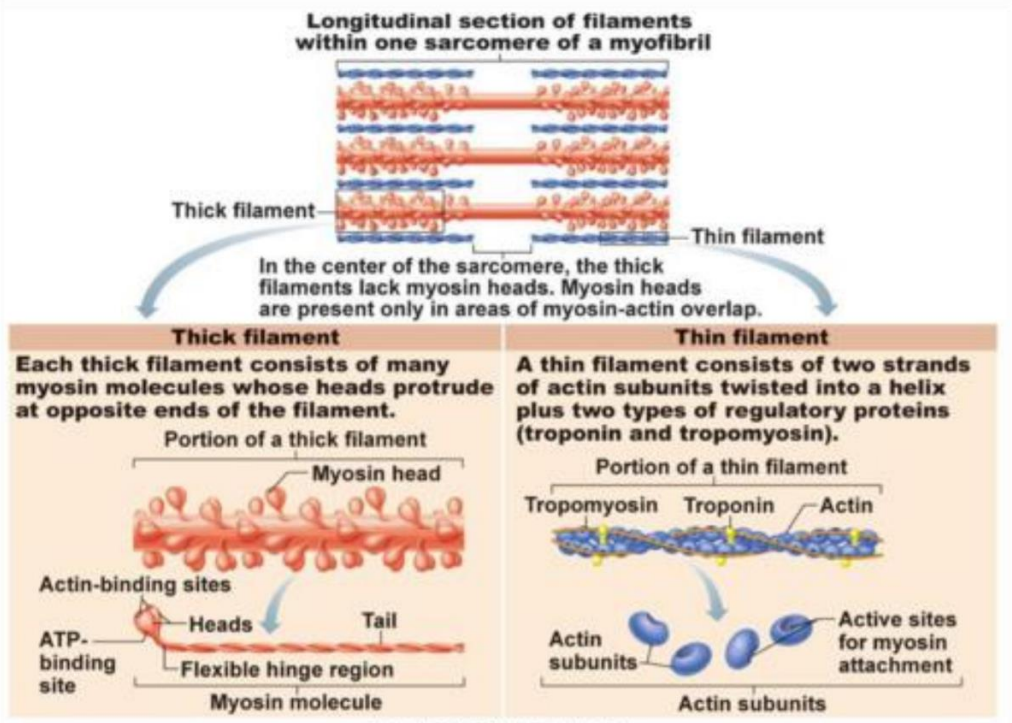
By the displacement of tropomyosin by **calcium**. If we have high Ca^{2+} concentration, Ca^{2+} will bind to troponin C and will induce conformational changes in these regulatory proteins, and then the tropomyosin will be displaced from the binding sites resulting in interaction between thick and thin filaments and the movement of the muscle.

Note: 4 Calcium ions are needed to bind to 1 troponin C.



Notice how the tropomyosin is displaced in the presence of Ca^{2+}.

The doctor mentioned that this slide is useful regarding the differences between thick and thin filaments:



When the muscle contracts, the muscle's length shortens with the following changes:

- I band shortens
- H zone shortens
- The sarcomere shortens

*** A band does not change

To summarize, the interaction can occur in the presence of calcium resulting in binding of myosin to its site on thin filaments, then some other conformational changes result in tilting of the head, then detachment of the head.
So it is a cycle of 1: binding 2: power stroke 3: detachment 4: binding again.

Note: bending of the cross bridges = tilting = power stroke.

As we already know, the presence of Calcium results in binding of cross bridges with actin molecules, after that bending of the head (also called power stroke) resulting in pulling the thin filaments towards the center of the sarcomere.
To detach the head, it must be **dephosphorylated and another ATP molecule should be added.**
(whenever there is a Pi attached to the myosin head, we consider it phosphorylated)

- **Let's go through the process with more details: (this notes describe the picture below)**
- We have mentioned that myosin head has an ATP-ase site. At this site ATP binds, where it splits into ADP and Pi. This needs Mg++ to attach the ATP before ATP-ase can split ATP molecule. This breakdown of ATP occurs before the head links to actin. (low Mg^{2+} concentration will result in muscle spasms.)

