Al-Mazaya University College
Department of Medical Lab Technology

Human Physiology

Lecture No. 2

Physiology of the Muscular System

(Neuro muscular)

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The **muscular system**

- The **muscular system** is the biological system of humans that **produces movement**. The muscular system, in vertebrates, is controlled through the **nervous system**, although some muscles, like cardiac muscle, can be completely autonomous.

- Thus, the nervous and muscle systems are closely **interconnected.** The nervous system 'communicates' with muscle via **neuromuscular** (**myoneural**) **junctions**. These junctions work very much like a synapse between neurons.

Functions of muscular system

- 1. **Locomotion**
- 2. **Vasoconstriction** and **vasodilatation**- constriction and dilation of blood vessel Walls are the results of smooth muscle contraction.
- 3. **Peristalsis –** wavelike motion along the digestive tract is produced by the Smooth muscle.
- 4. **Cardiac motion**
- 5. **Posture maintenance-** contraction of skeletal muscles maintains body posture and muscle tone.
- 6. **Heat generation –** about 75% of **ATP** energy used in muscle contraction is released as heat.

Muscle

- The muscle is a **contractile tissue** and is derived from the mesodermal layer of embryonic germ cells.
- Its function is to **produce force and cause motion**, either **locomotion or movement** within internal organs.
- Much of muscle contraction occurs **without conscious** and is necessary for survival, like the contraction of the **heart or peristalsis**, which pushes food through the digestive system.

Characteristics of muscle:

1. **Excitability** - responds to stimuli (e.g., nervous impulses)
2. **Contractility** - able to shorten in length
3. **Extensibility** - stretches when pulled
4. **Elasticity** - tends to return to original shape & length after contraction or extension.

Types of Muscles

- **1. Smooth muscle** or "**involuntary muscle**" consists of **spindle** shaped muscle cells found within the **walls of organs** and structures such as the esophagus, stomach, intestines, bronchi, uterus, ureters, bladder, and blood vessels. Smooth muscle cells contain only **one nucleus** and no striations.
- **2. Cardiac muscle** is also an **"involuntary muscle"** but it is **striated** in structure and appearance. Like smooth muscle, cardiac muscle cells contain only **one nucleus**. Cardiac muscle is found only within the heart.

Skeletal muscle

3. **Skeletal muscle or "voluntary muscle"** is anchored by tendons to the **bone** and is used to effect **skeletal movement** such as **locomotion**. Skeletal muscle cells are **multinucleated** with the nuclei peripherally located. Skeletal muscle is called **'striated'** because of the longitudinally **striped** appearance under light microscopy.

Functions

- a. **Support** of the body.
- b. Aids in **bone movement**.
- c. Helps maintain a constant body **temperature**.
- d. Assists with the movement of cardiovascular and **lymphatic vessels** through contractions.
- e. **Protection of internal organs** and contributing to joint stability.

Subtypes of Skeletal Muscles:

- **Type I: Slow Twitch, Slow oxidative, or "Red" Muscles**
- These are dense with **capillaries** and **rich in mitochondria** and myoglobin, giving the muscle tissue its characteristic red color. It can carry **more oxygen** and sustain **aerobic** activity. They are designed for **enduration** , and can contract for **long periods** of time (ex. Solues) .
- **Type II: Fast Twitch, "White " Muscles**
- White or fast skeletal muscle fibers , have **few mitochondria** , **reduced ability** to carry on aerobic respiration and tend to **fatigue rapidly** . (ex. extra ocular muscles) . Designed for **speed** , fatigue easily.
-

Kinds of White Muscles

White muscles have three major kinds that are, **in order of increasing contractile speed**:

a) **Type IIa,** which, **like slow muscle**, is aerobic, **rich in mitochondria** and capillaries and **appears red.**

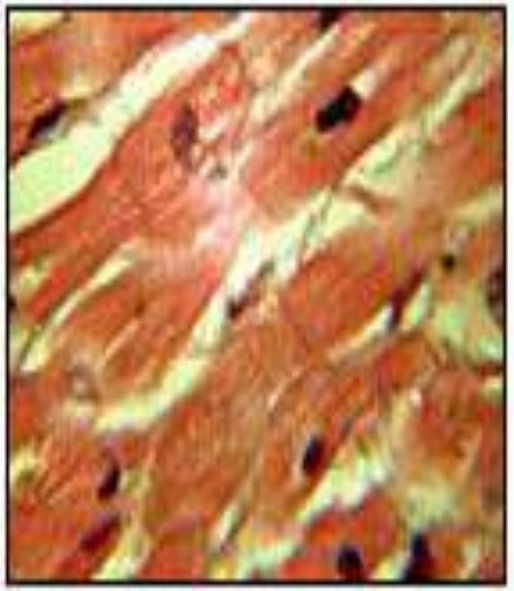
- b) **Type IIx** (also known as type IId), which is **less dense in mitochondria** and myoglobin. This is the **fastest** muscle type in humans. It can **contract more quickly** and with a greater amount of force than oxidative muscle, but can **sustain only short**, anaerobic bursts of activity before muscle contraction becomes **painful** (often attributed to a build-up of **lactic acid**).
- c) **Type IIb**, which is **anaerobic, glycolytic,** "white" muscle that is even less dense in mitochondria and myoglobin.

