بسم الله الرحمن الرحيم

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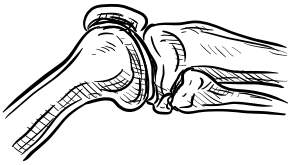

PHYSIOLOGY

MID | Lecture 3

Skeletal Muscle Contraction (pt.1)

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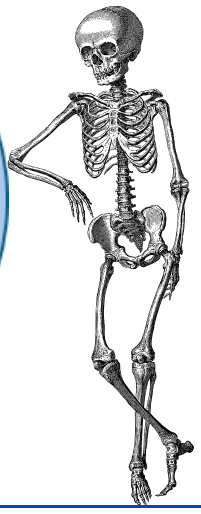
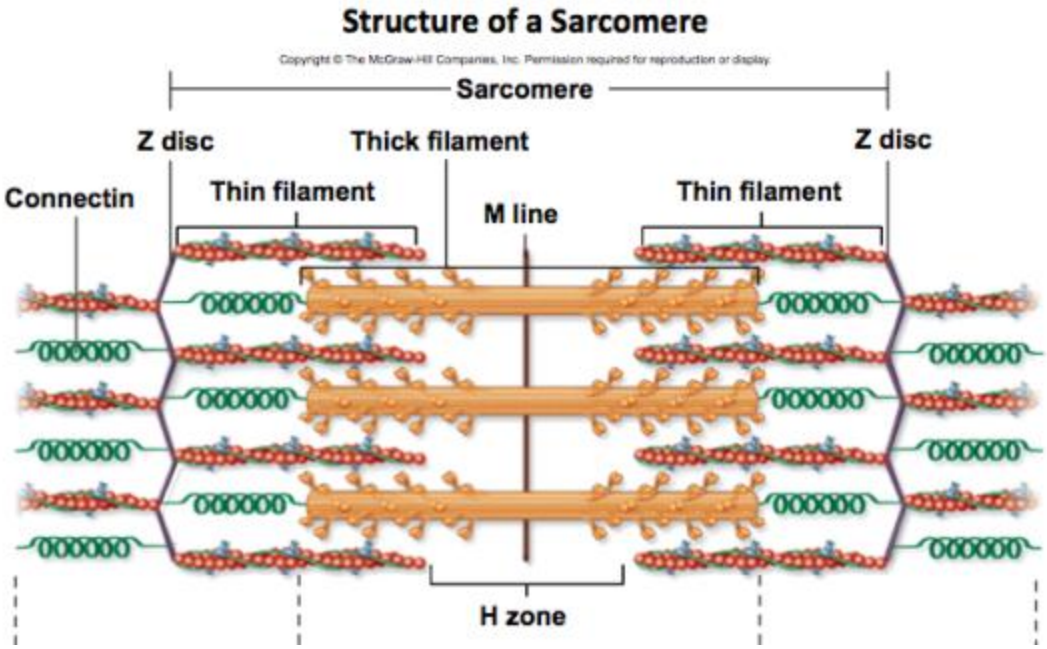
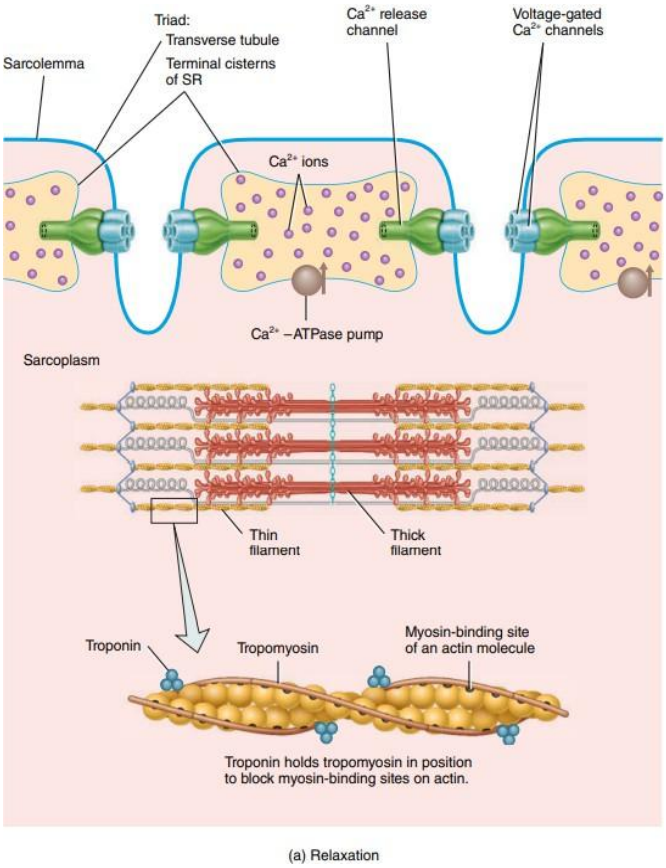


