CBCS 3RD SEM MAJOR : PAPER 3026 UNIT4

MUSCLE

BY DR. LUNA PHUKAN

1.HISTOLOGY OF DIFFERENT TYPES OF MUSCLE

Muscle classification: muscle tissue may be classified according to a morphological classification or a functional classification.

Morphological classification (based on structure)

There are two types of muscle based on the morphological classification system

1. Striated
2. Non striated or smooth.

Muscle function:

1. contraction for locomotion and skeletal movement
2. contraction for propulsion
3. contraction for pressure regulation

Functional classification

There are two types of muscle based on a functional classification system

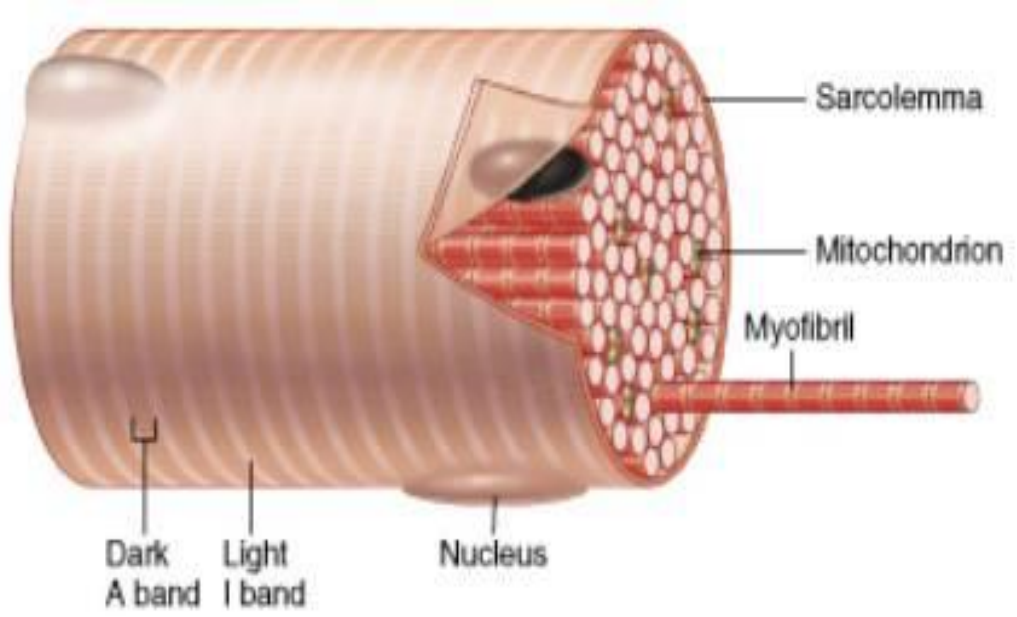
1. Voluntary
2. Involuntary.

Types of muscle: there are generally considered to be three types of muscle in the human body.

Skeletal muscle: which is striated and voluntary
Cardiac muscle: which is striated and involuntary
Smooth muscle: which is non striated and involuntary

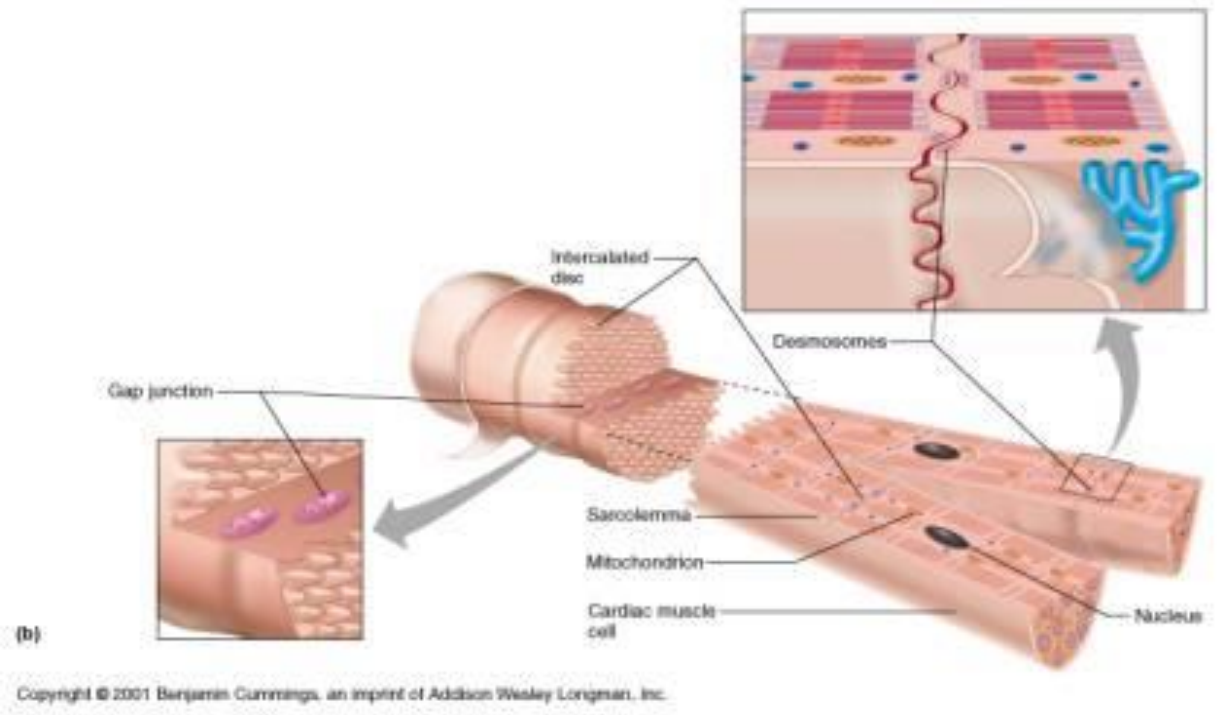
Characteristics of skeletal muscle

Skeletal muscle cells are elongated or tubular. They have multiple nuclei and these nuclei are located on the periphery of the cell. Skeletal muscle is striated. That is, it has an alternating pattern of light and darks bands that will be described later.



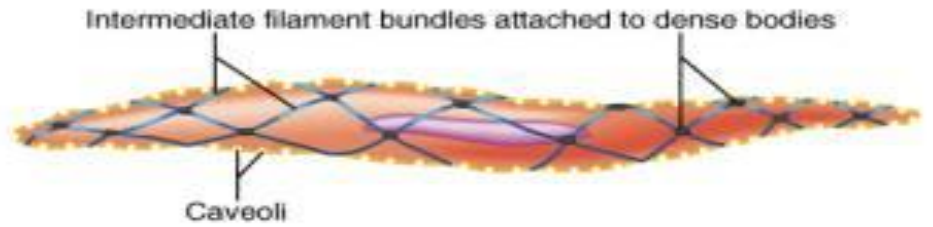
Characteristics of Cardiac muscle

Cardiac muscle cells are not as long as skeletal muscles cells and often are branched cells. Cardiac muscle cells may be mononucleated or binucleated. In either case the nuclei are located centrally in the cell. Cardiac muscle is also striated. In addition cardiac muscle contains intercalated discs

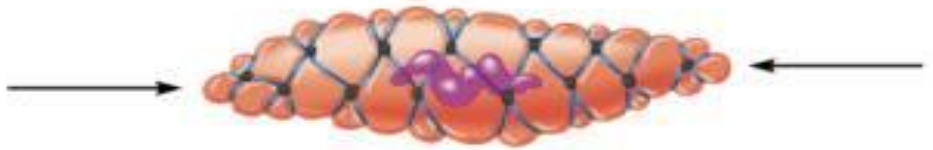


Characteristics of Smooth muscle

Smooth muscle cell are described as spindle shaped. That is they are wide in the middle and narrow to almost a point at both ends. Smooth muscle cells have a single centrally located nucleus. Smooth muscle cells do not have visible striations although they do contain the same contractile proteins as skeletal and cardiac muscle, these proteins are just laid out in a different pattern.



(a) Relaxed smooth muscle cell

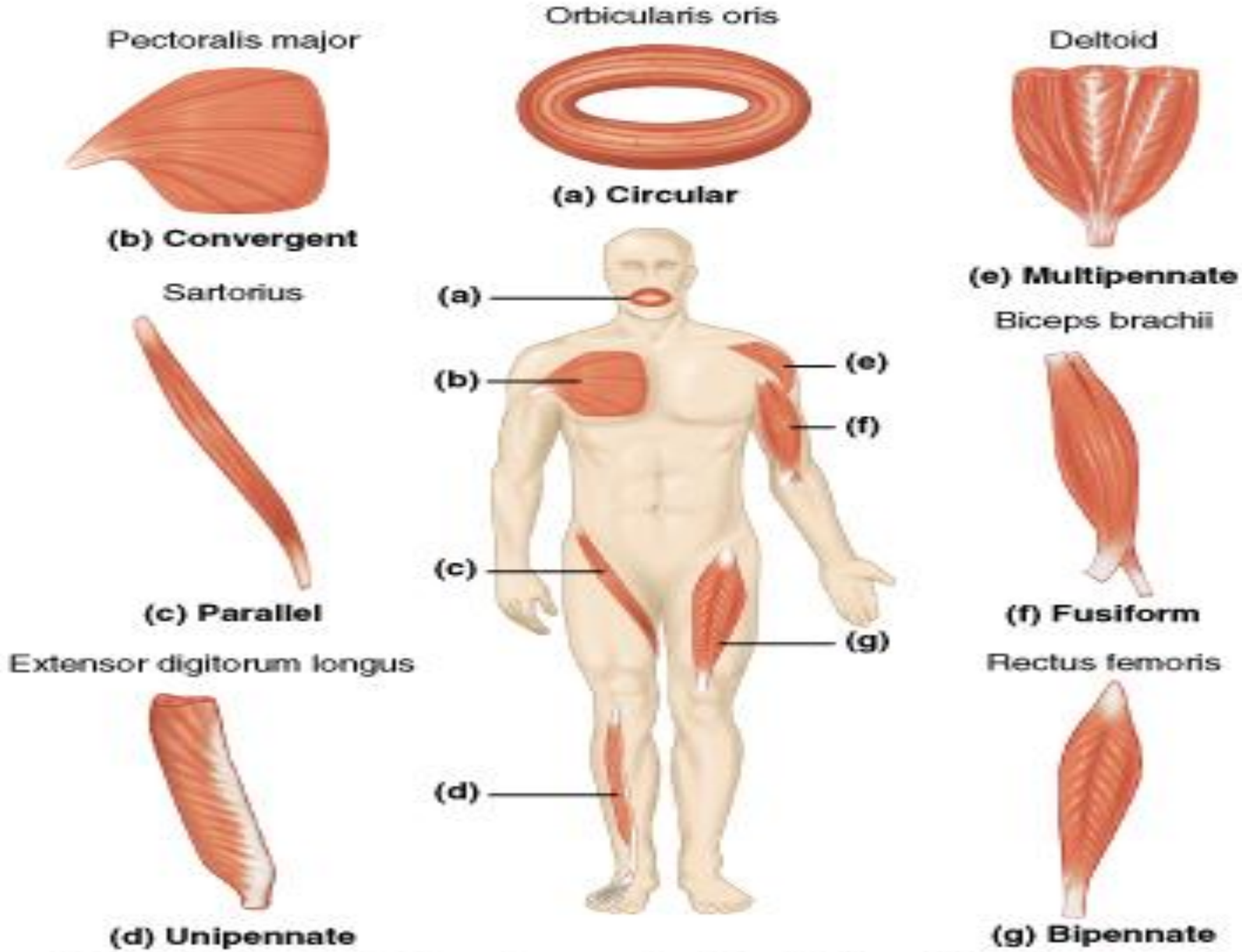


(b) Contracted smooth muscle cell

For the purposes of this class we will focus mainly on skeletal muscle.

Shapes of skeletal muscles:

1. Parallel or fusiform: as their name implies their fibers run parallel to each other. These muscles contract over a great distance and usually have good endurance but are not very strong. Examples: Sartorius muscle and rectus abdominus muscle.
2. Convergent: the muscle fibers converge on the insertion to maximize the force of muscle contraction. Examples: Deltoideus muscle and Pectoralis Major muscle.



3. pennate: many fibers per unit area. These types of muscles are strong but they tie or quickly. There are three types of pennate muscle.

- unipennate
- bipennat
- multipennete

4. Circular: the muscle fibers surrounded opening to act as a sphincter. Examples: Orbicularis oris and Orbicularis oculi muscles.

5. fusiform: some texts classify parallel muscles that are slightly wider in their middle (spindle shaped) as fusiform. This term will not be used in this course.

Muscle terminology

myofiber or myocyte: a muscle cell

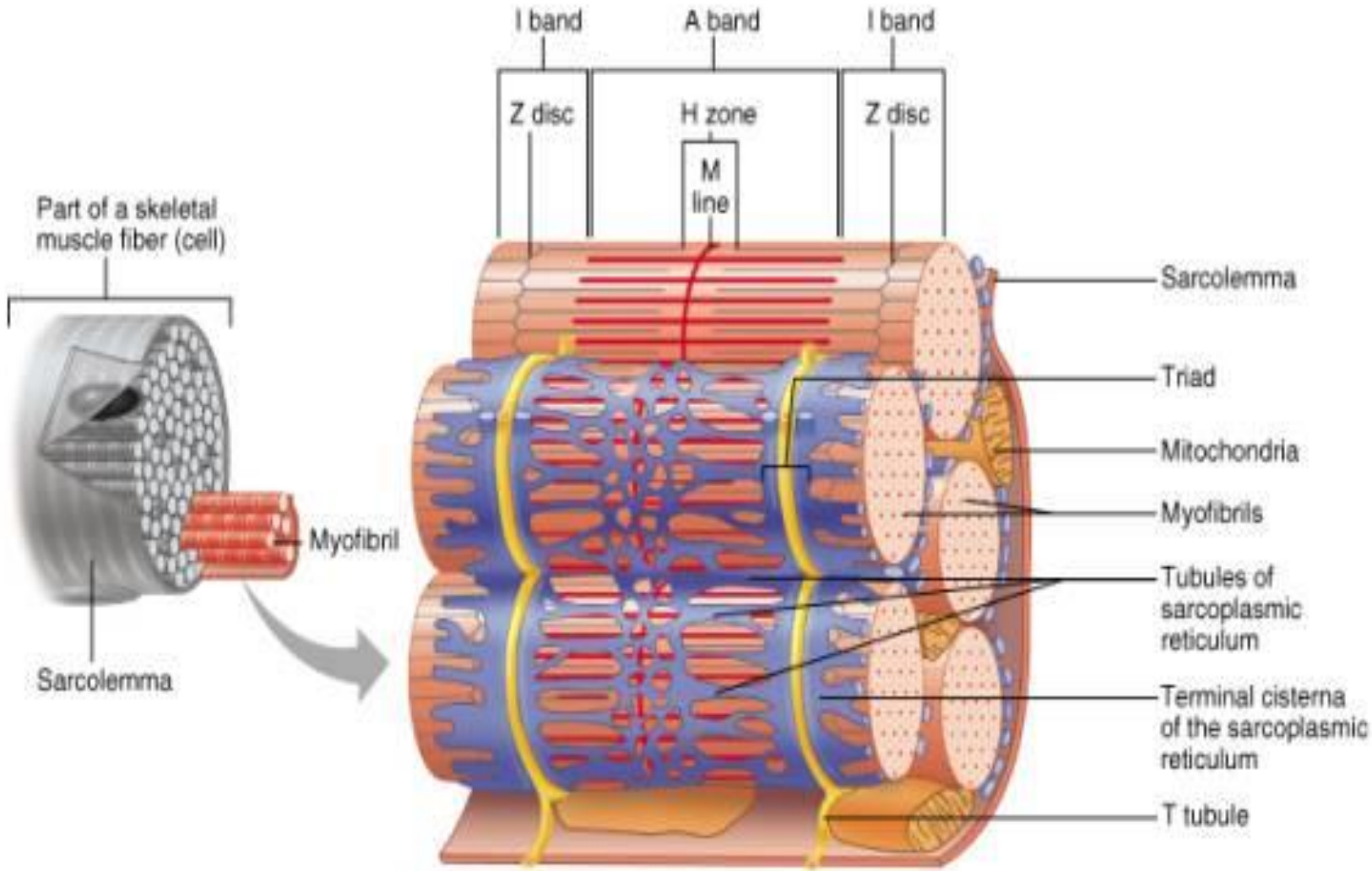
sarcolemma: the plasma membrane of a muscle cell

sarcoplasm: the cytoplasm of the muscle cell

sarcoplasmic reticulum: the endoplasmic reticulum of a muscle cell

sarcosome: the mitochondria of a muscle

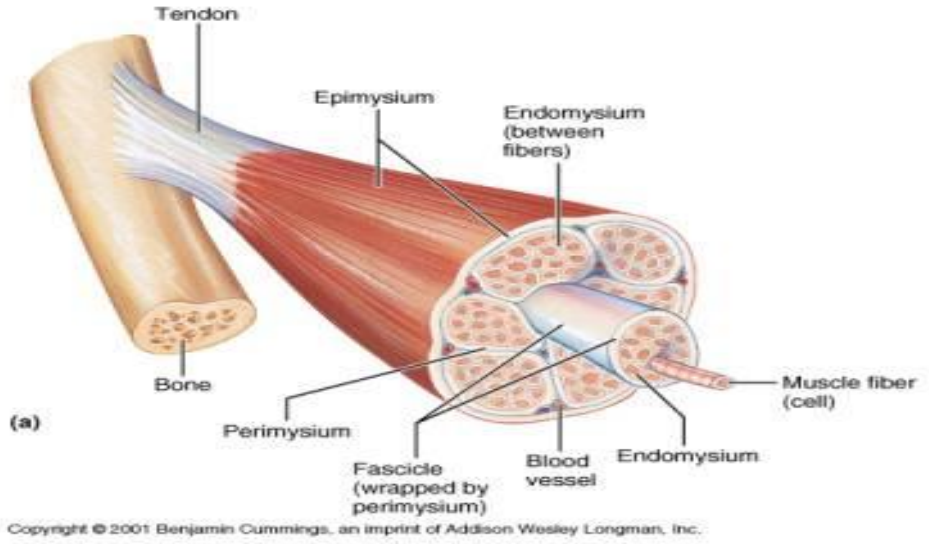
sarcomere: the contractile or functional unit of muscle



For the purposes of this class we will focus mainly on skeletal muscle.
Muscles have three major areas:
1. a belly or Gaster
2. an origin: a tendinous connection of the muscle to a bone, usually the bone that is stabilized.
3. an insertion: a tendinous connection of the muscle to a bone, usually the bone to be moved.

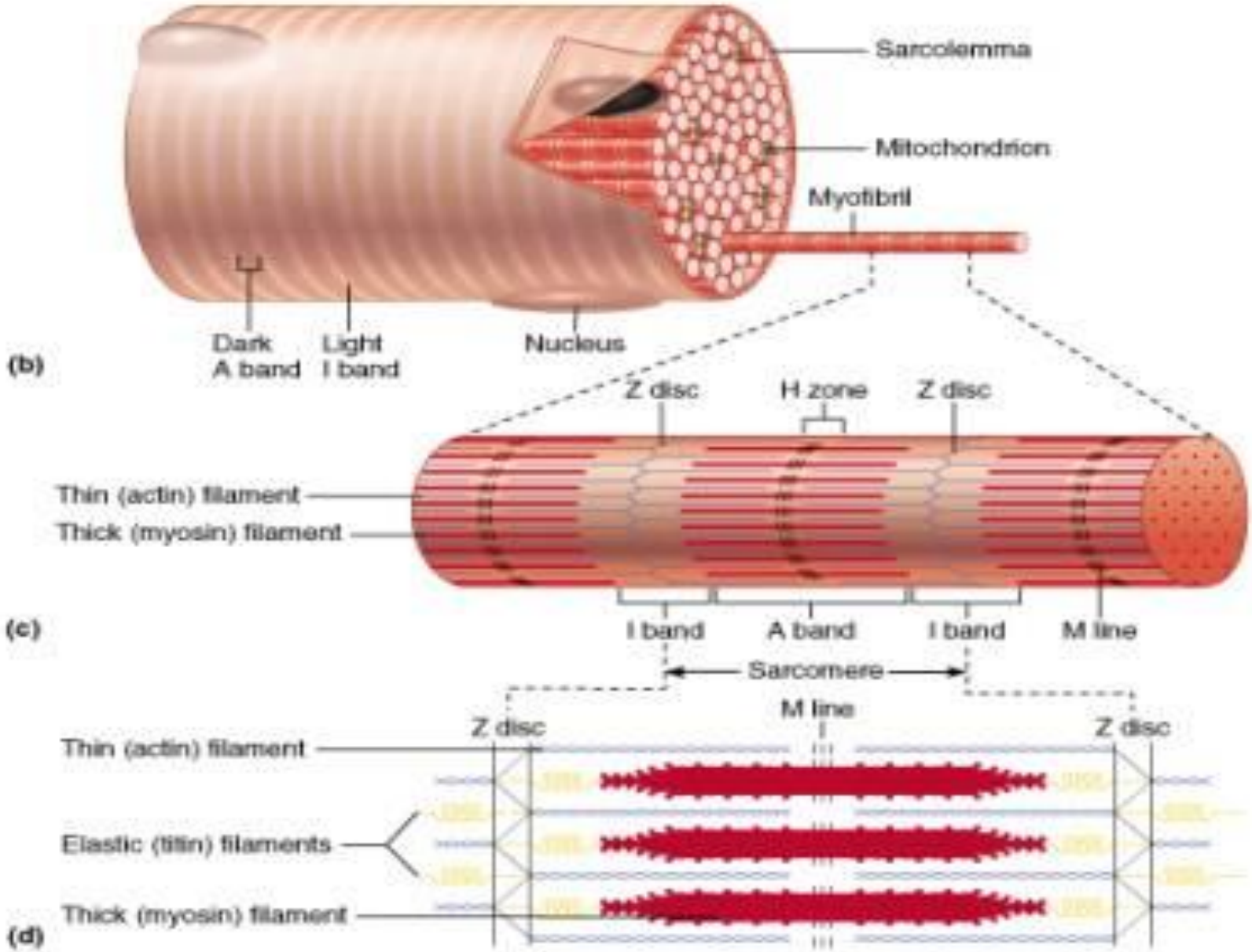
Skeletal muscle is designed as a bundle within a bundle arrangement. We will start with a whole muscle and then work our way down to the microscopic level of the muscle

The entire muscle is surrounded by a connective tissue called the epimysium.



The muscle is made up of smaller bundles known as fascicles. Fascicles are actually bundles of individual muscle cells (myofibers or myocytes). These bundles are surrounded by a connective tissue sheath called the perimysium.

