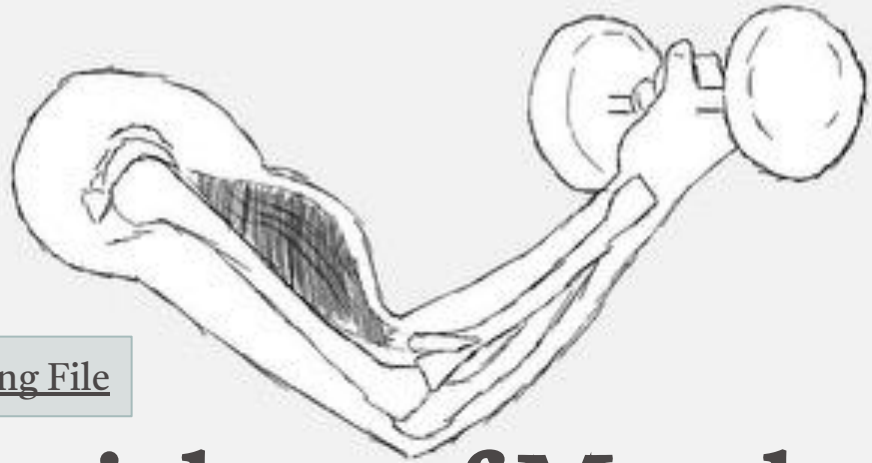


Editing File

Physiology of Muscle Contraction

Color Index:
-Main Text -Important -Notes
-Boy Slides -Girl Slides -Extra

Ty to Hasan Alsugahyir for sketch (445 - inshallah) <3

Objectives

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

02 Motor end plate potential and how action potential and excitation-contraction coupling are generated in skeletal muscle.

03 The molecular mechanism of skeletal muscle contraction & relaxation.

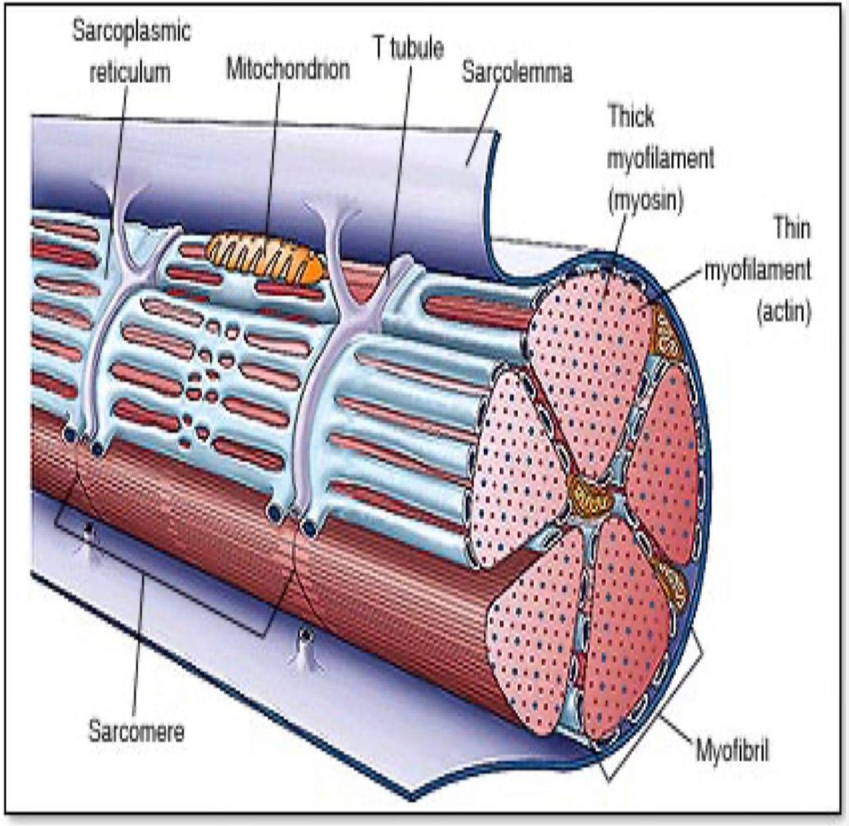
04 Sliding filament mechanism.

05 The general mechanism of skeletal muscle contraction.

06 Drugs/ diseases affecting neuromuscular transmission.

The Histology of the Muscle

- Each muscle cell fiber is covered by sarcolemma (cell-membrane)
  (simply: its plasma membrane with different name)
- Sarcoplasm: the matrix inside muscle fiber, in which myofilaments suspended
  (simply: its cytoplasm with different name)
- T-tubules: extend from one side of muscle to other (extension from sarcolemma to allow action potential to travel through cell).
- Sarcoplasmic reticulum: endoplasmic reticulum in sarcoplasm, full of Ca (sER but in muscle -> used for Ca+2 storage).



