

MUSCULOSKELETAL SYSTEM

#

Physiology

Lecture 3

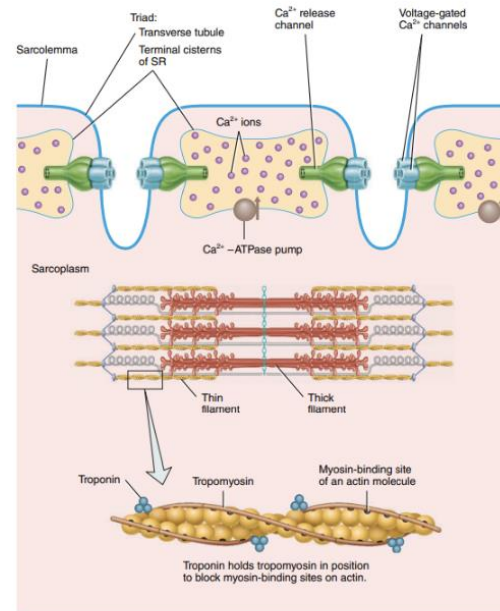
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Students Club

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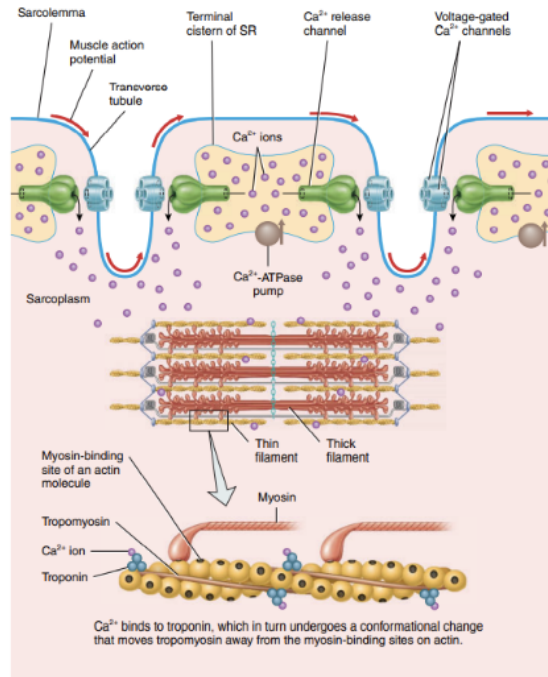
Relaxation



- **Myosin-Actin interaction:**
- A pure actin filament without the presence of the troponin-tropomyosin complex (but in the presence of magnesium ions and ATP) binds instantly and strongly with the heads of the myosin molecules.
- The active sites on the normal actin filament of the relaxed muscle are inhibited or physically covered by the troponin-tropomyosin complex.
- Consequently (As a result), the sites cannot attach to the heads of the myosin filaments to cause contraction.
- The muscle being relaxed means that there's no actin-myosin interaction which means the myosin heads can't pull the actin filaments causing the motion of muscle. It's actually really simple!

