Editing file

Physiology of muscle contraction

•Red : important
•Black : in male / female slides
•Pink : in female slides only
•Blue : in male slides only
•Green : notes
•Gray : extra
•Guyton

Objective

- The general mechanism of skeletal muscle contraction
- how excitation-contraction coupling are generated in skeletal muscle
- ▫ The molecular mechanism of skeletal muscle contraction & relaxation
- ▫ Sliding filament mechanism.

Histology of muscle

From Guyton
Sarcoplasmic reticulum is composed of two major parts ;
1- large chambers called **terminal cisternae**
2- long longitudinal that surround all surfaces of the actual contracting myofibrils
See the figure in the next slide

- Each muscle fiber is covered by **Sarcolemma**
- Each muscle cell (fiber) contain thousands of **Myofibrils**
- Myofibrils contain **Actin filaments (thin)** & **Myosin filaments (thick)** which make the dark band (A-band) and light band (I-band)
- **Sarcoplasm** the matrix inside muscle fiber in which myofilaments suspended
- **Sarcoplasmic reticulum** is endoplasmic reticulum inside sarcoplasm full of Ca

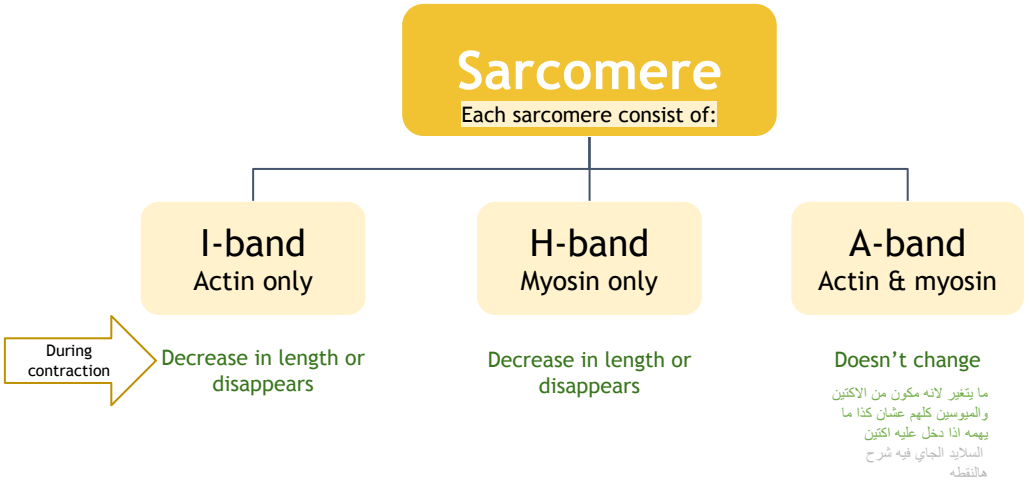
  Function to storage Calcium we need for contraction ; Sarcoplasmic reticulum=specialized endoplasmic reticulum for muscle cell
- **T-tubules** extend from one side of muscle to other to transmit the AP to the interior part of the muscle each sarcomere has two T-tubule located at the A-I bands junction