The Histology of the Muscle

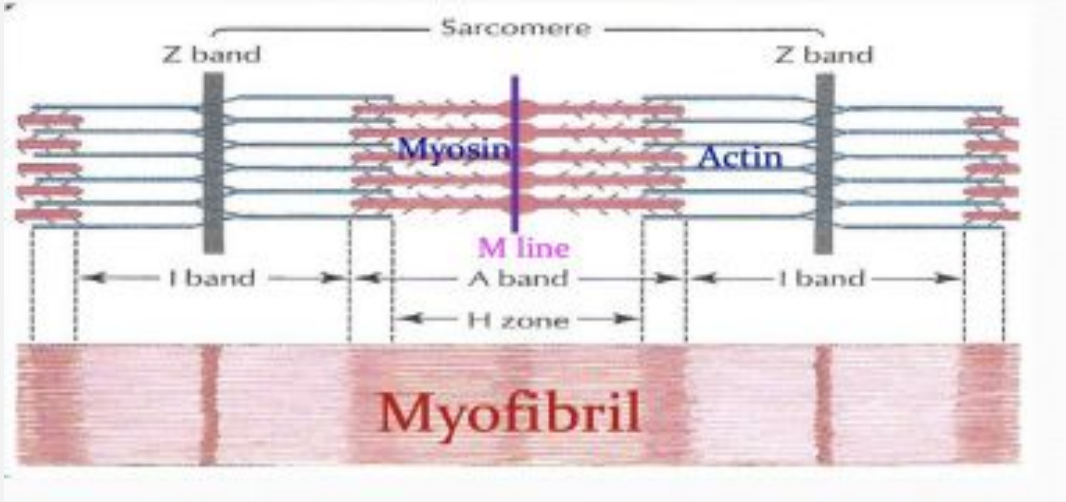
https://youtu.be/JbbVbwX0av8?si=EDcAAEOYRkiQCUXd
Highly Recommended introductory video!!

- Each muscle fiber (cell) has a few hundreds - thousands of myofibrils.
- Each myofibril contains actin filaments (thin) & myosin (thick) filaments.
- Each myofibril (skeletal & cardiac) is striated: consisting of dark bands (A-bands) and light (I-bands).
- Sarcomere: the functional/contractile unit of muscle (myofibril) - the zone between two Z lines/discs = 2 μm in length in resting state.
- Z discs/lines: lines extend all way across myofibrils.

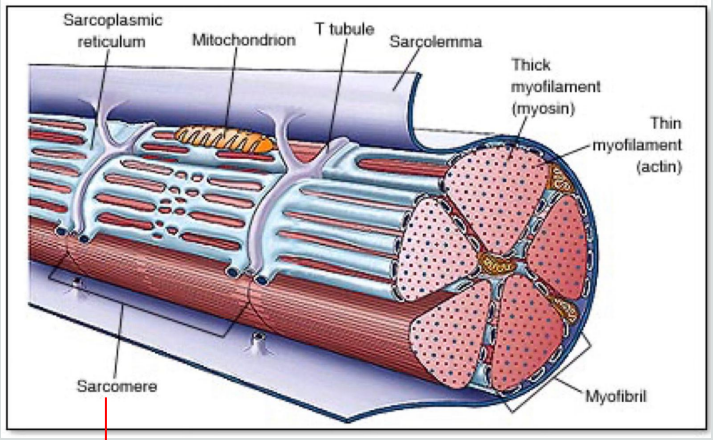
- **Bands**: region in the sarcomere that contains protein → can change in length (because Z lines will come together).
- **Filaments**: actual proteins (actin & myosin) → NEVER change in length.
- During contraction: I & H bands get shorter (the filaments length is not affected), while A band length isn't affected.

The Histology of the Muscle

Extra visualization for the previous slide



Female Slides Only



Sarcomere: the functional/contractile unit of muscle (myofibril) - the **zone between two Z lines/discs = 2 µm in length in resting state**

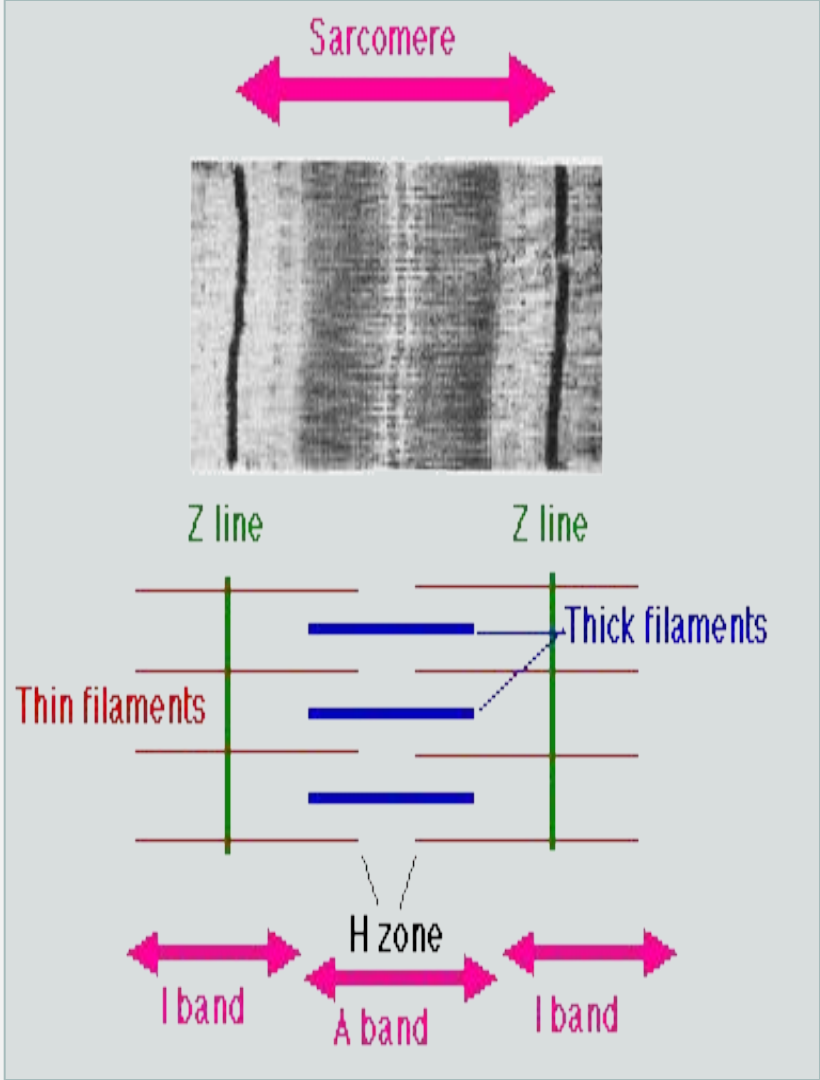
I Band: Actin only

A band: Actin & myosin

H Band: Myosin only

Myofibril

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



Molecular Characteristics of the Contractile Filaments

Muscle Proteins

Myosin Thick Filament

Composed of multiple myosin molecules (contractile proteins), each has:

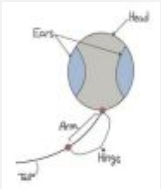
- ➢ Head (has ATP site)
- ➢ Arm
- ➢ Tail
- ➢ Hinge (joint)

❖ Head + Arm = cross bridge .

□ عبارة عن نتوءات طالعة من الميوسين

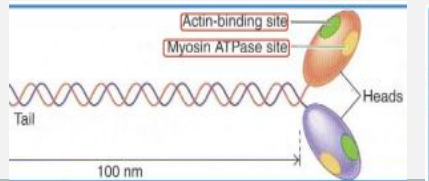
❖ Each myosin head contains:

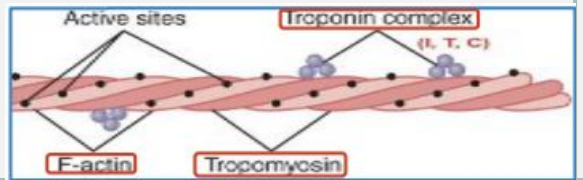
- ➢ Actin binding site
- ➢ Myosin ATPase site



تشبه عصا الغولف ولها أذنين:
الأولى ترتبط مع ATP
الثانية ترتبط مع الأكتين

لو ماكان موجود Myosin ATPase site ما رح يصير (Contraction)





Actin Thin Filament

Double stranded backbone

Actin (Contractile protein)	Tropomyosin (Regulatory protein)	Troponin (Regulatory protein)
كأنه عقدين من اللؤلؤ لافين على بعض	كأنها عصابة تغطي على مكان ربط الميوسين بالاكتن	عبارة عن 3 كور كل وحده مرتبطة بشيء وحدة مع الأكتين وحدة مع الكالسيوم وحدة خيط التروبوميوزين
contains binding sites for myosin head (activated by Ca+) during contraction.	String which covers the active site.	❖ Complex (I - T - C) **T:** binds with tropomyosin. **I:** inhibits myosin-actin interaction. **C:** binds with Ca.

The Muscle Action Potential (AP)

Muscle RMP = -90 mV
(same as in nerves)

Duration of AP = 1-5 ms.
(longer than the nerve AP " about 1 ms ").

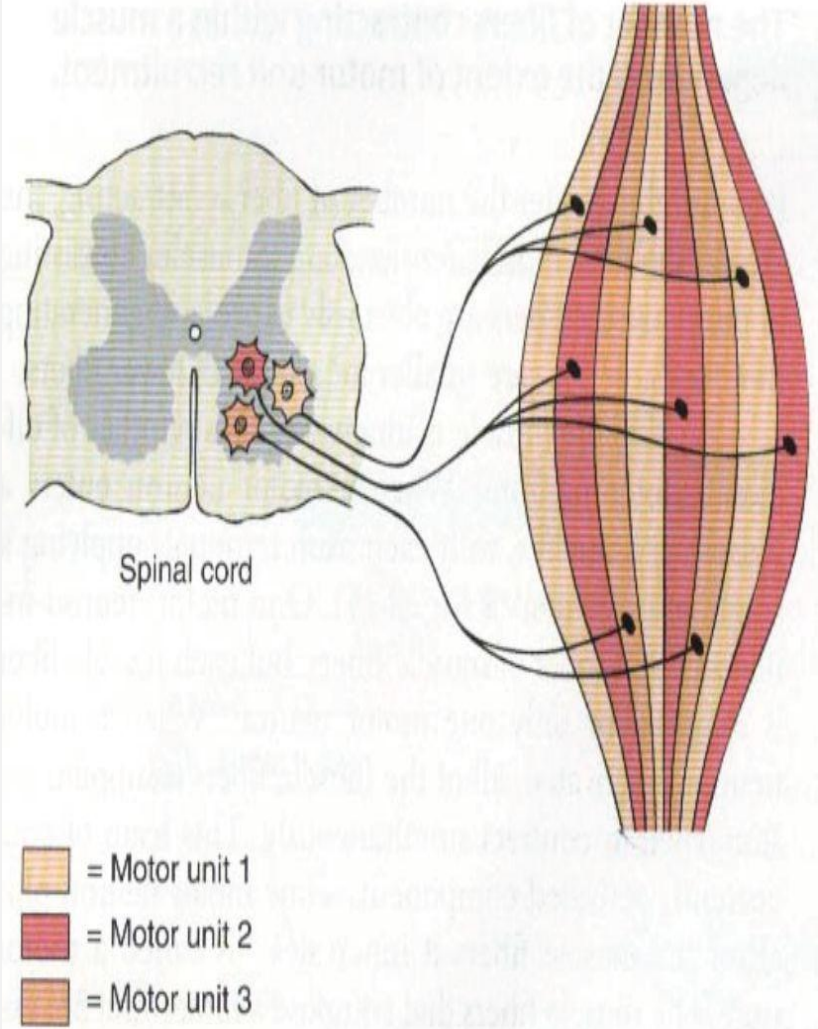
Conduction Velocity = 3-5 m\s
(slower than big nerves).

