Physiology 439

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Physiology of Skeletal Muscle Contraction

Editing file

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Red: Important
Black: In Male & Female slides
Blue: In male slides
Pink: In female slides
Gray: Notes & extra information

Objectives

01 The physiologic anatomy of the skeletal muscle and NM junction.

02 The general mechanism of skeletal muscle contraction.

03 Motor End Plate potential and how action potential and excitation-contraction coupling are generated in skeletal muscle.

04 The molecular mechanism of skeletal muscle contraction & relaxation.

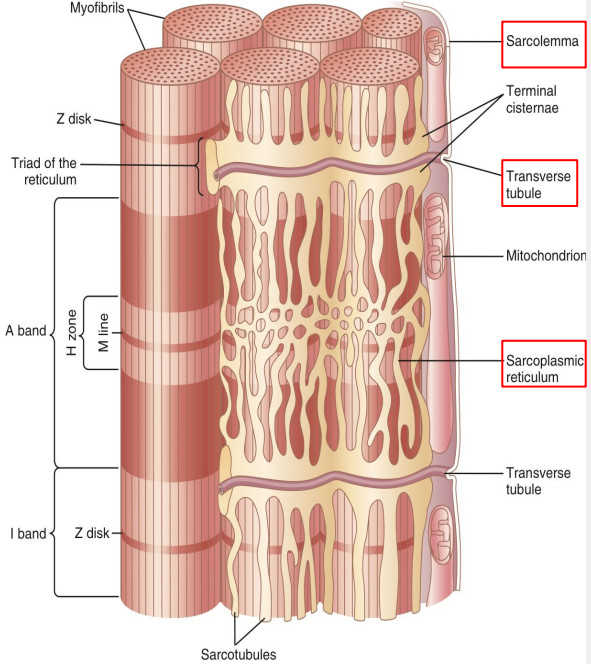
05 sliding filaments mechanism

06 Drugs/ diseases affecting the neuromuscular transmission.

helpful video

The muscle action potential and histology

- Muscle RMP = -80 to -90 mV (**same as in nerves**)
- Duration of AP = 1-5 ms (**longer duration than nerve AP)** which is usually about 0.2-1 ms
- Conduction Velocity = 3-5 m/s (**slower than big nerves)which is (39-65 m/s)**
- Each muscle cell fiber is covered by a cell- membrane called **Sarcolemma.**
- **Sarcoplasm** is the matrix inside muscle fiber in which myofilaments suspended.
- **Sarcoplasmic reticulum** it is endoplasmic reticulum inside the sarcoplasm full of Ca. (مخزن كالسيوم)
- **T- tubules**:- extend from one side of muscle to other.

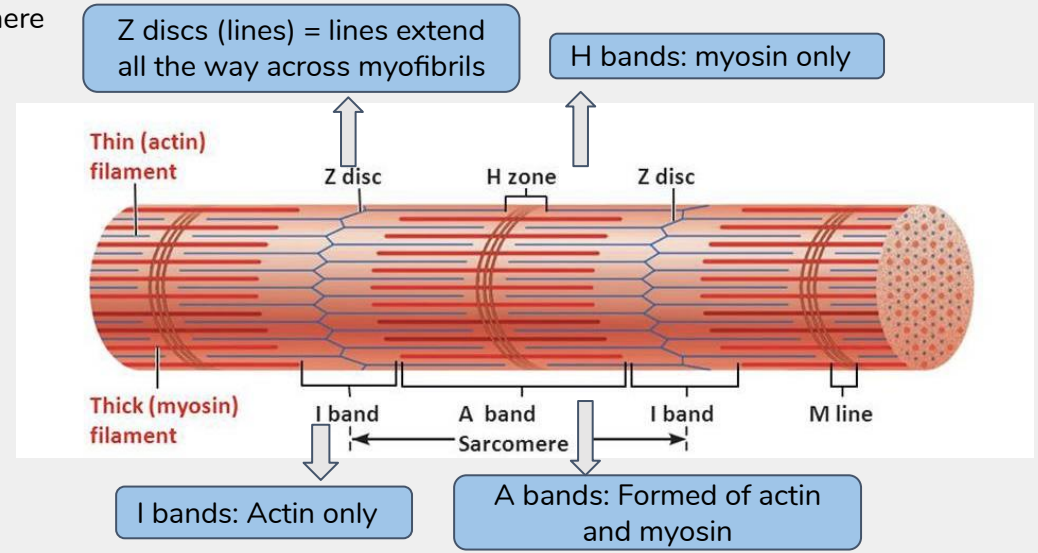


The histology of the muscle

- 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**)
  Titin filaments keep the myosin and actin filaments in place.