Comparison between Muscle Types

- Cardiac and skeletal muscles are **striated** in that they contain **sarcomere** and are packed into highly-regular arrangements of bundles; smooth muscle has neither. **Striated muscle** is often used in **short, intense bursts**, whereas **smooth muscle** sustains **longer or even near-permanent contractions.**
- **Nucleus:** smooth and cardiac muscles are uninculcated (one nucleus per cell), skeletal muscle is multinucleated (several nuclei per cell).
- **Transverse tubule (T tubule):** well developed in skeletal and cardiac muscles to transport calcium. Absent in smooth muscle.
- **Intercalated disk:** specialized intercellular junction that only occurs in **cardiac muscle**.
- **Control:** skeletal muscle is always under **voluntary** control, with some exceptions (the tongue and pili arrector muscles in the dermis). smooth and cardiac muscles are under **involuntary** control.

Skeletal muscle

Smooth muscle



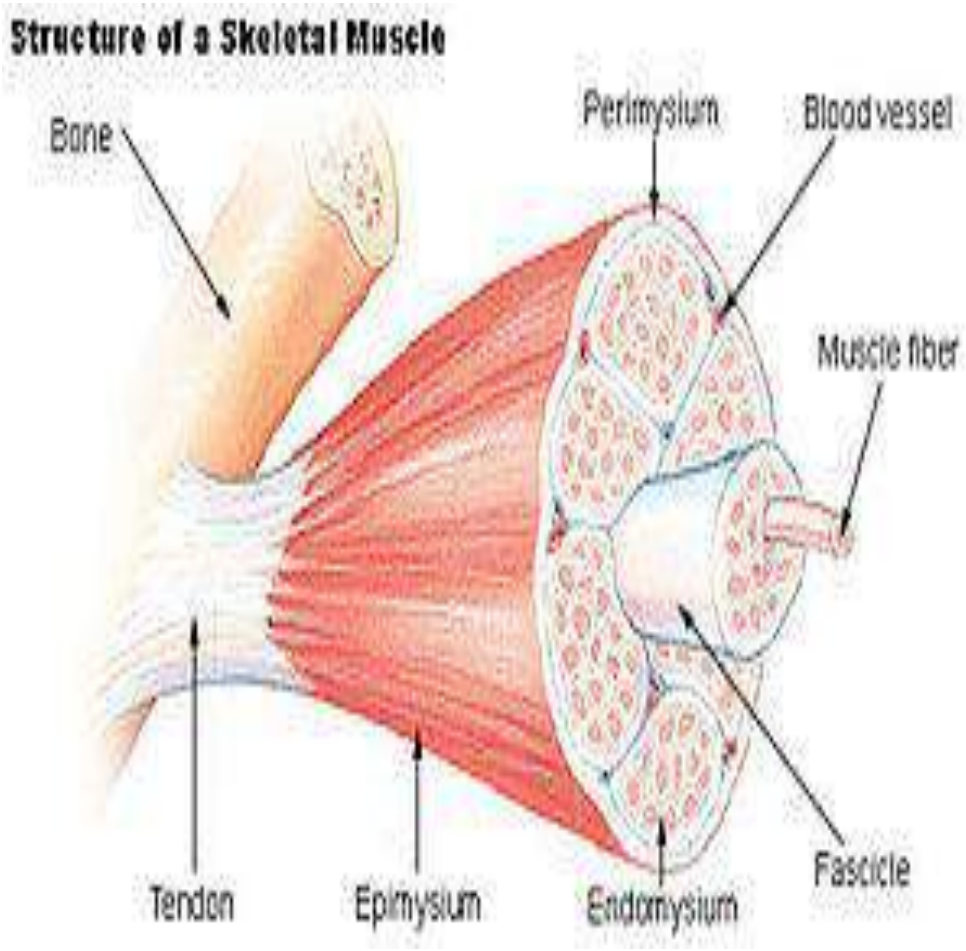
Cardiac muscle

Skeletal Muscle Structure

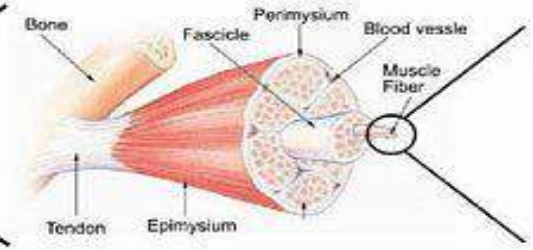
- **Muscle** is composed **of muscle cells** (sometimes known as "muscle **fibers**"). Within the cells are **myofibrils**; myofibrils contain **sarcomeres** which are composed of **actin and myosin**.

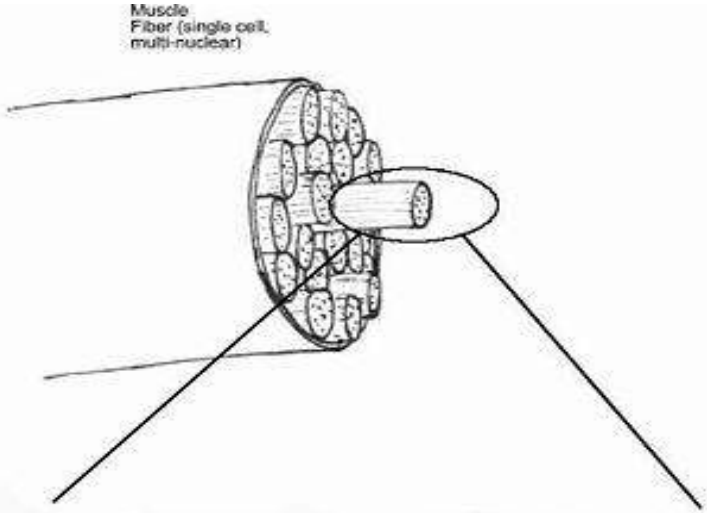
- Individual muscle cells are lined with **endomysium**.
- Muscle cells are bound together by **perimysium** into **bundles** called **fascicles**.
- These bundles are then grouped together to form muscle, and is lined by **epimysium**.

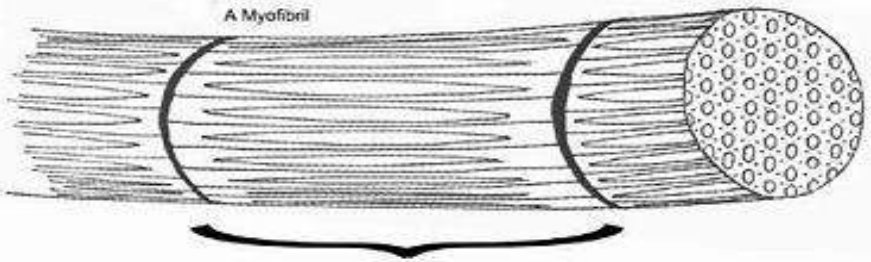
- Muscle **spindles** are distributed throughout the muscles, and provide sensory feedback information to the central nervous system.