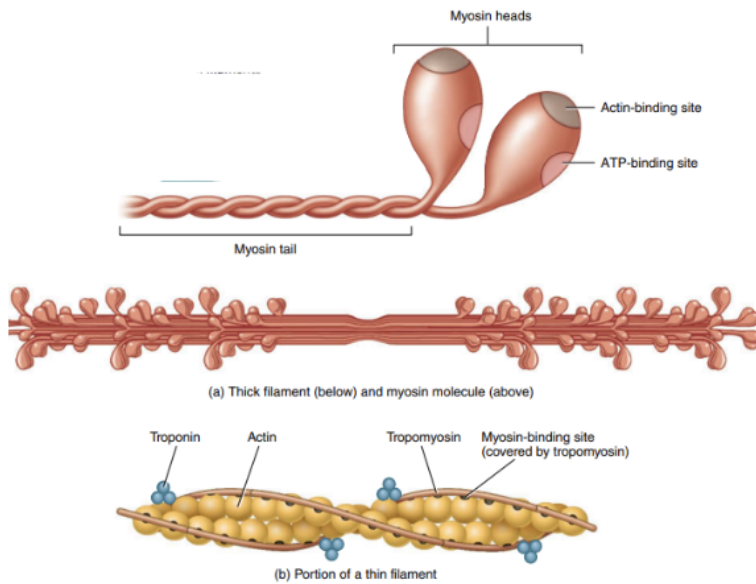


Contraction



(b) Contraction

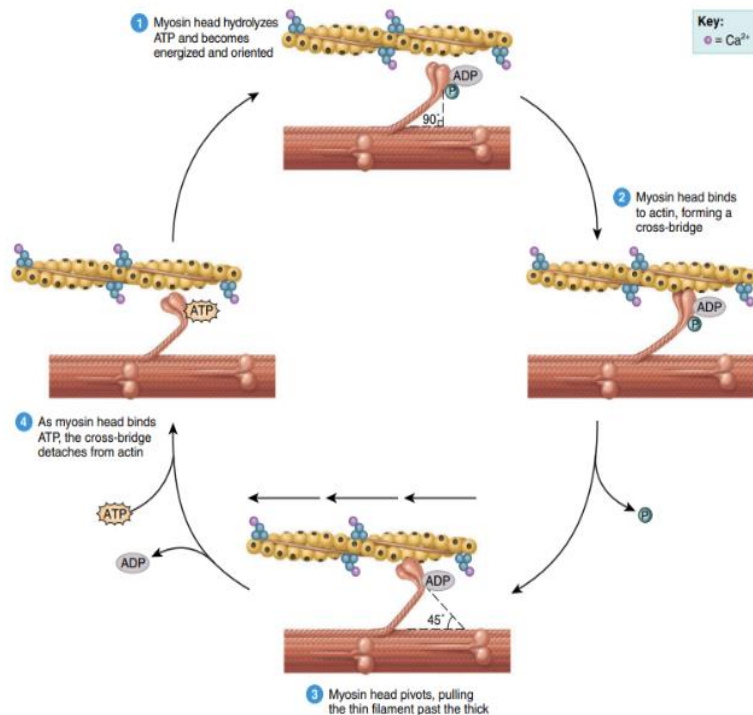
Thick and thin filaments



- **Excitation-contraction coupling:**

- The series of events occurring from the generation of the action potential (AP) in the skeletal muscle fibres to the beginning of muscle tension. (Sandow, 1950). [Check the photo below and read the explanation after it!](#)

Contraction cycle



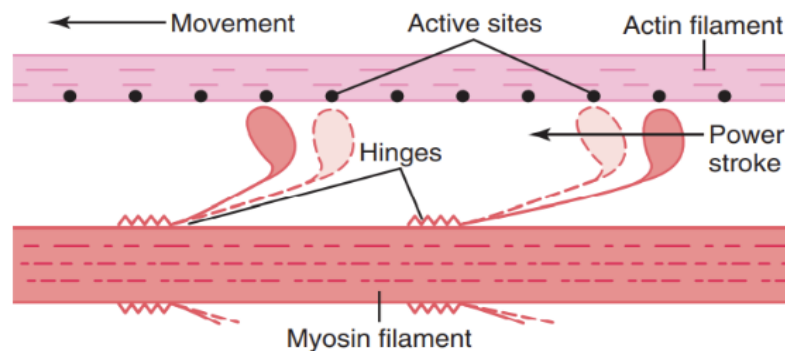
- **The Contraction cycle:**

- 1. Before contraction begins, the heads of the cross-bridges bind with ATP. The ATPase activity of the myosin head immediately cleaves the ATP but leaves the cleavage products, ADP plus phosphate ion, bound to the head. In this state, the conformation of the head is such that it extends perpendicularly toward the actin filament but is not yet attached to the actin.
- 2. When the troponin-tropomyosin complex binds with calcium ions, active sites on the actin filament are exposed and myosin heads can now actually bind.