رمضان مبارك

Click on the “**A band”** for a quiz on the last lecture



Relaxation



(a) Relaxation

This figure shows the structure of a relaxed muscle fiber, here the figure shows the plasma membrane that surrounds the muscle fiber, which is called the sarcolemma, the indentations of the sarcolemma which are called the T tubules, the sarcoplasmic reticulum and its receptors that are attached to the sarcolemma at the T tubules, these receptors play a critical rule in regulating the diffusion of calcium out of the sarcoplasmic reticulum, and finally the relaxed sarcomere with its different regions of overlapping and non-overlapping filaments.

Myosin-Actin interaction

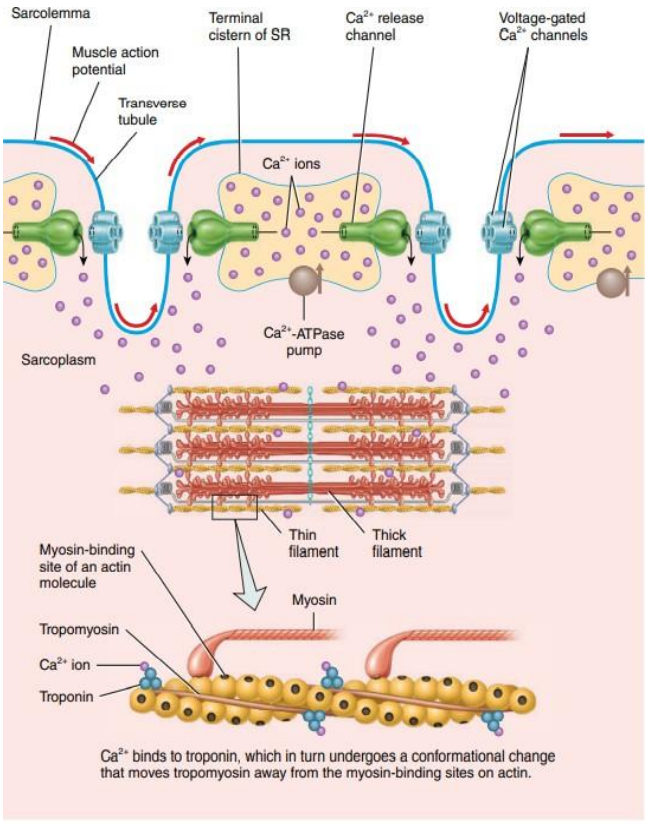
A pure actin filament without the presence of the troponin-tropomyosin complex (but in the presence of magnesium ions and ATP) binds instantly and strongly with the heads of the myosin molecules.

The active sites on the normal actin filament of the relaxed muscle are inhibited or physically covered by the troponin-tropomyosin complex.

Consequently, the sites cannot attach to the heads of the myosin filaments to cause contraction.

