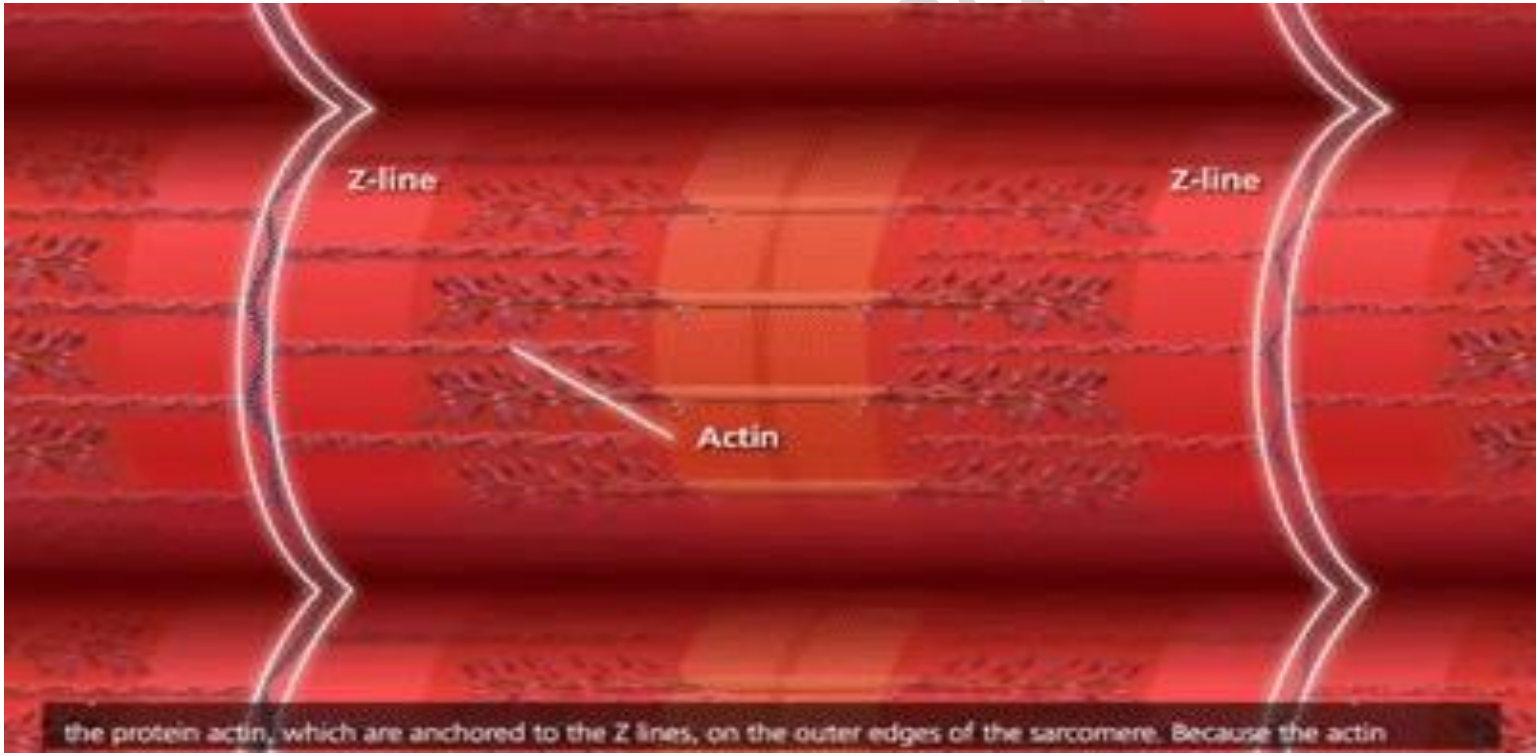
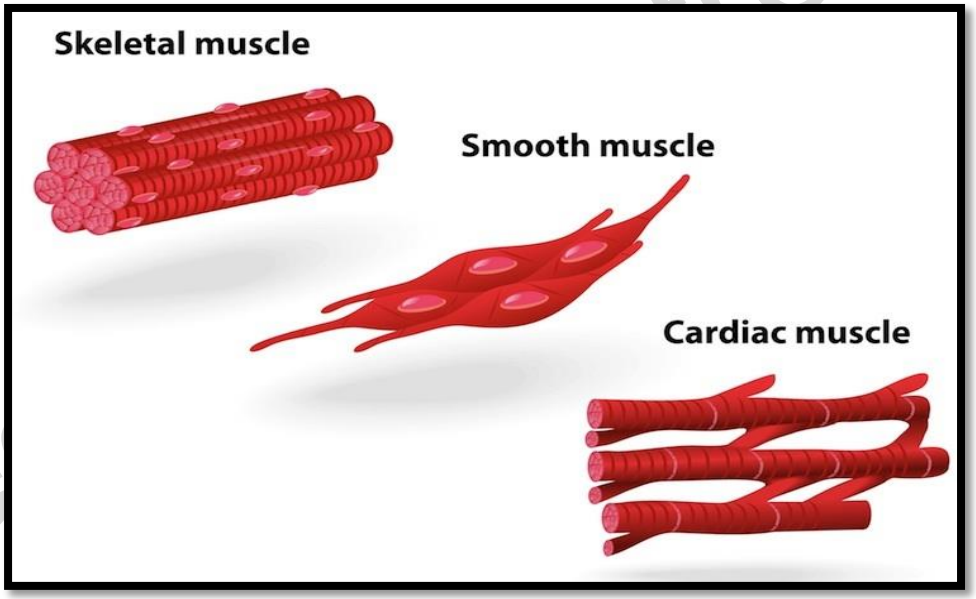
Mechanism of muscle contraction



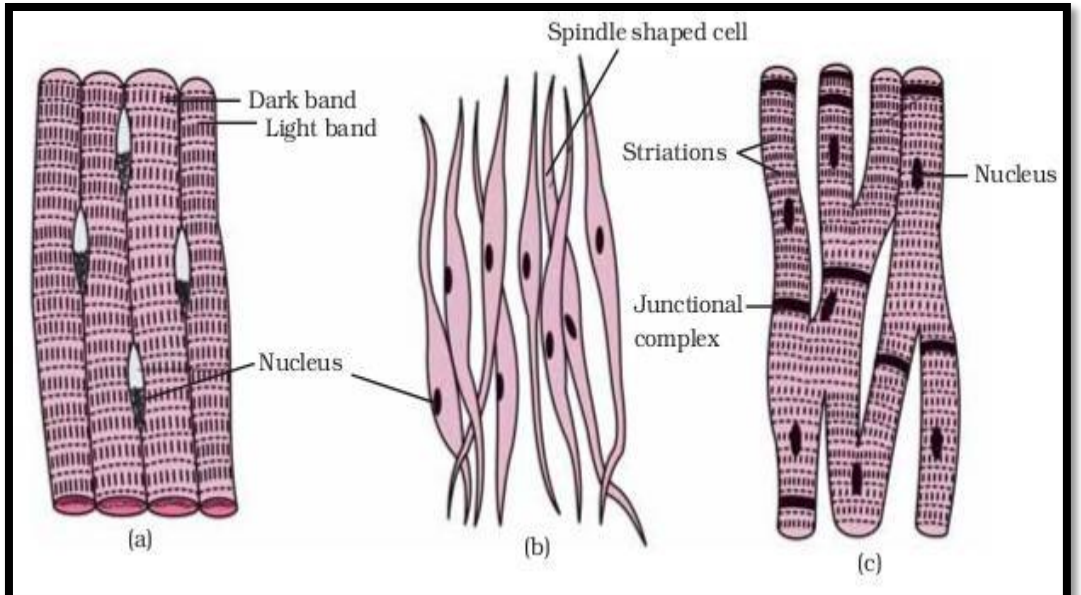
Classification of Muscle Tissue

Functionally

- Skeletal Muscle
- Cardiac Muscle
- Smooth Muscle

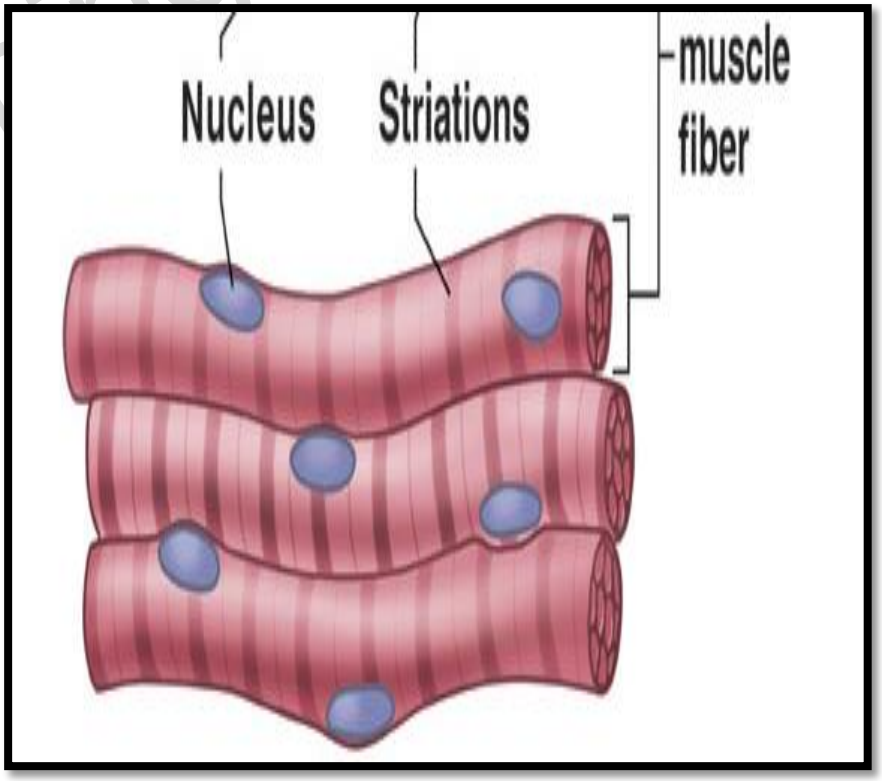


- **Appearance**
- Striated
- Nonstriated



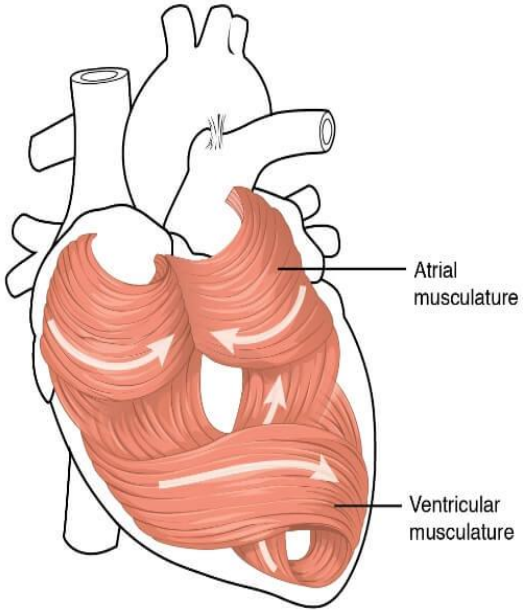
Skeletal Muscle fiber

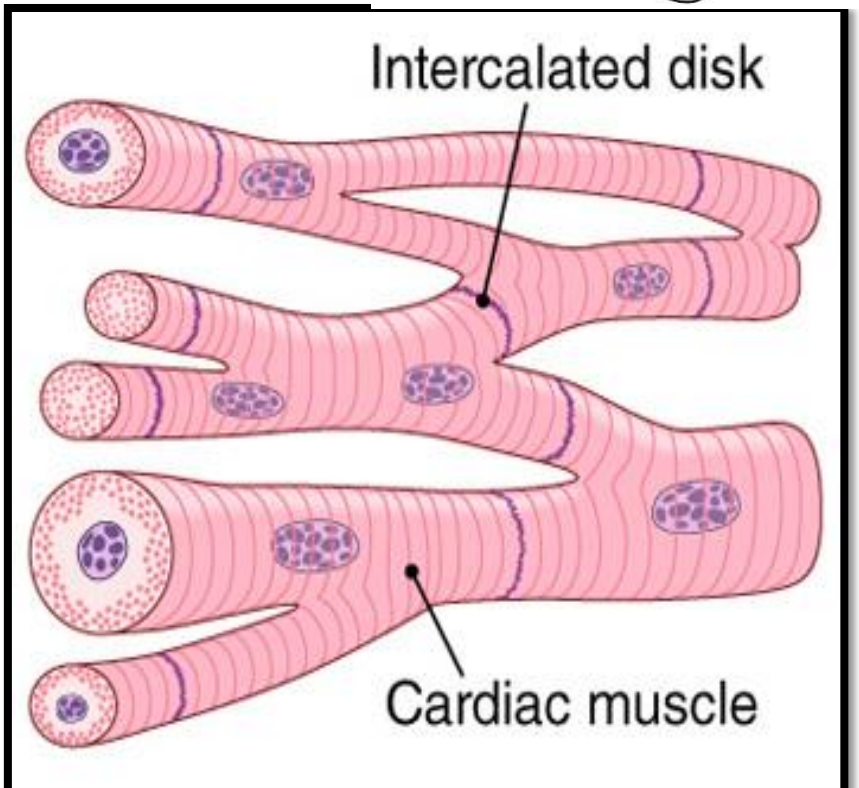
- Long cylindrical cells
- Many nuclei per cell
- Striated
- Voluntary
- Rapid contractions



Cardiac Muscle

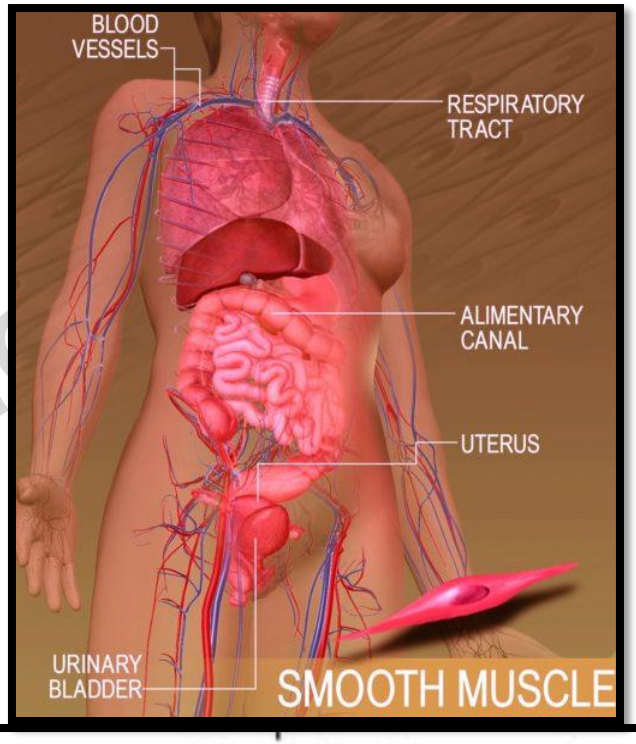
- Branching cells
- One or two nuclei per cell
- Striated
- Involuntary
- Medium speed contractions
- **Forms syncitium.**

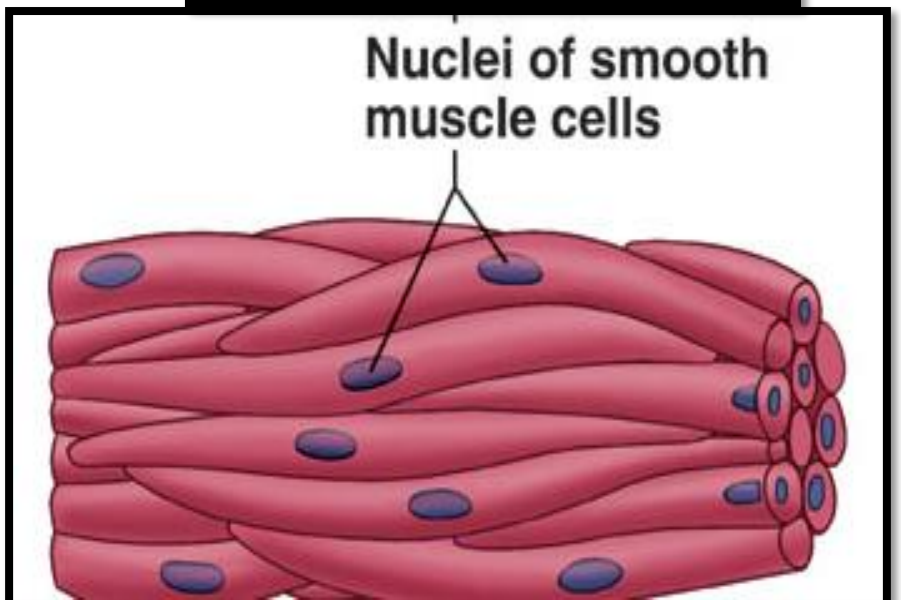


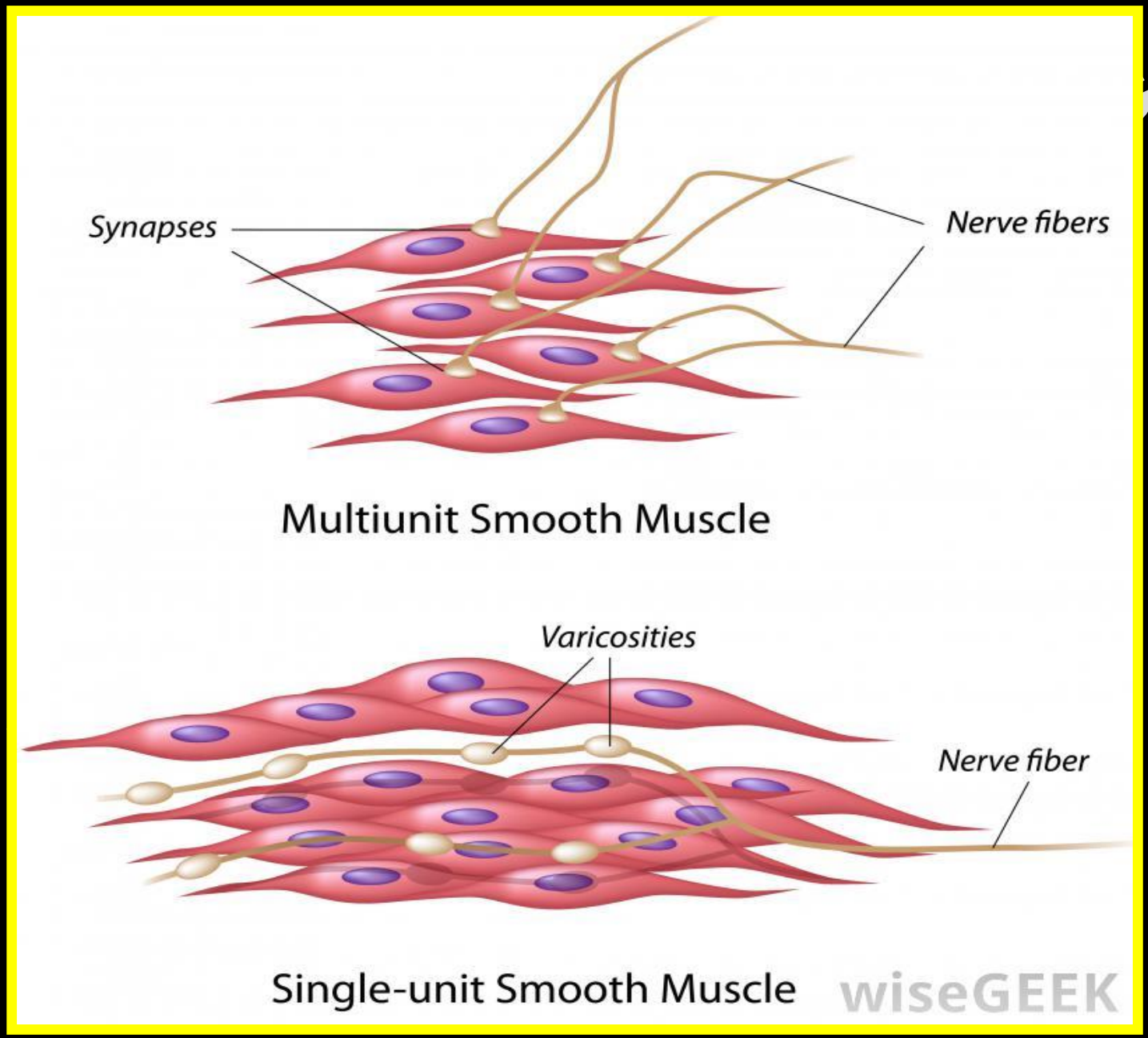


Smooth Muscle

- Spindle shaped cells
- One nucleus per cell
- Nonstriated
- Involuntary



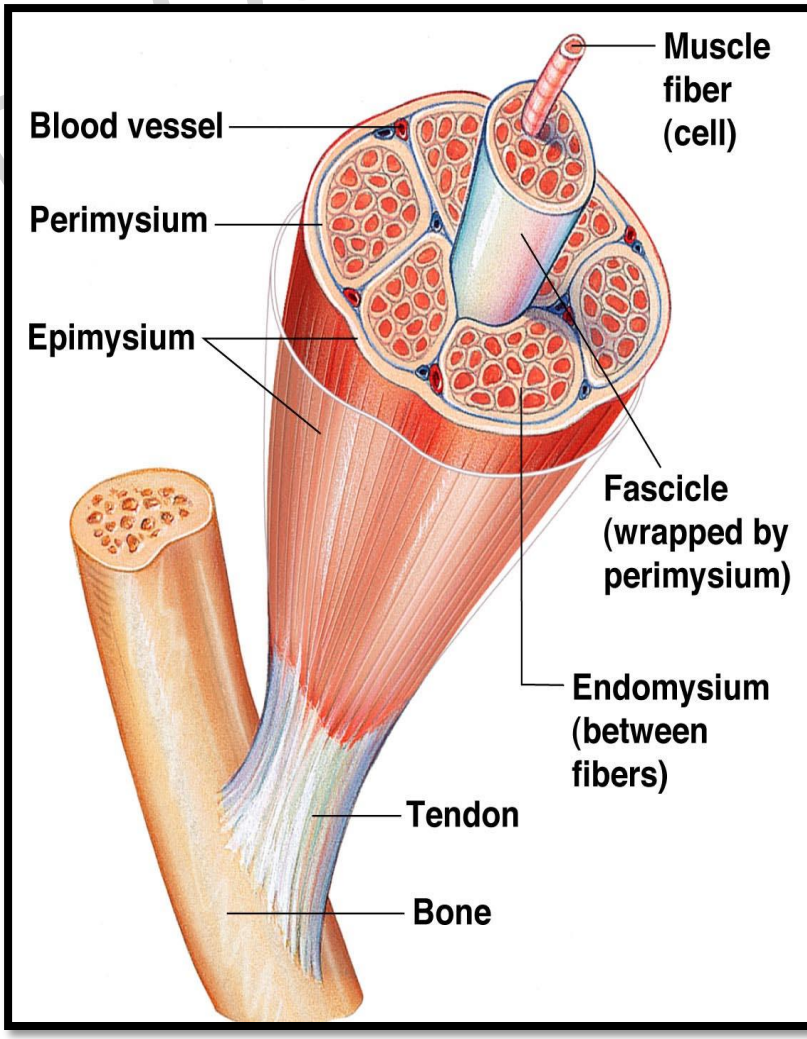


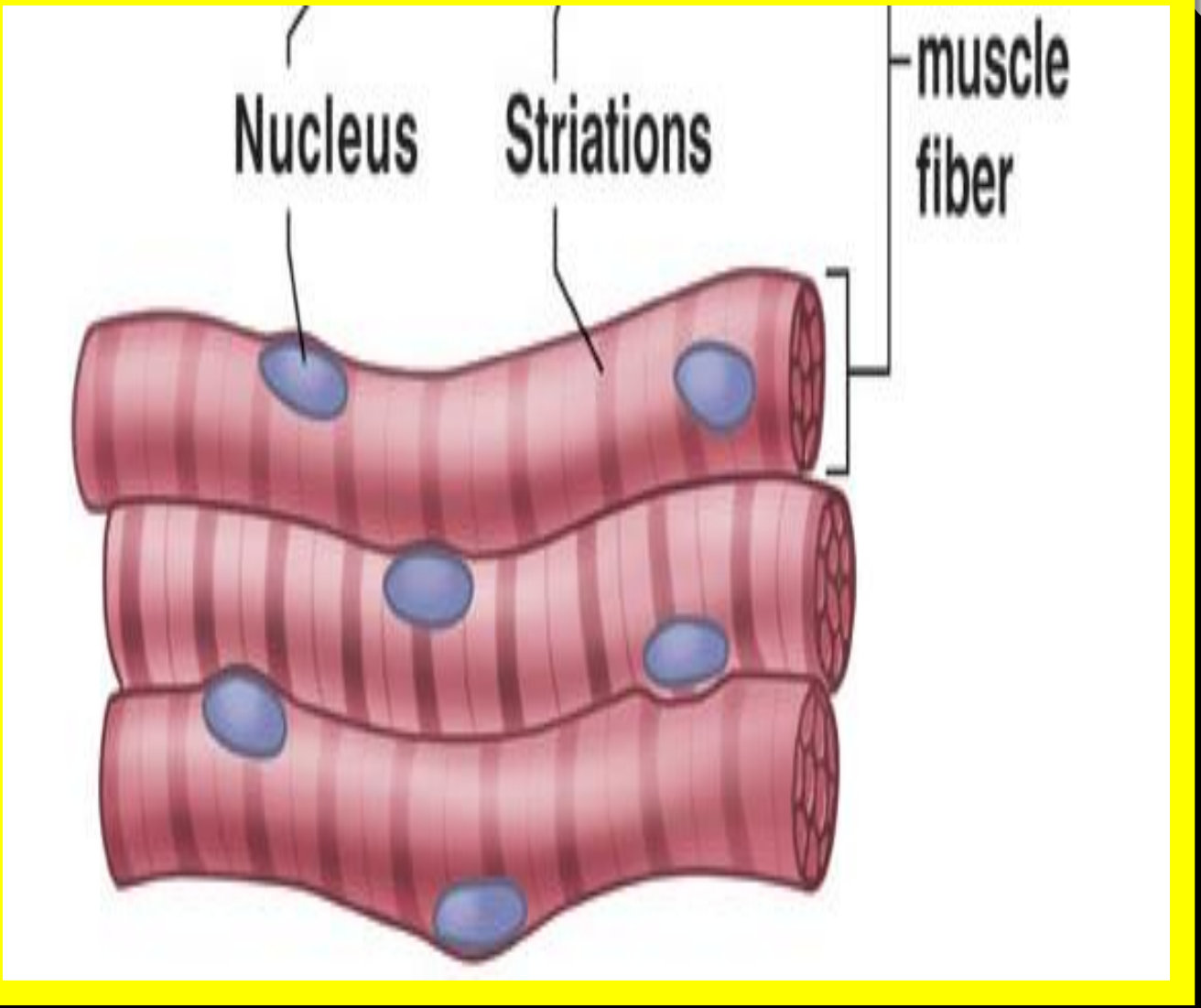

Synapses
Nerve fibers
Multiunit Smooth Muscle
Varicosities
Nerve fiber
Single-unit Smooth Muscle
wiseGEEK

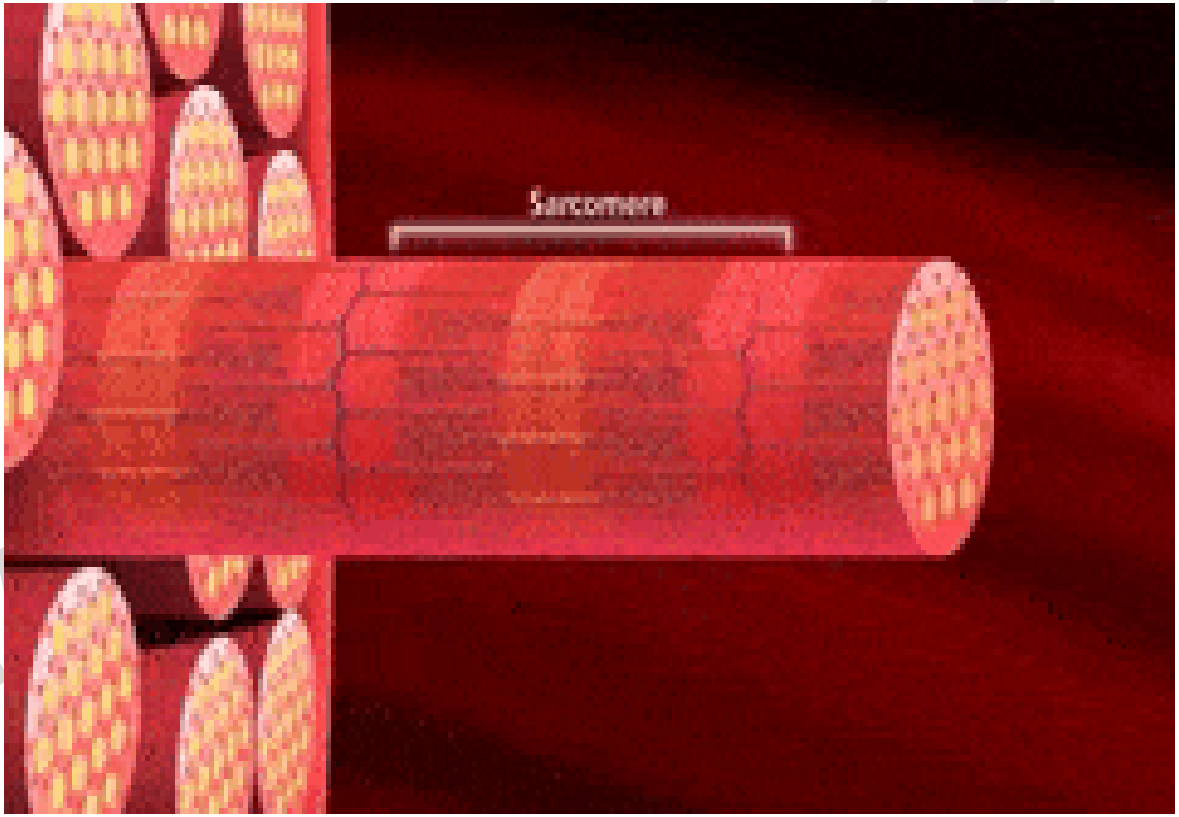
Structure of Skeletal Muscle: Connective Tissue Covering

- Muscle- Epimysium
- Fasciculus - Perimysium
- Muscle fibers- Endomysium/ sarcolemma

Muscle bundle consists of many muscle fibers.




Nucleus
Striations
muscle fiber


Sarcomere

Structure of muscle fiber

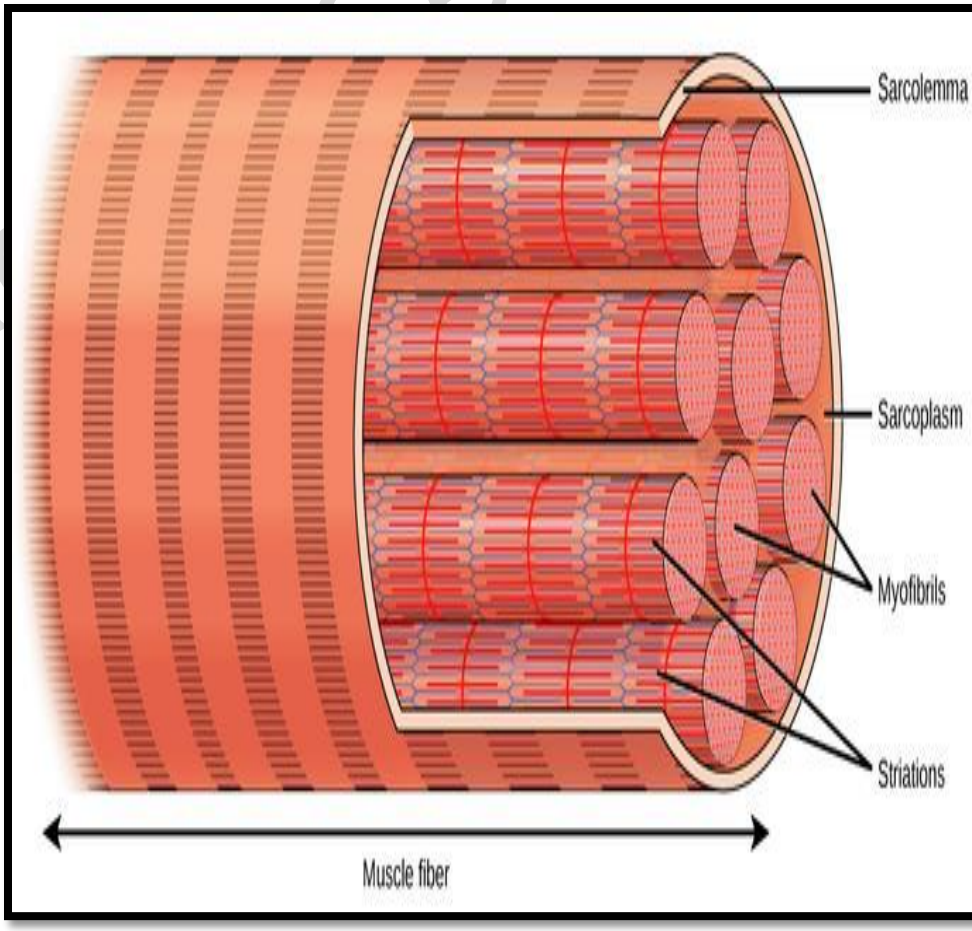
- **Muscle fiber-** 10 to 80µ in diameter each is composed of 1000s of **myofibrils**

- Each **myofibril** is in turn made up of myofilaments

- **Myofilaments**

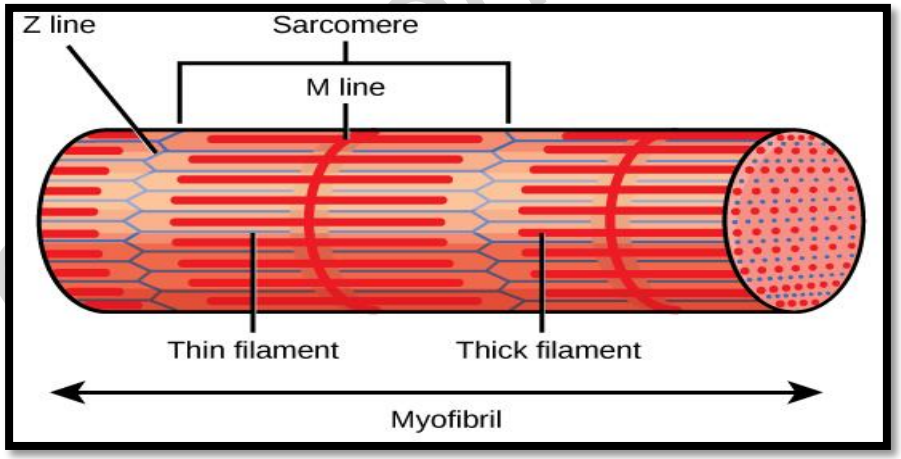
  (i) contractile- myosin , actin

  (ii) modulatory- tropomyosin, troponin

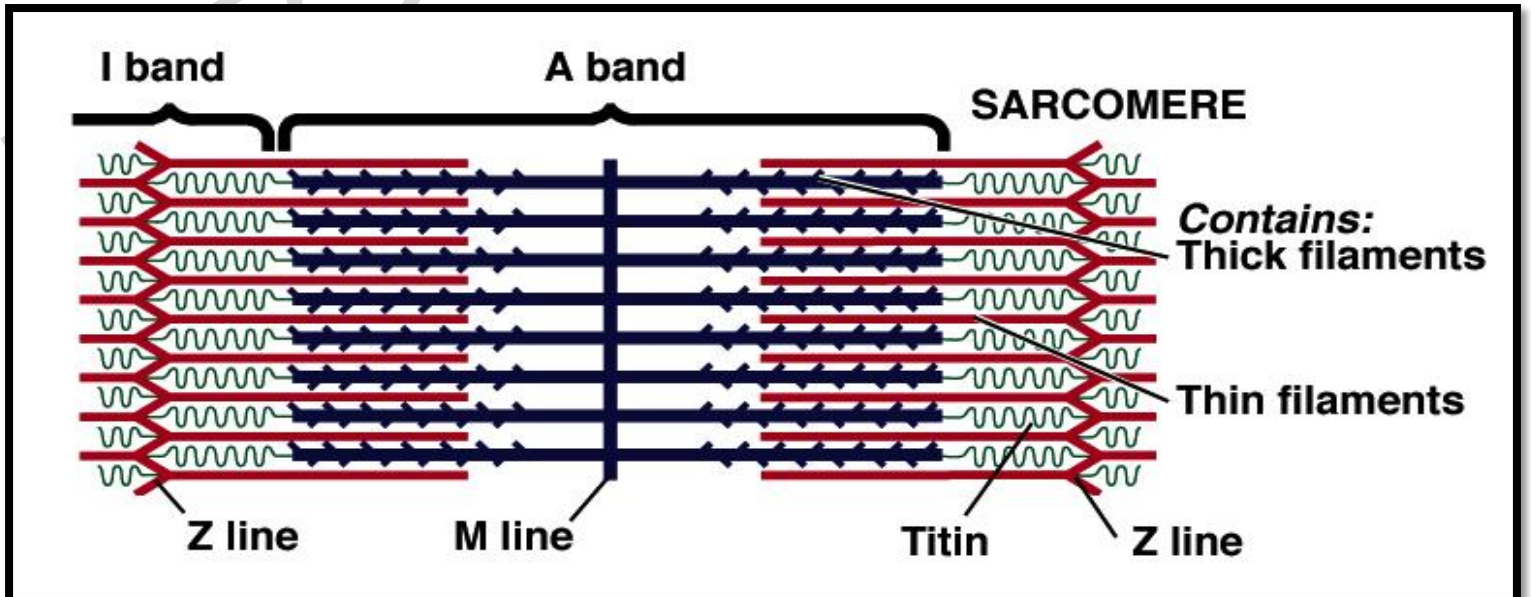


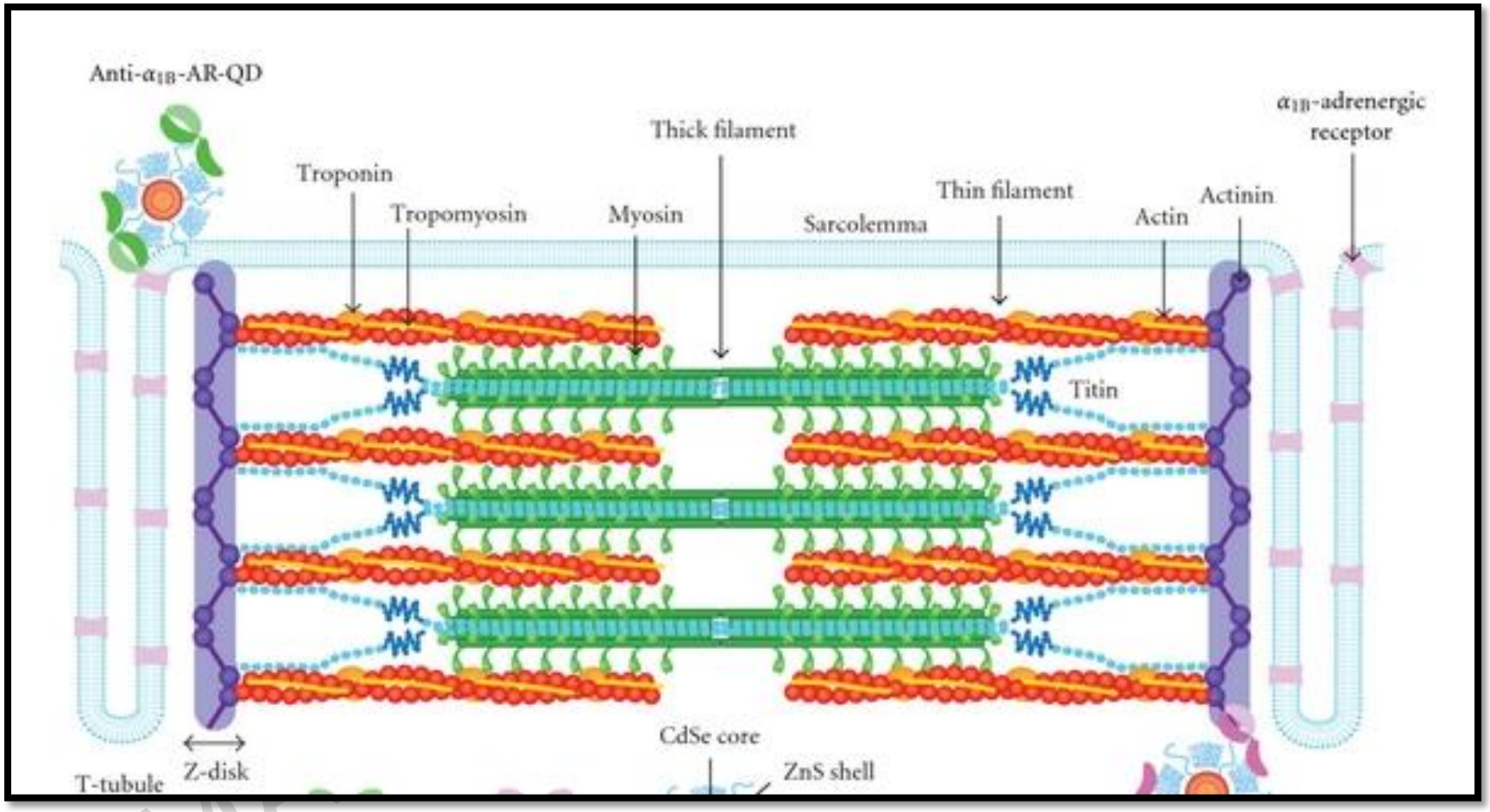
Structure of Sarcomere

- **Sarcomere- structural and functional unit of muscle fiber.**



- **Distance between two Z lines**





Actin Filaments are attached to Z line

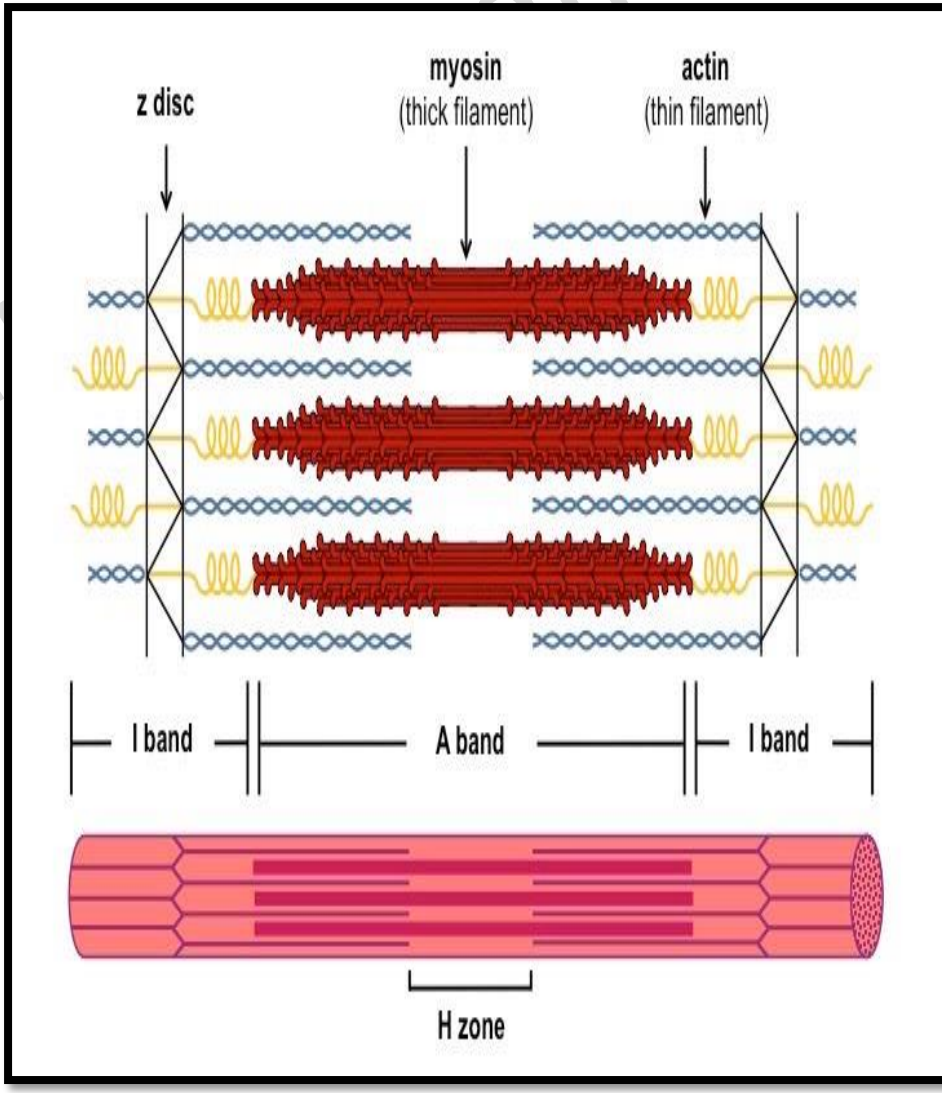
- **Myosin filaments are attached to Z line by Titin**

Structure of Sarcomere

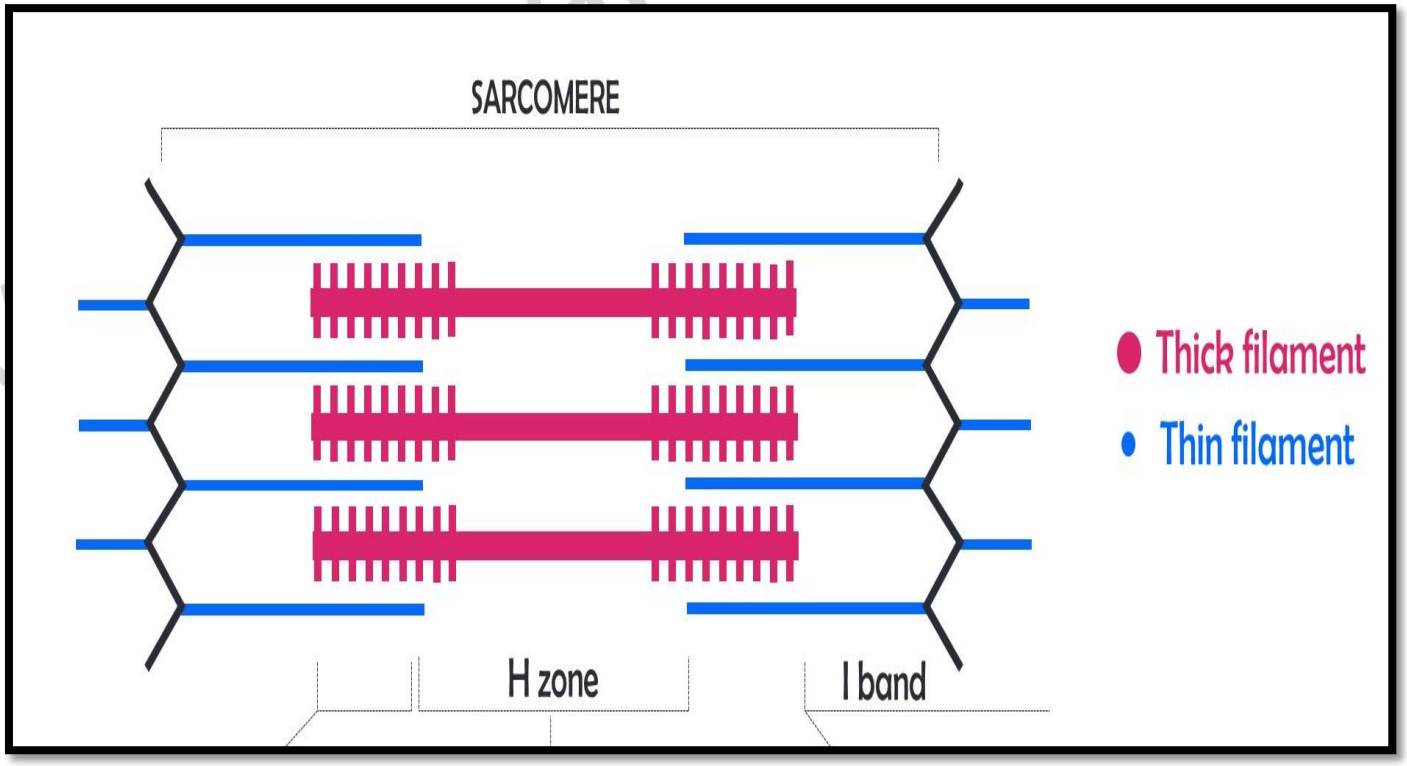
- Light band- Isotropic band- **I band (J band) -** only thin filaments