The light and dark bands give skeletal and cardiac muscle their striated appearance.

- **Sarcomere** is the functional unit (contractile unit) of muscle(myofibril), it is the zone between **two Z lines** (discs) = 2 micrometer in length in resting state.
- Inside each sarcomere there are **three** bands :
  1- A band
  2- I band
  3- H band



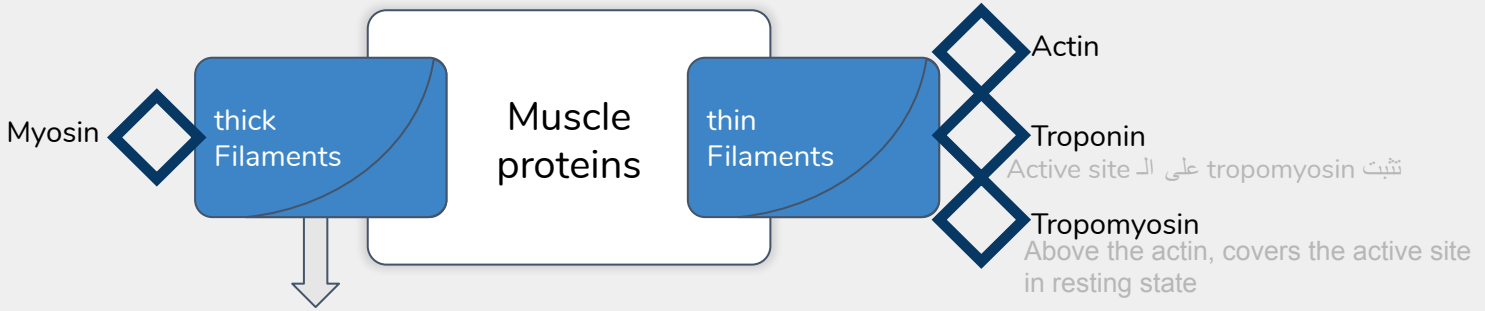
During contraction, I and H bands become shorter, while the A band does not change

Overview of muscle contraction

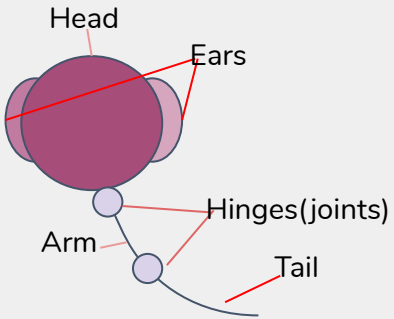
what causes the actin filaments to slide inward among the myosin filaments? Forces generated by interaction of the cross-bridges from the myosin filaments with the actin filaments

Sliding Filament Mechanism

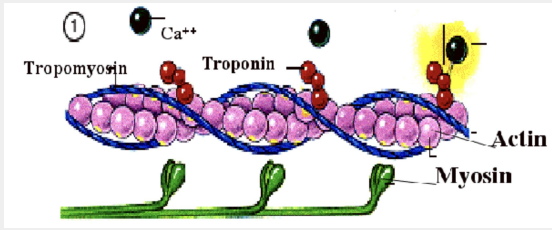
When contraction takes place Actin & Myosin slide upon each other and the distance between two z- discs decreases .



