7 Physiology of Skeletal Muscle Contraction

Very important

Extra information

Terms

For better understanding , we recommended you to study Integrated muscle lecture.
Chick histology team work :Integrated muscle

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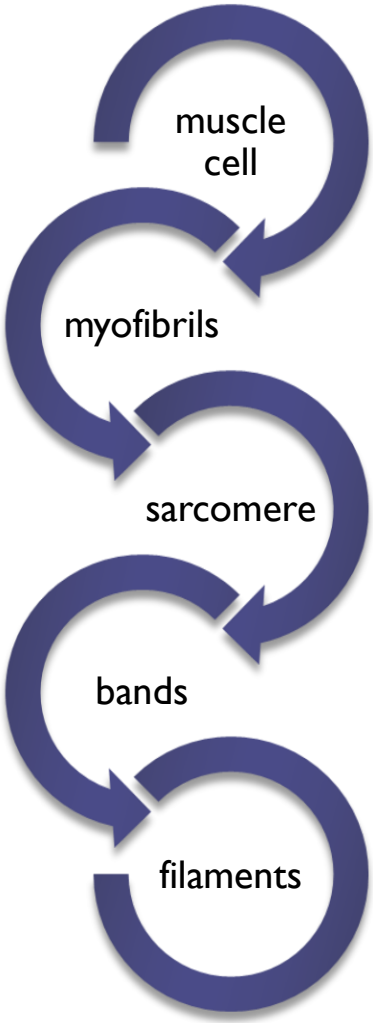
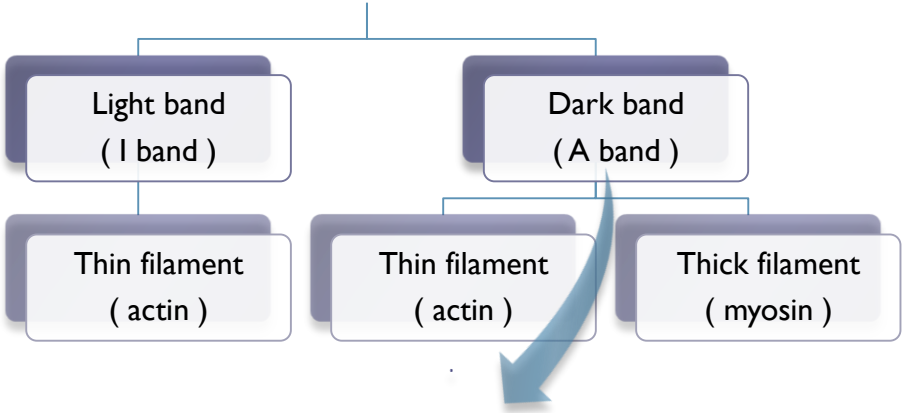
Over view



- The muscle cell contains thousand of (myofibrils)
- Each myofibril consists of (sarcomere) "which is the functional unit"

- The **sarcomere** consist of :



Between (A band) there is light band called (H band) → which contain myosin only

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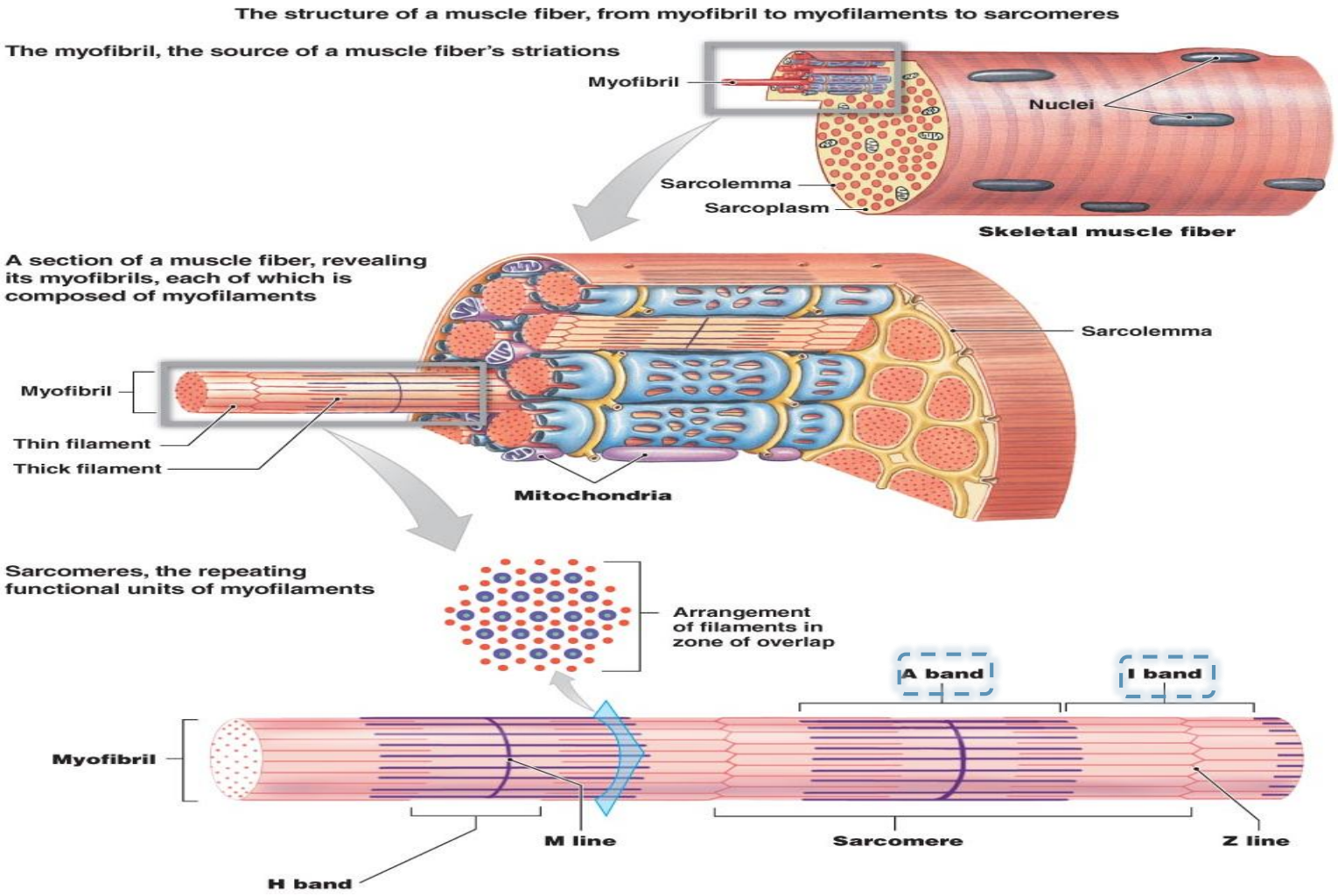
Over view



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Muscle Action Potential

Muscle Resting membrane potential	-90 mV "same as in nerves"
Duration of Action potential	1-5 ms "longer duration than nerve AP which is usually about 1 ms"
Conduction Velocity	3-5 m/s "slower than big nerves"

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Muscle Fibers

- Skeletal muscle is made up of many cylindrical ,multinucleated muscle cells (fibers).
- The fibers (cell) can be 10 to 100 ten micron in diameter and can be hundreds of centimeters long.
- Each muscle cell (Fiber) is covered by a cell-membrane called **Sarcolemma.**
- Each cell contains between a few hundreds to a few thousands **Myofibrils**.
- Each Myofibril contains :

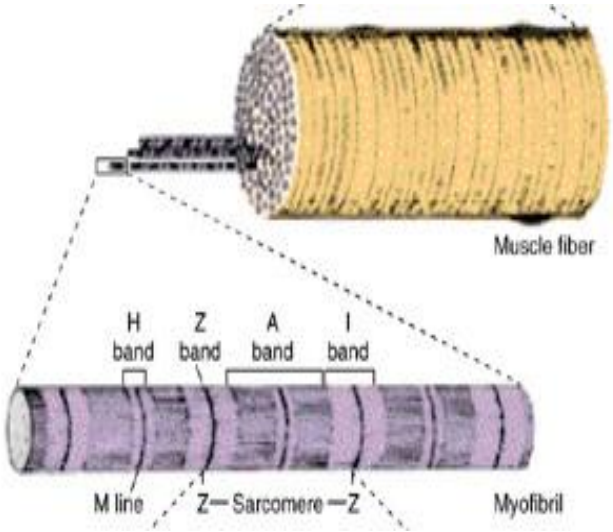
- Actin (thin) filaments.
- Myosin (thick) filaments .

[Each myofibril is made up of 3000 Actin and 1500 Myosin]

- Each myofibril is **striated** and consisting of :

- DArk bands (A-bands) It has pale area in the middle (H band) which divided by a dark line called (M line).
  "A band is mainly formed of thick filament (myosin)".

- LIght (I-bands) it has a dark line in the middle called (Z band).
  "I band is formed by thin filament (actin)".



Video

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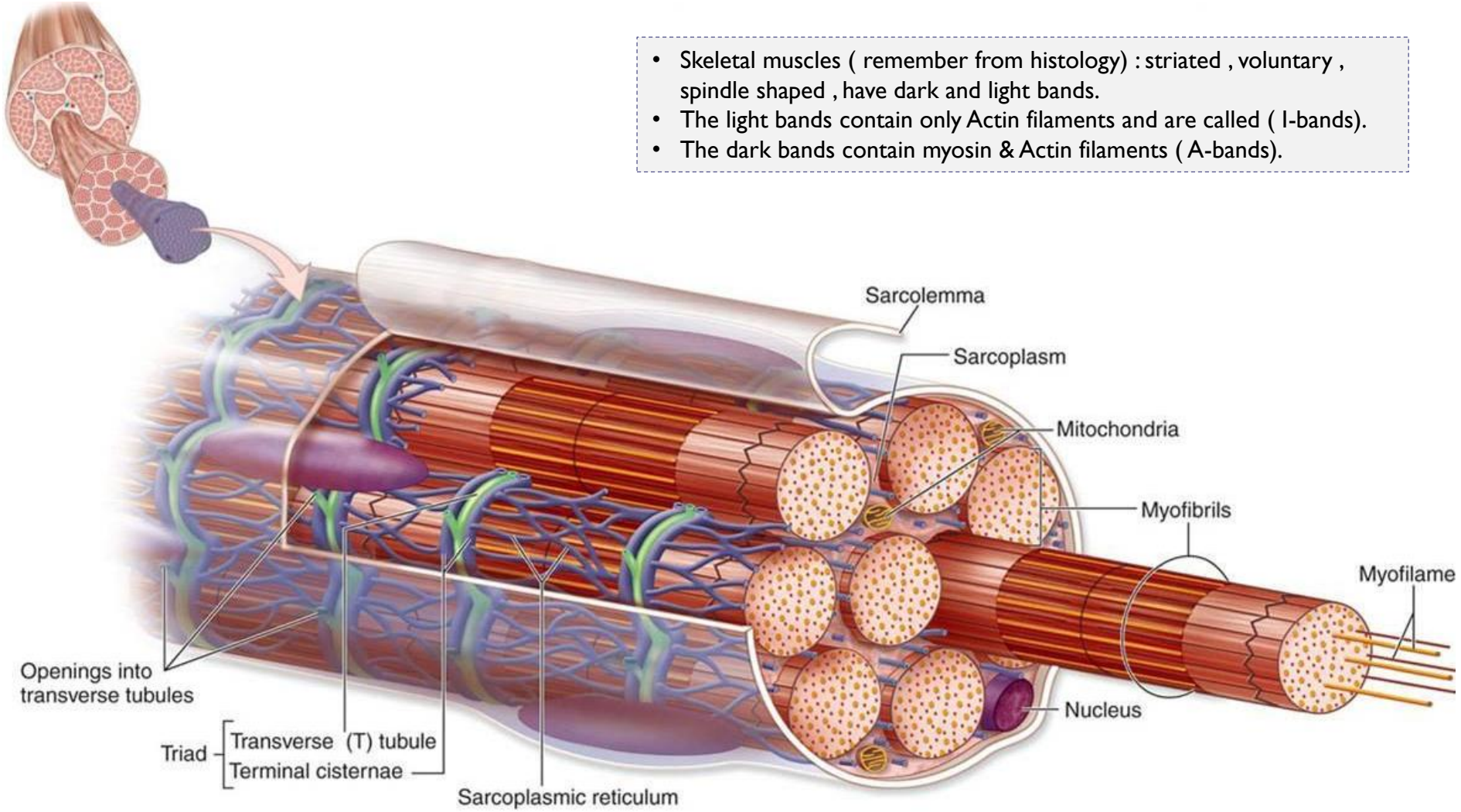
- Skeletal muscles (remember from histology) : striated , voluntary , spindle shaped , have dark and light bands.
- The light bands contain only Actin filaments and are called (I-bands).
- The dark bands contain myosin & Actin filaments (A-bands).