Contraction

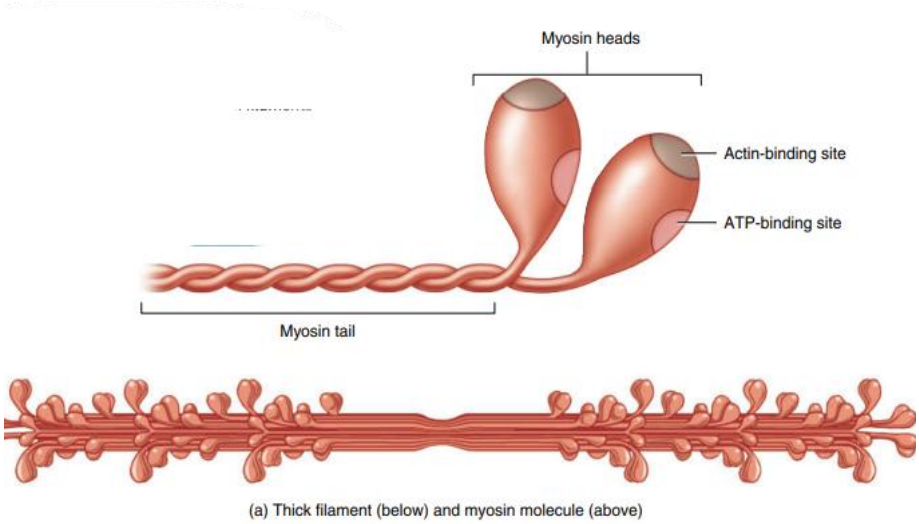
Once an action potential reaches the sarcolemma and get transmitted to the T tubules, and this will activate the receptors that open the way for the calcium ions to diffuse into the sarcoplasm, calcium binds to troponin, a conformational change of it will move tropomyosin away from the myosin binding sites on actin exposing these sites for the myosin heads to bind and the muscle to contract.



(b) Contraction

Thick and thin filaments

[This figure was discussed in detail in the previous lecture]



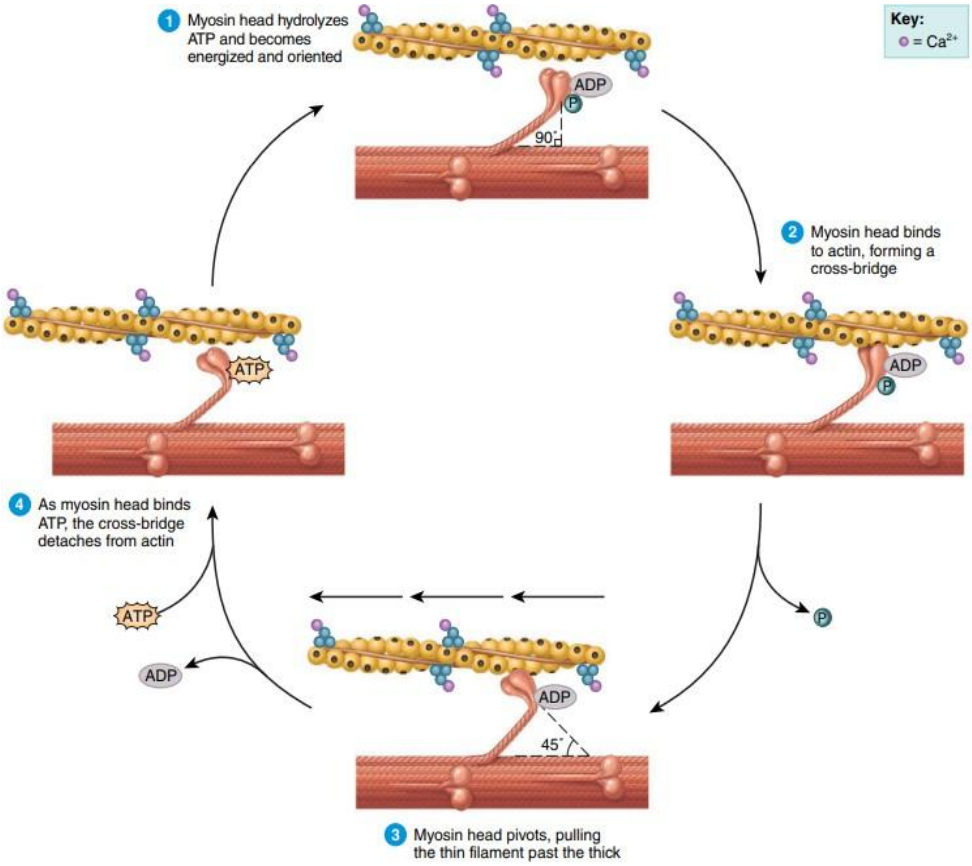
(a) Thick filament (below) and myosin molecule (above)

(b) Portion of a thin filament

Excitation-contraction coupling

The series of events occurring from the generation of the action potential (AP) in the skeletal muscle fibers to the beginning of muscle tension.