Each fascicle is made up of several muscle cells known as myocytes. They may also be called myofibers or muscle fibers. Each muscle cell is surrounded by a connective tissue sheath known as the endomysium. This sheath is very important in the physiology of muscle contraction because it electrically insulates the individual muscle cells from each other

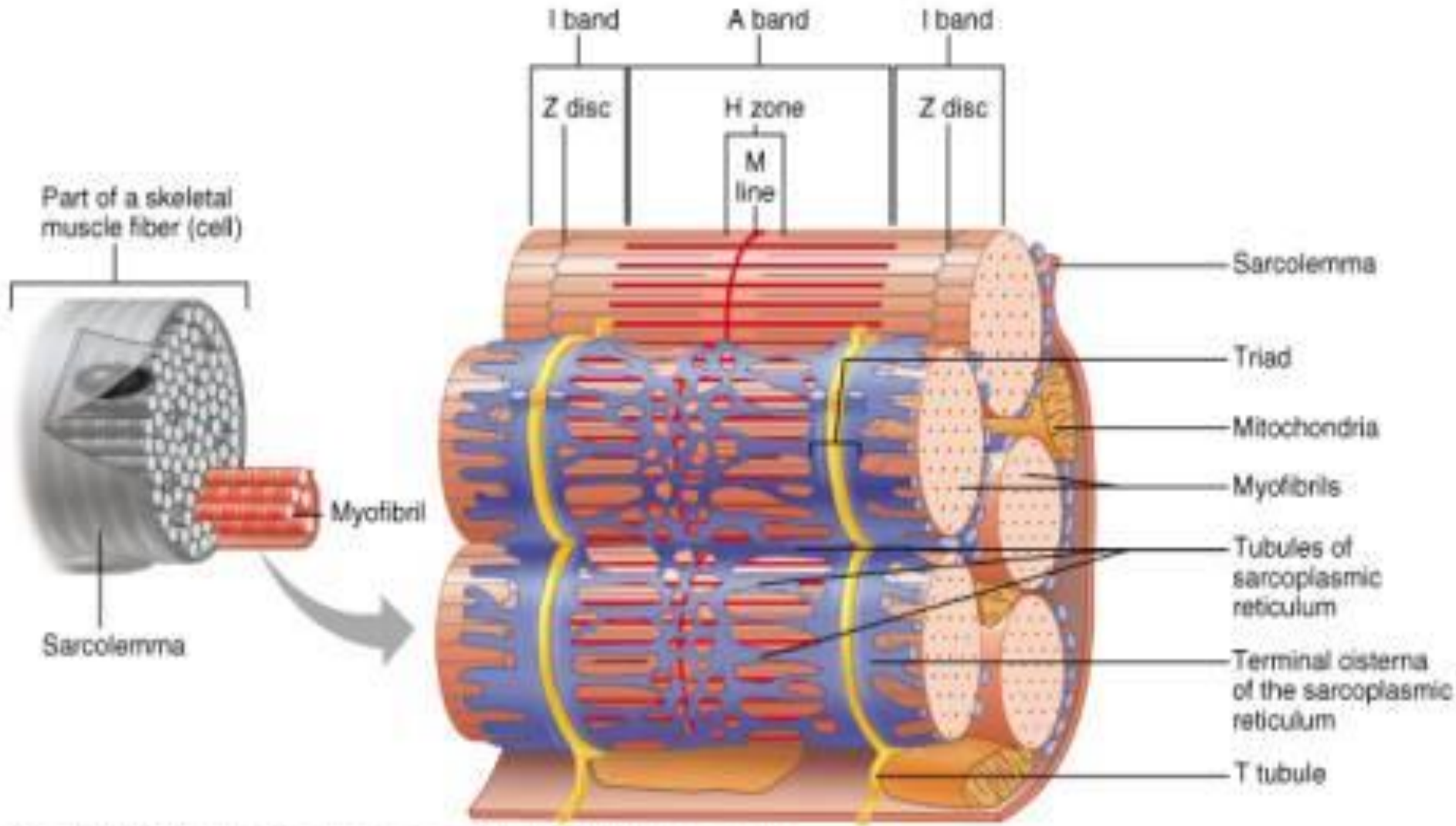


At the ends of the muscle all of the connective tissue sheaths (epimysium, perimysium, and endomysium) converge to form a tendon which will connect the muscle to its attachment site.

Each muscle fiber (muscle cell) contains all of the organelles that we find in other cell types.

Although these organelles are the same as in other cells they are given special names.

Note that the prefixes sarco and myo both refer to muscle. Therefore if you see a word with either of these prefixes you should immediately think MUSCLE.



The nucleus contains the genetic material of the muscle cell.

The sarcolemma is the name given to the plasma membrane of the muscle cell.

There are specialized invaginations of the sarcolemma that run transversely across the cell. These invaginations are known as T tubules (short for transverse tubules).

The T tubules are essential for carrying the depolarization brought to the cell by a motor nerve impulse down into the muscle cell where it can have an affect on the terminal cisternae.
We will cover more about this in the unit on the physiology of muscle contraction.
The cytosol is the cytoplasm of the muscle cell.

The sarcoplasmic reticulum is the endoplasmic reticulum of the muscle cell. There are sac-like regions of the sarcoplasmic reticulum known as terminal cisternae.

The terminal cisternae act as calcium storage sites. The calcium ions stored in the terminal cisternae are essential in muscle contraction. We will cover more about this in the unit on the physiology of muscle contraction.

NOTE: this is not calcium storage for use in general body physiology as we would see with bone tissue, but rather is calcium storage for muscle contraction.

In skeletal muscle two terminal cisternae are associated with a T tubule to form a structure known as a triad. This differs from cardiac muscle where one terminal cisternae associates with one T tubule to form a diad.

Mitochondria are sites of energy production (ATP synthesis) in the muscle cell as in all other cells of the body, except for mature red blood cells.

A myofibril is a cylindrical bundle of contractile proteins found within the muscle cell. Note that there are several myofibrils within each muscle cell. It is the arrangement of the contractile proteins within the myofibril that cause the striated appearance of skeletal and cardiac muscle.

Myofibrils are composed of individual contractile proteins called myofillaments. These myofilaments are generally divided into thick and thin myofilaments.

The thin myofilaments are composed mainly of a protein known as actin. Actin filaments are anchored into the z-line of a sarcomere.

The thick myofilaments are composed mainly of the protein myosin.

It is the orderly overlapping of the actin and myosin filaments that give cardiac and skeletal muscle their striated appearance (light and dark bands).
The A band is the dark band and corresponds to the length of a bundle of myosin filaments. Because muscle contraction is a sliding of the myofilaments past each other we do not see any of the myofilaments actually shorten. However the width of the banding patterns change as the degree of overlap changes. Because the A band corresponds to the length of the myosin filaments, and these filaments do not shorten, the width of the A band also does not shorten.

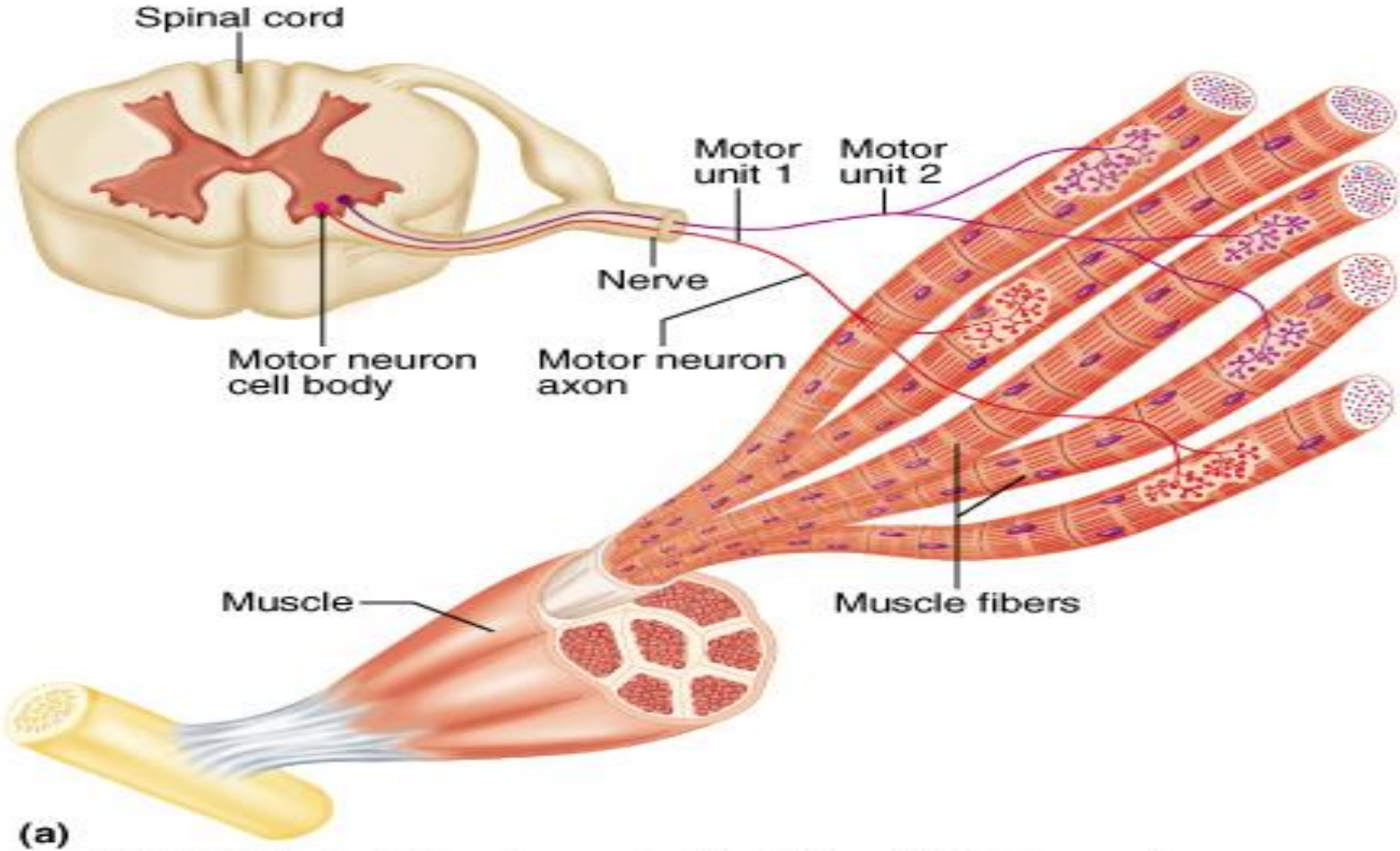
The light bands are known as I bands. The I bands are composed mainly of actin filaments. Each I band is bisected by a protein disc known as the Z-line. Actin filaments are anchored into the Z-line. During muscle contraction the actin filaments slide over the myosin filaments which results in a shortening of the I band.

In the middle of the A band is a somewhat lighter area known as the H zone. This zone corresponds to the area where we have myosin not overlapped by actin (the area between the thin filaments). During muscle contraction the actin sliding over the myosin encroaches into this area so that the H zone shortens. In the middle of the H zone we see a dark band known as the M line. The M line is comprised of protein fibers that function to anchor the myosin filaments.

The area between two Z lines is known as a sarcomere. The sarcomere is the functional or contractile unit of muscle.

To recap, a whole muscle if made up of many smaller bundles known as fascicles. Each fascicle is made up of many muscle cells (myofibers). Myofibers contain cylindrical bundles of myofibrils which in turn contain many smaller bundles of myofilaments.

Muscles contract when they receive a motor impulse from a motor nerve. These nerve impulses serve only a limited number of muscle fibers. The muscle fibers served by a single motor neuron make up a structure known as a motor unit.



(a)

. Motor units allow for selective contraction of muscle fibers so that we may control the strength and extent of muscle contraction. Without motor units a nerve impulse to the muscle would result in the entire muscle contracting to its full extent. That would make every motion that we make an "all or none" motion. This type of movement would make life nearly impossible

Note that this diagram shows a neuromuscular junction of one motor neuron with one muscle fiber. In a motor unit the motor neuron branches to form neuromuscular junctions with several muscle fibers. To repeat, a motor neuron and all of the muscle fibers it supplies is called a MOTOR UNIT.

2.ULTRASTRUCTURE OF SKELETAL MUSCLE

The Muscular System

Muscles are responsible for all types of body movement – they contract or

- shorten and are the machine of the body
- Three basic muscle types are found in the body
- Skeletal muscle
- Cardiac muscle
- Smooth muscle

Characteristics of Muscles

- Muscle cells are elongated
- (muscle cell = muscle fibber)
- Contraction of muscles is due to the movement of microfilaments
- All muscles share some terminology
- Prefix myo refers to muscle
- Prefix mys refers to muscle
- Prefix sarco refers to flesh

Skeletal Muscle Characteristics

- Most are attached by tendons to bones
- Cells are multinucleate
- Striated – have visible banding
- Voluntary – subject to conscious control
- Cells are surrounded and bundled by connective tissue = great force, but tires easily

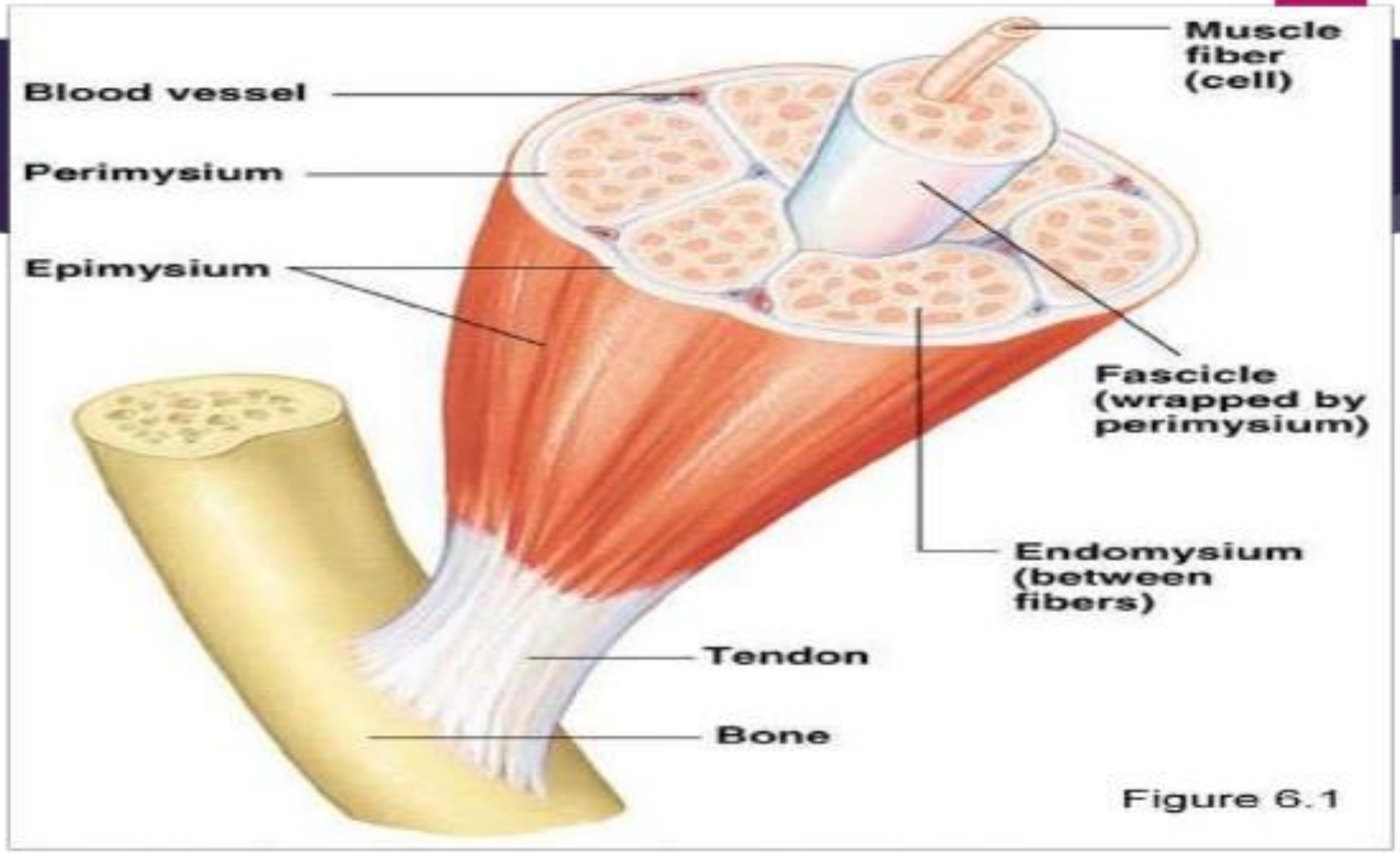
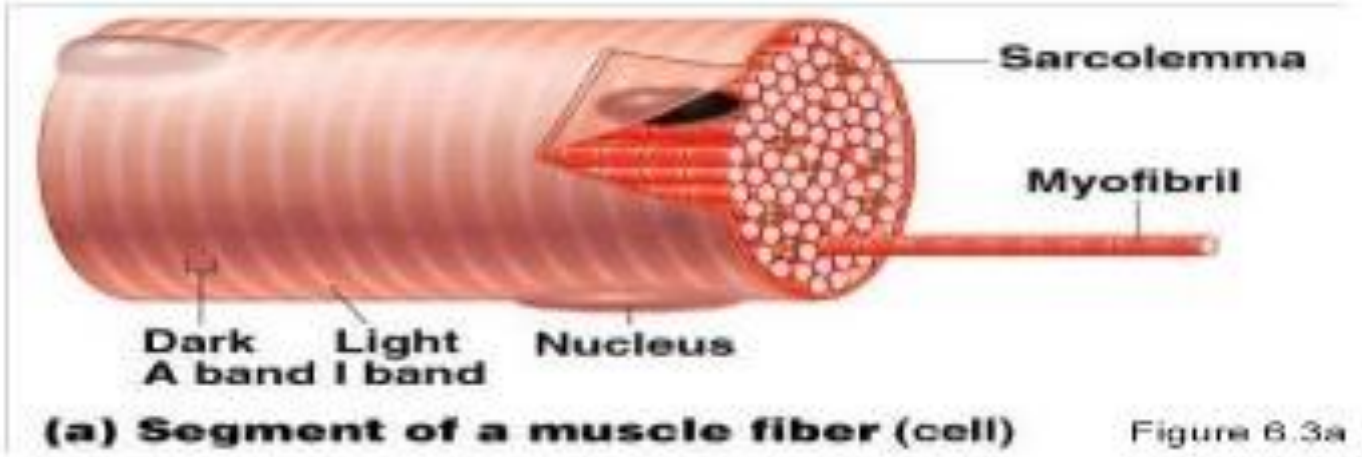

Blood vessel
Perimysium
Epimysium
Muscle fiber (cell)
Fascicle (wrapped by perimysium)
Endomysium (between fibers)
Tendon
Bone

Figure 6.1

- Cells are multinucleate
- Nuclei are just beneath the sarcolemma



(a) Segment of a muscle fiber (cell)

Figure 6.3a

Sarcolemma – specialized plasma membrane

Sarcoplasmic reticulum – specialized smooth endoplasmic reticulum

Myofibril

- Bundles of myofilaments

Myofibrils are aligned to give distinct bands

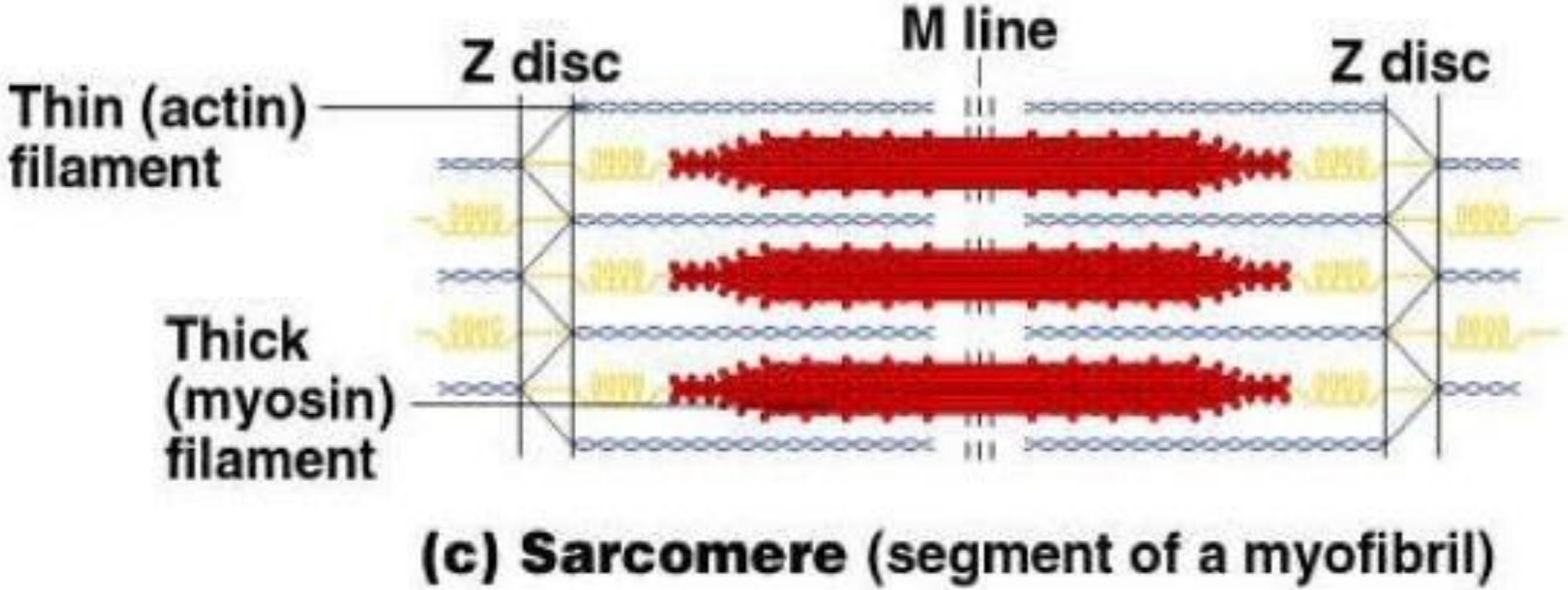
- •I band = light band
- •A band = dark band

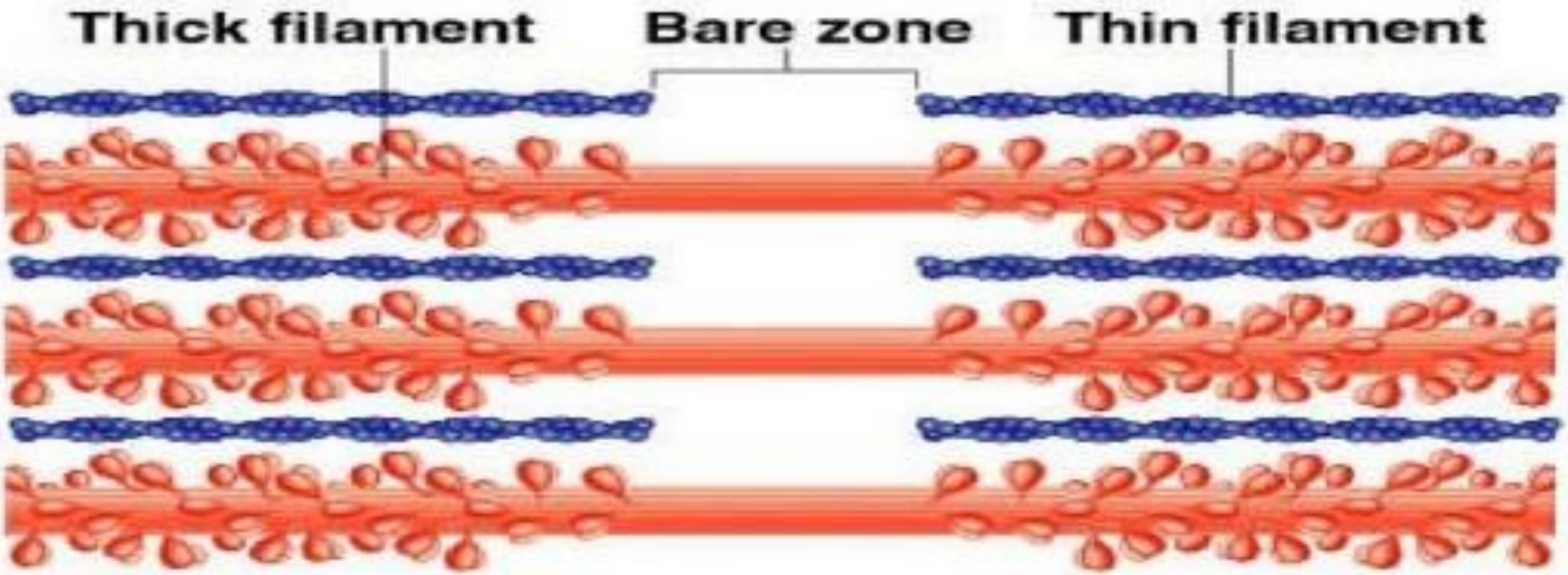
Sarcomere

Contractile unit of a muscle fiber

Organization of the sarcomere

- •Thick filaments = myosin filaments
- •Composed of the protein myosin
- •Has ATPase enzymes


M line
Z disc
Z disc
Thin (actin) filament
Thick (myosin) filament
(c) Sarcomere (segment of a myofibril)



(d) Myofilament structure (within one sarcomere)

Properties of Skeletal Muscle Activity (single cells or fibers)

- Irritability – ability to receive and respond to a stimulus
- Contractility – ability to shorten when an adequate stimulus is received

Skeletal muscle is one of three major muscle types, the others being cardiac muscle and smooth muscle.