Video

Muscle Fibers

- **Sarcoplasm :**

  Matrix inside muscle fiber in which myofilaments suspended.

- **Sarcoplasmic reticulum :**

  It is endoplasmic reticulum inside sarcoplasm full of Ca+. "مخزن الكالسيوم"

- **T- tubules :**

  Extend from one side of muscle to other.

  * What is the function of T-tubules ?

- **Sarcomere :**

  contractile unit of muscle, it is the zone between two Z lines (discs)=2 micrometer in length in resting state.

- **Z discs (lines) :**

  lines extend all way across myofibrils.

Transmission of Action potentials occur along transverse tubules (t-tubules) that penetrate all the way through the muscle fiber from one side of the fiber to the other. T-tubule action potentials cause release of calcium ions inside the muscle fiber which initiate the contraction.
"Although it wasn't written in our slides it is very important to know T-tubules function!"

Video

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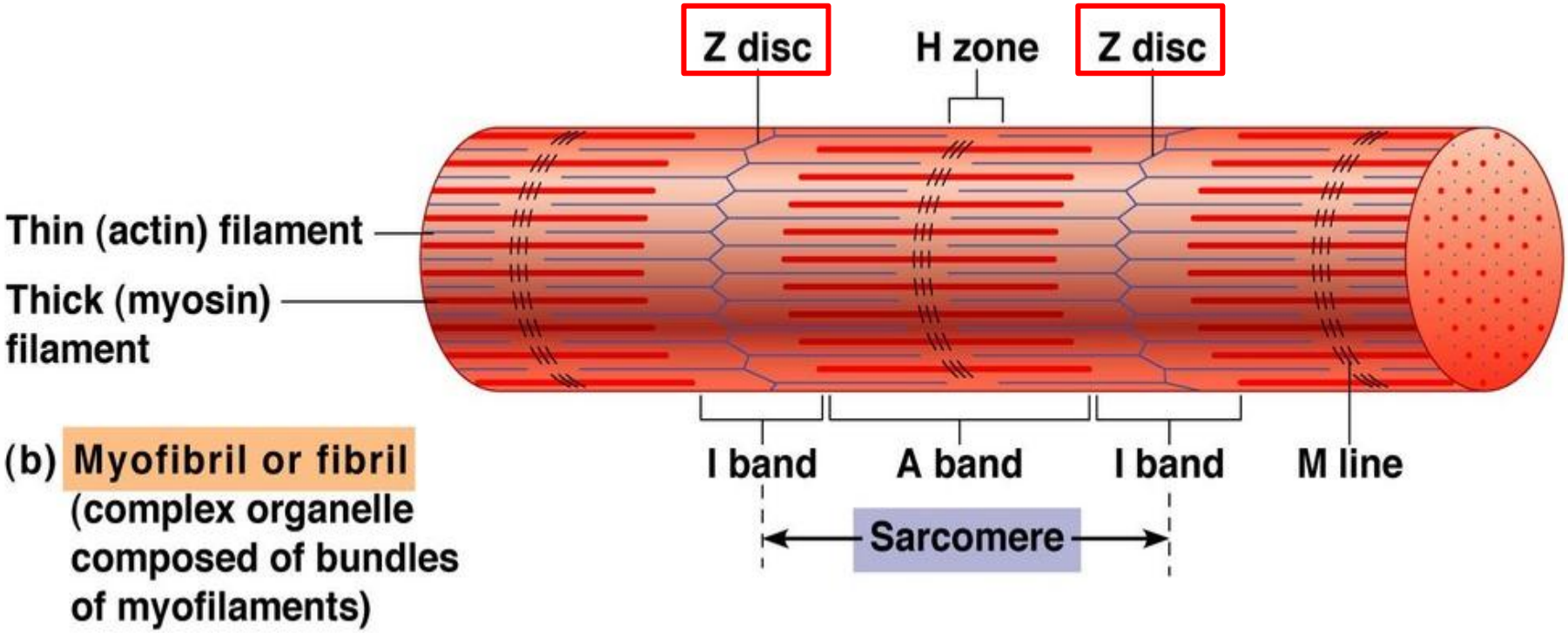
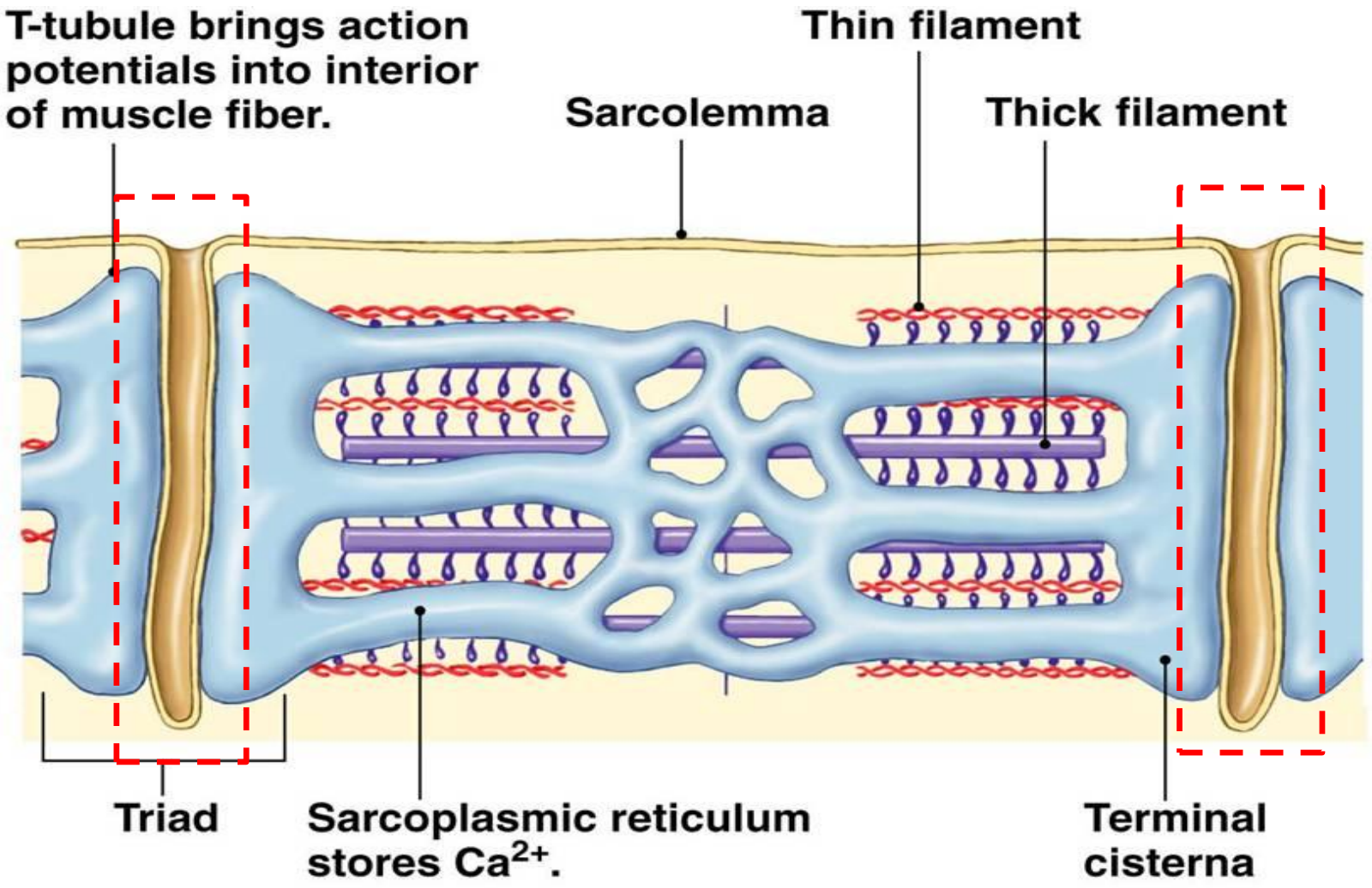


- The distance between 2 Z lines > sarcomere > the functional unit of contraction.
- T-tubule "transverse tubule" : عرضياً cell membrane يقطع الـ
  "invagination of sarcolemma" they contain ECF.
- Sarcoplasmic reticulum surrounds the T-tubule and it is "مخزن الكالسيوم"



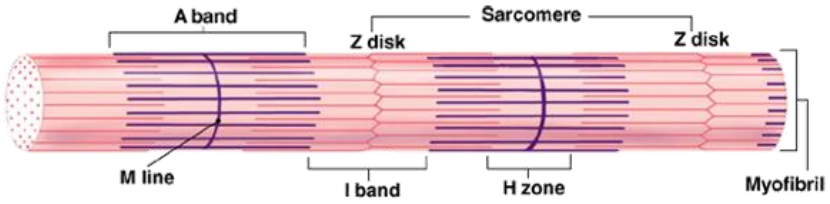
T-tubule (or transverse tubule) is a deep invagination of the sarcolemma which is the plasma membrane of skeletal muscle cells. These invaginations allow depolarization of the membrane to quickly penetrate to the interior of the cell.