Female Slides Only

The Motor Unit

Motor unit: Somatic motor neuron (Anterior Horn Cell, Axon) and all the muscle fibers it innervates .

40% of body are skeletal muscles .

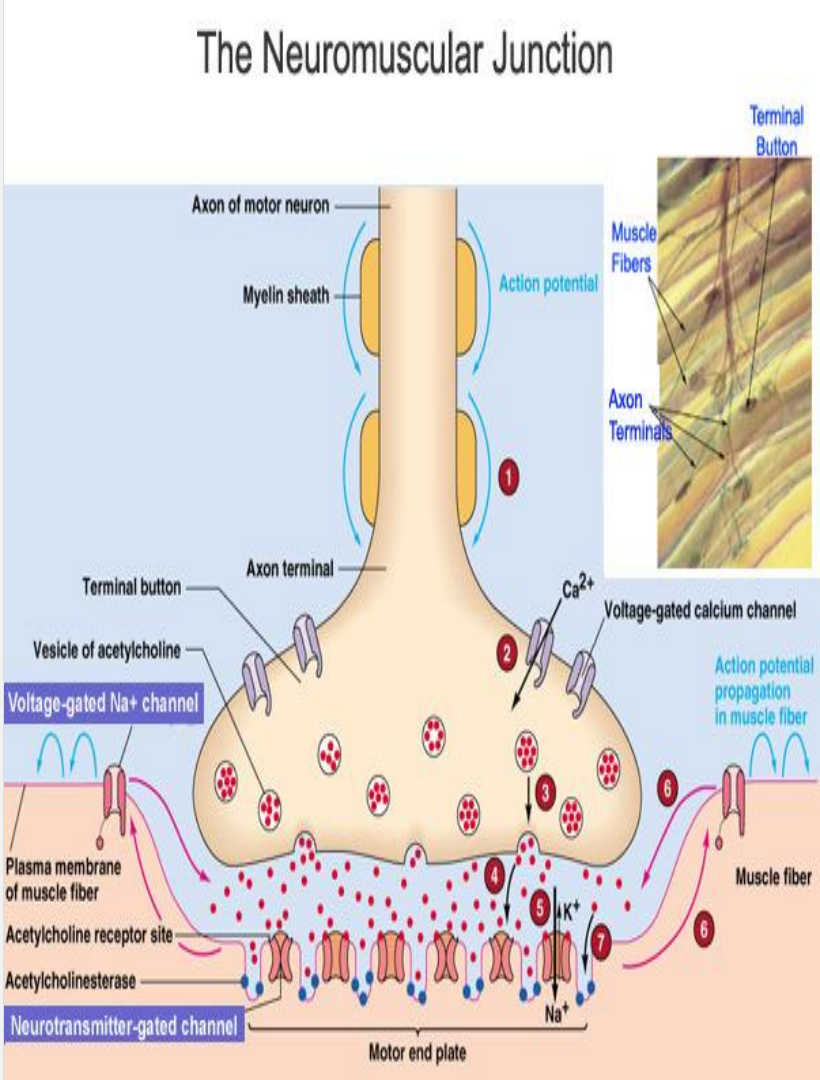


Neuromuscular junction (NMJ)

Transmission of impulses from nerve endings to skeletal muscle fibers occurs via : (NMJ)

2 molecules of Ach must attach to the receptor

Ach channels open and allow (Na+,Ca+,K+) ions to move through easily; but not negative ions such as (cl-)