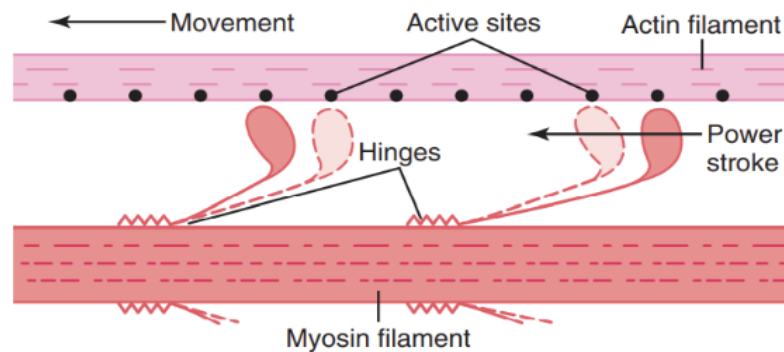
- 3. The bond between the head of the cross-bridge and the active site of the actin filament causes a conformational change in the head, prompting the head to tilt toward the arm of the cross-bridge and providing the power stroke for pulling the actin filament.
- The energy that activates the power stroke is the energy already stored, like a “cocked” spring, by the conformational change that occurred in the head when the ATP molecule was cleaved earlier.
- 4. Once the head of the cross-bridge tilts, release of the ADP and phosphate ion that were previously attached to the head is allowed. At the site of release of the ADP, a new molecule of ATP binds. This binding of new ATP causes detachment of the head from the actin.
- 5. After the head has detached from the actin, the new molecule of ATP is cleaved to begin the next cycle, leading to a new power stroke. That is, the energy again “cocks” the head back to its perpendicular condition.

Walk-along theory of contraction



- **Simply:** Muscle contraction is the process by which muscle fibers shorten to generate force. Muscle cells contain proteins called actin and myosin that interact with one another and form cross-bridges to produce a contraction.

Walk-along theory of contraction



- Myosin head tilts toward the arm and to drag the actin filament along with it. This tilt of the head is called the **power stroke**.
- Immediately after tilting, the head then automatically breaks away from the active site. Next, the head returns to its extended direction. In this position, it combines with a new active site farther down along the actin filament.
- Umm... Basically whats happening here is that the myosin head is moving on those actin filaments but when it does move it kinda sticks to the actin filament moving it alongisde it! Ya3ni sho bdkom subject easier than that! But take it easy on the average pls 😊.