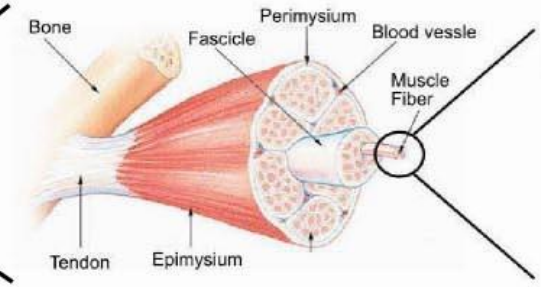
It is a form of striated muscle tissue which is under the voluntary control of the somatic nervous system.

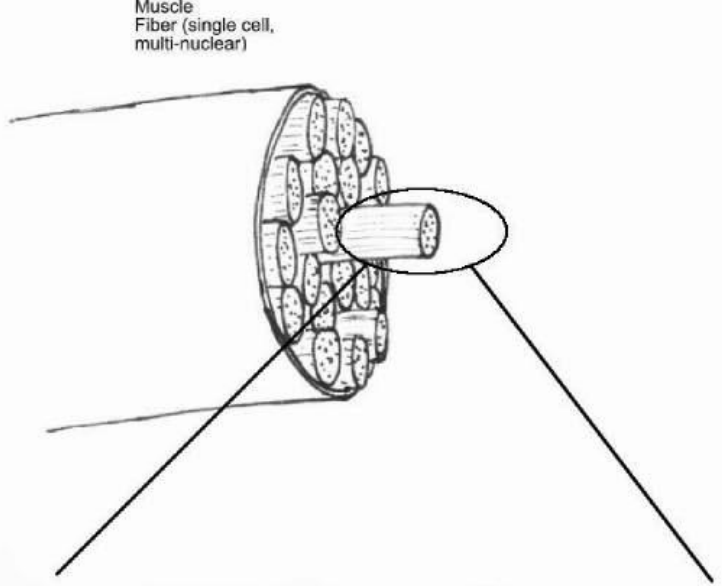
Most skeletal muscles are attached to bones by bundles of collagen fibers known as tendons.

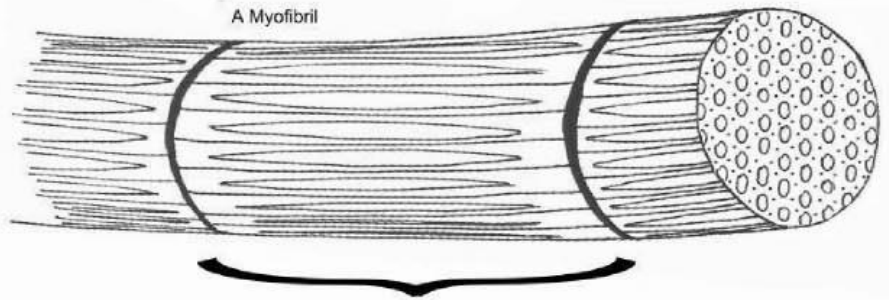
A skeletal muscle refers to multiple bundles (fascicles) of cells joined together called muscle fibers. The fibers and muscles are surrounded by connective tissue layers called fasciae.
Muscle fibers, or muscle cells, are formed from the fusion of developmental myoblasts in a process known as myogenesis. Muscle fibers are cylindrical and have more than one nucleus. They also have multiple mitochondria to meet energy needs.

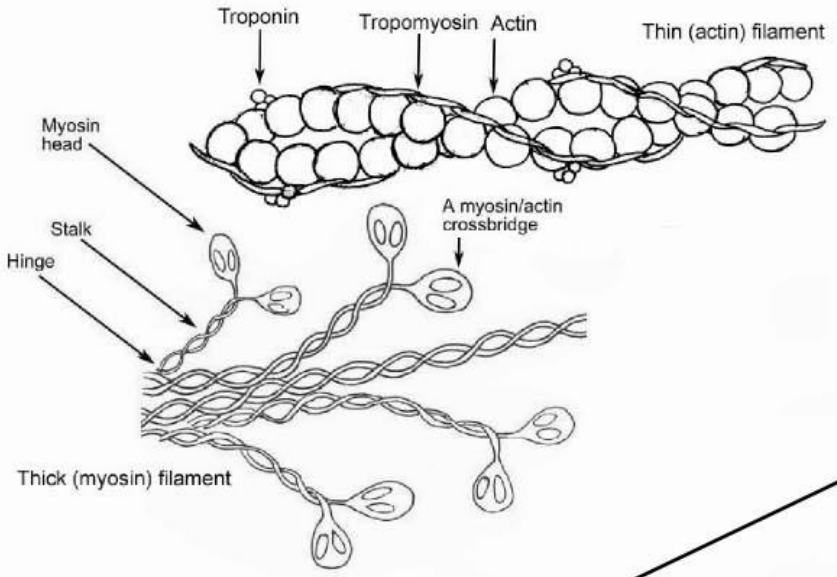
Muscle fibers are in turn composed of myofibrils. The myofibrils are composed of actin and myosin filaments, repeated in units called sarcomeres, which are the basic functional units of the muscle fiber.

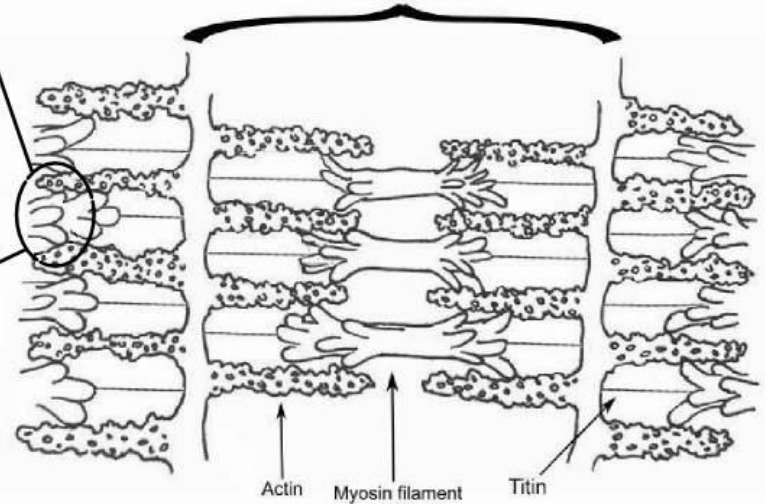
The sarcomere is responsible for the striated appearance of skeletal muscle and forms the basic machinery necessary for muscle contraction.


Bone
Fascicle
Perimysium
Blood vessle
Muscle Fiber
Tendon
Epimysium


Muscle Fiber (single cell, multi-nuclear)


A Myofibril

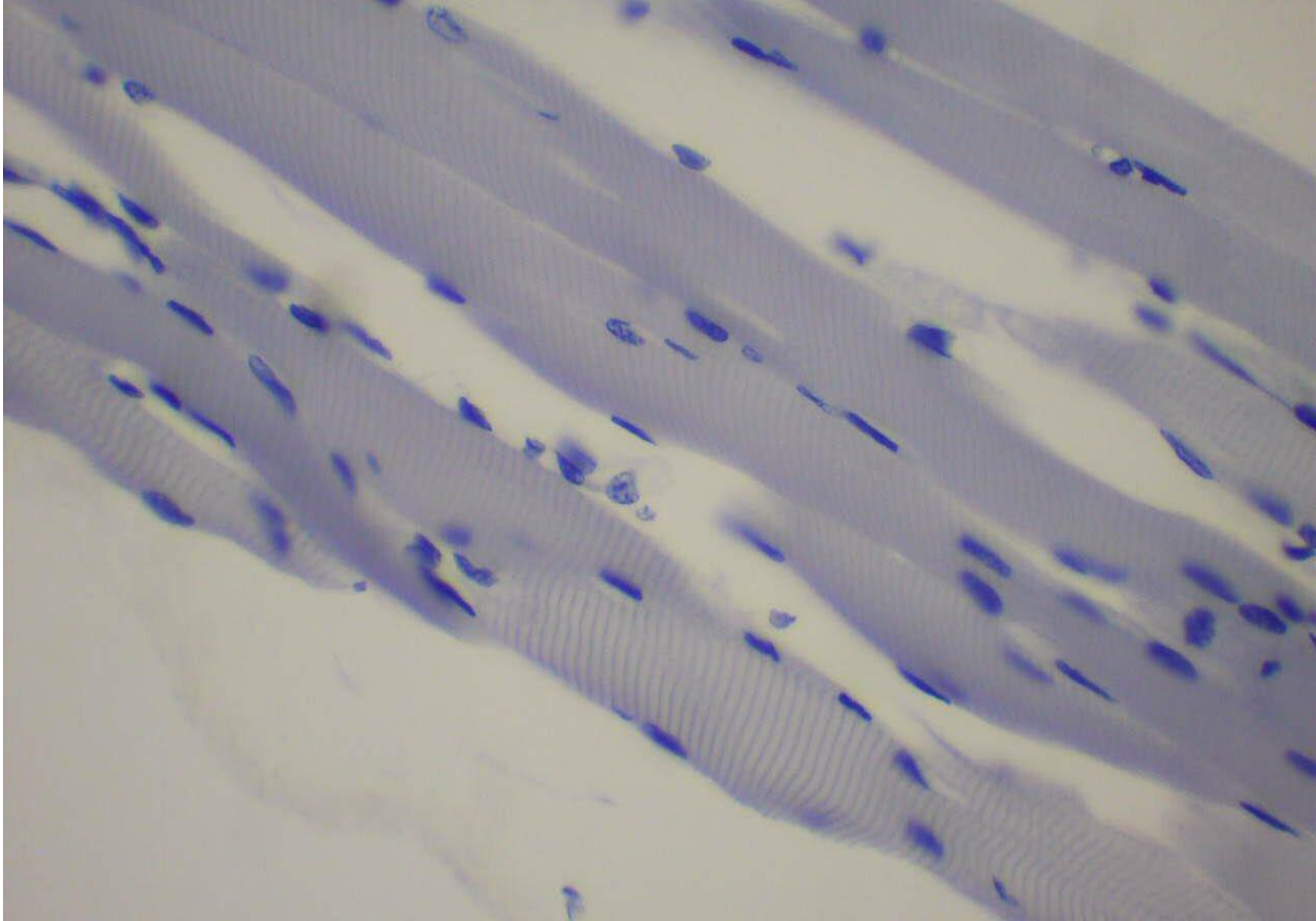

Troponin
Tropomyosin
Actin
Thin (actin) filament
Myosin head
Stalk
Hinge
A myosin/actin crossbridge
Thick (myosin) filament


One sarcomere
Actin
Myosin filament
Titin

MICROANATOMY OR ULTRASTRUCTURE

Skeletal muscle exhibits a distinctive banding pattern when viewed under the microscope due to the arrangement of cytoskeletal elements in the cytoplasm of the muscle fibers. The principal cytoplasmic proteins are myosin and actin (also known as "thick" and "thin" filaments, respectively) which are arranged in a repeating unit called a sarcomere. The interaction of myosin and actin is responsible for muscle contraction.

Skeletal muscle fibers show sarcomeres clearly.



Every single organelle and macromolecule of a muscle fiber is arranged to ensure form meets function. The cell membrane is called the sarcolemma with the cytoplasm known as the sarcoplasm.

In the sarcoplasm are the myofibrils. The myofibrils are long protein bundles about 1 micrometer in diameter each containing myofilaments. Pressed against the inside of the sarcolemma are the unusual flattened myonuclei. Between the myofibrils are the mitochondria.

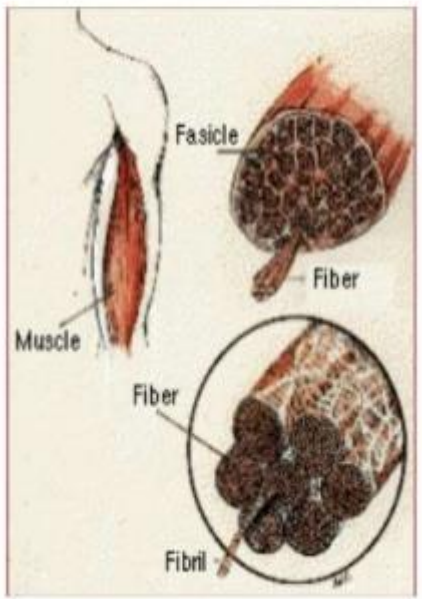
While the muscle fiber does not have smooth endoplasmic cisternae, it contains a sarcoplasmic reticulum. The sarcoplasmic reticulum surrounds the myofibrils and holds a reserve of the calcium ions needed to cause a muscle contraction. Periodically, it has dilated end sacs known as terminal cisternae.

These cross the muscle fiber from one side to the other. In between two terminal cisternae is a tubular infolding called a transverse tubule (T tubule). T tubules are the pathways for action potentials to signal the sarcoplasmic reticulum to release calcium, causing a muscle contraction. Together, two terminal cisternae and a transverse tubule form a triad.

3. MOLICULAR AND CHEMICAL BASIS OF MUSCLE CONTRACTION

Structure Of Skeletal Muscle

- Muscle
- Muscle Fascicle
- Muscle Fiber
- Myofibrils



Skeletal Muscle

A. Muscle Fiber

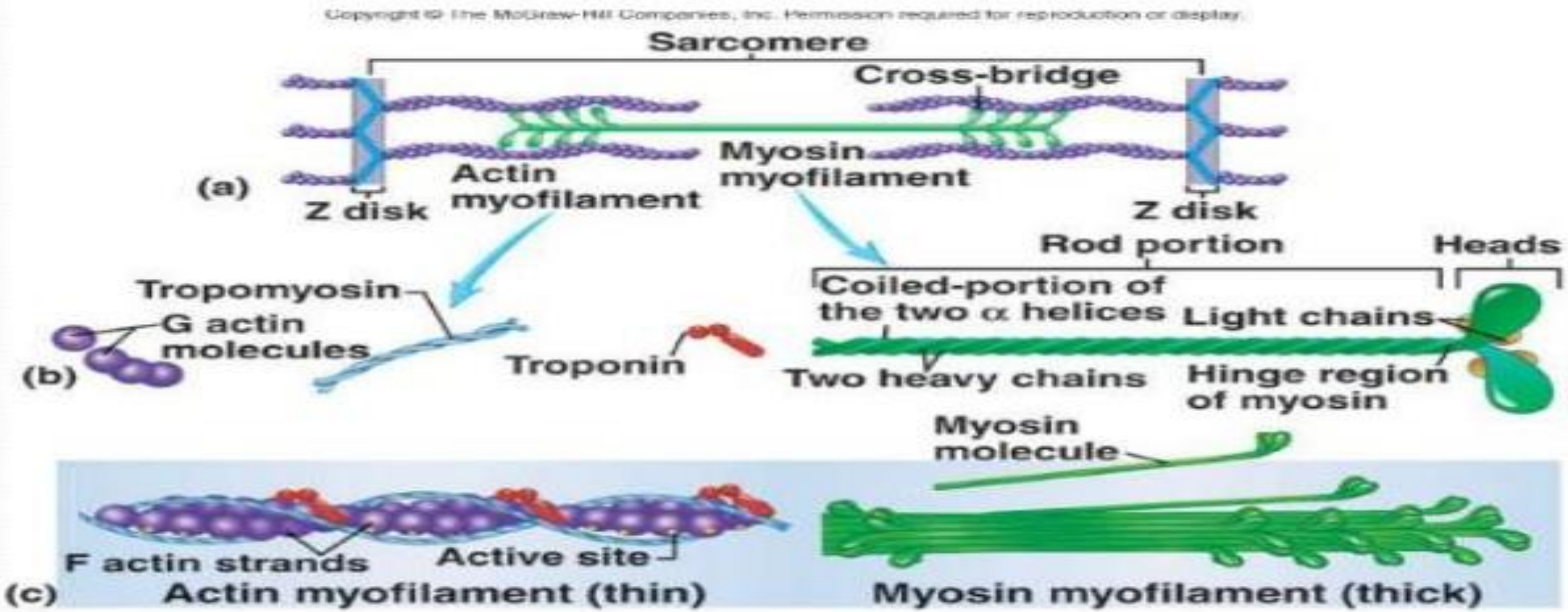
1. Sarcolemma
2. Sarcoplasm
3. Myofibrils – contractile elements → Actin
   → Myosin

a. Actin Filament

- F- actin strands
- Tropomyosin
- Troponin (T,I,C)

b. Myosin Filament

Structure Of Myofibril



Mechanism Of Muscle Contraction

- Step 1. Nerve impulse, travels towards the synaptic knob.

- Step 2. Ca++ ion from ECF enter into the synaptic knob through **calcium channels**.

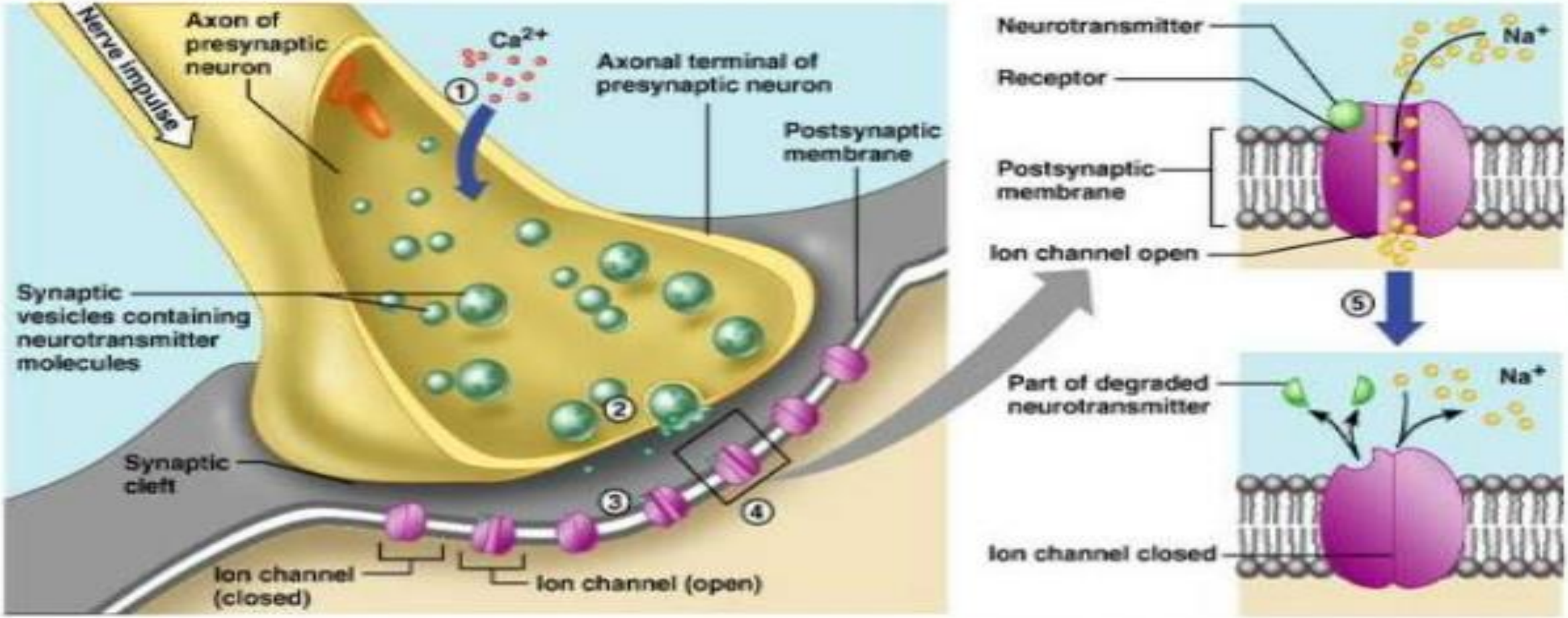
Mechanism Of Muscle Contraction

- Step 3. As Ca++ enter into synaptic knob, Ach. Vesicles ruptures and Ach. release out into synaptic cleft by exocytosis.

Mechanism Of Muscle Contraction

- Step 4. Ach diffuses across the neuromuscular junction and binds to the receptor sites on postsynaptic membrane.