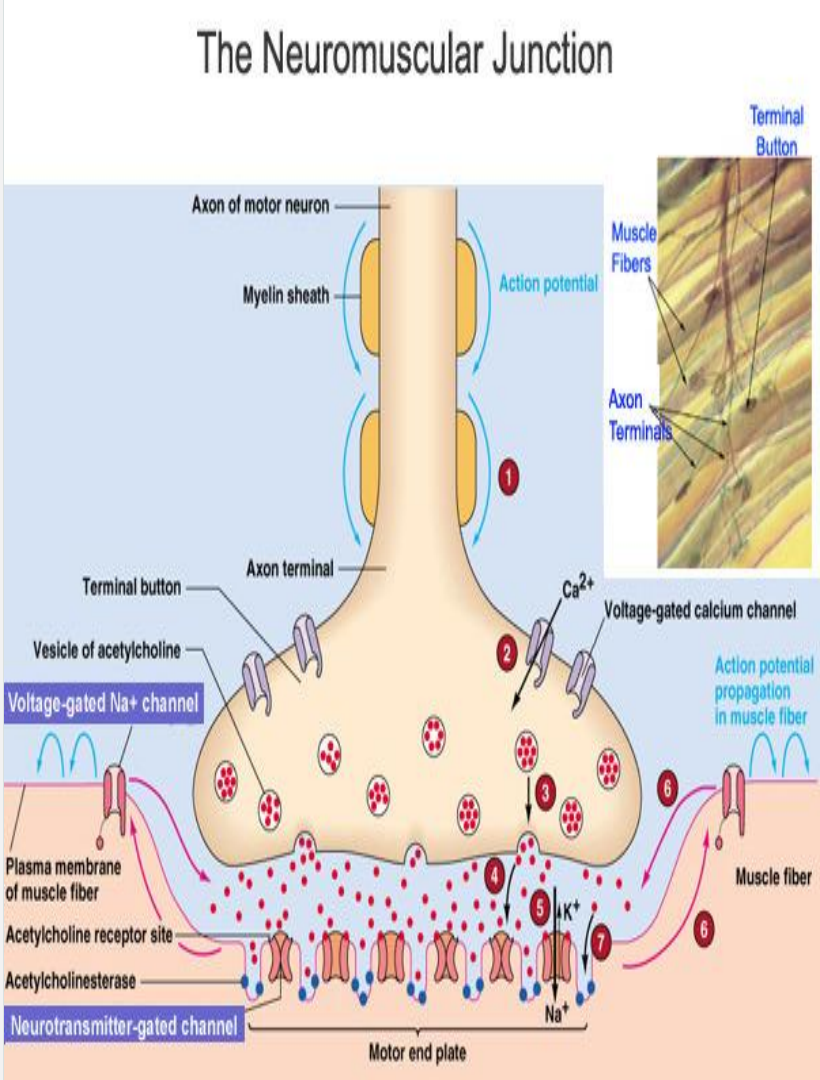


Neuromuscular junction (NMJ)

More (Na+) ions will pass through which creates a local positive potential change inside the muscle fiber membrane called (End Plate potential EPP)

EPP spreads along the muscle fiber

When Ach gated channels open , sudden influx of Na+ will increase electrical potential in the positive direction as much as 50-75 mV and creates a local EPP this will open voltage

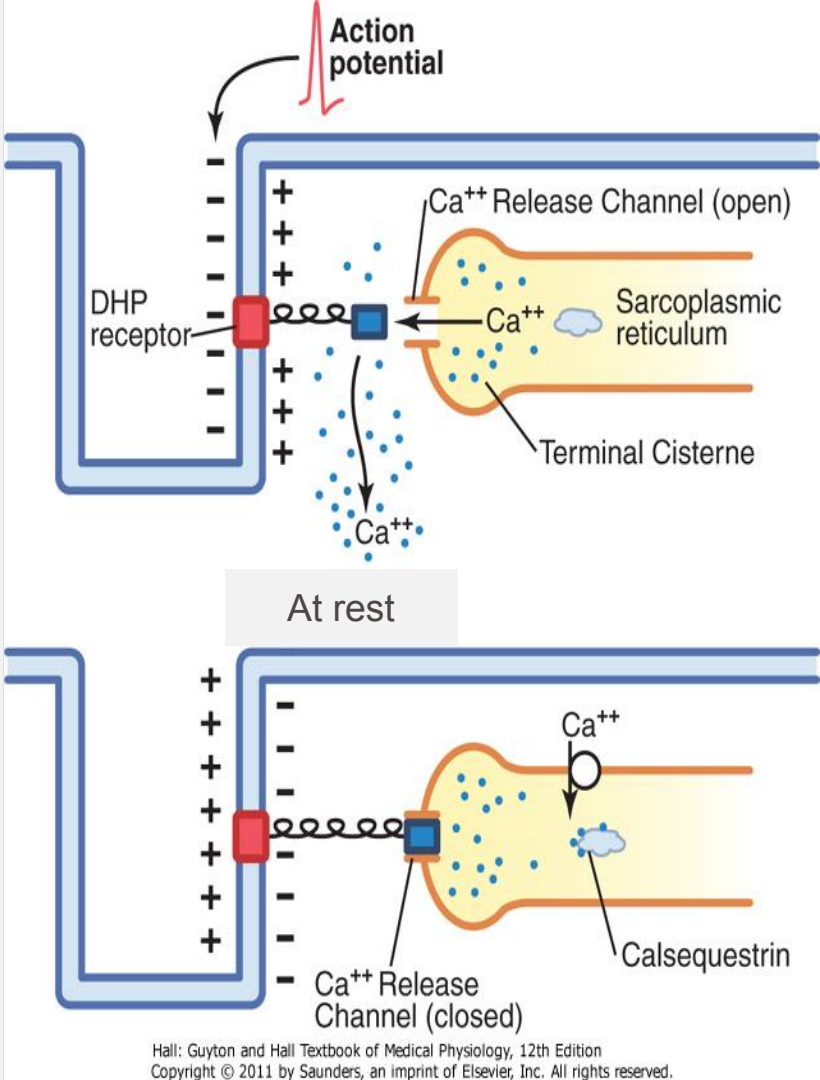


Release Ca by sarcoplasmic reticulum

As AP reaches the T-tubule, the voltage change is sensed by [***voltage-gated calcium channel*** dihydropyridine receptors (DHP)] linked to calcium release channels (Ryanodine receptors) which triggers the release of Ca^{++} initiating contraction.

Calcium pump removes calcium ions after contraction occurs.
Calcium binds to *calsequestrin*

AP= action potential



Molecular features of contractile filaments

Myosin filaments are composed of multiple myosin molecules.

Each Myosin molecule has

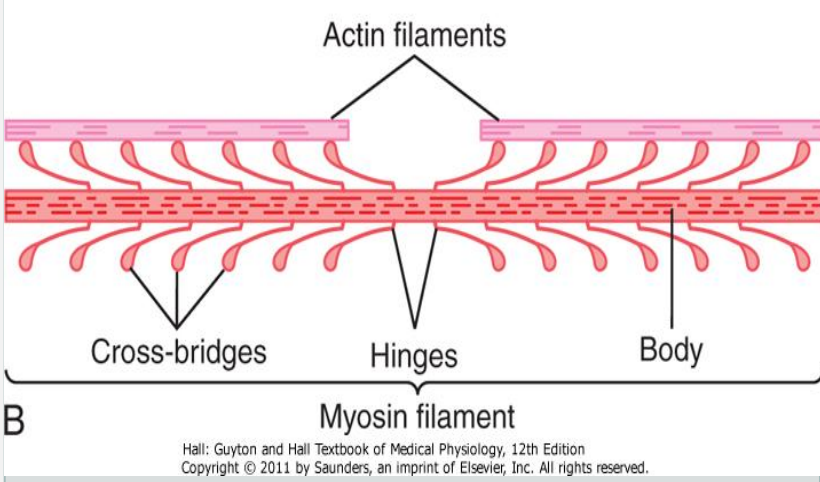
1- Head and each head contain:

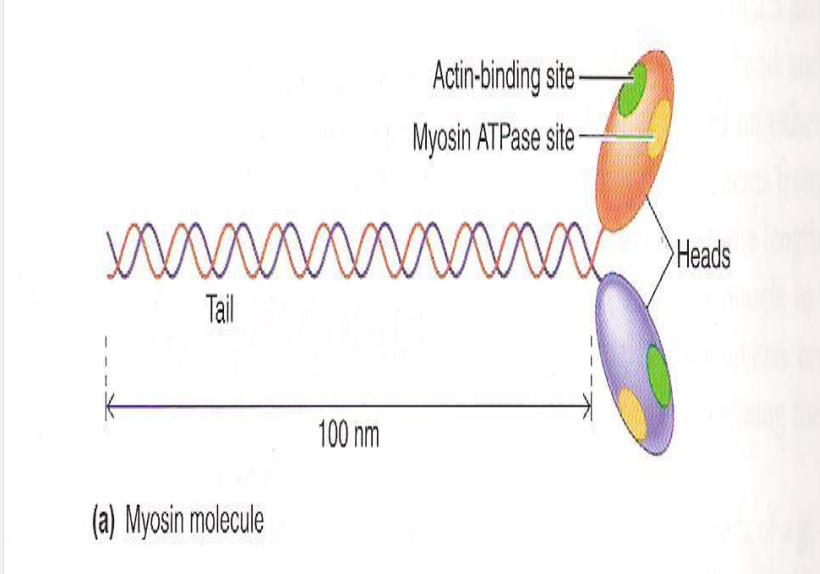
A- Actin binding site

B- Myosin ATPase site

2- Tail

3- Hinge (joint)





Molecular features of contractile filaments

- Actin Filaments are composed of

(Actin,Tropomyosin and Troponin)

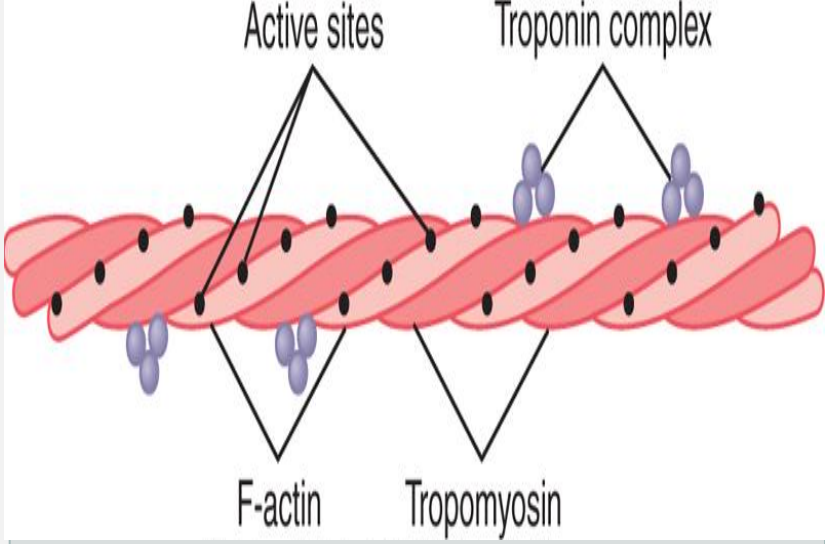
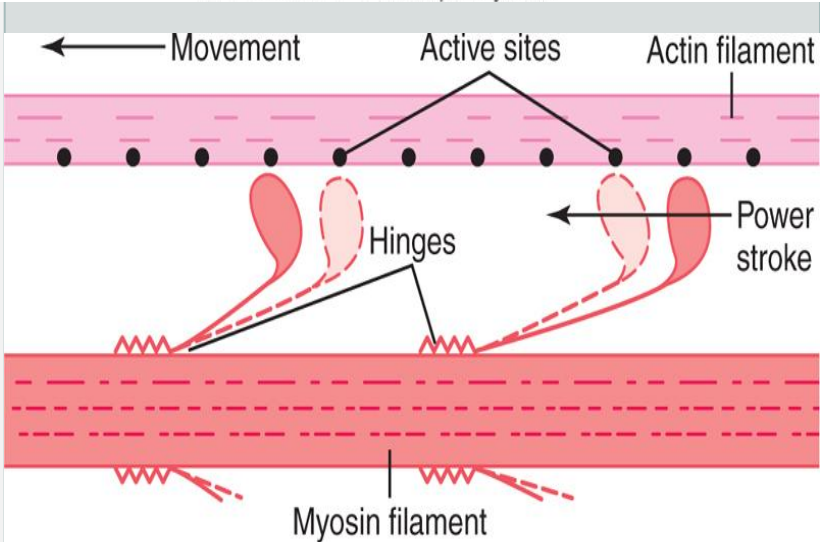


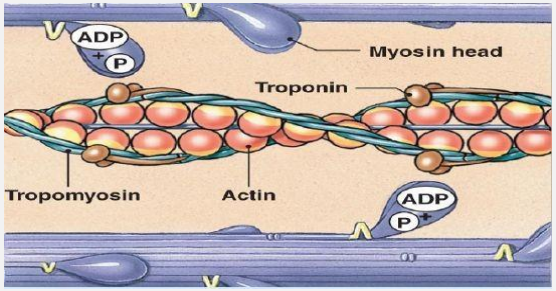
Figure to the right shows "Walk-along" mechanism for muscle contraction.
The heads of the cross-bridges bend back and forth and step by step walk along the actin filament, pulling the ends of two actin filaments toward the center of the myosin filament.