Sarcomere bands

Inside each sarcomere there are :

3 bands

1. **I band**
   - Formed of actin filament only
2. **H band**
   - Formed of myosin filament only
3. **A band**
   - Formed of actin and myosin filaments



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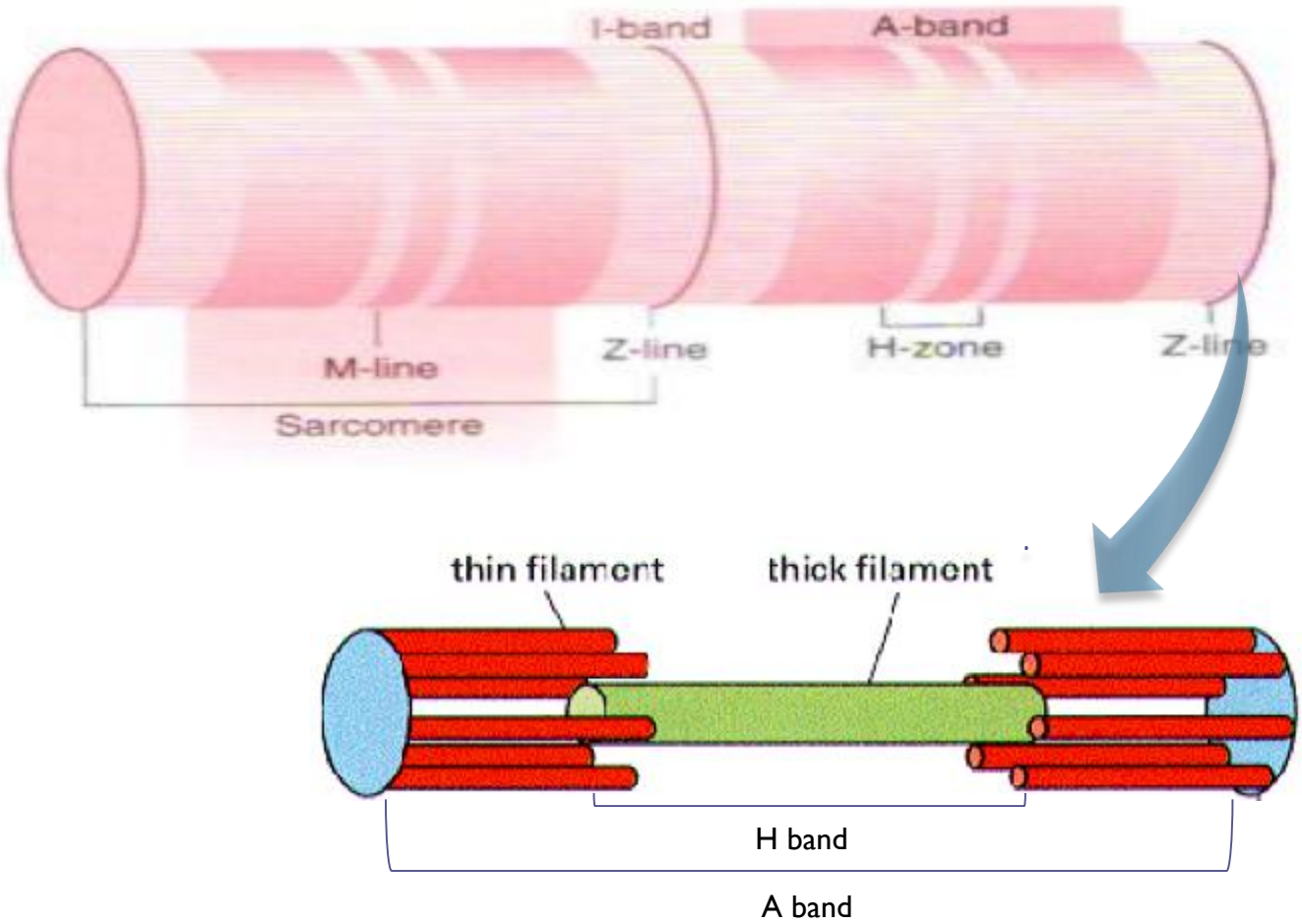
Sarcomere bands



Extra

Sarcomere : is one of the segments into which a fibril of muscle is divided.

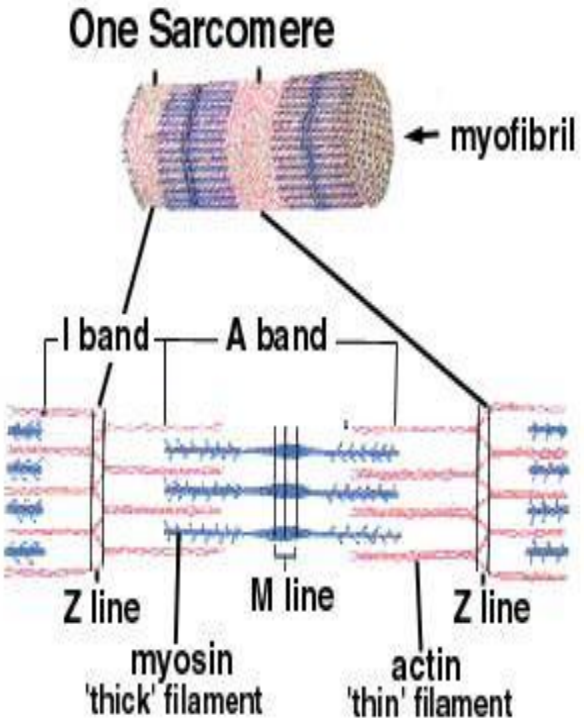
M line : provides an attachment for myosin filaments

Z line :provides an attachment for actin filaments

A band : is the darker band of the myofibril containing the myosin and actin filaments

H band : is the lighter section in the middle of the A band where only myosin is present

I band :is the lighter band of the myofibril containing only the actin filaments



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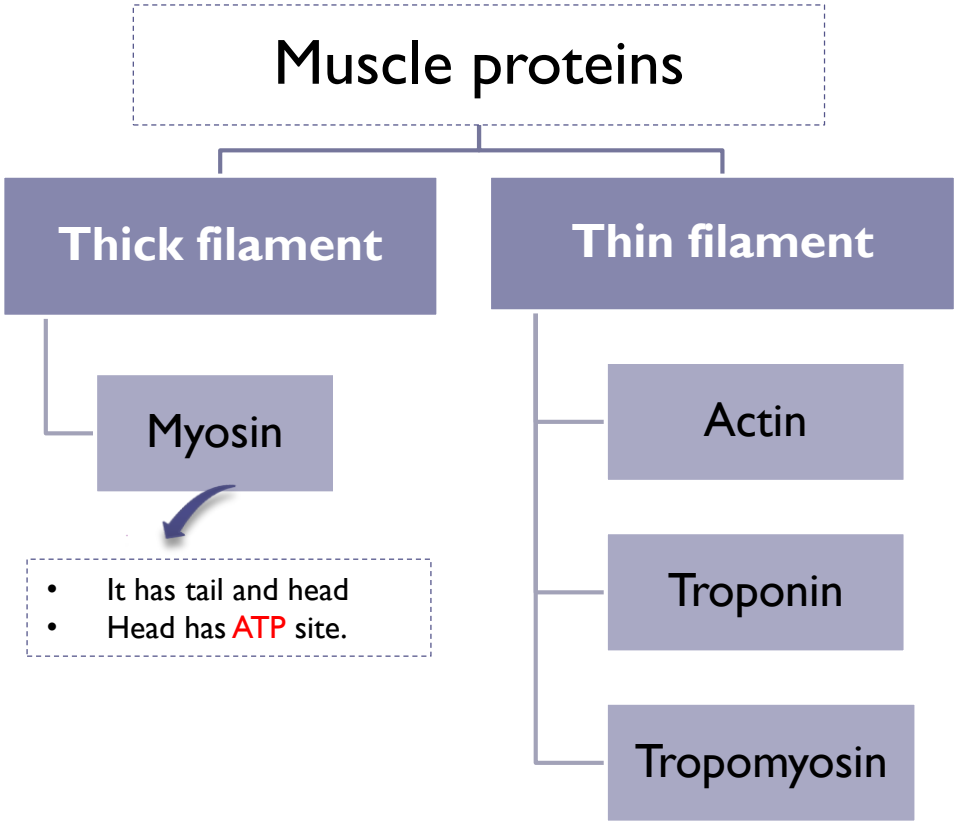
Muscle Contraction

- Contractile proteins are :
  Actin & myosin
- Regulatory proteins are:

1. Troponin :
   "excitatory to contraction"
2. Tropomyosin :
   "inhibitory to contraction"



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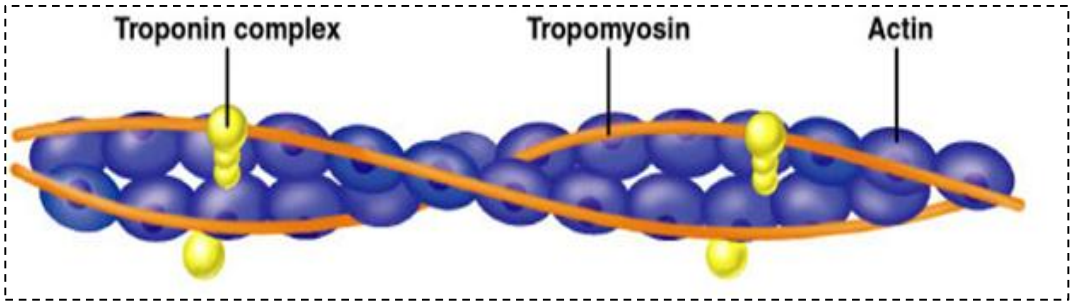
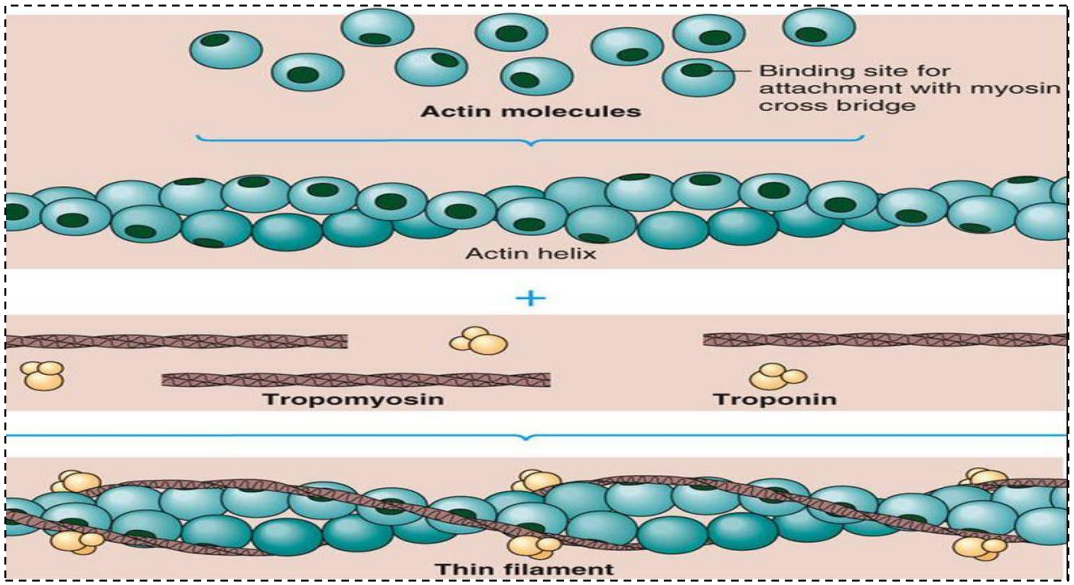
Thin Filament