Steps 1-4


Nerve impulse
Axon of presynaptic neuron
Ca^{2+}
Axonal terminal of presynaptic neuron
Postsynaptic membrane
Synaptic vesicles containing neurotransmitter molecules
Synaptic cleft
Ion channel (closed)
Ion channel (open)
Neurotransmitter
Receptor
Na^+
Postsynaptic membrane
Ion channel open
Part of degraded neurotransmitter
Ion channel closed

Mechanism Of Muscle Contraction

- Step 5. Stimulating of the receptor causes conformational change in post synaptic membrane and generate an action potential.

Ach. destroyed by an enzyme (**acetylcholinestrase**)

Mechanism Of Muscle Contraction

- Step 6. This action potential travels along the length of muscle fiber, and then penetrates deep into the muscle through the T-tubular system.

Mechanism Of Muscle Contraction

- Step 7. The electrical impulse stimulates the sarcoplasmic reticulum to release calcium into the (a contractile unit of a mofibril) area.

Mechanism Of Muscle Contraction

- Step 8. Calcium bind with tropnin-C and activates myosin ATPase.

  As myosin ATPase become active. Tropomyosin slipped off, G-action exposed.

  ATPase react with ATP.

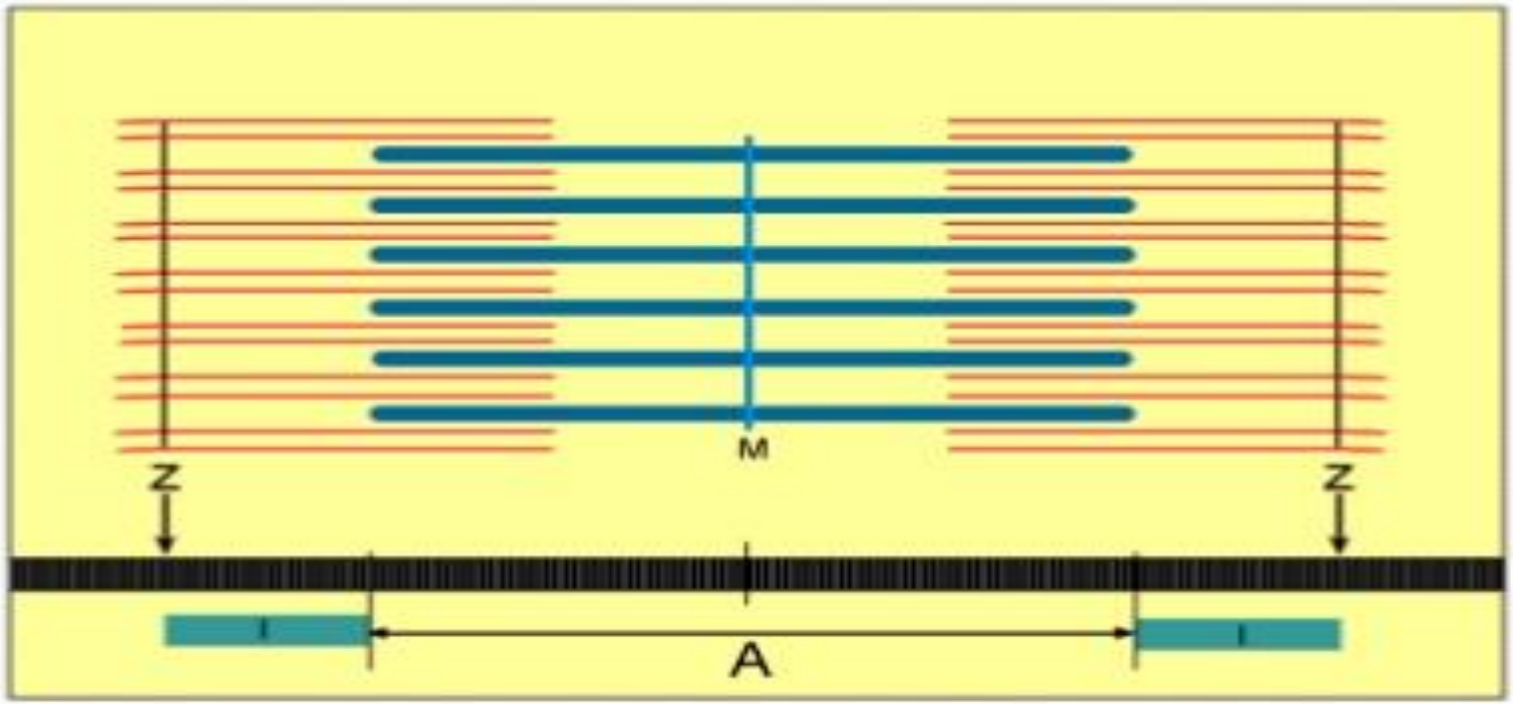
$$ATP + ATPase \xrightarrow{Ca^{++}} ADP + {\sim}P$$

Muscle contraction takes place.

Mechanism Of Muscle Contraction

- Muscle contraction occurs when calcium is pumped back into the sarcoplasmic reticulum, away from the actin and myosin.
- When Calcium moves in this way, the actin and myosin cannot interact, and the muscle relaxes.

SLIDING FILAMENT

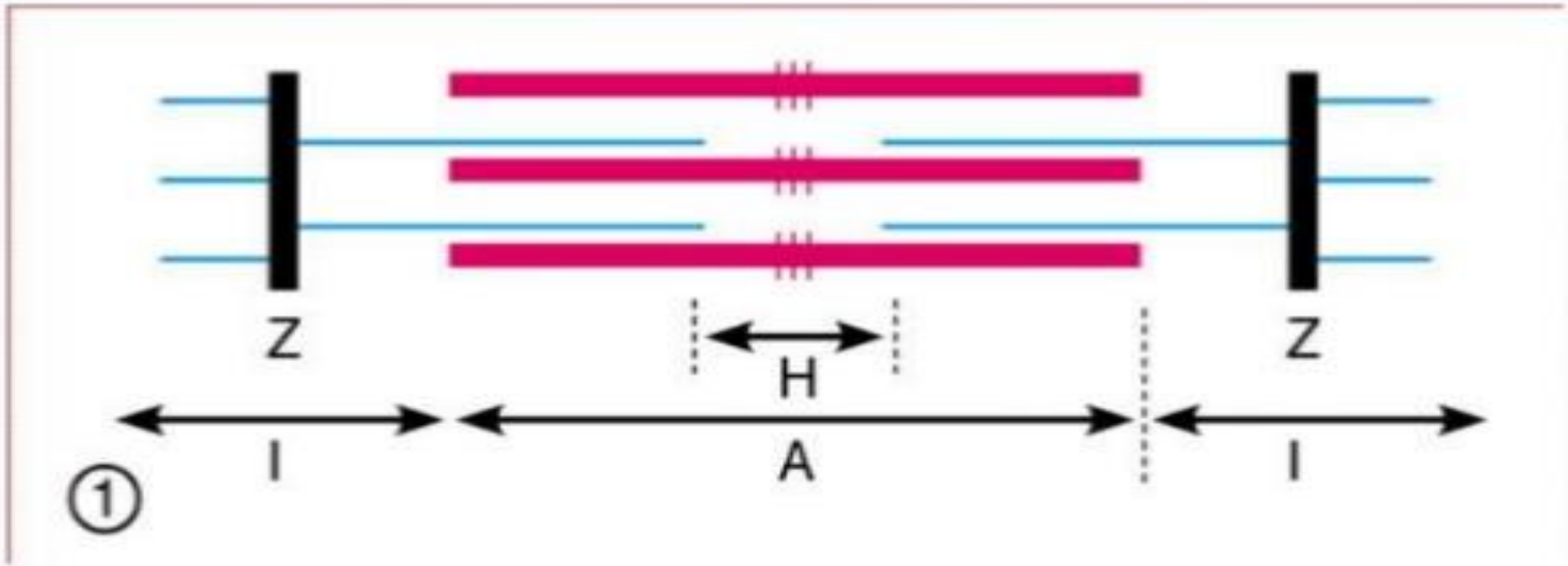


CONTRACTION

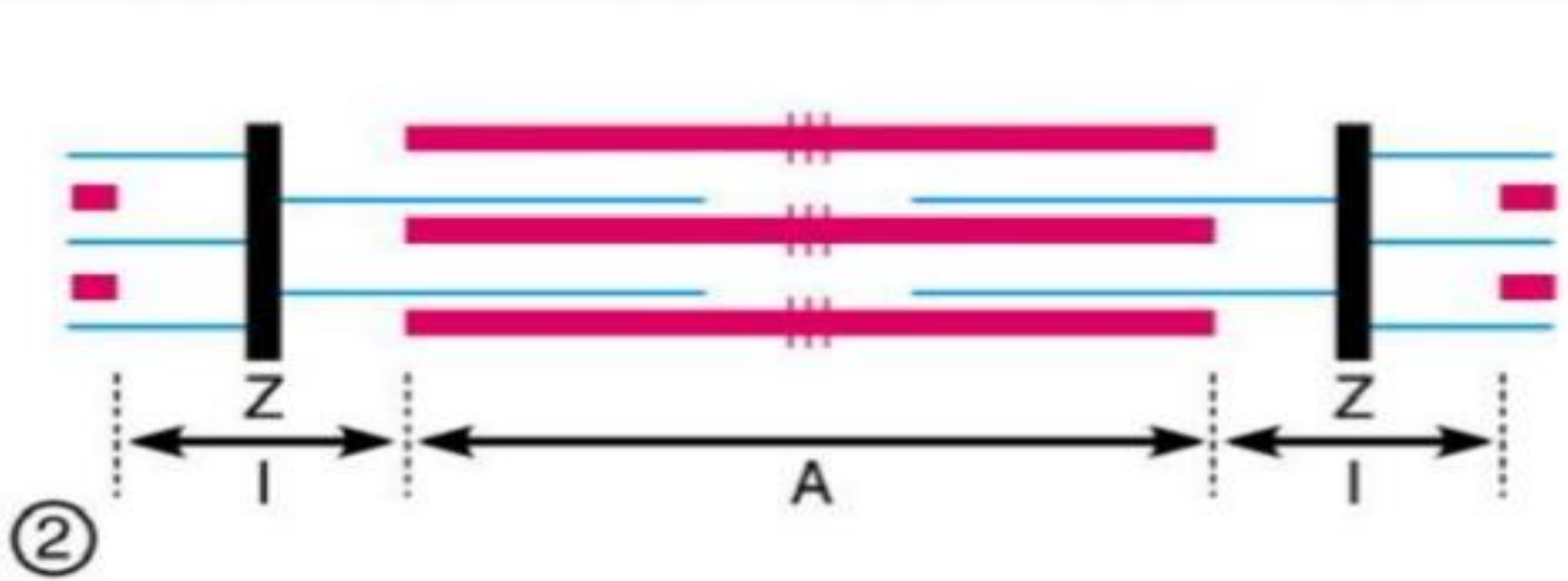
In Contraction

- I- band disappear
- H- band disappear
- M- band disappear
- Length of sarcomere decreases.

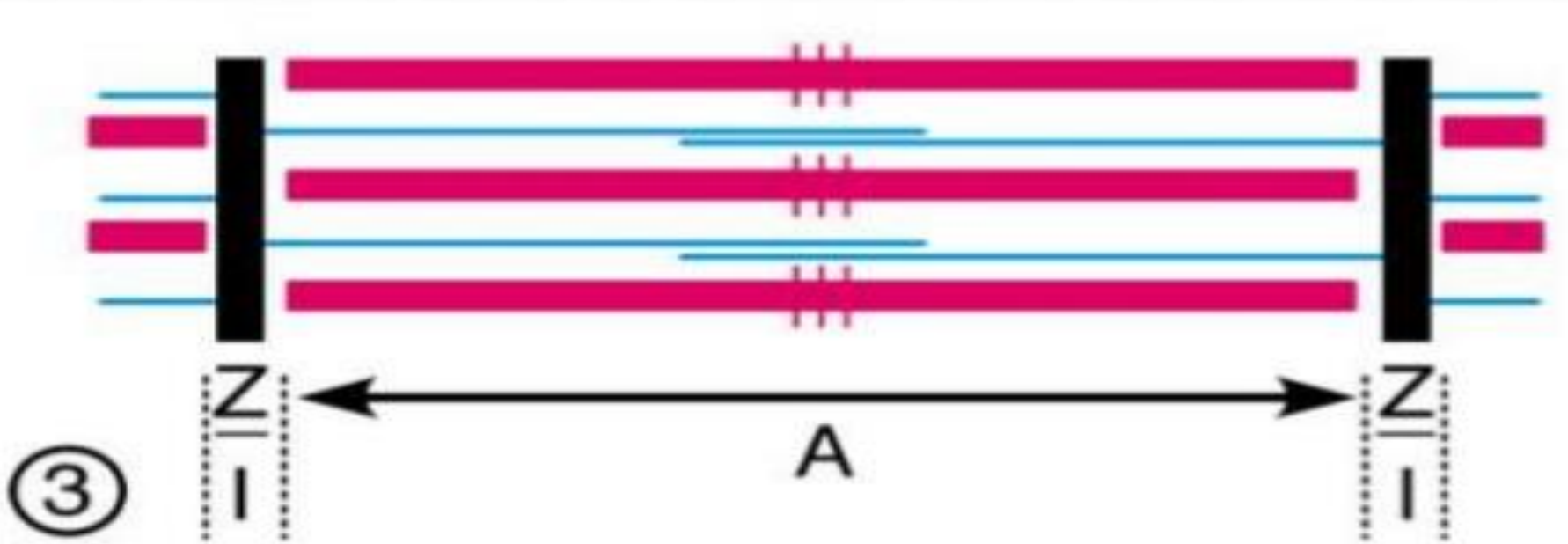
Sarcomere Relaxed



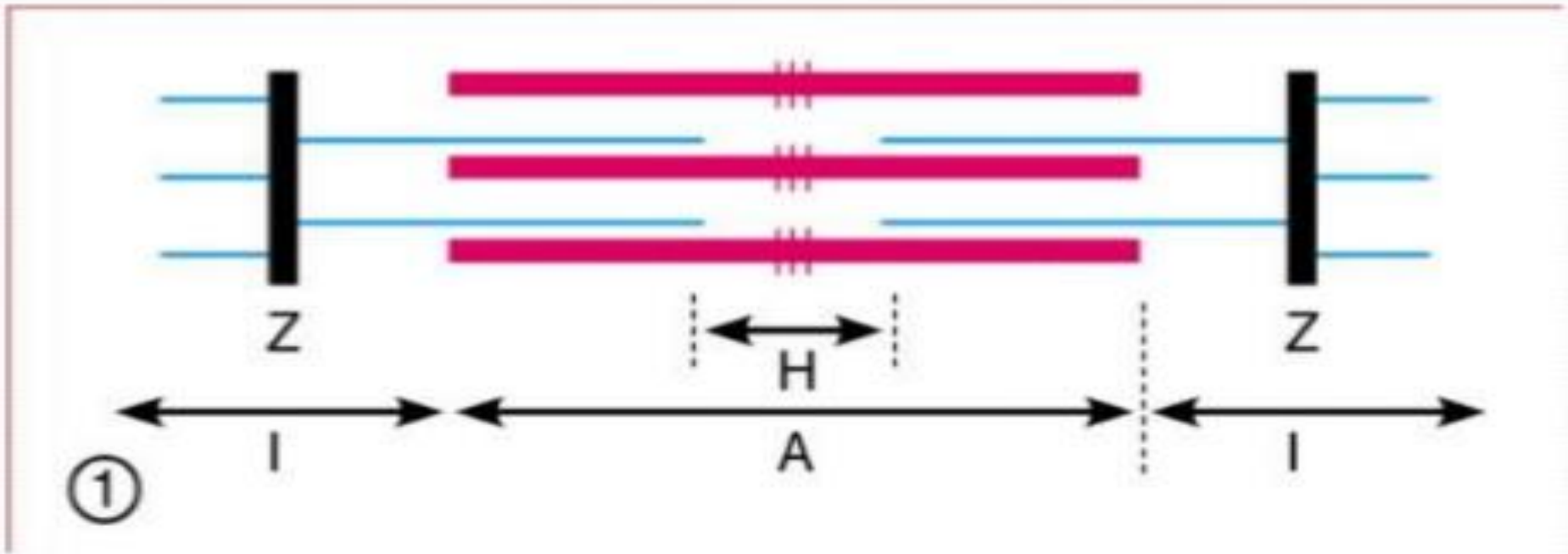
Sarcomere Partially contracted



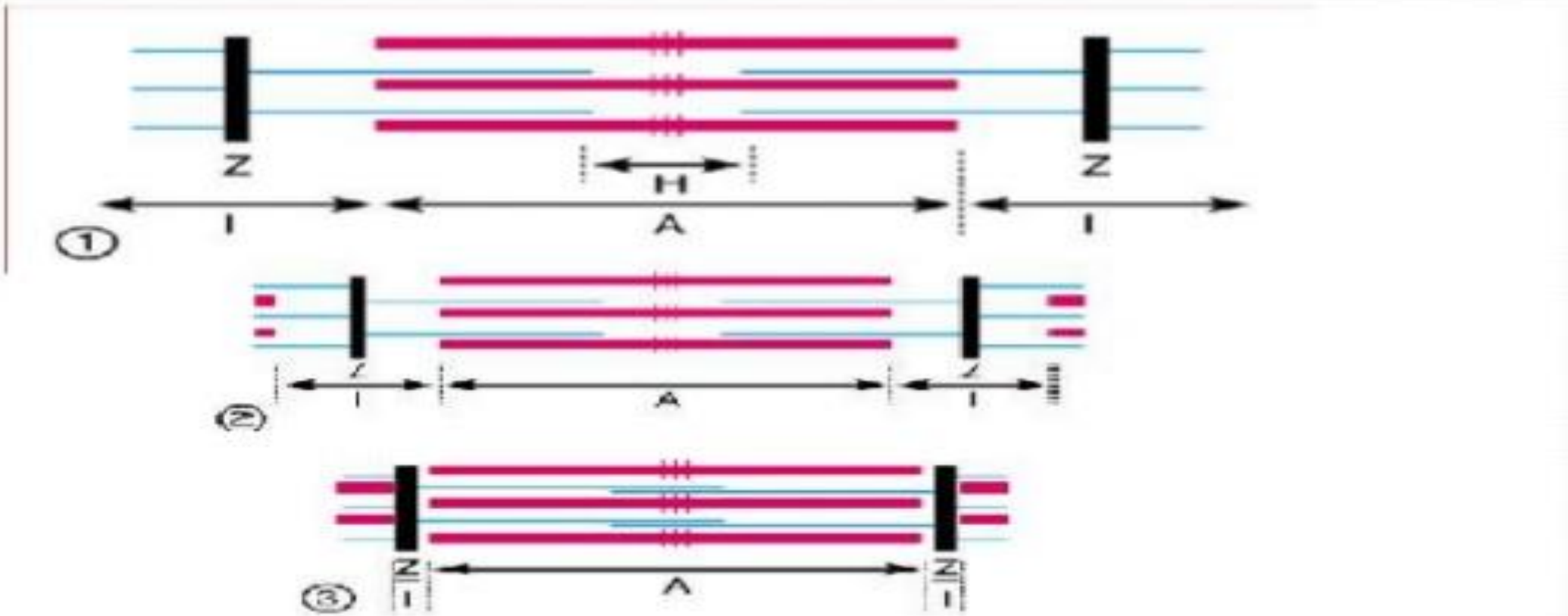
Sarcomere completely contracted



Sarcomere relaxed



Stages Of Muscle Contraction



Notice: To the Student

I have prepared the notes for “Muscle Contraction” in two different ways. It is left to the student to opt for the one he finds easier.

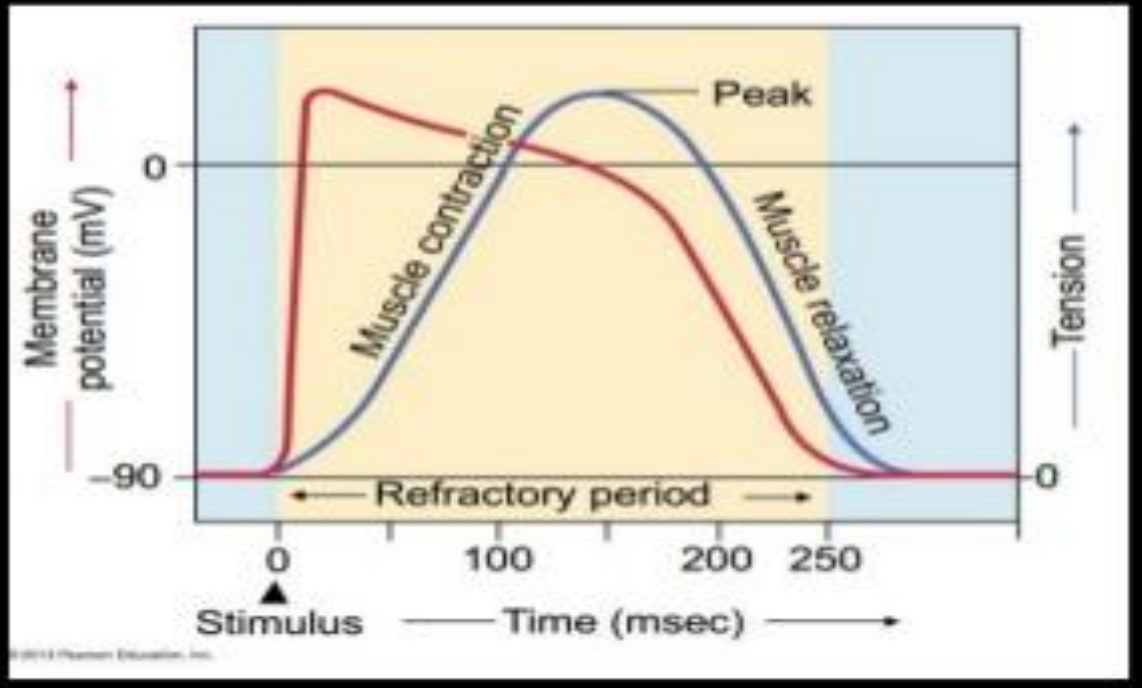
Dr. Luna Phukan

OBJECTIVES

- Process of Muscle Excitation.
- Process of Excitation-Contraction Coupling.
- Process of Muscle Contraction.
- Sequence of events during muscle contraction & relaxation when stimulated by nerve.
- Types of Muscle Contraction
- Isotonic & Isometric.