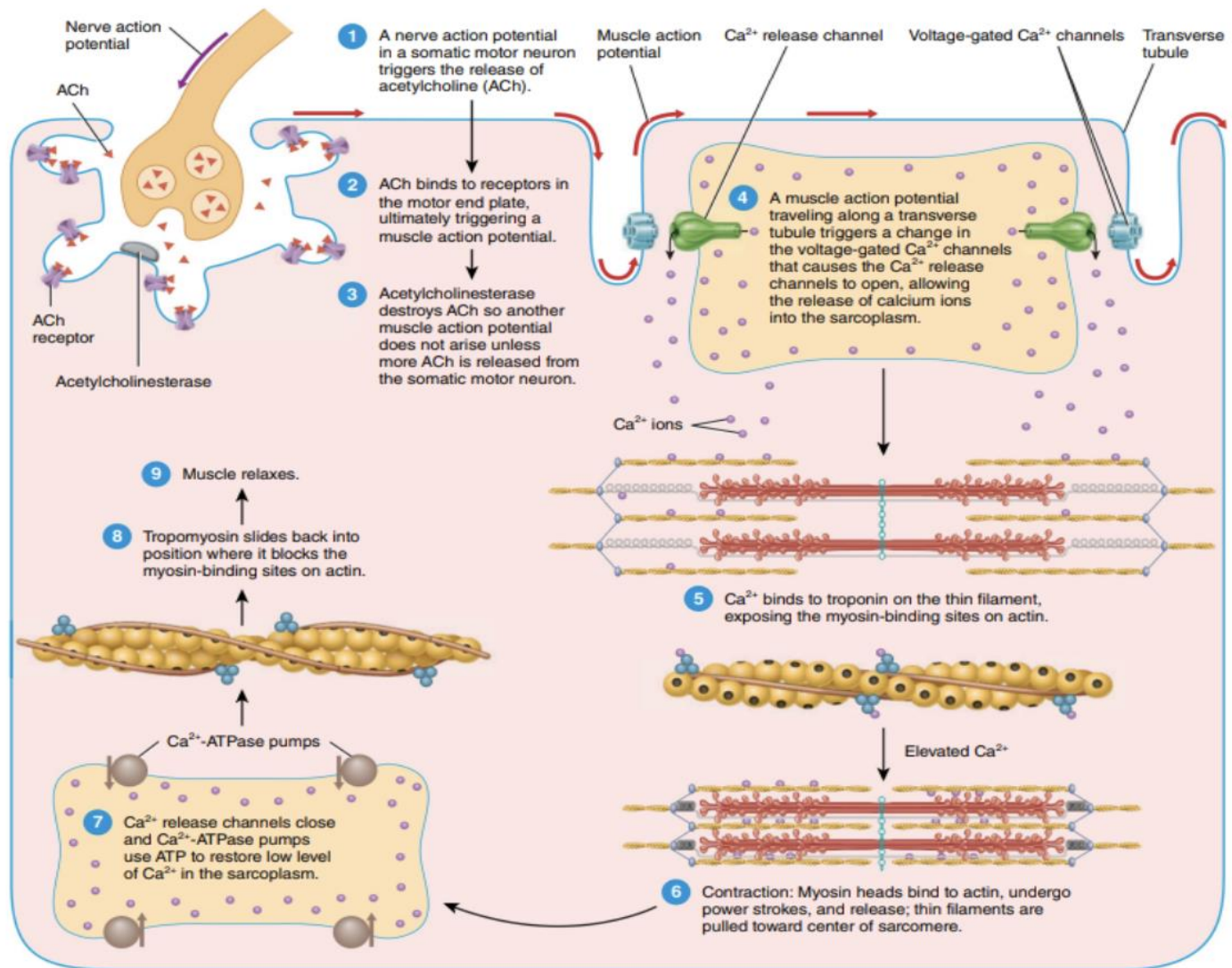
- **Calcium:**

- The normal resting state concentration ($<10^{-7}$ molar) of calcium ions in the cytosol that bathes the myofibrils is too little to elicit contraction.
- Therefore, the troponin-tropomyosin complex keeps the actin filaments inhibited and maintains a relaxed state of the muscle.
- Full excitation of the T tubule and sarcoplasmic reticulum system causes enough release of calcium ions to increase the concentration in the myofibrillar fluid to as high as 2×10^{-4} molar concentration, which is about 10 times the level required to cause maximum muscle contraction.

- **Calcium pump:**

- Once the calcium ions have been released from the sarcoplasmic tubules and have diffused among the myofibrils, muscle contraction continues as long as the calcium ion concentration remains high.
- However, a continually active calcium pump located in the walls of the sarcoplasmic reticulum pumps calcium ions away from the myofibrils back into the sarcoplasmic tubules.
- This pump can concentrate the calcium ions about 10,000- fold inside the tubules.
- The total duration of this calcium “pulse” in the usual skeletal muscle fiber lasts about $1/20$ of a second, although it may last several times as long in some fibers and several times less in others.





- ACTION POTENTIAL** → Muscle Action Potential → Calcium release → Troponin binds with Ca^{++} → Tropomyosin moves exposing myosin binding sites on actin → Contraction due to myosin movement → Ca^{++} channels close and Ca^{++} -ATPase allows Ca^{++} to enter back to the sarcoplasmic reticulum → Tropomyosin covers myosin binding sites → Muscle relaxes.



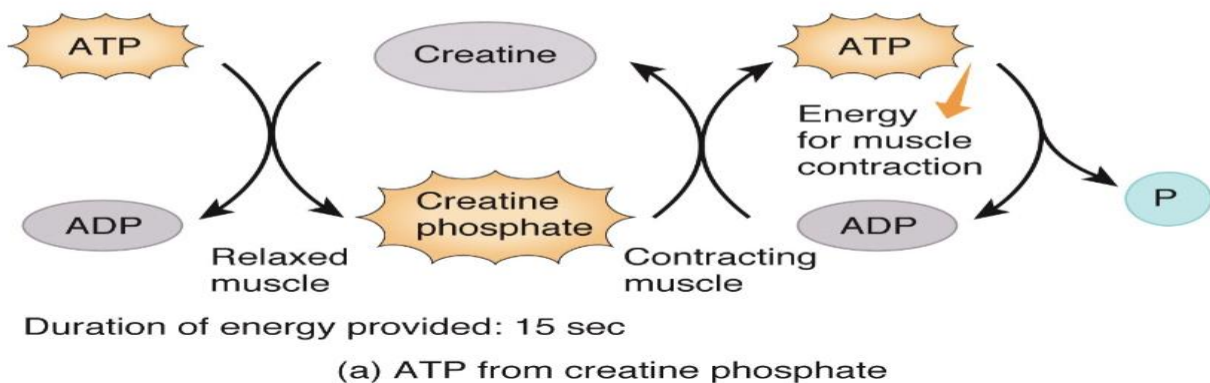
- [Now lets study these points in detail:](#)
- 1. An action potential travels along a motor nerve to its endings on muscle fibers.
- 2. At each ending, the nerve secretes a small amount of the neurotransmitter substance acetylcholine.
- 3. The acetylcholine acts on a local area of the muscle fiber membrane to open “acetylcholine-gated” cation channels through protein molecules floating in the membrane.
- 4. Opening of the acetylcholine-gated channels allows large quantities of sodium ions to diffuse to the interior of the muscle fiber membrane. This action causes a local depolarization that in turn leads to opening of voltage-gated sodium channels, which initiates an action potential at the membrane.
- 5. The action potential travels along the muscle fiber membrane in the same way that action potentials travel along nerve fiber membranes.
- 6. The action potential depolarizes the muscle membrane, and much of flows through the center of the muscle fiber. Here it causes the sarcoplasmic reticulum to release large quantities of calcium ions that have been stored within this reticulum.
- 7. The calcium ions initiate attractive forces between the actin and myosin filaments, causing them to slide alongside each other, which is the contractile process.
- 8. After a fraction of a second, the calcium ions are pumped back into the sarcoplasmic reticulum by a Ca^{++} pump and remain stored in the reticulum until a new muscle action potential comes along; this removal of calcium ions from the myofibrils causes the muscle contraction to cease.