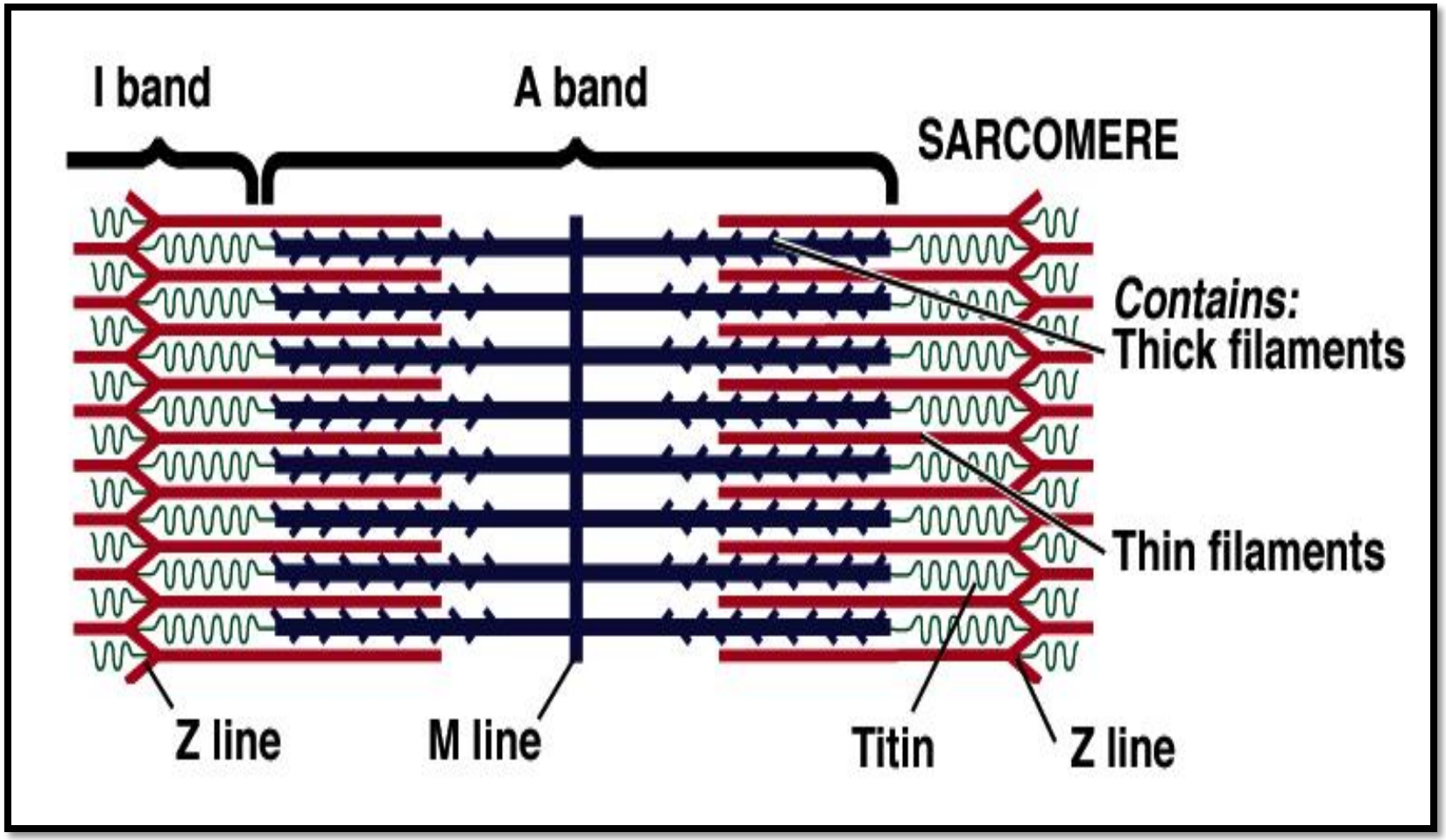
- Dark band- Anisotropic band- **A band (Q band)**

- **overlapping of thin & thick filaments**

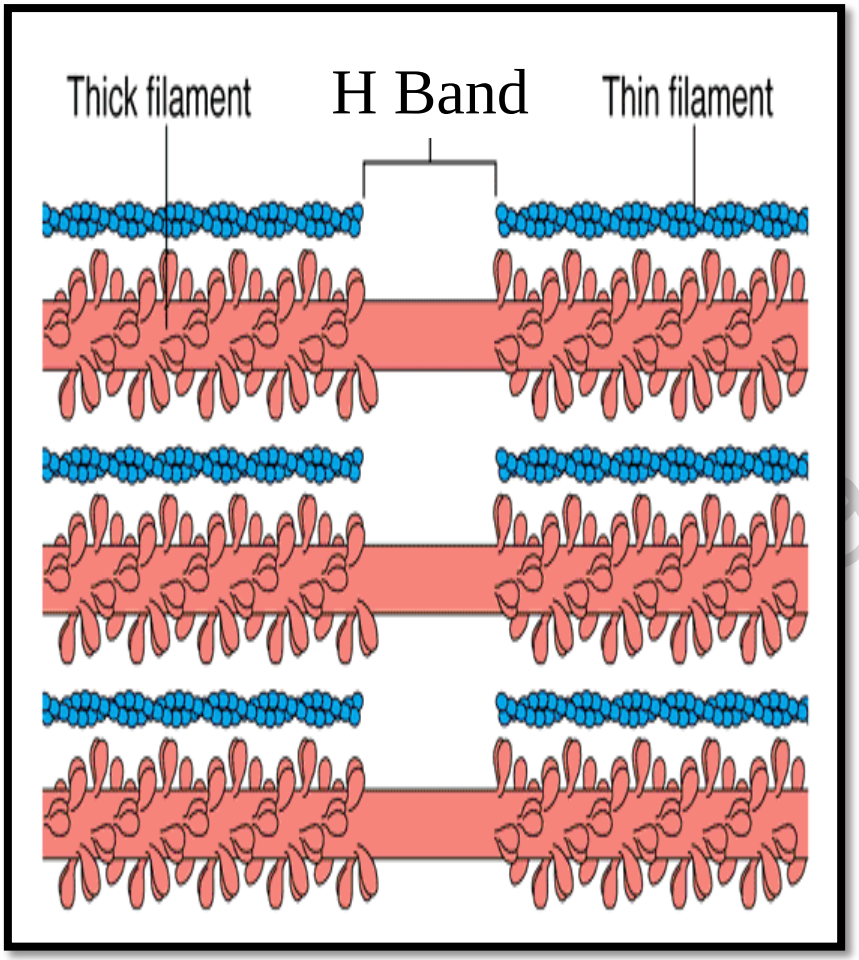


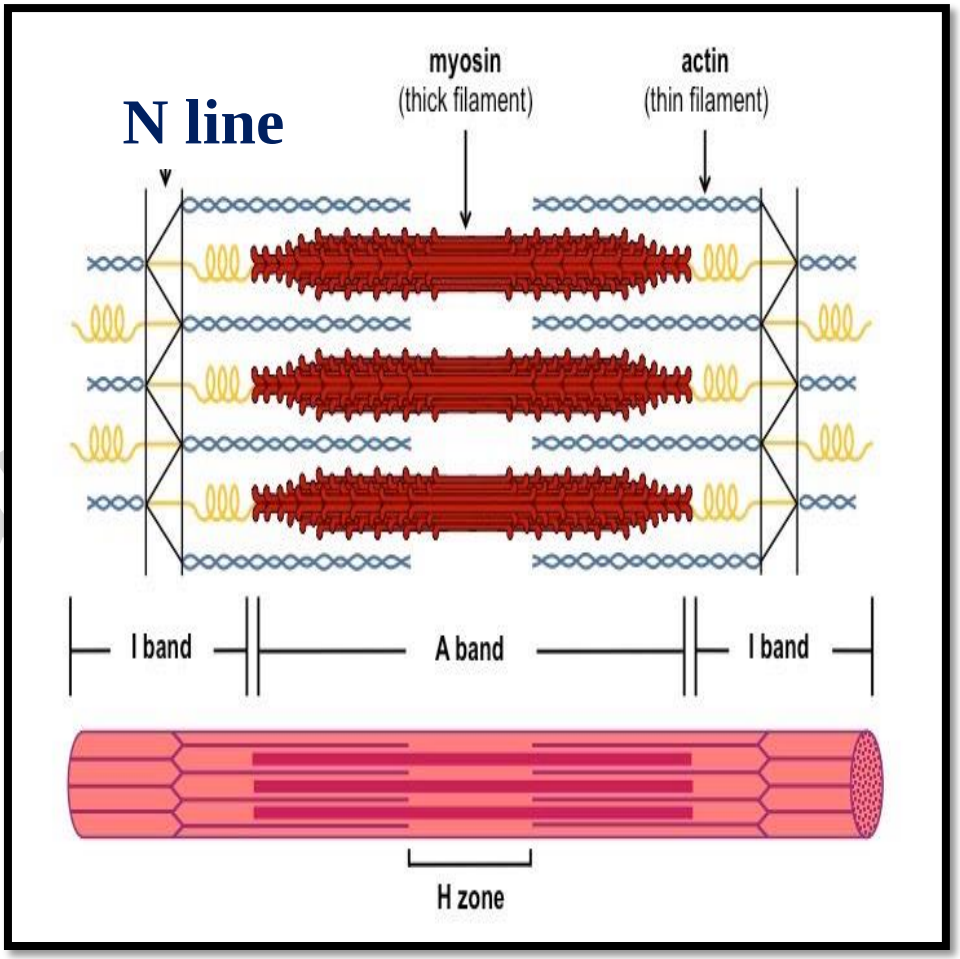
- **H zone (Henson's zone)-** lighter zone in A band
- here thin filaments do not overlap thick filaments
- **Z line (Zwischenscheibe)-** in the center of I band
  - **Dobie's line/ Krause membrane**





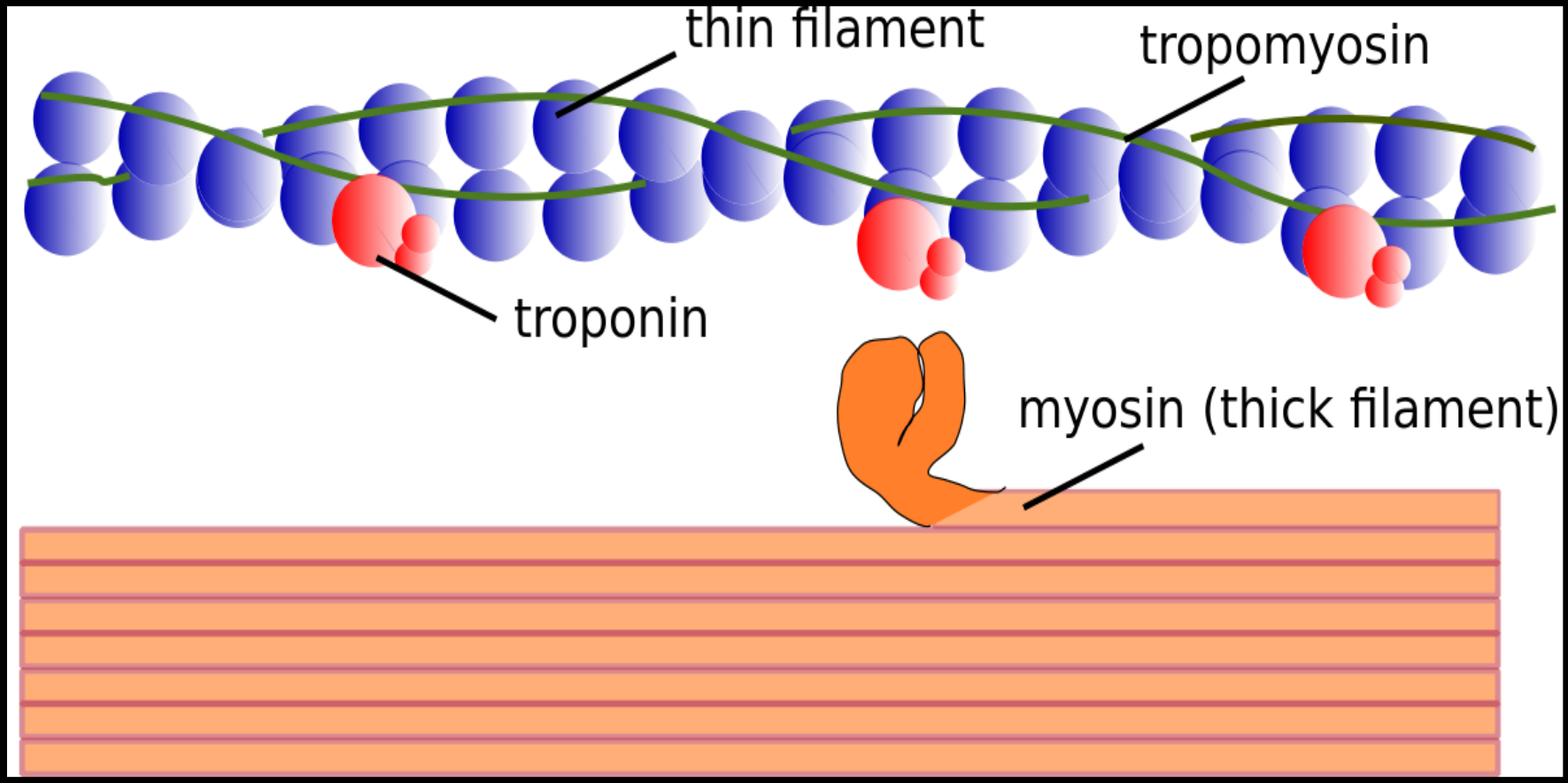
M line- in the center of A band





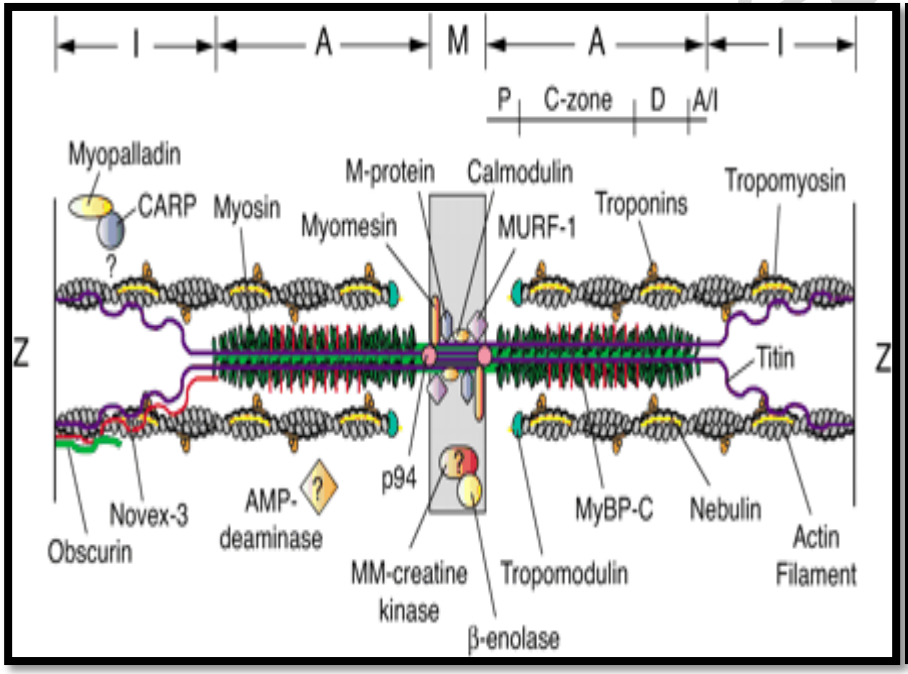
Myofilaments- thick & thin filaments

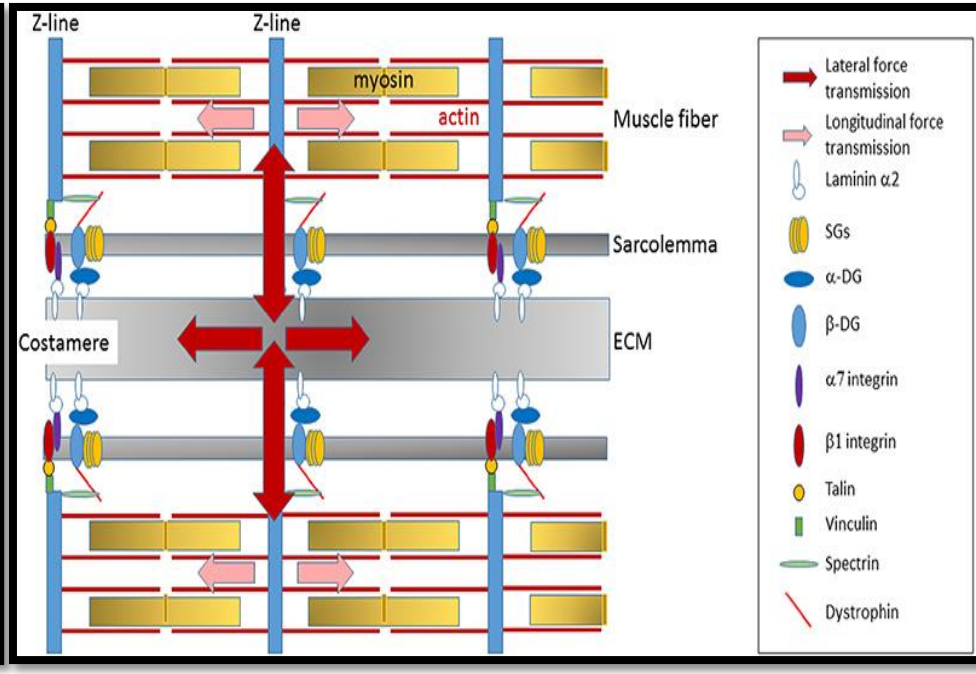
- **MYOFILAMENTS** – are protein microfilaments of sarcomere.



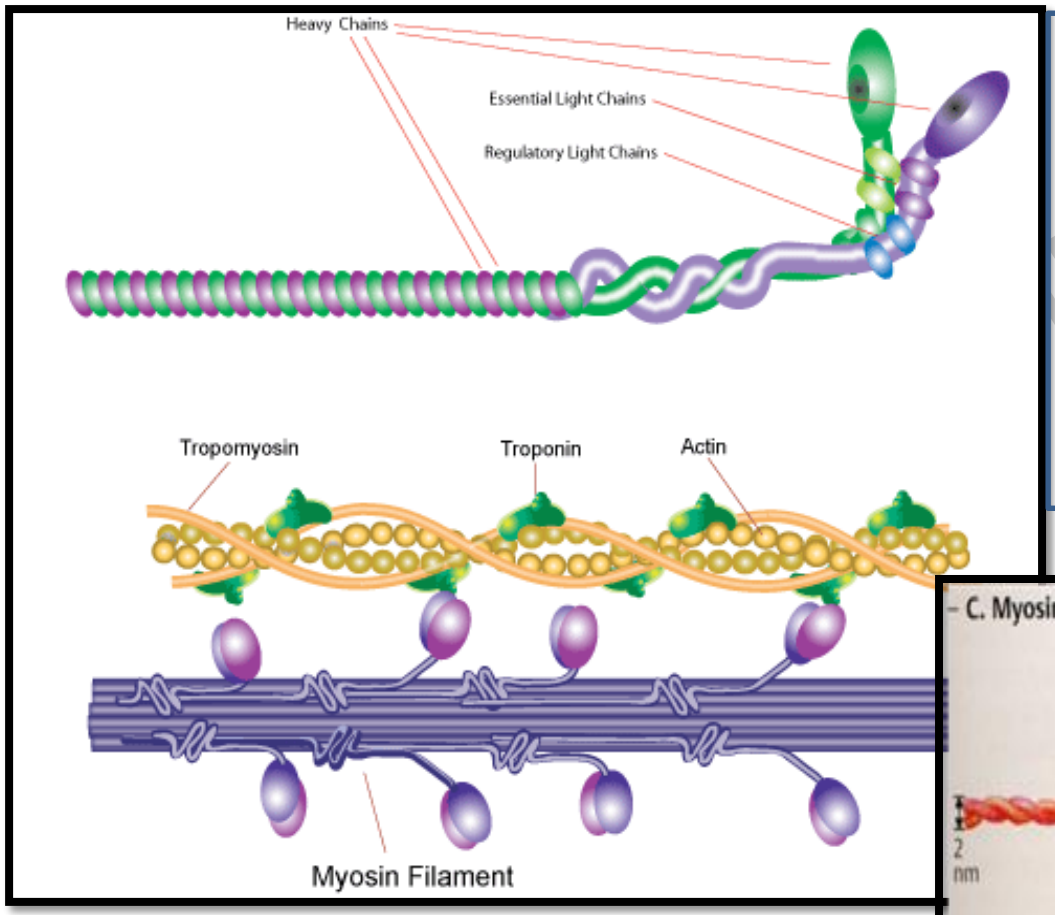
Myofilaments

- **Contractile proteins** : **Actin, Myosin**
- **Regulatory Proteins**: **Troponin, Tropomyosin**
- **Structural Proteins**: **Myomesin, Dystrophin**

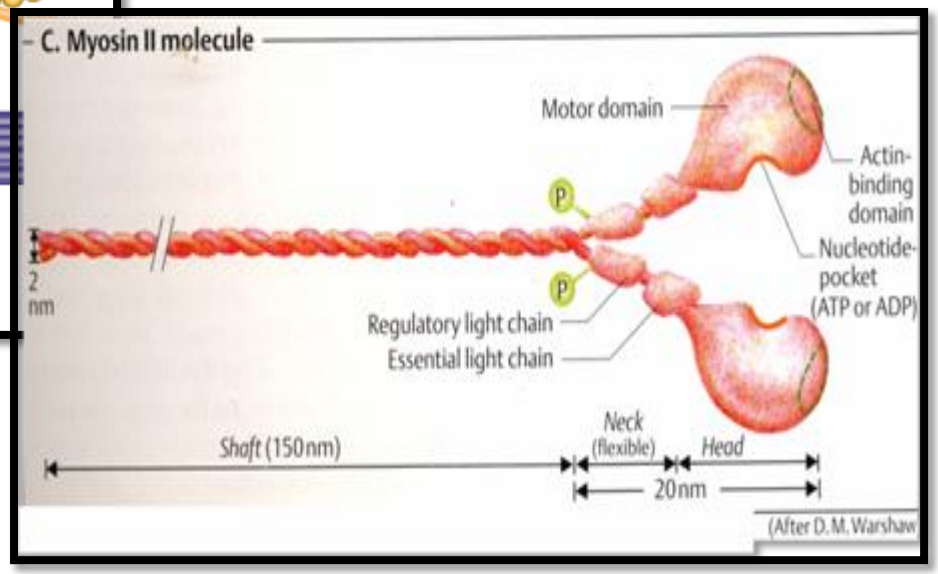




Myosin



- 2 Heads
- 2 tails wound in double helix
- Head has got 2 attachment sites for ATP and actin



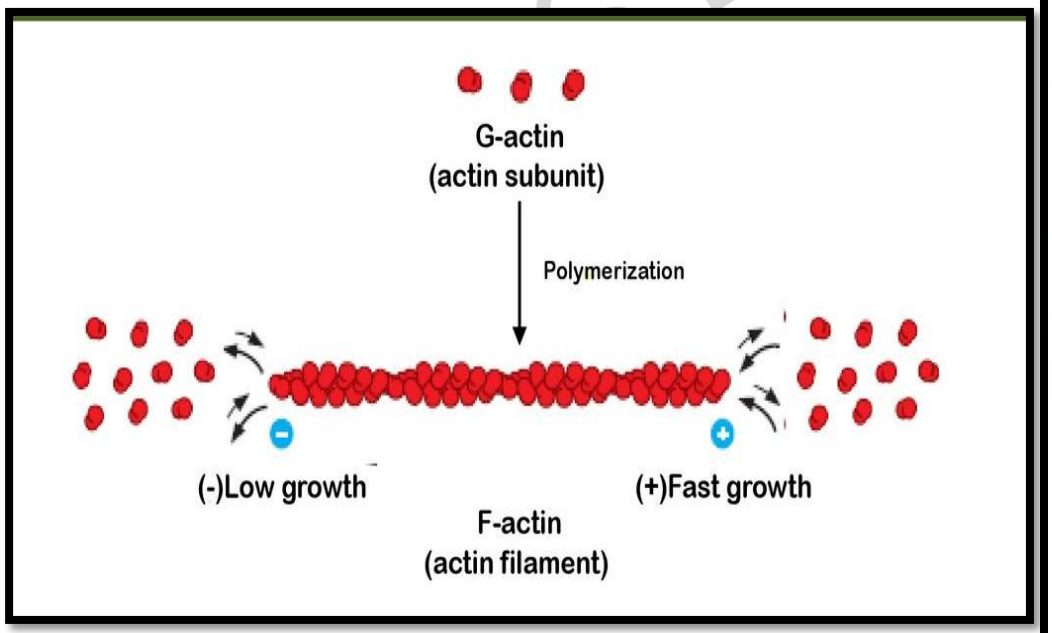
- **Thin Filaments**

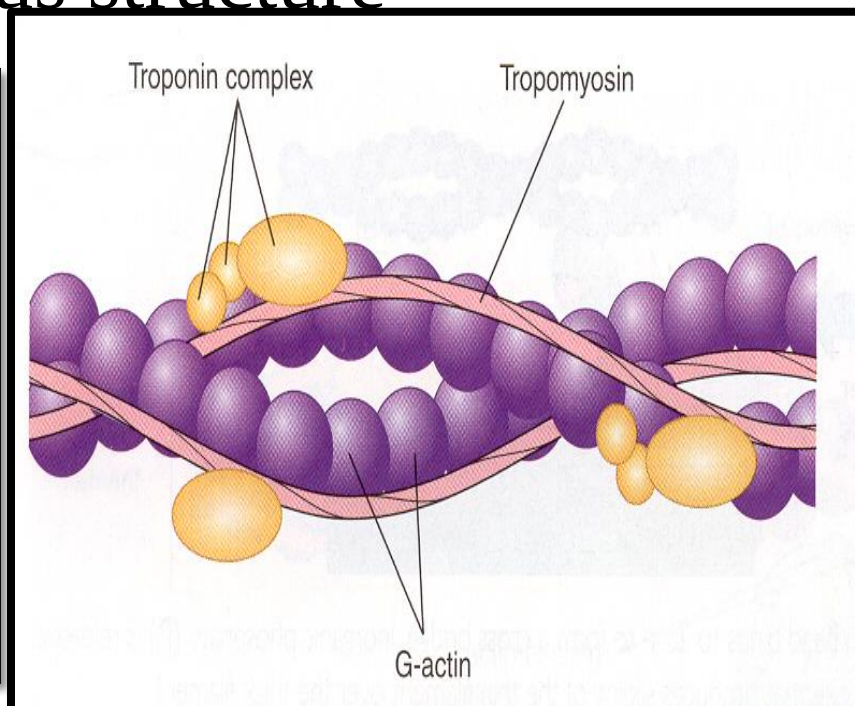
300- 400 **Actin** molecules in double helix

Each Actin molecule has a binding site for Myosin head (called actin active sites)

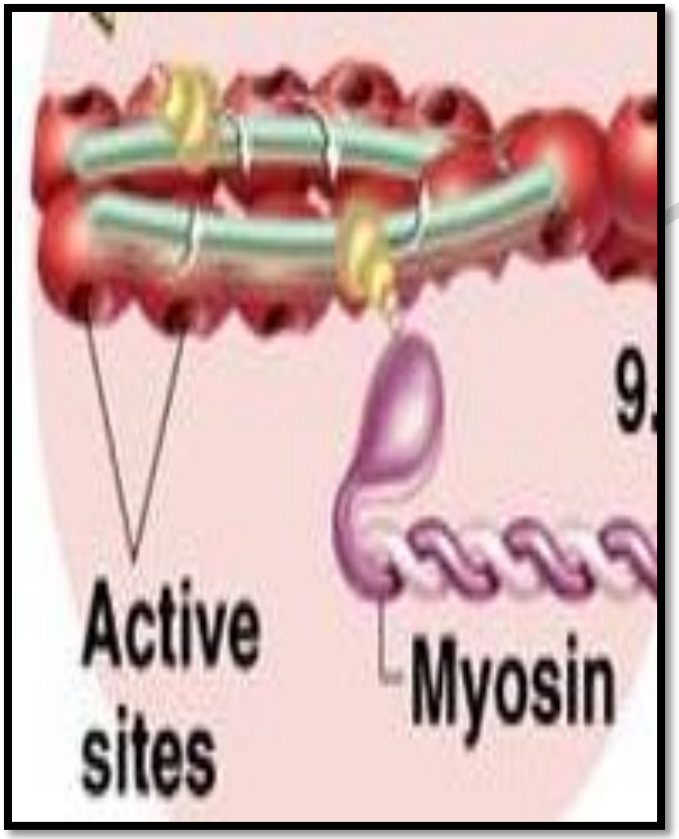
- G actin – monomeric globular structure

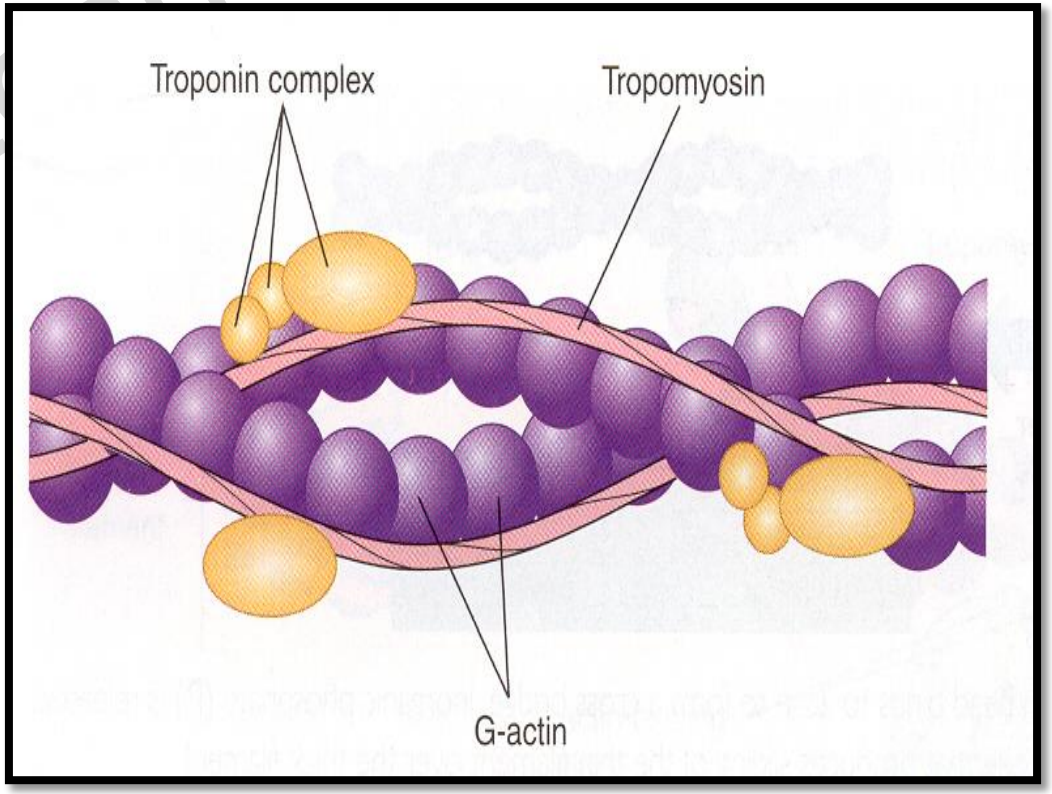
- F actin - polymeric fibrous structure





- **Tropomyosin** - long protein filaments that cover active sites of actin from Myosin head.
- At rest Tropomyosin prevents muscle contraction

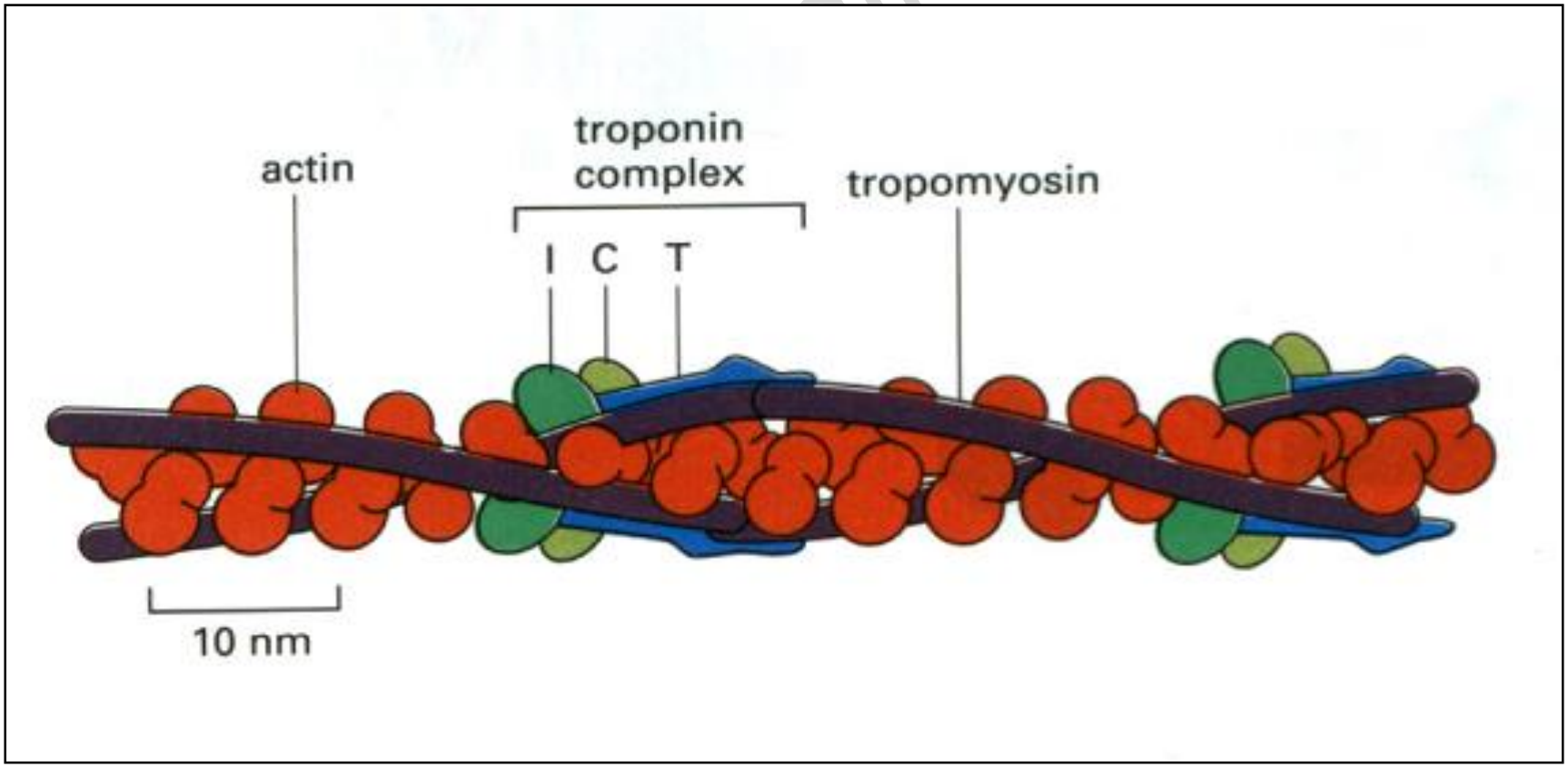




Troponin – Trimeric protein

- located at intervals on tropomyosin

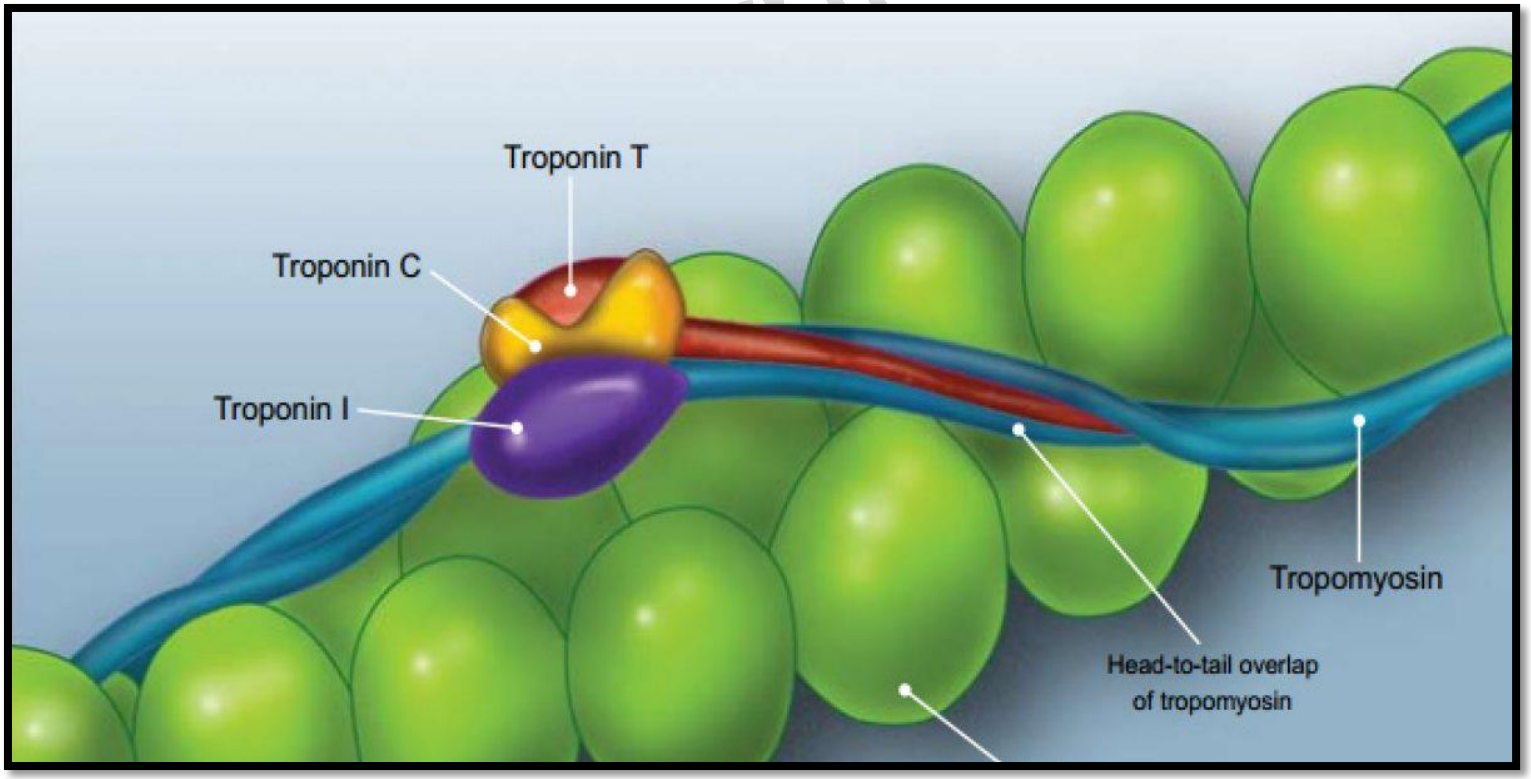
-made of 3 protein subunits (**TnI, TnC & TnT**)