Histology of muscle

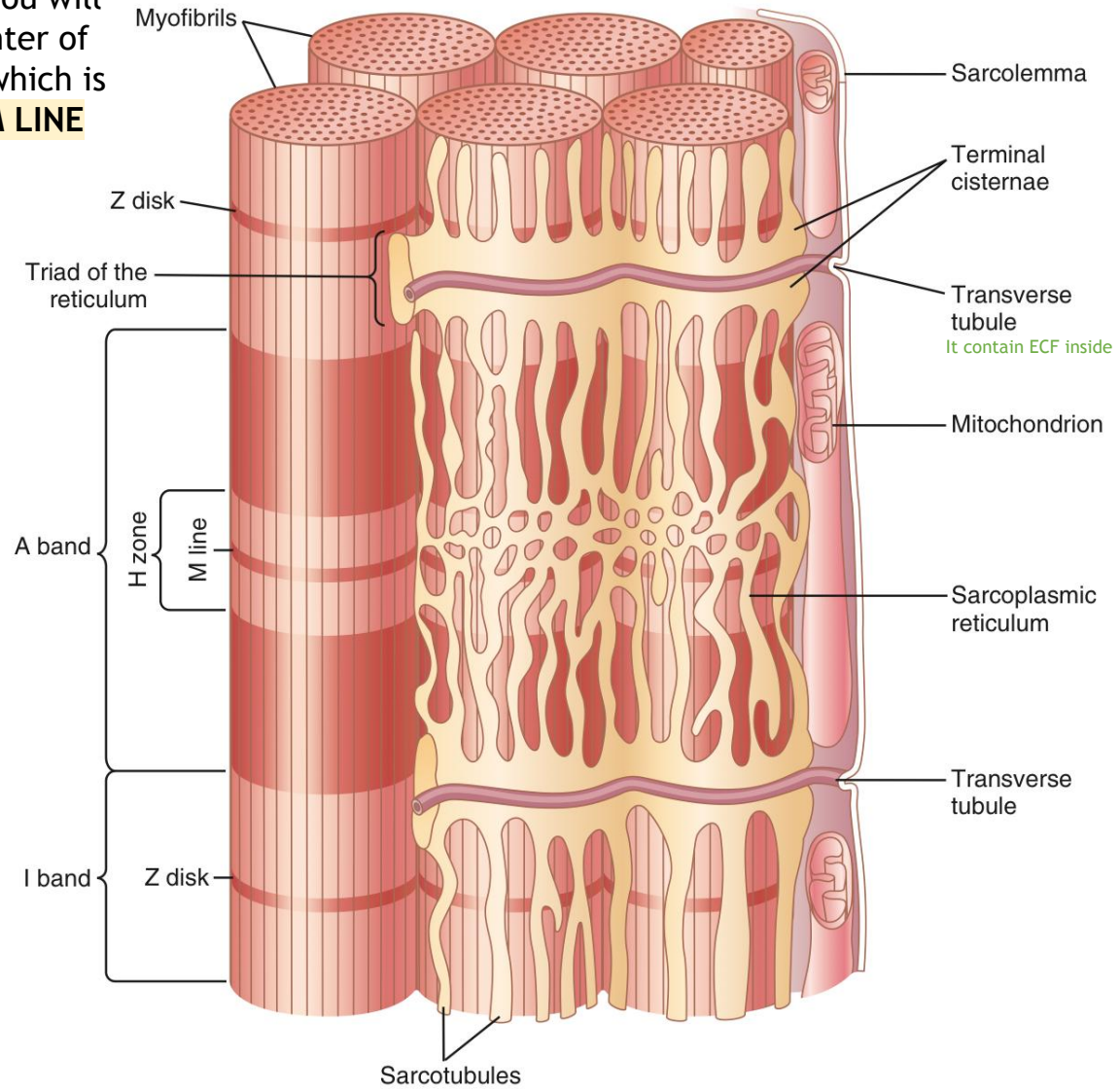
The functional unit of muscle is Sarcomere:

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



In the middle of a sarcomere you will find the Center of sarcomere which is called the **M LINE**



What is the function of muscle ? **To contract** ,so because of that we name the sarcomere as the functional unit = contractile unit because it's the responsible for contraction

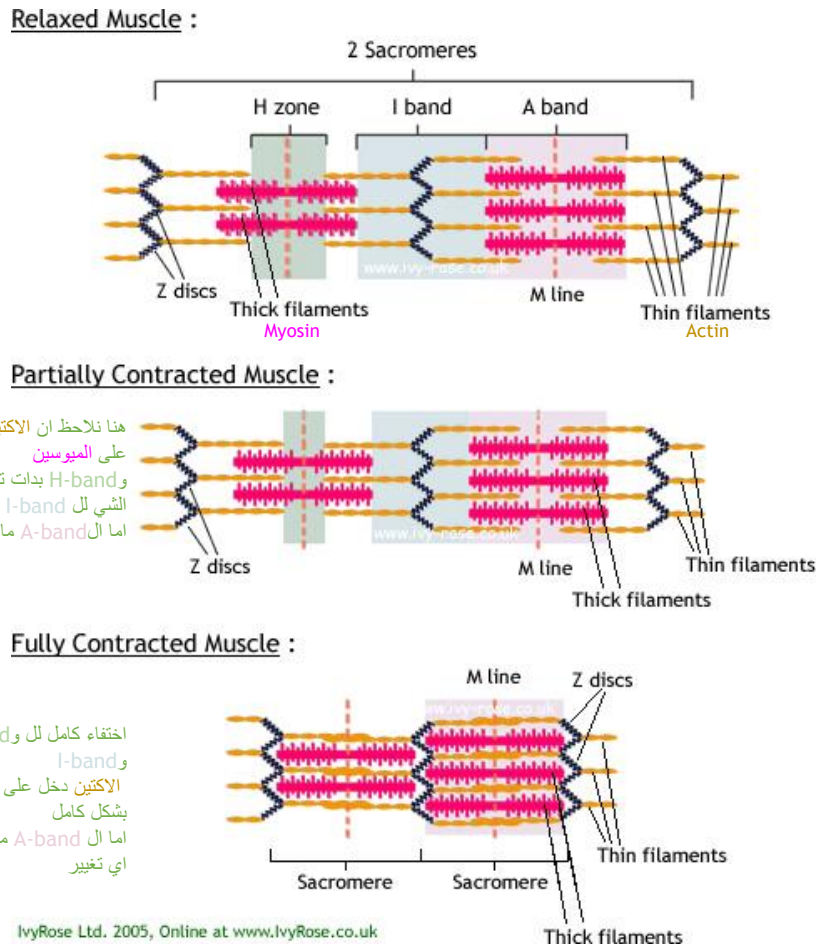
Note :-
Filaments: the actual proteins (Actin & myosin) and it doesn't change in length at all
Bands: the region in sarcomere contain the proteins

Overview of muscle contraction

Mechanism of muscle contraction: sliding filaments mechanism

When contraction take place Actin slides over myosin and the distance between two Z-discs decreases —> sarcomere decrease in length

Dr. Mohammed notes
the myosin does not move انتبه



In this way when each sarcomere contract and decrease in length the whole myofibril will contract due to a nerve signal

From Guyton:

I bands because they are isotropic to polarized light.