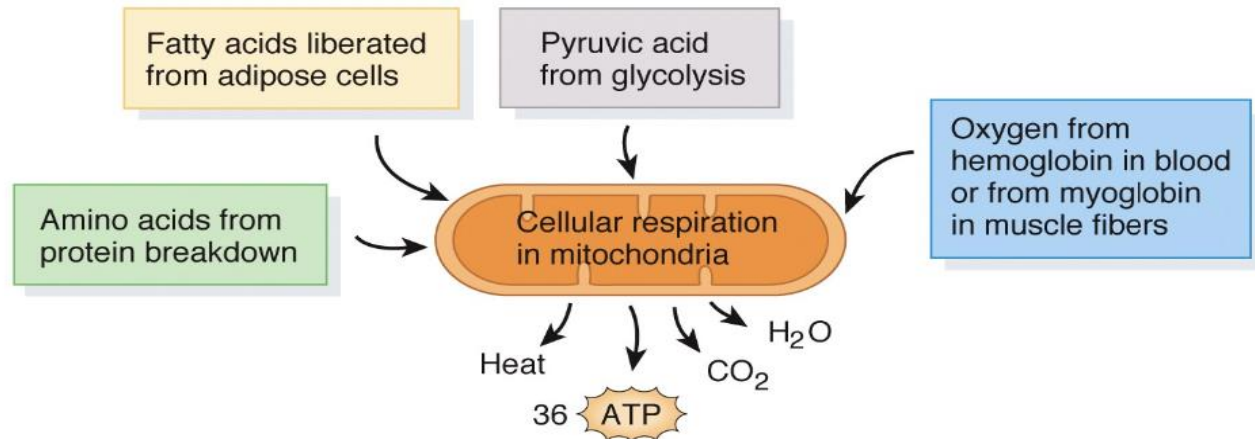
▪ **Processes require energy in muscle fiber:**

- 1. Most of the energy required for muscle contraction is used to actuate the walk-along mechanism by which the cross- bridges pull the actin filaments.
- 2. Pumping calcium ions from the sarcoplasm into the sarcoplasmic reticulum after the contraction is over.
- 3. Pumping sodium and potassium ions through the muscle fiber membrane to maintain an appropriate ionic environment for propagation of muscle fiber action potentials.
- The first source of energy** that is used to reconstitute the ATP is the substance **phosphocreatine**, which carries a high-energy phosphate bond similar to the bonds of ATP. The high-energy phosphate bond of phosphocreatine has a slightly higher amount of free energy than that of each ATP bond.
- Therefore, phosphocreatine is instantly cleaved, and its released energy causes bonding of a new phosphate ion to ADP to reconstitute the ATP.
- However, the total amount of phosphocreatine in the muscle fiber is also small—only about five times as great as the ATP. Therefore, the combined energy of both the stored ATP and the phosphocreatine in the muscle is capable of causing maximal muscle contraction for only 5 to 8 seconds.