Contraction cycle



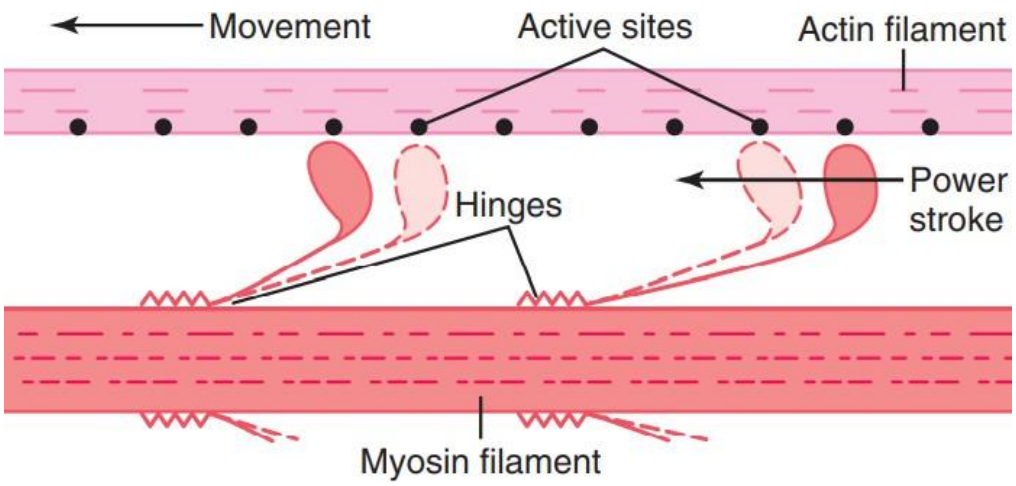
1. Before contraction begins, the heads of the cross-bridges bind with ATP. The ATPase activity of the myosin head immediately cleaves the ATP but leaves the cleavage products, ADP plus phosphate ion, bound to the head. In this state, the conformation of the head is such that it extends perpendicularly 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 uncovered and the myosin heads then bind with these sites.