[Thin Filament]



[Components of Thin Filament]

Thin filament consists of :

- Actin (double helix)

لديه : binding site with myosin [Active site]

- Tropomyosin :

عبارة عن خيط موجود على الـ double helix وتحديداً على الـ Active site

نظراً لأن هذا الخيط قابل للتحرك وغير ثابت , هنالك مكوّن آخر يعمل على تثبيته وهو :

- Troponin :" 3 balls " every ball will be attached to something :

- One ball with Tropomyosin
- One ball with Actin
-One ball with CALCIUM

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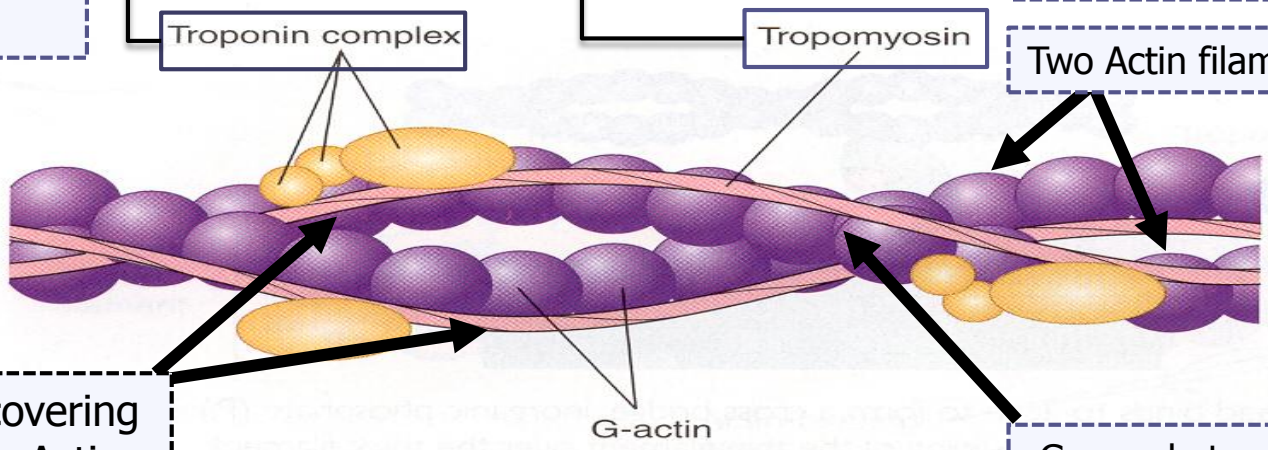
Thin filament

Actin is made of globular protein called G-actin.

3. Tropomyosin lies in the groove between the F-actin strands to cover the active sites on actin that bind the head of myosin.

2. Each two strands wind together to form double helix called Actin Filament

4. Troponin is attached to tropomyosin and to actin



Tropomyosin covering active sites on Actin

1. G-actins are attached together to form F-actin strand (chain)

Groove between the 2 F-actin strands

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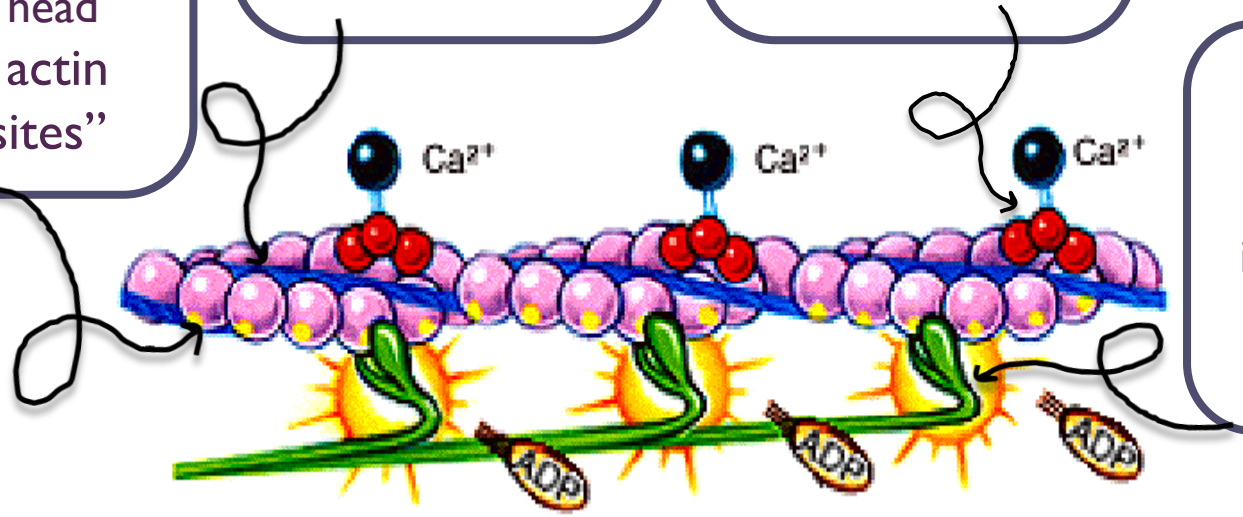
The rule of thin filament in muscle contraction

1- Each G-Actin molecule has a binding site for Myosin head "called actin active sites"

2- These active sites are covered and hidden from the Myosin head by the inhibitory protein Tropomyosin

3-When Troponin is activated by Ca++ it will move the Tropomyosin away from these sites and expose them for Myosin



4- Then myosin head will attach actin active sites immediately lead to formation of "cross-bridge"

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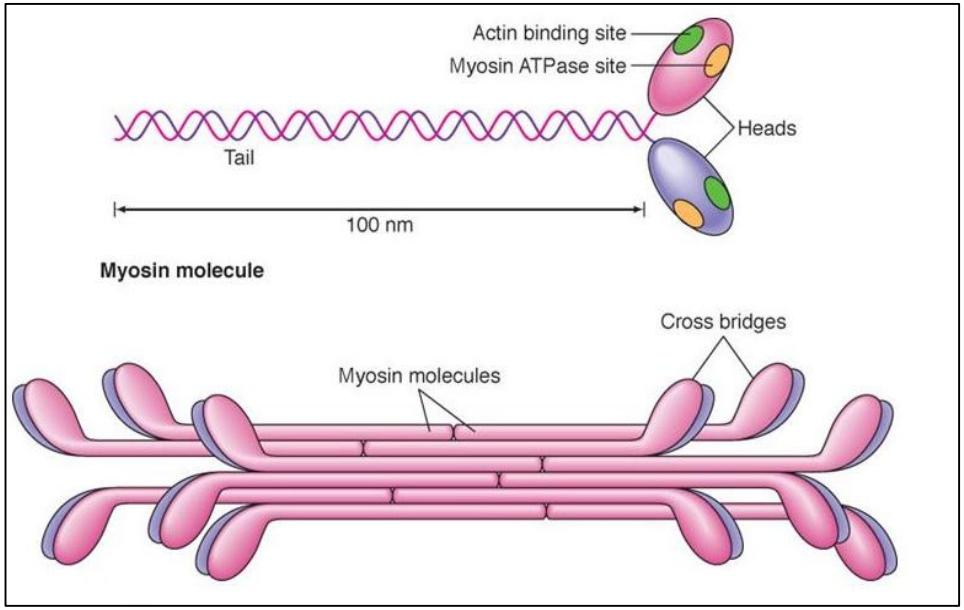
Thick Filament

Thick filaments contain only myosin

each myosin molecule contains :

- Head
- Hinge "joint"
- Tail

Each myosin head contains an ATP binding site as well as ATP-ase enzyme



- Each 200 myosin molecules aggregate to form a myosin filament , from the sides of which project myosin heads In all directions.

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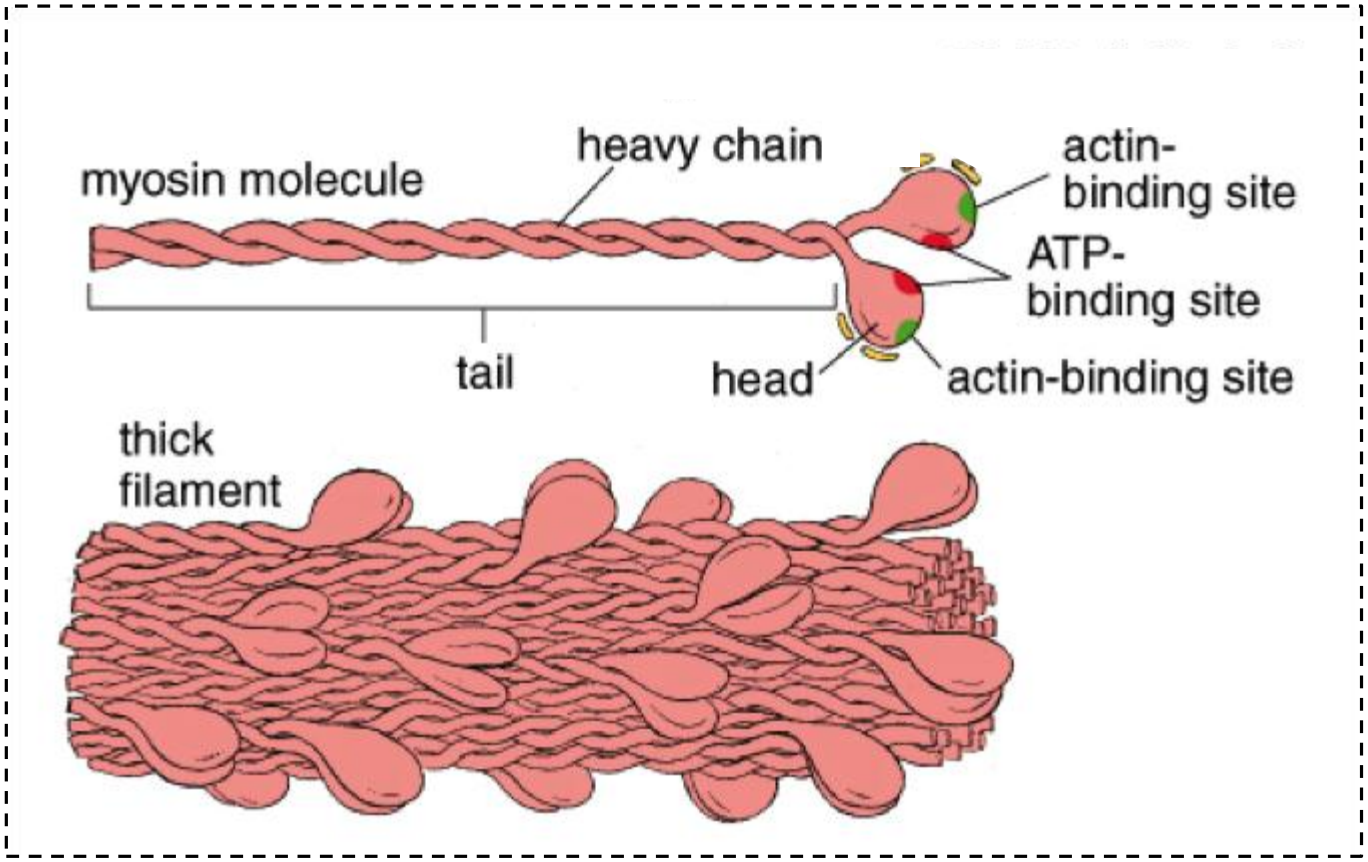


- Myosin tails are arranged to point toward the center of the sarcomere.
- The heads point to the sites of the myofilament band.