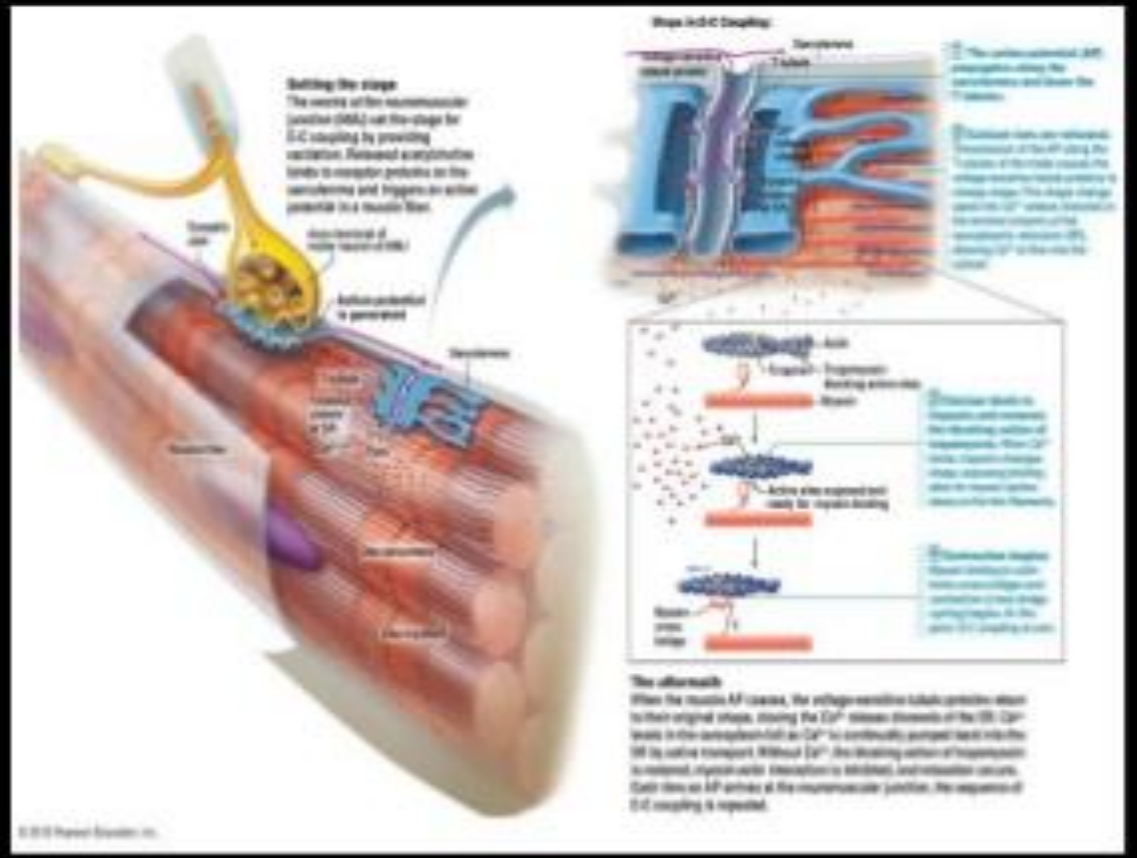
PROCESS OF MUSCLE EXCITATION.

- **Muscle** – excitable tissue.
- When stimulated shows response
  - **Electrical Response** – production of action potential.
  - **Mechanical Response** – contraction.



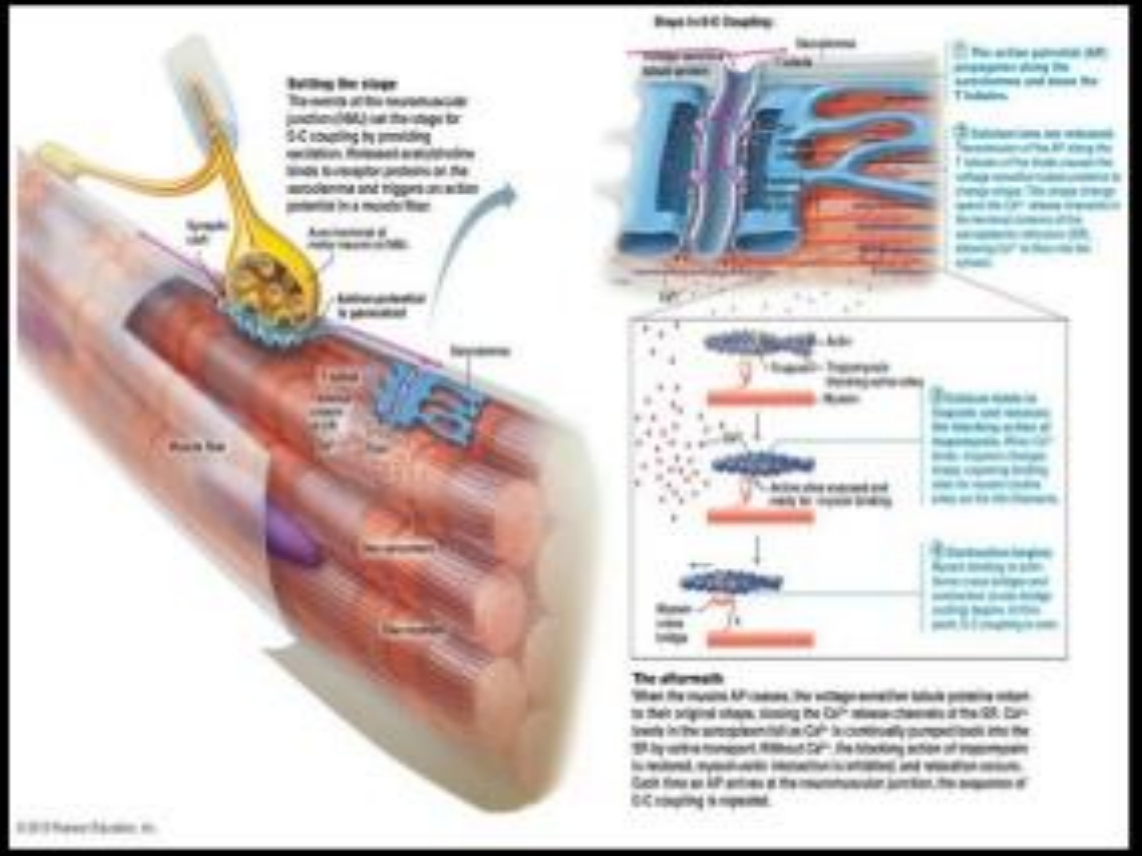
PROCESS OF MUSCLE EXCITATION.

- So, Excitation – Action Potential
- & Contraction – Muscle Contraction.
- Linking of these 2 events is done by coupling.
- Done by **Ca** ions.



PROCESS OF EXCITATION-CONTRACTION COUPLING.

- When **EPP** reaches threshold level , it produces action potential which propagates over muscle fibre & through it along transverse tubules.

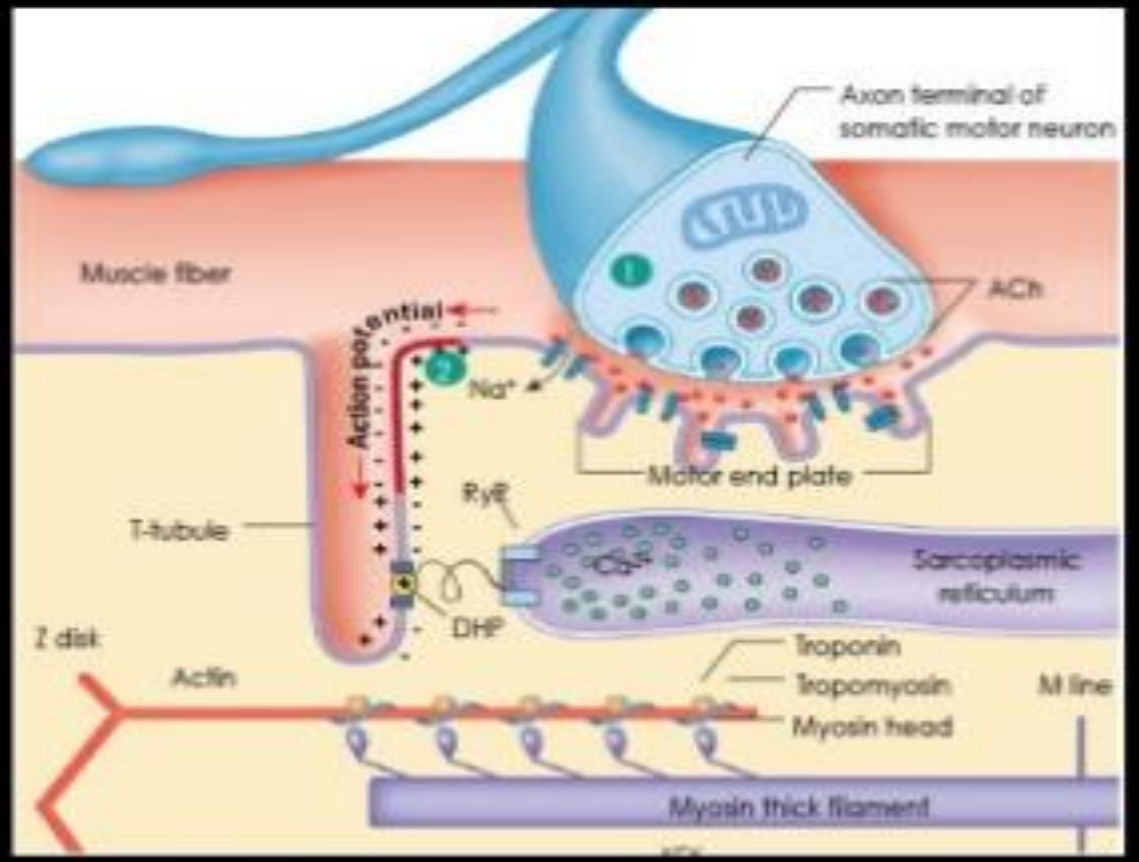


DIFFERENCE BETWEEN EXCITATION OF NERVE & MUSCLE.

FEATURES	NERVE	SKELETAL MUSCLE
RMP (mv)	-70	-90
THRESHOLD LEVEL (mv)	15	30-40
AP Magnitude (mv)	100-105	120-130
SPIKE POENTIAL DURATION (ms)	0.4-2	2-4
ABSOLUTE REFRACTORY PERIOD	0.4-2	1-3
EXCITABILITY	MORE	LESS
CONDUCTION VELOCITY	VARIABLE	LOW

PROCESS OF MUSCLE CONTRACTION.

- AP initiated in plasma membrane spread to surface & into muscle fibre through T tubules.
- When reaches tip of T Tubule activate voltage gated DHP **(Dihydropyridine Receptors)**



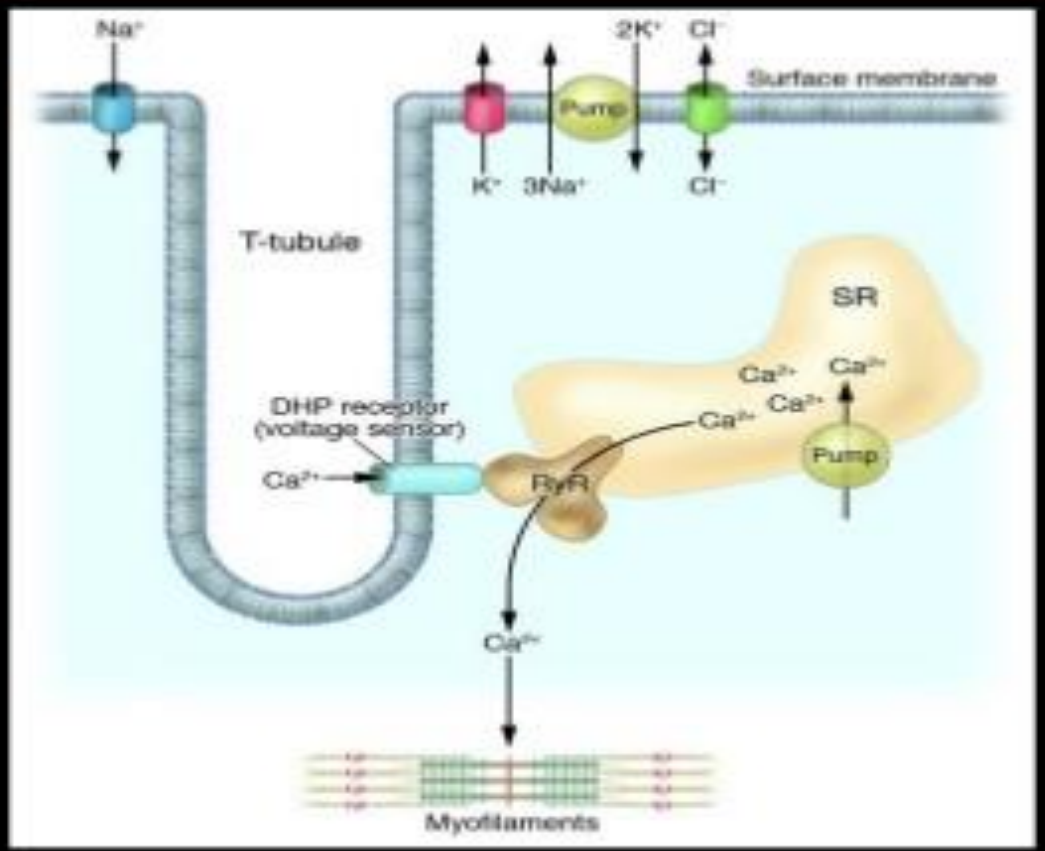
PROCESS OF MUSCLE CONTRACTION.

- Activated DHP receptors

triggers

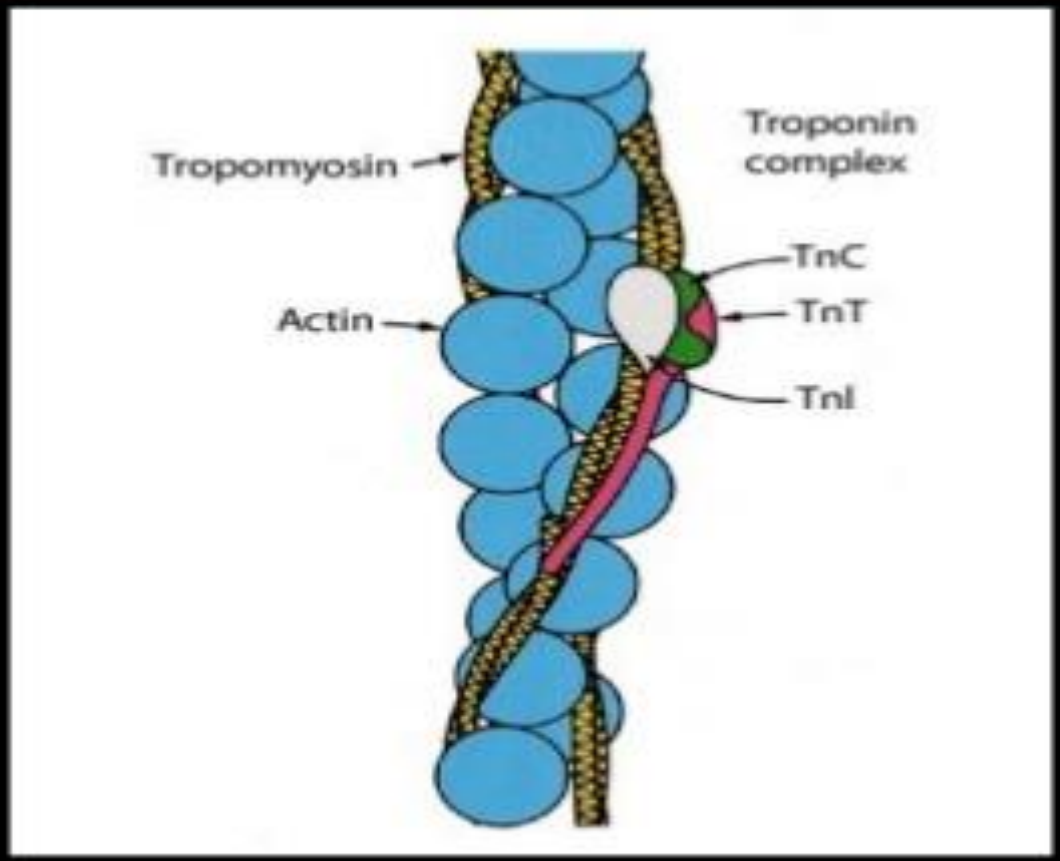
opening of Ca release channels on terminal cisterns i.e. **Ryanodine Receptors**

Ca diffuses into cytoplasm & ICF Ca increases (2000 times)



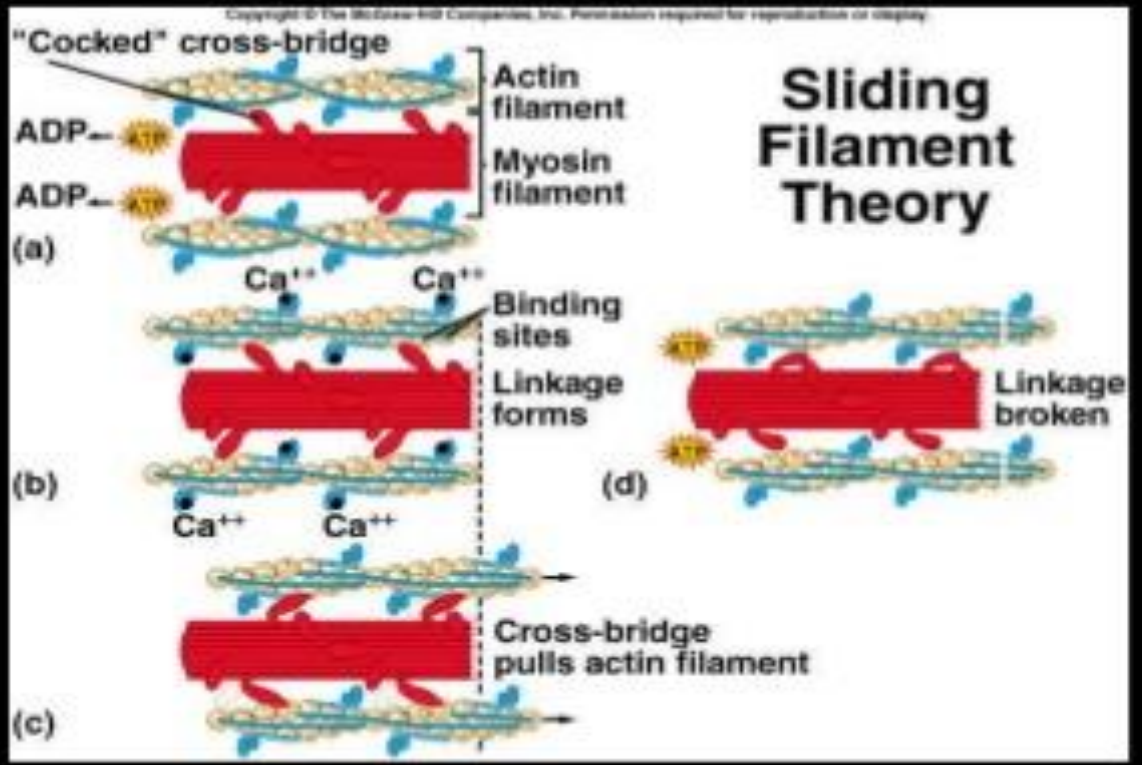
PROCESS OF MUSCLE CONTRACTION.

- Ca ion get attached to **Troponin-C** & starts chain of events
- So Ca acts as linkage between excitation & contraction process.



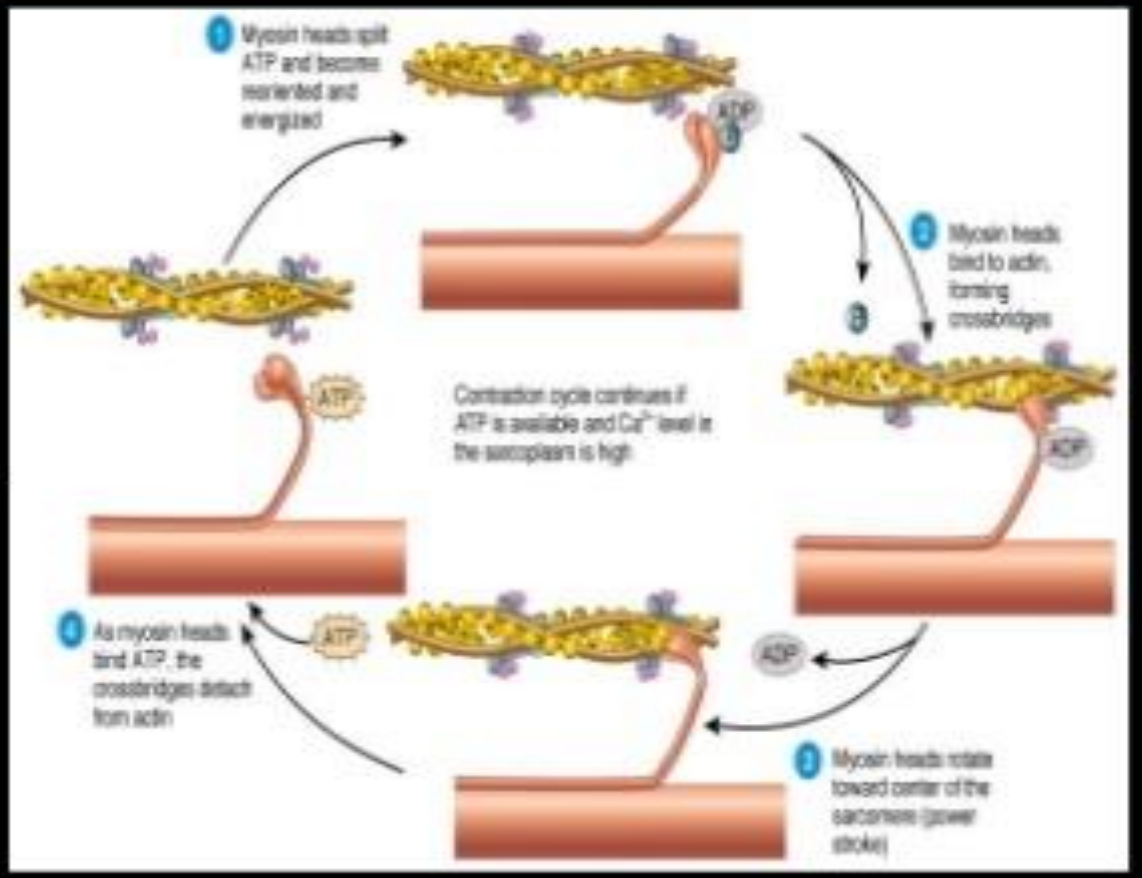
PROCESS OF MUSCLE CONTRACTION.