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

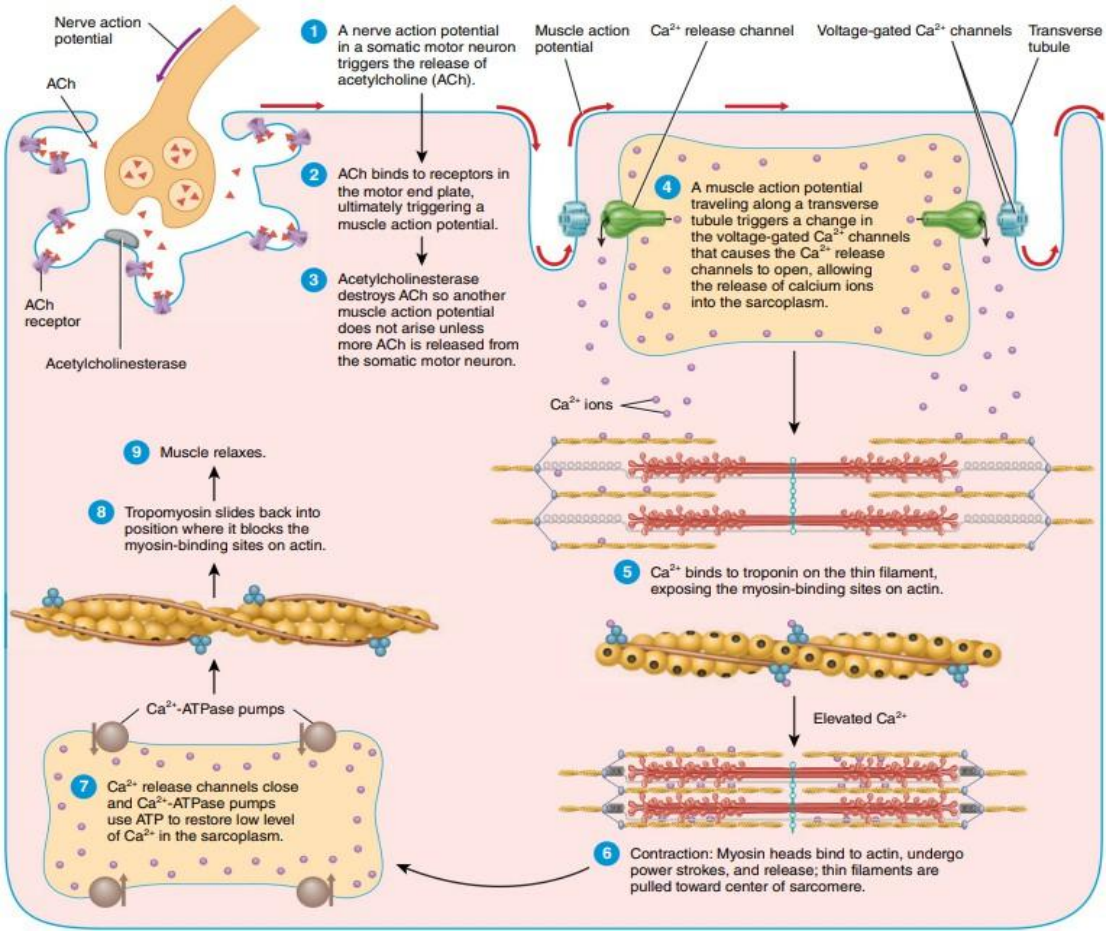


- Myosin head tilts toward the arm to drag the actin filament along with it. This tilt of the head is called the **power stroke**.
- Immediately after tilting, the head then automatically breaks away from the active site. Next, the head returns to its extended direction.In this position, it combines with a new active site farther down along the actin filament.

Calcium

- The normal resting state concentration (<10^{-7} molar) of calcium ions in the cytosol that bathes the myofibrils, this concentration 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 x 10^{-4} molar concentration, which is about 10 times the level required to cause maximum muscle contraction.

Calcium Pump (Ca^{+2} ATPase pump)



[this figure summarizes the excitation-contraction coupling events]

- 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.

As long as the stimulus exists, more calcium will diffuse out of the sarcoplasmic reticulum and more contraction will happen until there is no more calcium in to bind troponin.

- 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 uses ATP as it pumps the calcium ions back into the sarcoplasmic reticulum against their concentration gradient after the stimulus diminishes; this is crucial for the muscle to restore calcium for the next contraction.

- 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.

The coming page summarizes the mechanism by which skeletal fibers contract (and relax back); try to grasp the points well as they are predictably highly important for exam questions.

Mechanism of muscle contraction

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^{+2} 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.

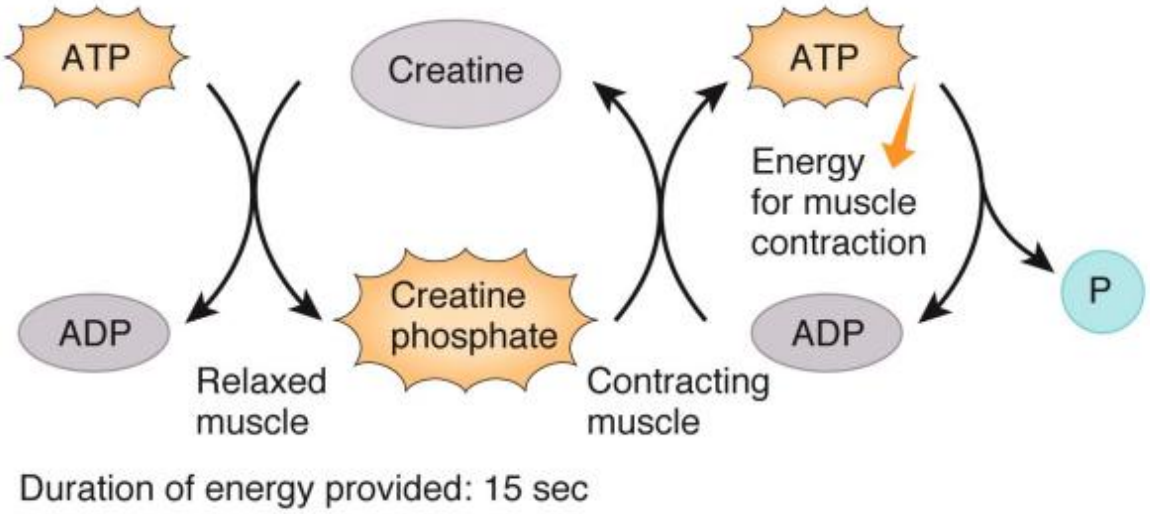
Processes that require energy in muscle fiber

