Physiology #1

مجموعة التفريغ السريع

MSS

Subject: *Muscle Physiology #1*

Done by: *See last page*

Doctor: *Mohammad Alqudah*

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EHSAN إحسان

Muscle Physiology

Outline:

I. Contraction: Mechanical Events
II. Neuromuscular junction
III. Characteristics of muscle contraction
IV. Muscle Metabolise Introduction and muscle functions
V. Skeletal Muscle Structure
VI. Muscle Contraction: Cell Events
VII. Muscle m
VIII. Types of Skeletal Muscle Fibers

The **primary function** of the muscles is **to contract**.
- contraction doesn't mean shortening of the muscle, for example if you left something against gravity and your arm is straight there is no shortening of the muscle, still your muscle is active and producing force. So, **muscle contraction** means **to activate** the muscle to produce force, (Either shortening of the whole muscle or without shortening).

Muscles perform many functions:
1) **movement** which depends on the type of the muscle, for example:
a- skeletal muscle plays a role in the local motion (movement of one bone toward another),
b- smooth muscle line the whole organ to propel contents of the GIT,
c- heart muscle provide pumping of blood to the body.

2) **Heat production**, during muscle contraction there is heat production.
3) **Protection,** for example the abdominal muscle protect the abdominal viscera (the stronger the muscle the more protection).

4) **Posture maintenance,** this is the action of muscle spindle it's like maintaining the body posture; it's involuntary function of the skeletal muscle.
5) **Joint stabilization,** it's the synergistic effect of muscles to stabilize the joints.

There are four basic characteristics of the muscle tissue:
1) **excitability**: it is the responsibility to a stimulus, if there is a nerve stimulus there will be an action potential in the muscle which leads to the second characteristic which is contractility.
2) **Contractility** it is the ability to produce force in response to stimulus. 3) **Elasticity** it is the ability of the muscle to recoil to its original length after stretching.
4) **Extensibility,** it is the ability of the muscle to be stretched.

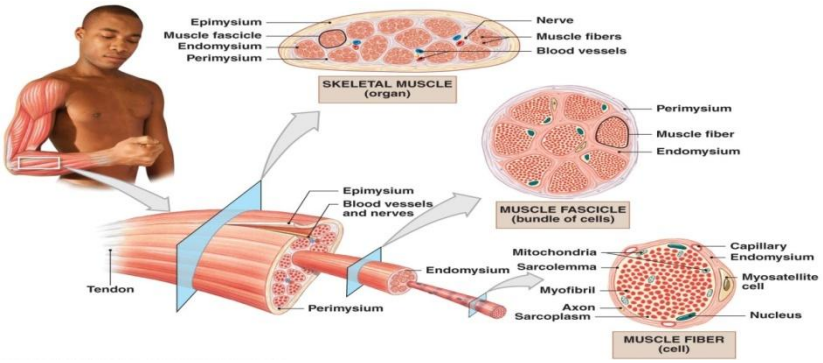
Classification of the muscles:
muscles can be classified according to histological (fine) structure, neuronal control and anatomy.
1) **Histologicaly**: there are striated muscles either by stripes or bands or smooth muscle.
2) **Anatomically:** there skeletal target and visceral.
3) **Neuronal control**: voluntary and involuntary muscle types.
the most common category of classification is skeletal muscle cardiac muscle smooth muscle, skeletal muscle attached to skeleton, cardiac muscle in the heart and smooth muscle are involuntary muscle like the muscles in GIT, UB (urinary bladder) and gallbladder.

Skeletal muscles are like cylinders, the muscle cell is cylindrical in shape, multi nucleated and the nuclei are located at the periphery and its most striking feature is those stripes or the banded appearance.

Cardiac muscles:are involuntary muscle, cylindrical with one nucleus in the center and its most striking feature is the intercalated disk between adjacent muscle fibers.