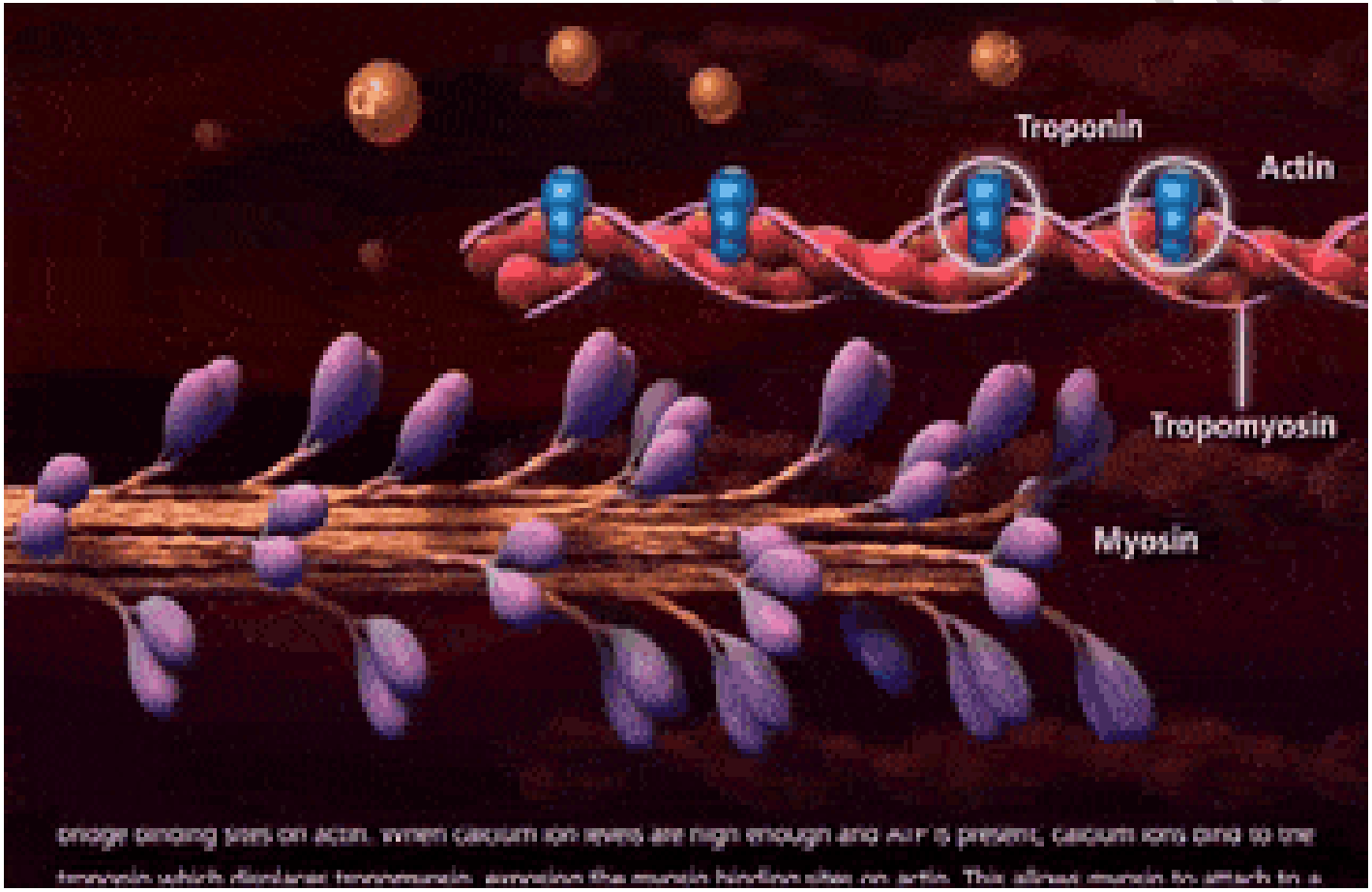


- **Troponin I** – binds the **C & T subunits**

Troponin T - Binds Troponin to **Tropomyosin**

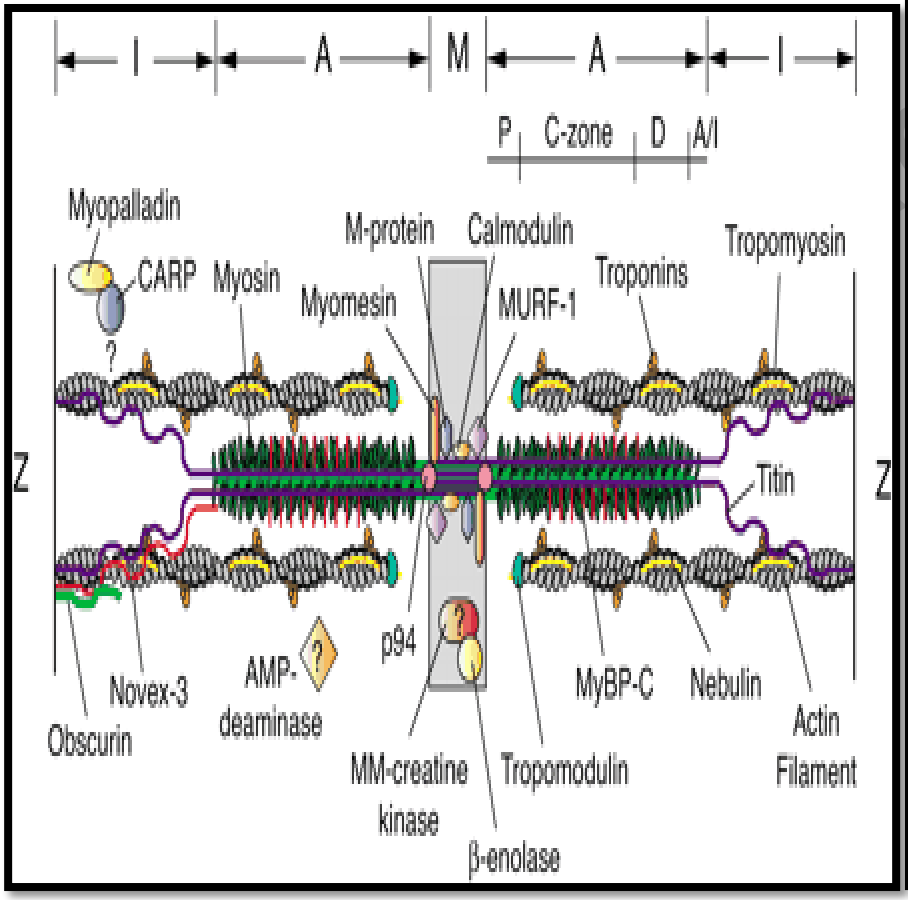
Troponin C – Binds to **calcium**

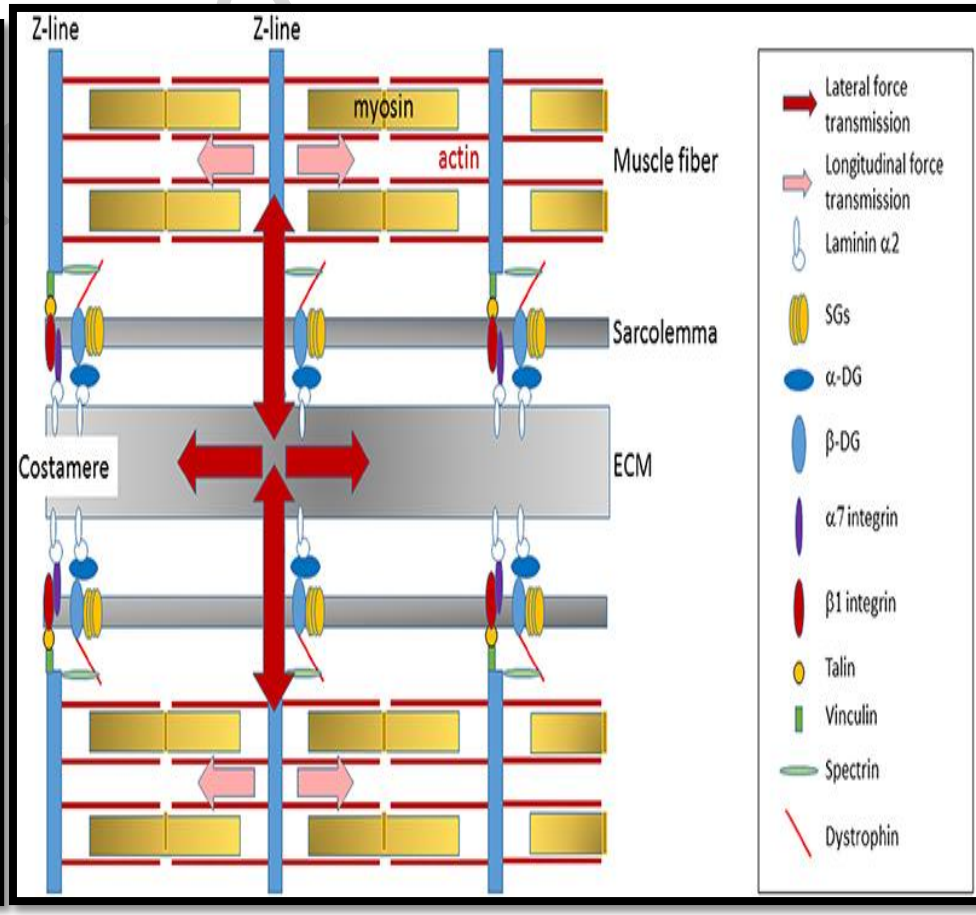


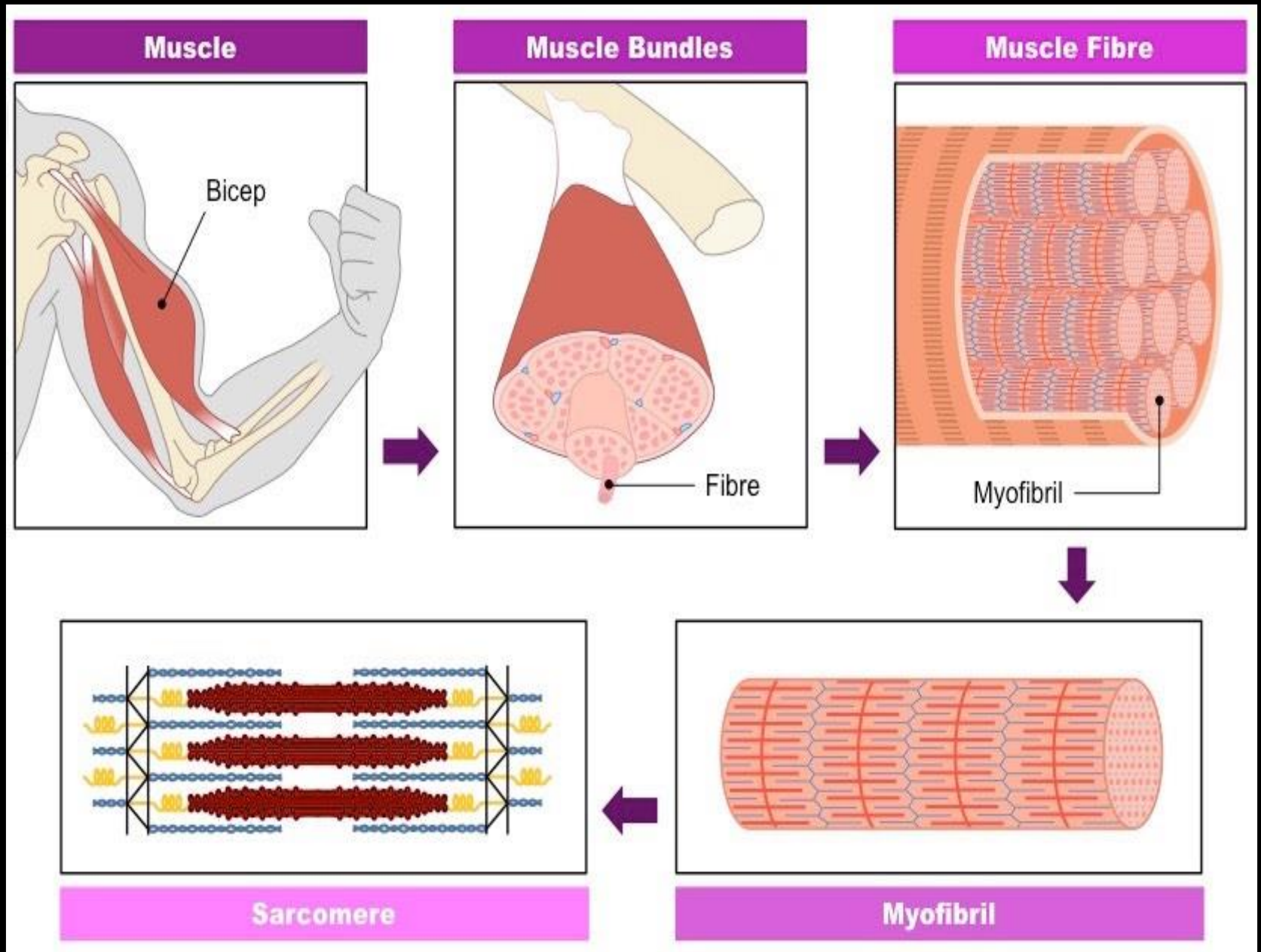

Troponin
Actin
Tropomyosin
Myosin

Myofilaments

Structural Proteins: **Myomesin, Dystrophin**

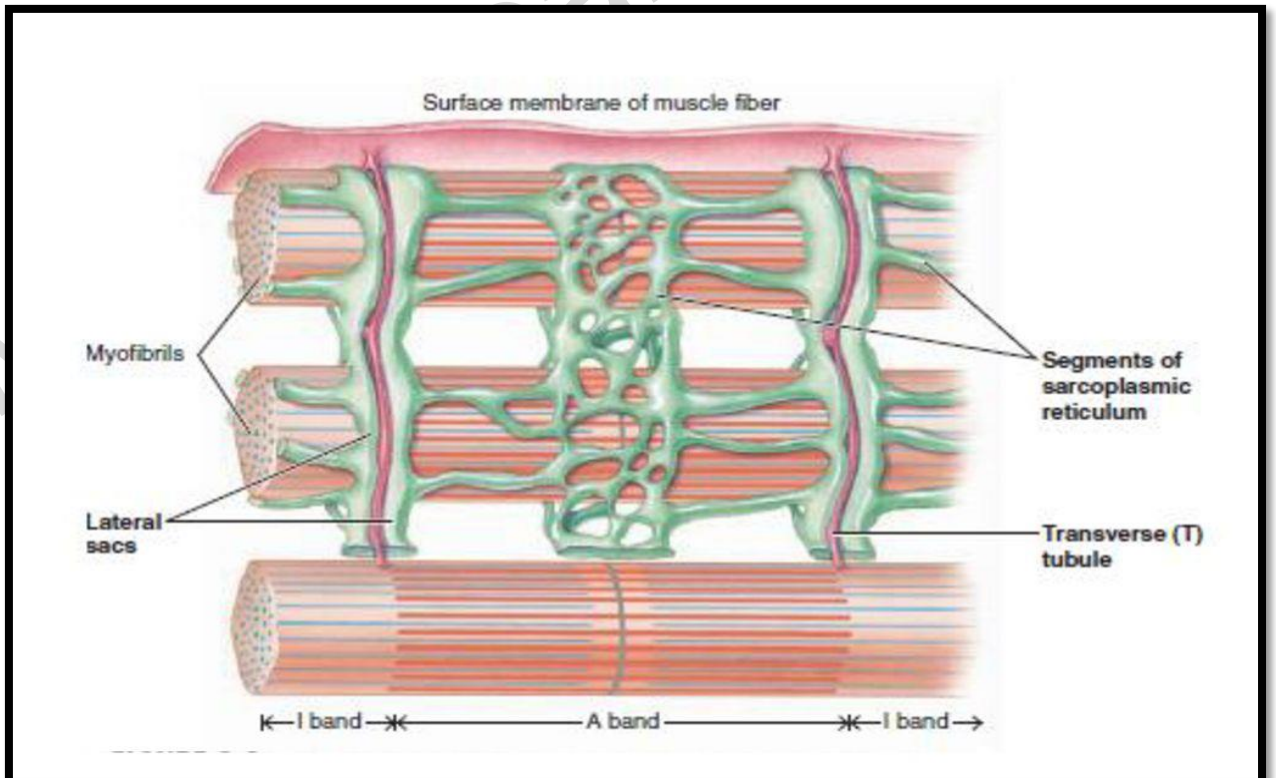





Muscle
Bicep
Muscle Bundles
Fibre
Muscle Fibre
Myofibril
Myofibril
Sarcomere

Sarcotubular system

- Network of Transverse and Longitudinal tubules present in sarcoplasm in close approximation to sarcomere.



Sarcotubular system

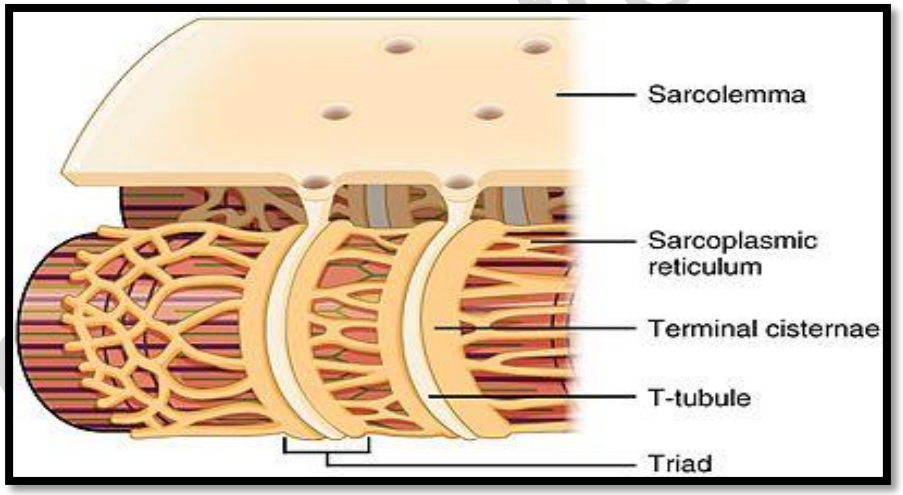
T-tubule

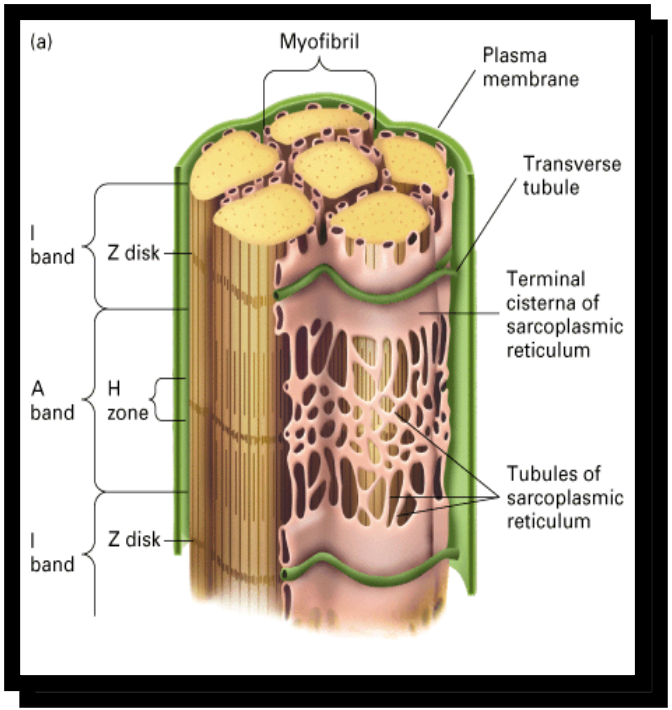
- inward extension of sarcolemma

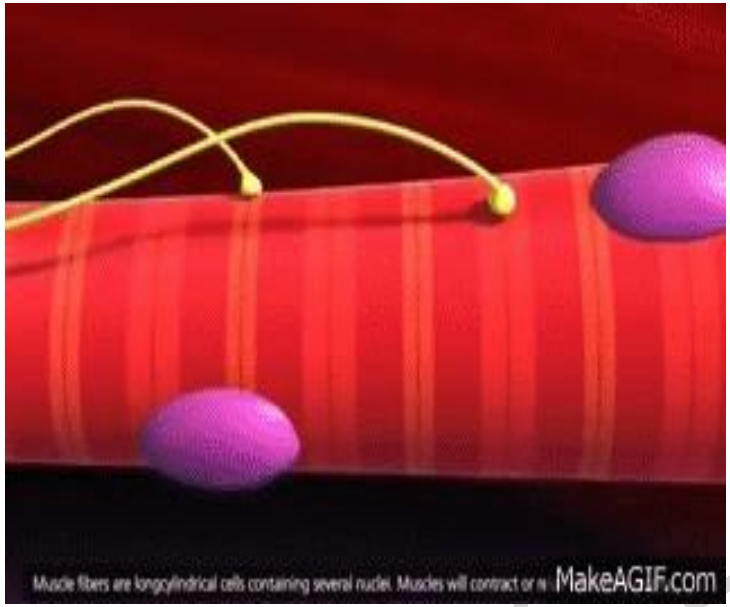
- opens to exterior contains ECF

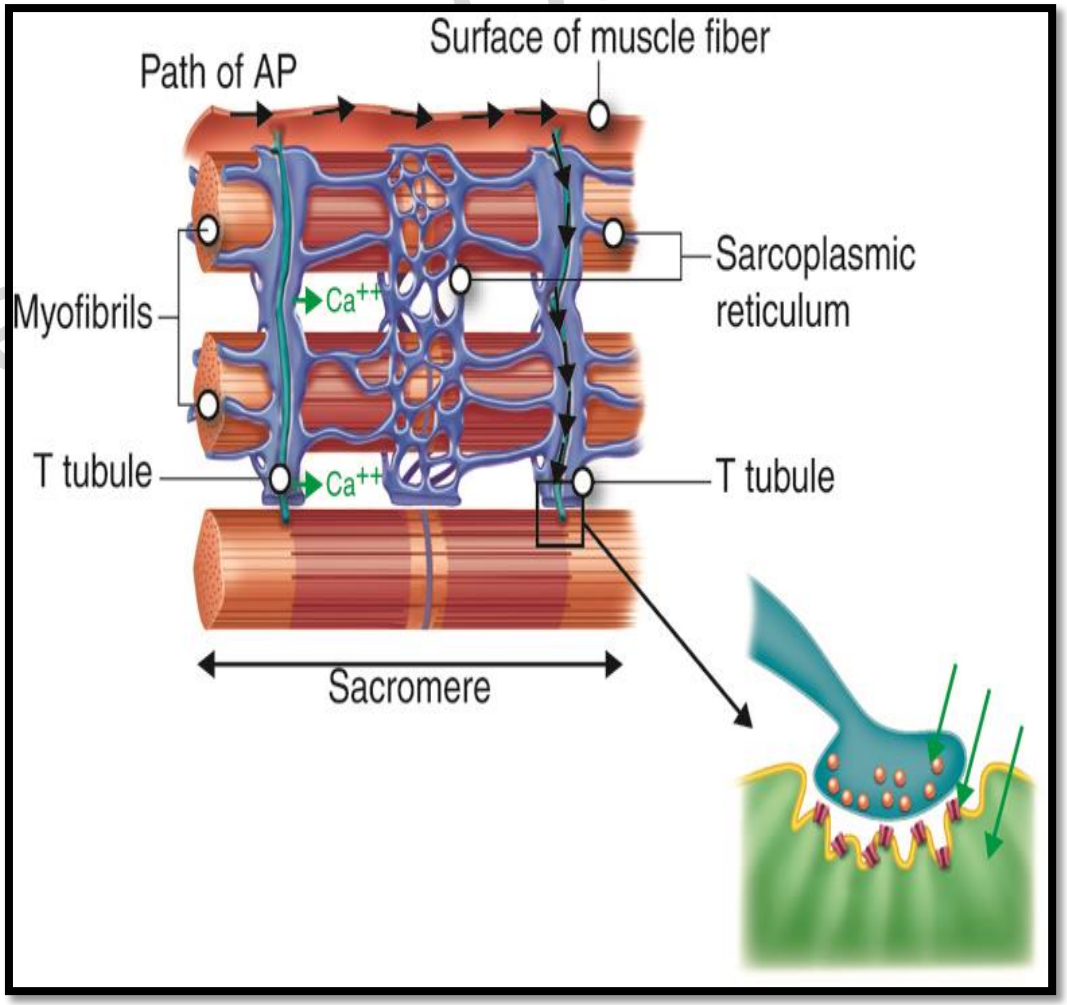
- run transverse to myofibrils

- **Transmission action potential to myofibrils**









Sarcotubular system

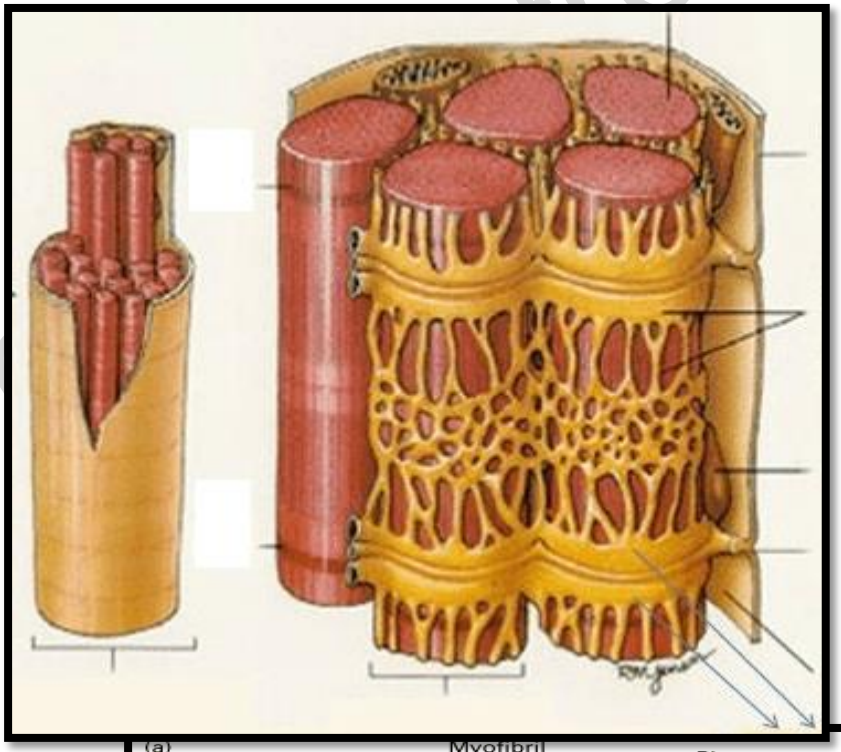
L-tubule

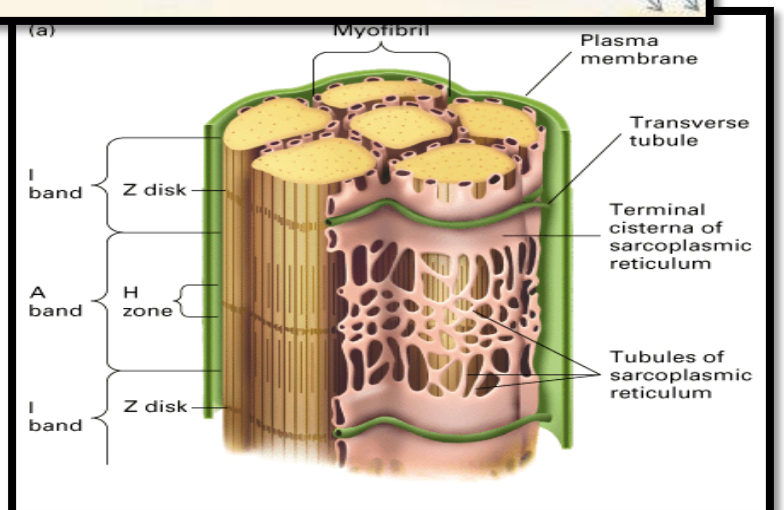
- sarcoplasmic reticulum

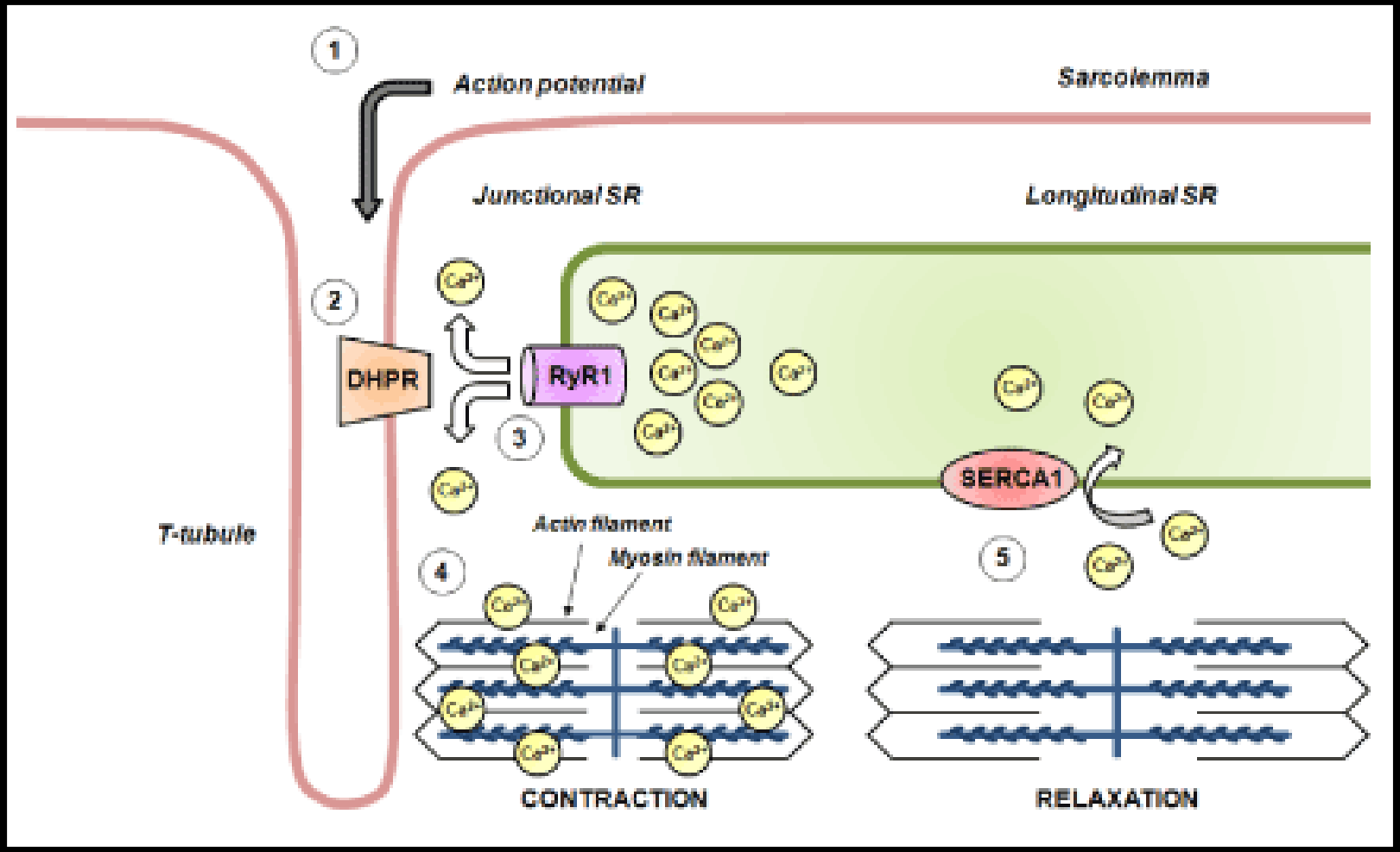
- run parallel to myofibrils

-terminates in dialated terminal cisternae

- Function: **stores calcium ions**







When a muscle is stimulated signals are carried to each myofibril by T- tubule

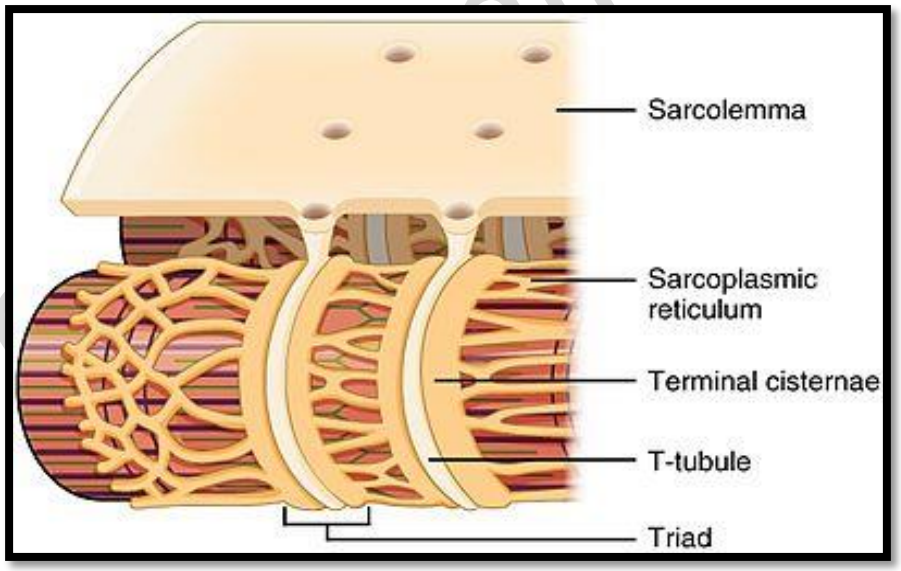
- **T- tublue inturn stimulates L-tubule to release Calcium ions**

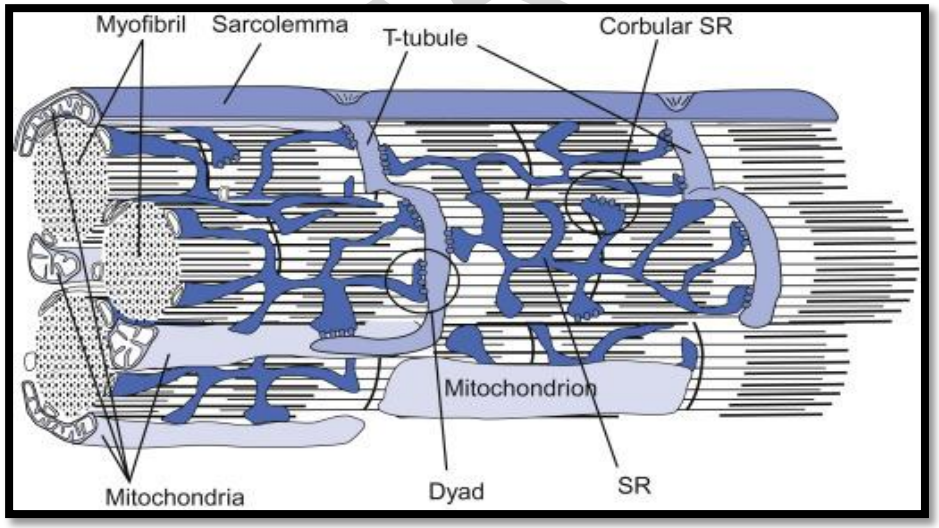
Sarcotubular system

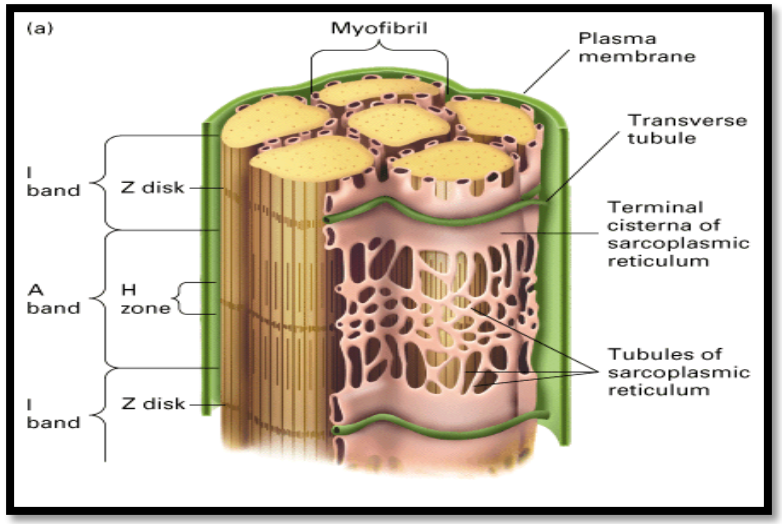
Triads-

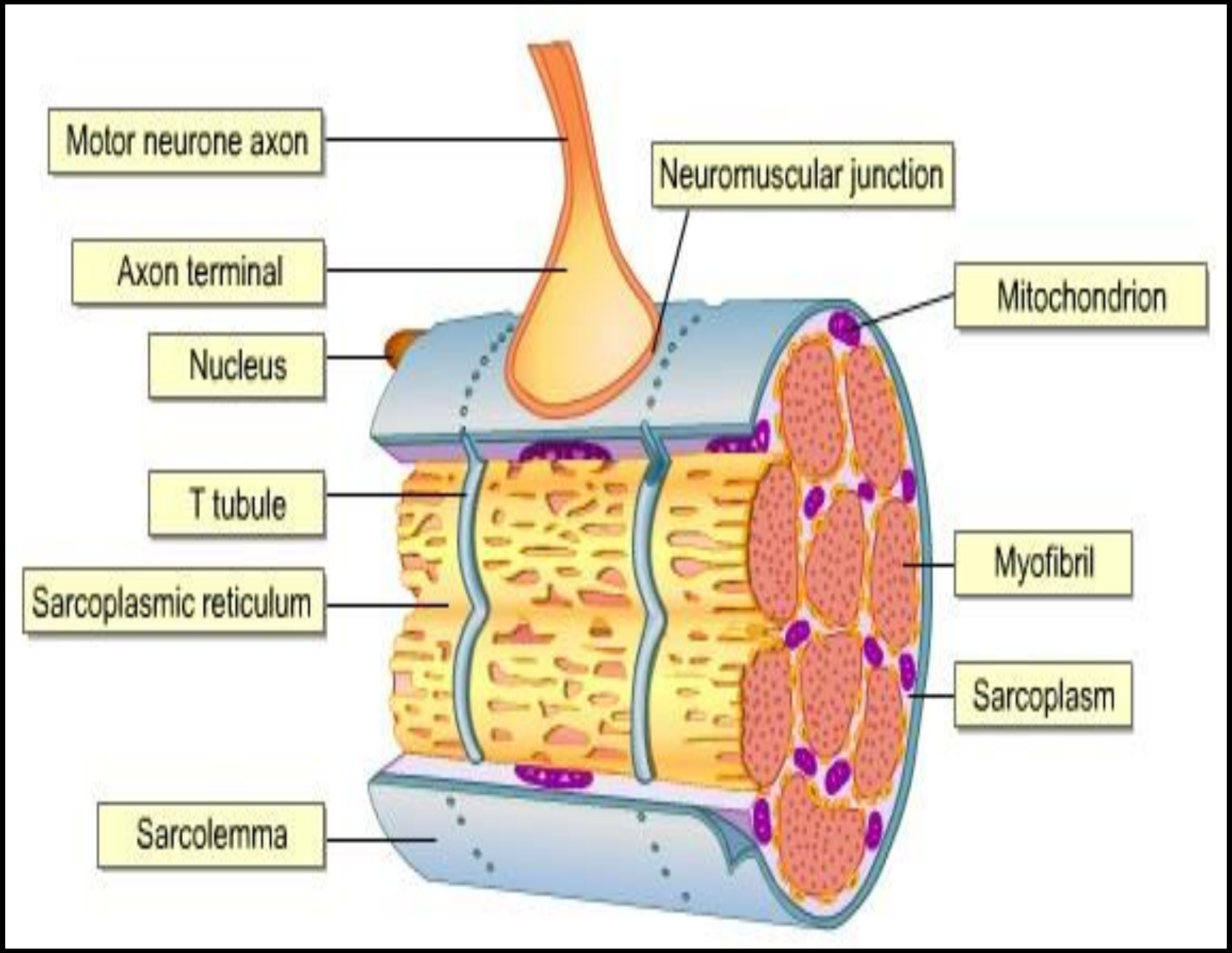
- two terminal cisternae abutting a T-tubule.

Dyad in cardio myocyte

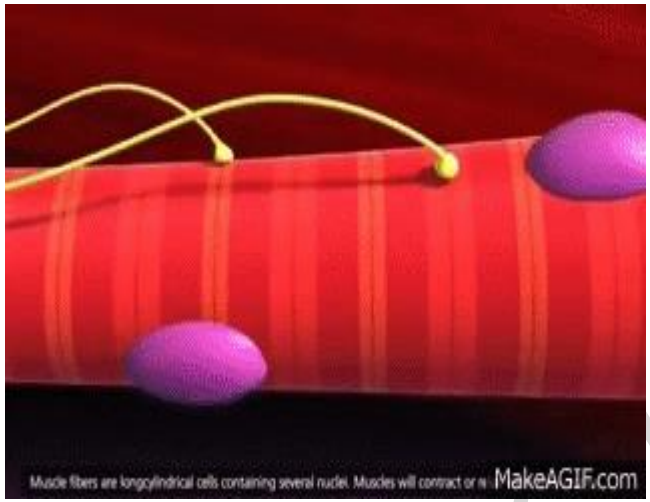


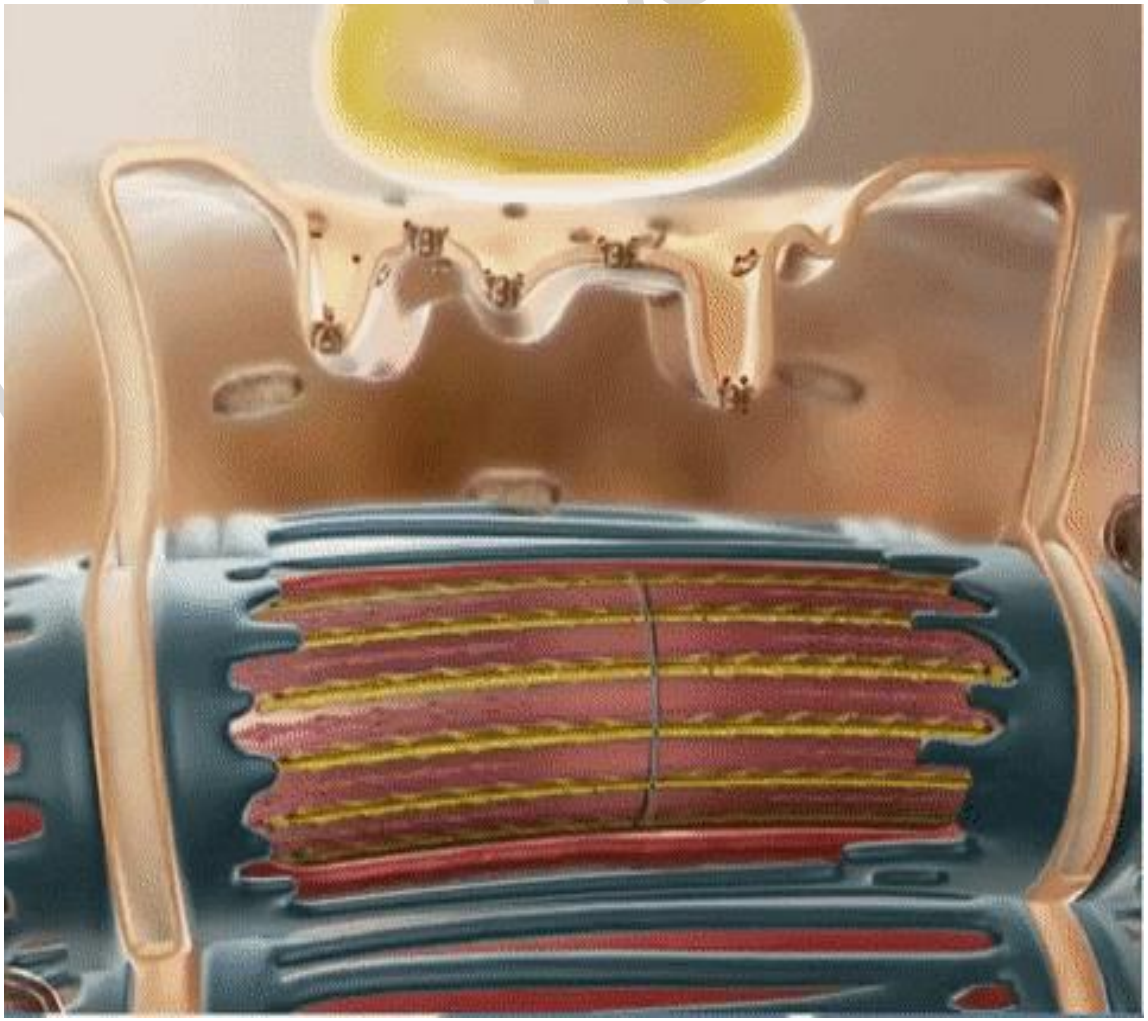


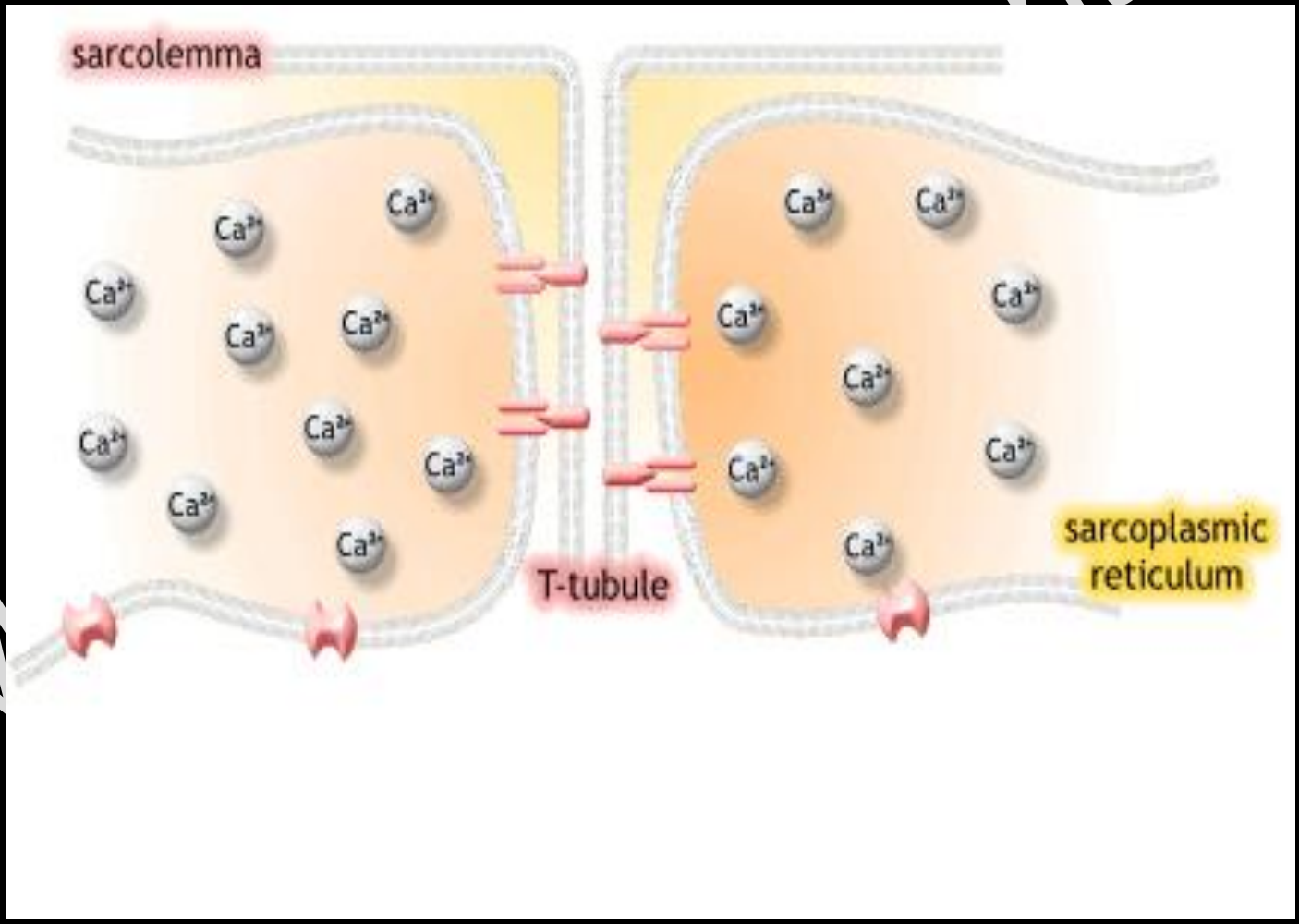


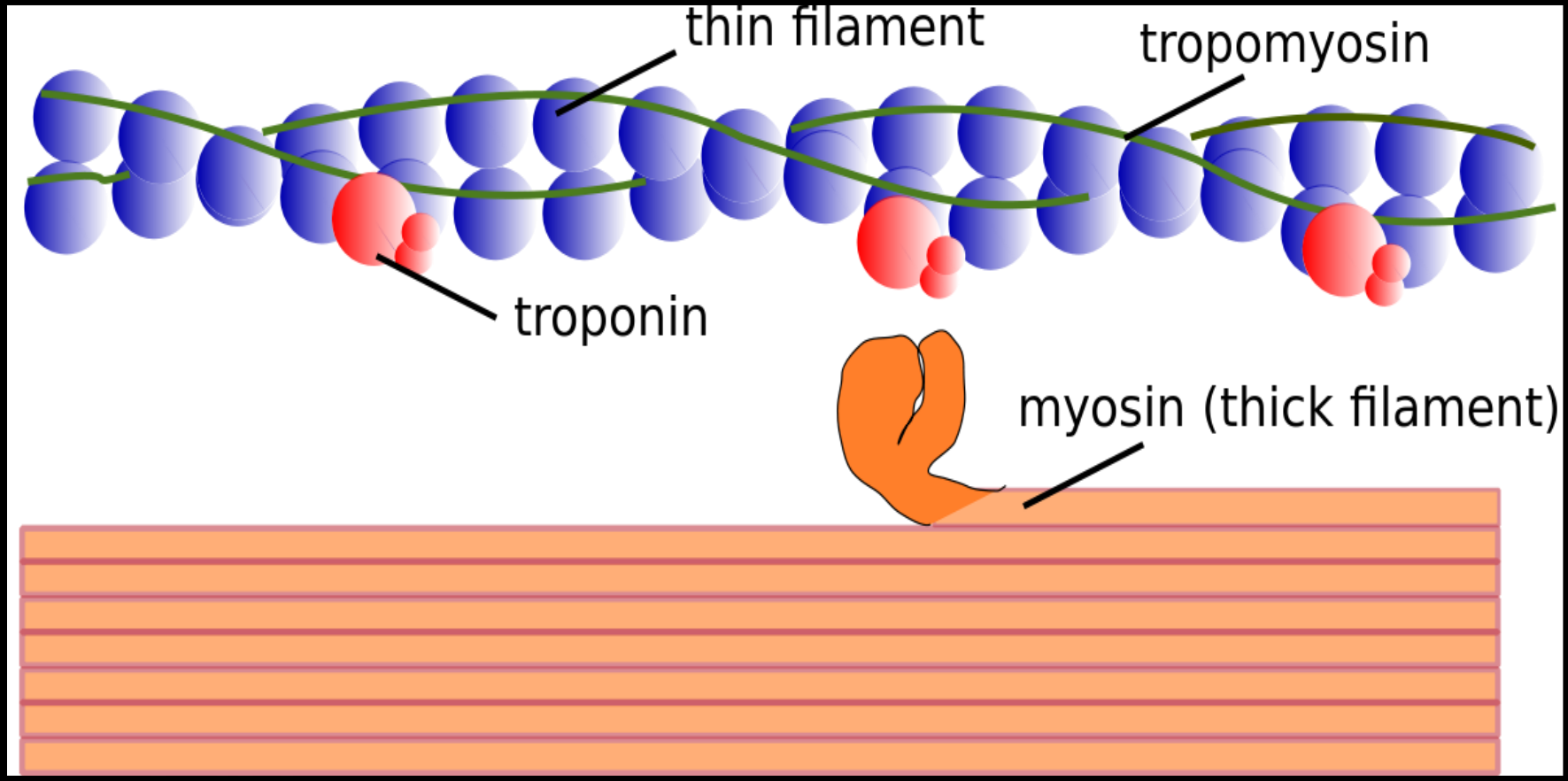

Motor neurone axon
Neuromuscular junction
Axon terminal
Mitochondrion
Nucleus
T tubule
Myofibril
Sarcoplasmic reticulum
Sarcoplasm
Sarcolemma