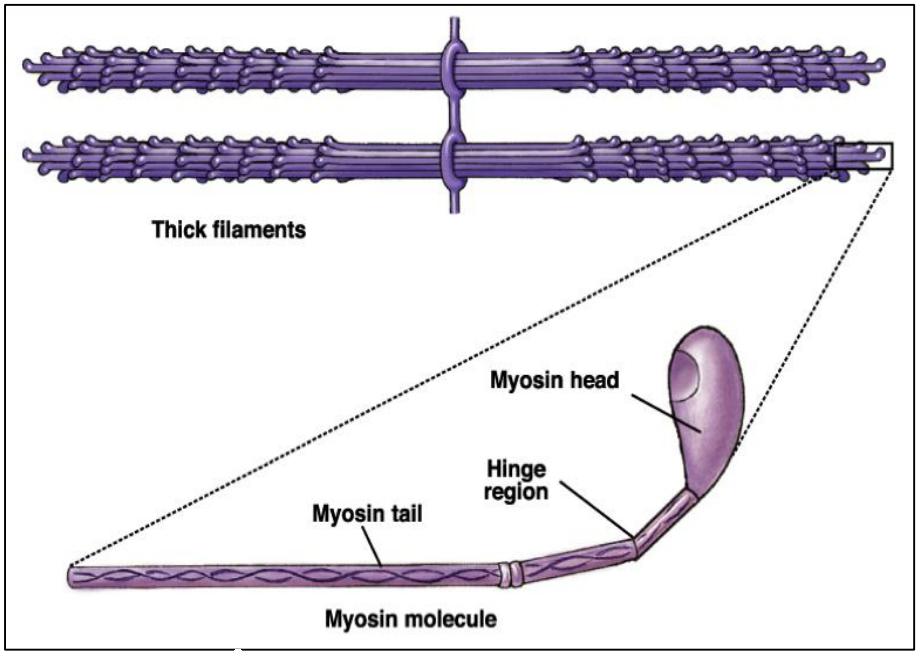
Video

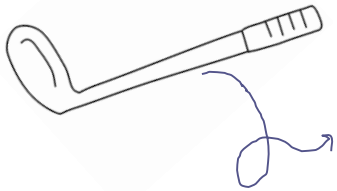
Thick Filament "Extra"

- Thick filament consists of myosin only.
- it has head and tail
- The head is connected to 2 binding sites "2 ears" :

- 1 Ear will be attached to Actin
- and the other will be attached to ATP
  الأذن المرتبطة مع الـ ATP تكون مرتبطة معه بشكل دائم .

- Head contains an enzyme "ATPase" which is responsible of degradation of ATP into (ADP+ phosphate) :
  يخزنهم داخله , مما يعني أن لديه طاقة دائمة كامنة
- Between the head and tail, there is a space called "Arm"





Myosin resembles "Golf stick"

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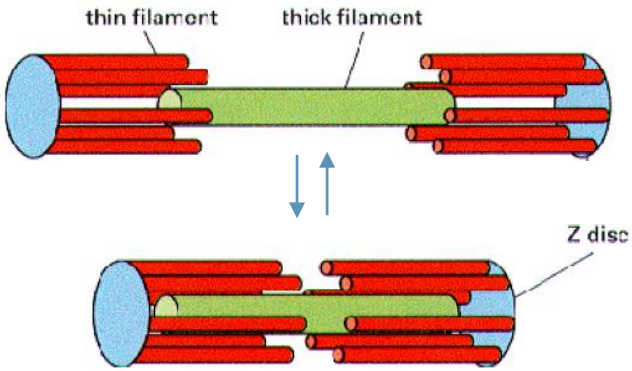
Sliding filament theory

When contraction takes place

Actin & Myosin slide upon each other

So the distance between two z-discs decreases

This process is called : Sliding Filament Mechanism



I-band gets smaller , and eventually may disappear
A-band does not become smaller or bigger

Video

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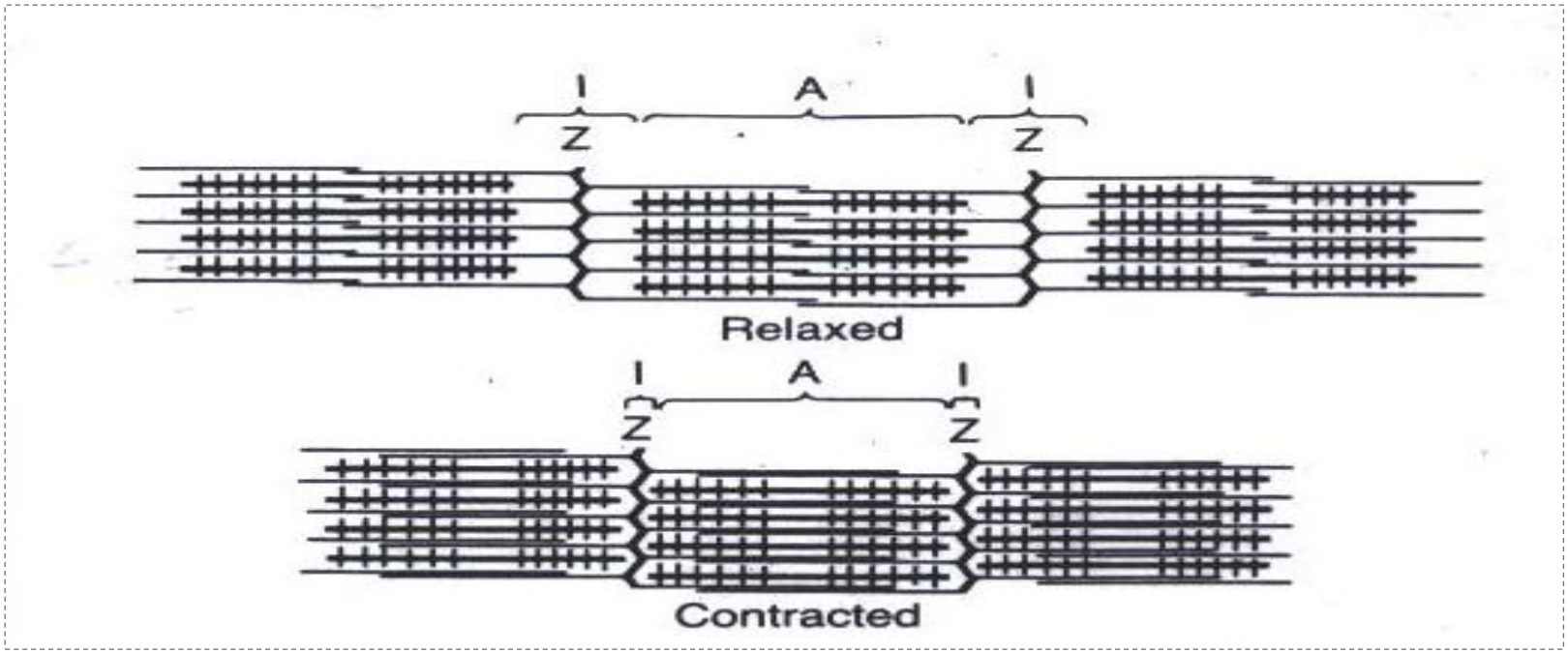
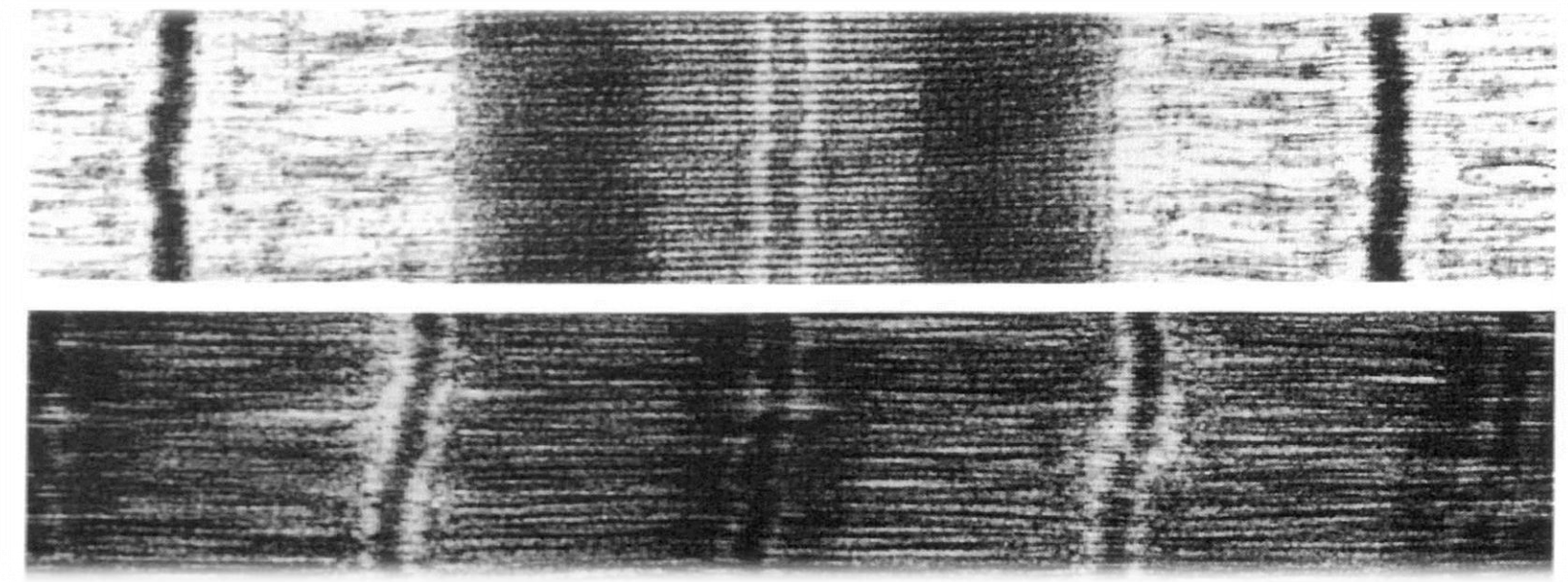
Sliding filament theory



The changes that happened on the length of the bands when there is contraction :
- A band → no changes in length
- I band → be shorter
- H band → be shorter, or even disappear

Video

EM Evidence for Sliding Filaments



"During muscle contraction the actin and myosin filaments do not shorten but they slide past each other"

Sliding filament theory: sliding of A & I bands
without shortening of FILAMENTS. "Actin & Myosin"

Video

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Overview about the mechanism of muscle contraction

Our hero here is calcium, so once the calcium binds to troponin conformational change takes place :
troponin : يغير مكان الـ **Tropomyosin** ويرفعه لأعلى بالتالي يجهّز الـ Active site للارتباط مع الميوسين