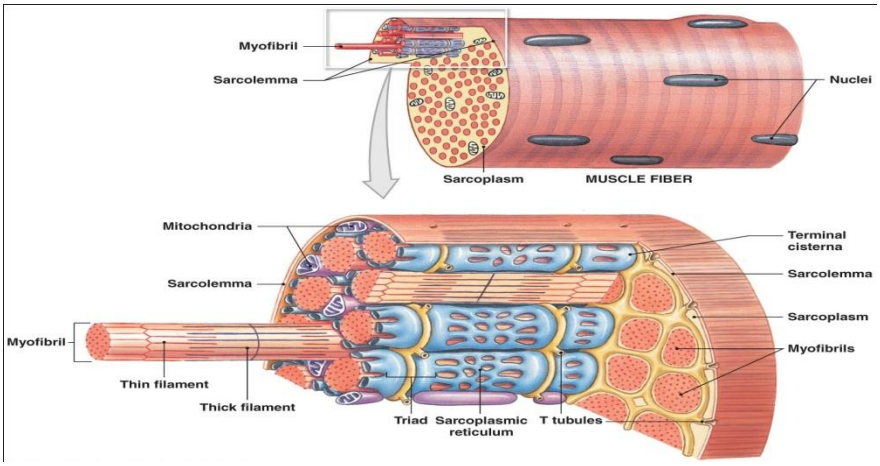
Smooth muscles are characterized by the absence of the close striations seen in the skeletal and cardiac muscles and they are involuntary with a single nucleus located in the center of the muscle cell.

We will focus on skeletal muscles, we will see how skeletal muscles contract and the molecular mechanism for contraction, the characteristics of contraction and the energy of contraction.

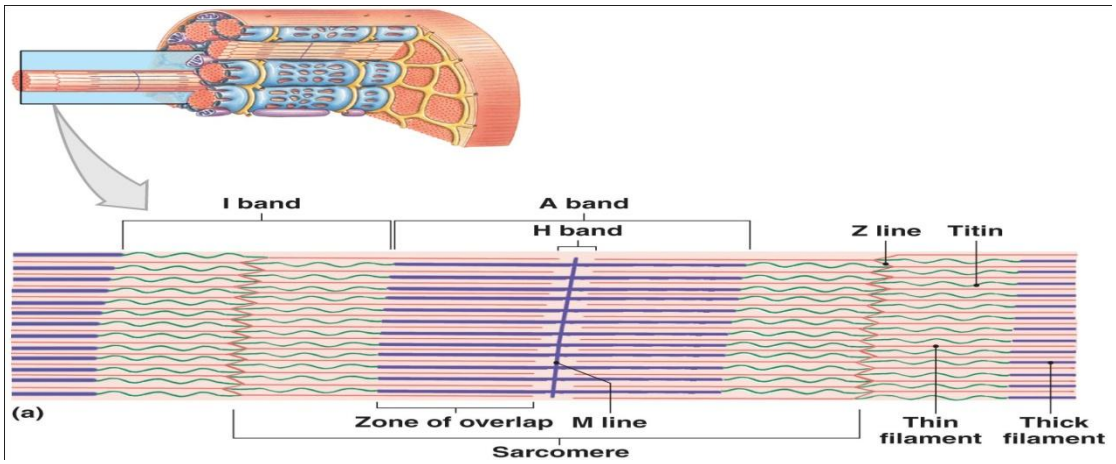


This is **skeletal muscle** which is composed of bundles of muscle fibers called **fascicles** and each fascicle is composed of a number of **muscle cells** or **muscle fibers**.

Skeletal muscle is a connective tissue that is highly innervated and vasculated.



muscle fiber is composed of plasma membrane of the skeletal muscle cell is called the (sarcolemma) , there is invagination of the muscle cell membrane, these long tubules called (T tubules) are continuous with the outside, the cytoplasm of the muscle cell is called the (myoplasm), each **muscle fiber** is composed of hundreds of thousands of cylindrical structures called the (**myofibrils**), the **myofibril** is composed of end to end or repeats of the functional units of the skeletal muscle which is called (the **sarcomere**) arranged end to end and this is what gives the skeletal muscle its striated appearance, the arrangement of the **myofilaments** in the myofibril gives the skeletal muscle its striated or banded appearance.