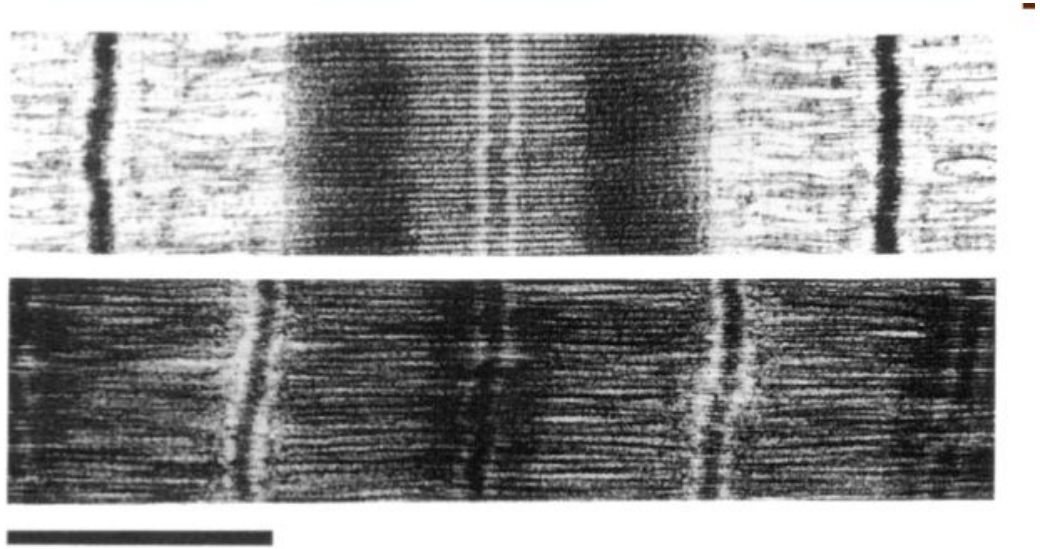
A bands because they are anisotropic to polarized light.

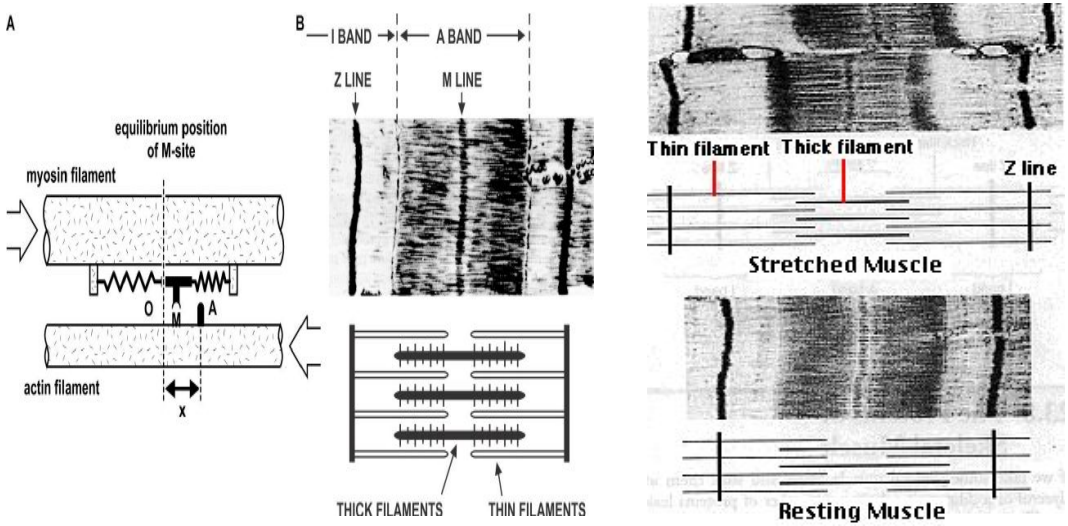
...

Titin a protein that act as a framework that holds the myosin and actin filaments in place so that the contractile machinery of the sarcomere will work.