Function of sarcotubular system

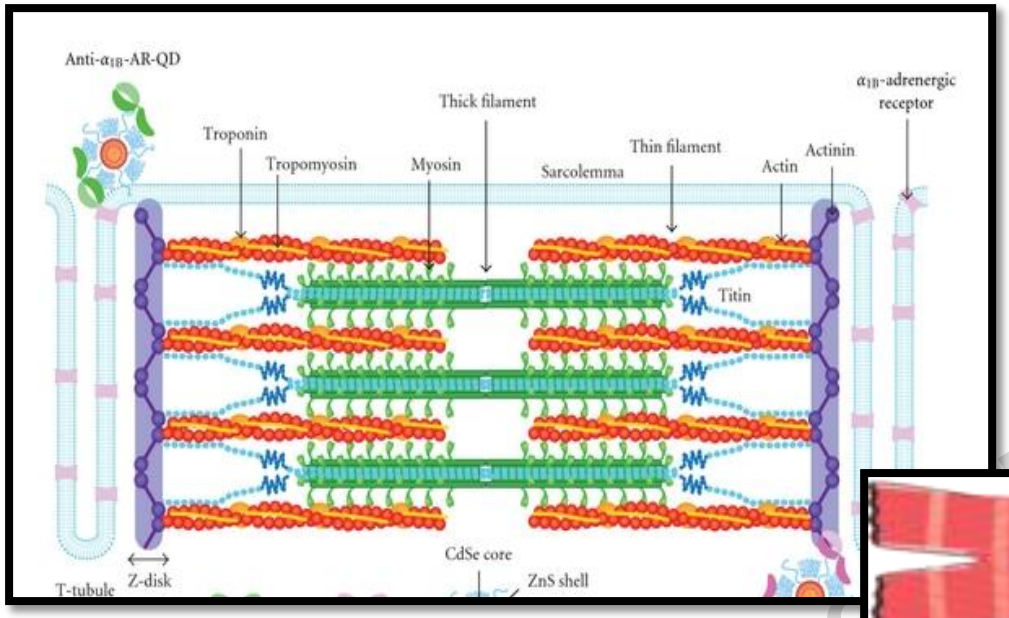




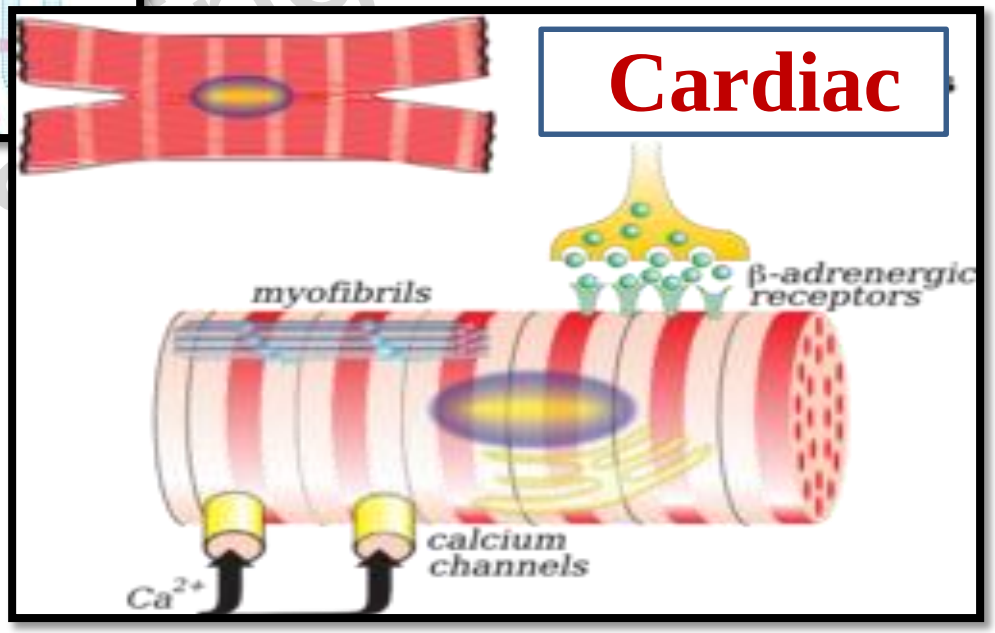

sarcolemma
Ca2+
T-tubule
sarcoplasmic reticulum

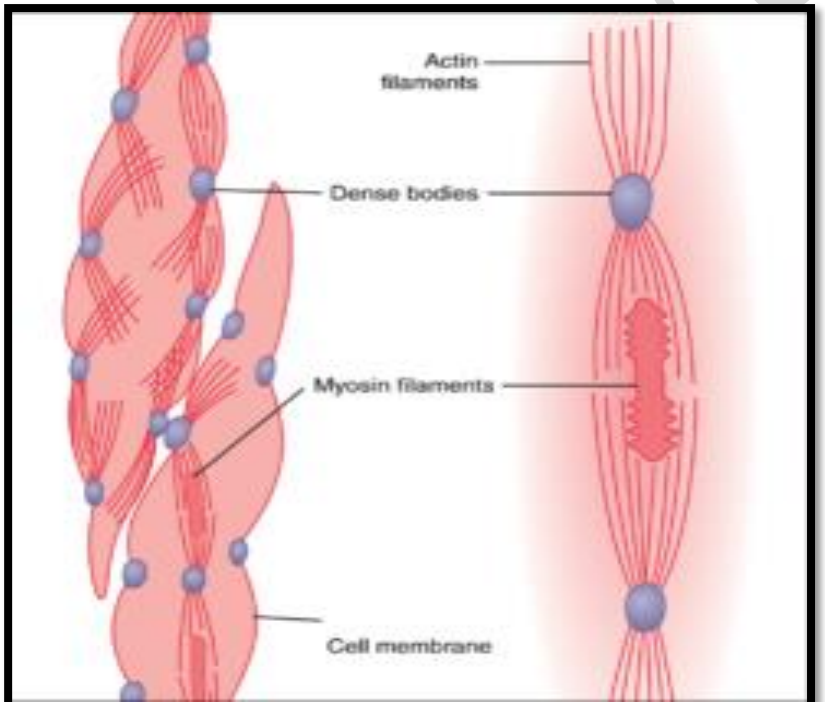


Calcium Ions bind with C unit of Troponoin and initiates muscle contraction



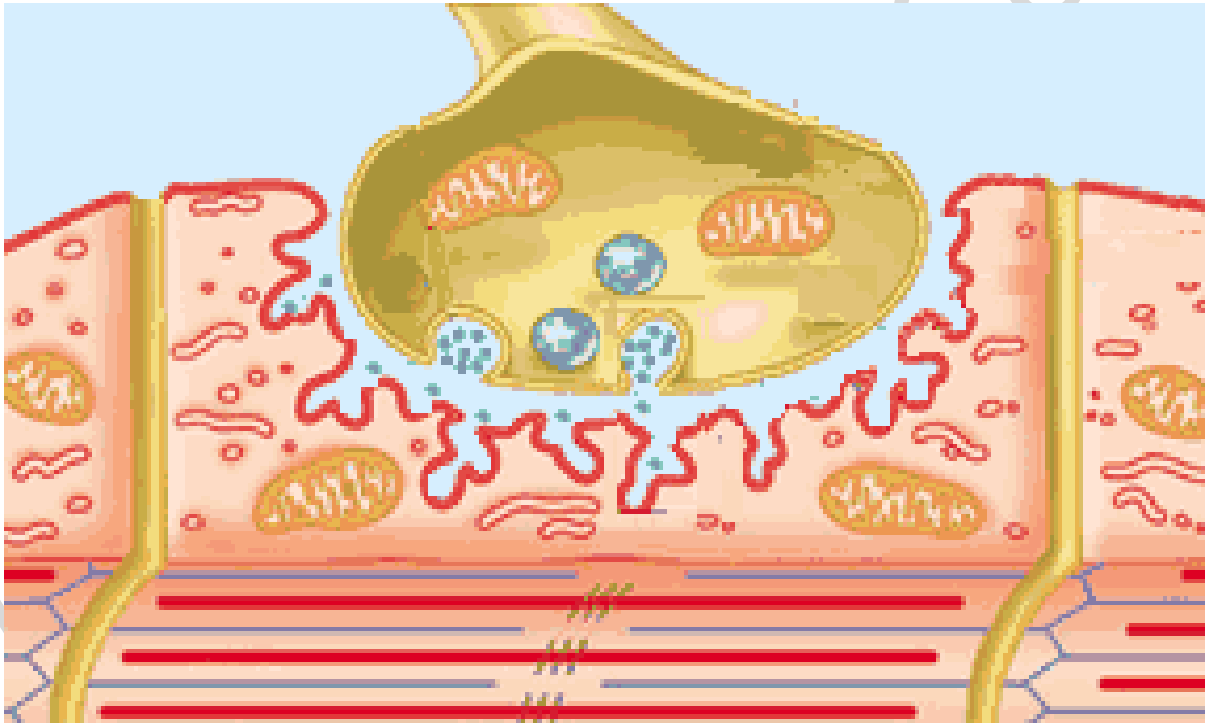
Skeletal Muscle



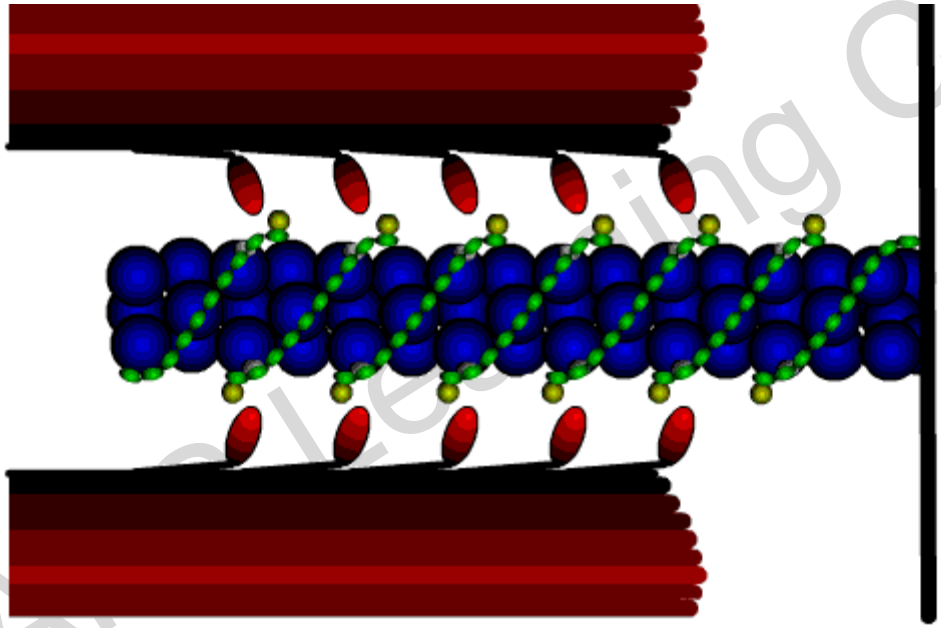


Smooth Muscle

Mechanism of Muscle contraction



Is explained by Sliding Filament Theory

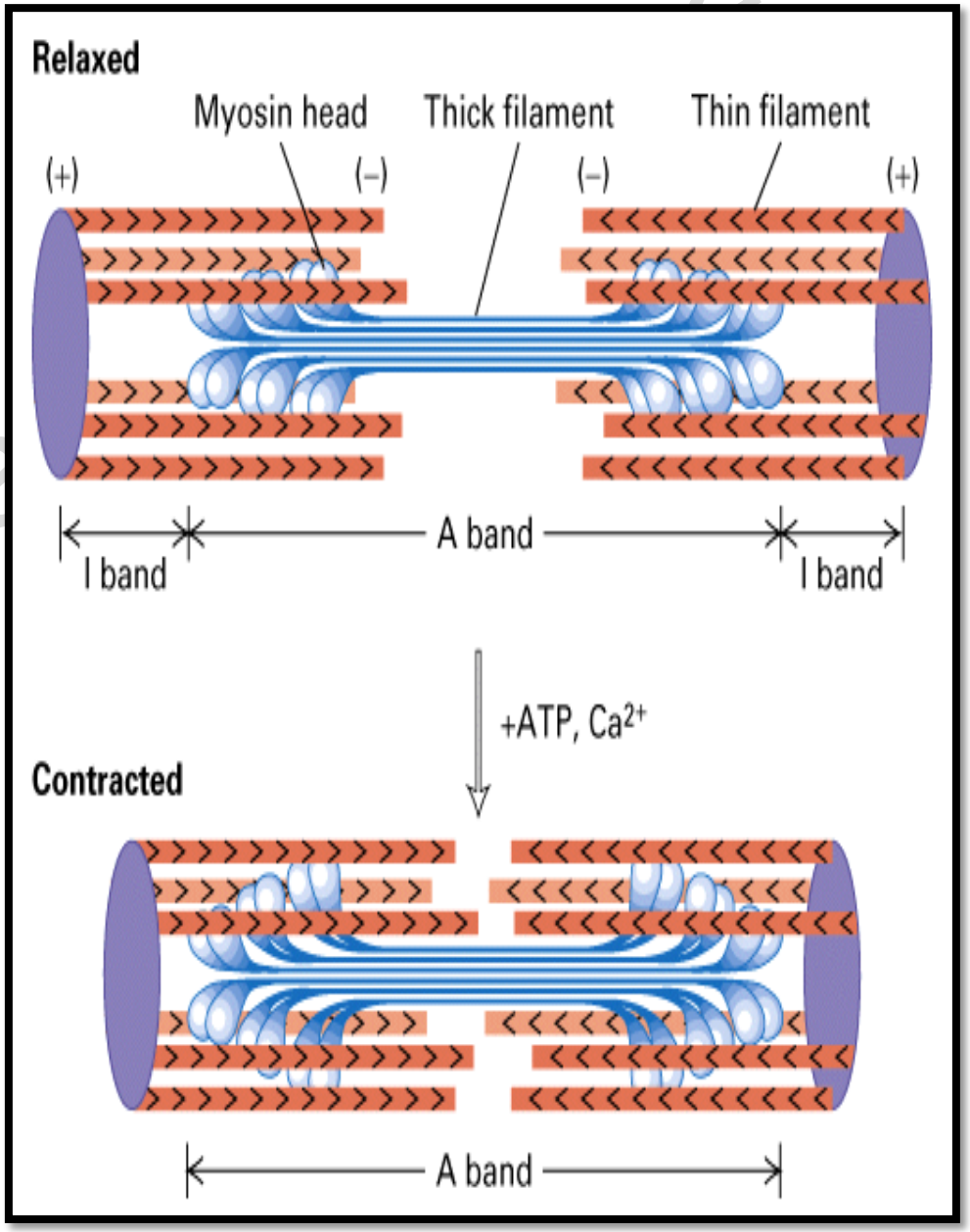


The action potential inhibits the calcium pumps, and calcium escapes from the **sarcoplasmic reticulum.**

- **Sliding Filament Theory**

- Andrew Huxley
- Ralph Niedergerke
- Hugh Huxley
- Jean Hanson

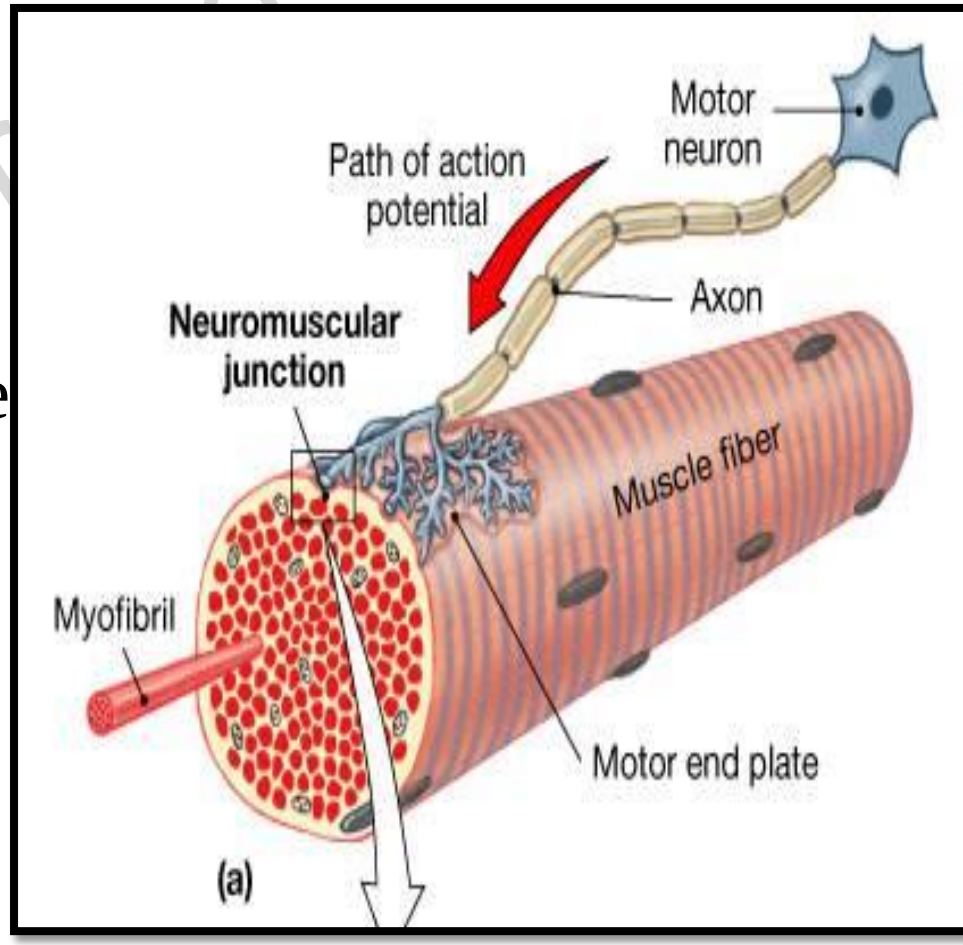
(1954)



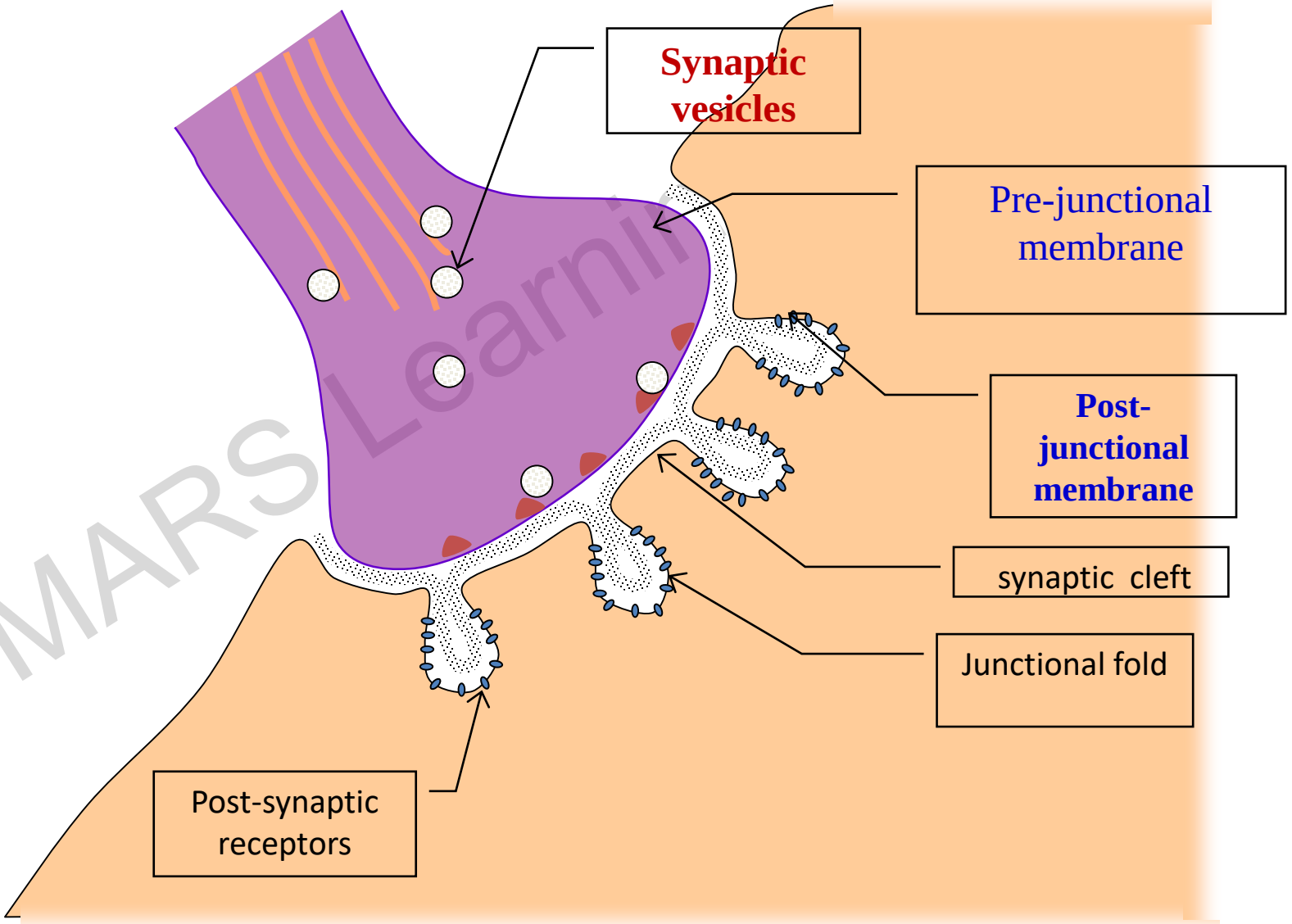
NMJ

- **Neuromuscular junction**

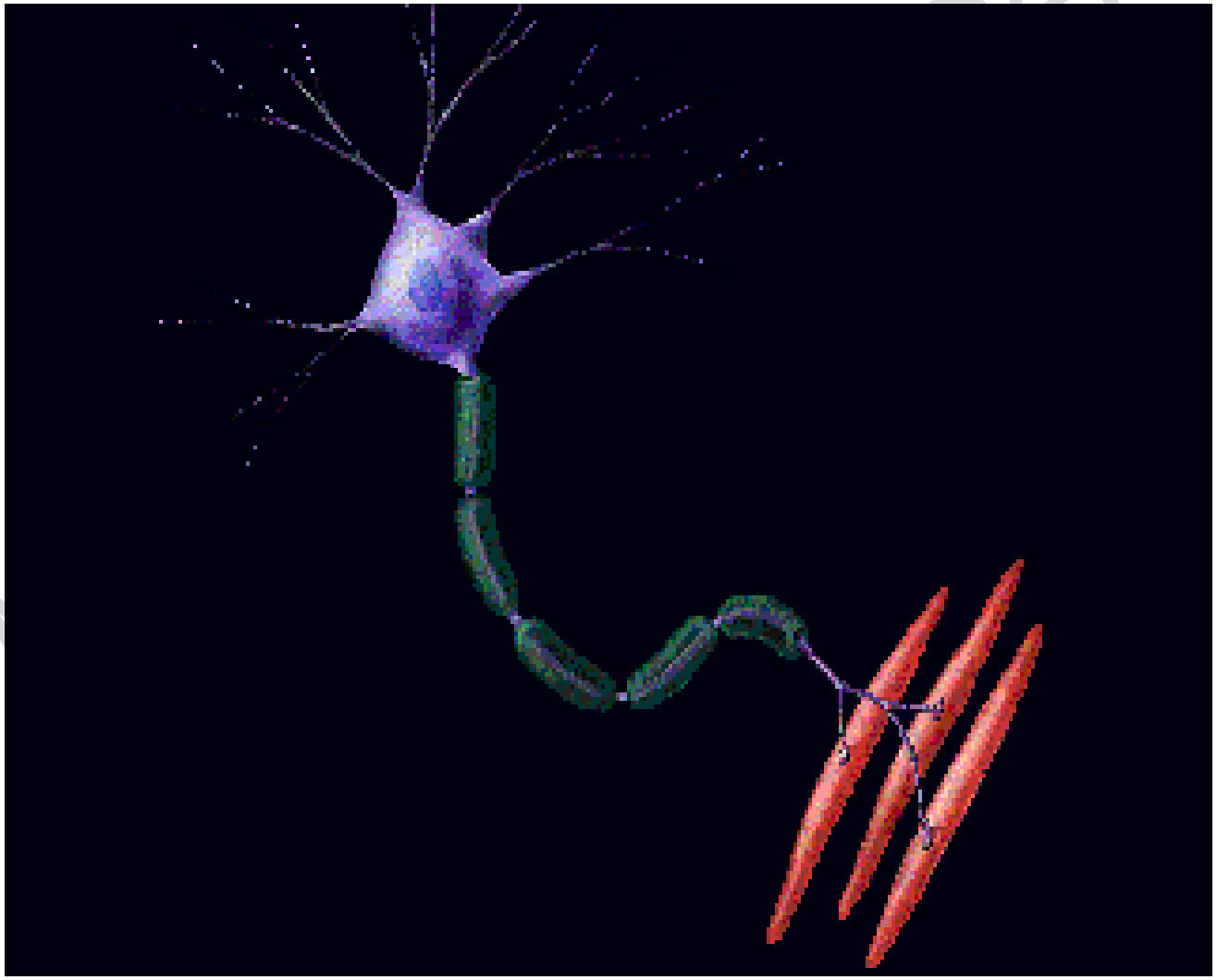
- Junction between nerve fibe and muscle fiber.

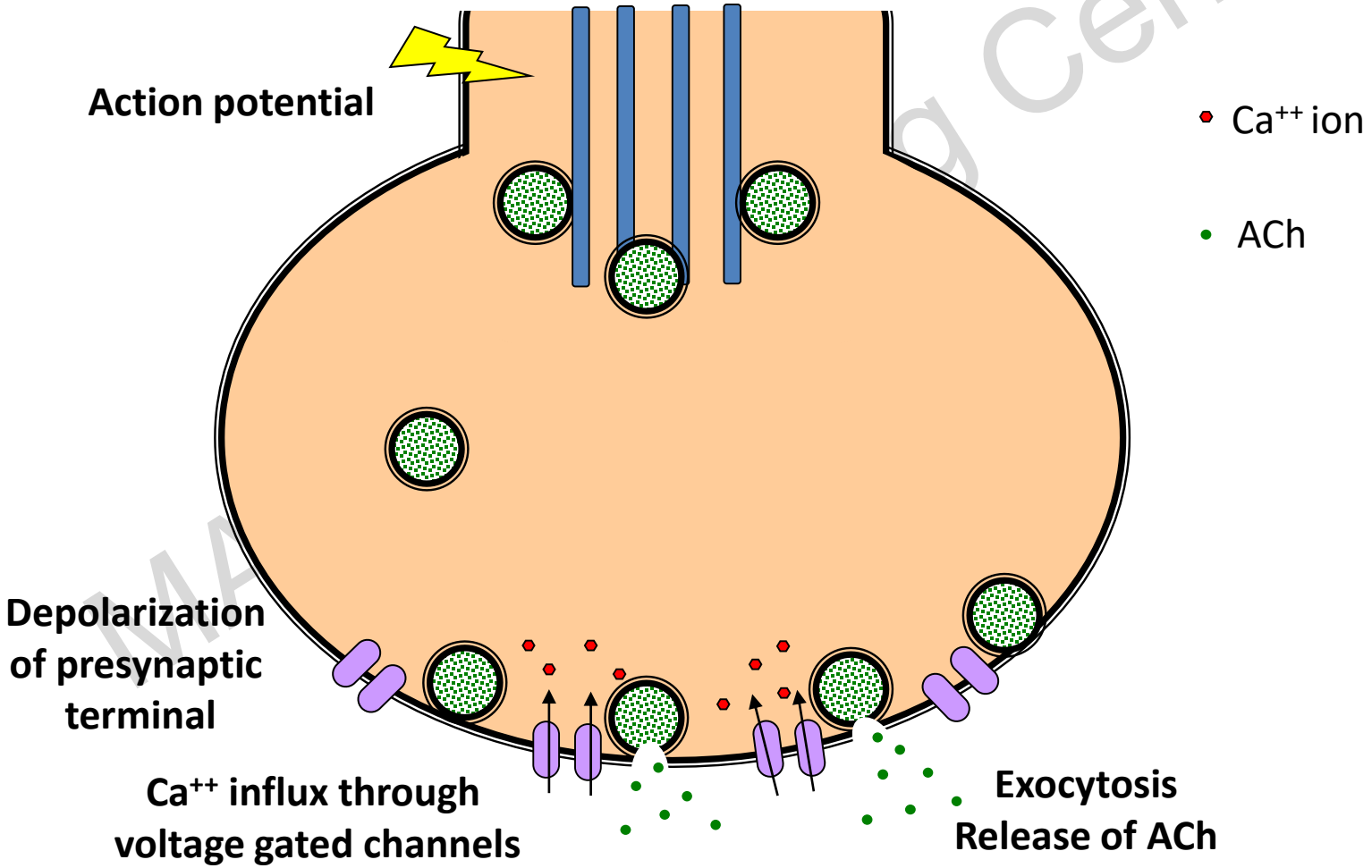


Neuromuscular junction



Neural signals/ Action potential moves down from the site of stimulation



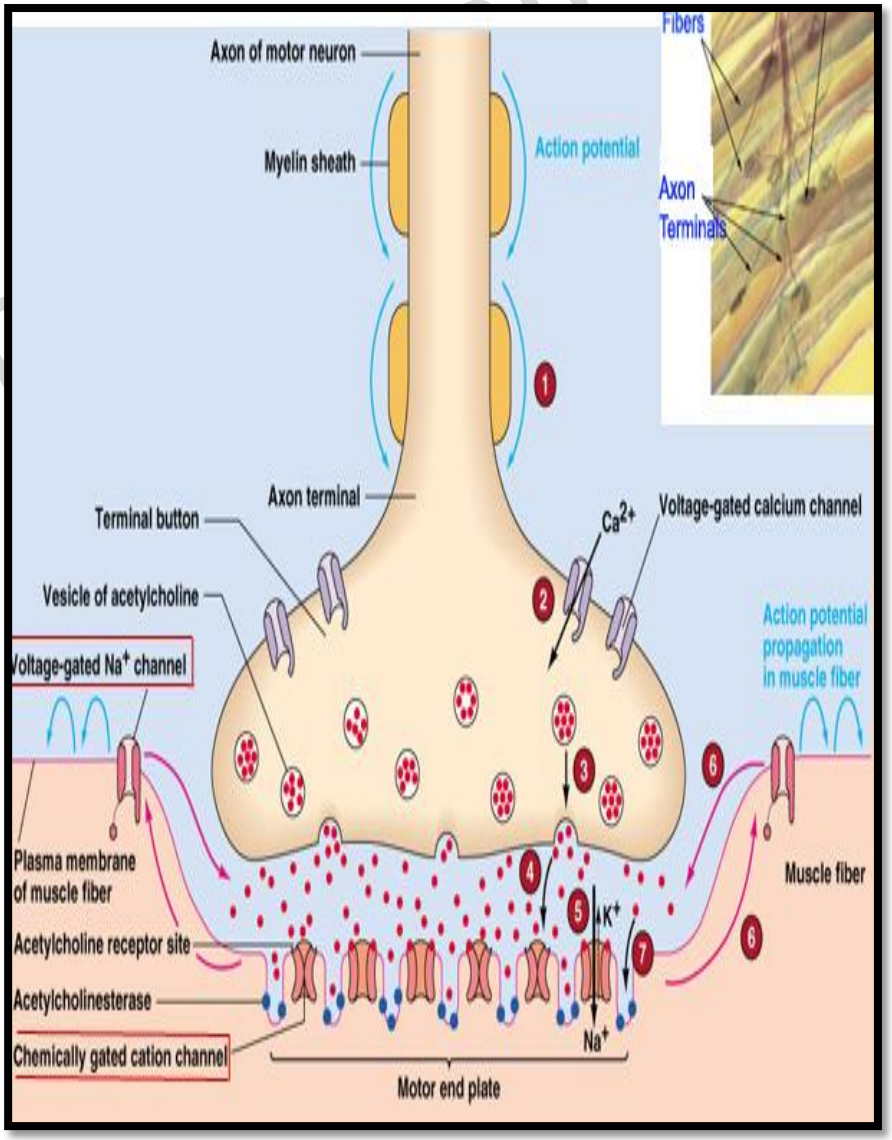

Action potential
Ca++ ion
ACh
Depolarization of presynaptic terminal
Ca++ influx through voltage gated channels
Exocytosis
Release of ACh

Neuromuscular Transmission –Pre – synaptic Events

Arrival of AP at Axon terminal

Ca2+ influx into axon terminal

Ca2+ mediated exocytosis of vesicles & Acetylcholine release

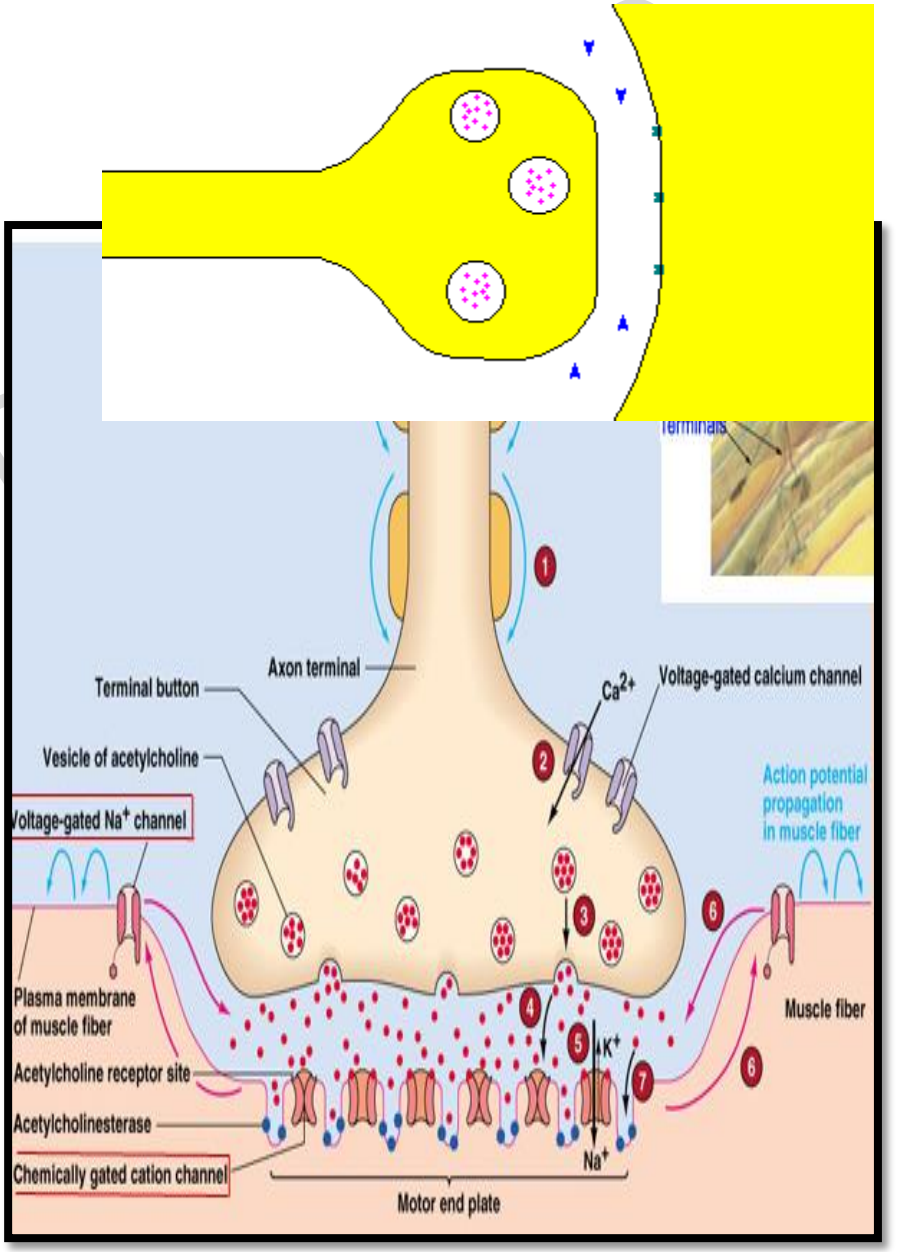


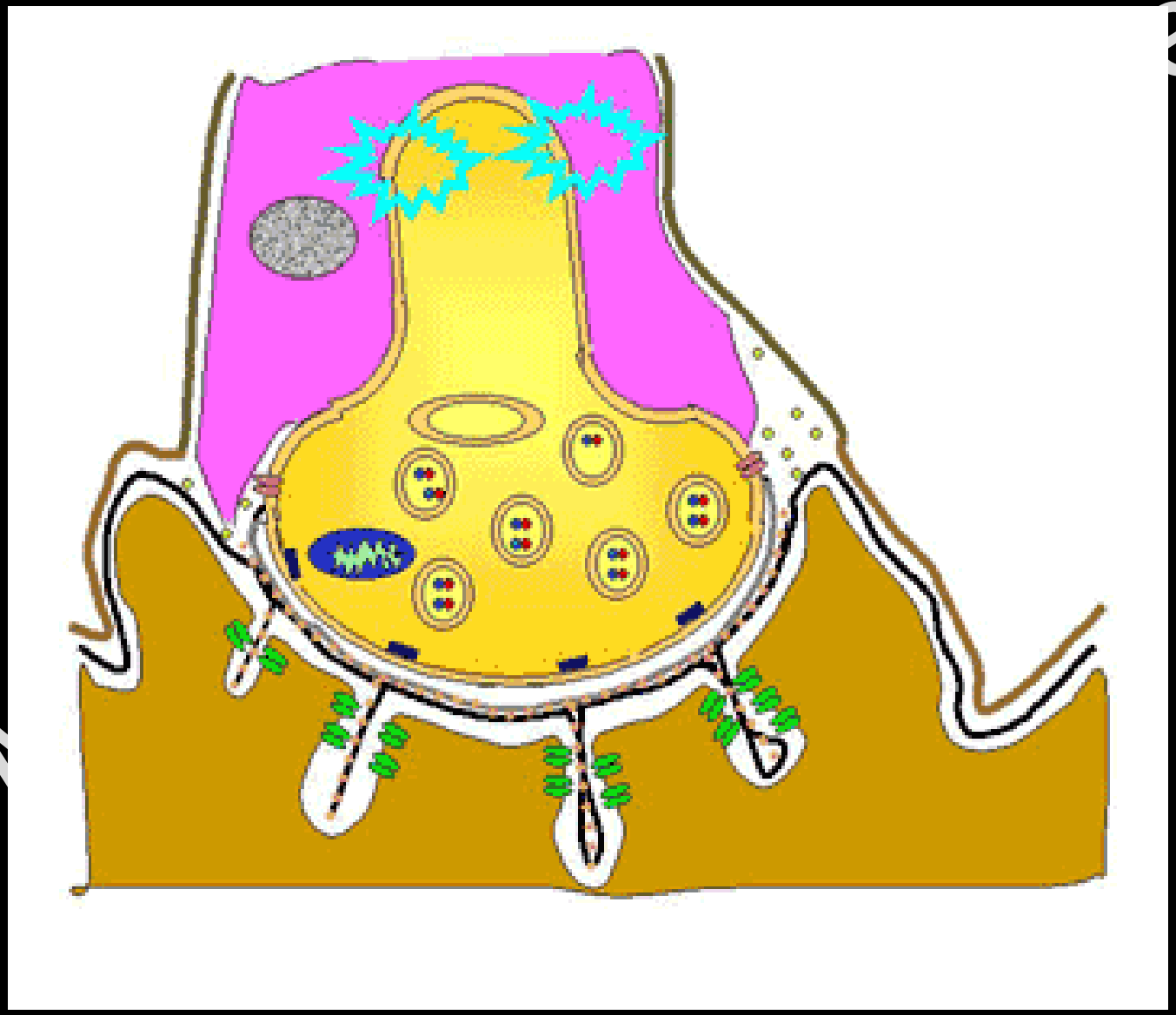
Neuromuscular Transmission –Pre – synaptic Events

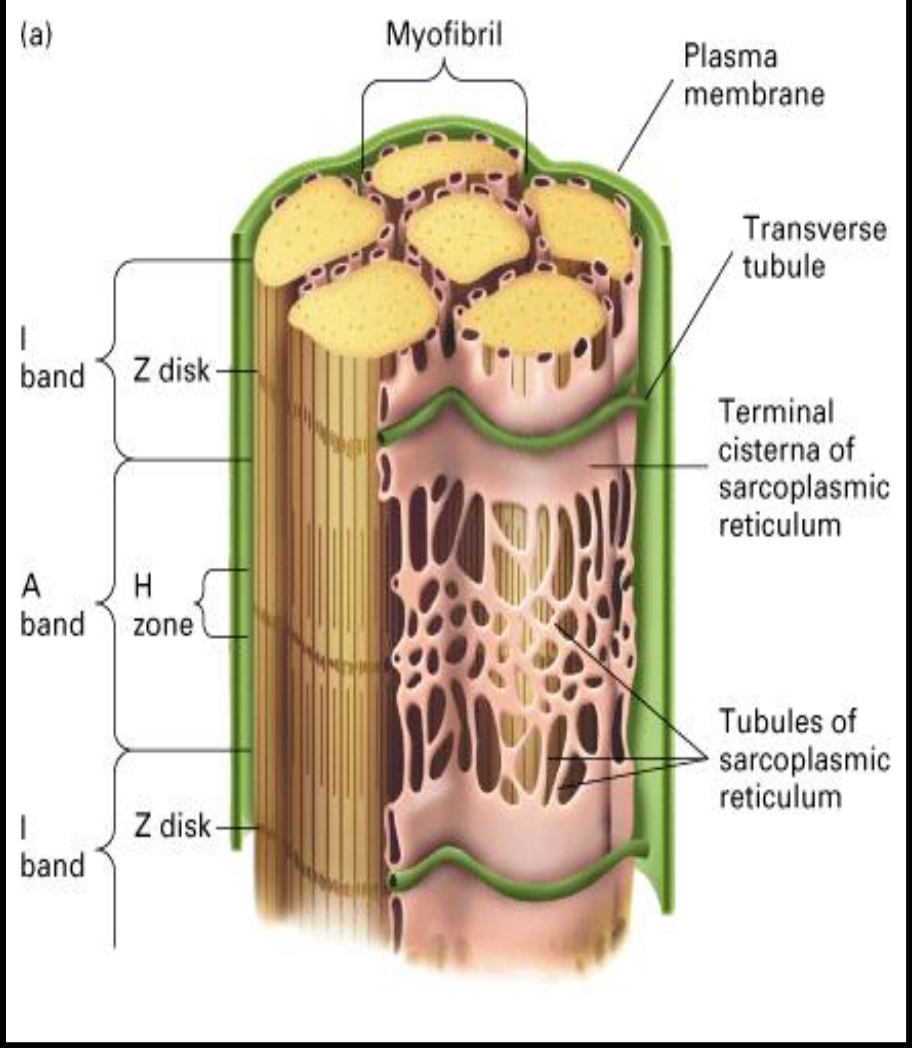
Binding of Ach to Ach receptors in post junctional membrane

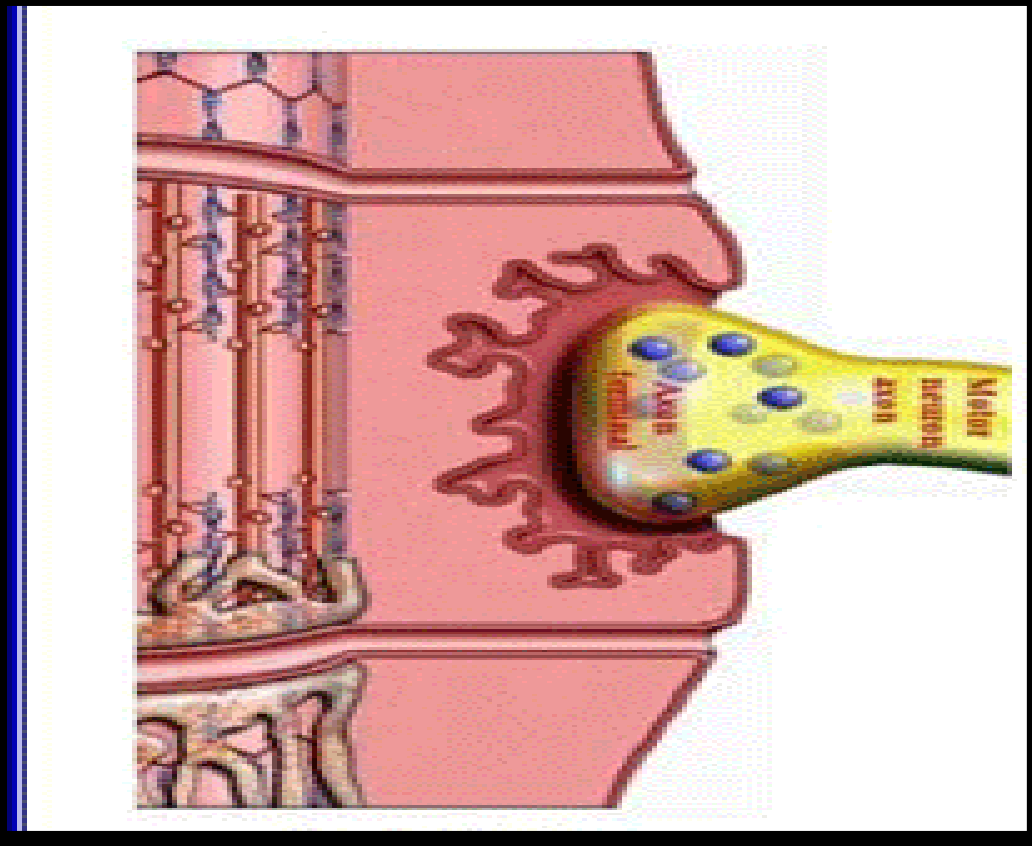
Na+ channels open & Na+ influx resulting in action potential in **sarcolemma**