This is a small section of the myofibril represent the functional unit of the muscle cell or the skeletal muscle.

this is the **sarcomere**, there are thick filaments and thin filaments and this is the (Z line) which demarcates the end of the sarcomere, the arrangement of the thick filaments and the thin filaments is like web repeats alternative bands of (I bands) composed of the thin filaments and the (A bands) which gives the skeletal muscle its striated appearance.

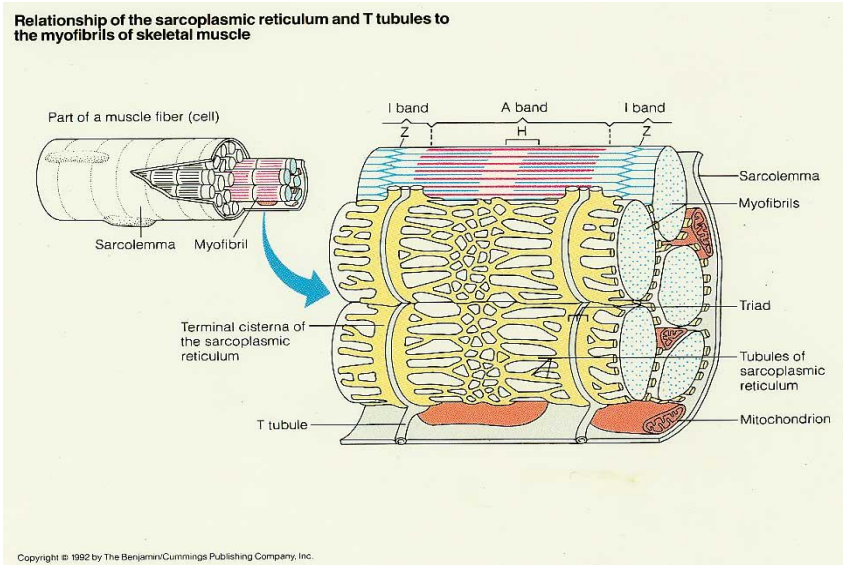
* How contraction takes place??

first there should be a stimulus, the stimulus is the **action potential** coming from the motive neuron, the action potential beats this terminal end of the neuron it will **depolarize the terminal end**, this will lead to **increase the permeability of calcium channels** on the plasma membrane of the terminal end and **influx of**

calcium ions to the end terminal with these neurotransmitter vesicles in the presynaptic membrane and the **release of neurotransmitter** into this gap or the synaptic cleft and this neurotransmitter specially (acetylcholine) will **bind to its receptor** on the postsynaptic membrane on the muscle cell membrane or the sarcolemma and this will initiate **action potential** in the muscle cell which will be transferred into contraction in the muscle cell.

Excitation –Contraction Coupling

"The process by which depolarization of the T-tubules converted to an intracellular calcium signal and the Subsequent activation of contraction is called Excitation-Contraction Coupling"



1.Motor neuron excitation

- action potential in the nerve cell

- action potential in muscle cell

- the T tubule conducts the action potential deep into the muscle

2. Ca^{+2} release from the SR into the myoplasm…

the T tubule conducts the action potential deep into the muscle (it is continuous with the sarcolemma), Sarcoplasmic reticulum stores calcium

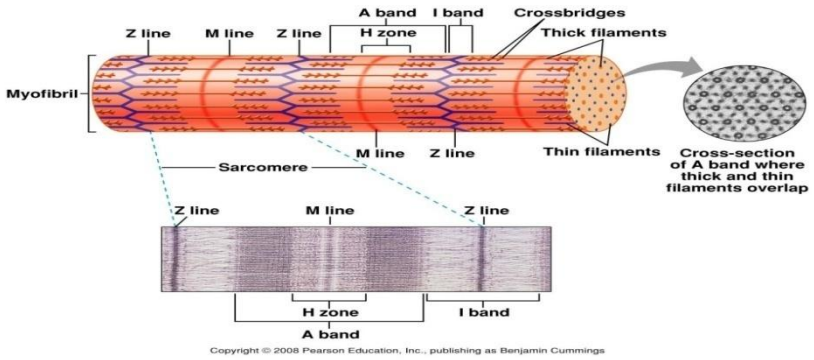
so when there is an action potential it will depolarize the muscle cell then the Transverse tubules (T tubules) will Transmit the action potential deep into the muscle cell. These tubules adjacent to Sarcoplasmic reticulum, this action potential will stimulate the release of the calcium from its stores , so the release of the calcium will stimulate the final signal for contraction which is the **increase** in the concentration of the calcium inside muscle cell.