<<— Dr. Mohammed notes: not important

EM Evidence for Sliding Filaments





Sliding Filament structure

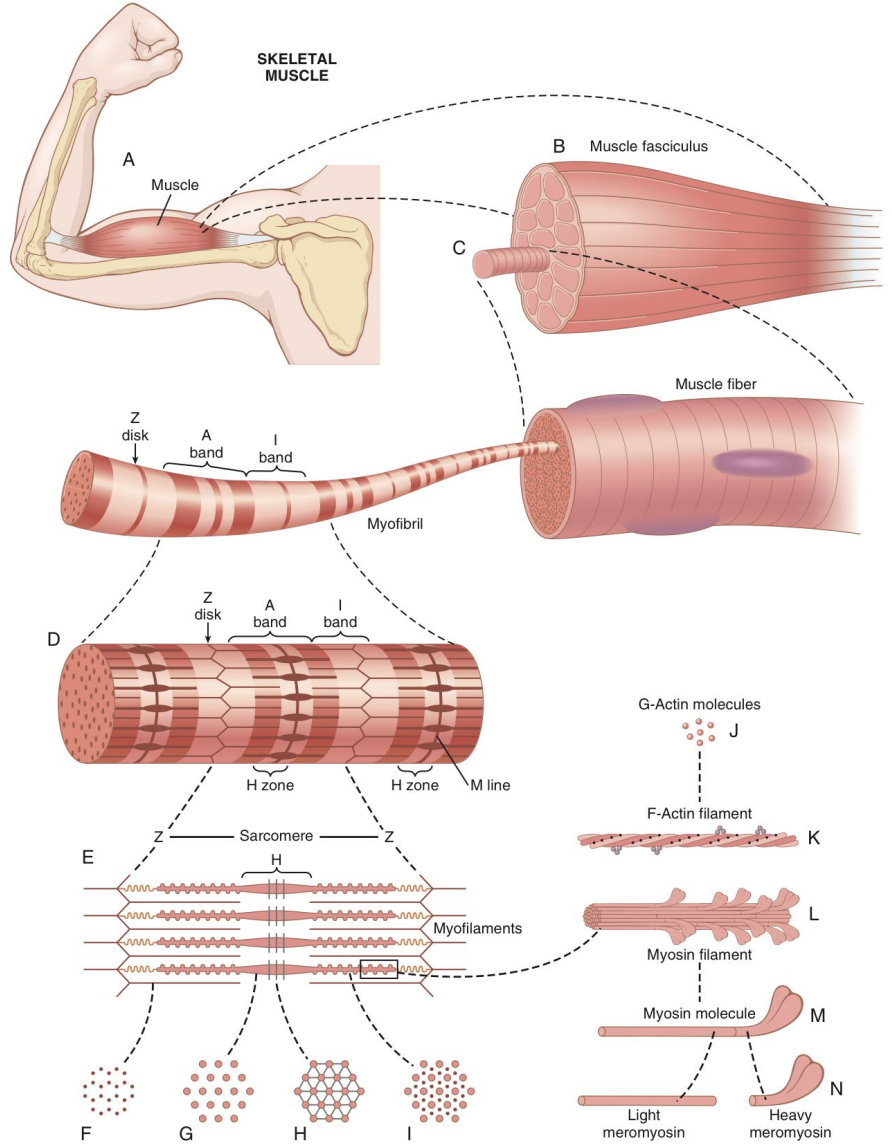


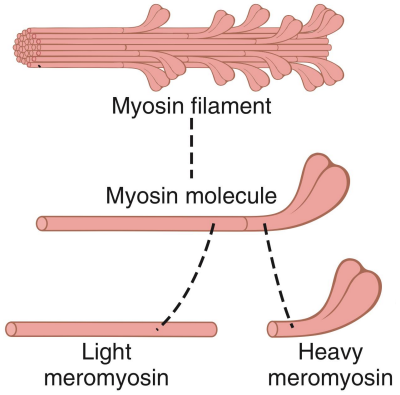
Figure 6-1. Organization of skeletal muscle, from the gross to the molecular level. *F, G, H,* and *I* are cross sections at the levels indicated.

Contraction mechanism

Simple defention of our heroes today ;

الشخصيات الرئيسيه :-

- **Muscle proteins**
  - **Thick filaments**
    - **Myosin**
  - **Thin filaments**
    - **Actin**
    - **Tropomyosin**
    - **Troponin**



See next slide

Two strands of Actin are forming the backbone of thin filament

Actin contain Active sites or binding sites where the myosin head will bind during contraction

Active site = ADP molecule

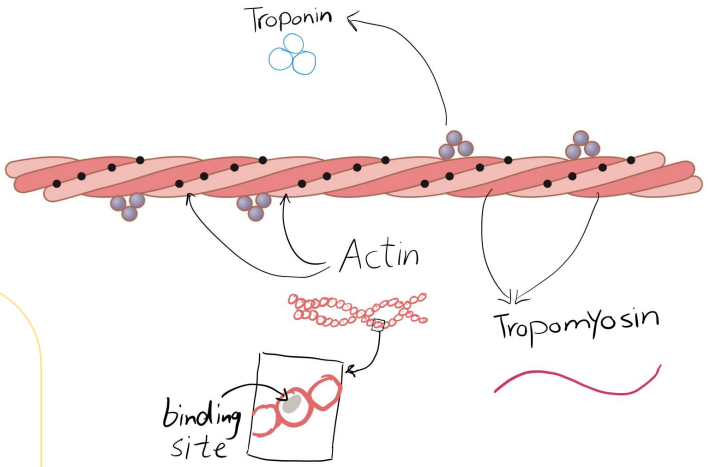
An inhibitory protein

Two strands of tropomyosin are wrapped around Actin above the binding sites in resting state to inhibit contraction