Each Myosin molecule has:



- The myosin head contains:
  1- Actin binding site
  2-Myosin ATPase site
- Head + tail = Cross bridge



Med 438 : the myosin does not move

Mechanism of muscle contraction (Excitation-Contraction coupling)

First step

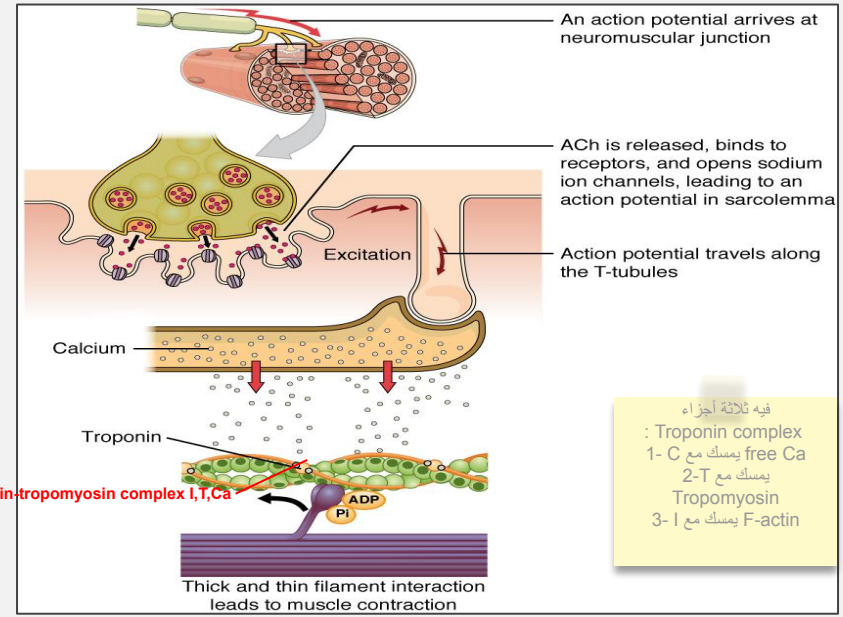
Acetylcholine released by motor nerve ➡ End plate potential (EPP) ➡ depolarization of Compound Muscle Action Potential (CMAP).

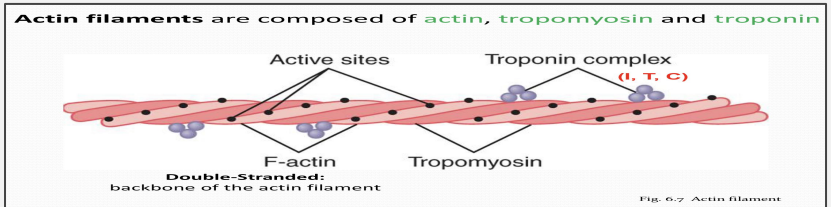
Second step

Spread of AP into T tubule ➡ release of Ca from sarcoplasmic reticulum (Reservoir of ca) into the cytoplasm.

Third step

Ca combines with troponin and cause conformational change ➡ troponin pull tropomyosin sideway ➡ exposing the active site on actin ➡ myosin heads with ATP on them, attached to actin active site.