Molecular mechanism of Muscle contraction:

muscle contraction takes place because of the sliding of the inter-digitations of the myofilament (thin and thick filament). Sliding of the filament will cause shortening of the functioning unit in the muscle cell which is the sarcomere that produce the force .there will be production of cross bridges between the thick and thin filament and this is the cause of force production (muscle activation = force production).

Characteristics of Contractile proteins

Sarcomeres: The contractile units of muscle & Structural units of myofibrils, form visible patterns within myofibrils. The myofibrils are organized into a repetitive pattern, the sarcomere. Its composed of thin (1 micrometer on each side) and thick (1.6 micrometer) filament mainly but its total length is less than 3.6 micrometer because of the inter-digitations between the thin and thick filament .



Muscle striations

A striped or striated pattern within myofibrils: alternating dark, thick filaments (A bands) and light, thin filaments (I bands)
The A band is anisotropic which means dissimilar (thin+thick filaments), and the I band is isotropic which means something similar (pure thin filament)

M Lines and Z Lines:

M line: the center of the A band at midline of sarcomere is a group of protein that keep the thick filament in register.

Z lines: the centers of the I bands at two ends of sarcomere and the junction between two adjacent thin filament

Zone of overlap: the densest, darkest area on a light micrograph where thick and thin filaments overlap

The H Band: the area around the M line has thick filaments but no thin filaments

Titin: Big MW (3.7 million Dalton)Strands of protein reach from tips of thick filaments (M line) to the Z line stabilize the filaments
forms a framework for myosin assembly

“animation for the Sliding mechanism or walk along theory : http://highered.mcgraw-hill.com/sites/0072495855/student_view0/chapter10/animation__sarcomere_contraction.html “

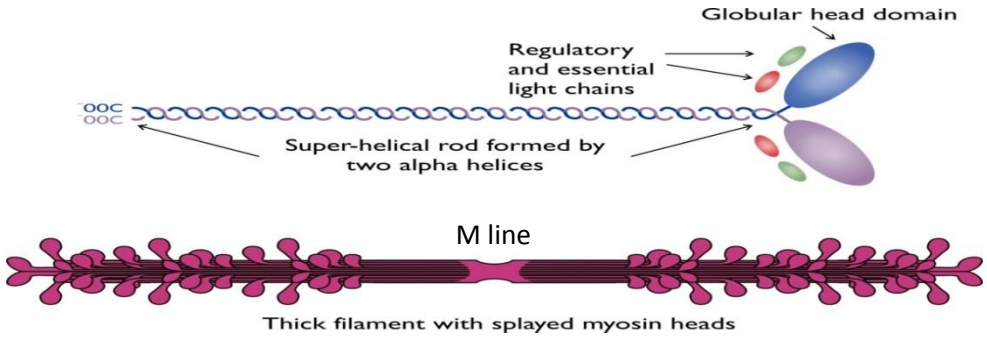
During the contraction A band will stay the same, I band will decrease, H zone will decrease and may even disappear.

Myosin Structure

Myosin: thick filament

Actin: thin filament

myosin protein is consist of 6 polypeptide , 2 heavy chain and 4 light chain (tail, hinge, head).
the 2 heavy chain Wraps around each other to form a roll structure tail and globular part called the head .
and 4 light chain , these are regulatory essential proteins , they are part of the head , 2 on each head .
the myosin filament arranged in this polarized chain where’s the head to the outside and the tails to the center .