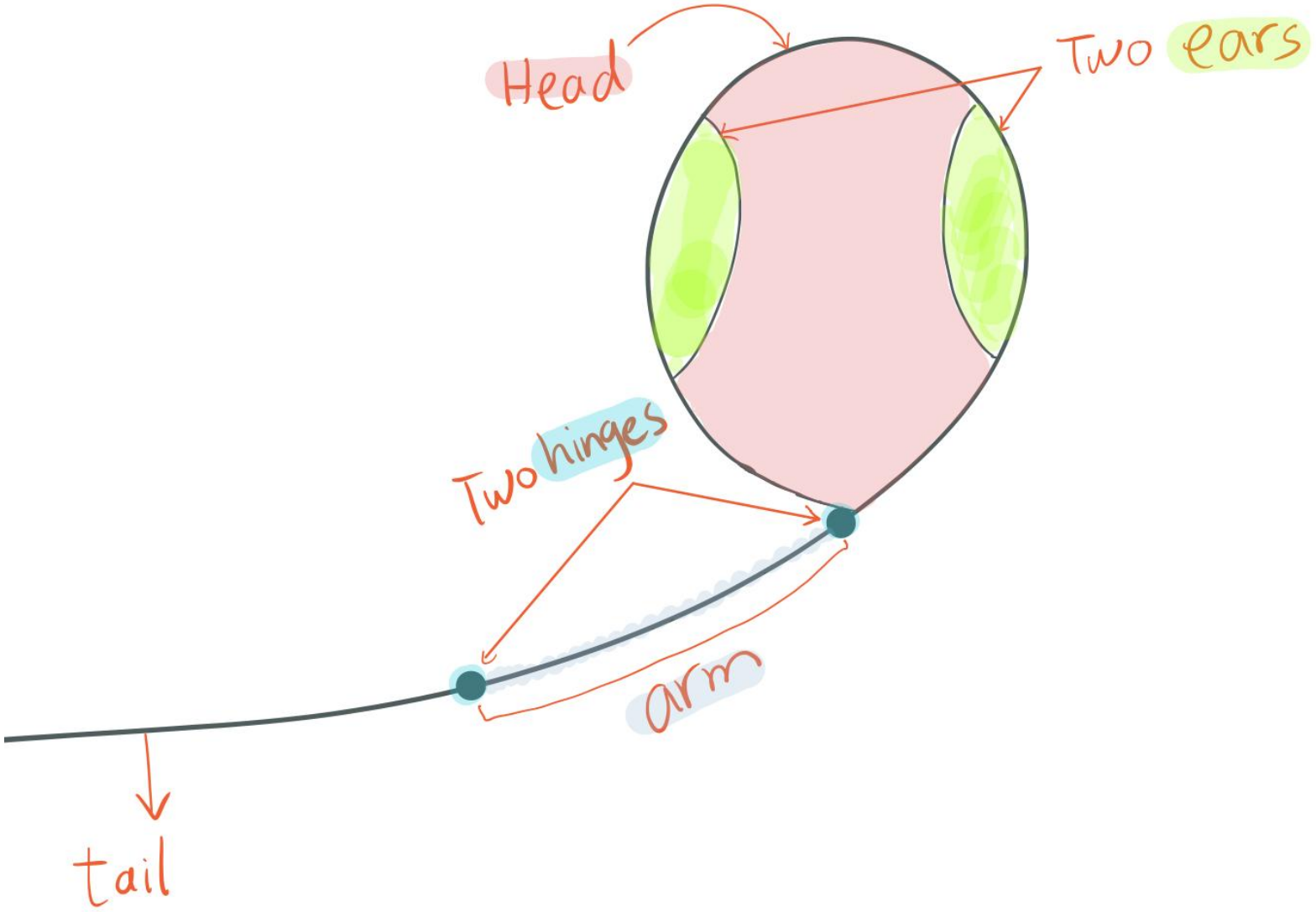
Composed of three bound protein subunits ;

1- bind with Actin
2-bind with tropomyosin
3-bind with calcium ions

يشبه المسمار وظيفته انه يتاكد ان tropomyosinال ثابت على Active sitesال



Thin filaments structure



- Arm + head = cross bridge
- The hinges make the myosin flexible and let it move at the site of arm and head
- Two ears function is to:

One ear to bind with Actin
Other ear to bind with ATP

Myosin structure

تشبه عصا الغولف

Excitation-Contraction mechanism

Helpful video

Excitation

1- Acetylcholine released by motor nerve
2- End Plate Potential
3- depolarization of muscle = AP
4- spread of AP inside muscle by T-tubule
5- the release of Ca ++ into sarcoplasm

Because AP is transmitted by T-tubule next to Sarcoplasmic reticulum, The AP stimulate Sarcoplasmic reticulum to release Ca by the opening of voltage gated Calcium channels with concentration gradient

⇐

عشان كذا الt-tubule مكانها جنب مخزن الكالسيوم (sarcoplasmic reticulum)

The calcium is البطل الرئيسي of our contraction story

- Contraction starts when Ca is present
- Contraction stops (relaxation) when Ca is absent