Spread of AP to the T-tubule

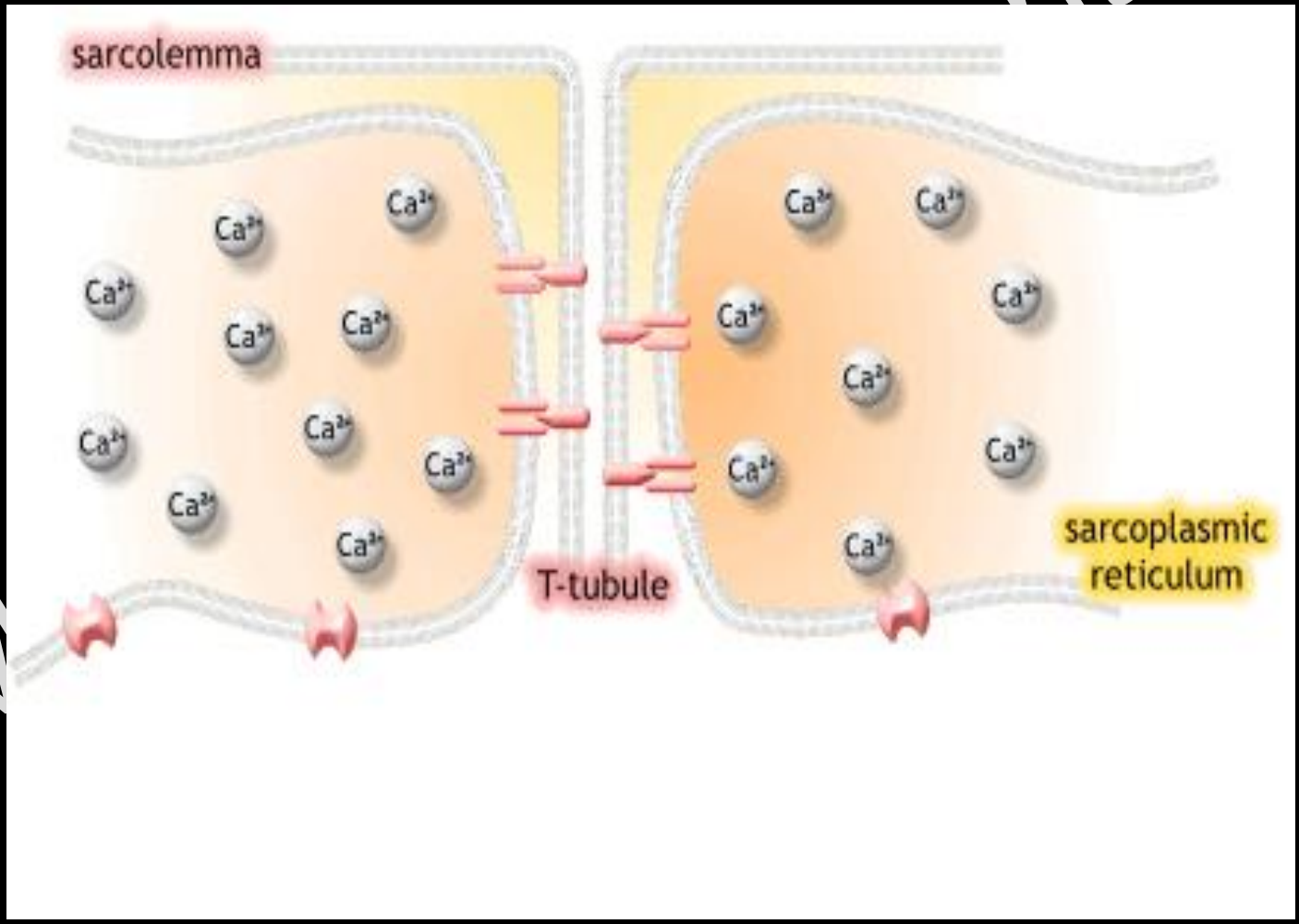





(a)
Myofibril
Plasma membrane
Transverse tubule
I band
Z disk
Terminal cisterna of sarcoplasmic reticulum
A band
H zone
Tubules of sarcoplasmic reticulum
I band
Z disk

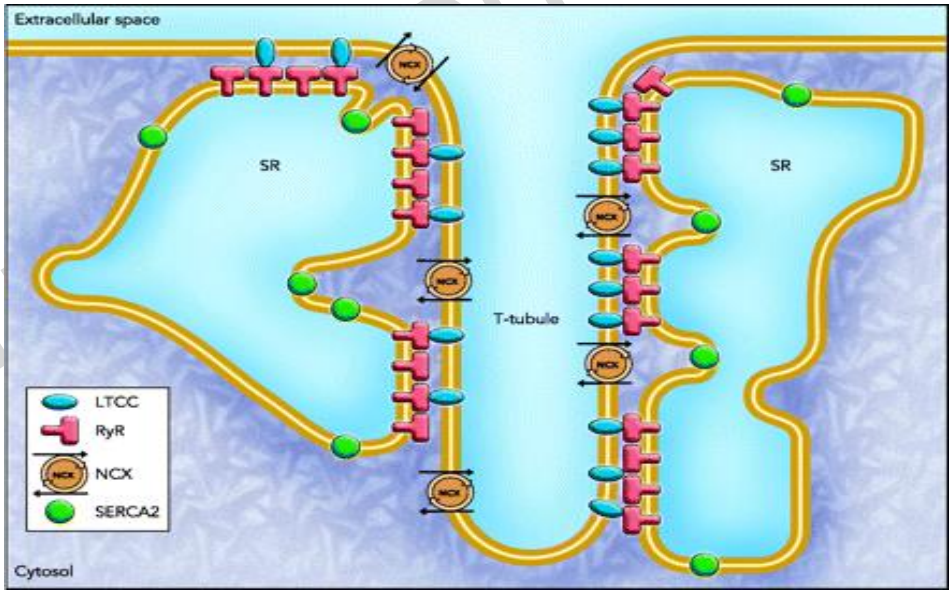

Myelin
Nerve
axon

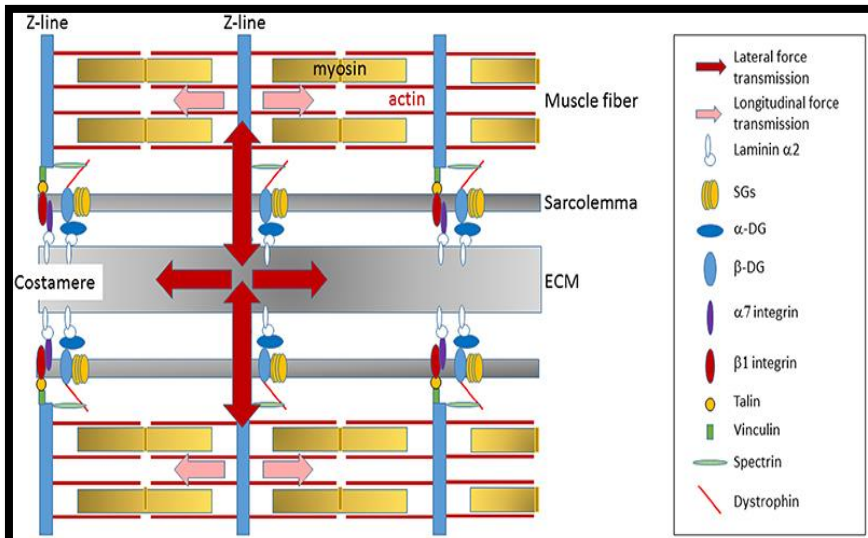
ntre


sarcolemma
Ca2+
T-tubule
sarcoplasmic reticulum

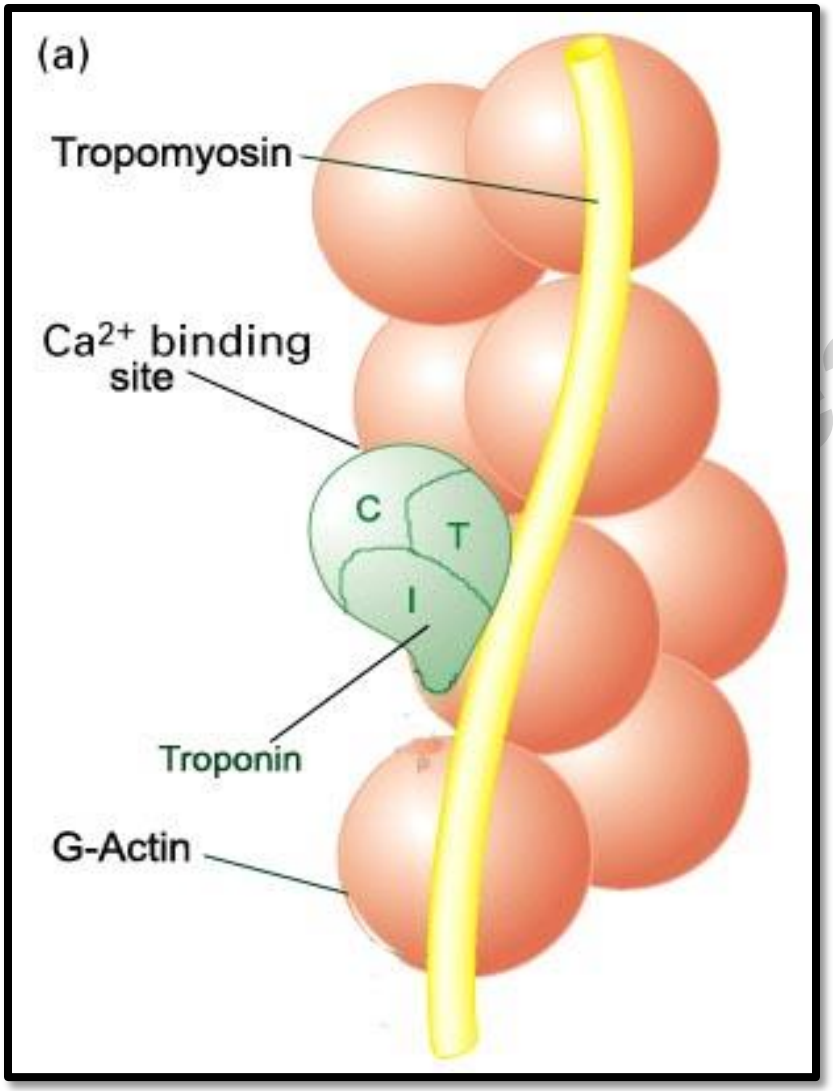
EXCITATION CONTRACTION COUPLING

- AP in sarcolemma
- Spreads along T tubules into interior of myofibril.
- **AP spreads to L tubule**
- **Via a protein -- dystrophin**
- Ca2+ released into sarcoplasm



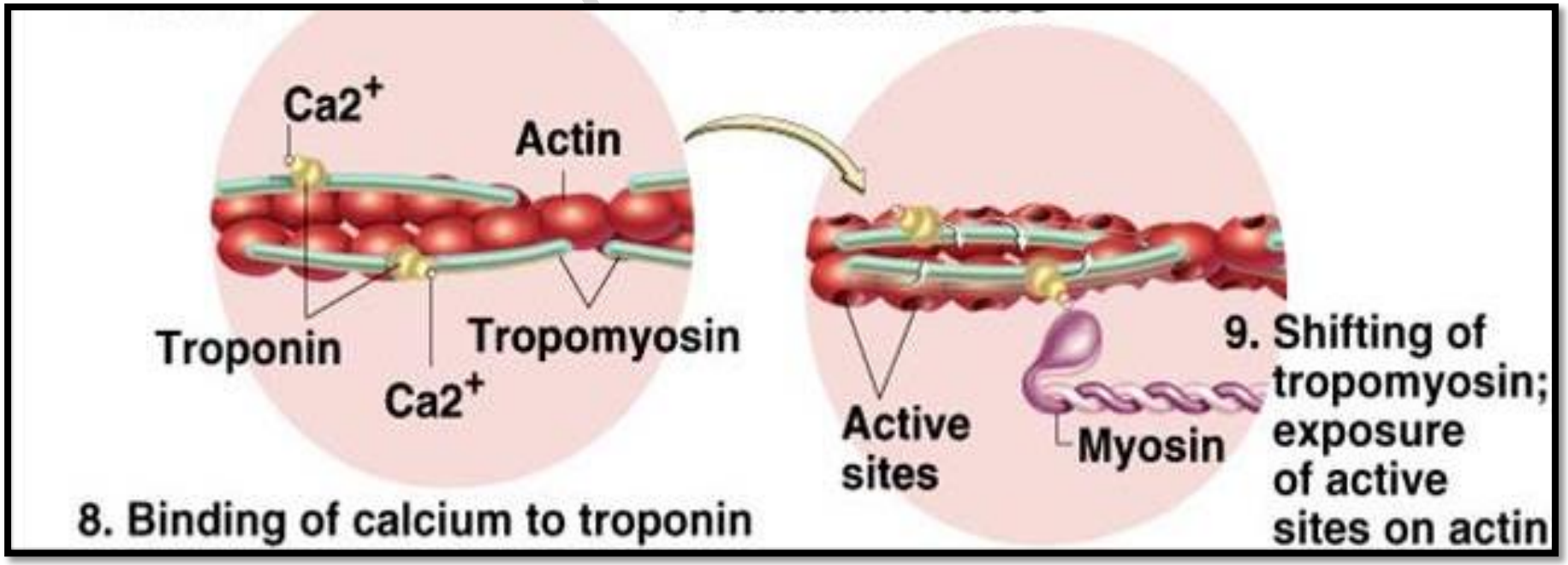


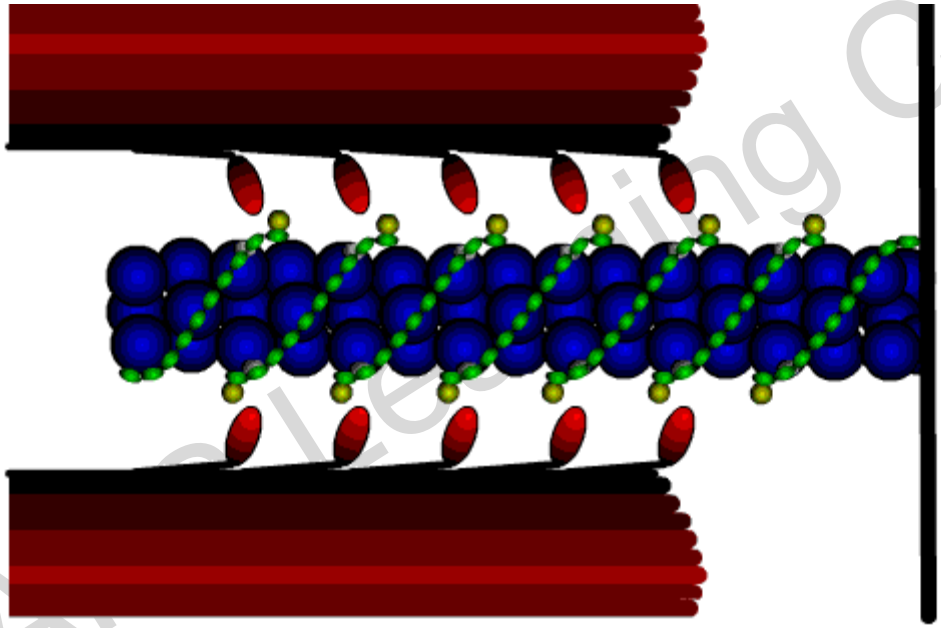
Calcium Activation of Contraction



- Ca ^{2} binds to **troponin C (TnC),** the calcium-binding subunit of the troponin molecule.
- protein found on the thin filament.

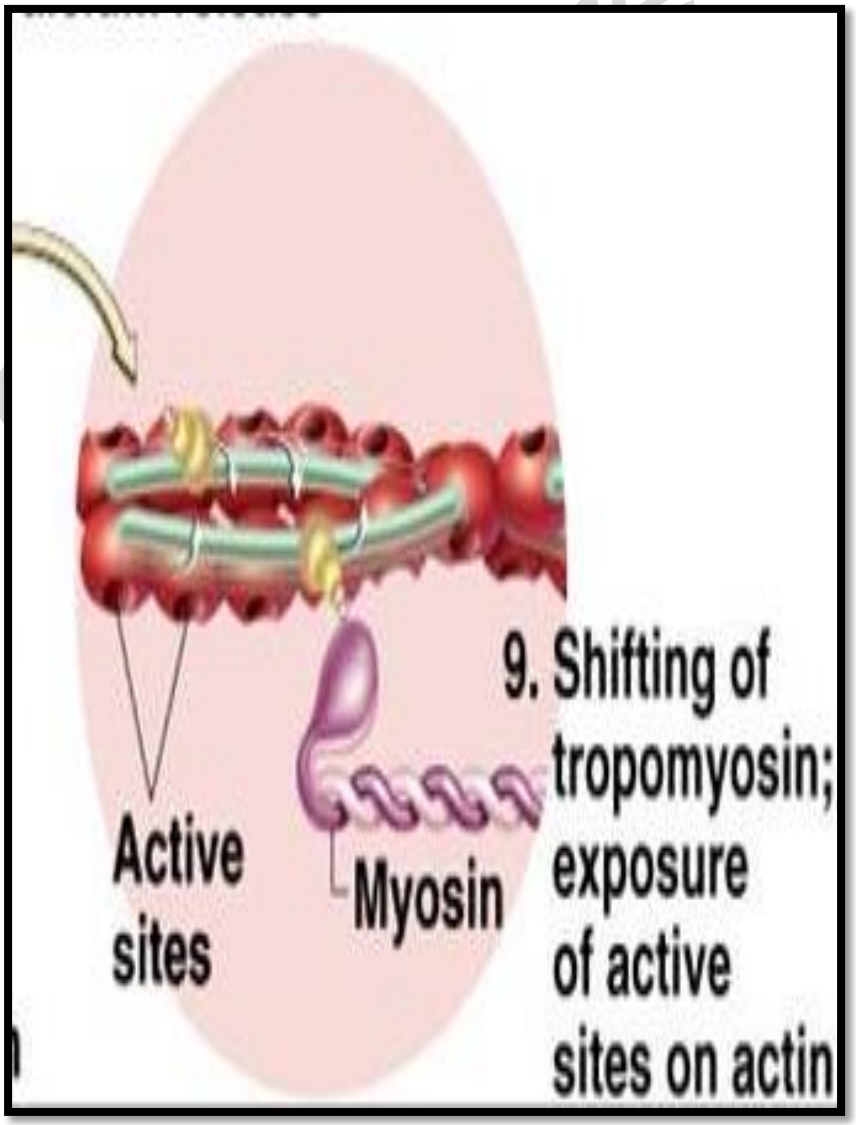
- When calcium binds to **TnC**,
- **tropomyosin** shifts away from active sites of actin.

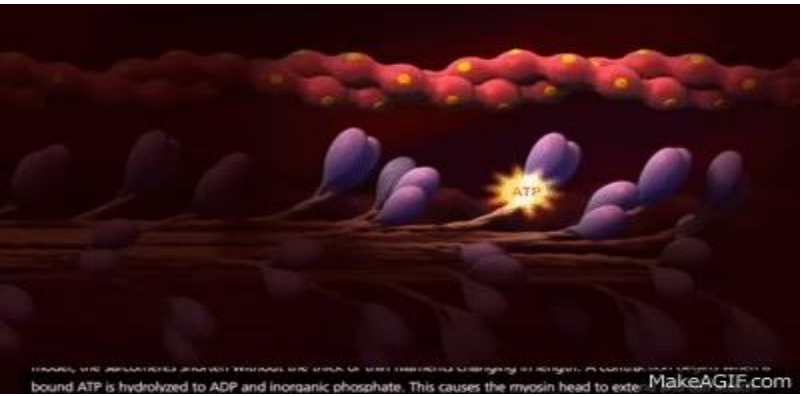




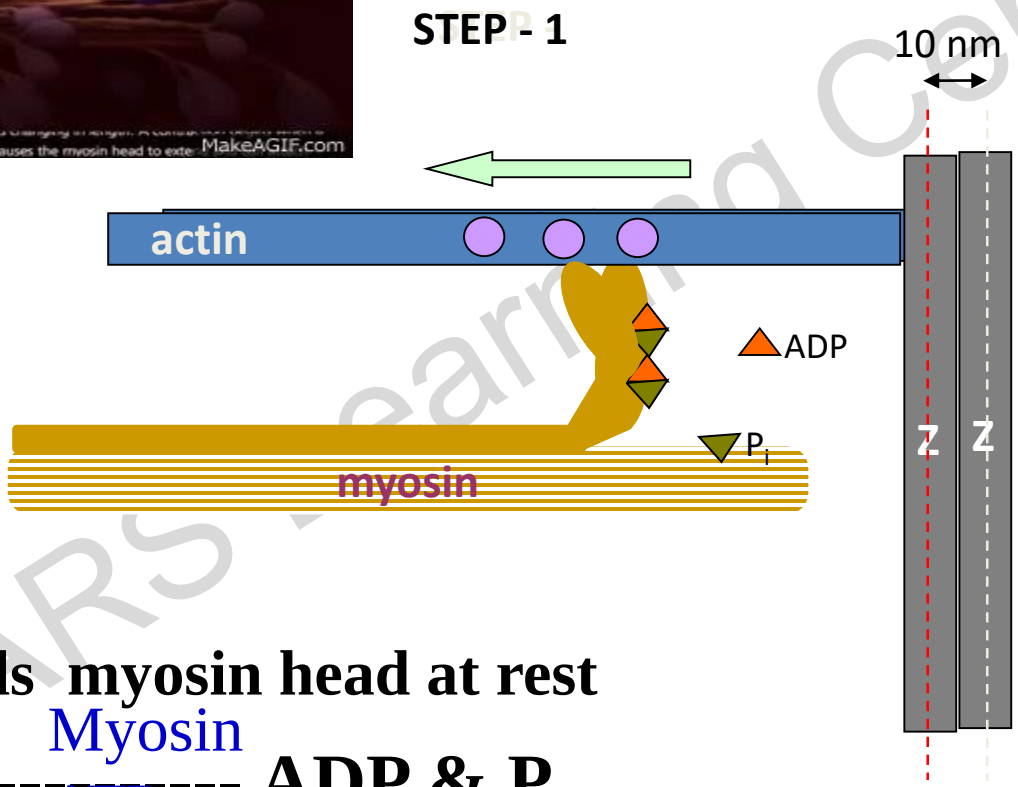
The action potential inhibits the calcium pumps, and calcium escapes from the **sarcoplasmic reticulum.**

- **Cross bridge cycle** starts
- Binding of myosin head to actin
- **Energy (ATP)** dependent process.





Cross bridge cycle



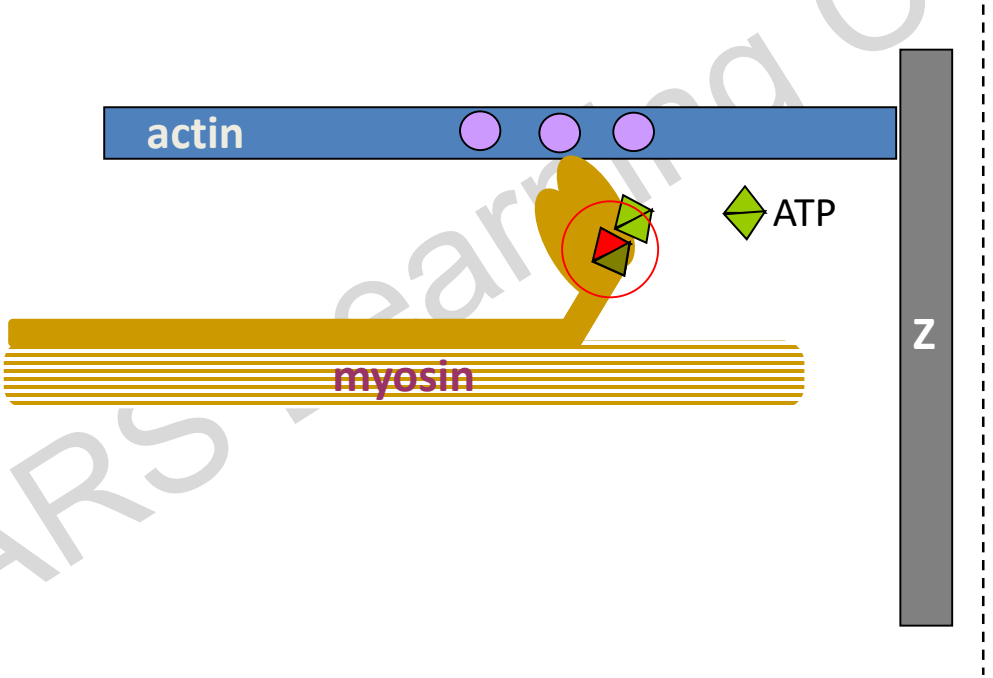
- **ATP binds myosin head at rest**
- **ATP** —(Myosin / ATPase)— **ADP & P_i**

- **Myosin head energized and attaches to exposed actin**

Power stroke

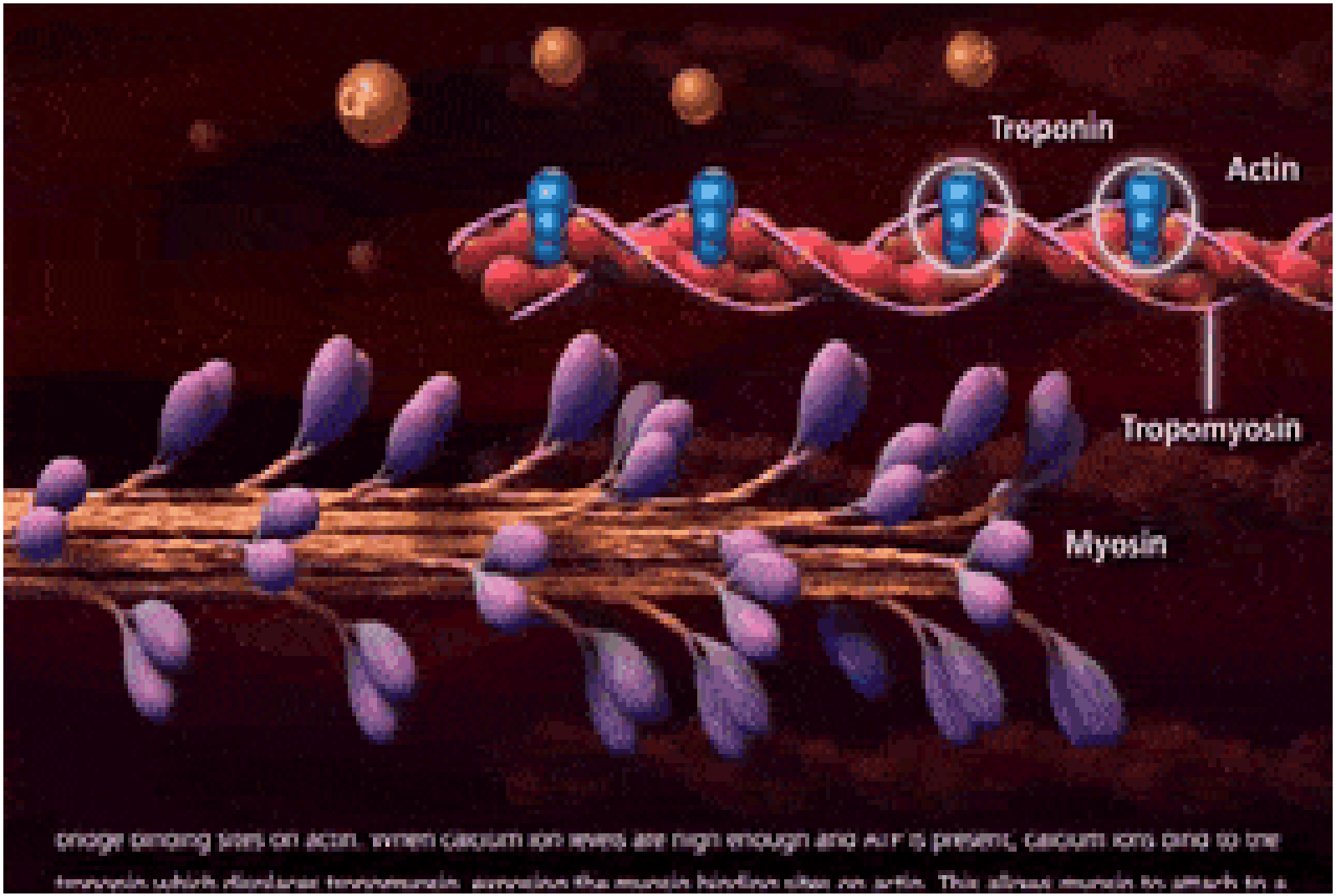
Cross bridge cycle

STEP - 3



- **Attachment of ATP to Myosin head**

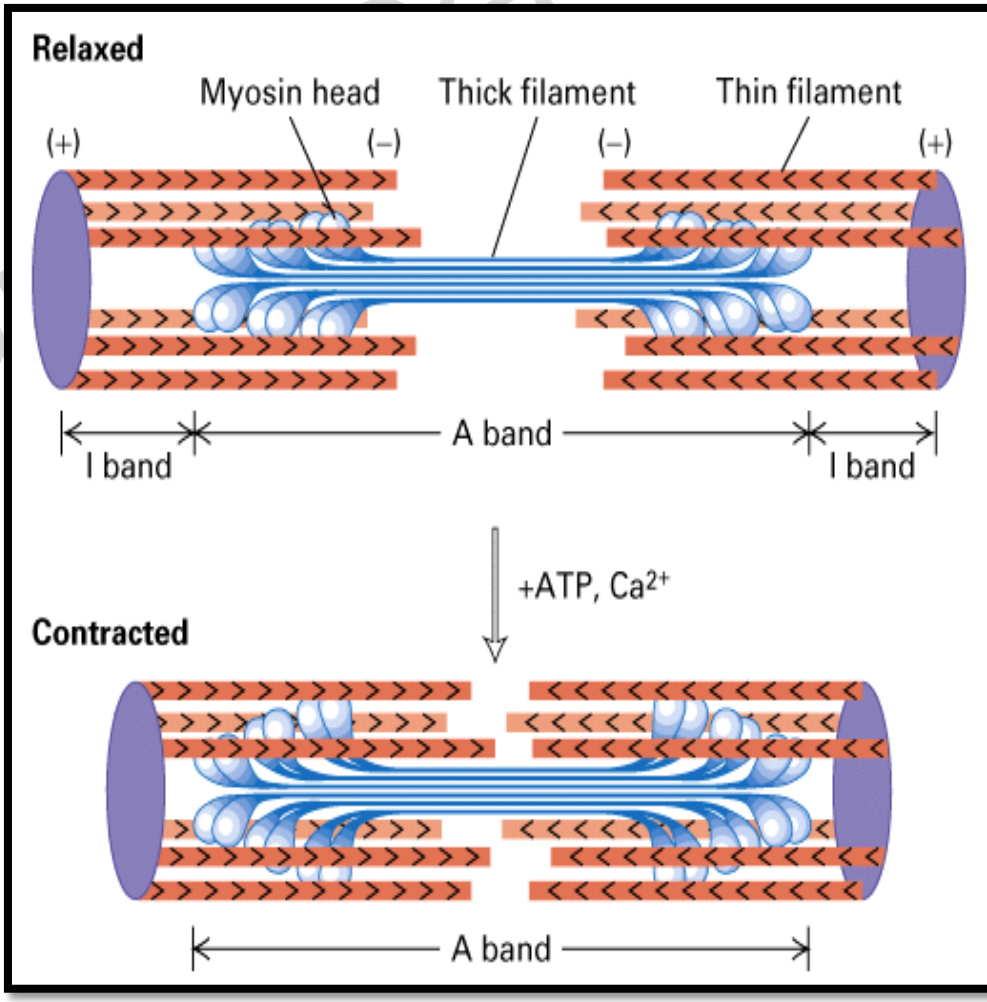
- **Cross bridge detachment**



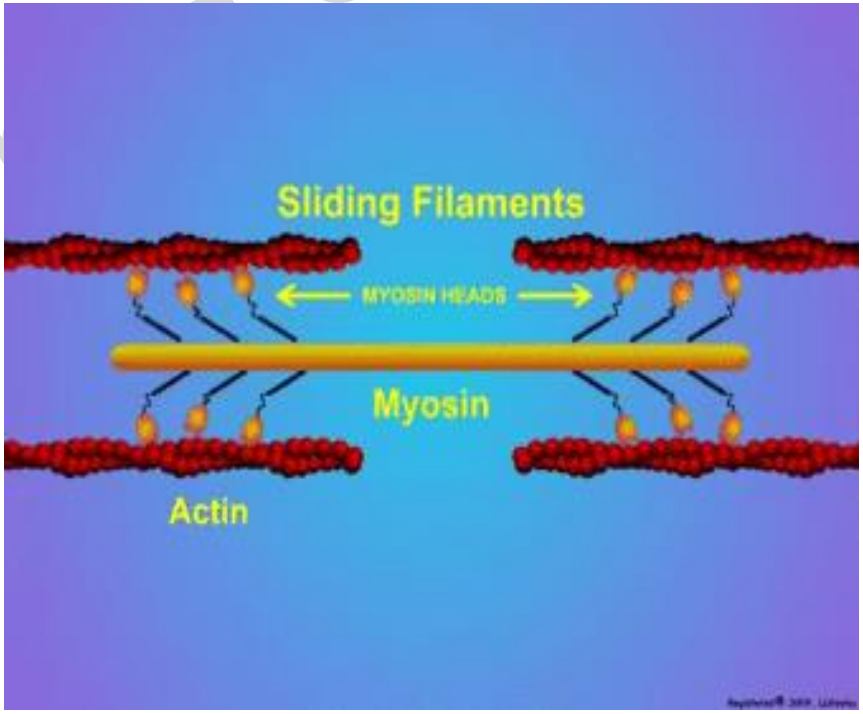
Sliding of Thin filament over thick filament

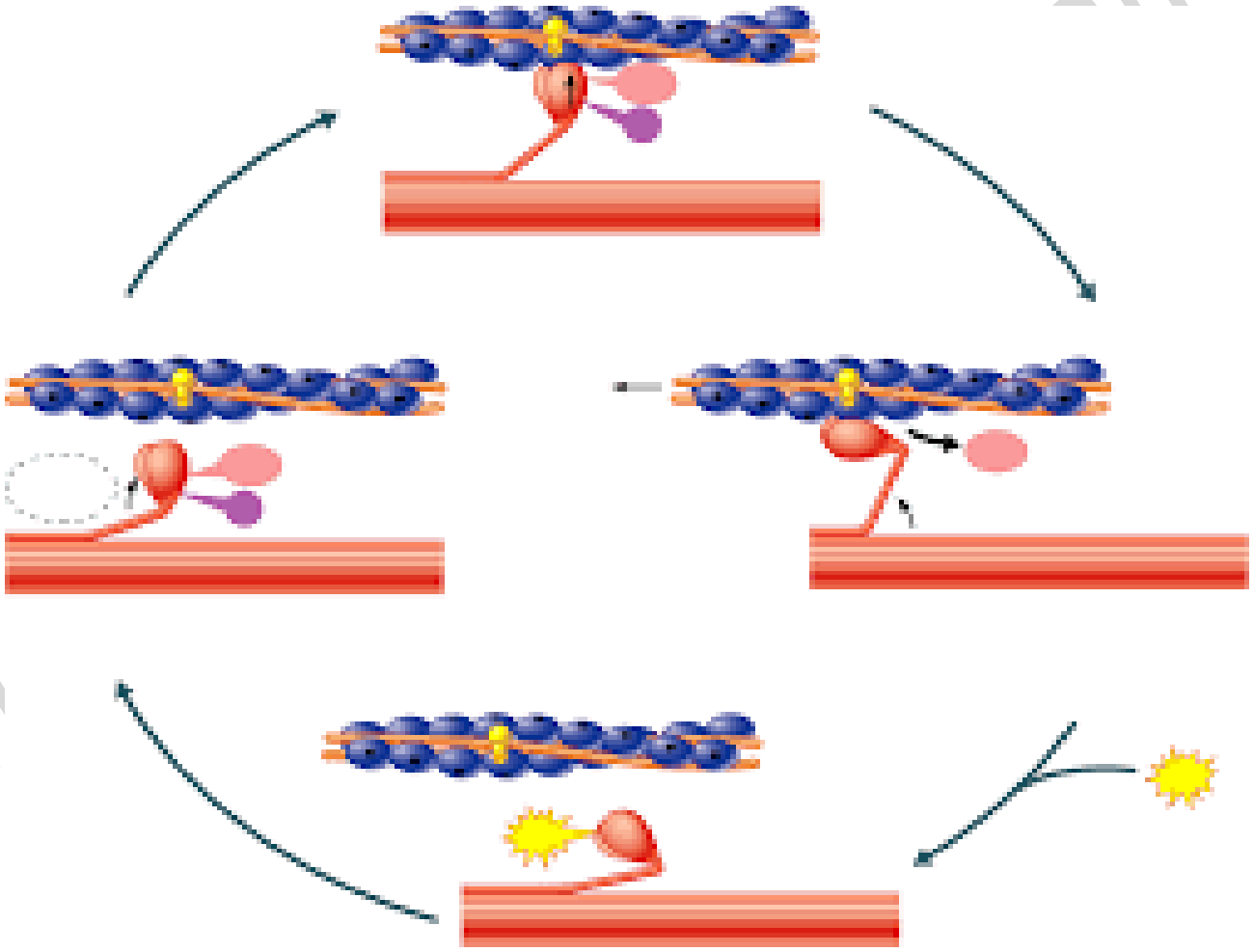
- Actin filament pulled to center

- After contraction width of **A band** remains <u>constant</u> but **Z lines** moves closer .

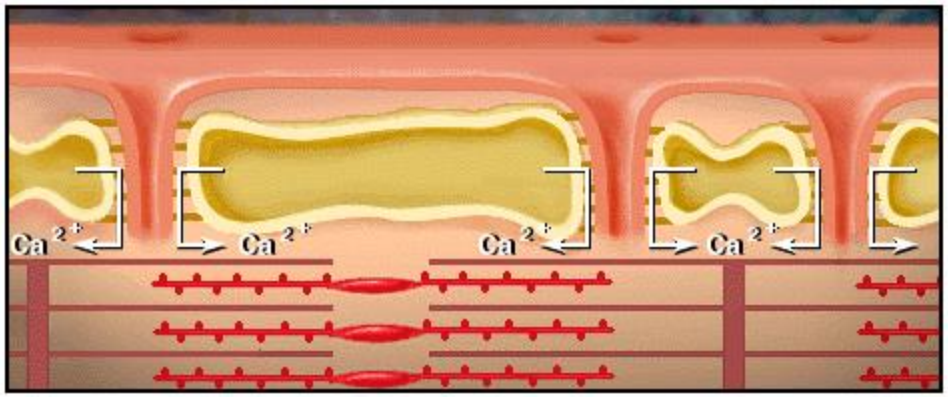


- Complete contraction of the muscle **cross bridge cycles** should repeat for 5 – 6 times





Muscle Relaxation



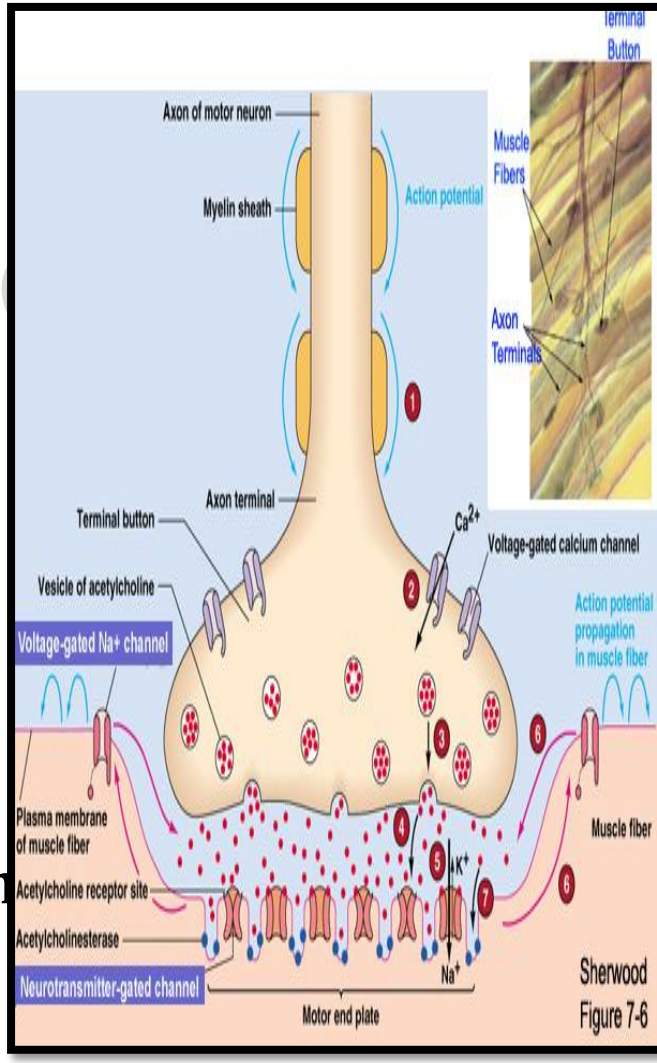
Steps in muscle relaxation

- **Synaptic cleft**

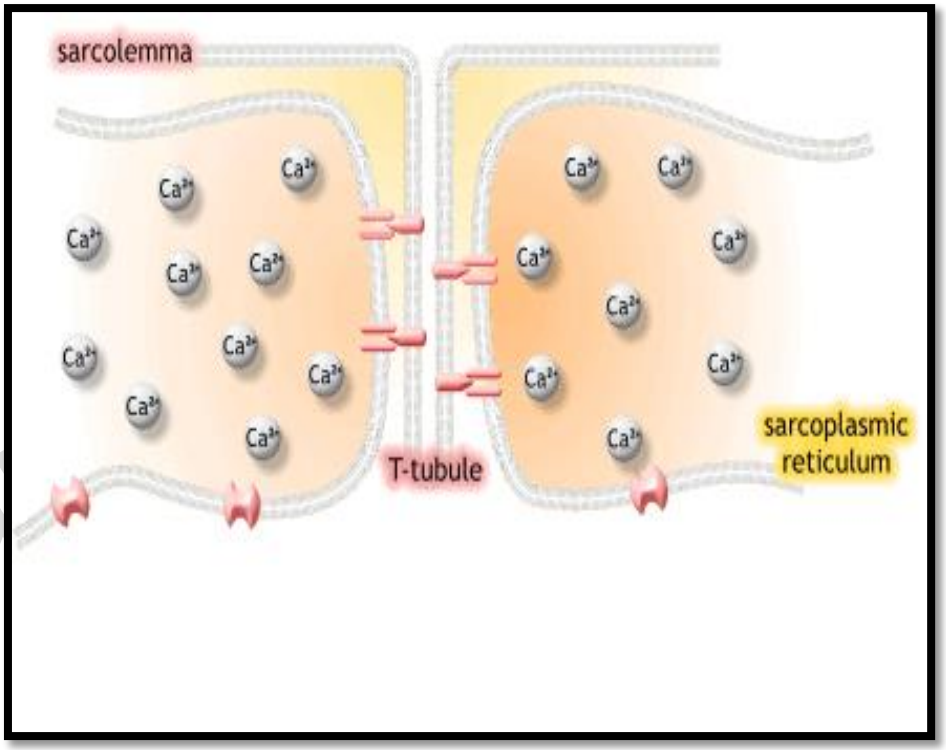
- gap between terminal button and muscle fiber
- 50 – 100 nm wide space

- **Contains enzyme cholinesterase which can destroy Ach neurotransmitter**

- **STOPS Action Poptential**

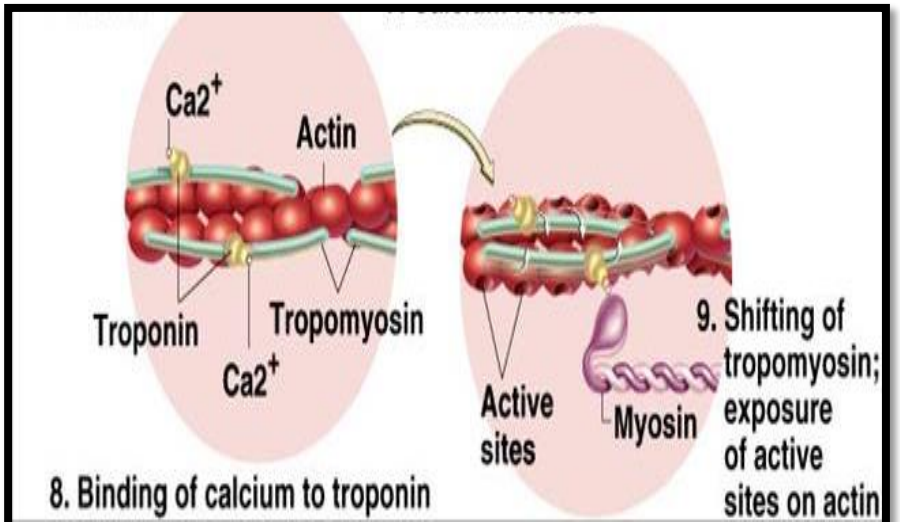


- ca^{2+} pumped back into **L - tubule**

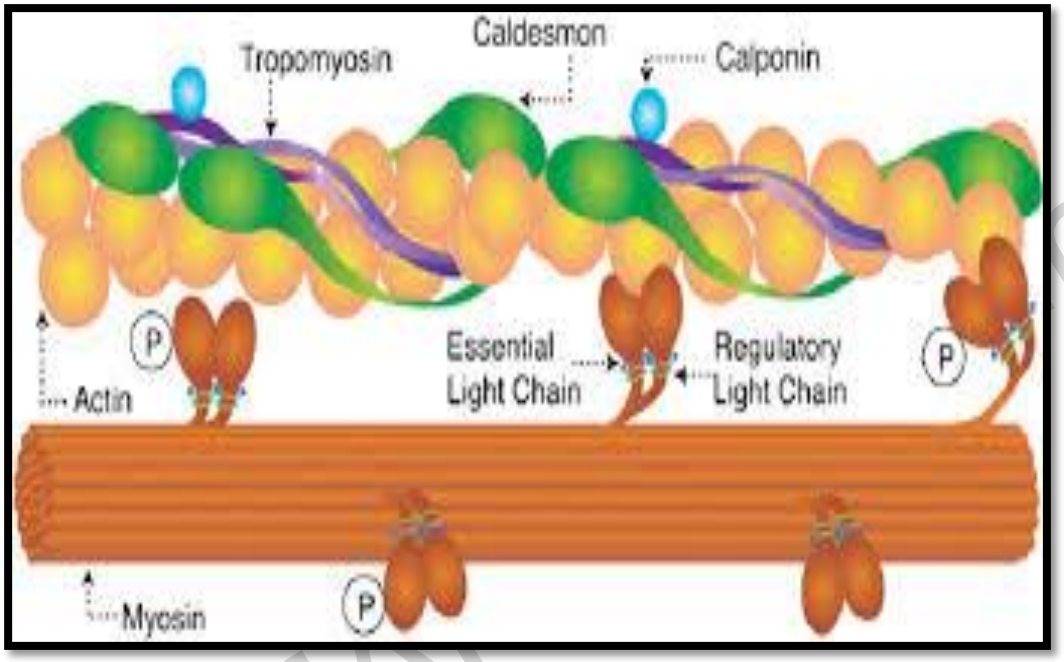


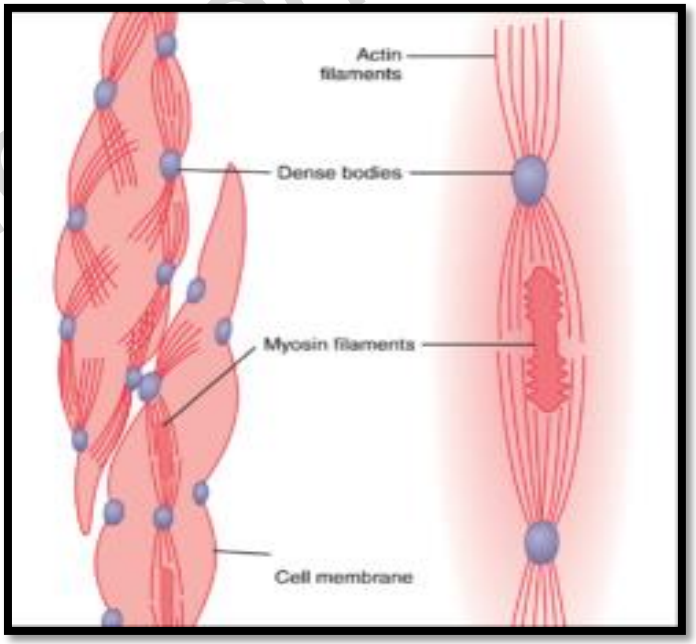
- ca^{2+} binds to calcium binding protein