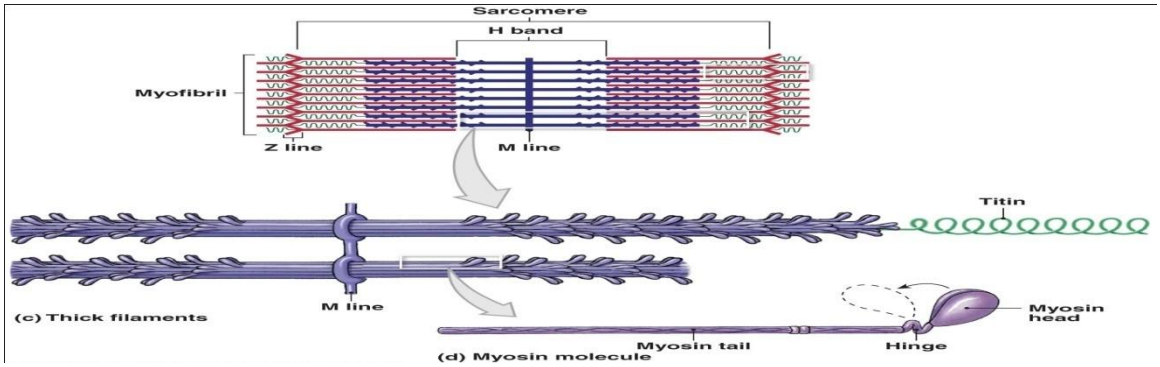


Its between the M line and the Z disc – the green line is the titen – and this the two heads, hinge, and the myosin tail.

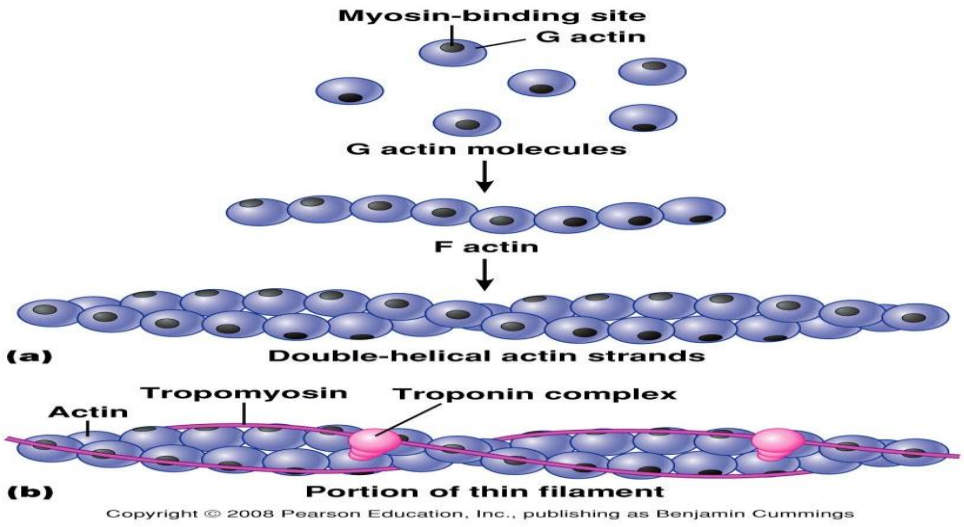
Myosin head has a binding site for ATP and another binding site for actin. The mechanism of sliding and cross bridging for a muscle contraction takes place in response for the attachment or the formation of cross bridges between the heads of thick filaments and the actin. ATP will transform to a mechanical energy to allow the formation of attachment.

Titin: a giant protein that serves as a template for myosin assembly

M Line: stabilize the myosin filaments.
theorized to aid in transmission of force from sarcomere to cytoskeletal intermediate filaments.



Actin



Composed of a monomer called **G-actin** – globular protein, about 42,000 kd MW- and will arrange into a Filamentous actin (F-actin). F filament form a double helix about 1 um in length in the sarcomere. you can see that 7 G-actin form half tail.
-we have another protein here called **tropomyosin**. It's the same length of half tail and covers the binding site of myosin on actin.