Muscle contraction

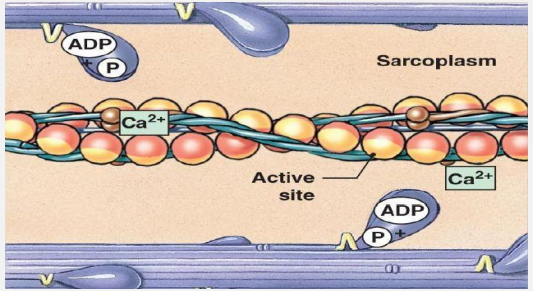
Important Slide

Resting sarcomere (Inactive Forces)



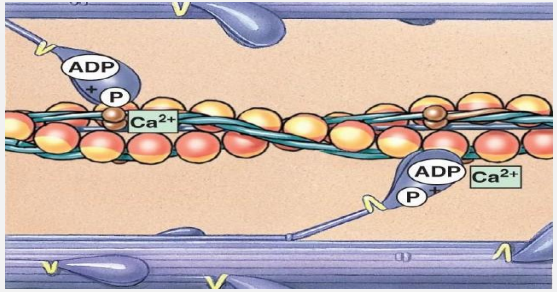
Heads of cross bridges bind with ATP. ATPase activity of the myosin head immediately cleaves ATP (releasing energy which is used in the power stroke) but leaves the cleavage products (ADP + phosphate ion) bound to the head .

Step 1 (Active-Site Exposure)



Troponin-tropomyosin complex binds with Ca++ → active sites on the actin filament are uncovered → myosin heads bind with these sites .

Step 2 (Cross Bridge Formation)

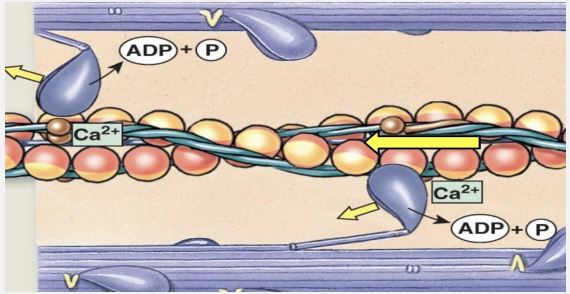


Active sites on the actin are exposed myosin heads bind to the actin, forming cross-bridges .

Muscle contraction

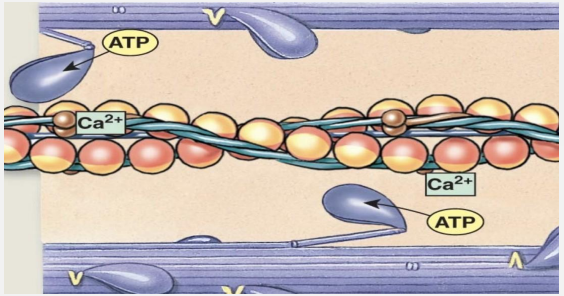
Important Slide

Step 3 (Pivoting of Myosin Head)



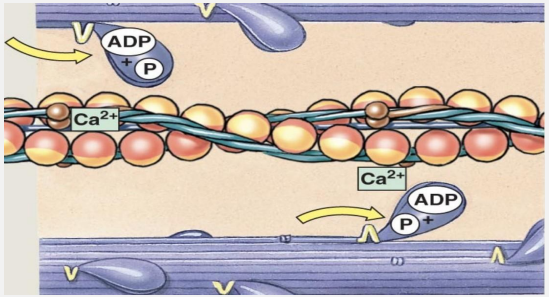
Binding head of the crossbridge with active site → causes conformational change in head → head tilt toward the arm of the crossbridge → power stroke is provided for pulling the actin filament.

Step 4 (Cross Bridge Detachment)



Head of the cross-bridge tilts → ADP & phosphate ion are released → new molecule of ATP binds → detachment of head from actin

Step 5 (Myosin Reactivation)

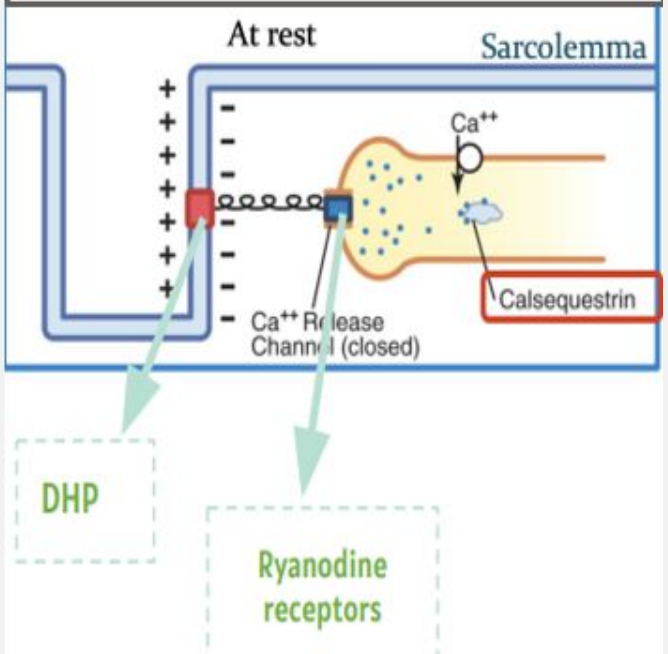


New ATP is cleaved to begin the next cycle which “cocks” the head back to its perpendicular condition, ready to begin the new power stroke cycle.