- Molecular basis of Muscle Contraction.
- **A.F.Huxley & H.E.Huxley** put forward **Sliding Filament theory / Rachet theory / Walk-along theory / Modern theory of Muscular Contraction.**



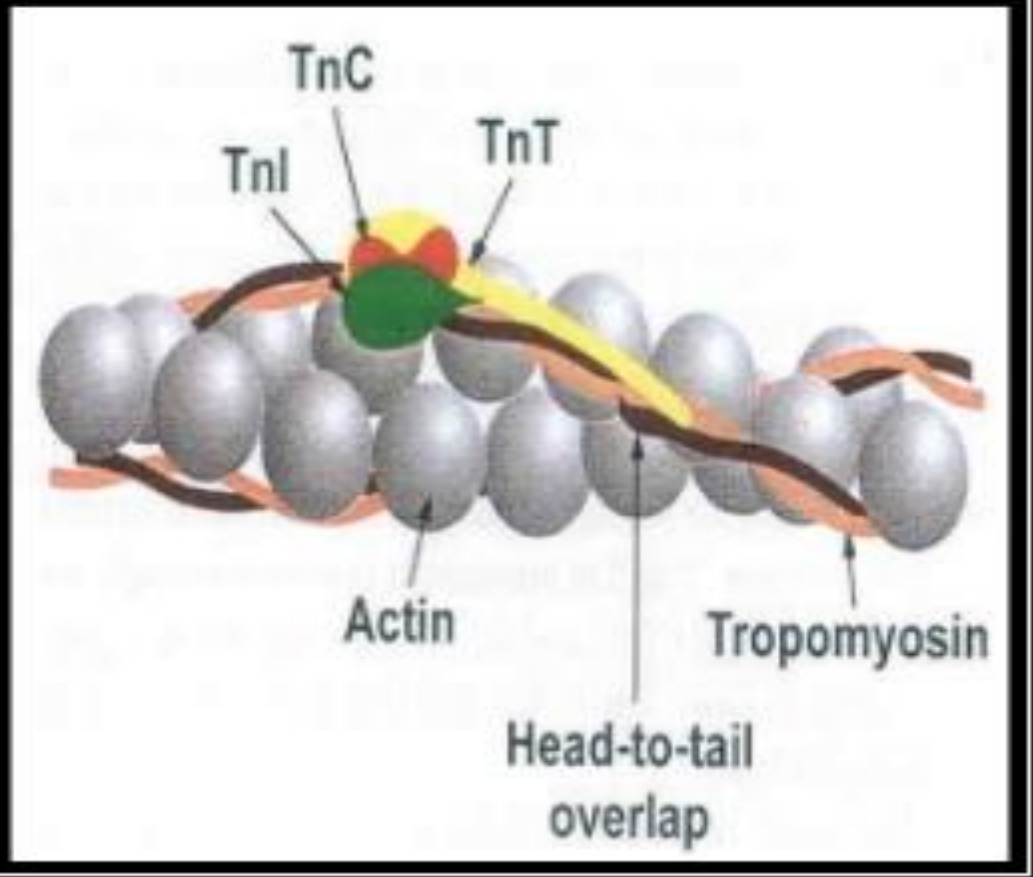
STEPS OF CROSS BRIDGE CYCLING.

- Initiation of cross bridge cycling.
- Formation of Actin-myosin complex
- Power stroke.
- Detachment of myosin head of cross bridge from the active site of an Actin filament.
- Reactivation of Myosin Head.



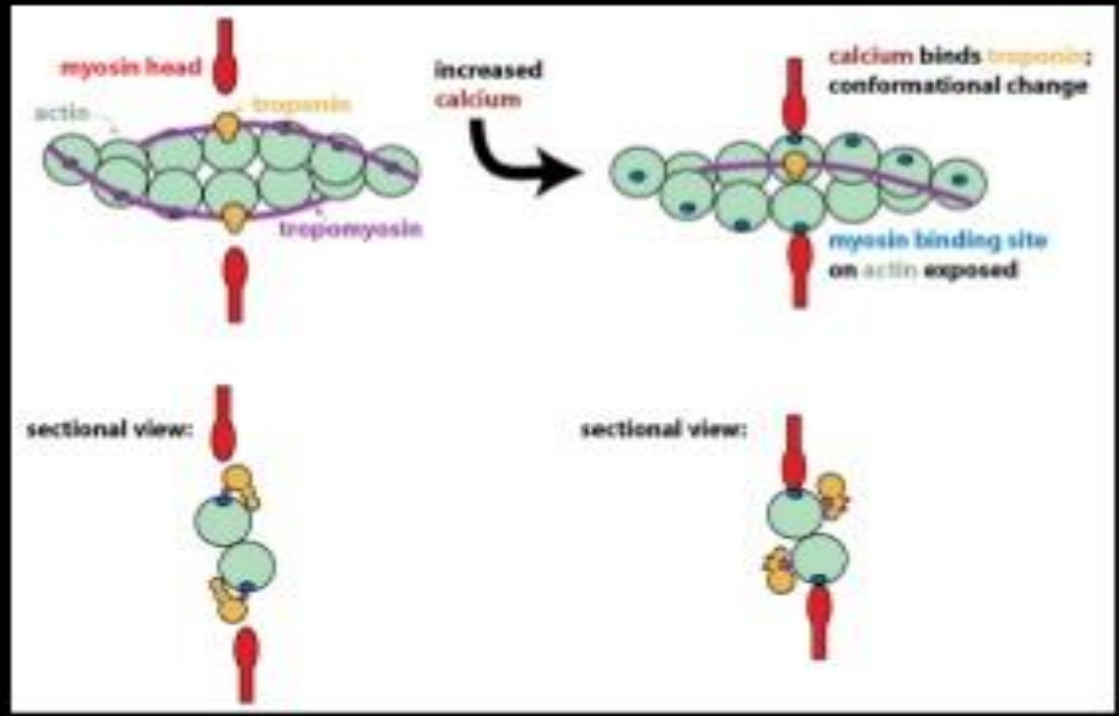
INITIATION OF CROSS BRIDGE CYCLING.

- **At Rest –**
  - Troponin I is lightly bound to actin
  - & Myosin binding sites on actin is covered by tropomyosin which lies in a groove between actin strands.
  - Troponin T attached to tropomyosin to form troponin-tropomyosin complex.



INITIATION OF CROSS BRIDGE CYCLING.

- **After Excitation** – Ca released in cytosol is attached to Troponin C.
- Causes conformational change & Tropomyosin to move laterally
- **Uncover** active binding sites on Actin.



FORMATION OF ACTIN-MYOSIN COMPLEX

- Head of myosin **binds** with **ATP**
- ATPase activity of head of myosin breaks ATP into ADP + Pi cleavage products.
- Head gets energy move perpendicular toward Actin & gets attached

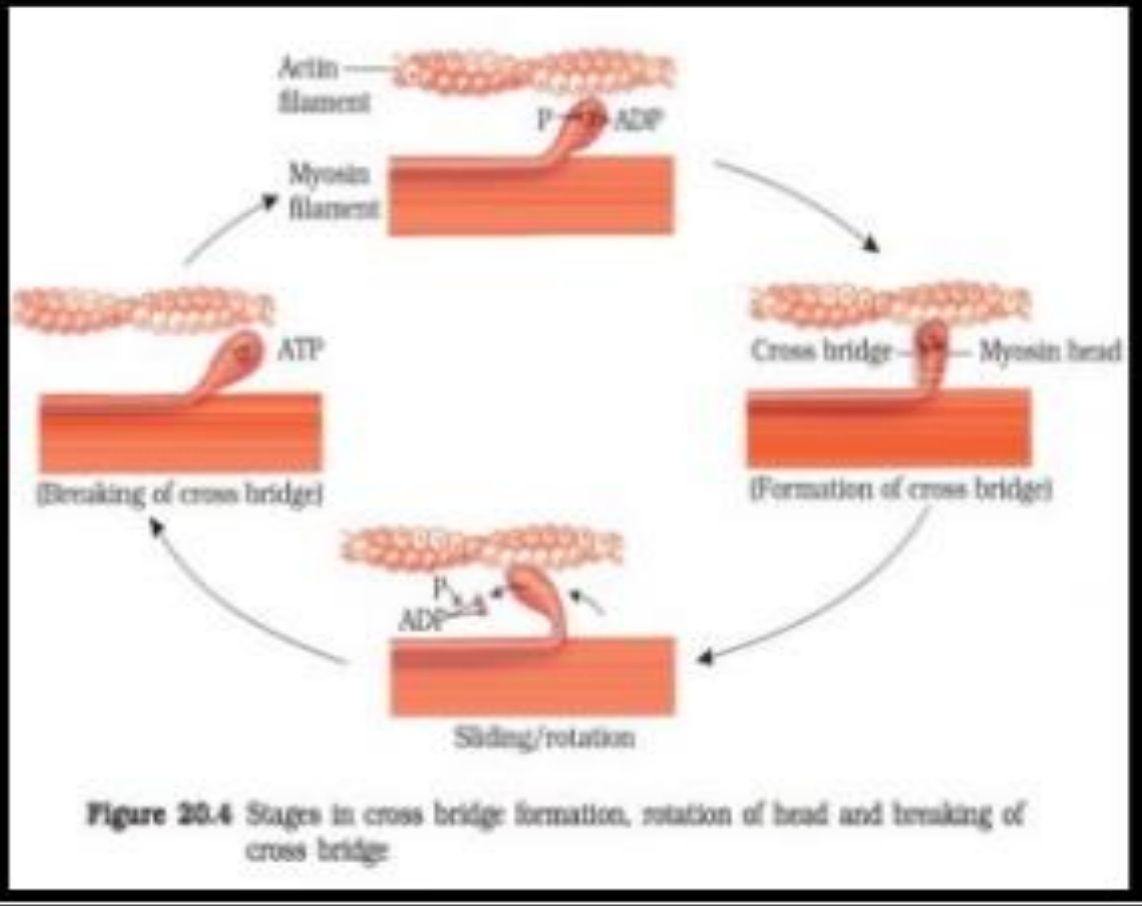
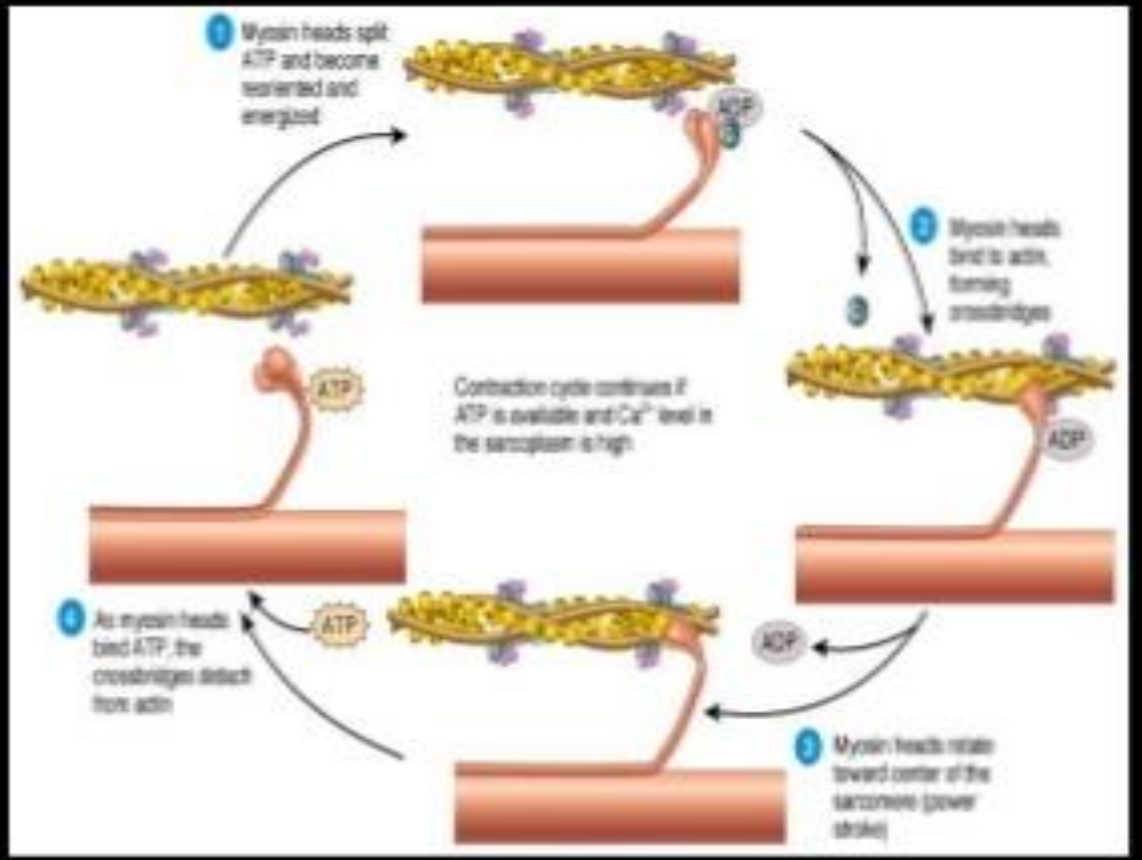


Figure 20.4 Stages in cross bridge formation, rotation of head and breaking of cross bridge

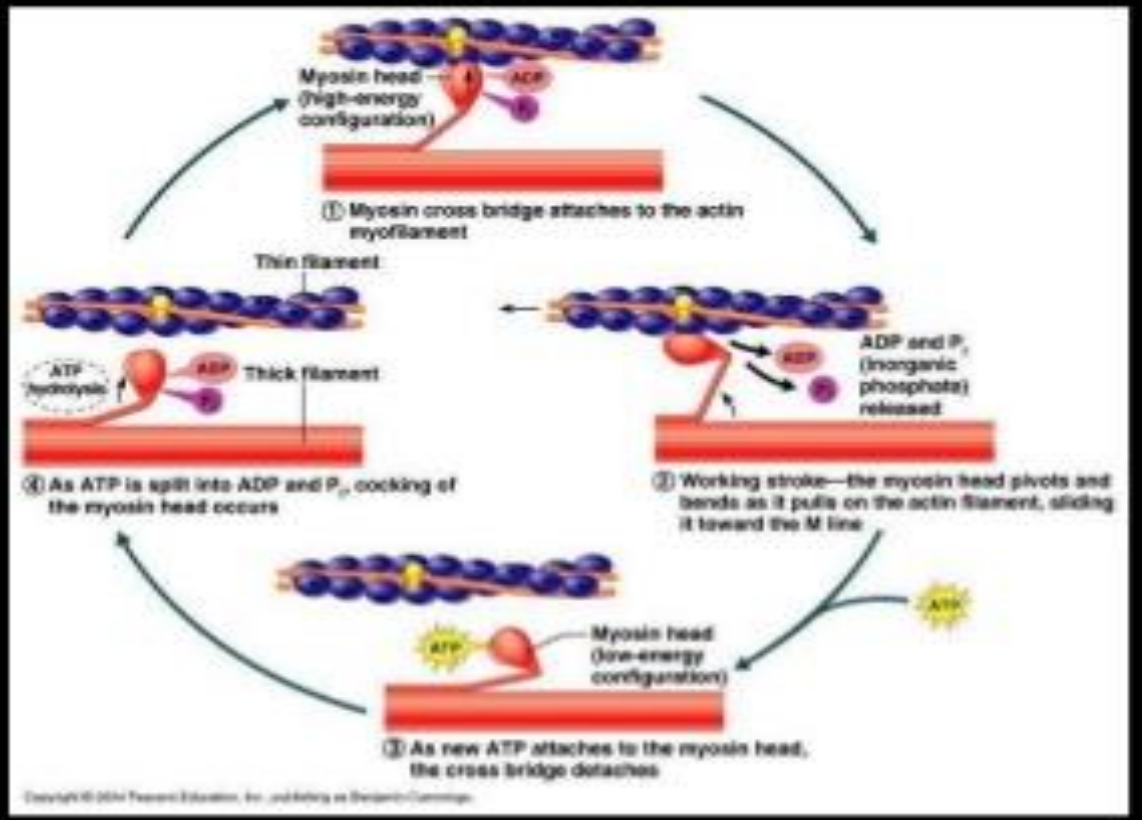
POWER STROKE.

- **Actin-Myosin-ADP-Pi complex** triggers
  - Release of Pi & ADP
  - Conformational change in myosin & myosin head flex toward arm.
- This movements generate mechanical force – **POWER STROKE.**



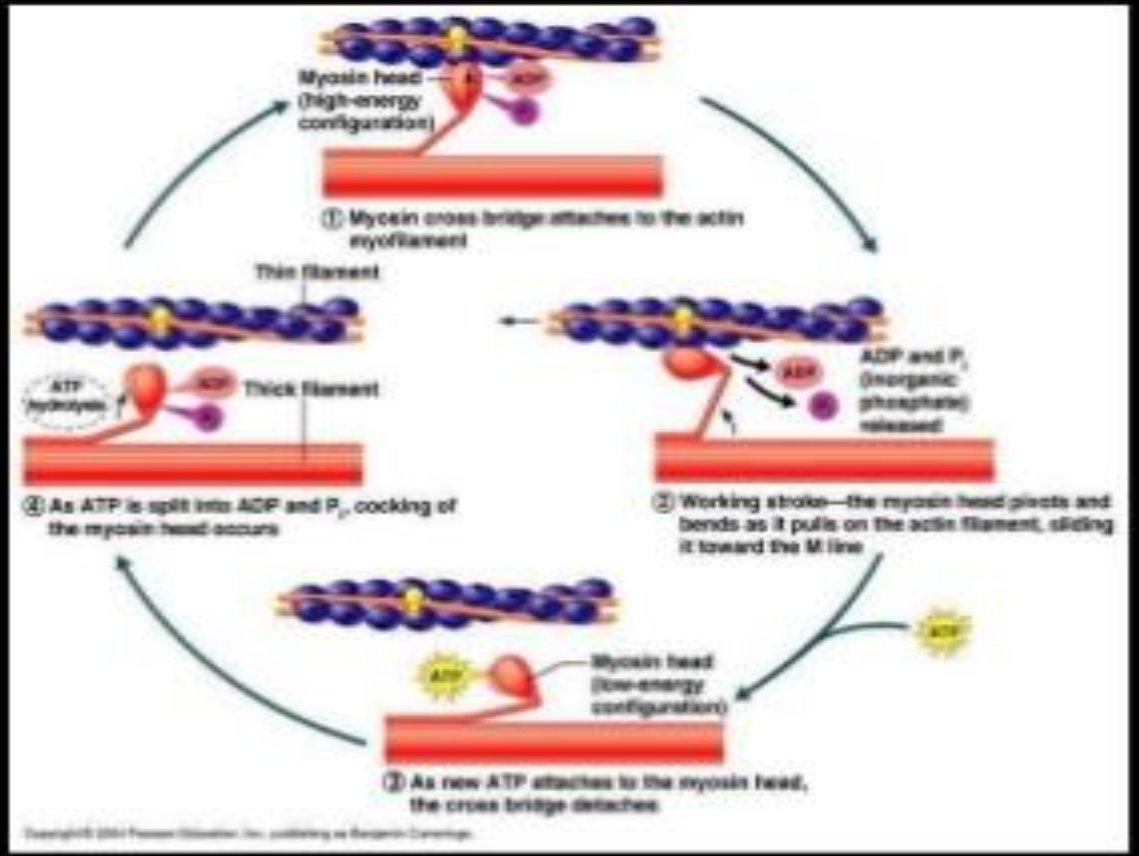
EFFECTS OF POWER STROKE

- **If load on muscle is Small** – Actin slides over myosin & muscle shortening.
- **If load is Large** – flexion of myosin head-stretching of elastic neck & no sliding.



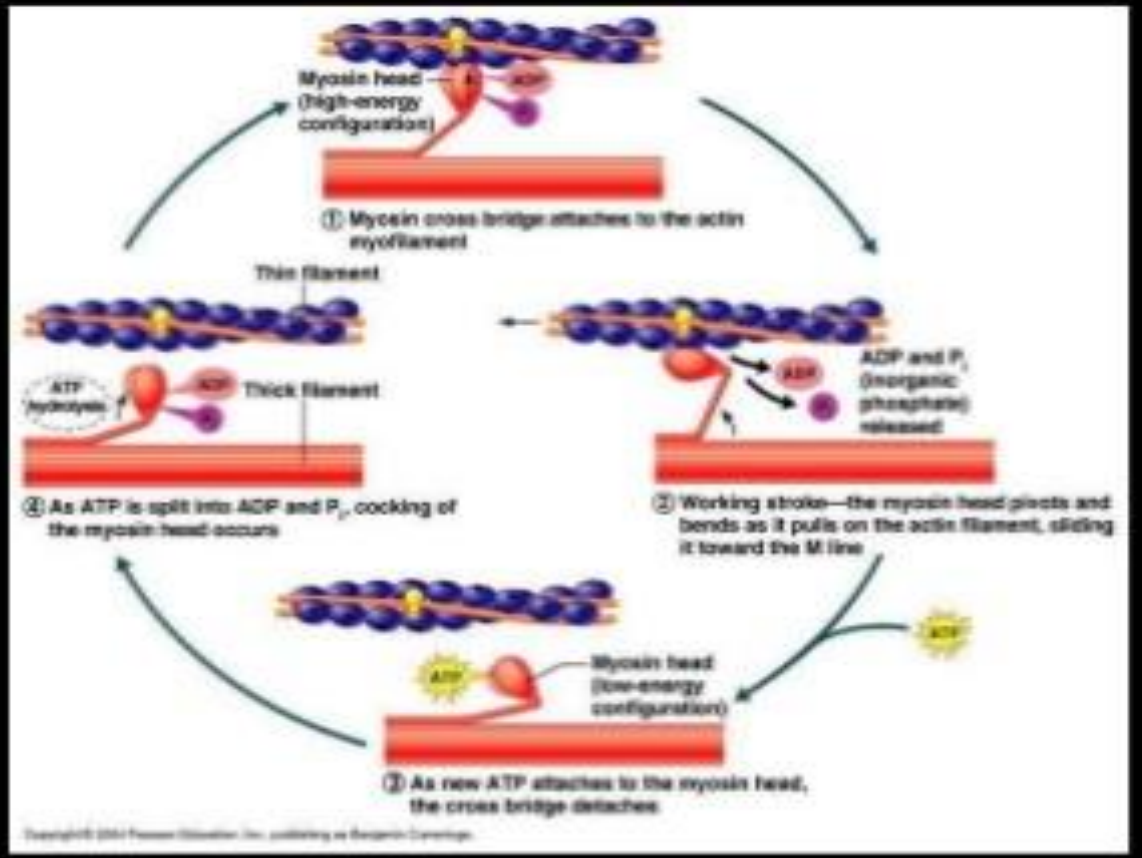
DETACHMENT OF MYOSIN HEAD OF CROSS BRIDGE FROM THE ACTIVE SITE OF AN ACTIN FILAMENT.

- Release of ADP & Pi make new ATP to attach to myosin head.
- This new ATP with myosin head has low affinity for Actin so **Dissociation** of myosin head with Actin occurs.