-Troponin :
It's a complex of three proteins (Troponin T , C , I) , their names come from their function.
*Troponin T binds to Tropomyosin.
*Troponin C binds to calcium.
*Troponin I inhibit the interaction between thick filament and thin filament.

we said that Tropomyosin covers the binding site of myosin on actin and it's attached to it by troponin T and as we said that the final signal for contraction is the increment in intracellular calcium in the cytosol of muscle cell , Ca2+ binds to receptor on troponin molecule and the Troponin-tropomyosin complex changes Exposing the active site of F-actin Thick Filaments (Contain twisted myosin subunits and titin strands that recoil after stretching).

The mysosin molecule:
1- Tail: binds to other myosin molecules

2-Head: made of two globular protein subunits reaches the nearest thin filament Myosin Action During contraction, myosin heads Interact with actin filaments, forming cross-bridges Pivot, producing motion

Skeletal Muscle Contraction (Sliding filament theory) , Thin filaments of sarcomere slide toward M line, alongside thick filaments The width of A zone stays the same Z lines move closer together. * The force depends on the number of cross bridges formed between actin and myosin.

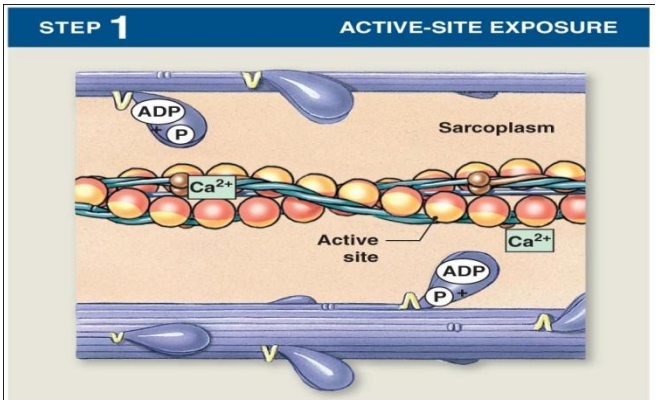
Nebulin : is another giant protein that keep thin filaments in its register. you can see this a relaxed sarcomere and there is a slide digitation between thin and thick filaments , and this is a partialy contracted sarcomere and a shortening of the distance between the two Z lines and this is a fully contarcted sarcomere.

Muscle Contraction: Mechanical Events

Acto-myosin cross bridge cycle:

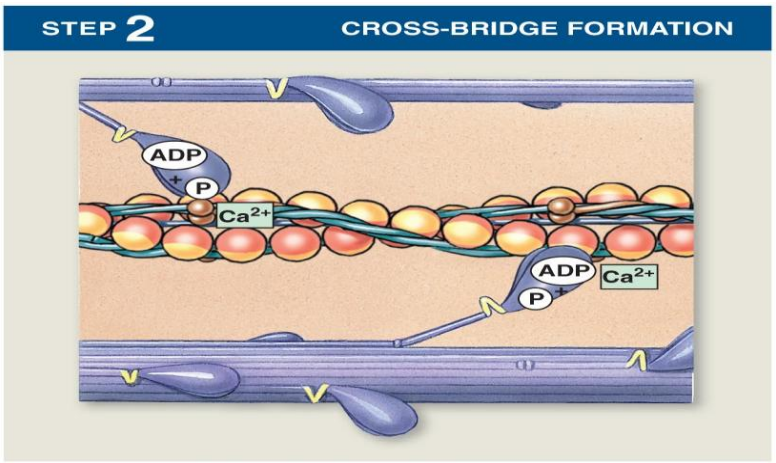
- Myosin heads bind to actin filaments
- ATP hydrolysis allows the myosin head to walk along the actin filament
- Myosin is an actin-activated ATPase

we have what we call "actomyosin cross bridge cycle". We said that myosin will bind to actin filament and this is the reason for the formation of cross bridges. ATP hydrolysis allow myosin heads to WALK along the actin filaments. Myosin is an actin-activated ATPs; this means that myosin itself can hydrolyze ATP into ADP and inorganic P, but once it's attached to thin filament, actin will facilitate hydrolysis of ATP and accelerate the process of contraction.