Sources of Muscle Energy



Sources of Muscle Energy



Duration of energy provided: Minutes to hours

(c) ATP from aerobic cellular respiration

- **The second important source of energy**, which is used to reconstitute both ATP and phosphocreatine, is “**glycolysis**” of glycogen previously stored in the muscle cells.
- Rapid enzymatic breakdown of the glycogen to pyruvic acid and lactic acid liberates energy that is used to convert ADP to ATP; the ATP can then be used directly to energize additional muscle contraction and also to re-form the stores of phosphocreatine.
- The importance of this glycolysis mechanism is two-fold:
 - 1. the glycolytic reactions can occur even in the absence of oxygen, so muscle contraction can be sustained for many seconds and sometimes up to more than a minute, even when oxygen delivery from the blood is not available.
 - 2. the rate of formation of ATP by the glycolytic process is about 2.5 times as rapid as ATP formation in response to cellular foodstuffs reacting with oxygen.
- However, so many end products of glycolysis accumulate in the muscle cells that glycolysis also loses its capability to sustain maximum muscle contraction after about 1 minute due to fatigue from lactic acid.



- **The third and final source of energy is oxidative metabolism**, which means combining oxygen with the end products of glycolysis and with various other cellular foodstuffs to liberate ATP.
- •More than 95 percent of all energy used by the muscles for sustained, long term contraction is derived from oxidative metabolism.

- Its important to understand that the muscle fibers in our bodies exist In mainly three forms, they are either slow fibers or fast fibers (which are two types) as we will learn in the table beneath. The muscles in our bodies are always mixed (meaning they contain both fibers) BUT one is more dominant than the other depending on the function and speed of action of that muscle.

- **Characteristics of slow fibers:**
 - **Slow Fibers (Type 1, Red Muscle).**
 1. Slow fibers are smaller than fast fibers.
 2. Slow fibers are also innervated by smaller nerve fibers.
 3. Compared with fast fibers, slow fibers have a more extensive blood vessel system and more capillaries to supply extra amounts of oxygen.
 4. Slow fibers have greatly increased numbers of mitochondria to support high levels of oxidative metabolism.
 5. Slow fibers contain large amounts of myoglobin, an iron- containing protein similar to hemoglobin in red blood cells. Myoglobin combines with oxygen and stores it until needed, which also greatly speeds oxygen transport to the mitochondria. The myoglobin gives the slow muscle a reddish appearance and hence the name red muscle.



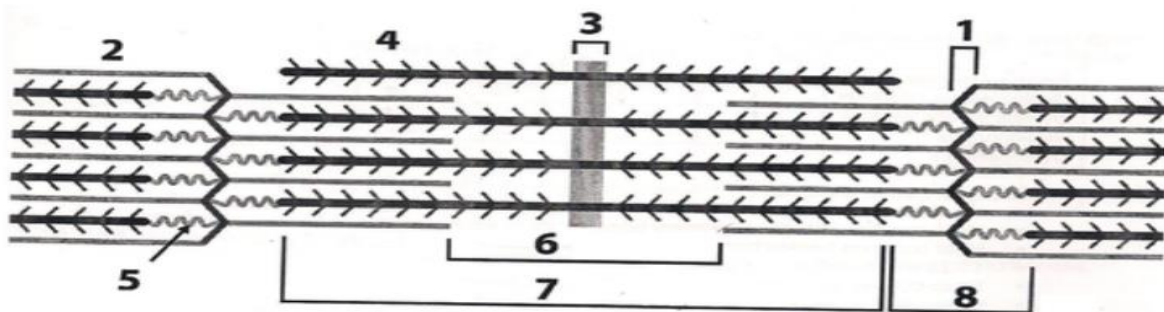
○ Fast Fibers (Type II, White Muscle).

1. Fast fibers are large for great strength of contraction.
 2. An extensive sarcoplasmic reticulum is present for rapid release of calcium ions to initiate contraction.
 3. Large amounts of glycolytic enzymes are present for rapid release of energy by the glycolytic process.
 4. Fast fibers have a less extensive blood supply than do slow fibers because oxidative metabolism is of secondary importance.
 5. Fast fibers have fewer mitochondria than do slow fibers, also because oxidative metabolism is secondary. A deficit of red myoglobin in fast muscle gives it the name white muscle.
- Every muscle of the body is composed of a mixture of fast and slow muscle fibers, with still other fibers gradated between these two extremes.
 - Muscles that react rapidly, including the anterior tibialis, are composed mainly of “**fast**” fibers with only small numbers of the slow variety. Conversely, muscles such as soleus that respond slowly but with prolonged contraction are composed mainly of “**slow**” fibers.