Events of Muscle Relaxation

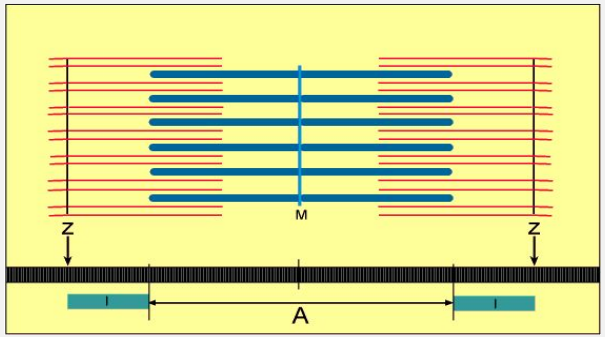
- Acetylcholinesterase removes acetylcholine from the synaptic cleft.
- Ca is pumped back by Calcium pump into sarcoplasmic reticulum after contraction occurs.
  - Calcium binds to calsequestrin.
- Ca detached from troponin → tropomyosin return to its original position
- Tropomyosin blocks myosin binding site on actin, preventing the formation of cross bridge → relaxation
- In order to release the head of myosin from actin, a new ATP is needed to come & combine with head of myosin .

- Ca moves from sarcoplasmic reticulum to cytoplasm:
  High conc. → lowc onc.
  (no energy required).
- Ca moves from cytoplasm to sarcoplasmic reticulum:
  - Low conc. → high conc.
    (energy required).



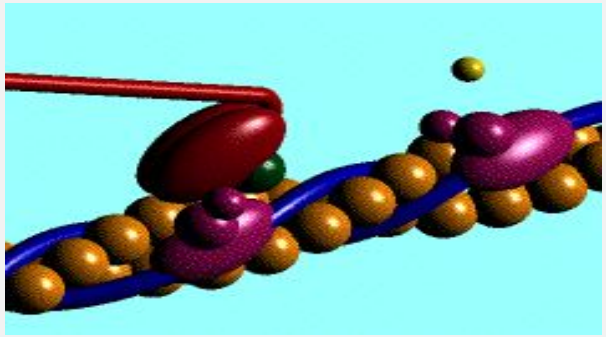
What causes the actin filaments to slide inward among myosin filaments?

Forces generated by interaction of the cross bridges from the myosin



What is Rigor mortis?

Contracture of skeletal muscles that begins several hours after death due to loss of (ATP)



Summary (from team 443)

Very important note: All the process of contraction & Relaxation requires Energy (In one cycle we need 3 ATP).

- During contraction, I and H bands become shorter, while the A band does not change.
- Calcium is needed in nerves for exocytosis & release of Ach.
- Calcium is needed in muscles for contraction.
- Muscle relaxation is an active process (needs ATP).
- Muscle AP spreads through T-tubules
- 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 .
- Ca++ combines with Troponin , activating it.
- Troponin pulls away Tropomyosin, This uncovers the active sites in Actin for Myosin.
- Myosin combines with these sites , This causes cleavage (breakdown) of ATP and release of energy.
- Myosin and Actin slide upon each other causing contraction ,A new ATP comes and combines with the Myosin head this causes detachment (separation)of Myosin from Actin .
- Note: Muscle relaxation is an active process, because it needs ATP.

MCQs

Q1: Troponin C function ?			
A- binds with tropomyosin	B- binds with actin	C- binds with Ca	D-all
Q2: Actin binding site and Myosin ATPase site are present in:			
A-Myosin arm	B-Actin	C-Myosin hinge	D-Myosin head
Q3:duration of Muscle Action Potential is:			
A-1-5 ms	B-3-5 ms	C-1-4 ms	D- 2-4 ms
Q4:which of the following decreases in length during the contraction of a skeletal muscle fiber?			
A- A band of the sarcomere	B-I band of the sarcomere	C- Z disc of the sarcomere	D-none; they all slide but don't change in length

Answers: C -> D -> A ->B

MCQs

Q5:- which of the following blocks myosin heads, preventing contraction?			
A-tropomyosin	B-troponin	C-Calcium	D-actin filaments
Q6:Which of the following is the functional unit of the skeletal muscle?			
A-Sarcolemma	B-Sarcomere	C-Myofibril	D- actin & myosin
Q7:during muscle contraction, Ach binds to nicotinic receptors in? *(not from 🎁)*			
A-parts of Sarcolemma	B-Sarcoplasmic reticulum	C-Terminal Cisternae	D- Axon terminal

Ach binds to nicotinic receptors that are on the sarcolemma of the muscle which is a part of the **Motor End Plate** (not all sarcolemma)

Answers: 5- A 6- B 7-A

SAQs

Q1: Each myosin head contains:

A1: a- Actin binding site
b-Myosin ATPase site

Q2: What is the importance of Power Stroke?

A2: Pulling Actin filaments toward center of sarcomere.

Q3: Does muscle relaxation require energy (ATP)?

A3: yes it does, we need ATP in order to pump Ca++ back into the sarcoplasmic reticulum.

Q4: Explain the excitation-contraction coupling in skeletal muscles

A4: - slide 16

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Aram Alzahrani

Noor Altalag