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.

Sources of energy for muscle contraction

- **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.
- When the muscle is at rest, creatine molecules receive a phosphate group from ATP producing phosphocreatine that act as an energy storage molecule, these moelcules provide the energy that is needed for the quick, intense muscle contractions such in high jumps or sudden sprints as this energy sotrage lasts for a short period of time.
- 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.

This scheme shows how ATP is used to make **creatine phosphate, which in turn supplies the muscle** with a fast, "tappable" ATP source.



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. The amount of energy available for the function of the muscle in this case depends on the amount of stored glycogen.

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:

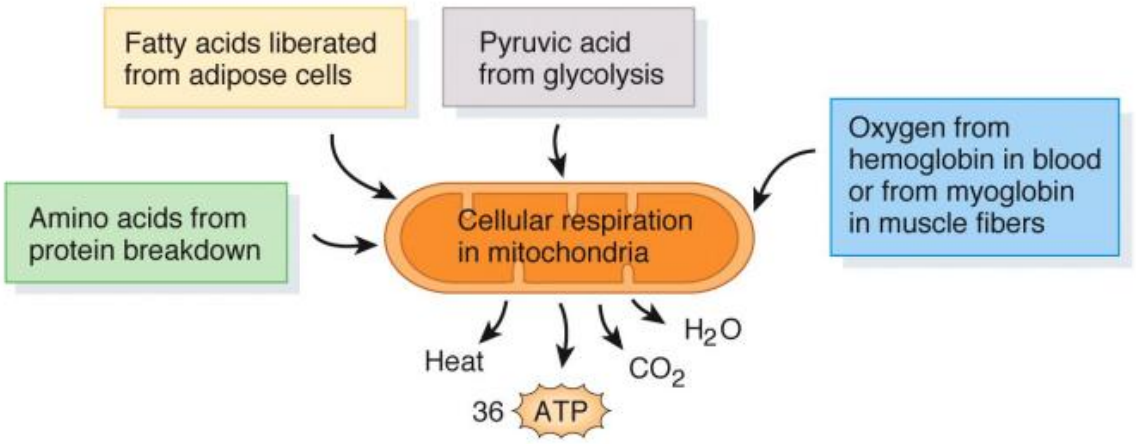
1. the glycolytic reactions can occur even in the absence of oxygen, so muscle contraction can be sustained for many seconds and sometimes up to more than a minute, even when oxygen delivery from the blood is not available.
2. the rate of formation of ATP by the glycolytic process is about 2.5 times as rapid as ATP formation in response to cellular foodstuffs reacting with oxygen.

However, so many end products of glycolysis, such as lactic acid, accumulate in the muscle cells that glycolysis also loses its capability to sustain maximum muscle contraction after about 1 minute. The muscle is said to be fatigued in this case (due to lactic acid accumulation); this usually happens when there is no adequate oxygen supply or when the muscle is not adapted to using aerobic respiration (see next page).

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, such as amino acids and fatty acids, to liberate ATP.

More than 95 percent of all energy used by the muscles for sustained, long-term contraction is derived from oxidative metabolism.

This scheme below shows the third way of getting energy for muscle physiologic functions. Keep in mind that this is the way that makes the fibers endure continuous activity for long periods of time since it accounts for about 36 ATP out of each glucose molecule, yet a downside is the long time it takes for this cascade to be active.