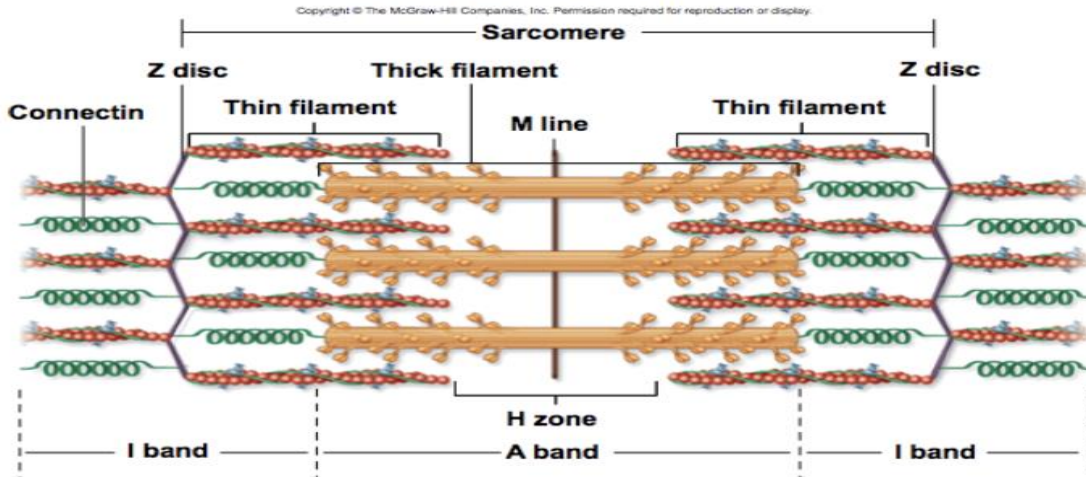
	SLOW OXIDATIVE (SO) FIBERS	FAST OXIDATIVE–GLYCOLYTIC (FOG) FIBERS	FAST GLYCOLYTIC (FG) FIBERS
STRUCTURAL CHARACTERISTIC			
Myoglobin content	Large amount.	Large amount.	Small amount.
Mitochondria	Many.	Many.	Few.
Capillaries	Many.	Many.	Few.
Color	Red.	Red-pink.	White (pale).
FUNCTIONAL CHARACTERISTIC			
Capacity for generating ATP and method used	High, by aerobic respiration.	Intermediate, by both aerobic respiration and anaerobic glycolysis.	Low, by anaerobic glycolysis.
Rate of ATP hydrolysis by myosin ATPase	Slow.	Fast.	Fast.
Contraction velocity	Slow.	Fast.	Fast.
Fatigue resistance	High.	Intermediate.	Low.
Creatine kinase	Lowest amount.	Intermediate amount.	Highest amount.
Glycogen stores	Low.	Intermediate.	High.
Order of recruitment	First.	Second.	Third.
Location where fibers are abundant	Postural muscles such as those of neck.	Lower limb muscles.	Extraocular muscles.
Primary functions of fibers	Maintaining posture and aerobic endurance activities.	Walking, sprinting.	Rapid, intense movements of short duration.



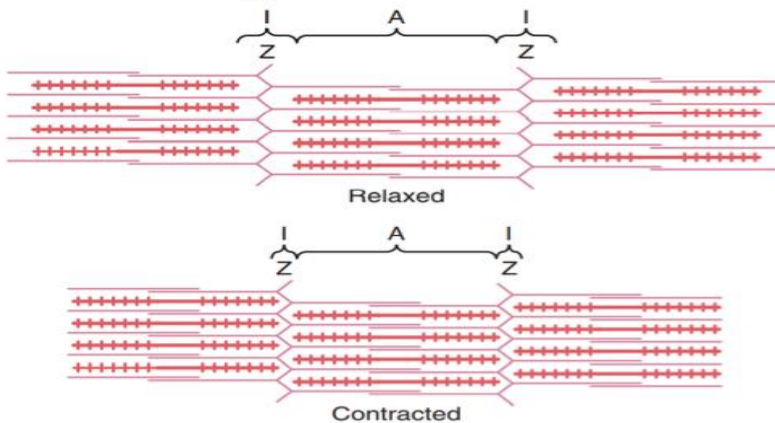
Name it!