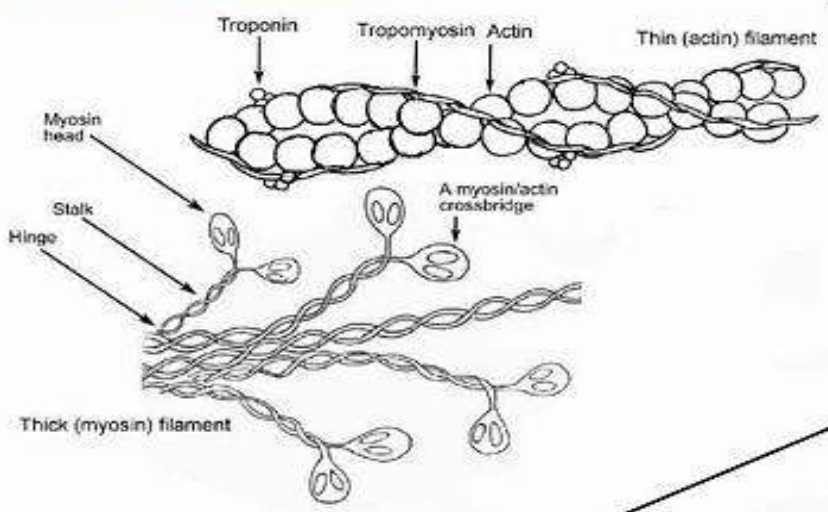


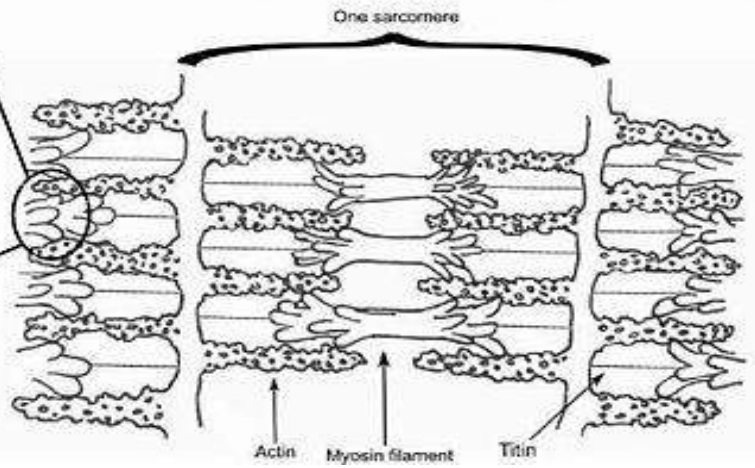
A top-down view of skeletal muscle











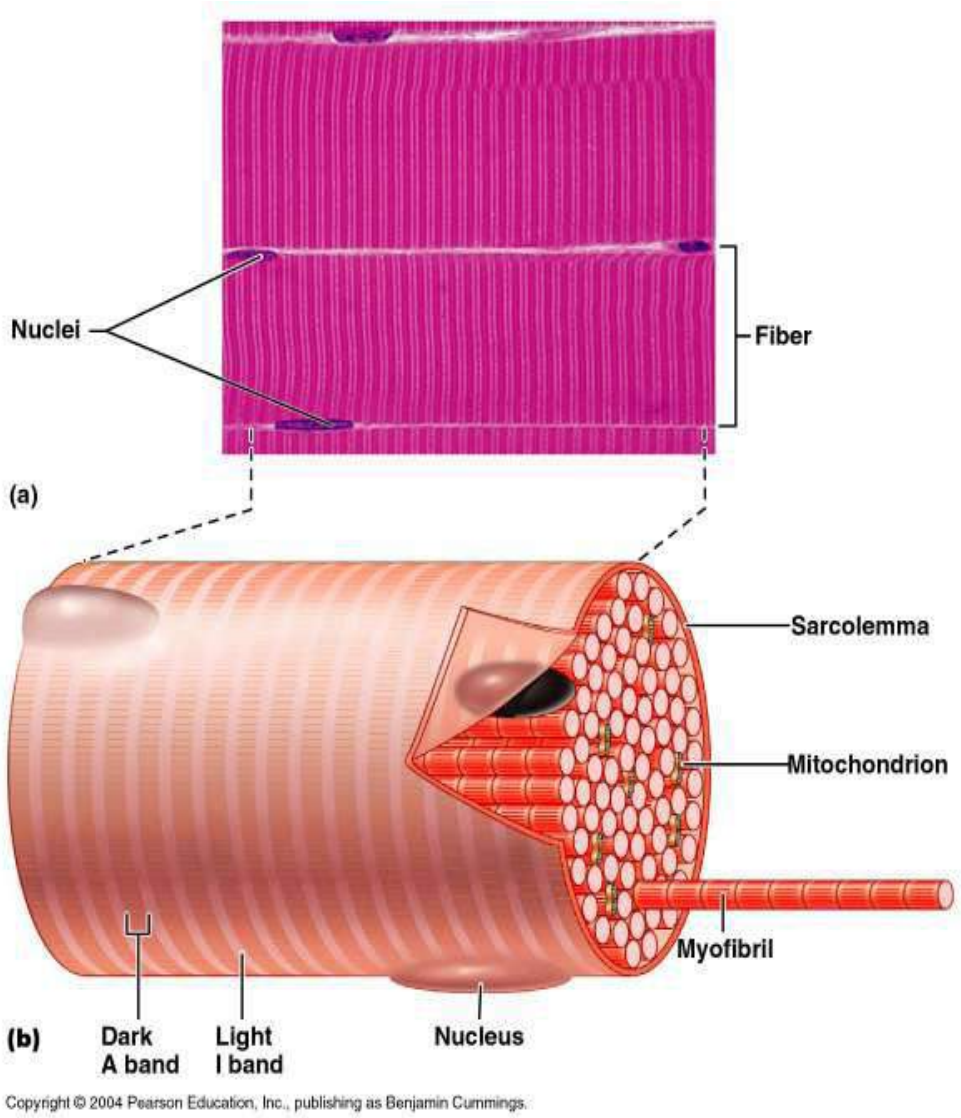
Skeletal Muscle Fiber (Muscle cell)

1. Each skeletal **muscle fiber** is a single muscle cell , which is the unit of contraction .
2. Muscle fibers are **cylindrical** cells with many nuclei .
3. The cell membrane is called . **Sarcolemma**, the cytoplasm is called **Sarcoplasm** .
4. The sarcoplasm contains abundant , parallel **thread** like **myofibrils** , that run in parallel fashion .
5. The myofibrils contain **2 kinds of protein filaments** .