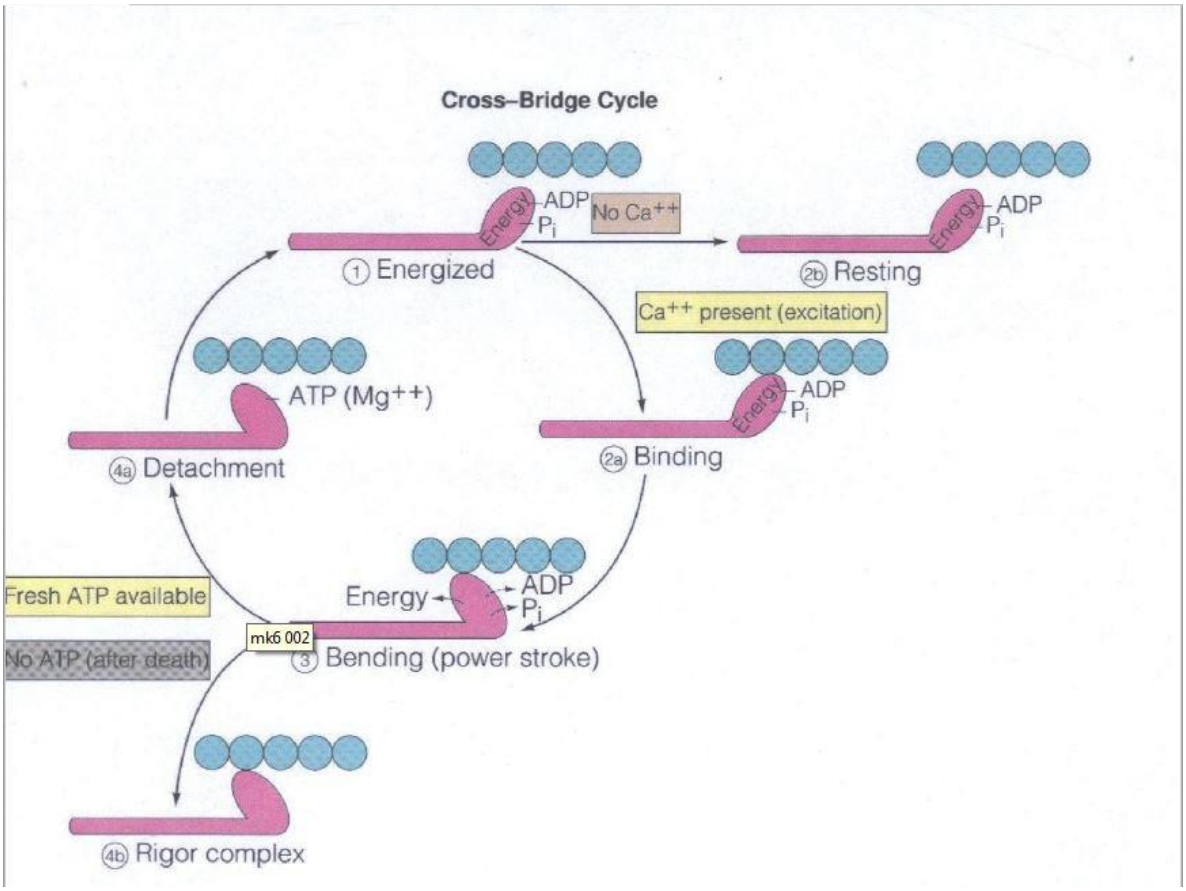
- The resulted ADP and Pi remain bound to myosin and the generated energy from splitting is stored within the cross bridge. During relaxation of the muscle, the head is energized. (without binding)

- When the muscle fiber is excited, the increase in Ca++ concentration in the sarcoplasm, pulls tropmyosin-troponin complex out of their blocking position. This will enable myosin head to attach to actin.