The first step when the muscle is **relaxed** there will be a binding of ADP and inorganic P to the myosin head , there is no calcium , the binding of ADP and inorganic P to the myosin head makes myosin with a high affinity for actin , but the binding site for myosin is covered by tropomyosin.
The myosin is charged ; this means that it has energy to be converted to a mechanical work , but its high affinity for actin and at the same time active site is covered by tropomyosin.

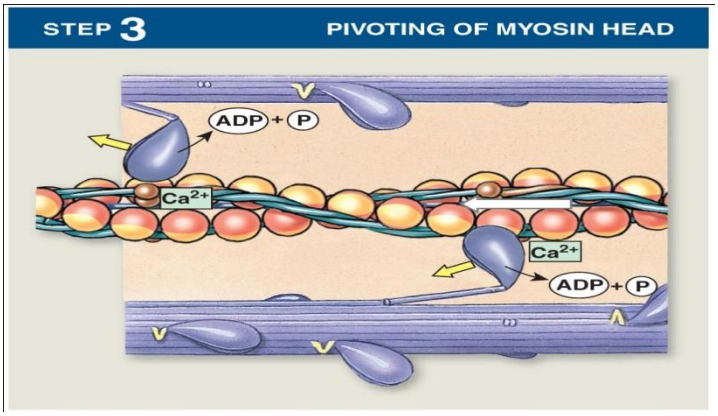
action potential stimulates the muscle and thought t-tubules toward sarcoplasmic reticulum , there will be release of calcium from internal store into cytosol so there will be increase in intracellular calcium, calcium will bind to troponin C and this will cause a conformational change in the troponin-tropomyosin complex, rolling the tropomyosin away from the active sites on actin.
Thus allowing them to interact with energized myosin heads.



Now, the binding sites – these in yellow- available for the high affinity myosin , so there will be attachement of actin and myosin and the

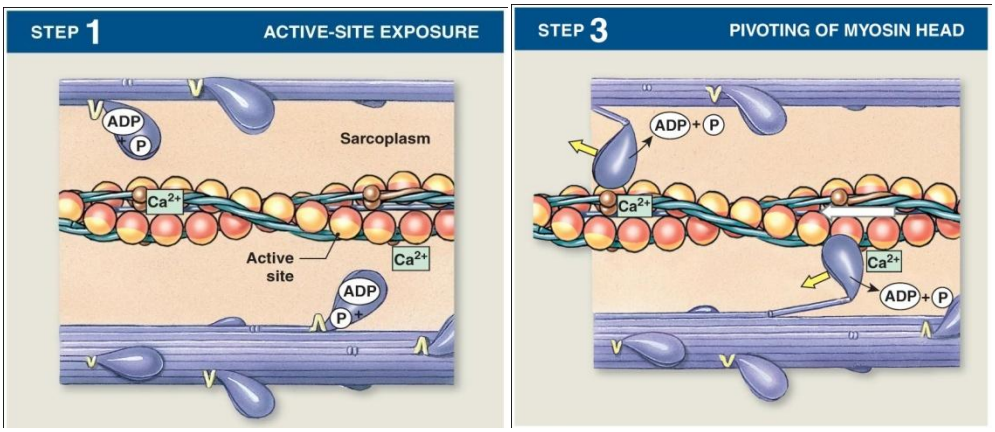
formation of cross bridges. There will be release of inorganic P and ADP. This will induce a conformational change in the myosin head and hinge to what is called power stroke .