Mechanism of muscle contraction

Fourth step

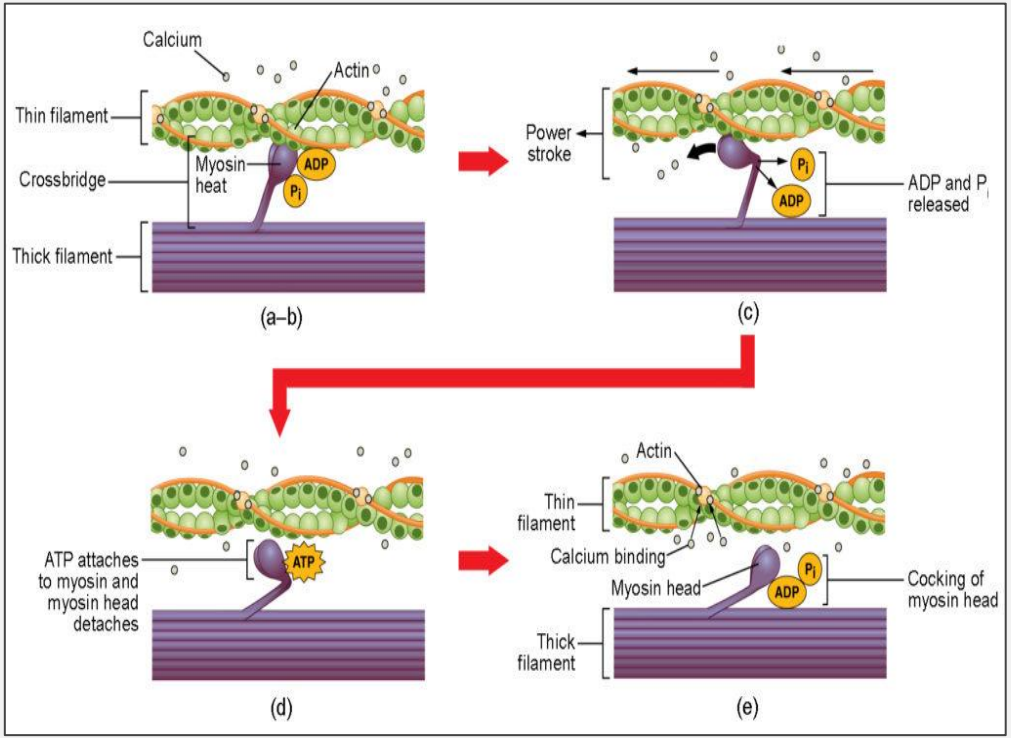
myosin cross bridges bend pulling actin toward center of sarcomere (Power stroke) using energy of ATP ➡ ADP & P released Linkage between actin & myosin broken as new ATP binds to myosin cross bridge ➡ ATP hydrolyzed and cross bridge go back to its original conformation.

Fifth step

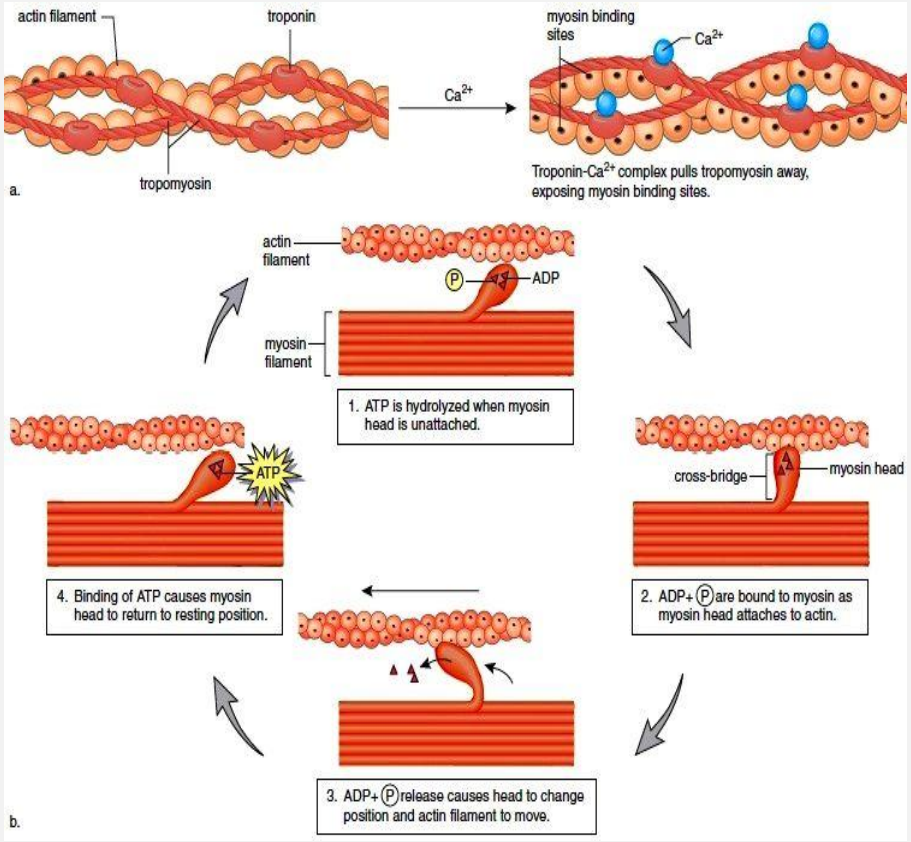
When a new ATP occupies the vacant site on the myosin head, this triggers detachment of myosin from actin, The new ATP is cleaved to begin the next cycle which "cocks" the head back to its perpendicular condition

Sixth step

The free myosin swings back to its original position, & attached to another actin, & the cycle repeat itself.