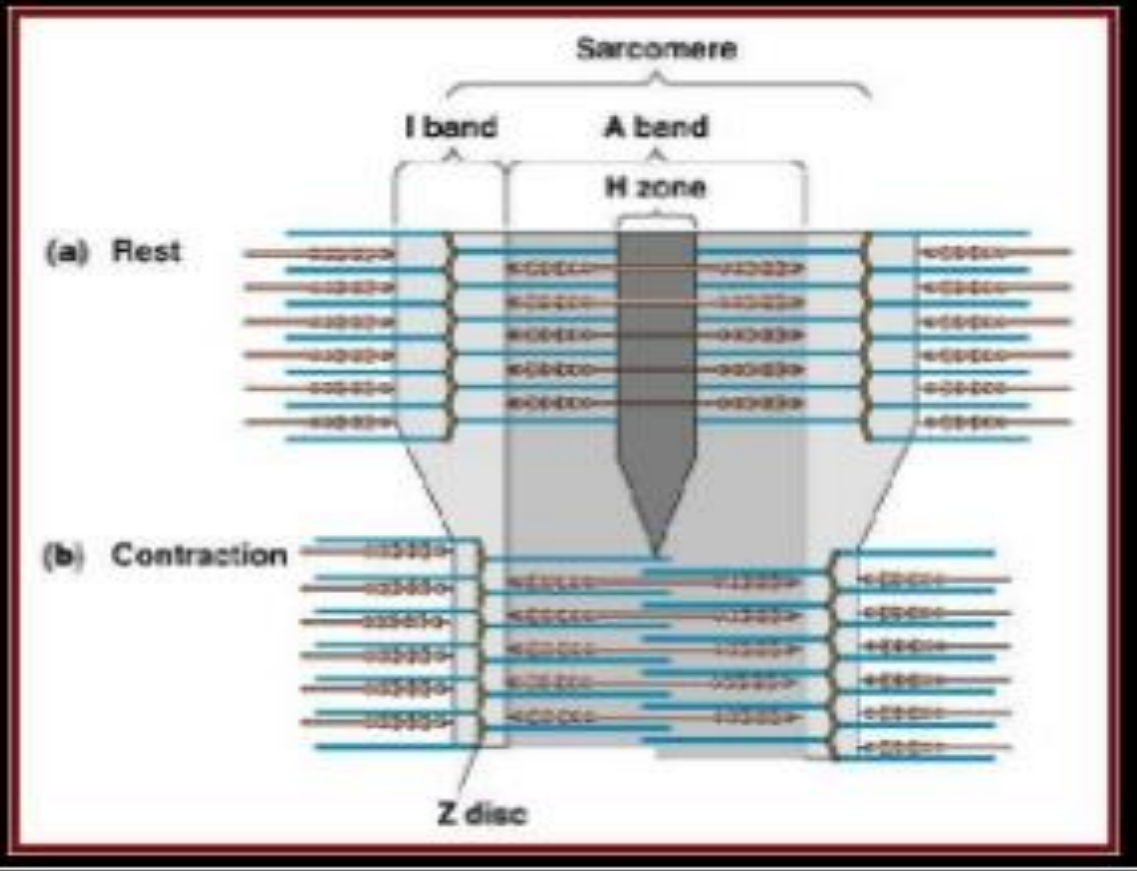
REACTIVATION OF MYOSIN HEAD.

- This bound ATP splits again into ADP & Pi
- Which again give energy to myosin head & **reactivate** it.
- Again energized head move towards Actin filaments & gets attached to it.



CHANGES AT SARCOMERE LEVEL DURING MUSCLE CONTRACTION.

- Width of A band remains constant.
- H zone Disappears.
- I band width decreases.
- Z line move closer.
- The Sarcomere shortens.



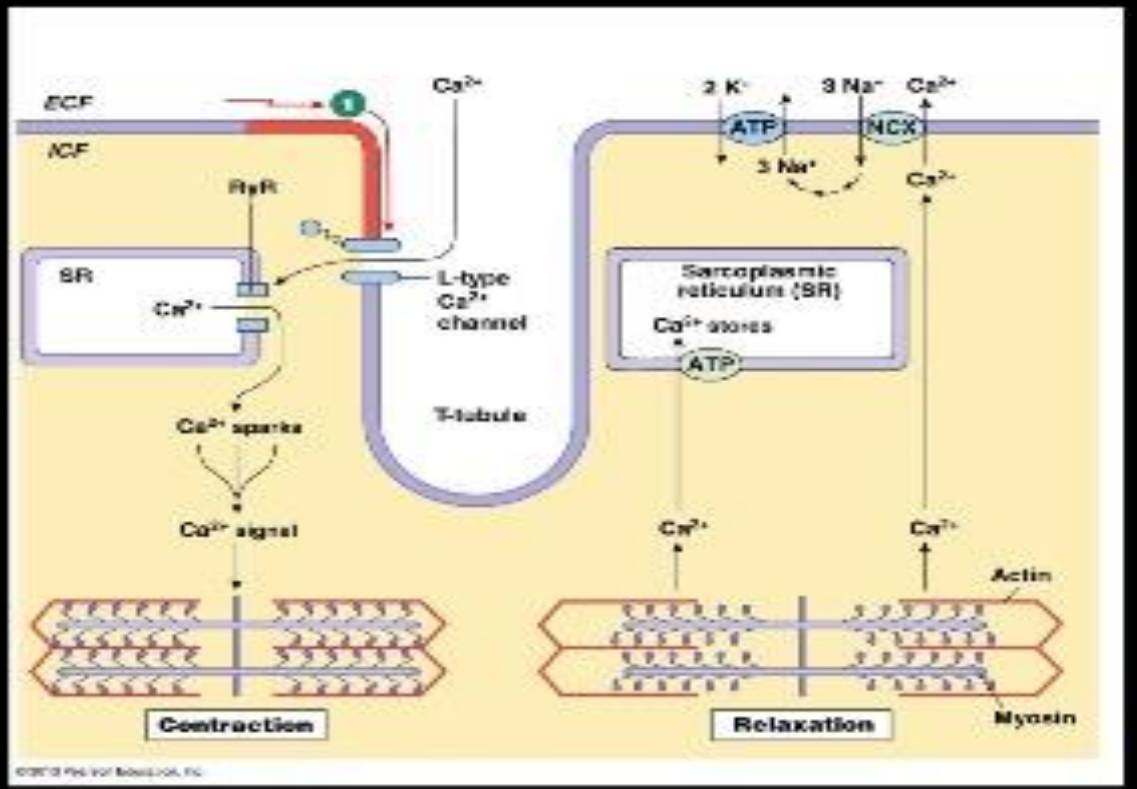
STEPS IN MUSCLE RELAXATION.

- After a few ms Ca pump transport Ca from Sarcoplasm

- **Sarcoplasmic Reticulum**

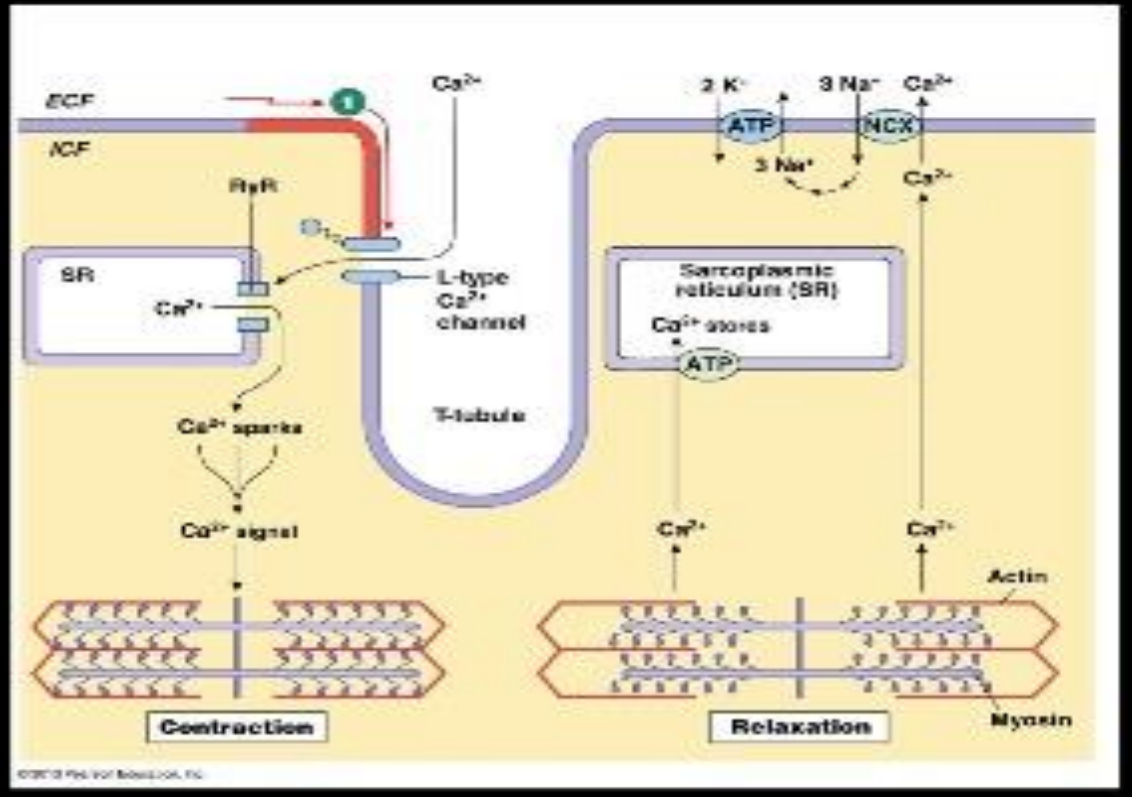
discharge to

Terminal Cisterns.



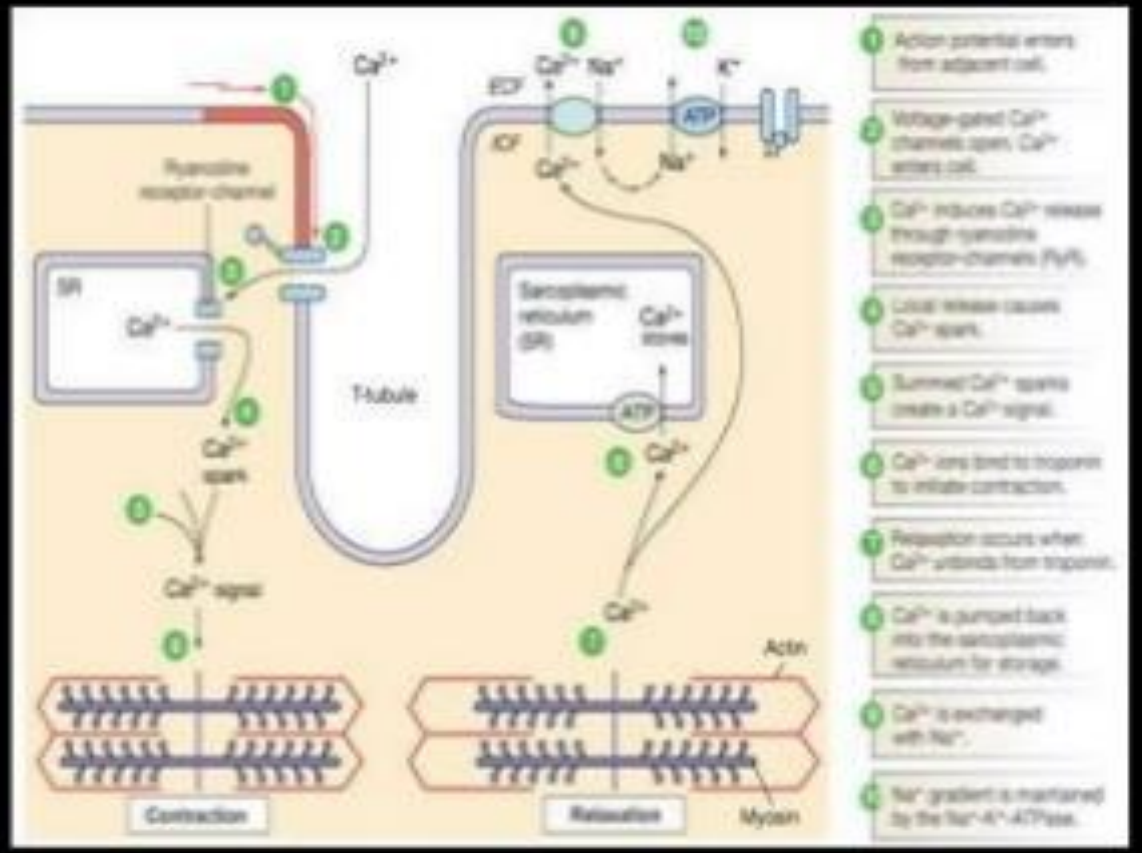
STEPS IN MUSCLE RELAXATION.

- **Removal** of Ca from Troponin
- **Rotate** Troponin-Tropomyosin Complex
- **Cover active sites** , closes cross bridge cycle & relaxes Muscle.

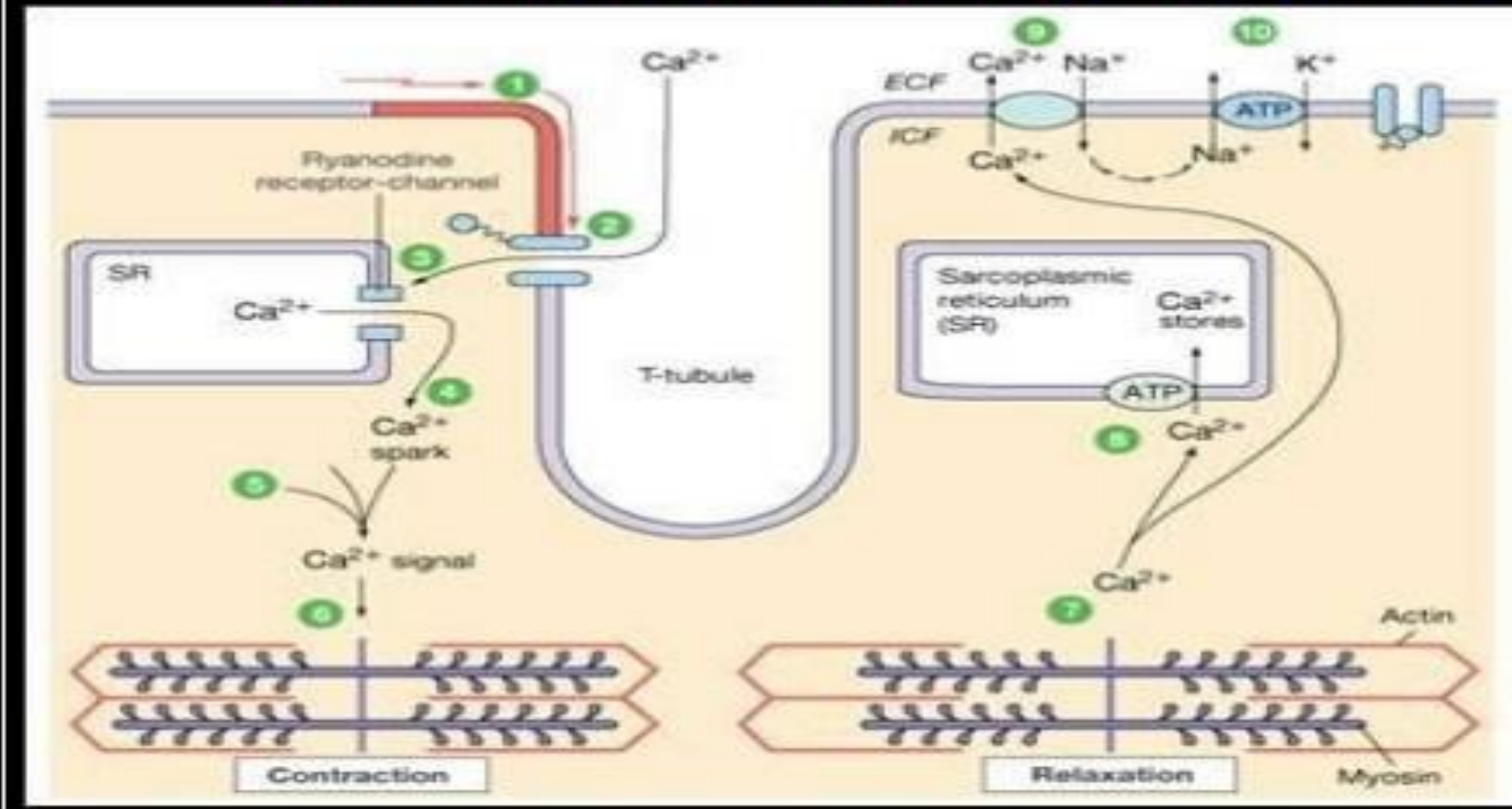


ROLE OF ATP IN MUSCLE CONTRATION & RELAXATION.

- ATP hydrolysis gives energy to cross bridges -- provide **Force**.
- ATP binding to Myosin **Dissociate** cross bridges & begin new cycle.
- Ca ATPase by hydrolysis of ATP provide energy for Ca pump to **transport Ca back** – ending contraction & **Muscle Relaxes**.



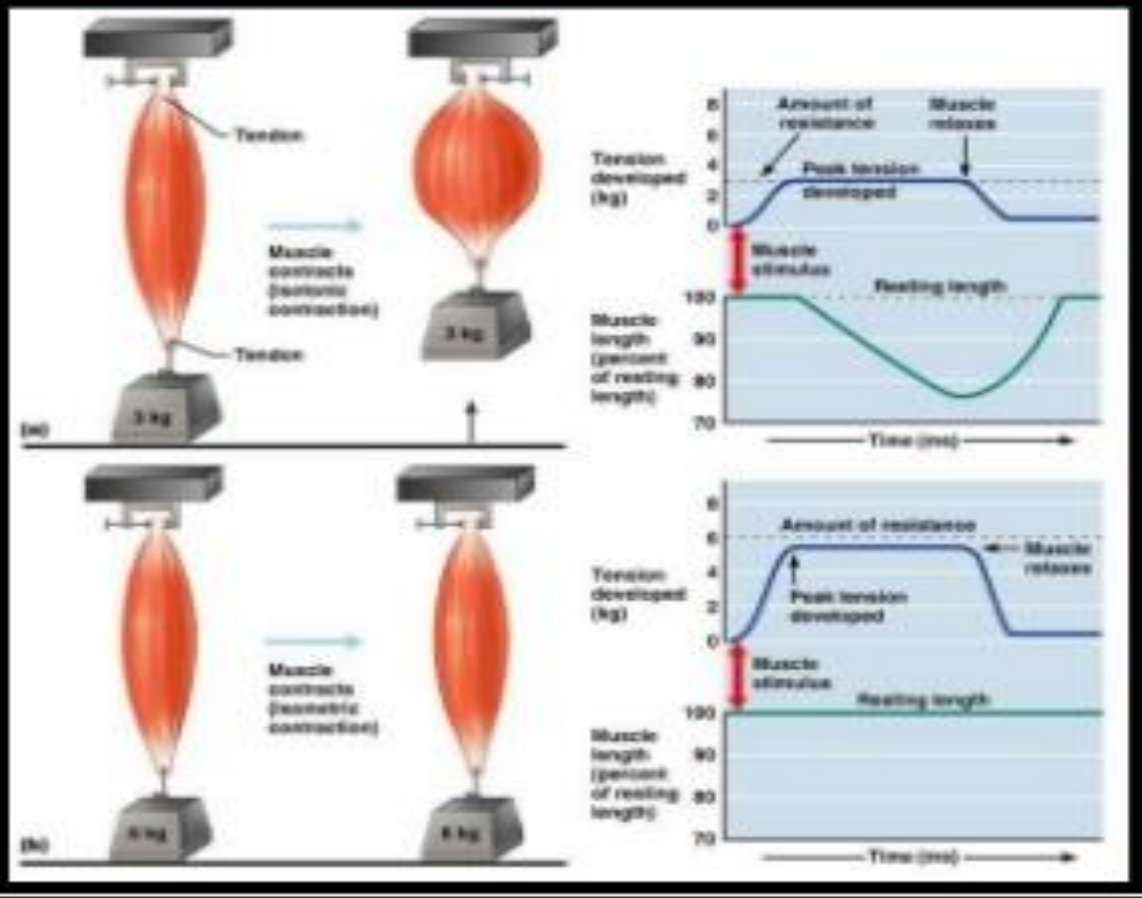
SEQUENCE OF EVENTS DURING MUSCLE CONTRACTION & RELAXATION



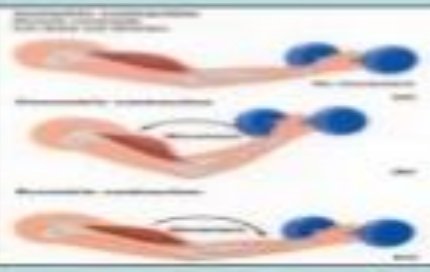
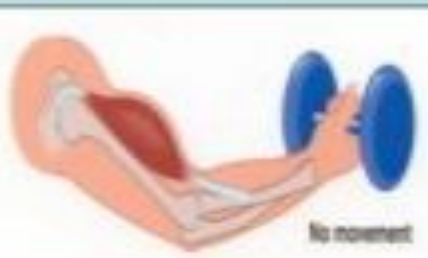
1. Action potential enters from adjacent cell.
2. Voltage-gated Ca^{2+} channels open. Ca^{2+} enters cell.
3. Ca^{2+} induces Ca^{2+} release through ryanodine receptor-channels (RyR).
4. Local release causes Ca^{2+} spark.
5. Summed Ca^{2+} sparks create a Ca^{2+} signal.
6. Ca^{2+} ions bind to troponin to initiate contraction.
7. Relaxation occurs when Ca^{2+} unbinds from troponin.
8. Ca^{2+} is pumped back into the sarcoplasmic reticulum for storage.
9. Ca^{2+} is exchanged with Na^{+}.
10. Na^{+} gradient is maintained by the Na^{+}-K^{+}-ATPase.

CONTRACTILE RESPONSE.

- Muscle stimulated
- Excited
- Response – Contraction
- Manifested by
  - **Shortening (Iso-Tonic)**
  - **Developing Tension (Iso-Metric)**
  - **Both**



TYPES OF MUSCLE CONTRACTION ISOTONIC & ISOMETRIC.

Isotonic contraction		Isometric contraction
Concentric	Eccentric	
		
• Concentric contraction in the biceps brachii during the **upward phase** of exercise • Biceps brachii produces tension and **shortens** • It pulls the **forearm upwards to cause flexion** of the elbow	• Eccentric contraction in the biceps brachii during the **downward phase** of exercise • Biceps brachii produces tension and **lengthens** • It **slows the lowering of the forearm and controls extension of the elbow**	• Isometric contraction occurs in the biceps brachii when the muscle is **holding the weight still** • Biceps brachii develops tension and **stays the same length** •It **stops flexion and extension of the elbow**

OBJECTIVES WE HAVE SEEN

- Process of Muscle Excitation.
- Process of Excitation-Contraction Coupling.
- Process of Muscle Contraction.
- Sequence of events during muscle contraction & relaxation when stimulated by nerve.
- Types of Muscle Contraction
- Isotonic & Isometric.

End of muscle contraction

4. Characteristic of Muscle Twitch: MOTOR UNIT, Summation and Tetanus

Muscle twitching is also called muscle fasciculation. Twitching involves small muscle contractions in the body. Your muscles are made up of fibers that your nerves control. Stimulation or damage to a nerve may cause your muscle fibers to twitch. Most muscle twitches go unnoticed and aren't cause for concern.