Rigor Mortis : In the absence of ATP, the muscles remain in a contraction state as the myosin head stayed attached to actin (ATP is the cause of separation) and this what Happens the muscles of the body



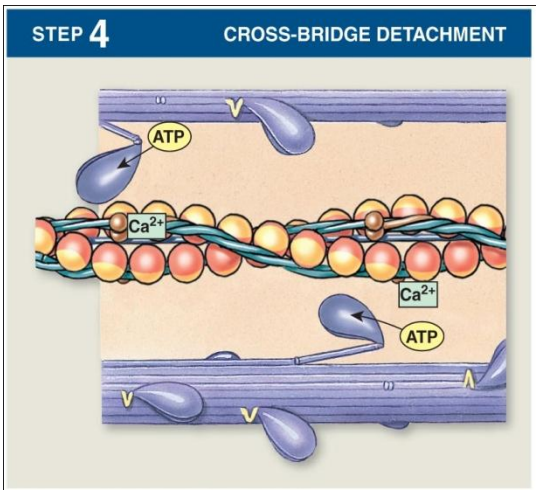
This will induce a conformational change in the myosin head and the hinge to cause the stroke power. And still the myosin with high activity form will be shifted 45º toward the M line, pulling the thin filaments toward the center of the sarcomer.

The rest and contracted position



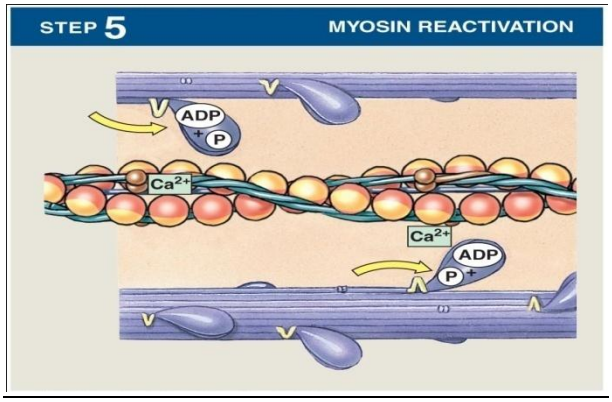
Then, ADP and the phosphate group are released.

Step 4



Another molecule of ATP will bind to the myosin head; shifting the myosin from a high affinity state to a low affinity one. So the myosin head will deattach from the actin filament.

Step 5



ATP will hydrolyze charging the myosin head and moving it back to its perpendicular position.

As long as there is ATP and Ca^{2+} the cycle is going again and again, producing more cross bridges and force until the contraction reaches the max strength.

The force depends on the number of the cross bridges which are formed.

This animation reviews the whole process:

http://media.pearsoncmg.com/bc/bc_0media_ap/apflix/ap/ap_video_player.html?cbc

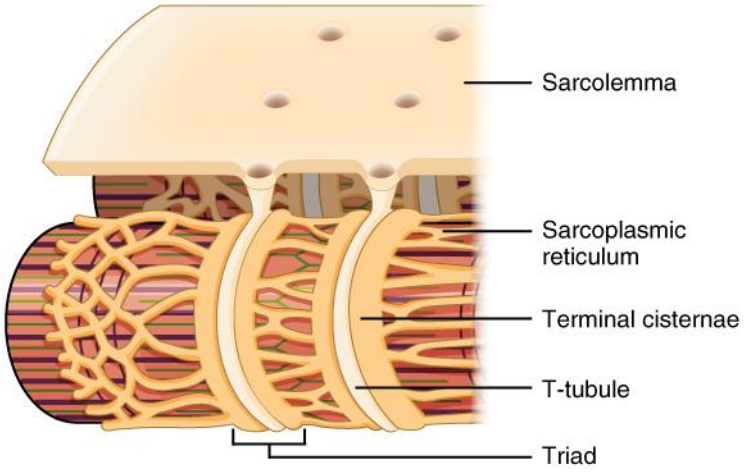
The relation between the plasma membrane with T tubules and sarcoplasmic reticulum

The fluid in the T tubules is part of the extracelluer fluid, and it slides between two sacks (endoplasmic reticulum cesterna)

Triad:

A T tubule surrounding by 2 cisternae on both sides.

- **there is 2 triad per sarcomere;** to insure the proximity of the Ca^{2+} to the filaments.
- It's function is allowing the action potential to reach deeper in the muscle



Tomorrow's lecture will be about the Neuro-Muscular junction & the characteristics of the muscle contraction.

Trust us.. ☺

NOTES:

أحمد طلفاح

وائل أبو السمن

أسامة الزعبي

معن شطناوي

خالد الروابدة ^_^