Contraction

6- Ca++ combines with troponin and cause conformational change
7- troponin pull tropomyosin sidaway from Actin active sides
- now Active sites are uncovered and Actin is free
8- myosin head attach to actin active site immediately

Myosin is already activated by ATP and waiting for Actin to be free

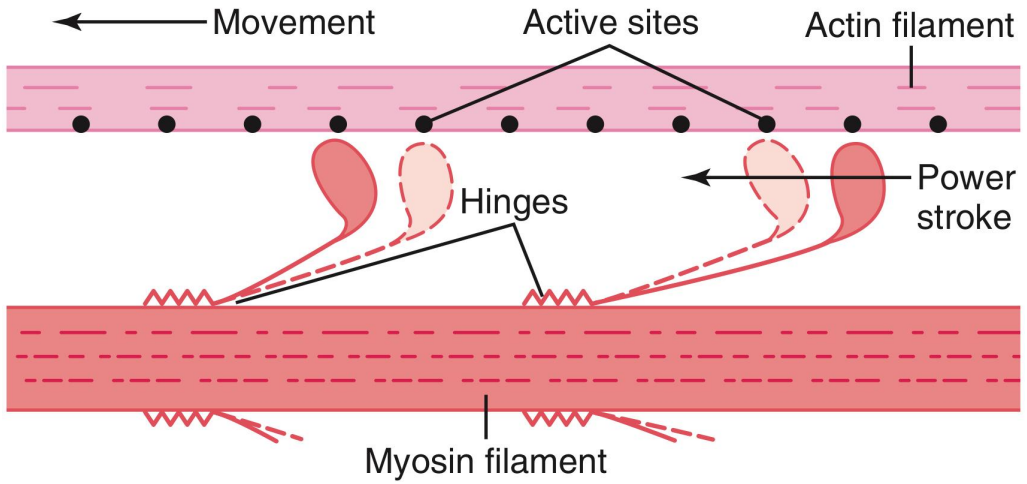
How is Myosin activated ?
There is an enzyme called Esterase floating in the head of myosin
This enzyme function is to break the high energy bond of ATP to get a phosphate and ADP molecule (this process provides the needed energy) ,so the activated myosin is attached to ADP+phosphate

Continued ..

Helpful video

9- myosin cross bridge (head + arm) bend pulling actin toward the centre of sarcomere (powerstroke) using the energy of ATP
10- ADP & phosphate released
11- linkage between actin & myosin broken as new ATP binds to myosin
12- a new ATP hydrolyzed and cross bridge go back to its original conformation and this detachment myosin from actin
13- the free myosin swings back to its original position, & attached to another actin, & the cycle repeat itself