A fasciculation, or muscle twitch, is a spontaneous, involuntary muscle contraction and relaxation, involving fine muscle fibers. They are common, with as much as 70% of people experiencing them. They can be benign, or associated with more serious conditions. When no cause or pathology is identified, they are diagnosed as benign fasciculation syndrome

The most effective way to detect fasciculations may be surface electromyography (EMG). Surface EMG is more sensitive than needle electromyography and clinical observation in the detection of fasciculation in people with amyotrophic lateral sclerosis.

Deeper areas of contraction can be detected by electromyography (EMG) testing, though they can happen in any skeletal muscle in the body.

Fasciculations arise as a result of spontaneous depolarization of a lower motor neuron leading to the synchronous contraction of all the skeletal muscle fibers within a single motor unit. An example of normal spontaneous depolarization is the constant contractions of cardiac muscle, causing the heart to beat. Usually, intentional movement of the involved muscle causes fasciculations to cease immediately, but they may return once the muscle is at rest again.

Tics must also be distinguished from fasciculations. Small twitches of the upper or lower eyelid, for example, are not tics, because they do not involve a whole muscle, rather are twitches of a few muscle fibre bundles, that are not suppressible.

Causes

Fasciculations have a variety of causes, the majority of which are benign, but can also be due to disease of the motor neurons. They are encountered by up to 70% of all healthy people, though for most, it is quite infrequent. In some cases, the presence of fasciculations can be annoying and interfere with quality of life. If a neurological examination is otherwise normal and EMG testing does not indicate any additional pathology, a diagnosis of benign fasciculation syndrome is usually made.

Risk factors

Risk factors for benign fasciculations are age, stress, fatigue, and strenuous exercise. Fasciculations can be caused by anxiety, caffeine or alcohol and thyroid disease. Magnesium deficiency is a common cause of fasciculation.

Other factors may include the use of anticholinergic drugs over long periods.[citation needed] In particular, these include ethanolamines such as diphenhydramine (brand names Benadryl, Dimedrol, Daedalon and Nytol), used as an antihistamine and sedative, and dimenhydrinate (brand names Dramamine, Driminate, Gravol, Gravamin, Vomex, and Vertirosan) for nausea and motion sickness. Persons with benign fasciculation syndrome (BFS) may experience paraesthesia (especially numbness) shortly after taking such medication; fasciculation episodes begin as the medication wears off.

Stimulants can cause fasciculations directly. These include caffeine, pseudoephedrine (Sudafed), amphetamines, and the asthma bronchodilators salbutamol (brand names Proventil, Combivent, Ventolin). Medications used to treat attention deficit disorder (ADHD) often contain stimulants as well, and are common causes of benign fasciculations. Since asthma and ADHD are much more serious than the fasciculations themselves, this side effect may have to be tolerated by the patient after consulting a physician or pharmacist.

The depolarizing neuromuscular blocker succinylcholine causes fasciculations. It is a normal side effect of the drug's administration, and can be prevented with a small dose of a nondepolarizing neuromuscular blocker prior to the administration of succinylcholine, often 10% of a nondepolarizing NMB's induction dose.

Even if a drug such as caffeine causes fasciculations, that does not necessarily mean it is the only cause. For example, a very slight magnesium deficiency by itself (see below) might not be enough for fasciculations to occur, but when combined with caffeine, the two factors together could be enough.

Motor unit

A motor unit is made up of a motor neuron and the skeletal muscle fibers innervated by that motor neuron's axonal terminals.

Groups of motor units often work together to coordinate the contractions of a single muscle; all of the motor units within a muscle are considered a motor pool. The concept was proposed by Charles Scott Sherrington.

All muscle fibers in a motor unit are of the same fiber type. When a motor unit is activated, all of its fibers contract. In vertebrates, the force of a muscle contraction is controlled by the number of activated motor units.

The number of muscle fibers within each unit can vary within a particular muscle and even more from muscle to muscle; the muscles that act on the largest body masses have motor units that contain more muscle fibers, whereas smaller muscles contain fewer muscle fibers in each motor unit. For instance, thigh muscles can have a thousand fibers in each unit, while extraocular muscles might have ten.

Muscles which possess more motor units (and thus have greater individual motor neuron innervation) are able to control force output more finely.

Motor units are organized slightly differently in invertebrates; each muscle has few motor units (typically less than 10), and each muscle fiber is innervated by multiple neurons, including excitatory and inhibitory neurons.

Thus, while in vertebrates the force of contraction of muscles is regulated by how many motor units are activated, in invertebrates it is controlled by regulating the balance between excitatory and inhibitory signals.

Recruitment (vertebrate)

The central nervous system is responsible for the orderly recruitment of motor neurons, beginning with the smallest motor units. Henneman's size principle indicates that motor units are recruited from smallest to largest based on the size of the load. For smaller loads requiring less force, slow twitch, low-force, fatigue-resistant muscle fibers are activated prior to the recruitment of the fast twitch, high-force, less fatigue-resistant muscle fibers. Larger motor units are typically composed of faster muscle fibers that generate higher forces.

The central nervous system has two distinct ways of controlling the force produced by a muscle through motor unit recruitment: spatial recruitment and temporal recruitment.

Spatial recruitment is the activation of more motor units to produce a greater force. Larger motor units contract along with small motor units until all muscle fibers in a single muscle are activated, thus producing the maximum muscle force. Temporal motor unit recruitment, or rate coding, deals with the frequency of activation of muscle fiber contractions.

Consecutive stimulation on the motor unit fibers from the alpha motor neuron causes the muscle to twitch more frequently until the twitches "fuse" temporally. This produces a greater force than singular contractions by decreasing the interval between stimulations to produce a larger force with the same number of motor units.

Using electromyography (EMG), the neural strategies of muscle activation can be measured. Ramp-force threshold refers to an index of motor neuron size in order to test the size principle. This is tested by determining the recruitment threshold of a motor unit during isometric contraction in which the force is gradually increased.

Motor units recruited at low force (low-threshold units) tend to be small motor units, while high-threshold units are recruited when higher forces are needed and involve larger motor neurons.
These tend to have shorter contraction times than the smaller units. The number of additional motor units recruited during a given increment of force declines sharply at high levels of voluntary force. This suggests that, even though high threshold units generate more tension, the contribution of recruitment to increase voluntary force declines at higher force levels.

To test motor unit stimulation, electrodes are placed extracellularly on the skin and an intramuscular stimulation is applied.

After the motor unit is stimulated, its pulse is then recorded by the electrode and displayed as an action potential, known as a motor unit action potential (MUAP). When multiple MUAP's are recorded within a short time interval, a motor unit action potential train (MUAPT) is then noted.

The time in between these pulses is known as the inter-pulse interval (IPI). In medical electrodiagnostic testing for a patient with weakness, careful analysis of the MUAP size, shape, and recruitment pattern can help in distinguishing a myopathy from a neuropathy.

Motor unit types (vertebrate)

Motor units are generally categorized based upon the similarities between several factors:

Physiological
Contraction speed in Isometric contractions

Rate of rise of force
Time to peak of a twitch contraction (response to a single nerve impulse)
FF — Fast fatigable — high force, fast contraction speed but fatigue in a few seconds.

FR — Fast fatigue resistant — intermediate force, fatigue resistant — fast contraction speed and resistant to fatigue.
FI — Fast intermediate — intermediate between FF and FR.
S or SO — Slow (oxidative) — low force, slower contraction speed, highly fatigue resistant.

Biochemical
Histochemical (the oldest form of biochemical fiber typing)
Glycolytic enzyme activity (e.g. glycerophosphate dehydrogenase (GPD))
Oxidative enzyme activity (e.g. succinate dehydrogenase -SDH)
Sensitivity of Myosin ATPase to acid and alkali
These generally designate fibers as:

I (Slow oxidative, SO) — Low glycolytic and high oxidative presence. Low(er) myosin ATPase, sensitive to alkali.
IIa (Fast oxidative/glycolytic, FOG) — High glycolytic, oxidative and myosin ATPase presence, sensitive to acid.
IIb (Fast glycolytic, FG) — High glycolytic and myosin ATPase presence, sensitive to acid. Low oxidative presence.
IIi — fibers intermediate between IIa and IIb

Histochemical and Physiological types correspond as follows:

S and Type I, FR and type IIa, FF and type IIb, FI and IIi.

Immunohistochemical (a more recent form of fiber typing)

Myosin Heavy Chain (MHC)

Myosin Light Chain — alkali (MLC1)

Myosin Light Chain — regulatory (MLC2)

The Immunohistochemical types are as follows, with the type IIa, IIb and slow corresponding to IIa, IIb and slow (type I) histochemical types

Summation, in physiology, the additive effect of several electrical impulses on a neuromuscular junction, the junction between a nerve cell and a muscle cell.

Individually the stimuli cannot evoke a response, but collectively they can generate a response.

Successive stimuli on one nerve are called temporal summation; the addition of simultaneous stimuli from several conducting fibres is called spatial summation.

Summation, which includes both spatial and temporal summation, is the process that determines whether or not an action potential will be generated by the combined effects of excitatory and inhibitory signals, both from multiple simultaneous inputs (spatial summation), and from repeated inputs (temporal summation).

Depending on the sum total of many individual inputs, summation may or may not reach the threshold voltage to trigger an action potential

1. 

facilitation

2. 

inhibition

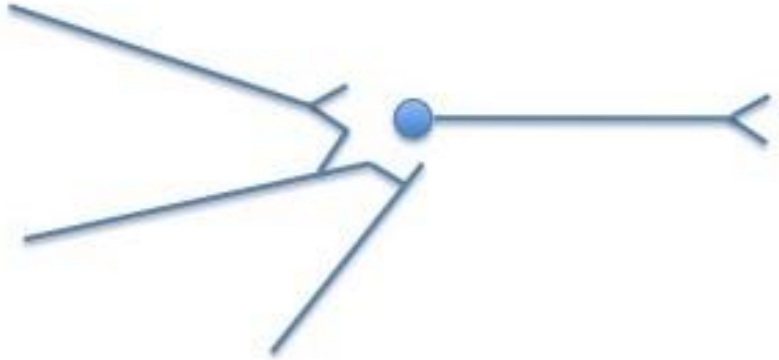
3. 

disfacilitation

disinhibition

4.

5. Spatial Summation



6. Temporal Summation

Basic ways that neurons can interact with each other when convertin g input to output

Neurotransmitters released from the terminals of a presynaptic neuron fall under one of two categories, depending on the ion channels gated or modulated by the neurotransmitter receptor.

Excitatory neurotransmitters produce depolarization of the postsynaptic cell, whereas the hyperpolarization produced by an inhibitory neurotransmitter will mitigate the effects of an excitatory neurotransmitter.

This depolarization is called an EPSP, or an excitatory postsynaptic potential, and the hyperpolarization is called an IPSP, or an inhibitory postsynaptic potential

The only influences that neurons can have on one another are excitation, inhibition, and—through modulatory transmitters—biasing one another's excitability.

From such a small set of basic interactions, a chain of neurons can produce only a limited response. A pathway can be facilitated by excitatory input; removal of such input constitutes disfacillitation.

A pathway may also be inhibited; removal of inhibitory input constitutes disinhibition, which, if other sources of excitation are present in the inhibitory input, can augment excitation.

When a given target neuron receives inputs from multiple sources, those inputs can be spatially summated if the inputs arrive closely enough in time that the influence of the earliest-arriving inputs has not yet decayed.

If a target neuron receives input from a single axon terminal and that input occurs repeatedly at short intervals, the inputs can summate temporally.

Types

At any given moment, a neuron may receive postsynaptic potentials from thousands of other neurons.

Whether threshold is reached, and an action potential generated, depends upon the spatial (i.e. from multiple neurons) and temporal (from a single neuron) summation of all inputs at that moment.

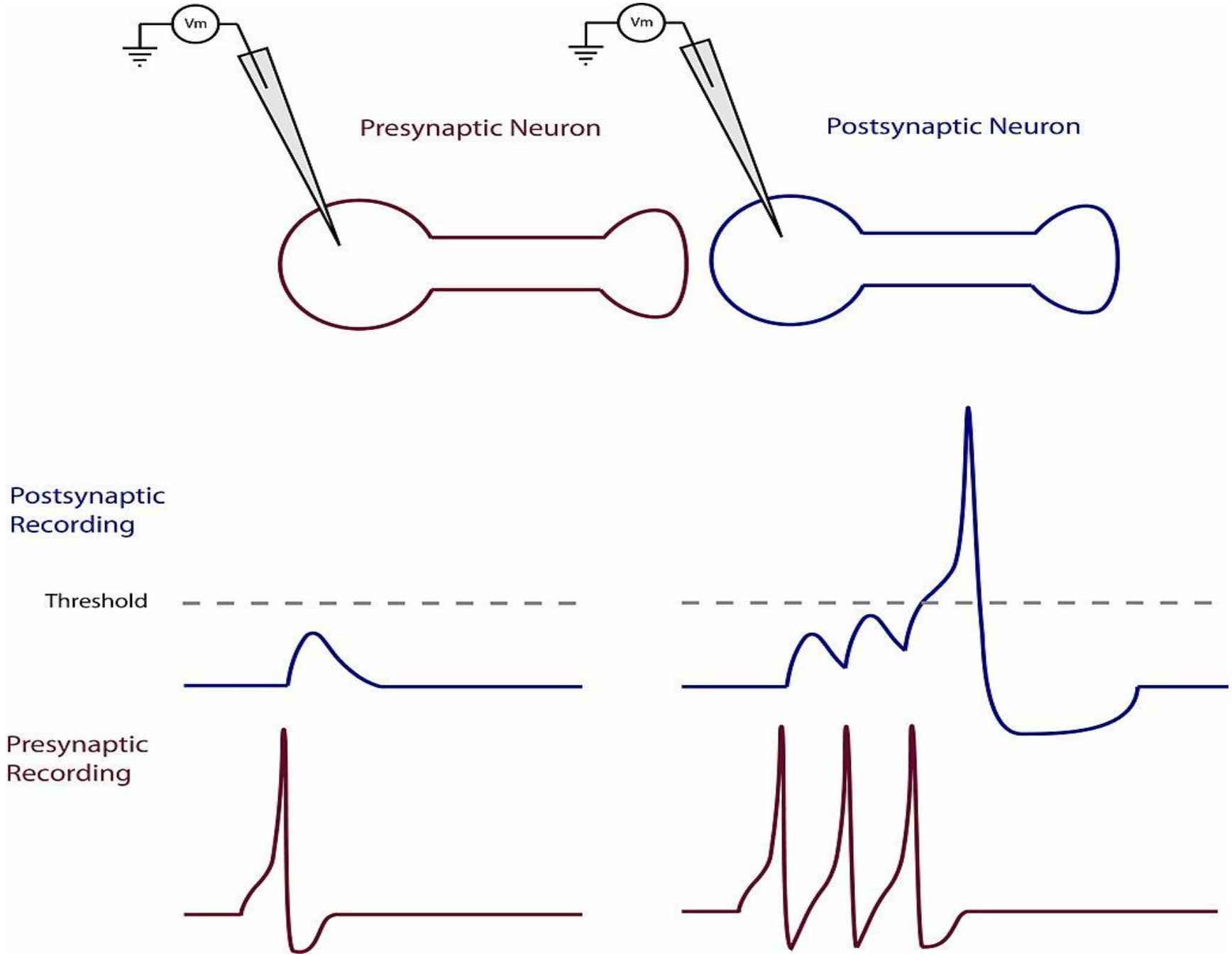
It is traditionally thought that the closer a synapse is to the neuron's cell body, the greater its influence on the final summation.

This is because postsynaptic potentials travel through dendrites which contain a low concentration of voltage-gated ion channels.

Therefore, the postsynaptic potential attenuates by the time it reaches the neuron cell body. The neuron cell body acts as a computer by integrating (adding or summing up) the incoming potentials.

The net potential is then transmitted to the axon hillock, where the action potential is initiated.

Another factor that should be considered is the summation of excitatory and inhibitory synaptic inputs. The spatial summation of an inhibitory input will nullify an excitatory input. This widely observed effect is called inhibitory 'shunting' of EPSPs


Vm
Vm
Presynaptic Neuron
Postsynaptic Neuron
Postsynaptic Recording
Threshold
Presynaptic Recording

Spatial summation

Spatial summation is a mechanism of eliciting an action potential in a neuron with input from multiple presynaptic cells. It is the algebraic summing of potentials from different areas of input, usually on the dendrites.

Summation of excitatory postsynaptic potentials increases the probability that the potential will reach the threshold potential and generate an action potential, whereas summation of inhibitory postsynaptic potentials can prevent the cell from achieving an action potential.

The closer the dendritic input is to the axon hillock, the more the potential will influence the probability of the firing of an action potential in the postsynaptic cell

Temporal summation

Temporal summation occurs when a high frequency of action potentials in the presynaptic neuron elicits postsynaptic potentials that summate with each other.

The duration of a postsynaptic potential is longer than the interval between action potentials. If the time constant of the cell membrane is sufficiently long, as is the case for the cell body, then the amount of summation is increased.

The amplitude of one postsynaptic potential at the time point when the next one begins will algebraically summate with it, generating a larger potential than the individual potentials. This allows the membrane potential to reach the threshold to generate an action potential

Mechanism

Neurotransmitters bind to receptors which open or close ion channels in the postsynaptic cell creating postsynaptic potentials (PSPs). These potentials alter the chances of an action potential occurring in a postsynaptic neuron. PSPs are deemed excitatory if they increase the probability that an action potential will occur, and inhibitory if they decrease the chances.

Glutamate as an excitatory example

The neurotransmitter glutamate, for example, is predominantly known to trigger excitatory postsynaptic potentials (EPSPs) in vertebrates. Experimental manipulation can cause the release of the glutamate through the non-tetanic stimulation of a presynaptic neuron.

Glutamate then binds to AMPA receptors contained in the postsynaptic membrane causing the influx of positively charged sodium atoms. This inward flow of sodium leads to a short term depolarization of the postsynaptic neuron and an EPSP. While a single depolarization of this kind may not have much of an effect on the postsynaptic neuron, repeated depolarizations caused by high frequency stimulation can lead to EPSP summation and to surpassing the threshold potential.

GABA as an inhibitory example

In contrast to glutamate, the neurotransmitter GABA mainly functions to trigger inhibitory postsynaptic potentials (IPSPs) in vertebrates.

The binding of GABA to a postsynaptic receptor causes the opening of ion channels that either cause an influx of negatively charged chloride ions into the cell or an efflux of positively charged potassium ions out of the cell.

The effect of these two options is the hyperpolarization of the postsynaptic cell, or IPSP. Summation with other IPSPs and contrasting EPSPs determines whether the postsynaptic potential will reach threshold and cause an action potential to fire in the postsynaptic neuron.

EPSP and depolarization

As long as the membrane potential is below threshold for firing impulses, the membrane potential can summate inputs. That is, if the neurotransmitter at one synapse causes a small depolarization, a simultaneous release of transmitter at another synapse located elsewhere on the same cell body will summate to cause a larger depolarization.

This is called spatial summation and is complemented by temporal summation, wherein successive releases of transmitter from one synapse will cause progressive polarization change as long as the presynaptic changes occur faster than the decay rate of the membrane potential changes in the postsynaptic neuron.

Neurotransmitter effects last several times longer than presynaptic impulses, and thereby allow summation of effect. Thus, the EPSP differs from action potentials in a fundamental way: it summates inputs and expresses a graded response, as opposed to the all-or-none response of impulse discharge.

IPSP and hyperpolarization

At the same time that a given postsynaptic neuron is receiving and summating excitatory neurotransmitter, it may also be receiving conflicting messages that are telling it to shut down firing. These inhibitory influences (IPSPs) are mediated by inhibitory neurotransmitter systems that cause postsynaptic membranes to hyperpolarize.

Such effects are generally attributed to the opening of selective ion channels that allow either intracellular potassium to leave the postsynaptic cell or to allow extracellular chloride to enter. In either case, the net effect is to add to the intracellular negativity and move the membrane potential farther away from the threshold for generating impulses.

TETANUS

tetanus: When the frequency of muscle contraction is such that the maximal force is tension is generated without any relaxation of the muscle. ... Tetanus is an infection caused by a bacterium called Clostridium tetani. Spores of tetanus bacteria are everywhere in the environment, including soil, dust, and manure. The spores develop into bacteria when they enter the body.

twitch: The period of contraction and relaxation of a muscle after a single stimulation. A single contraction is called a twitch.

A muscle twitch has a latent period, a contraction phase, and a relaxation phase. A graded muscle response allows variation in muscle tension.

Tetanic contraction

A tetanic contraction (also called tetanized state, tetanus, or physiologic tetanus, the latter to differentiate from the disease called tetanus) is a sustained muscle contraction evoked when the motor nerve that innervates a skeletal muscle emits action potentials at a very high rate. During this state, a motor unit has been maximally stimulated by its motor neuron and remains that way for some time. This occurs when a muscle's motor unit is stimulated by multiple impulses at a sufficiently high frequency. Each stimulus causes a twitch. If stimuli are delivered slowly enough, the tension in the muscle will relax between successive twitches. If stimuli are delivered at high frequency, the twitches will overlap, resulting in tetanic contraction. A tetanic contraction can be either unfused (incomplete) or fused (complete).

An unfused tetanus is when the muscle fibers do not completely relax before the next stimulus because they are being stimulated at a fast rate; however there is a partial relaxation of the muscle fibers between the twitches.
Fused tetanus is when there is no relaxation of the muscle fibers between stimuli and it occurs during a high rate of stimulation. A fused tetanic contraction is the strongest single-unit twitch in contraction.

When tetanized, the contracting tension in the muscle remains constant in a steady state. This is the maximal possible contraction.

During tetanic contractions, muscles can shorten, lengthen or remain constant length.

Tetanic contraction is usually normal (such as when holding up a heavy box). Muscles often exhibit some level of tetanic activity, leading to muscle tone, in order to maintain posture; for example, in a crouching position, some muscles require sustained contraction to hold the position.

Tetanic contraction can exist in a variety of states, including isotonic and isometric forms—for example, lifting a heavy box off the floor is isotonic, but holding it at the elevated position is isometric.

Voluntary sustained contraction is a normal (physiologic) process (as in the crouching or box-holding examples), but involuntary sustained contraction exists on a spectrum from physiologic to disordered (pathologic).

Muscle tone is a healthy form of involuntary sustained partial contraction. In comparison with tetanic contraction in an isometric state (such as holding up a heavy box for several minutes), it differs only in the percentage of motor units participating at any moment and the frequency of neural signals; but the low percentage and low frequency in healthy tone are the key factors defining it as healthy (and not tetanic).

Involuntary sustained contraction of a hypertonic type, however, is a pathologic process.

On the mild part of the spectrum, cramps, spasms, and even tetany are often temporary and nonsevere.

On the moderate to severe parts of the spectrum are dystonia, trismus, pathologic tetanus, and other movement disorders featuring involuntary sustained strong contractions of skeletal muscle.

THANK YOU