- myosin will come and bind with the actin since the active site of actin is exposed now
- مجرد ارتباط الأكتين مع الميوسين ليس بانقباض ولكنه خطوة مبدئية للعملية
- متى يبدأ الميوسين باستخدام الطاقة المخزنة لديه ؟ عند ارتباطه مع الأكتين
- Right after myosin bind with actin, the myosin will use the energy that's stored inside it by change it from chemical to mechanical and release the (ADP+P) .
- When (ADP+P) are released ,the head of myosin will bend > this movement is called [power stroke].
- مع كل Power stroke نستخدم كالسيوم جديد
- To detachment the actin from the myosin we need a new ATP
- نحتاج ATPجديدة لفصل الأكتين عن الميوسين ثم يرتبط الميوسين مع أكتين آخر
- في حال عدم وجود ATP جديدة , لن ينفصل الأكتين والميوسين وستستمر العضلة منقبضة
- In this stage the myosin become active again so it bind to another actin and "cycle repeated"

- [The story from the beginning]:

The acetylcholine will be released from axon terminal and bind to the receptors in the end plate
This binding will open Na+ gated channel and start end plate potential
Once the Na+ is enough then the action potential start "one of its properties that it's propagate / the action potential to reach the inside muscle it need the T-tubule which transfer the action to the sarcoplasmic reticulum"
[The importance of T-tubule is to make the whole muscle contracted "deep contracted"]
So it will reach the sarcoplasmic reticulum and open the Ca++ gated channel "the Ca++ here doesn't need ATP" because it's from high to low concentration
Then the Ca++ will bind to actin so the active site will exposed and the myosin will come and bind to actin
And this cycle will complete , the muscle still contract until we remove the Ca++ by ATP
To complete the contraction we need stimulus every second to stimulate the action potential to release Ca++

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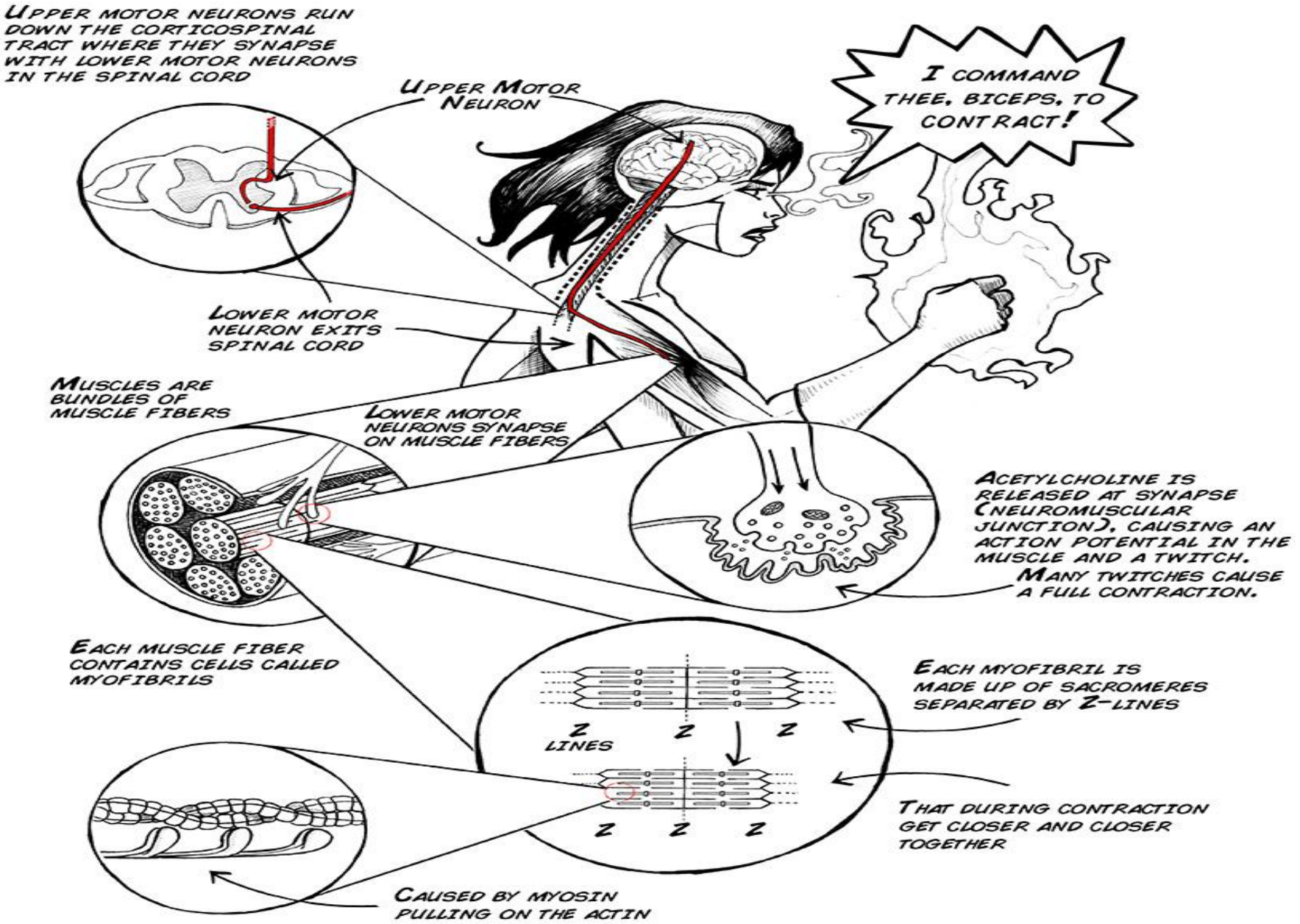
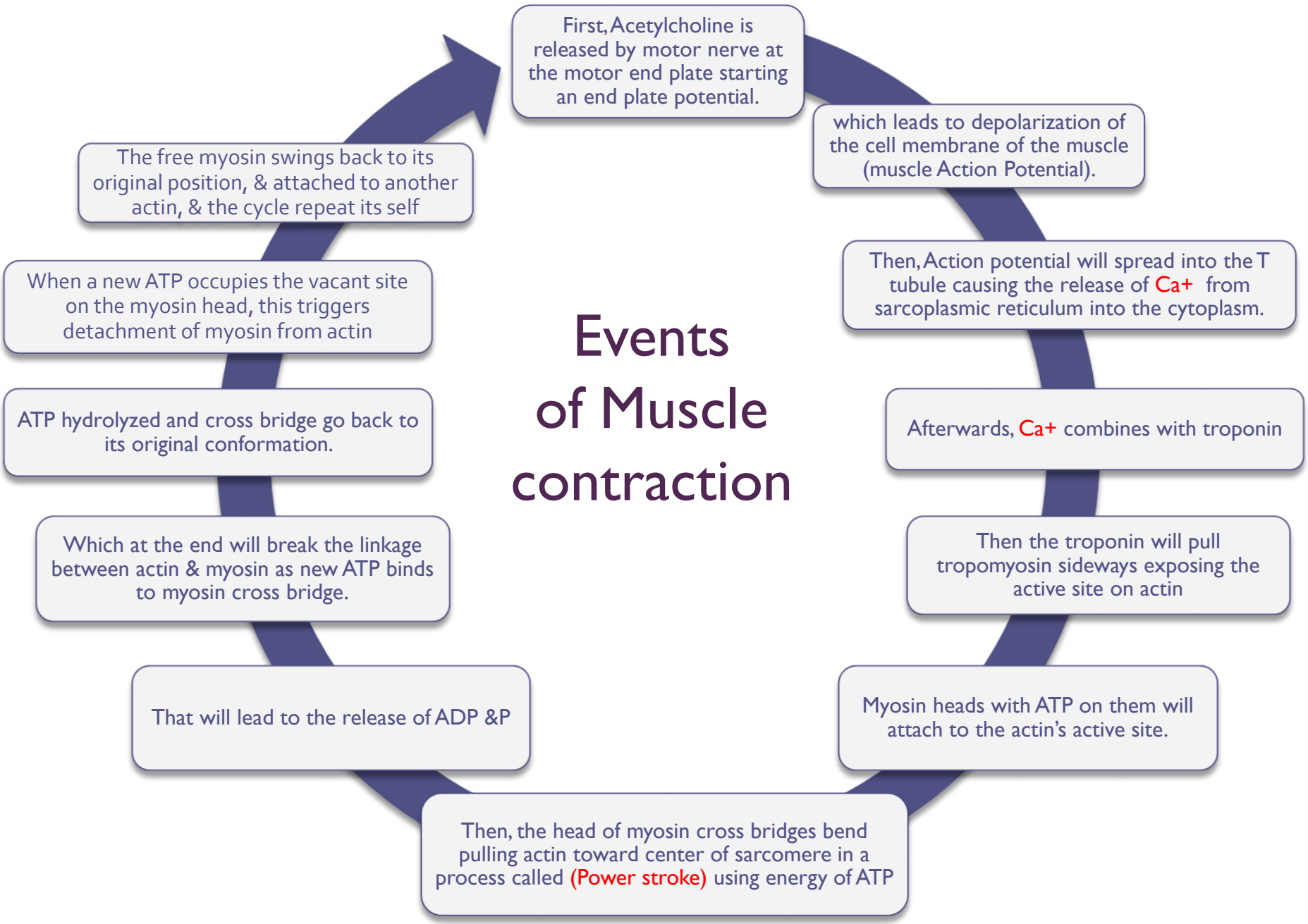

Upper motor neurons run down the corticospinal tract where they synapse with lower motor neurons in the spinal cord
Upper Motor Neuron
I command thee, biceps, to contract!
Lower motor neuron exits spinal cord
Muscles are bundles of muscle fibers
Lower motor neurons synapse on muscle fibers
Acetylcholine is released at synapse (neuromuscular junction), causing an action potential in the muscle and a twitch. Many twitches cause a full contraction.
Each muscle fiber contains cells called myofibrils
Each myofibril is made up of sacromeres separated by Z-lines
Z lines
Z
Z
Z
Z
Z
Z
That during contraction get closer and closer together
Caused by myosin pulling on the actin

Events of Muscle contraction



Muscle contraction

1- The EPP at the motor end-plate triggers a muscle AP

2- Muscle AP spreads down inside the muscle through the Transverse Tubules **(T-tubules)** to reach the Sarcoplasmic Reticulum.

3- In the SR "sarcoplasmic reticulum" the muscle AP opens calcium channels (in the walls of the SR) calcium passively flows out (by concentration gradient) of the SR into muscle cytoplasm then Ca++ combines with Troponin

4- The activated troponin pulls the inhibitory protein tropomyosin away from the myosin binding sites on actin → and once these sites on Actin are exposed (uncovered) → myosin heads quickly bind to them.

5- This binding activates the enzyme ATPase in the Myosin Head → it breaks down ATP releasing energy → which is used in the "Power Stroke" to move the myosin head.