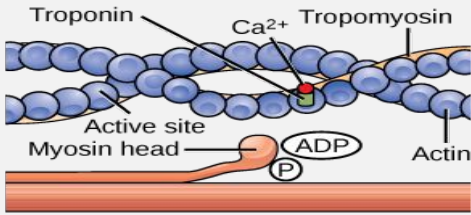


Mechanism of muscle contraction

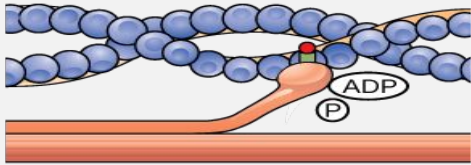


EXTRA

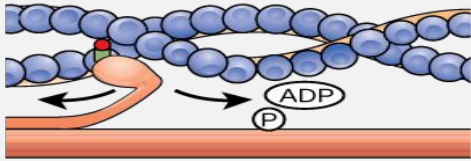
1. The active site on actin is exposed as Ca^{2+} binds troponin.



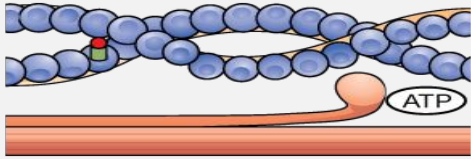
2. The myosin head forms a cross-bridge with actin.



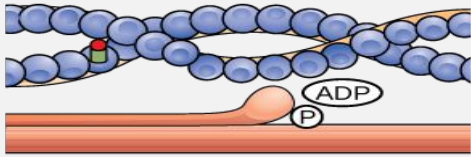
3. During the power stroke, the myosin head bends, and ADP and phosphate are released.