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

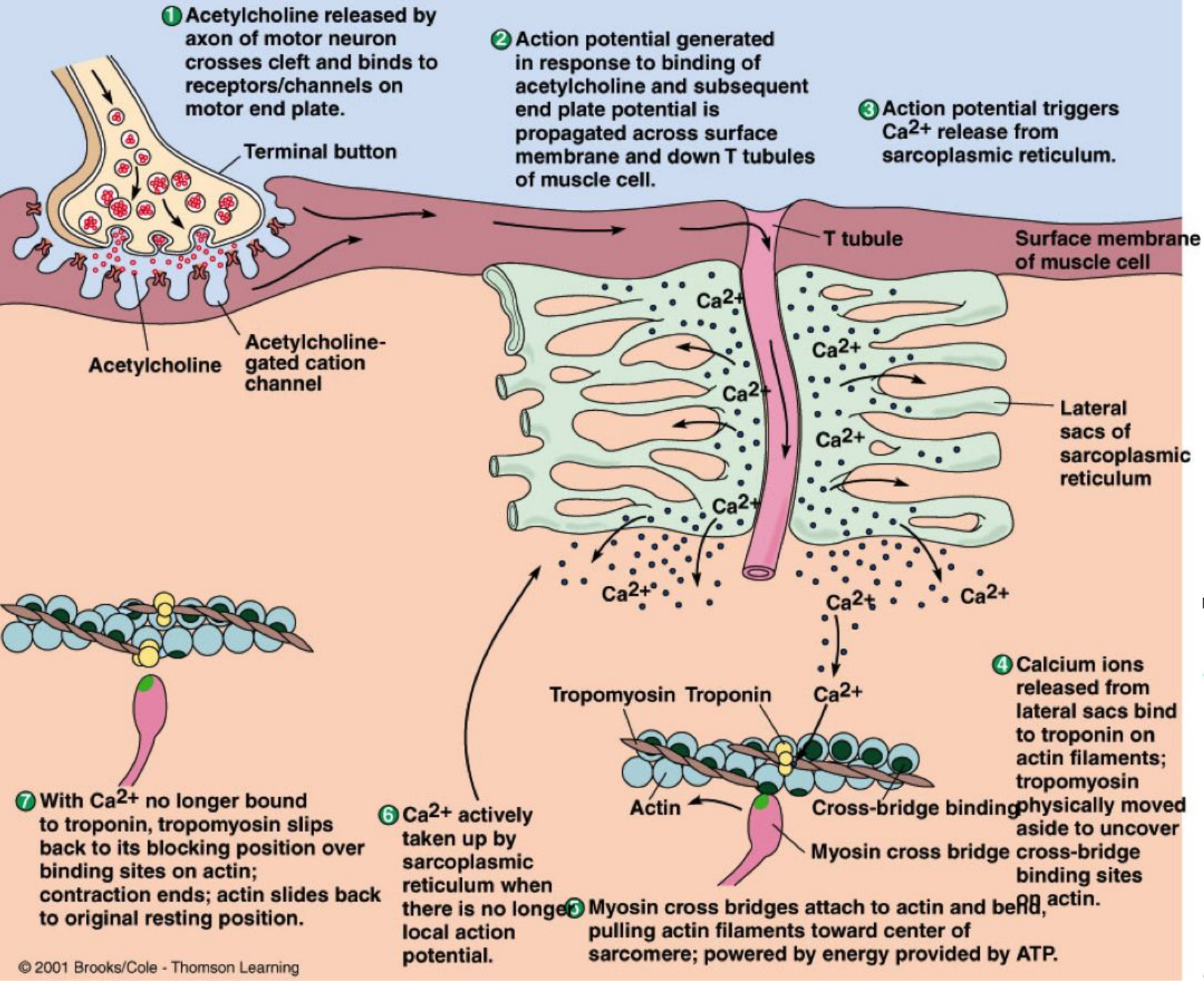


Relaxation

14- Ca is pumped back into sarcoplasmic reticulum
15- when Ca goes, the Active sites will be covered again by tropomyosin
16- relaxation happen

Contraction	Relaxation
Calcium is present	Calcium is absent
Active sites covered	Active sites Uncovered
myosin & actin are attached	myosin & actin are not attached

The calcium is re-uptake by sarcoplasmic reticulum by calcium pump against concentration gradient when the contraction stops

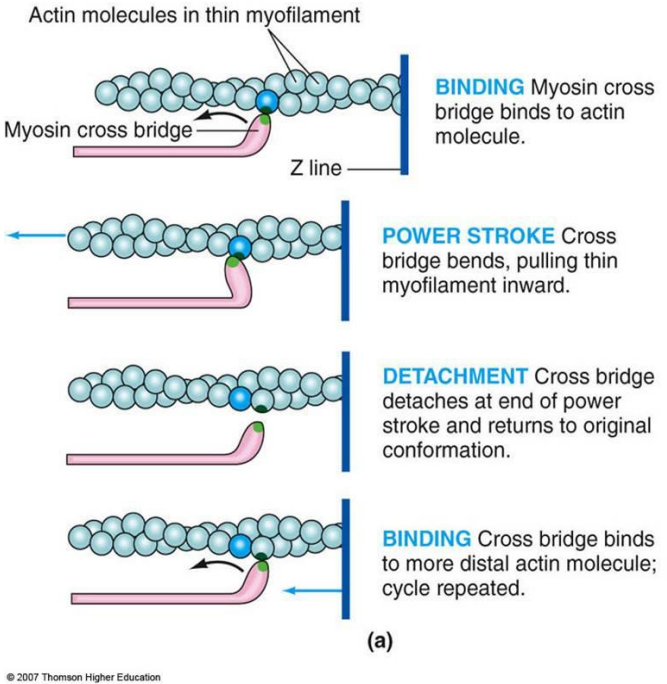


Dr. Mannan note :

How many ATPs are use for each contraction cycle ? **Three**

1- to activate a Myosin to produce power stroke
2- to unbind Myosin from Actin active site
3- to pump the calcium back to SR