Power stroke : tilting of the cross-bridge head (myosin head) and dragging (pulling) of actin filament

* نفس الخطوات السابقة لكن تم شرحها مرة أخرى في السلايدات بصياغة مختلفة

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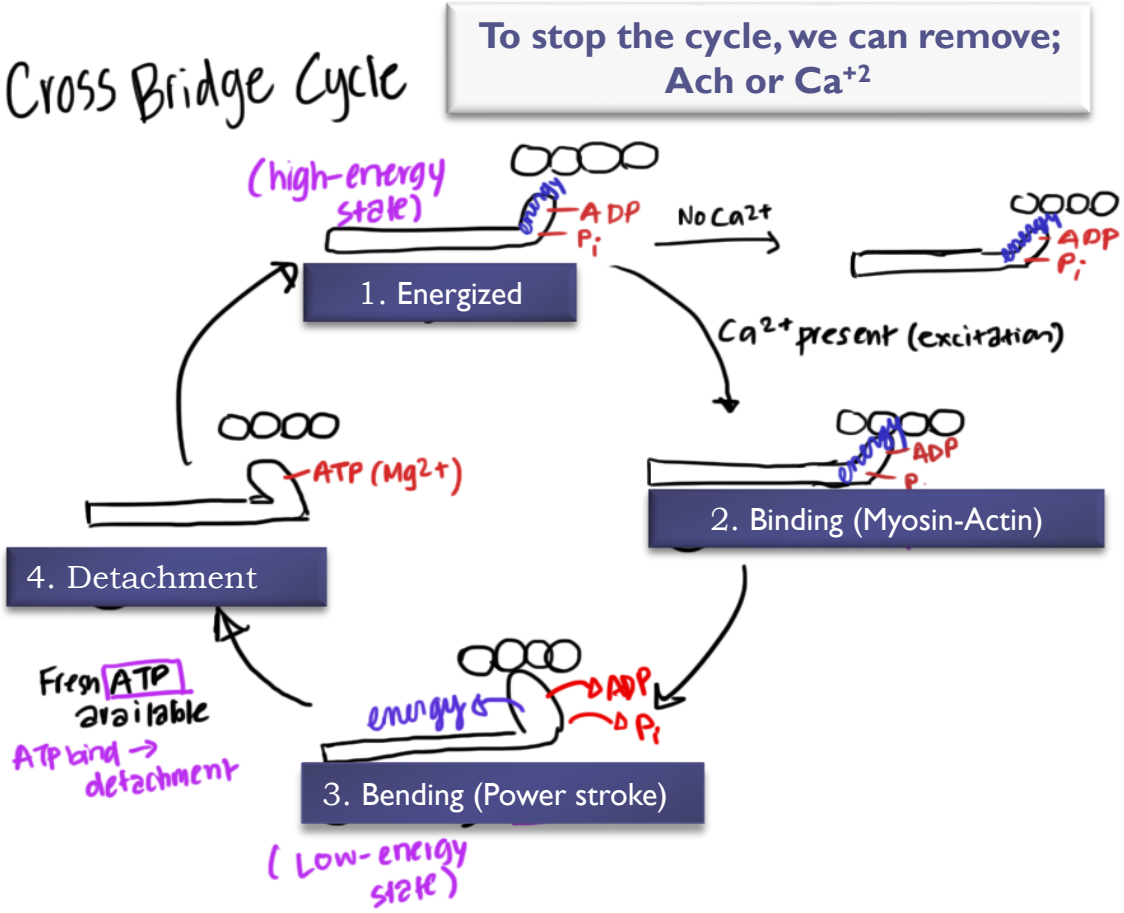
The Cross-Bridge Cycle



Video

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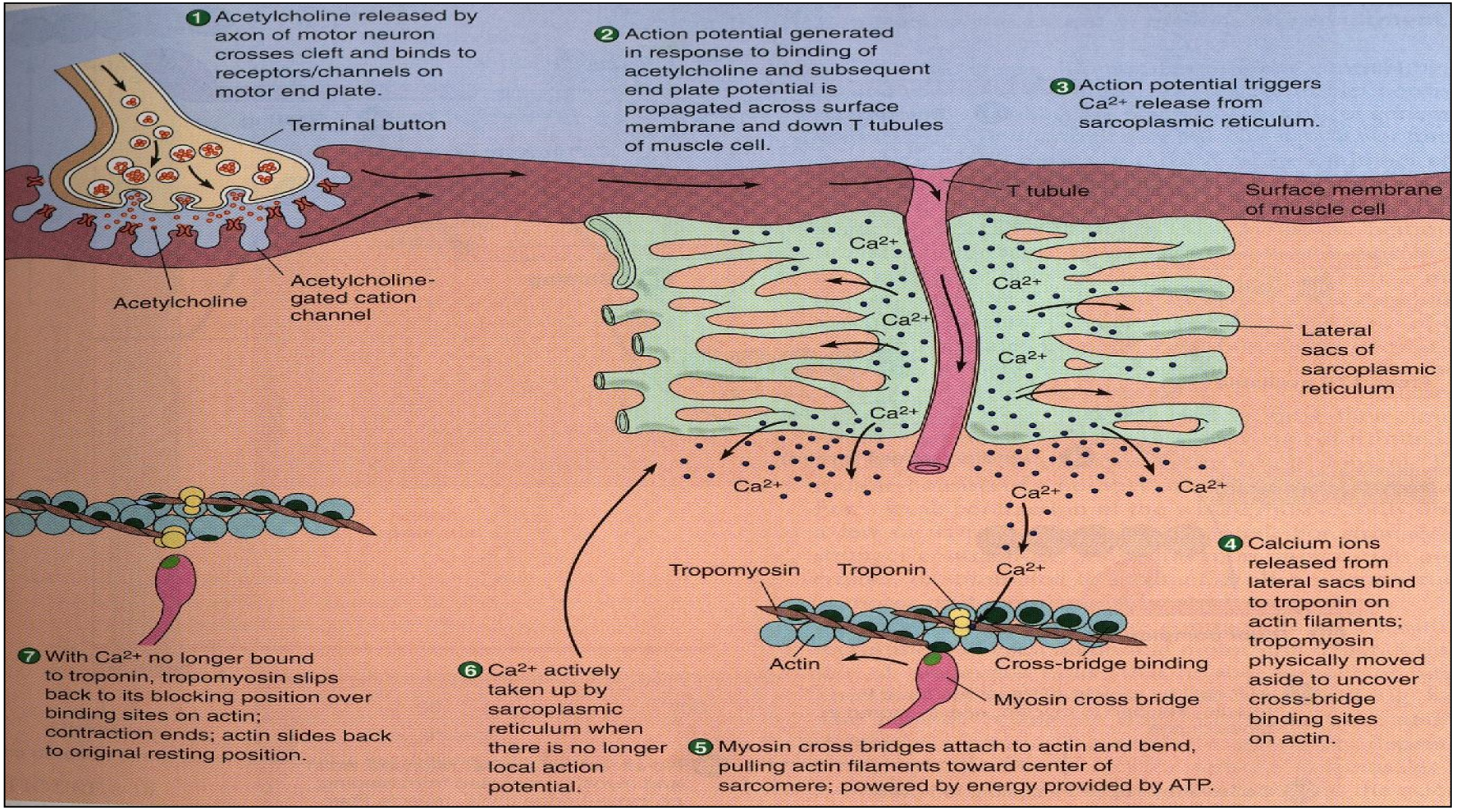
Molecular Mechanism of Muscle Contraction
"Excitation – Contracting coupling"



The sequence of events that convert action potentials in a muscle to contraction is known as Excitation – Contracting coupling mechanism.

Overview about the mechanism of muscle Relaxation

First we have to know that if : No calcium = No contraction
That means we need to remove calcium if we want the muscle to relax. How ?

- To stop the cycle of contraction and start relaxation we need to detachment the Ca++ which bind to the troponin, because with present of Ca++ the active site of actin exposed and the myosin already has energy and ready to bind .
  [No AP > relaxation "يحتاج طاقة لإعادة الكالسيوم"]
- Tropomyosin return to its original position
- Tropomyosin inhibit contraction "لازم نرفعه عن مكانه عشان يصير الكونتراكشن"
- Calcium will go back to Sarcoplasmic reticulum through calcium pump "from low to high" which requires energy
- No calcium = No contraction , No AP = No Ca++ outflux , No excitation = No calcium

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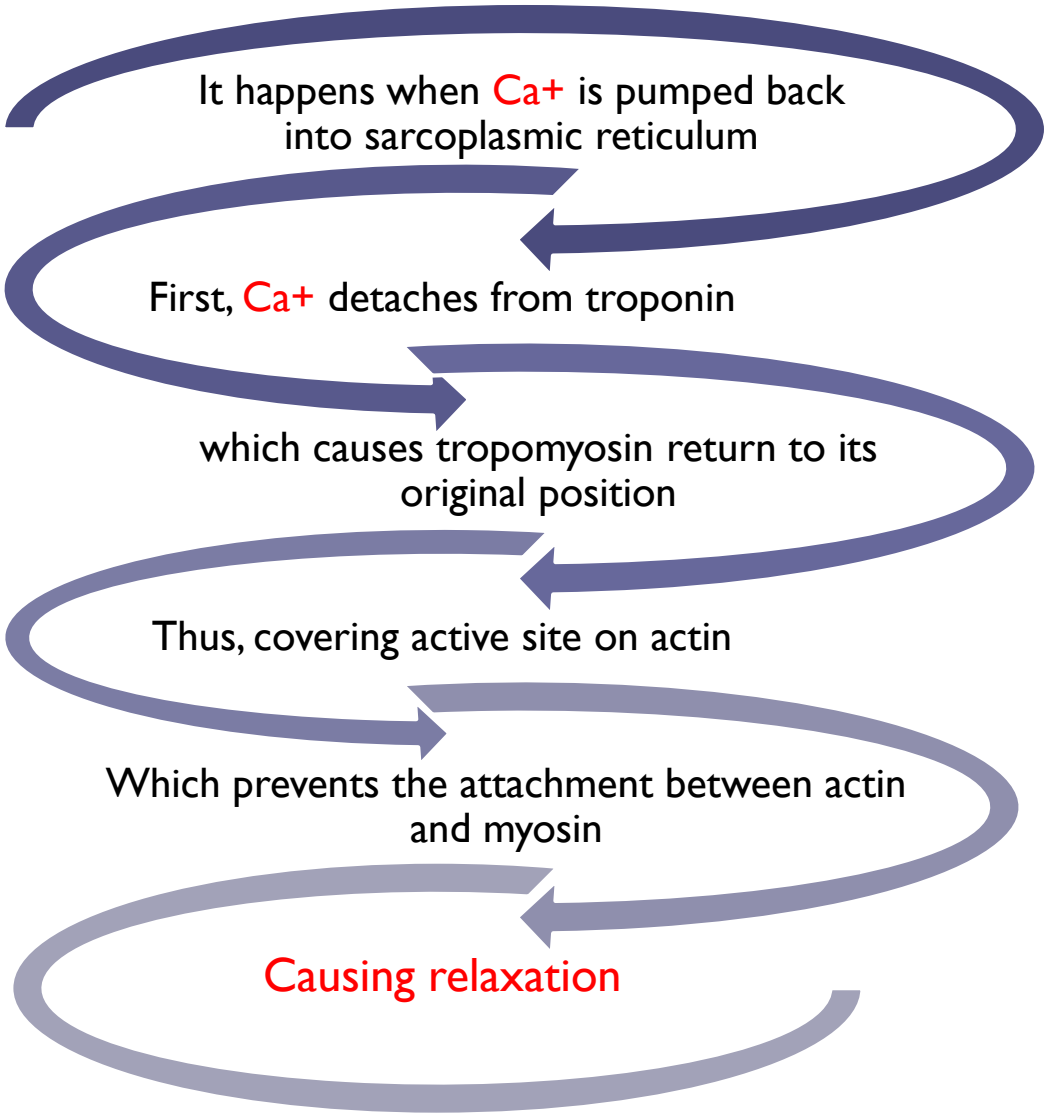
Events of Muscle relaxation