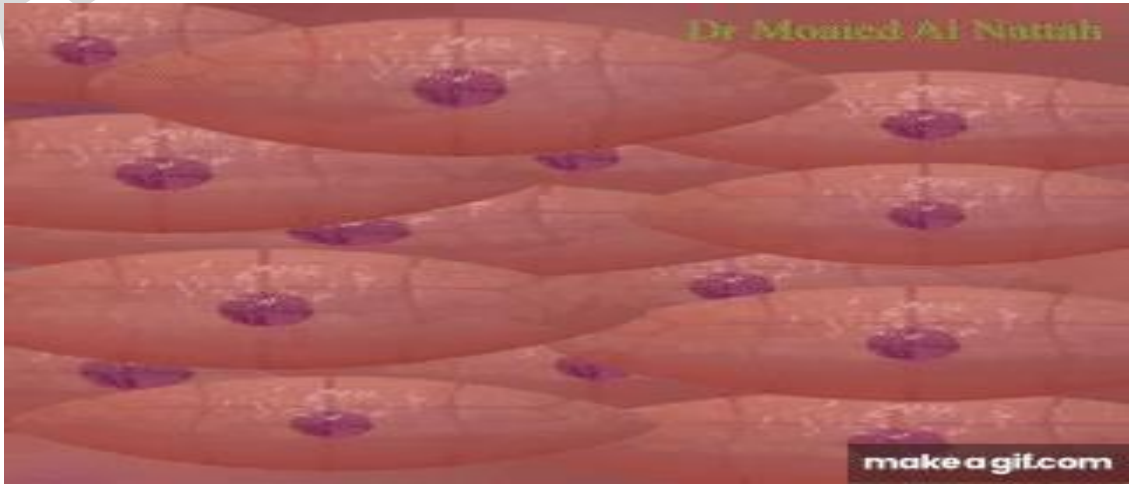
Calsequestrin

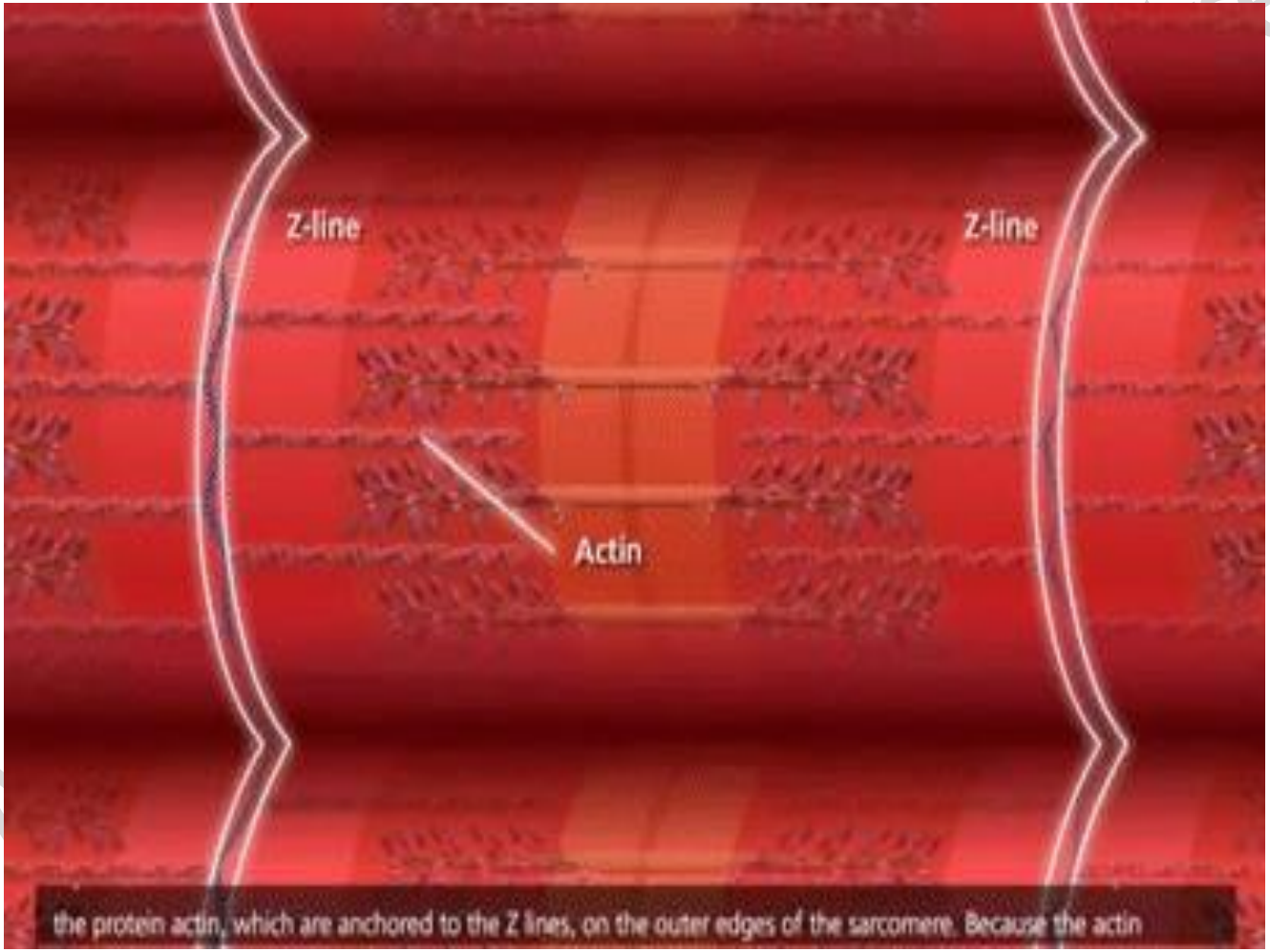


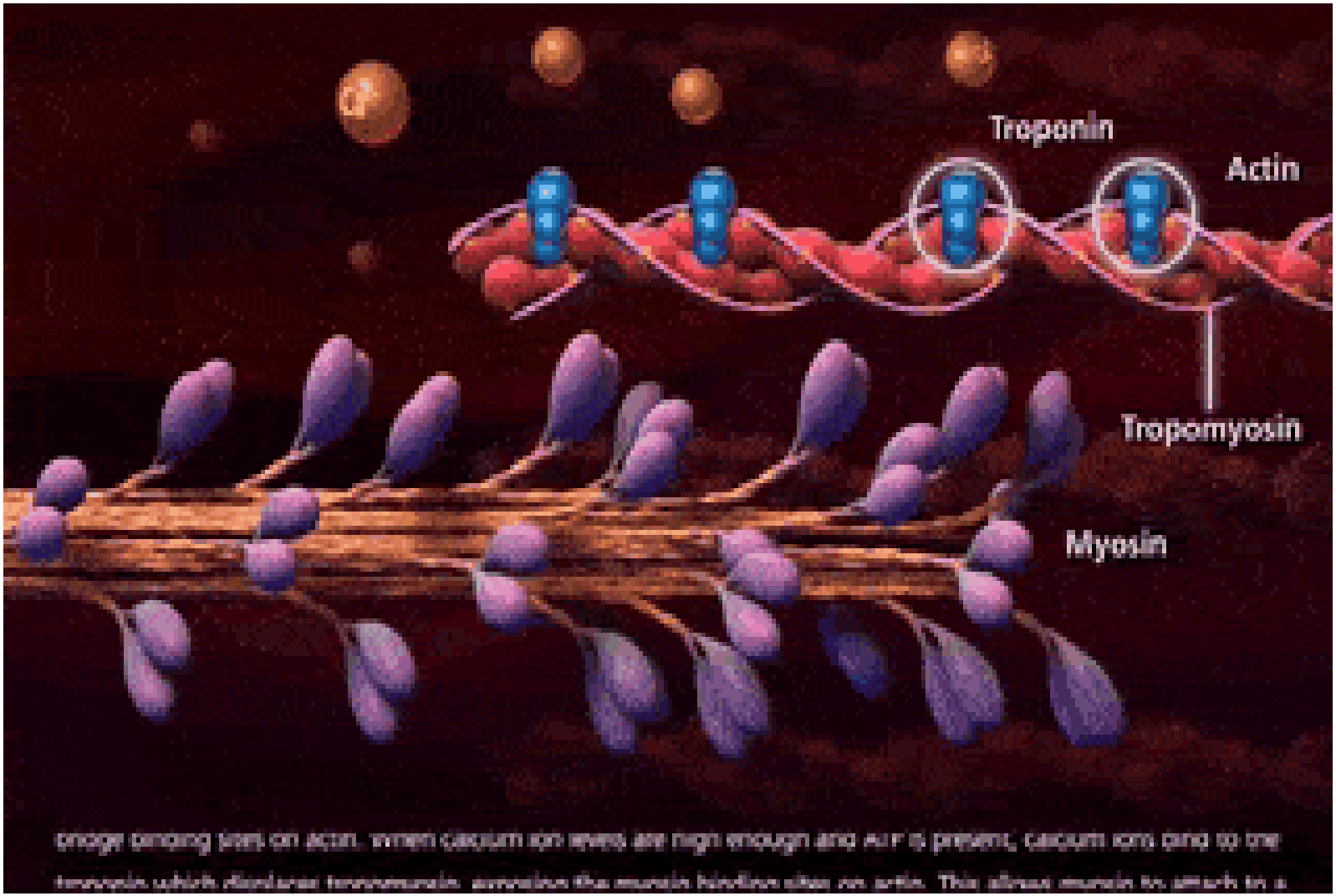
Smooth muscle contraction





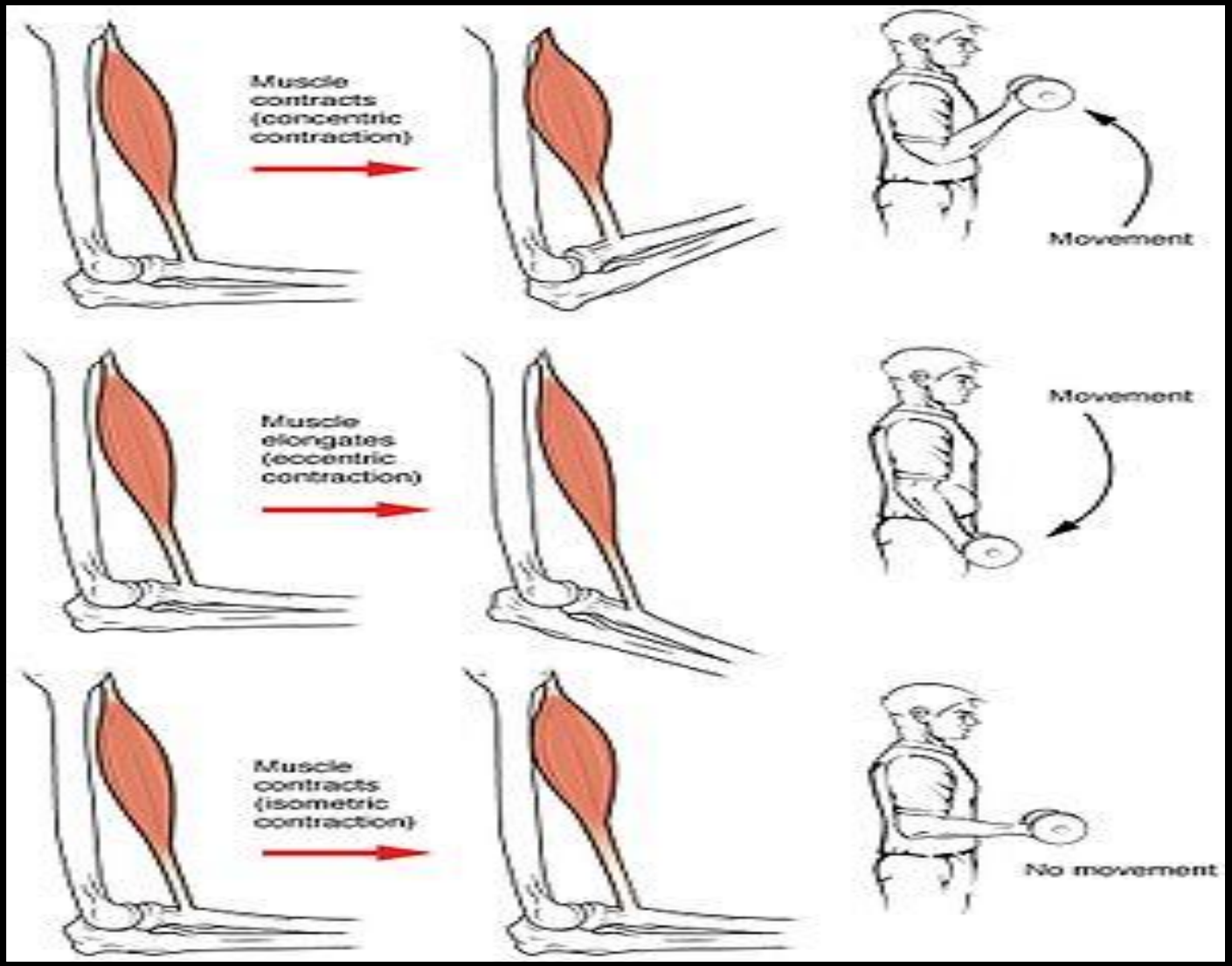



Z-line
Z-line
Actin
the protein actin, which are anchored to the Z lines, on the outer edges of the sarcomere. Because the actin

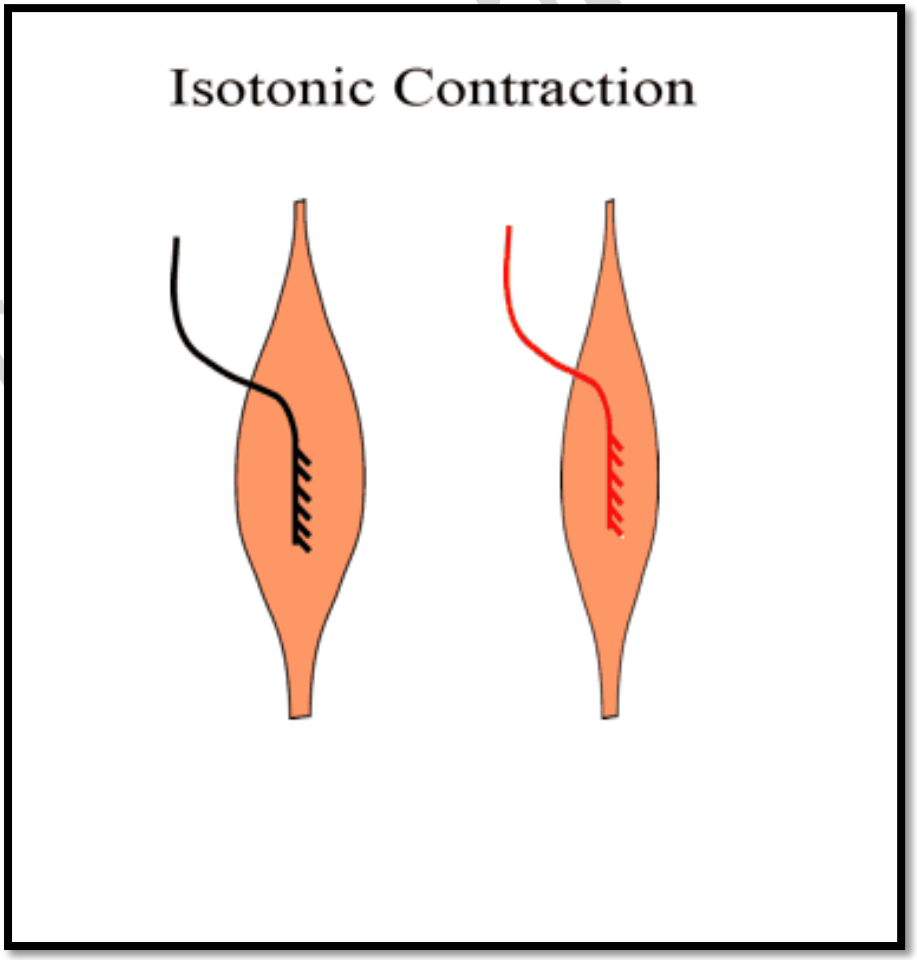


Sliding of Thin filament over thick filament

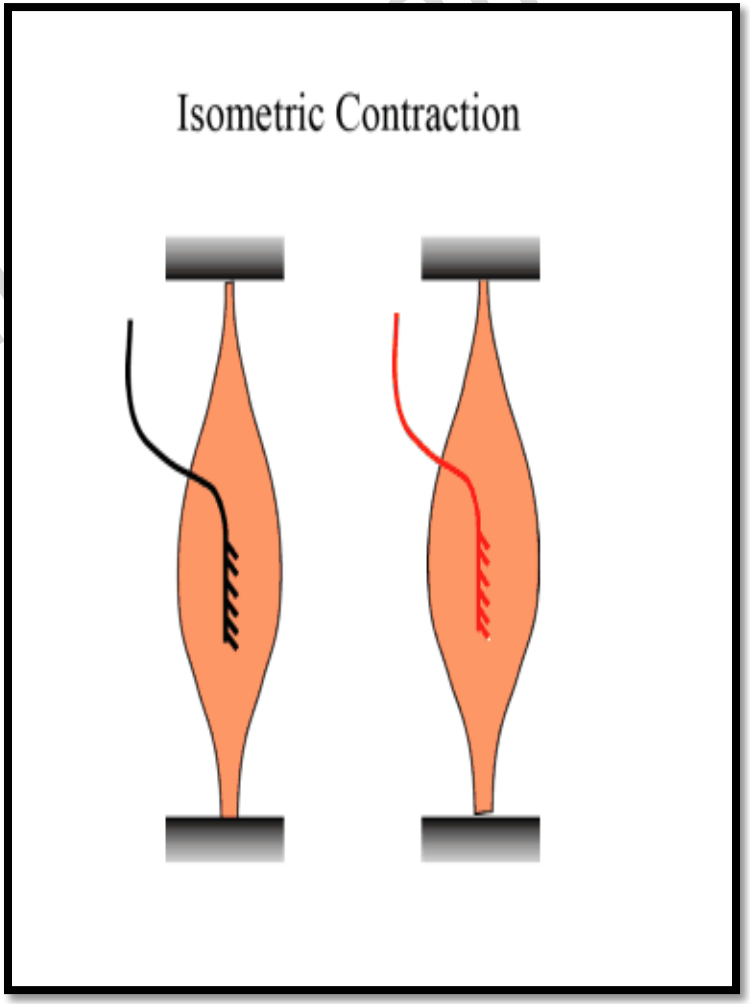
Types of muscle contraction



- **Isotonic Contraction**
- Tension remains same
- Change in length
- External work is done
- **Ex:**
- Contraction of leg muscles in walking, running.
- Contraction while lifting weight



- **Isometric Contraction**
- Length remains same
- Tension increases
- No external work done
- **Ex;**
- Contraction of muscles in maintaining posture
- Contraction of arm muscles while pushing wall



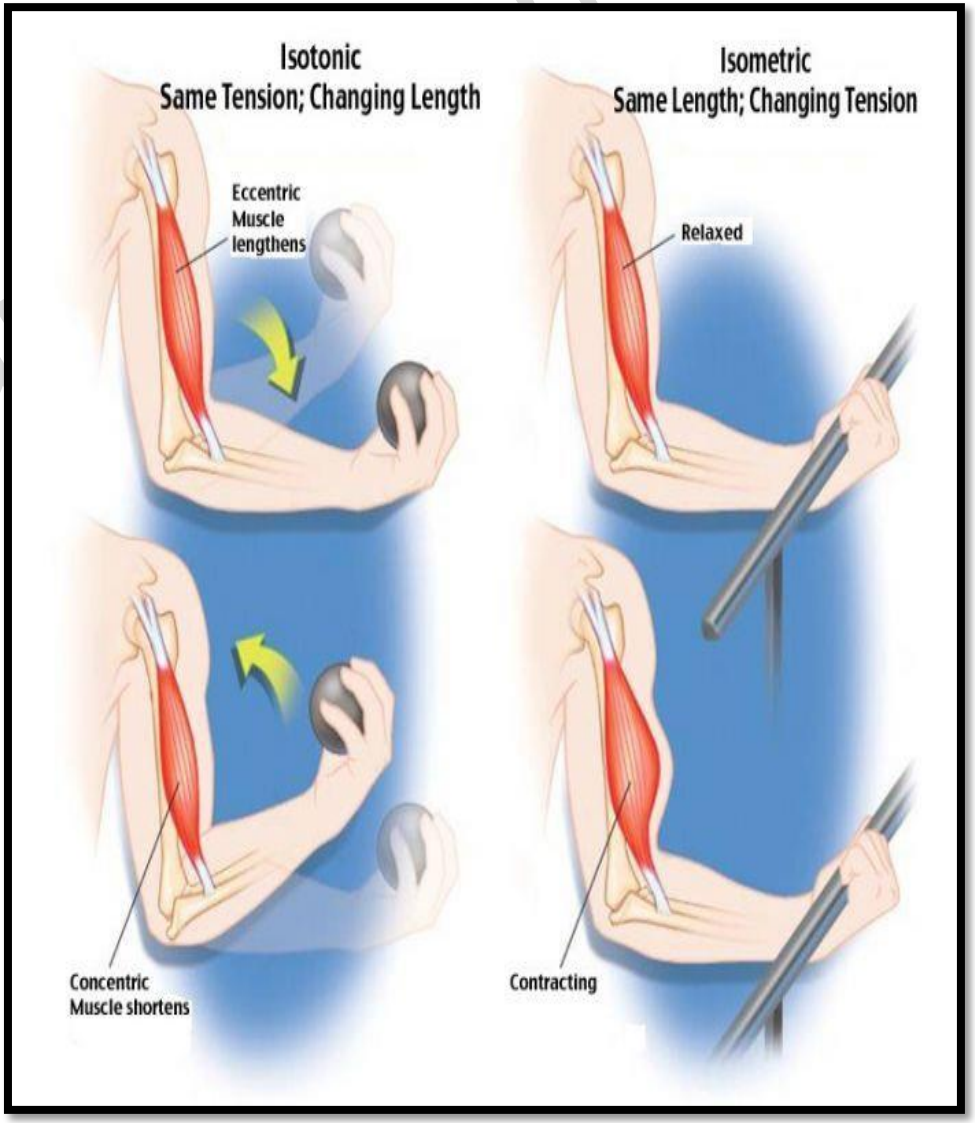
Isotonic Vs Isometric

- **Isotonic Exercise**

- Walking, Swimming,
- Wt lifting , Cycling
- Push ups, Pull ups

- **Isometric Exercise**

- Pushing against wall



Energy Source in Exercise

Aerobic Vs Anaerobic

- **Aerobic Exercise :**

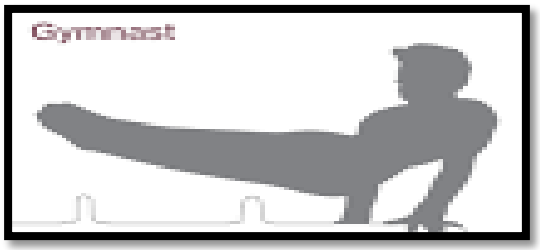
- Rhythmic activity sustained for long duration

- *Walking, jogging, skipping, treadmill, step-ups, dancing, football, basketball*

- **Anaerobic Exercise:**

- Short duration, high intensity exercise (2-3 min)

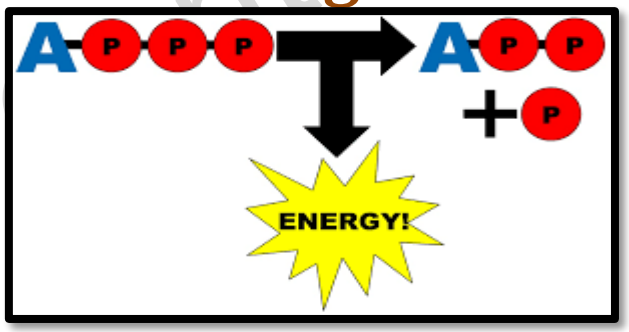
- *Sprinting, high jump, swimming(100m), running(400m) weight lifting, gymnastics.*



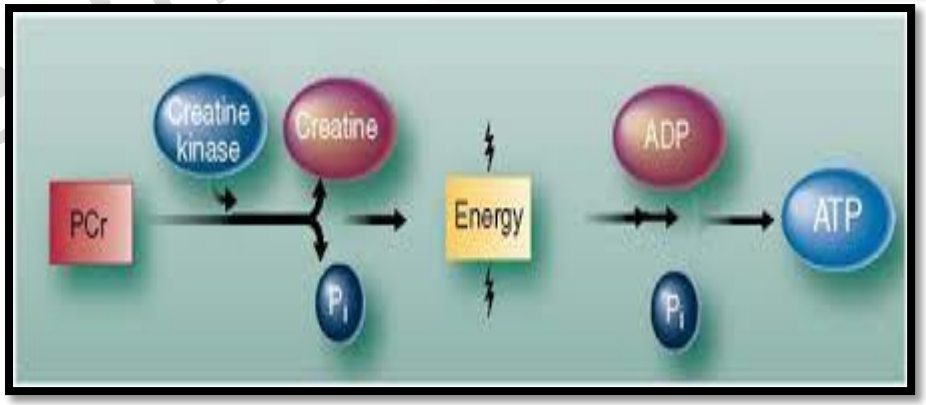
Energy Source in Exercise

Muscle is capable of burning multiple fuels during exercise

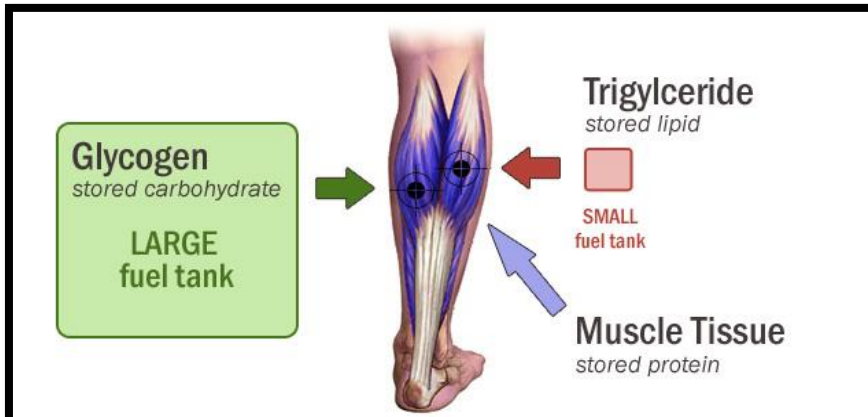
1. ATP



2. Creatine Phosphate



3. Glycogen
4. Fatty Acids
5. Muscle Proteins

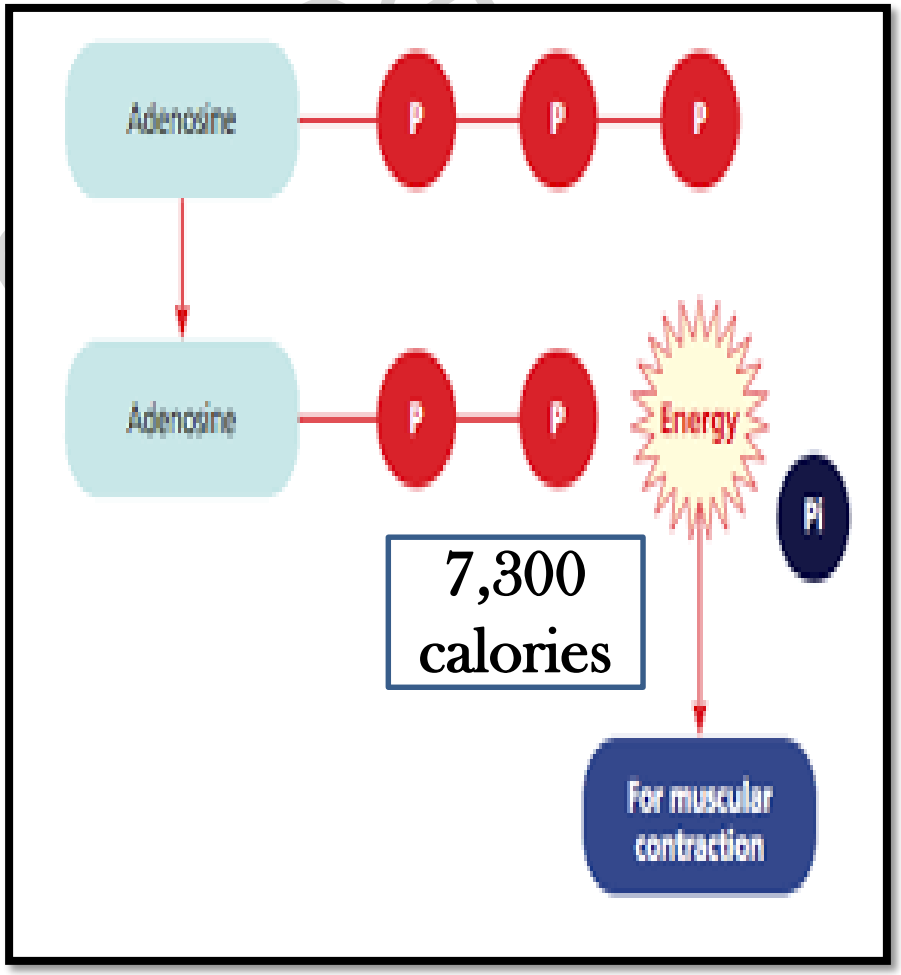


6. Lactic acid

Energy Source in Exercise

1. ATP stored in muscle

- ATP reserve is small
- Can sustain exercise only for first 2 -3 seconds
- How is energy provided for prolonged exercise ?
- By ATP regeneration

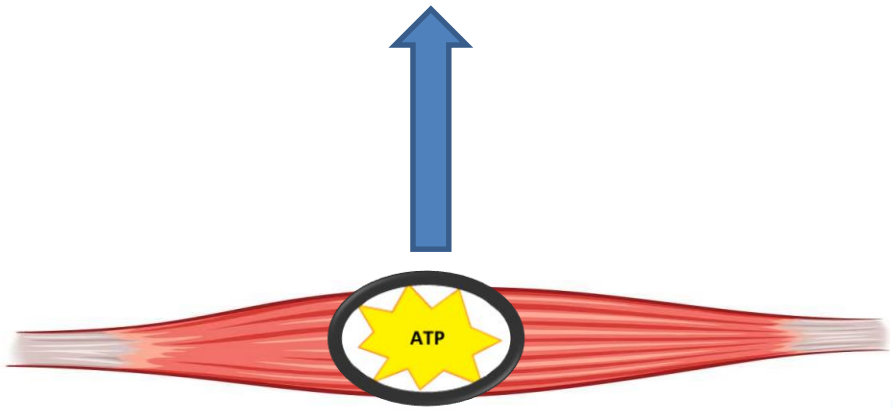


2. Glycolysis (Anaerobic)

1.Creatine phosphate (Anaerobic)

3. Oxidative Phosphorylation (Aerobic)

ATP Regeneration

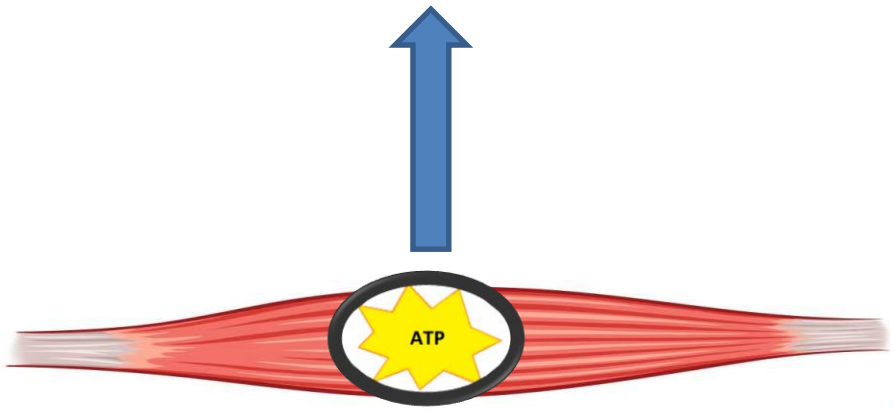


2. Glycolysis (Anaerobic)

1.Creatine phosphate (Anaerobic)

3. Oxidative Phosphorylation (Aerobic)

ATP Regeneration



Which mechanism is used for ATP regeneration

Aerobic

Oxidative phosphorylation

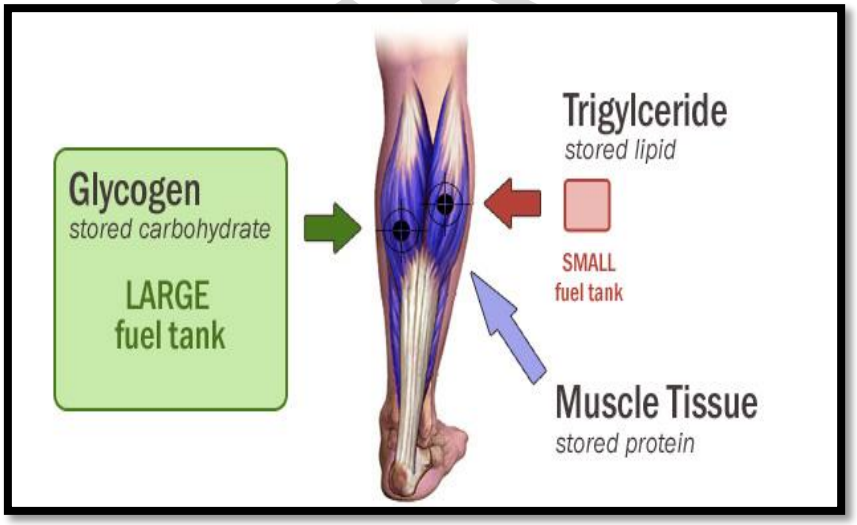
Anaerobic

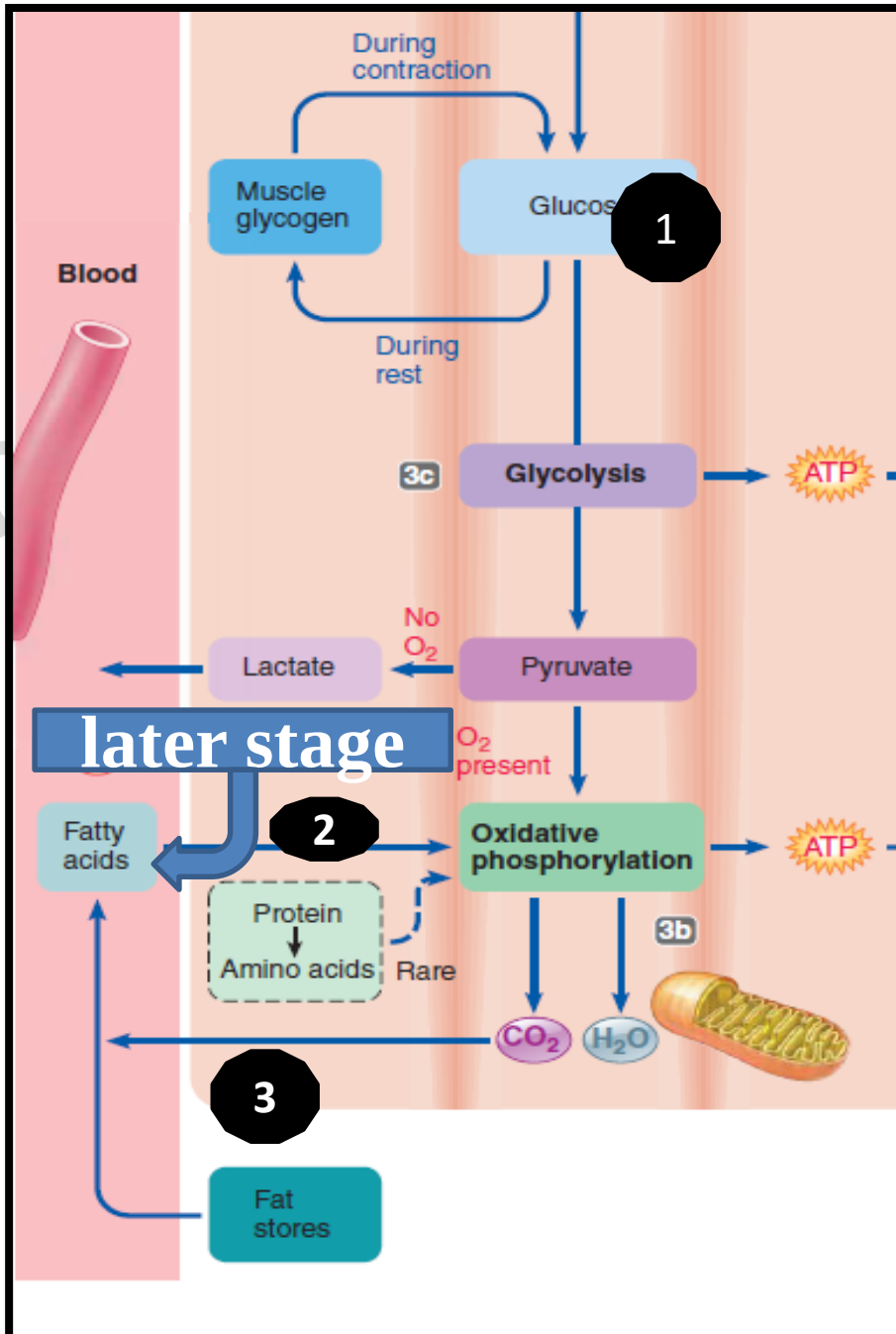
Creatine Phosphate system

Anaerobic Glycolysis

Aerobic Exercise

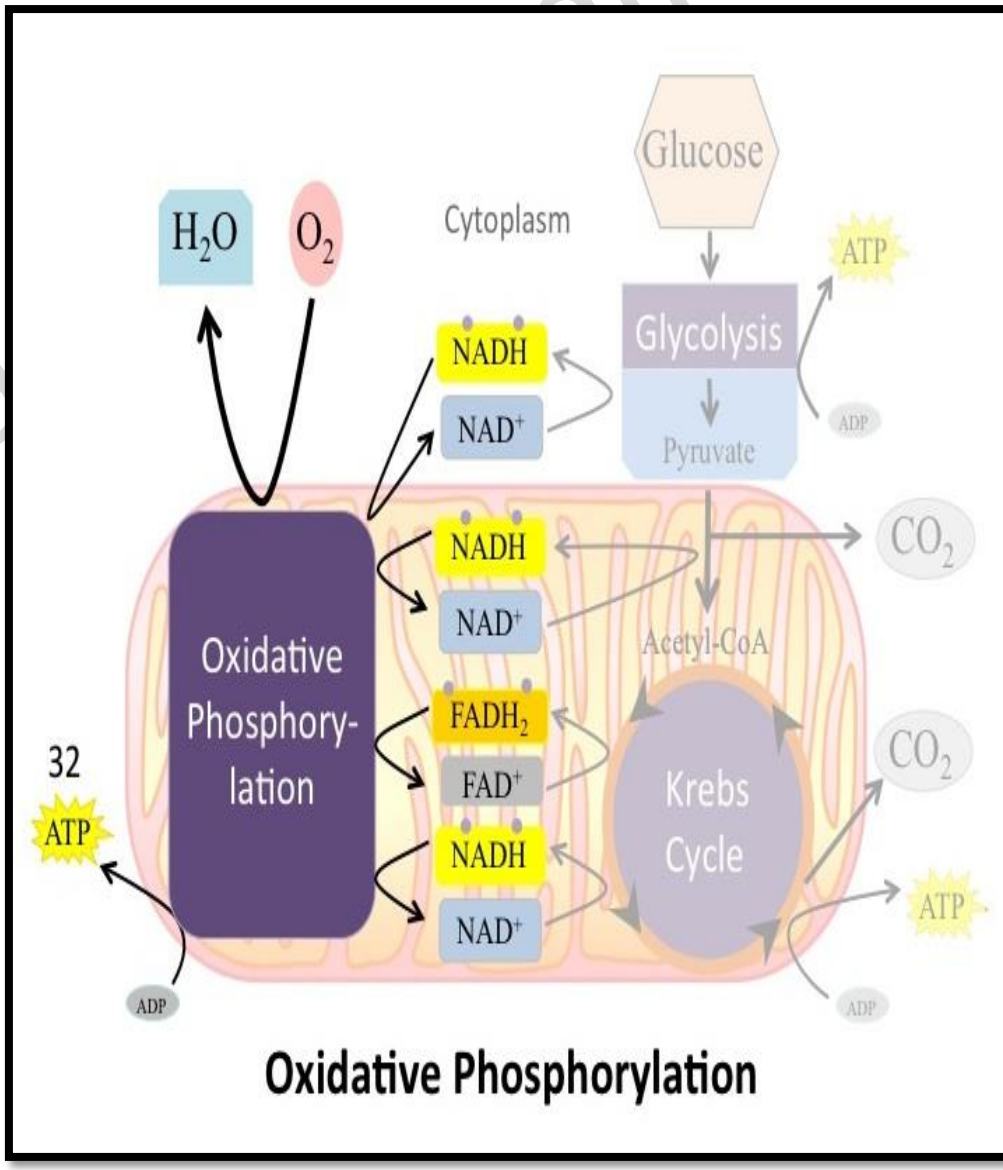
- After exhaustion of stored ATP
- Regeneration is by oxidative phosphorylation of *(nutrients)* glucose, fatty acids & proteins





Oxidative Phosphorylation in Aerobic Exercise

- Inside muscle Mitochondria utilizing Oxygen
- **1 glucose = 32-34 ATP's**
- Very slow process due to multistep pathway.