- When attached, myosin head can use stored energy to bend. After this power stroke, the head releases ADP and Pi from their site. At this point, the detachment of myosin head will take place ONLY when another ATP molecule binds to myosin head. After detachment the new molecule is cleaved, the head returns to its position and energized by splitting ATP.

- The cycle continues as long as we have high Ca++ concentration inside the sarcoplasm (cytosol) to keep active sites on actin ready for interaction with myosin.

- ATP is necessary for the detachment of cross bridges from actin. Not enough ATP will cause muscle to stiff because of the inability cross bridges to detach from actin after bending. This phenomenon is called rigor mortis (a stiffness of skeletal muscle after 3-4 hours of death).



Requirement of energy for contraction:

The role of ATP is important for muscle activity for the following:

- For the power stroke
- For the Ca2+ pump to pump Ca2+ into the sarcoplasmic reticulum
- Na+ and K+ pumps through the sarcolemma which is important for excitability.

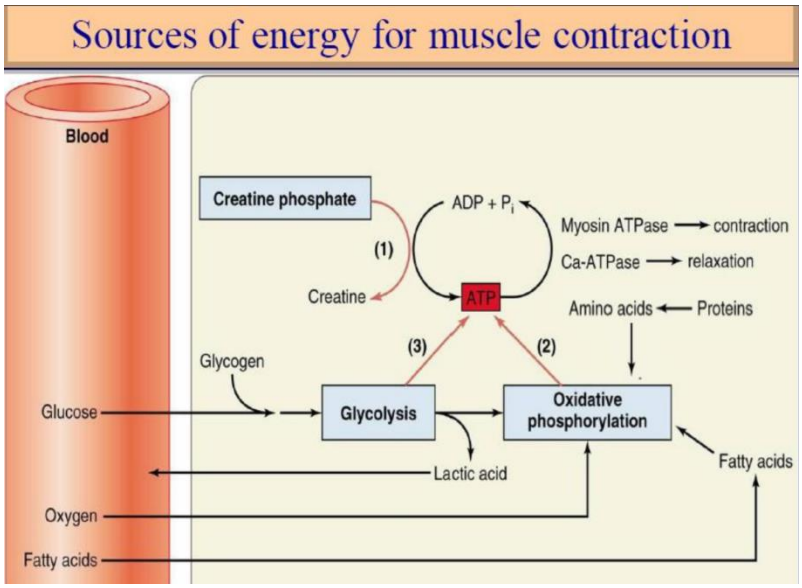
The amount of ATP inside the muscle is enough for a few seconds only, so the ATP must be replenished constantly.
ATP can be replenished in 3 ways:

1) From a macro energetic molecule (energy stored in a molecule and contains phosphate groups) as an immediate source called **creatine phosphate**. This is enough to replenish ATP for a few minutes
2) **Glycolysis** (it is fast, it doesn't need O2 and can cause accumulation of lactic acid).
3) **Oxidative phosphorylation** (takes place in the mitochondria, slow, releases more ATP than glycolysis and needs a constant supply of O2).

We have 2 types of skeletal muscles in our body:

1. Fast muscles
2. Slow muscles

Fast muscles	Slow muscles
Depends mainly on glycolysis as their ATP source	Depends mainly on oxidative phosphorylation as their ATP source
Contract faster	Contract slower
Cause muscle fatigueness due to accumulation of lactic acid	Doesn't cause muscle fatigueness
Doesn't need oxygen so it has less myoglobin	Needs oxygen so it has more myoglobin
White color	Red color because it is more vascularized and it has more myoglobin
Less amount of mitochondria	Higher amount of mitochondria
Used in 100 meter run	Used in marathons



How to get more slow or fast fibers?
If people are trained from childhood in sports that needs fast fibers, number of fast fibers increases.
If people are trained from childhood in sports that needs slow fibers, number of slow fibers increases.

If you have any questions regarding this sheet don't hesitate to contact me ☺