4. A new molecule of ATP attaches to the myosin head, causing the cross-bridge to detach.

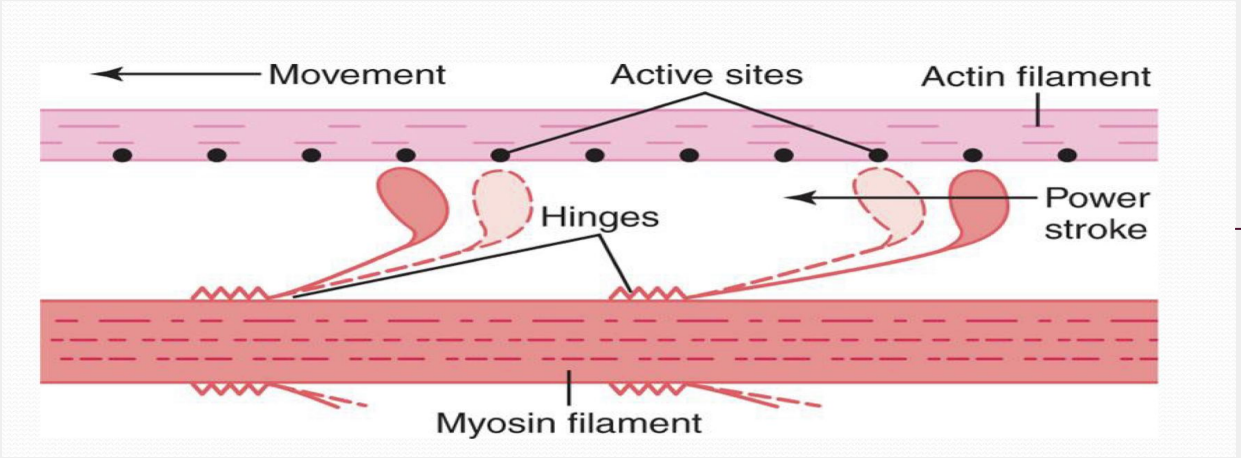


5. ATP hydrolyzes to ADP and phosphate, which returns the myosin to the "cocked" position.



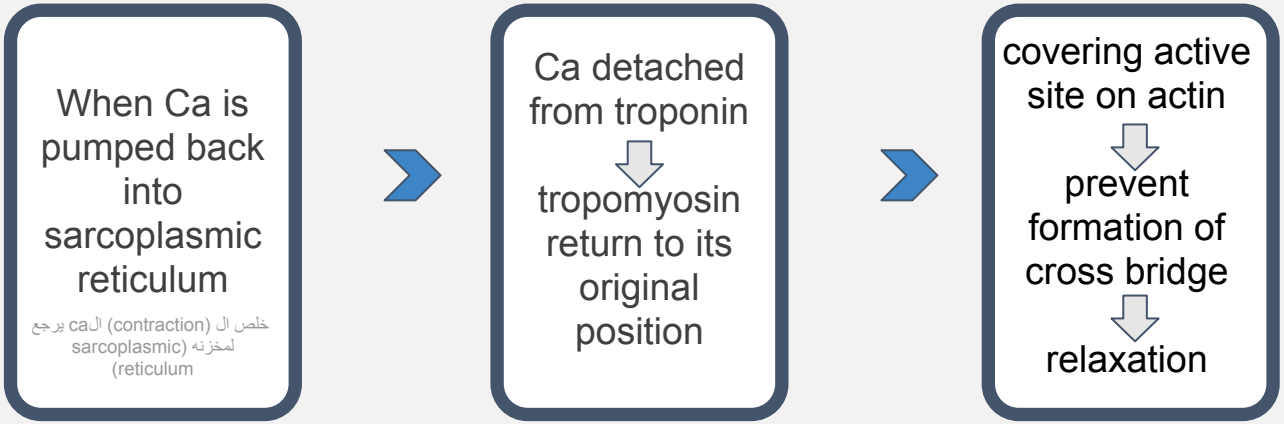
Mechanism of contraction

"**Walk-along**" mechanism for muscle contraction.
The heads of the cross-bridges bend back and forth and step by step walk along the actin filament, pulling the ends of two successive actin filaments toward the center of the myosin filament.



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

Muscle relaxation



Muscle relaxation is active process (needs ATP)

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Comparison between contraction and relaxation

Contraction:

- Ca is present
- Active site uncovered
- Myosin & Actin are attached

Relaxation:

- Ca is absent
- Active site covered
- Myosin & Actin are not attached

ATP is needed for three things:

1- Detachment of myosin from actin active sites.

2- Power stroke .

3- Pumping C++ back into the Sarcoplasmic reticulum

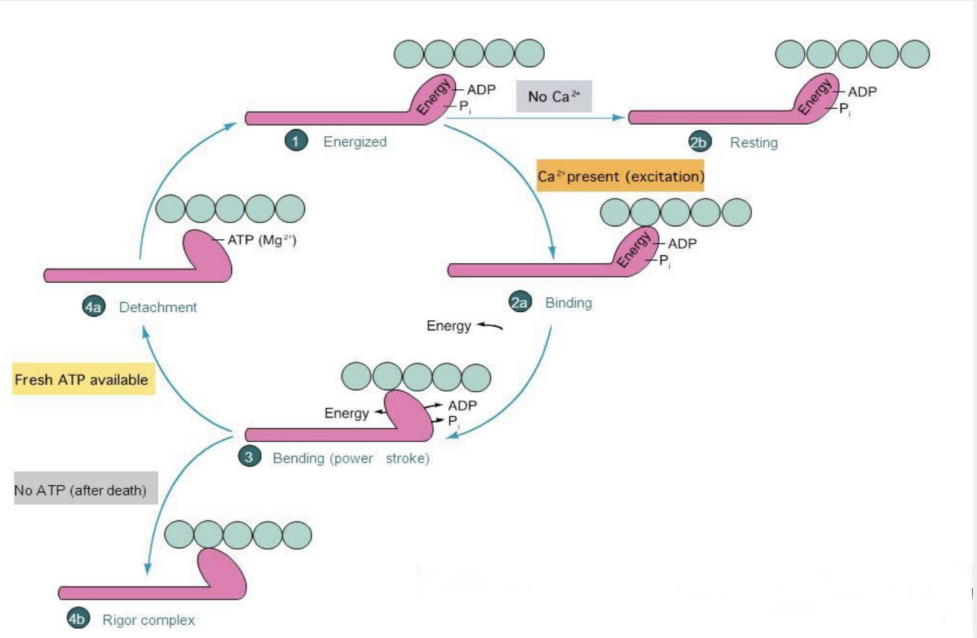
Ca:

- needed in nerve for : exocytosis(release of Ach).
- needed in muscle for: contraction.