Anaerobic exercise

Short duration high intensity exercise

Powerful and maximal muscle contractions

Blood vessels compressed

Affects oxygen delivery to muscles

Anaerobic Exercise

ATP regeneration

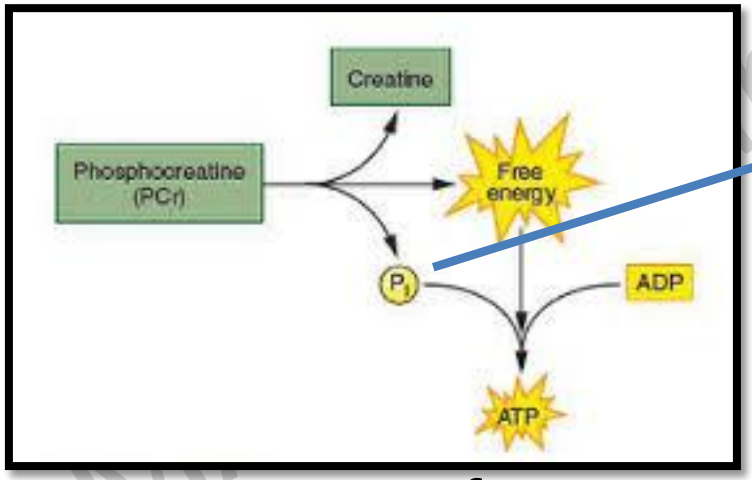
In absence of Oxygen

Creatine Phosphate system

Glycolysis

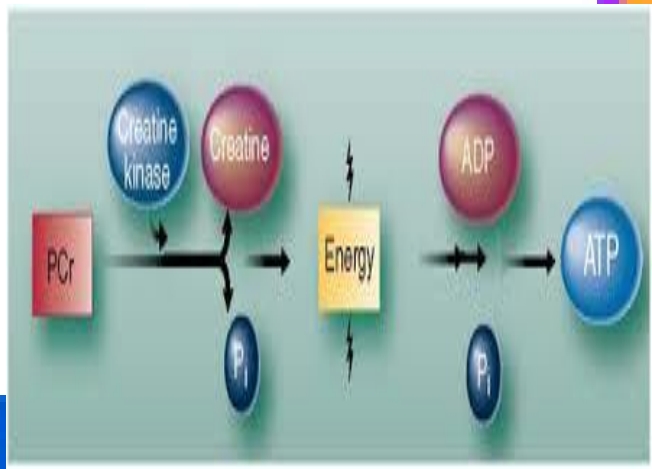
Creatine Phosphate System

- Source of ATP in anaerobic condition
- **Creatine phosphate is stored in Sarcoplasm**



10,300 cal/molecule

- Reaction is very fast
- Sustains exercise for 8 -10 seconds



Anaerobic Exercise

ATP regeneration

In absence of Oxygen

Creatine Phosphate system

Anaerobic Glycolysis

ATP from Glycolysis

- 1 glucose = 2 ATP's

- Pyruvic acid formed

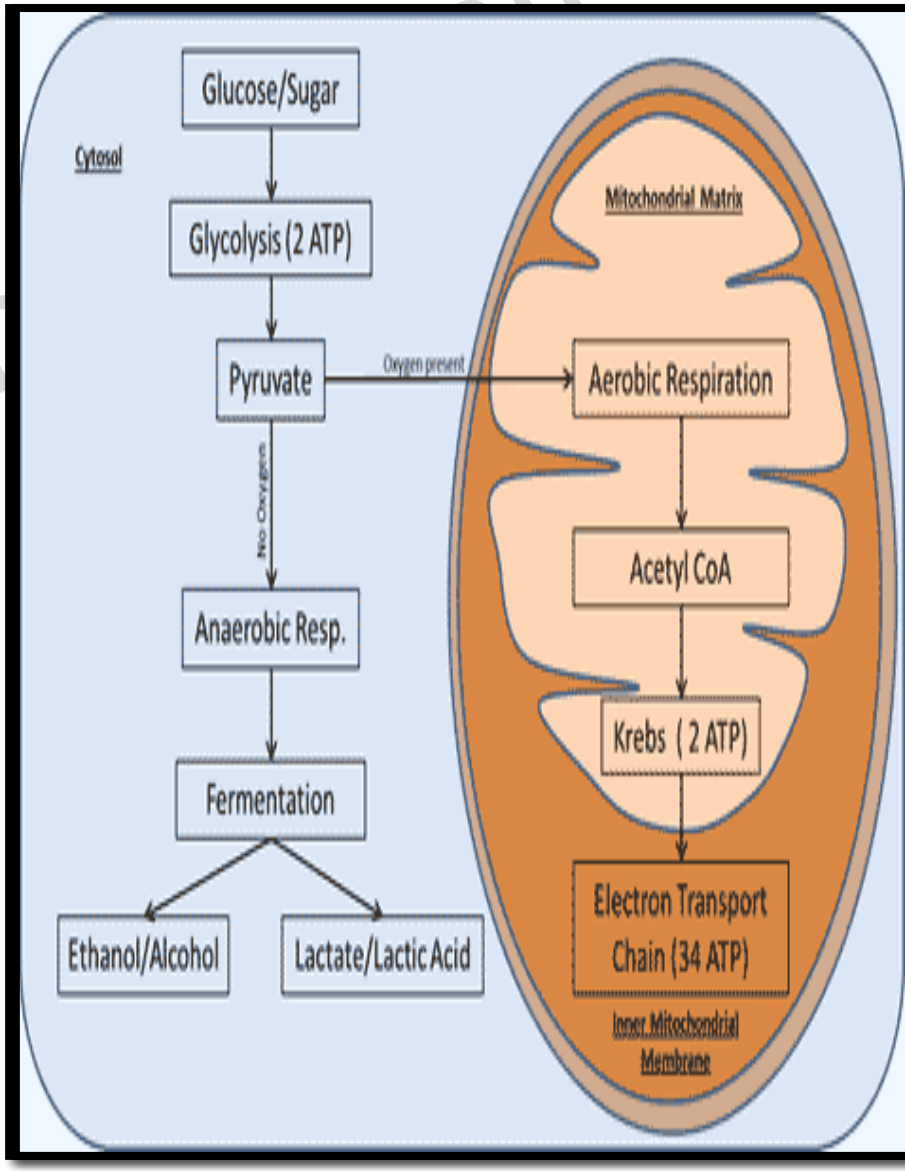
Sufficient oxygen

Insufficient oxygen

Enters mitochondria

Converted to Lactic acid

Oxidative phosphorylation

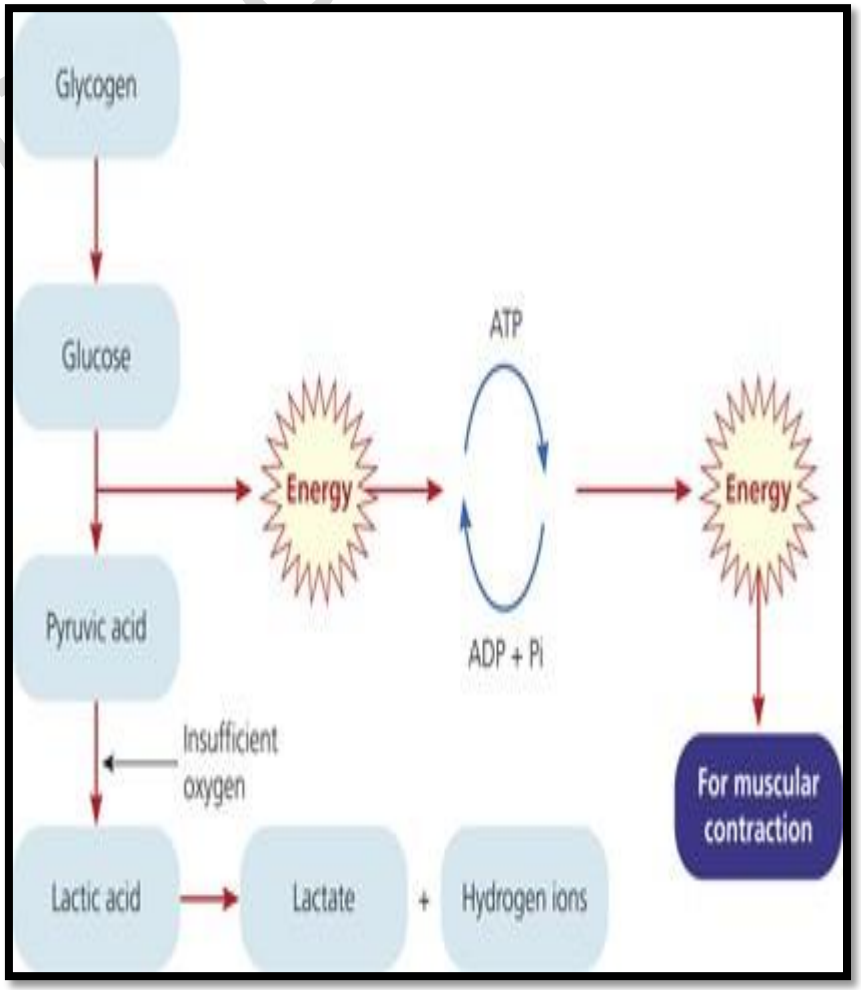


ATP from anaerobic Glycolysis

- Very quick
- But, ATP production is less

- **Lactate accumulation in muscle**
  - muscle soreness
  - stiffness
  - Fatigue

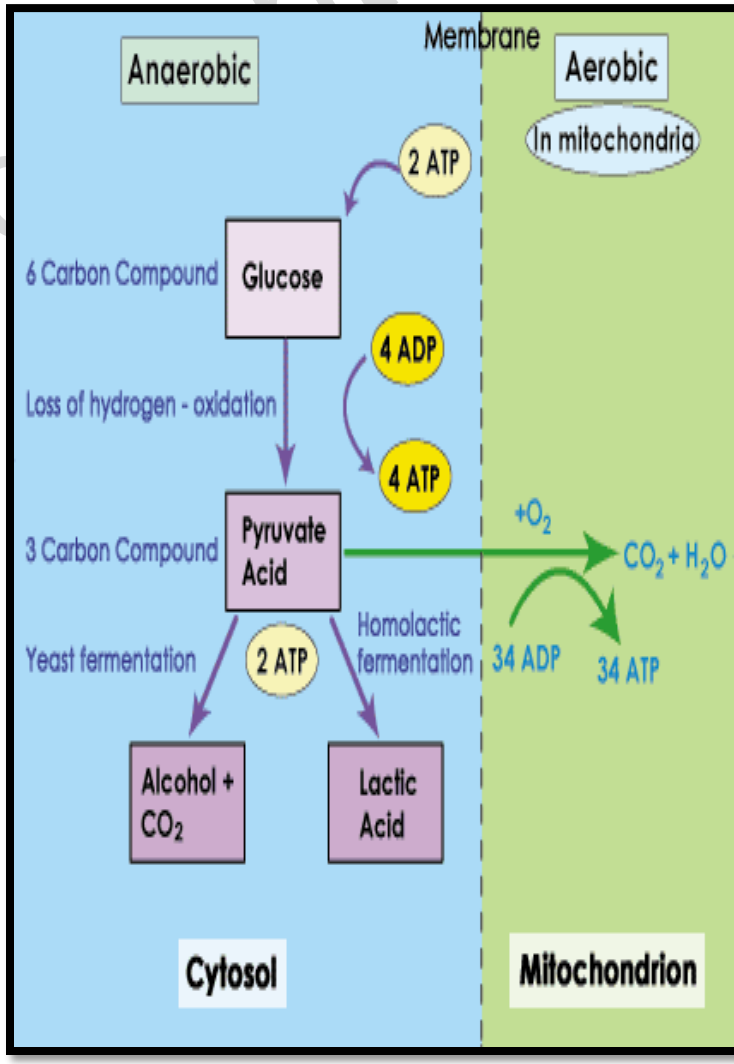
- **Anaerobic exercise can be sustained only for a short duration.**



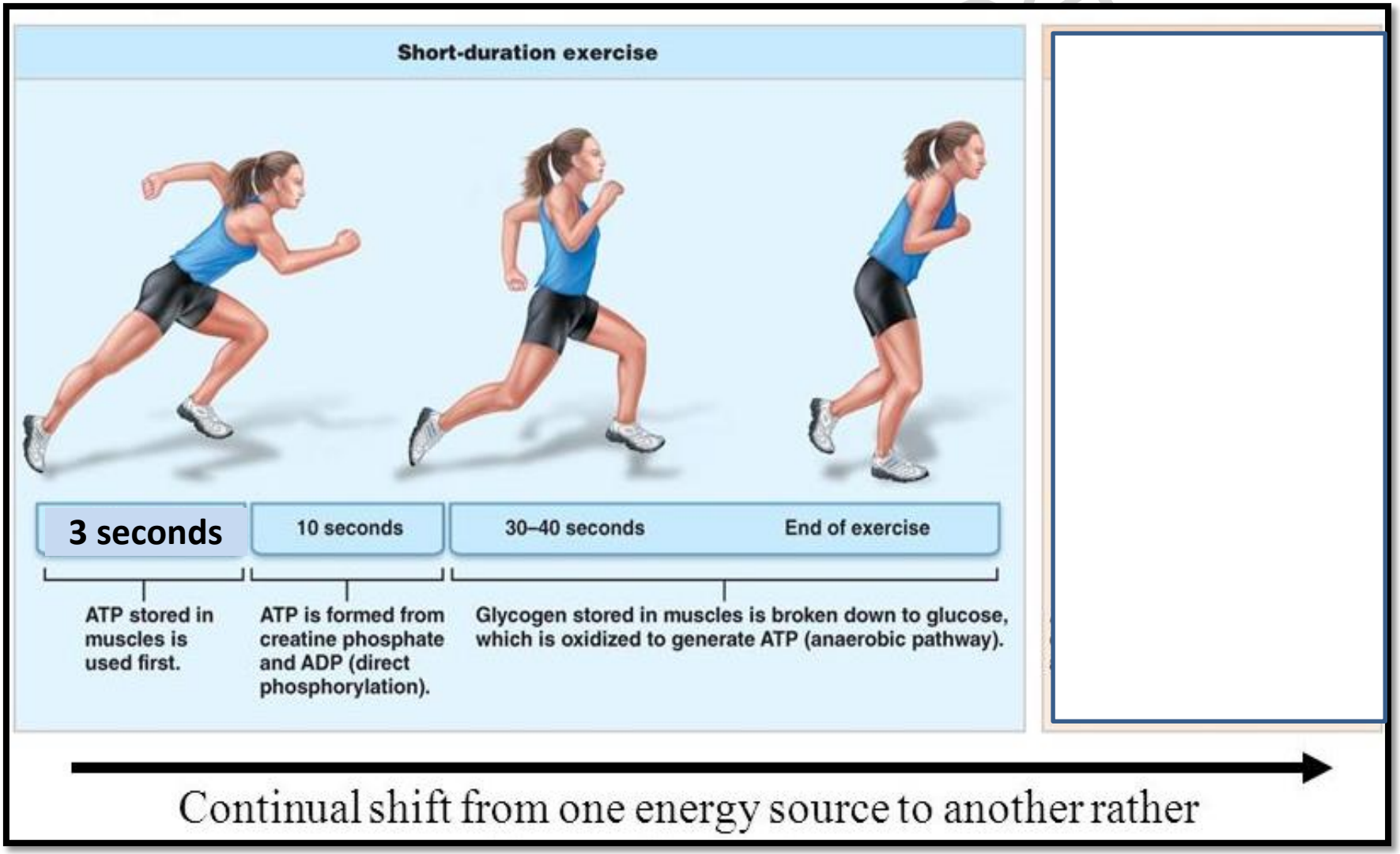
Anaerobic Respiration

- **In absence of oxygen**
- **Pyruvate ---- ethanol + lactic acid & Energy**
- **Lactic acid accumulation**

Fatigue , cramps



The type of fuel burned for energy depends on duration and intensity of exercise.



Sprinter

Phosphagen system

8-10 seconds (100 m)

Swimmer

Glycogen-lactic acid system

1.3–1.6 minutes (400 m)

Marathon runner

Aerobic respiration

Unlimited time (15 Km)

Glycolysis

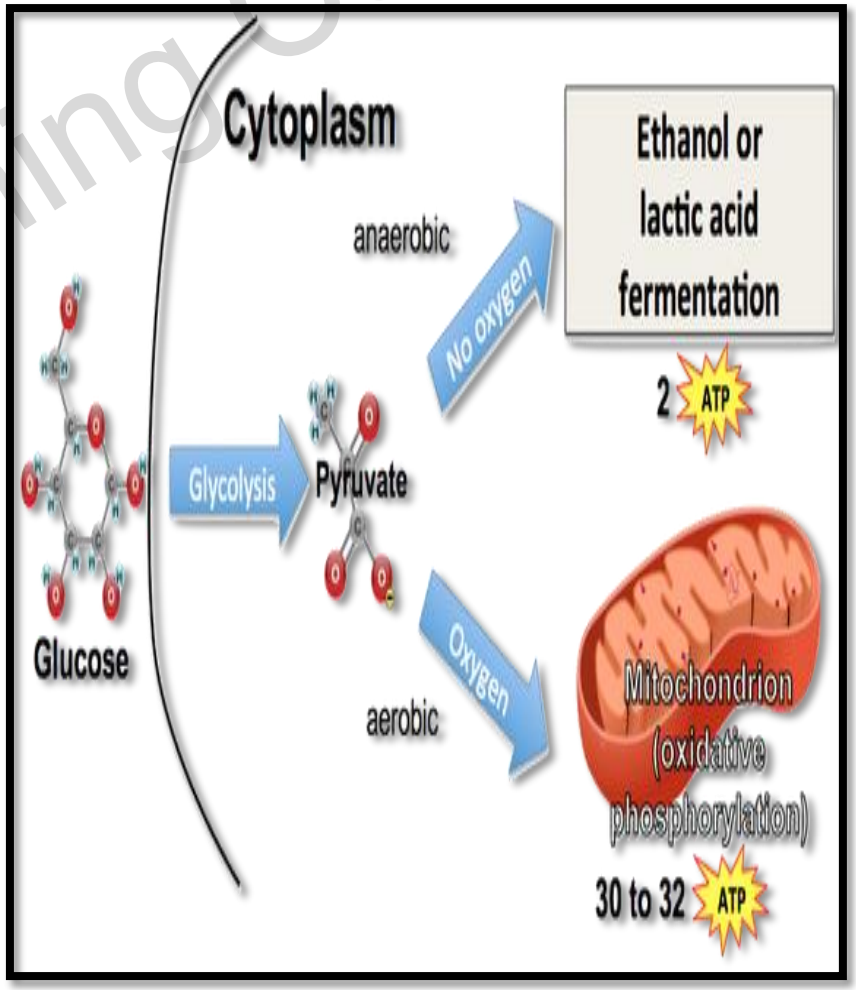
Pyruvate

No oxygen

- **Lactic Acid**
- **Energy**

oxygen

- **CO2**
- **water**
- **Energy**



Muscle twitch

- Twitch is a quick, jerky contraction of muscle for a single stimulus.

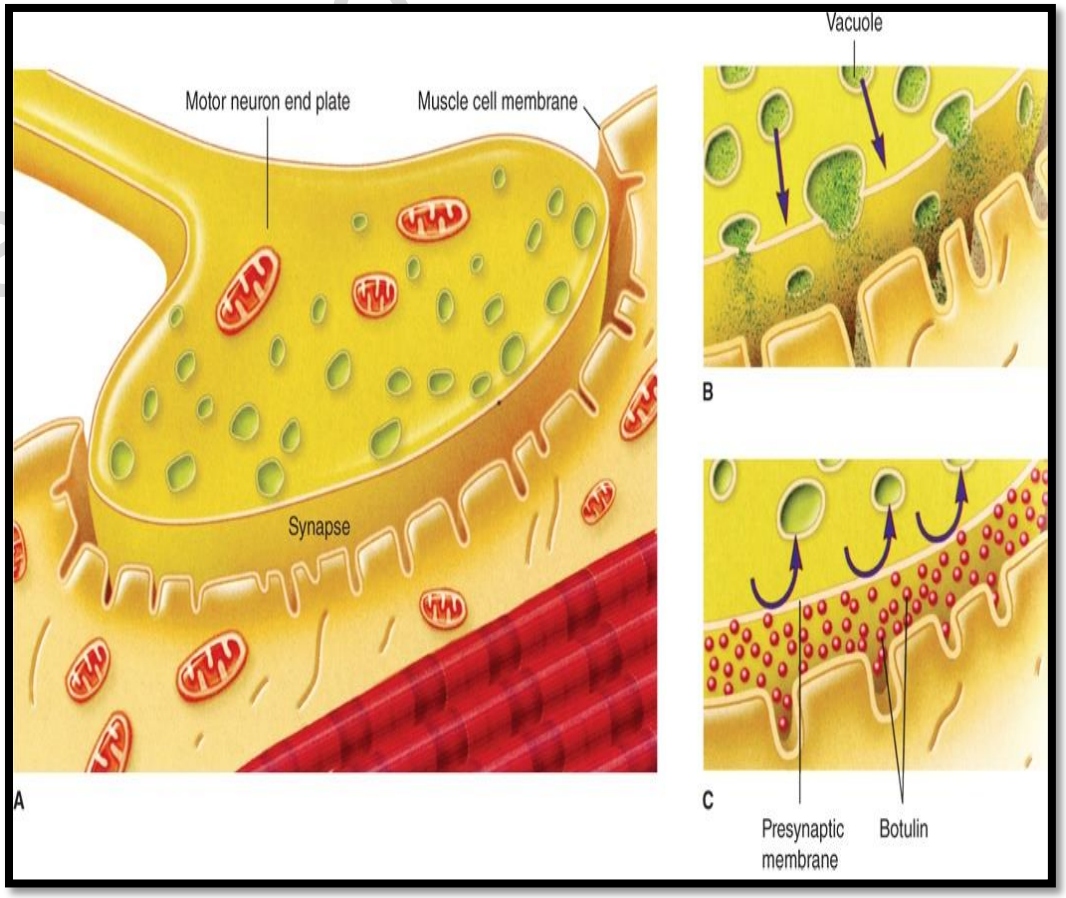
Muscle spasm

Tetanus

- **Prolonged painful contraction of muscle due to repeated stimulation.**

- **Bacterial infection**

Clostridium Tetani



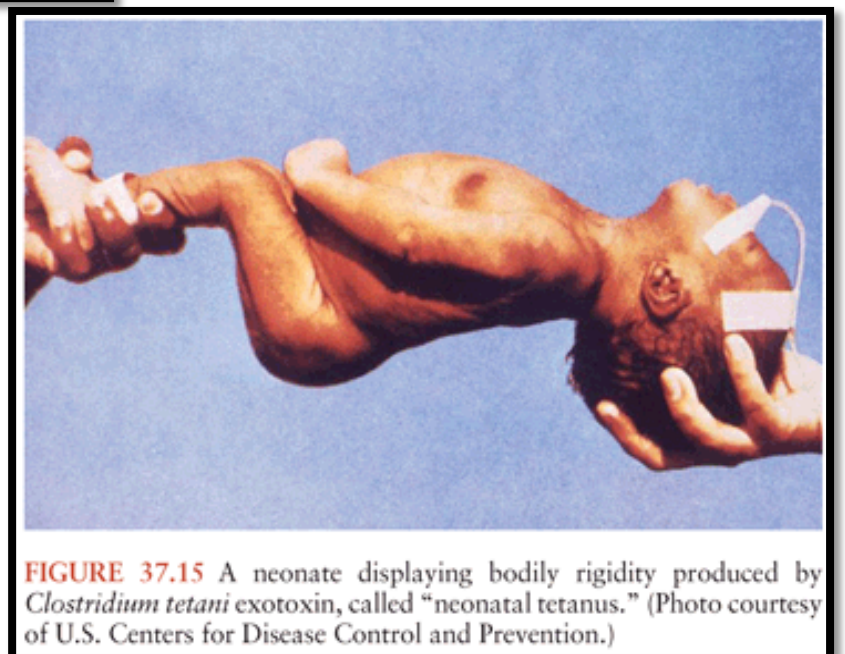


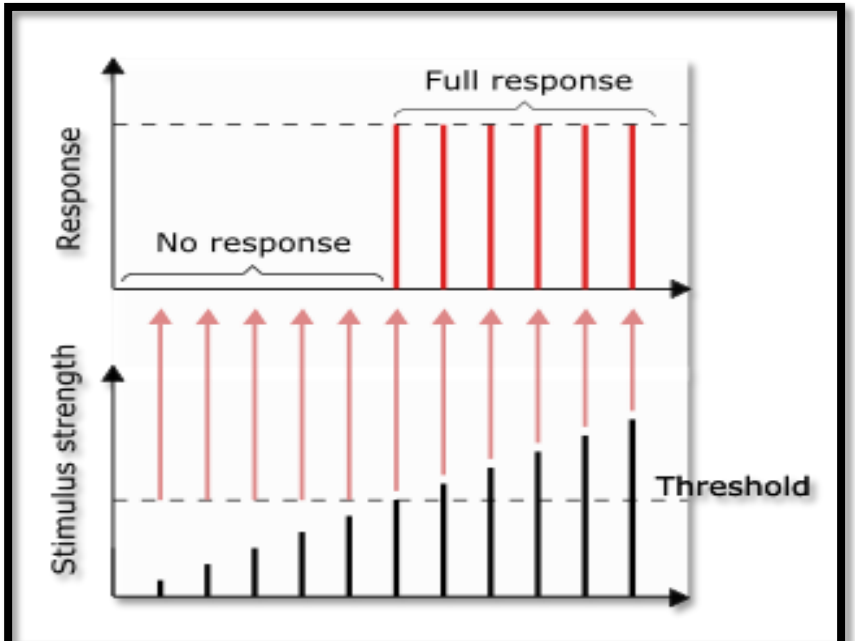
FIGURE 37.15 A neonate displaying bodily rigidity produced by *Clostridium tetani* exotoxin, called "neonatal tetanus." (Photo courtesy of U.S. Centers for Disease Control and Prevention.)

Properties of muscle fibers

1.All or none Law/ Bowditch's law

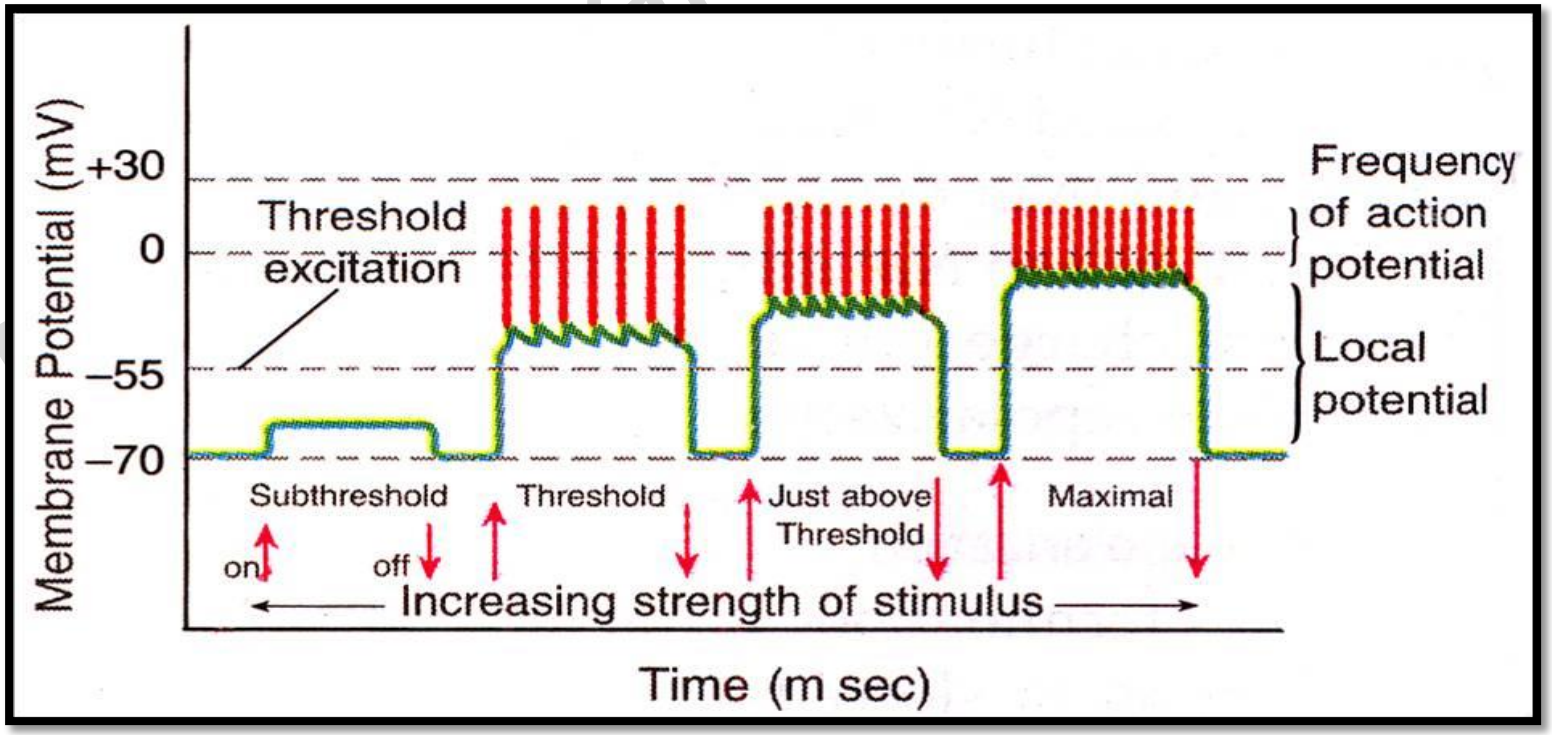
- States that response by a nerve or muscle depends on the strength of stimulus applied on it.

- Bodwitch (1871)

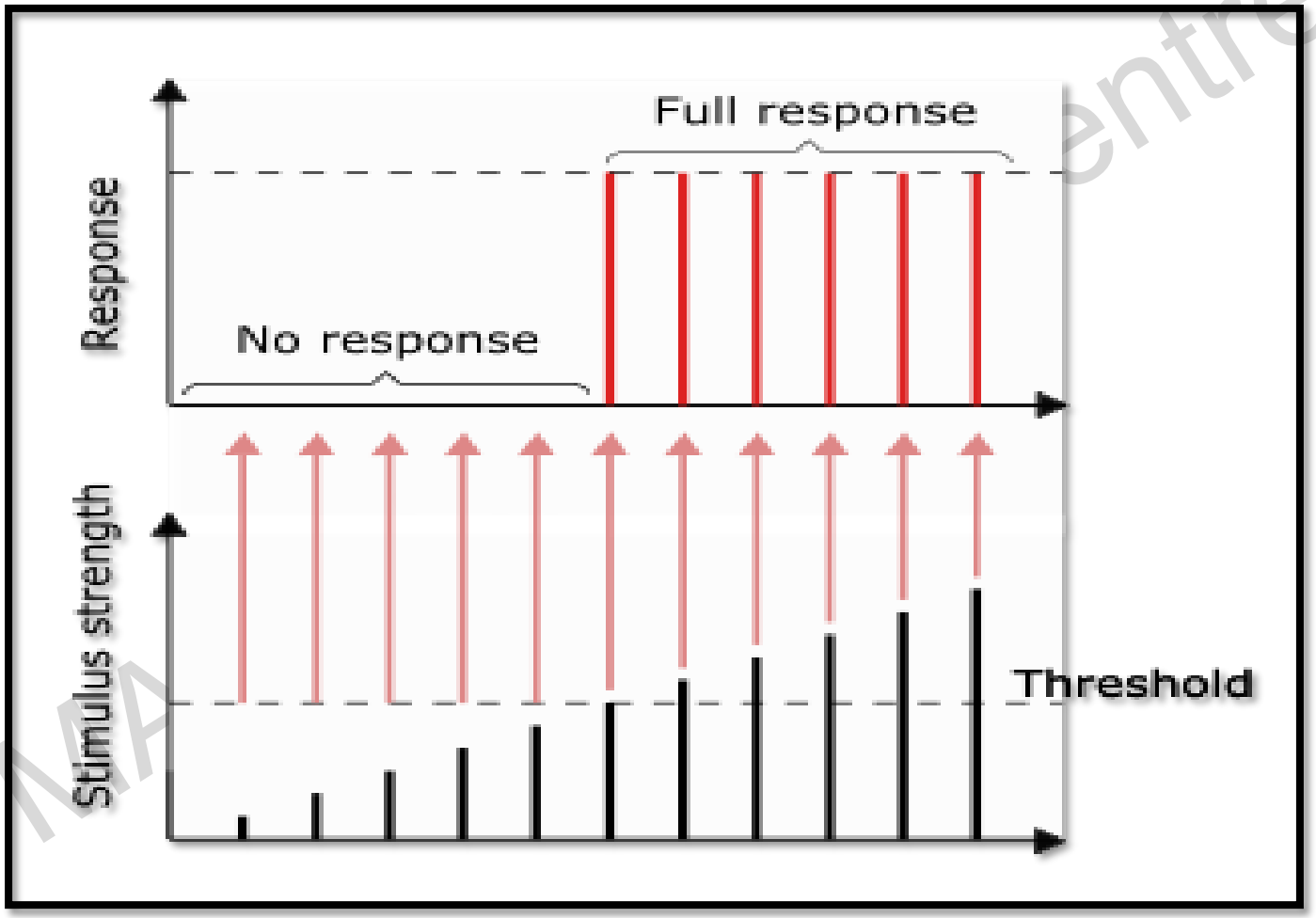


1.All or none Law/ Bowditch's law

- Sub threshold stimulus : no contraction
- Threshold intensity : full fledged contraction
- Supra threshold stimulus :no change in amplitude.

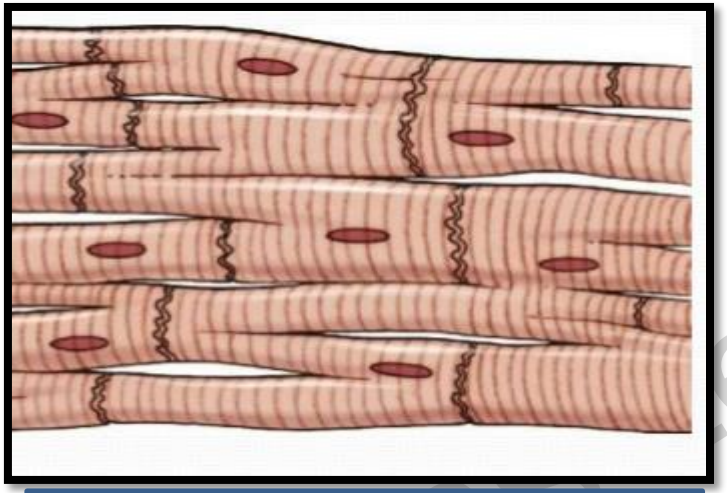


All or none Law

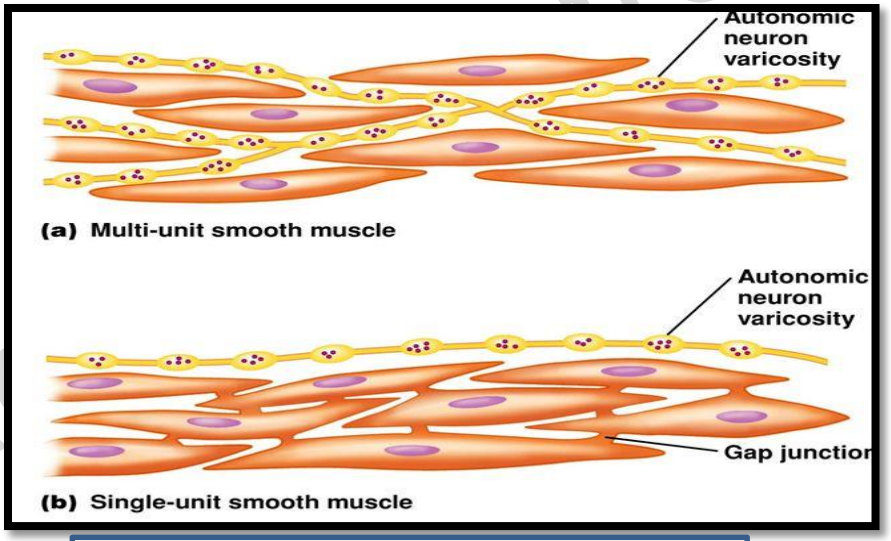


When a stimulus is applied either muscle responds to its maximum or does not respond at all depending on the strength of stimulus

All or none law property is followed by :

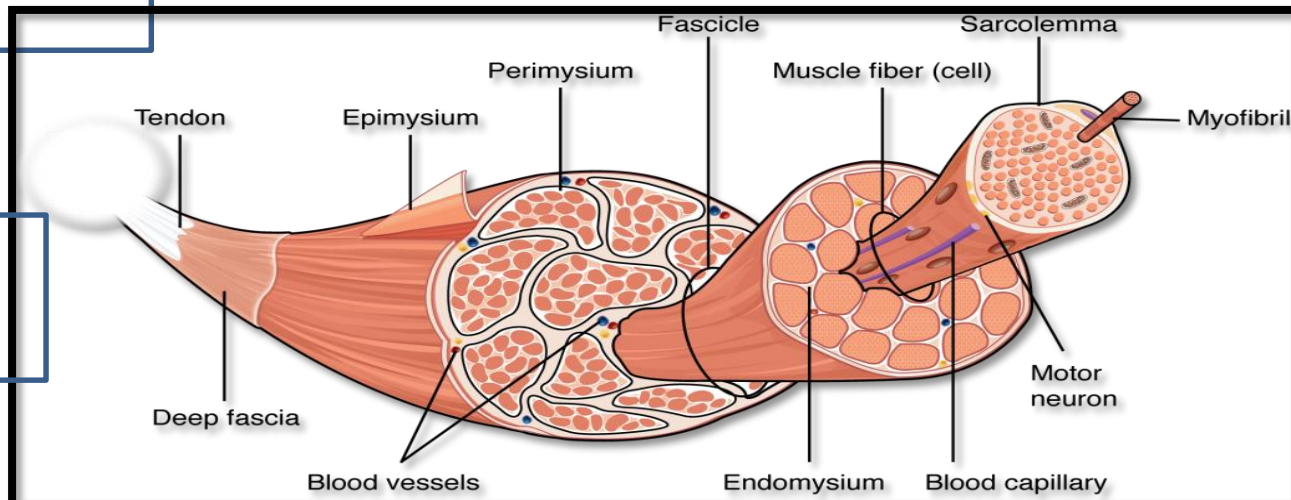


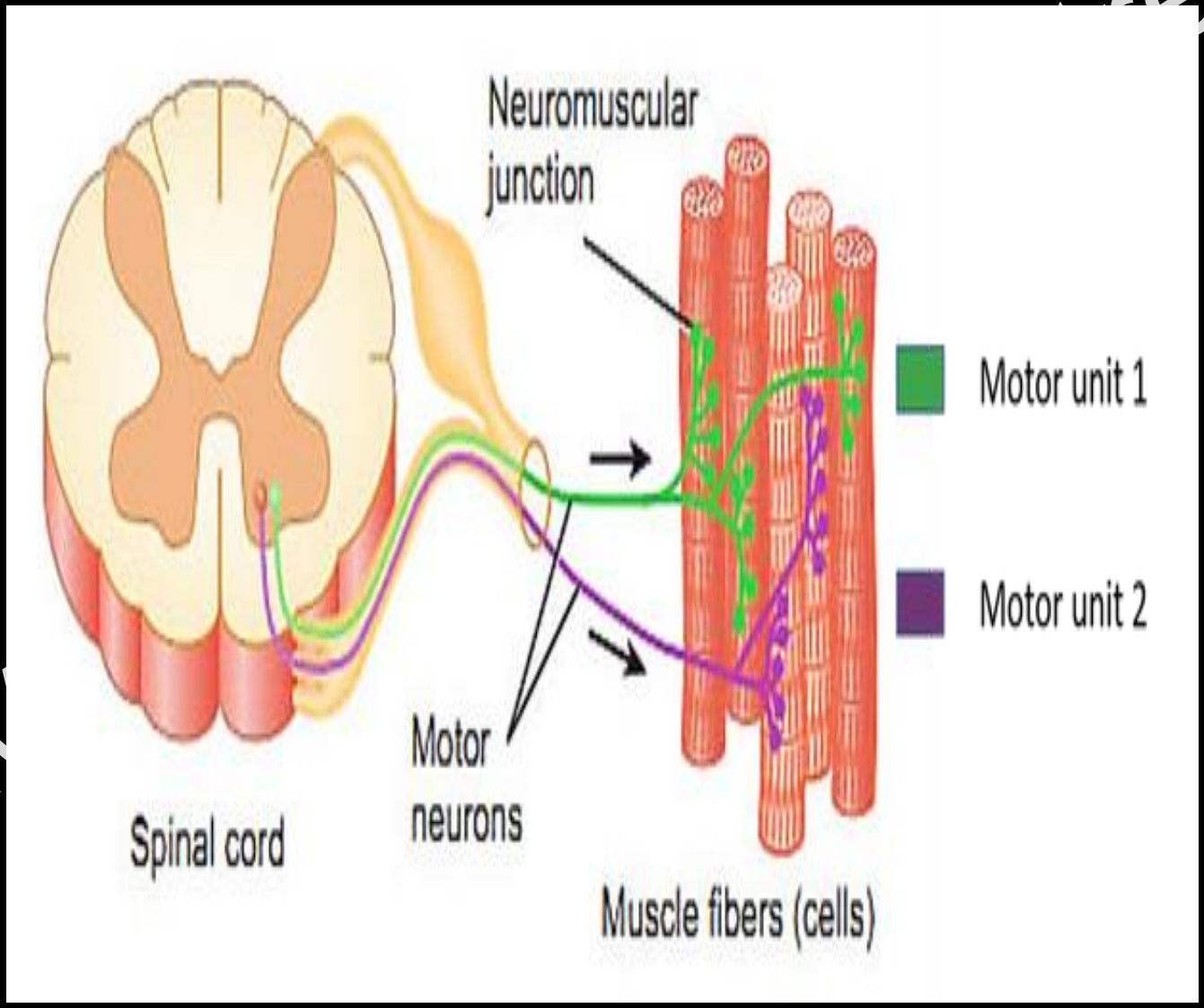
Cardiac muscle



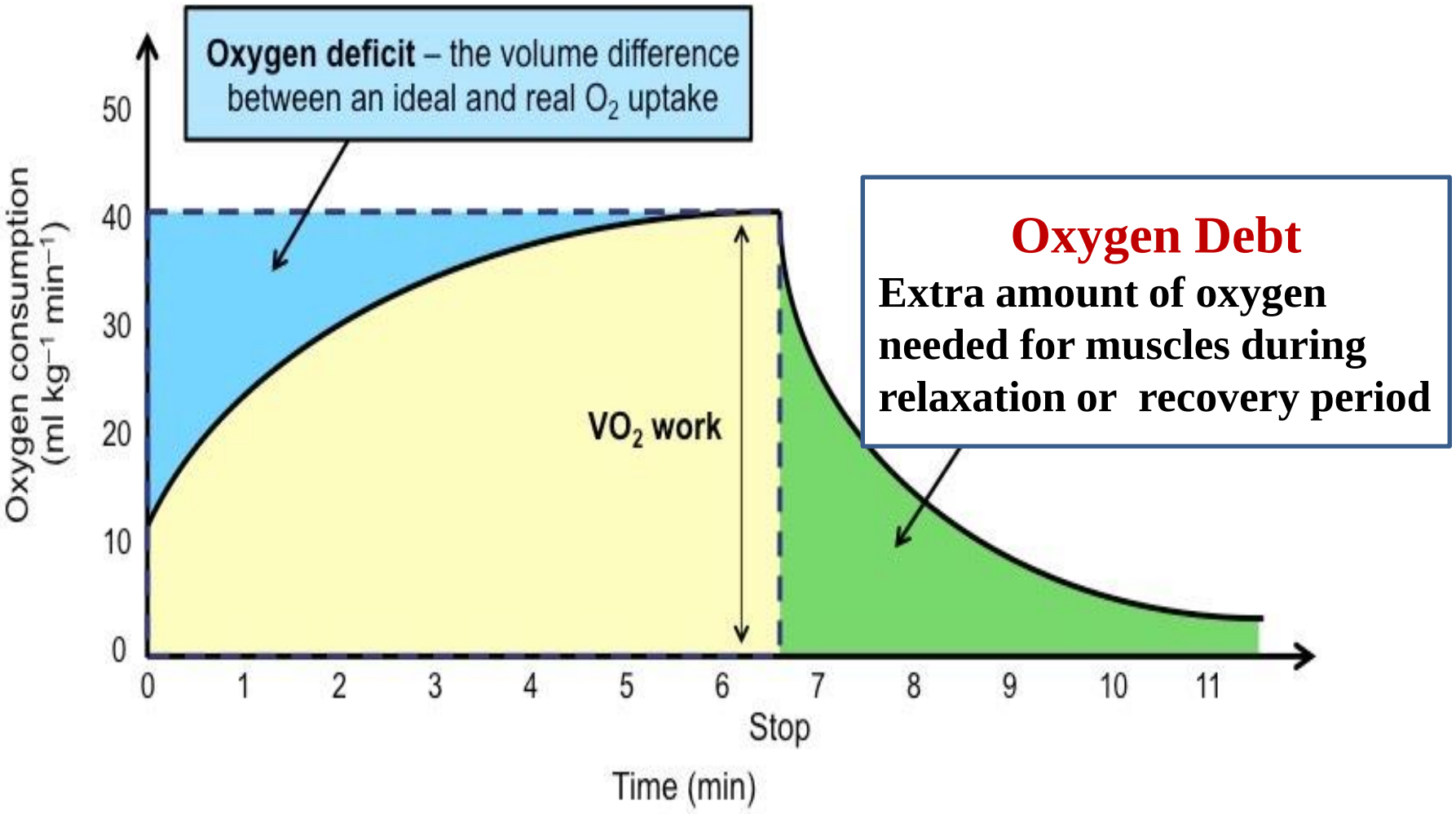
smooth muscle fiber

Individual Skeletal muscle fiber




Neuromuscular junction
Motor unit 1
Motor unit 2
Motor neurons
Spinal cord
Muscle fibers (cells)

Oxygen Debt

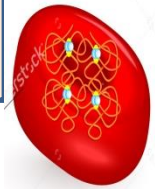

Oxygen deficit – the volume difference between an ideal and real O_2 uptake
Oxygen Debt
Extra amount of oxygen needed for muscles during relaxation or recovery period
VO_2 work
Oxygen consumption (ml kg⁻¹ min⁻¹)
0
10
20
30
40
50
0
1
2
3
4
5
6
7
8
9
10
11
Stop
Time (min)

During Exercise

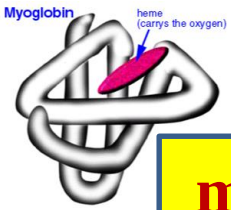
Body stores 2 Litres of Oxygen

0.5L

0.25L



1L



0.3L

myoglobin

All the stored O2 gets utilized in first few seconds of exercise for energy

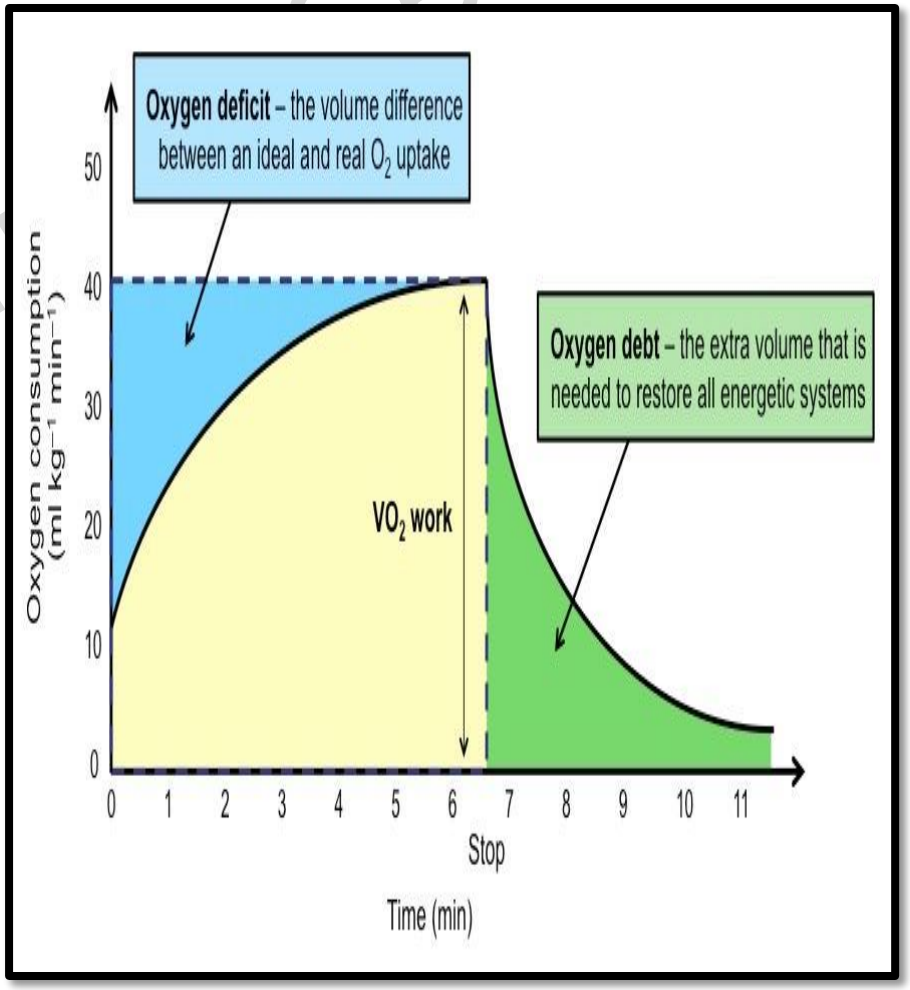
Later shifts to anaerobic respiration -- lactic acid accumulation

Significance of Oxygen Debt

1) Replenish O2 stores

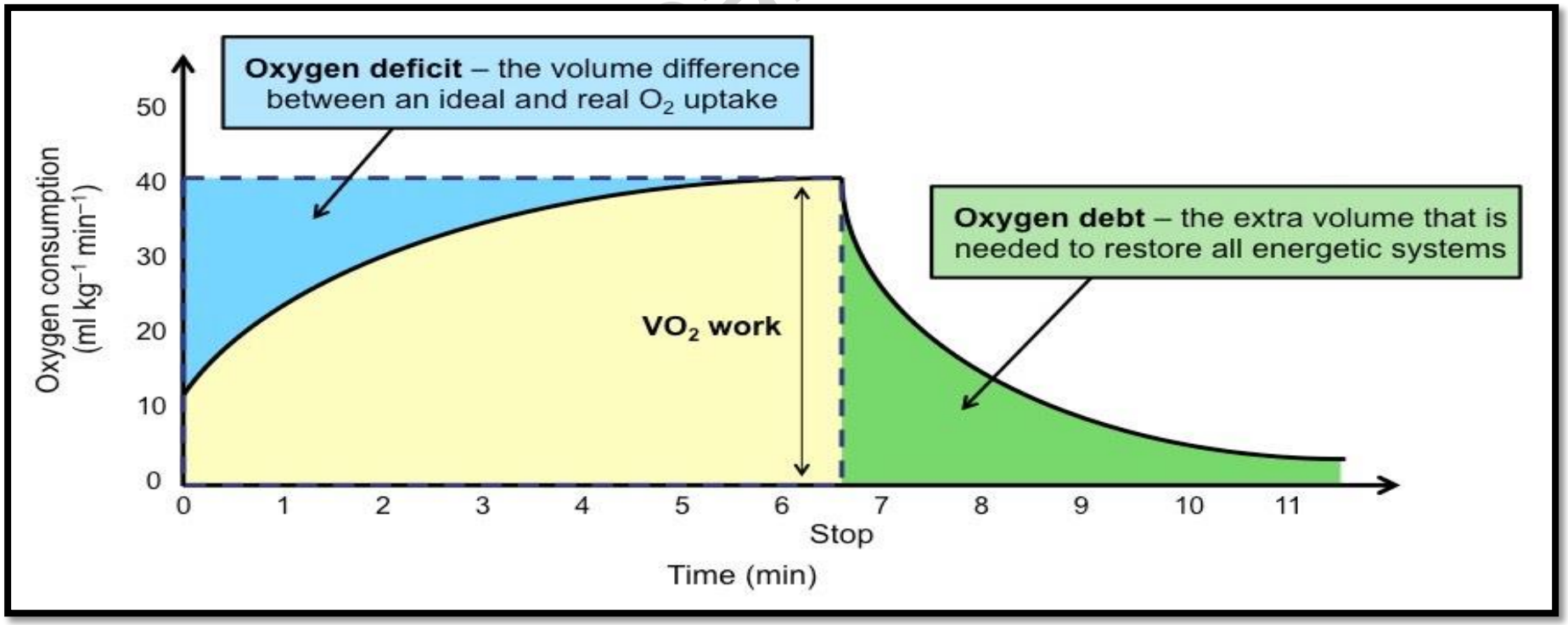
2) Replenish ATP & Phospho creatinine

3) Removes Lactic acid



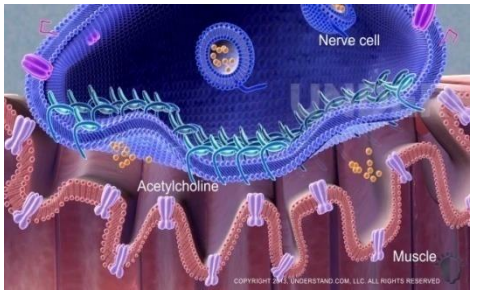
During Anaerobic Exercise

- Oxygen demand far exceeds oxygen supply
- Thus after exercise excess oxygen intake is needed



3. Muscle Fatigue

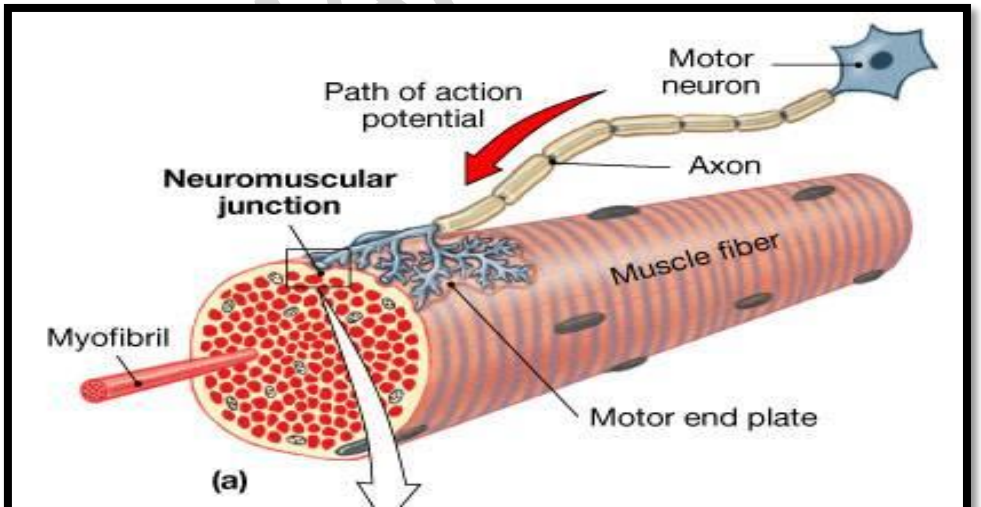
- Temporary exhaustion of muscle
- Reduced force of contraction of muscles due to prolonged stimulation.