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Comparison

Muscle Fiber Contracted	Muscle Fiber Relaxed
• There is cross-bridge binding	• No cross-bridge binding
• Active site on Actin exposed	• Active site on Actin covered
• There is a power stroke due to binding of actin with myosin.	• No power stroke because troponin-tropomyosin complex covers the Actin's active site

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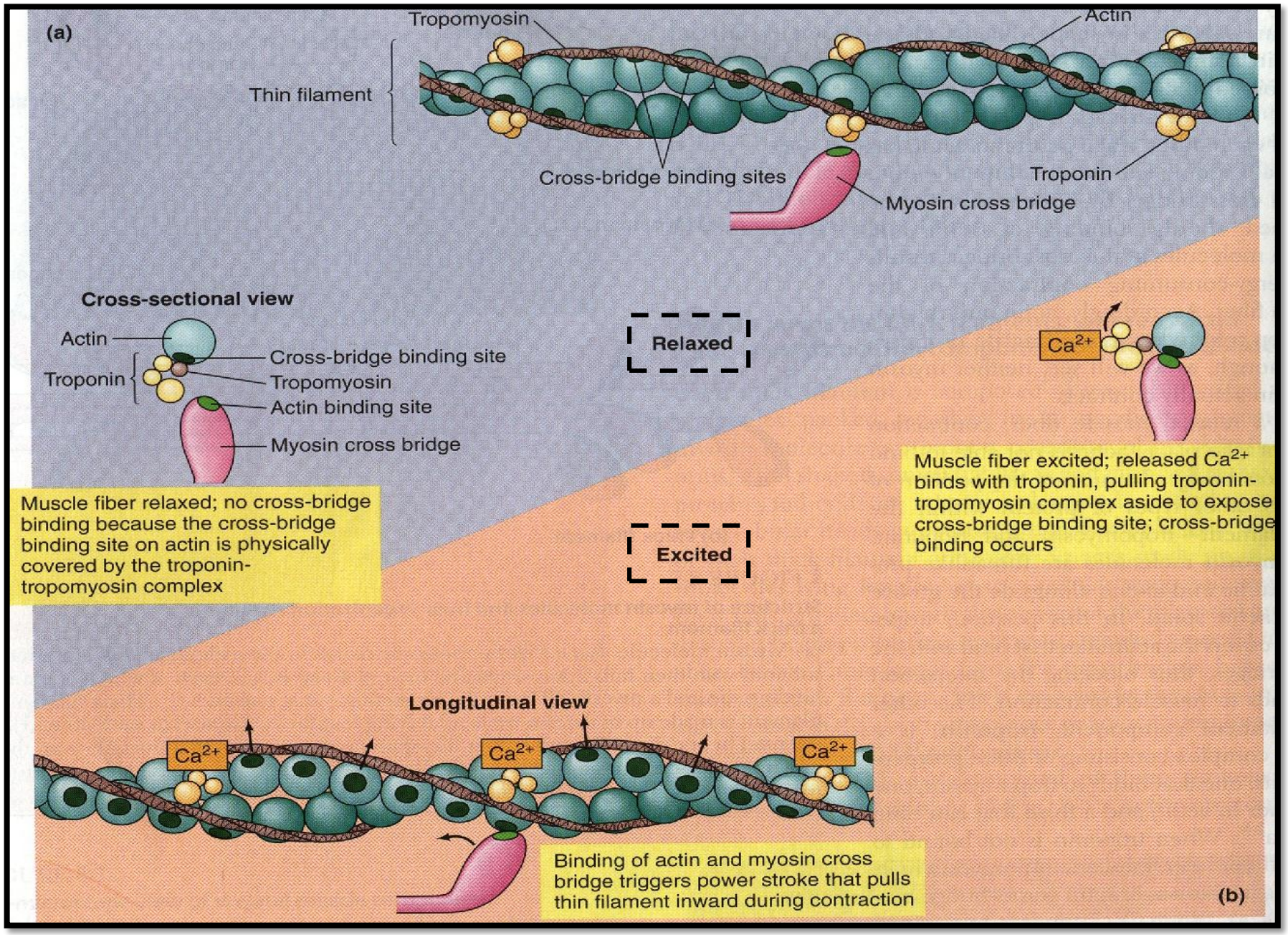

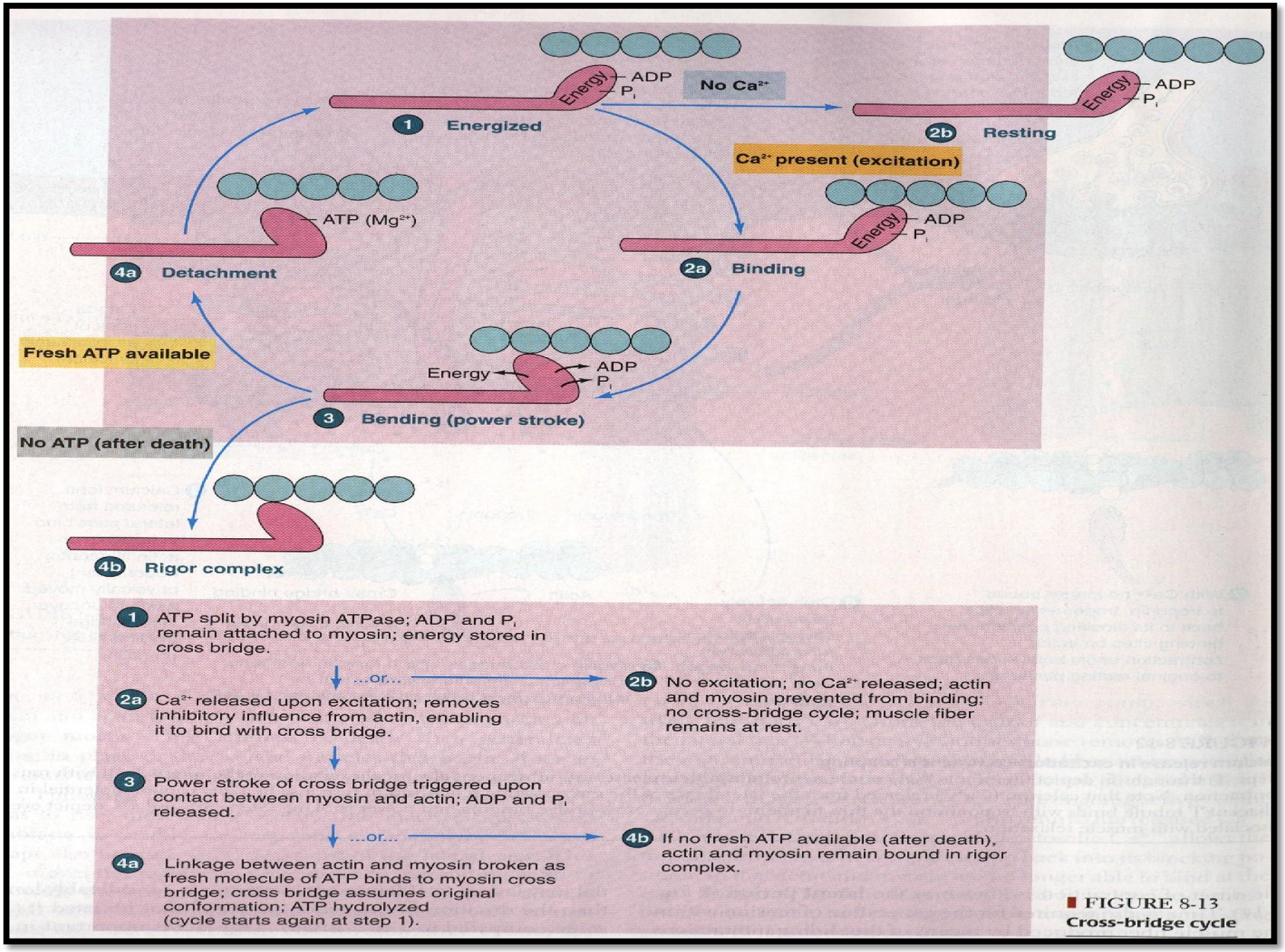

FIGURE 8-13
Cross-bridge cycle

Summary

1. Muscle AP spreads through T-tubules
2. it reaches the sarcoplasmic reticulum where → opens its Ca++ channels → calcium diffuses out of the sarcoplasmic reticulum into the cytoplasm → increased Ca++ concentration in the myofibrillar fluid.
3. Ca++ combines with Troponin , activating it .
4. Troponin pulls away Tropomyosin
5. This uncovers the active sites in Actin for Myosin
6. Myosin combines with these sites.
7. This causes cleavage (breakdown)of ATP and release of energy
8. This released energy that used to produce Power Stroke
9. Myosin and Actin slide upon each other → contraction
10. A new ATP comes and combines with the Myosin head → this causes detachment (separation)of Myosin from Actin .
11. Therefore , on order to release the head of Myosin from Actin , a new ATP is needed to come and combine with the head of Myosin .

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Important points

*What is Rigor Mortis ?

Rigor mortis : several hours after death, all muscles of the body do into a state of contracture called "rigor mortis" that means the muscles become contract and rigid. The rigidity results from loss of all ATP which is required to cause separation of the cross-bridges from the actin filaments during the relaxation process.
"مثال : الشخص الذي يموت وهو مبتسم"

*ATP is needed for 3 things : what are they ? "VERY IMPORTANT"

ATP is needed for **3** things :

(1) Power stroke
(2) Detachment of myosin from actin active sites
(3) Pumping C++ back into the Sarcoplasmic reticulum

*Is muscle relaxation a passive or active process ?

it is active ; Why ? Because it needs ATP through pumping of Ca^{+2} back into SR.

Important points

***What happens to A-band and I-band during contraction ?**

- I-Band gets smaller (may disappear)
- A-Band doesn't change (not become smaller or bigger)

***Ca++ is needed in nerve & muscle : when and where ?**

- In nerve → needed for exocytosis and release of Ach.
- In Muscle → needed for contraction .

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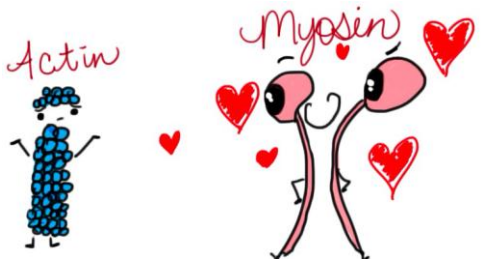
QUIZ1 & QUIZ2



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