Summary

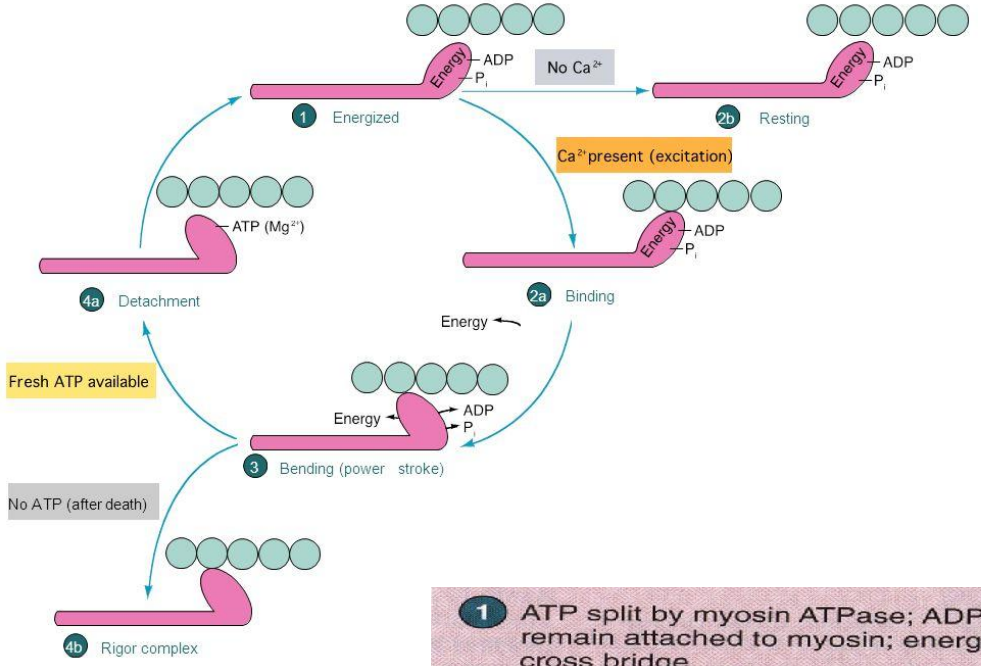


Rigor complex

Rigor complex (mortis)
when Myosin bind to Actin active site during contraction but there is no ATP to unbind them !
This happen after death

عشان كذا بعض الناس يموتون وهم مبتسمين لان العضلات تستمر منقبضة

بس بعد يومين تتحلل البروتينات وبيروح الانقباض



1 ATP split by myosin ATPase; ADP and P_i remain attached to myosin; energy stored in cross bridge.

...or...

2a Ca^{2+} released upon excitation; removes inhibitory influence from actin, enabling it to bind with cross bridge.

2b No excitation; no Ca^{2+} released; actin and myosin prevented from binding; no cross-bridge cycle; muscle fiber remains at rest.

3 Power stroke of cross bridge triggered upon contact between myosin and actin; ADP and P_i released.

...or...

4a Linkage between actin and myosin broken as fresh molecule of ATP binds to myosin cross bridge; cross bridge assumes original conformation; ATP hydrolyzed (cycle starts again at step 1).

4b If no fresh ATP available (after death), actin and myosin remain bound in rigor complex.

From Guyton
(Not included in the slides only for your information)

Energy during muscle contraction

Sarcoplasm have tremendous number of mitochondria supply the contracting myofibrils with large amounts of energy in the form of adenosine triphosphate (ATP) formed by the mitochondria.

What is the sources of energy for muscle contraction ? You will take it more detailed later (L8)

1- **phosphocreatine**

2- **glycolysis of glycogen** stored in muscle

Glycolysis is good because ;

I. it doesn't need oxygen
II. is fast

3- **oxidative metabolism** of cellular foodstuff (the Major source) liberate 95% of energy

Why muscle use energy during contraction ?

- Most of the energy required for muscle contraction is used to actuate the walk-along mechanism

but small amounts are required for

(1) pumping calcium ions from the sarcoplasm into the sarcoplasmic reticulum after the contraction is over

(2) pumping sodium and potassium ions through the muscle fiber membrane to maintain an appropriate ionic environment for propagation of muscle fiber action potentials.

Quiz

SAQ

Q1- What happens to A-band and I-band during contraction ?Q was written in female slides

Q2- Ca++ is needed in nerve & muscle : when and where ?Q was written in female slides

Answers

SAQ1-

A-band ➡ doesn't change

I-band ➡ decrease in length or disappear

SAQ2-

In nerve ➡ needed for exocytosis (& release of Ach)

In Muscle ➡ needed for contraction .

1) Is muscle relaxation a passive or active process ? Why ? Q was written in female slides	
A.	Active , because it work 24 hours a day
B.	Passive, because it work 3 hours a day
C.	Active ; because it needs ATP
D.	Passive , because it doesn't need ATP

2) when Ca is release from SR by AP how it will diffuse through the cell membrane of SR ?	
A.	Voltage gated calcium channels
B.	Calcium pump
C.	Na/ k pump
D.	Glucose channel

3) Which of the following statements about the role of calcium (Ca^{2+}) during skeletal muscle contraction is correct?	
A.	Ca^{2+} released into a myofibril by the action of a nerve impulse binds to a site on the myosin head to initiate contraction.
B.	Ca^{2+} released into a myofibril by the action of a nerve impulse binds to a site on tropomyosin to initiate contraction.
C.	Ca^{2+} released into a myofibril by the action of a nerve impulse binds to a site on the actin to initiate contraction.
D.	Ca^{2+} released into a myofibril by the action of a nerve impulse binds to a site on troponin to initiate contraction.

4) Which of the following statements about the contraction of skeletal muscle is correct?	
A.	The power stroke of skeletal muscle contraction occurs when the myosin head hydrolyses ATP
B.	The power stroke of skeletal muscle contraction occurs when the myosin head binds ATP
C.	The power stroke of skeletal muscle contraction occurs when the myosin head releases ATP.
D.	The power stroke of skeletal muscle contraction occurs when the myosin head releases ADP and Pi.

Answers key: 1) C 2) A 3) D 4) D

Team leaders

- Elaf Almusahel
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Thank you

♂ team members

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  - Meshari Alzeer
  - Mohammed Alhamad
  - Omar Alghadir
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@physiology438

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Summary file for your revision