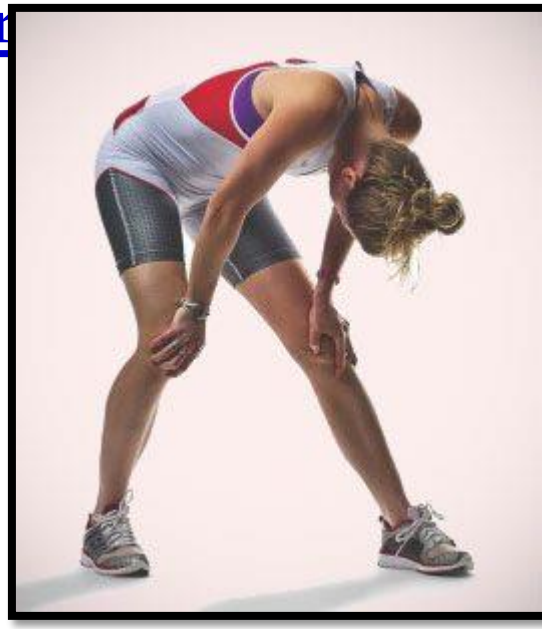


- **Reason:**

- Accumulation of lactic acid

- **Site of Fatigue : reduced neurotransmitter**



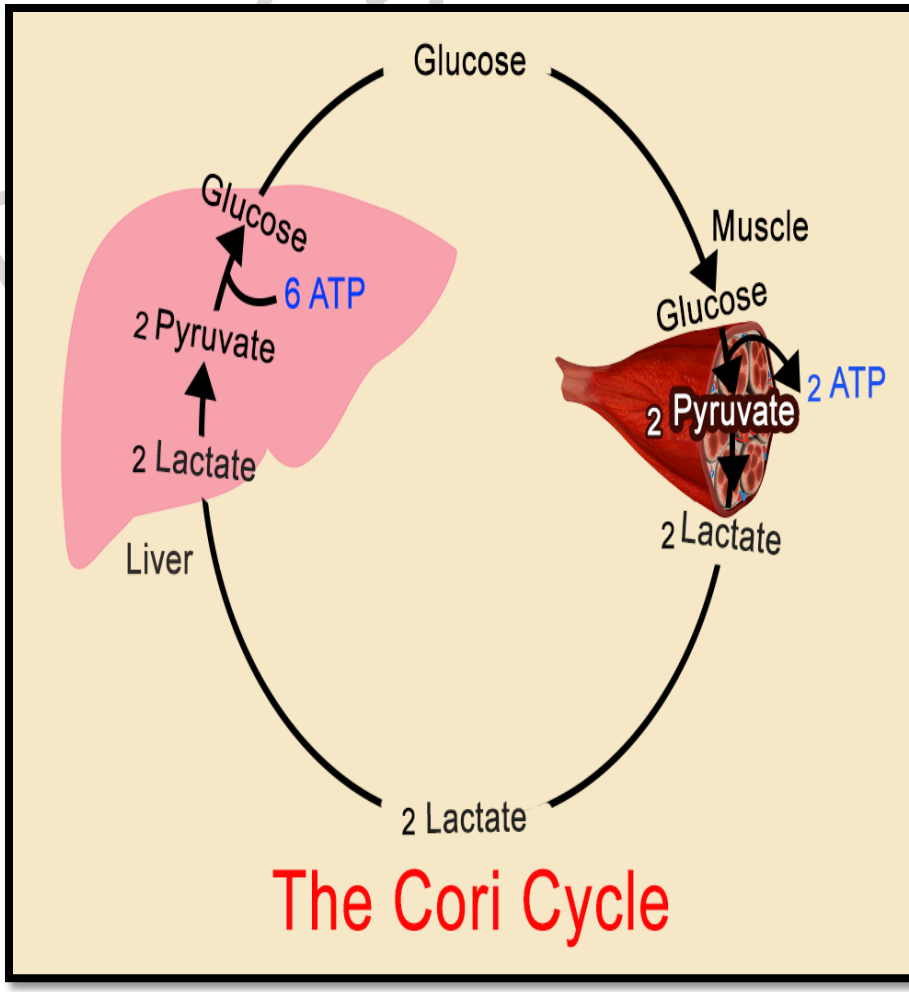


4. Cori's Cycle

- **Pathway of conversion of**
  lactate ⟶ glucose
  Glucose ⟶ Lactate
- **In anaerobic exercise**
- Formation of lactic acid in muscles
- Conversion of lactate to glucose in liver.

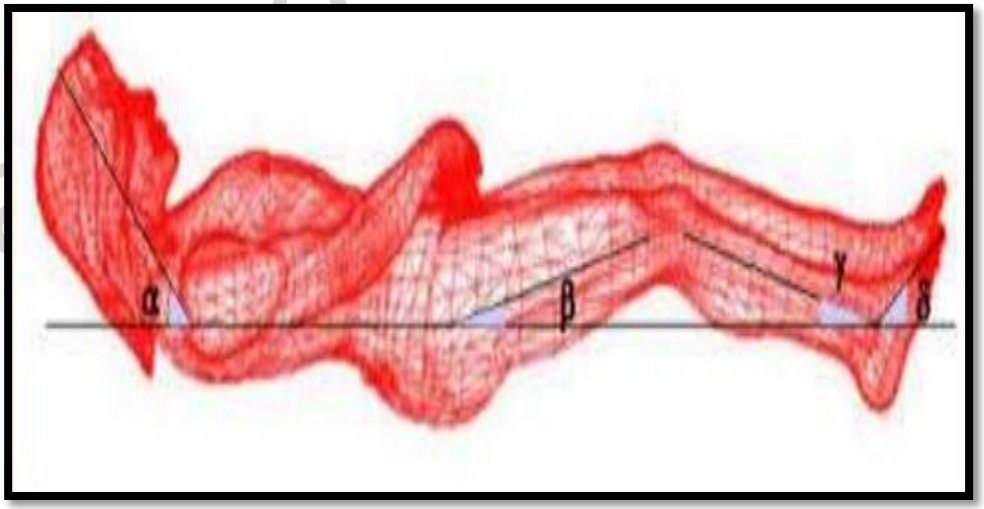
- **Reason:**

- **Reduces lactic acid accumulation**
- **Continous glucose supply.**



5. Rigor mortis

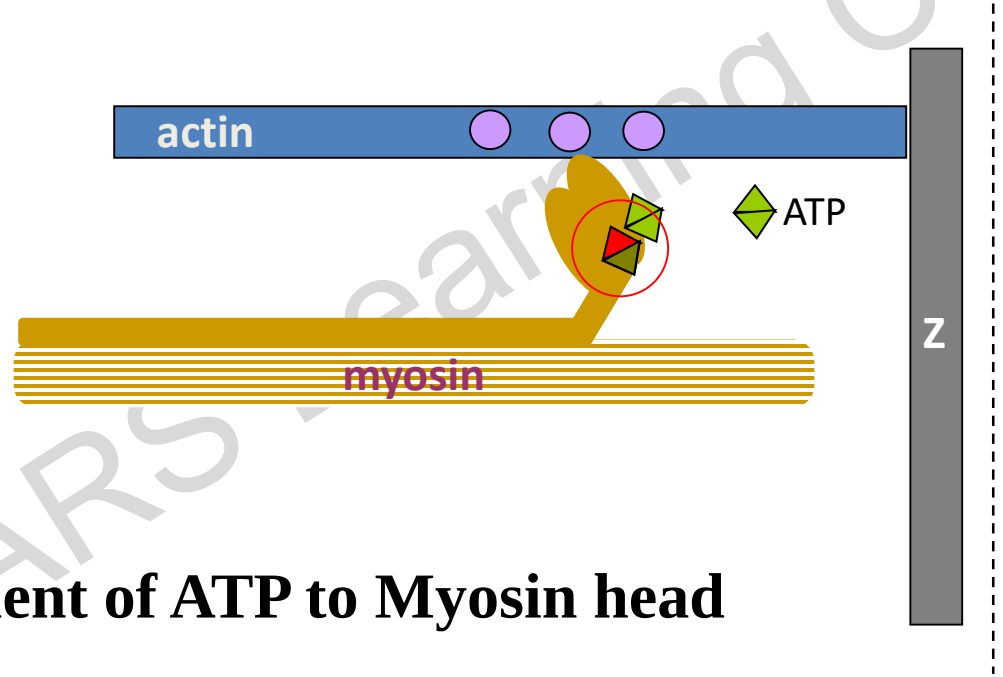
- Stiffening of muscles & joints few hours after death.



- First – lower jaw

- **Reason :**
- Lack of ATP for cross bridge detachment

Cross bridge cycle



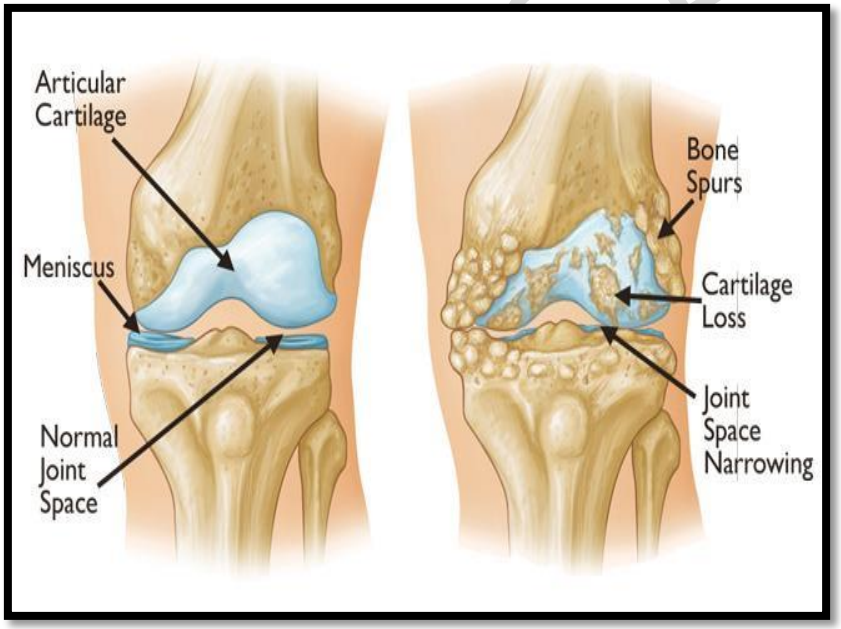
- **Attachment of ATP to Myosin head**
- **ATP----------$^{\text{Myosin ATPase}}$ ADP & P_i**
- **Cross bridge detachment**

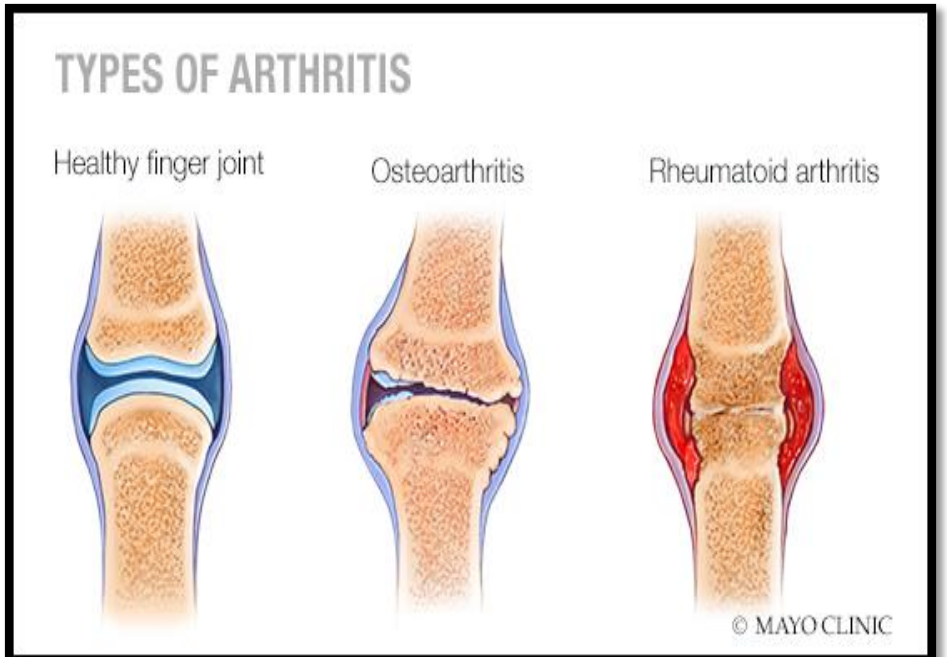
Arthritis

- Inflammation of joints
- Features : pain and stiffness in joints

- **Osteoarthritis**
- Degeneration of articular cartilage
- Middle age or old age
- Large weight bearing bones are affected

- **Rheumatoid arthritis**
- Inflammation of synovial membrane
- Any age.
- Multiple small joints are affected



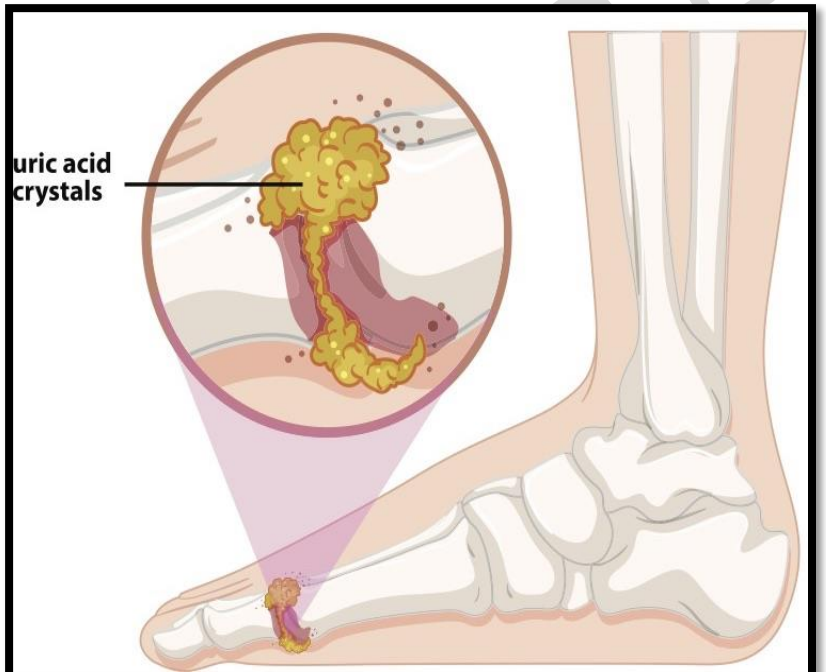


Gout

- Accumulation of crystals of

-uric acid

- sodium urate in synovial joints



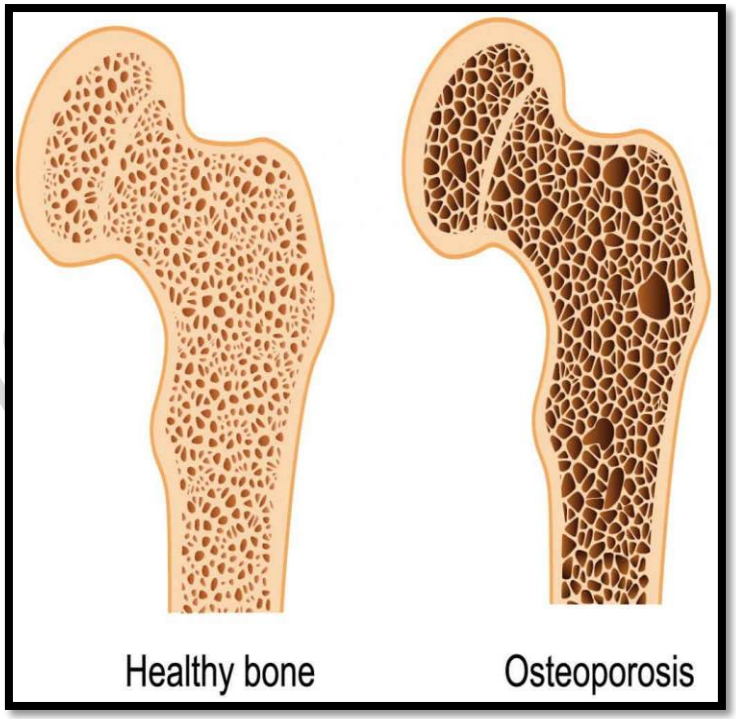
- **Reason:**

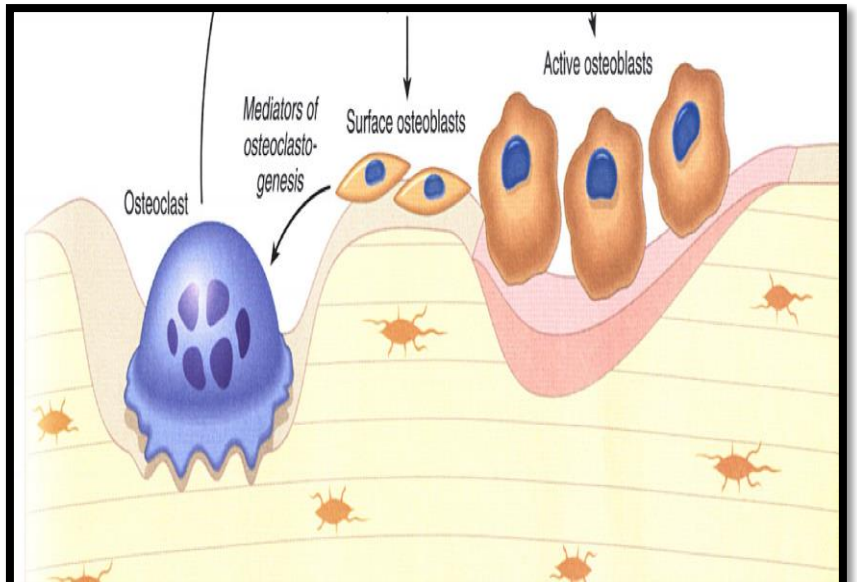
Genetic abnormality of purine metabolism

Osteoporosis

- **Reduced bone mass**
- **Cause:**

- Hypocalcaemia
- Hormone imbalance
- Parathyroid hormone excess
- Calitonin deficiency
- Estrogen deficiency



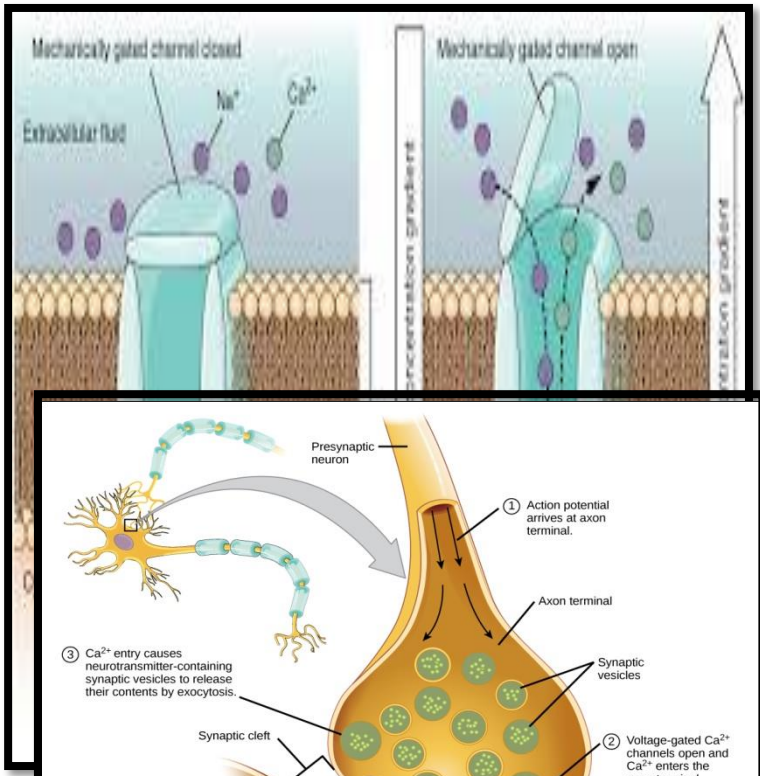


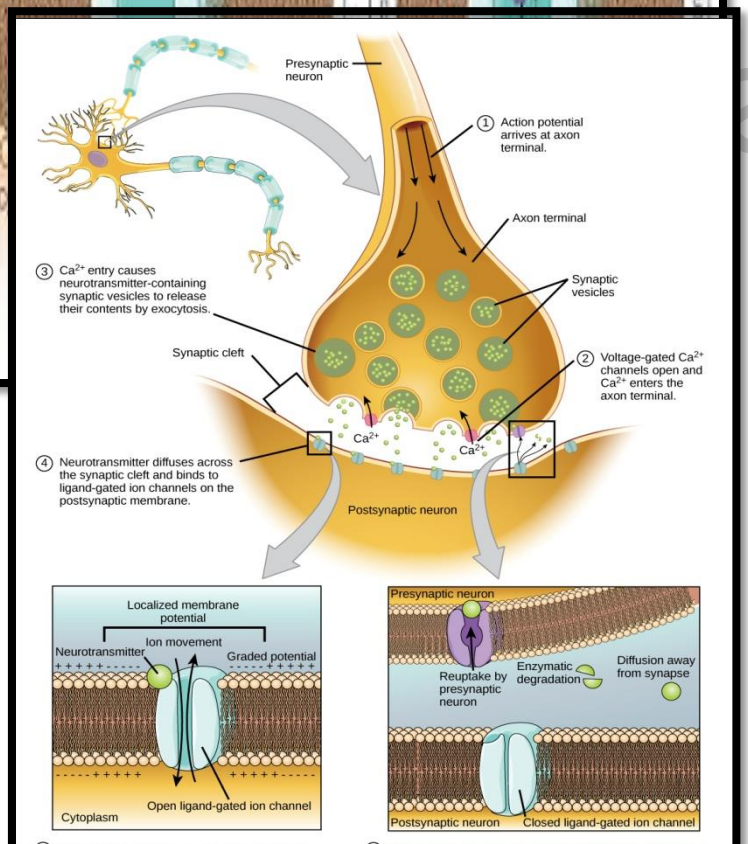
Tetany

- Repeated stimulus to the muscle leading to successive contractions without relaxation.
- **Reason:**

Hyperexcitibility of neurons due to severe calcium deficiency.

Hypocalcemia – excites Nervous system





Plasma Ca2+ ⟶ 6- 5mg/dl

↓

Neuronal permeability increases to Na+ ions , Super excited nerve fibers

↓

Initiates AP even for a subthreshold stimulus

↓

Tetanic muscle contraction

y2mate.com - chvostek_sign_r5YDqLwQH8g_1080p.mp4

Myasthenia gravis

- **Autoimmune disorder of NMJ**

  (Neuromuscular junction)

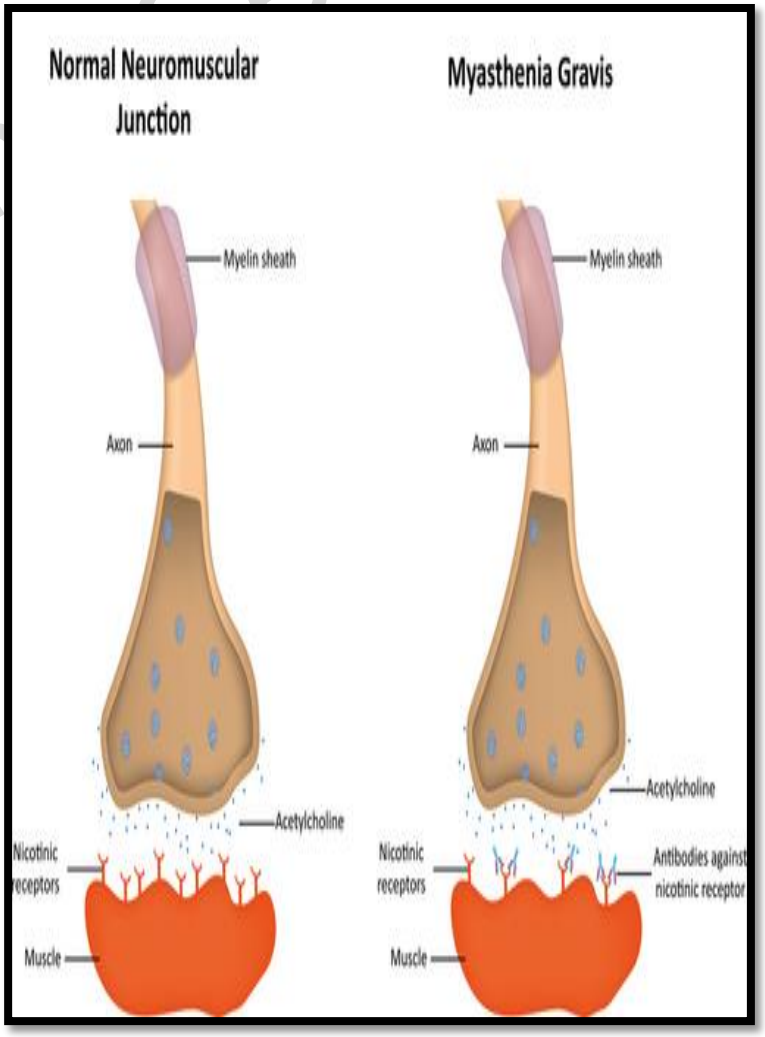
- **Cause:**

-Auto antibodies produced against

Ach Receptors

- So receptors are destroyed

- Muscle fiber is not stimulated



SYMPTOMS:

– Muscle weakness , rapid fatigue

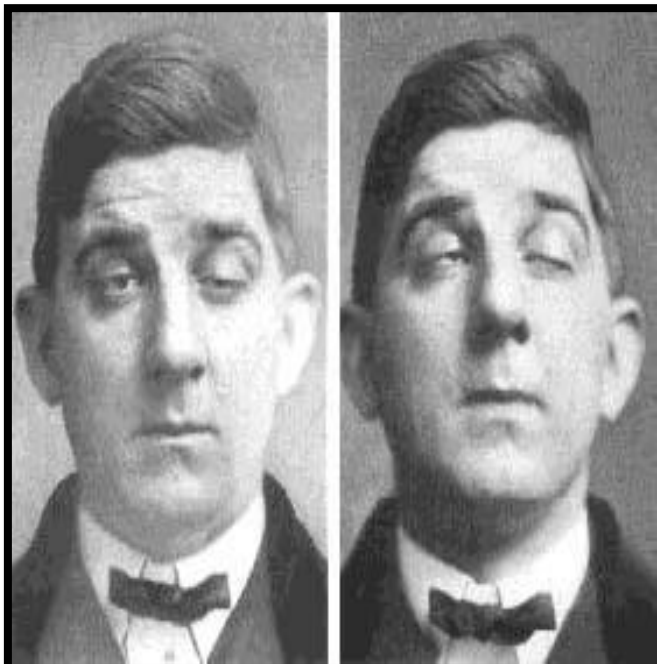
– Ptosis – drooping of eyelids

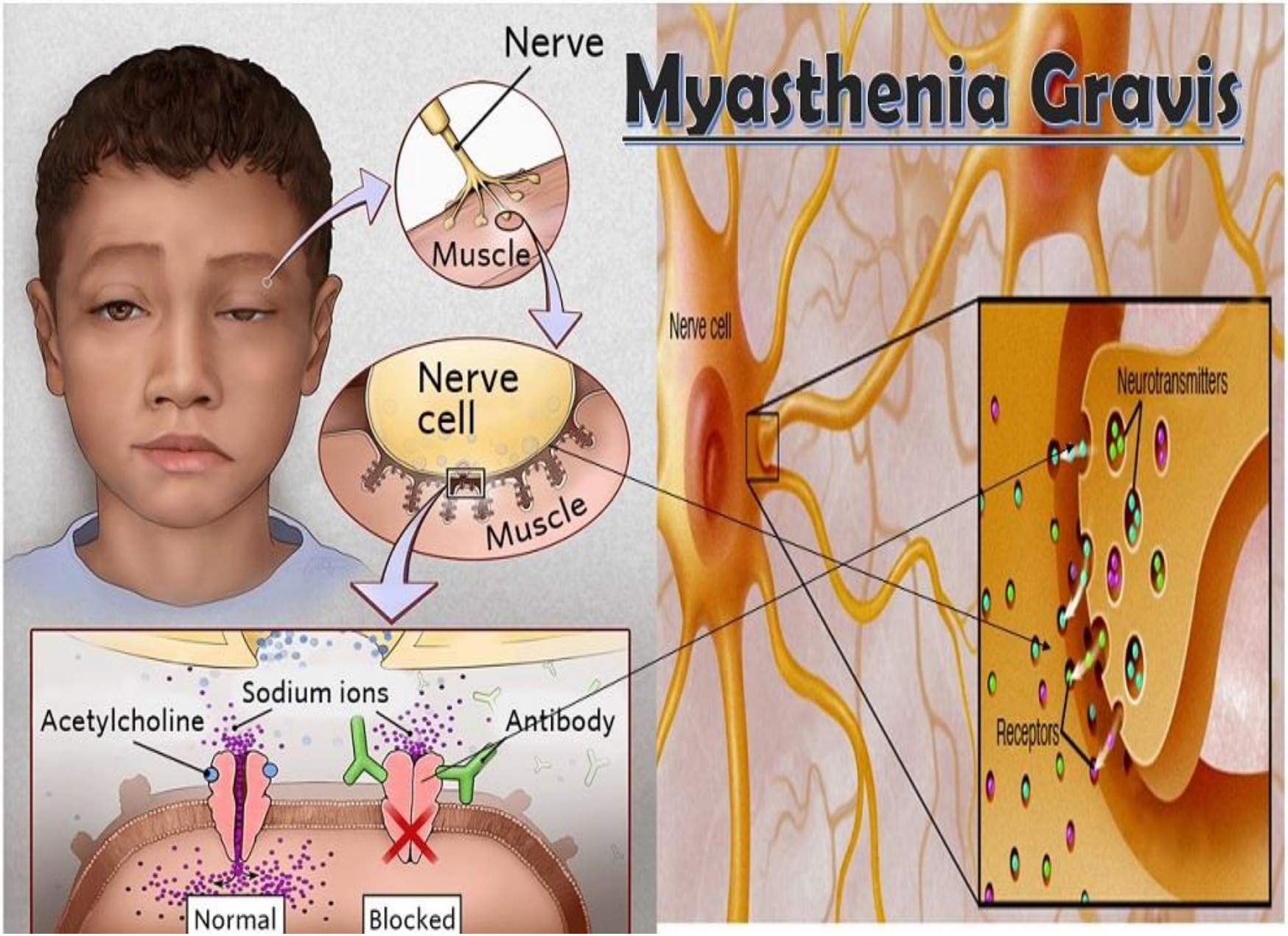
– Weakness of other ocular muscles

– Difficulty in swallowing, speech

– Weakness of muscles of extremities

– Respiratory muscle weakness




Myasthenia Gravis
Nerve
Muscle
Nerve cell
Muscle
Acetylcholine
Sodium ions
Antibody
Normal
Blocked
Nerve cell
Neurotransmitters
Receptors

BONE FRACTURES

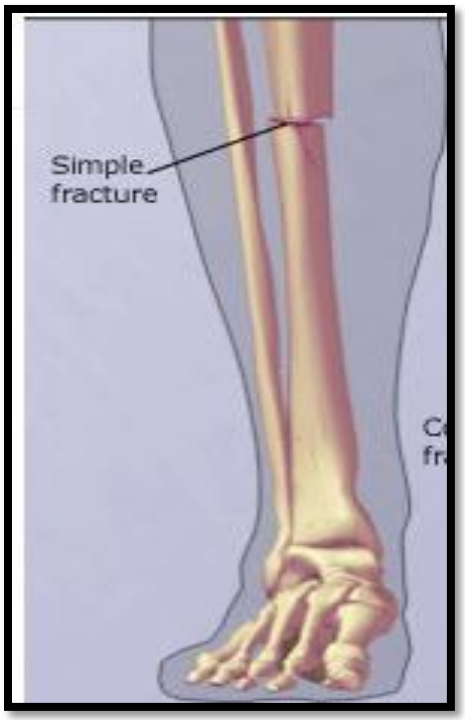
Types

1) Green stick Fracture

- Simple crack in the bone without breaking
- Hairline fracture

2) Simple fracture

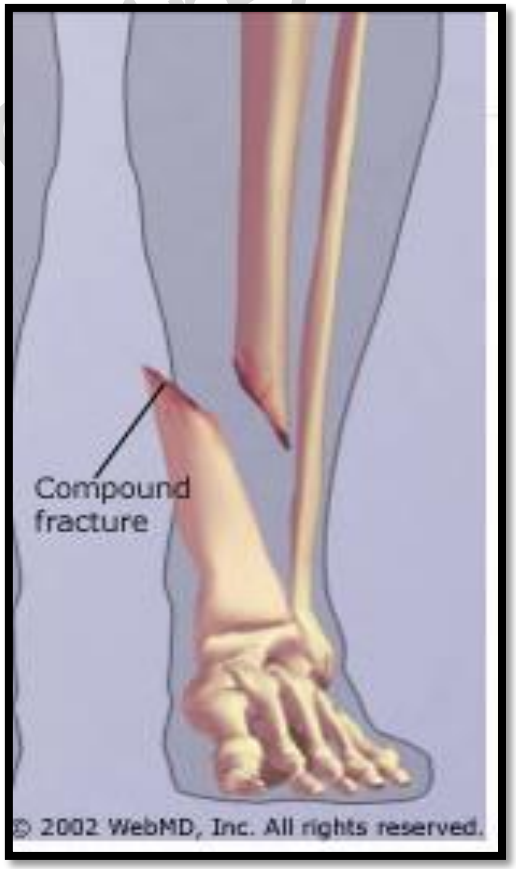
- Bone breaks into two parts
- Broken ends remain close to each other



Types

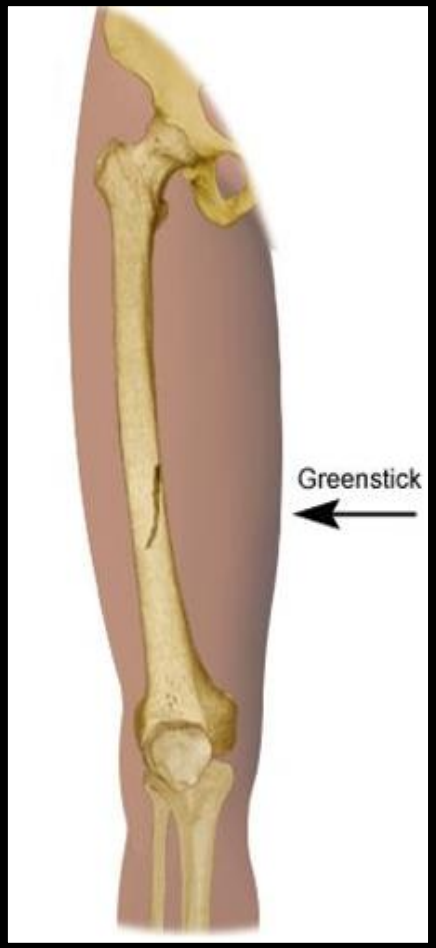
3) Compound Fracture

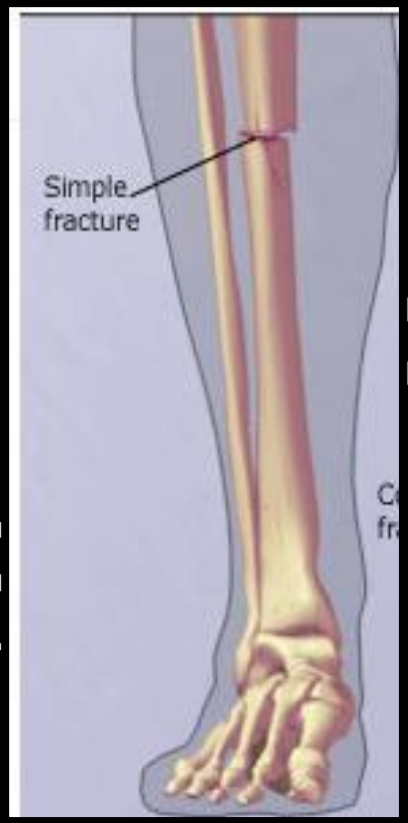
- Bone breaks into two or more parts
- Broken piece protrudes out of skin
- Damaging tissues around

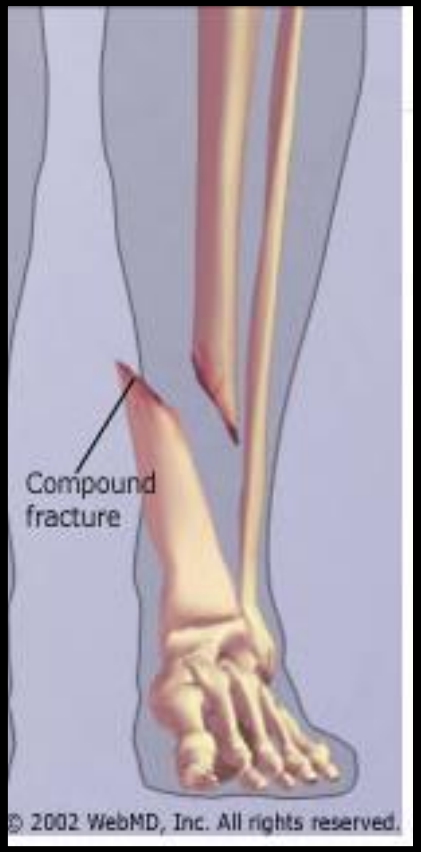


4) Comminuted Fracture

- Bone breaks into multiple pieces


Greenstick


Simple
fracture


Compound
fracture
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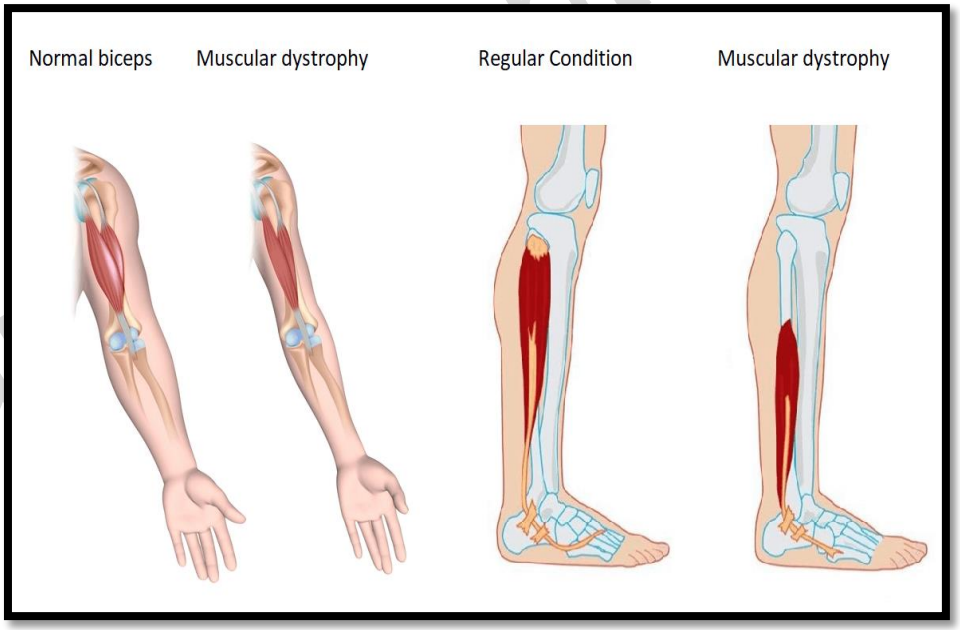
Comminuted

Dislocation

- Genetic disorder

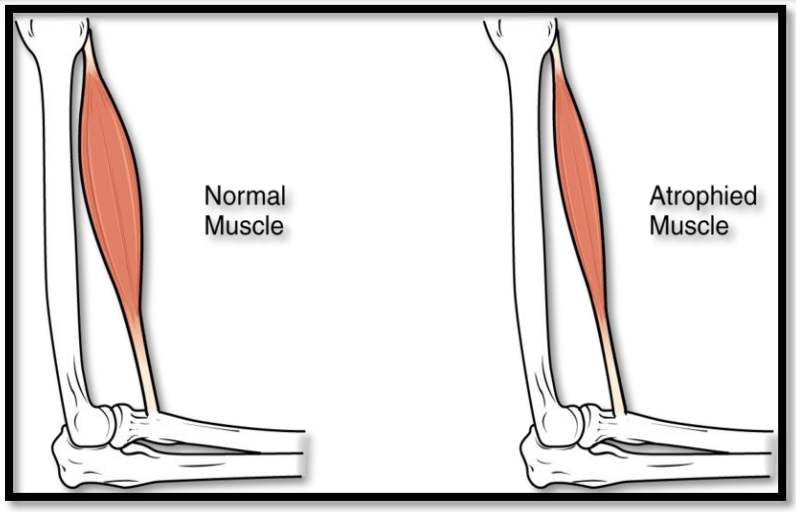


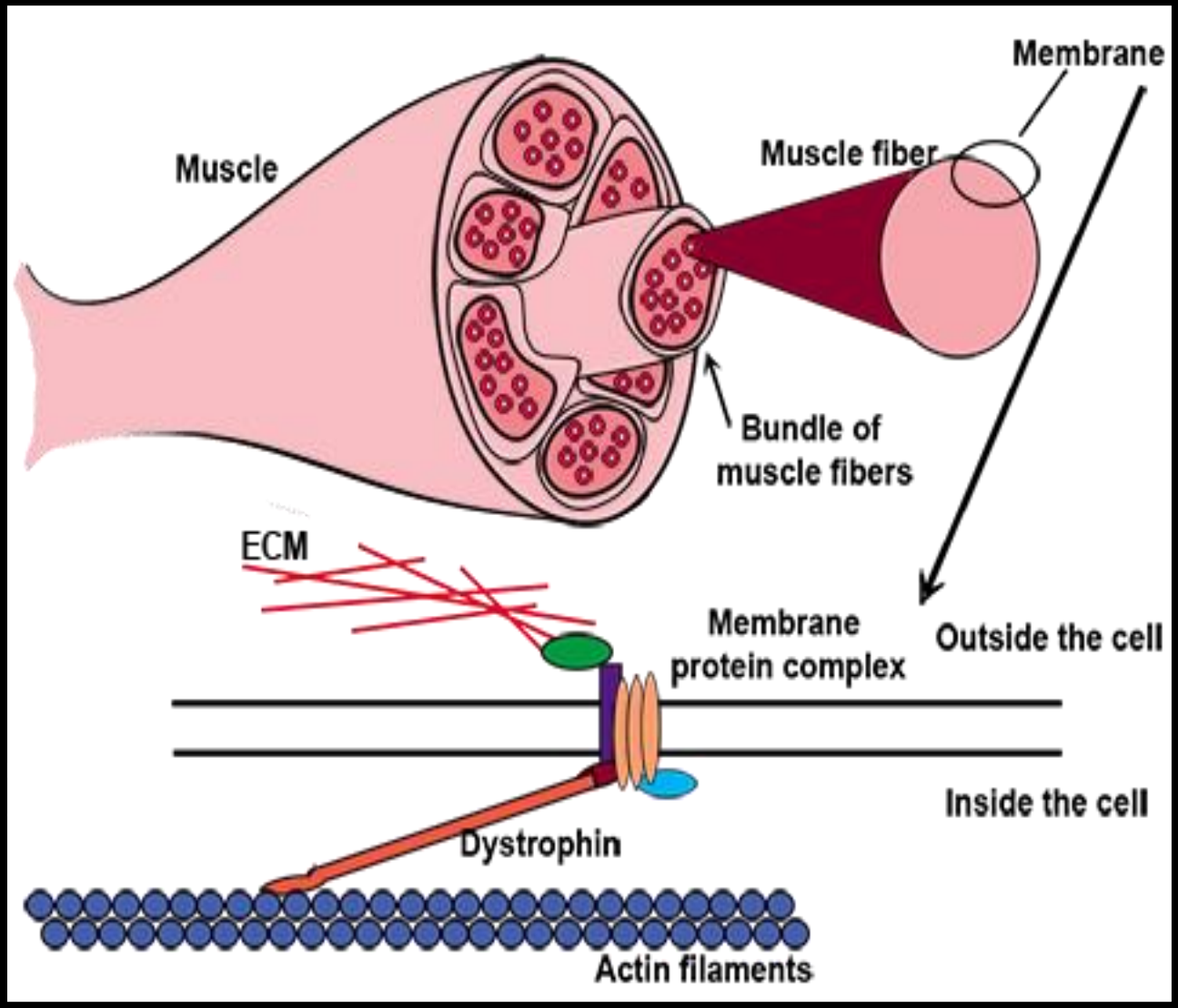
- **Cause:**

- Absence of **Dystrophin** – muscle protein.

- **Feature:**

- Progressive muscle degeneration and weakness.




Membrane
Muscle
Muscle fiber
Bundle of
muscle fibers
ECM
Membrane
protein complex
Outside the cell
Inside the cell
Dystrophin
Actin filaments

THANK YOU