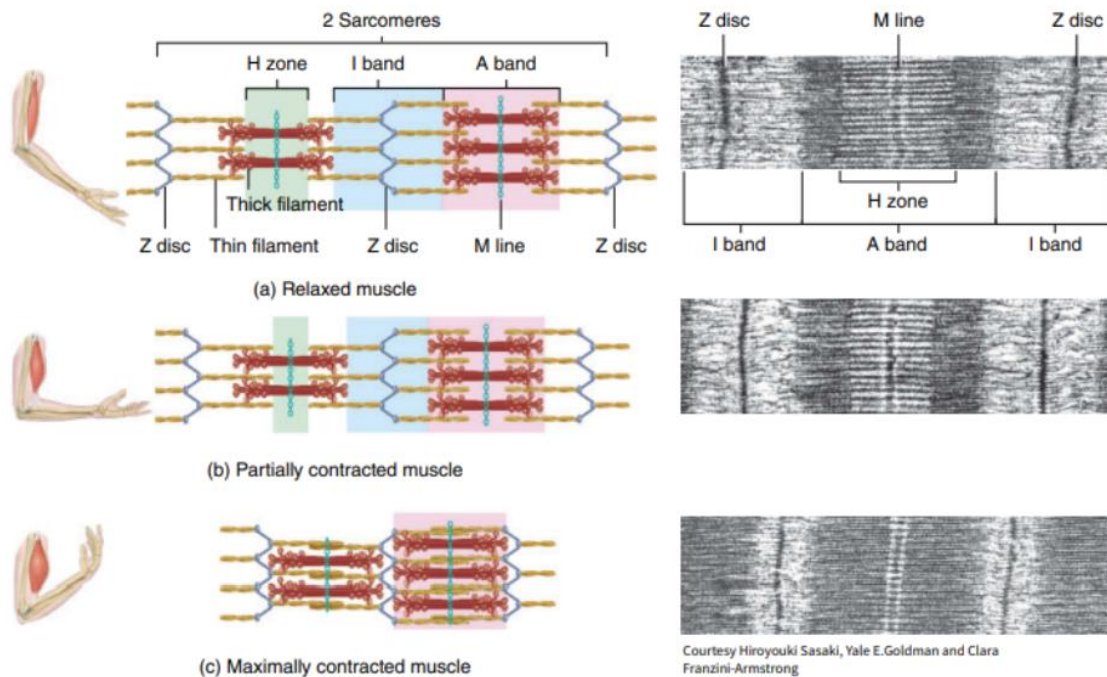
Structure of a Sarcomere



The sliding filament mechanism



Sarcomere changes during contraction



- The greater the number of cross-bridges in contact with the actin filament at any given time, the greater the force of contraction.
- The human body has many sizes of skeletal muscles, from stapedius muscle in the middle ear up to quadriceps.
- The energetics of muscle contraction vary considerably from one muscle to another. Therefore, mechanical characteristics of muscle contraction differ among muscles.



- For Example: shoulder and back muscles are rich in slow fibers preventing them from fatigue as they always need ATP to support our body, so they are rich in oxygen (extensive blood flow) low creatine phosphate and glycogen, so it depends on oxidative phosphorylation mainly.
 - As we said, all muscles are mixtures of these fibers
 - Aerobic respiration is important for large energy synthesis, and it has many sources not just glycogen and this occurs in mitochondria in the presence of oxygen producing high amounts of ATP but its slow.
- Test your knowledge!

What is the significance of the sliding filament mechanism in muscle contraction?

- A. It describes how ATP is utilized in muscle contraction
- B. It is the process by which muscle fibers are lengthened
- C. It describes how muscle filaments slide to cause contraction
- D. It explains the role of calcium ions in muscle contraction

What type of muscle fiber is characterized by high fatigue resistance and a rich blood supply?

- A. Type II muscle fibers
- B. Fast glycolytic (FG) fibers
- C. Slow muscle fibers
- D. Fast oxidative-glycolytic (FOG) fibers



What is the duration of energy provided by phosphocreatine during muscle contraction?

- A. Minutes to hours
- B. Around 5 to 8 seconds
- C. Essentially limitless due to constant replenishment
- D. Up to 30 seconds

What is the primary energy source for sustained, long-term muscle contraction?

- A. Creatine phosphate
- B. Cellular respiration in mitochondria
- C. Glycolysis
- D. ATP stored in muscle fibers

Which complex inhibits the active sites on actin filaments in relaxed muscles?

- A. The sarcoplasmic reticulum
- B. The troponin-tropomyosin complex
- C. Myosin heads
- D. Calcium ions