Duration of energy provided: Minutes to hours

Types of Muscle Fibers

Skeletal fibers can be divided into more than one type depending on their **speed of action**, which in turn depends on the type(s) of sources of energy they use. They can also be classified **by their color**, red or white, depending on their myoglobin content, which gives muscles a red color, so a muscle with more myoglobin appears more red.

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.

Types of muscle 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.

The table above is very important, so take your time looking at it and memorize it well as it makes life easier regarding muscle fiber types.

To see the doctor's explanation, please refer to (21:13 to 27:57) from this lecture.

There is a 3rd fiber type in between red and white. See the table above for more info.

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**.

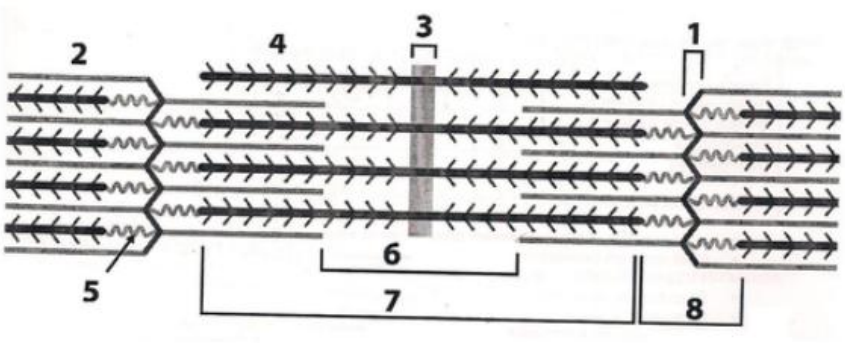
When we go to the gym, the real cause of improved fitness (اللياقة) — especially regarding muscles — is their adaptation to use prolonged energy sources, primarily through oxidative phosphorylation. This process reduces lactic acid formation, decreases fatigue, and helps us exercise for longer periods without feeling tired. As a result, the proportion of slow (red) fibers increases in our muscles.

Characteristics of whole muscle 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.

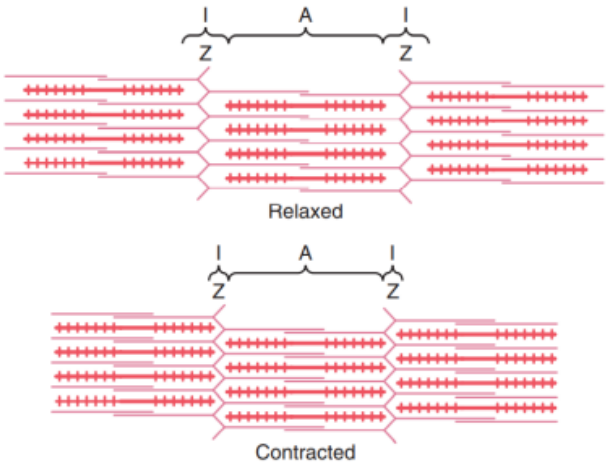
Name it!



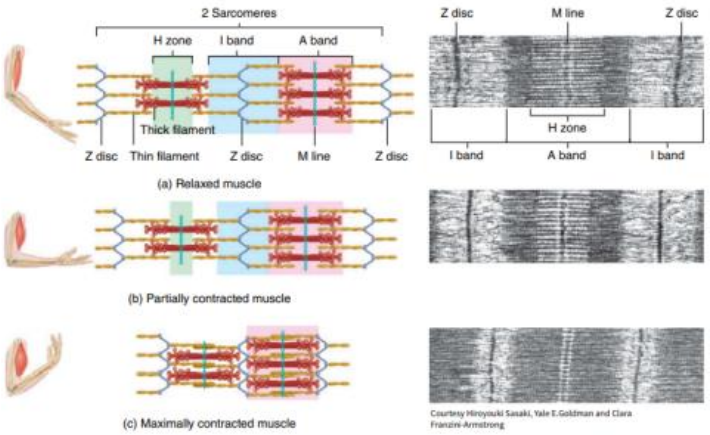
For the answers, please click here.

The greater the number of cross-bridges in contact with the actin filament at any given time, the greater the force of contraction.

The sliding filament mechanism



Sarcomere changes during contraction



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