Extra note : Muscle contraction: Ca is released from the SR through the (Voltage gated Ca channels), Muscle Relaxation: Ca is turned back to the SR through a (Ca pump) (E.g: SERCA pump)

Rigor mortis

- The contracture of skeletal muscles that begins several hours after death due to the loss of ATP.



إذا مات الشخص تكون عضلاته منقبضة لأن مافيه ATP يرجعها relax ولكن بعد كم يوم تتحلل البروتينات ويروح الانقباض

SUMMARY

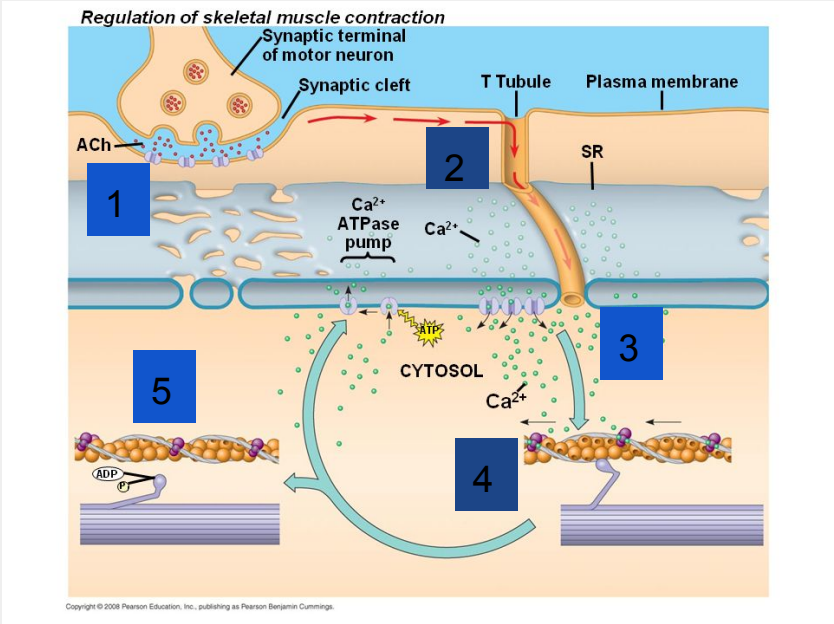
helpful video

1

ACH release from motor nerve > EPP > depolarization of CMAP

2

Spread of AP—>release of Ca from SR into cytoplasm



3

Ca combines with troponin > exposes the active site on actin and myosin attach to it

4

Myosin head rotate toward center of sarcomere (power stroke)

5

As myosin heads bind ATP, the cross bridges detach from actin

helpful video

QUIZ!

MCQs

Q1: muscle RMP is			
A) Same as nerves	B) Larger than nerves	C) smaller than nerves	D) Not relevant
Q2 : “cross bridge” refers to			
A) Arm+tail	B) tail+head	C) head+hinge	D) arm+head
Q3 : tropomyosin covers the active site at :			
A) the active state	B) the resting state	C) A + B	D) Not relevant
Q4 : During contraction Ca is :			
A) Present	B) Absent	C) Partially Present	D) Partially Absent
Q5 : During contraction Ca attached to :			
A) tropomyosin	B) troponin	C) myosin	D) actin
Q6 : the direction of actin filament in walk along mechanism:			
A) Toward the peripheral	B) upward	C) downward	D) Toward the center

SAQ

Q1: what is the sliding filaments mechanism?

Q2: what are three things needed for ATP ?

MCQs key answer :

1) A
2) D
3) B
4) A
5) B
6) D

SAQ answer key :

1) When contraction takes place Actin & Myosin slide upon each other and the distance between two z- discs decreases

2) slide 11

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Question bank