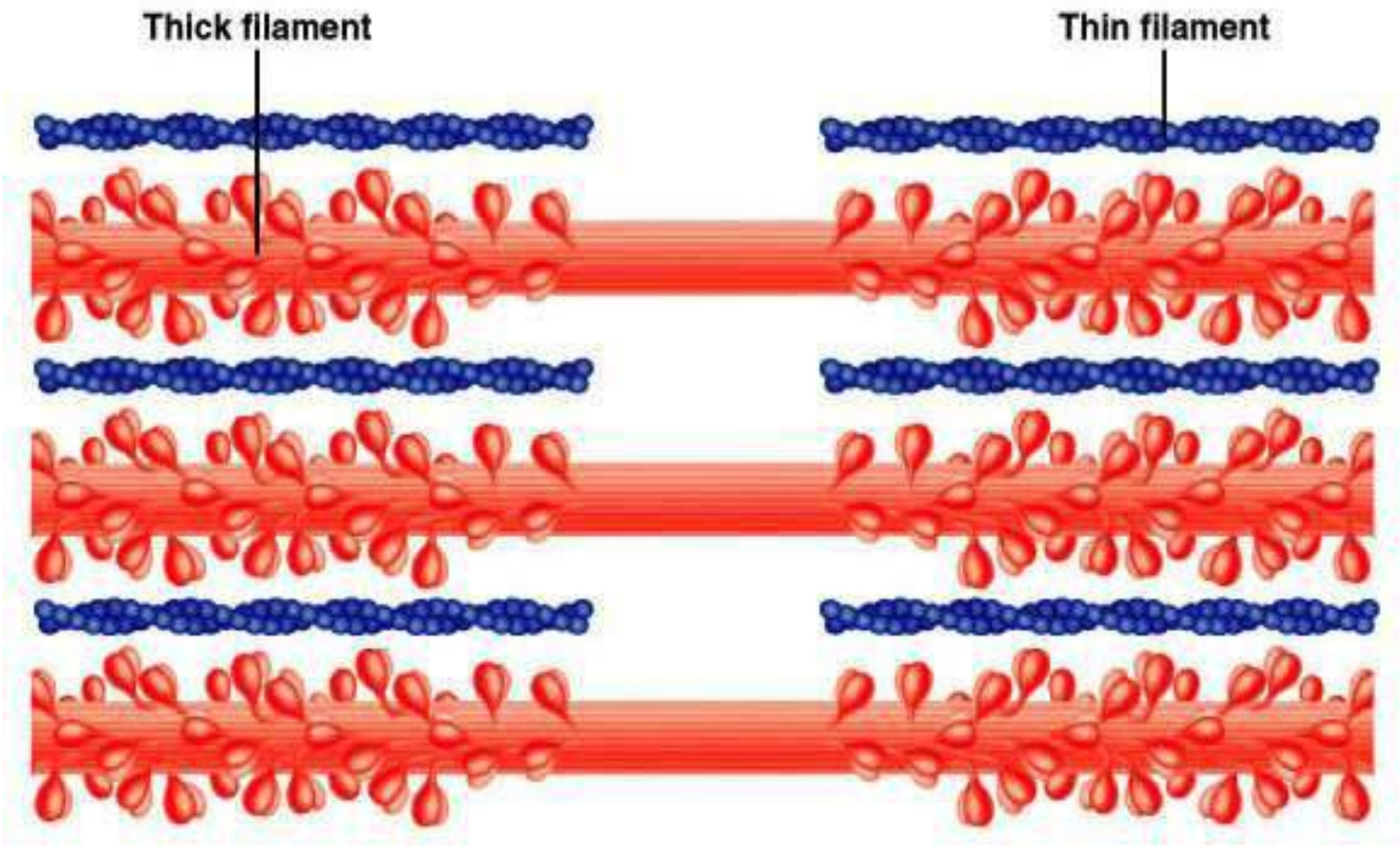
a. **Thick** filaments –composed of **Myosin** .

b. **Thin** filaments – composed of **Actin** , troponin and tropomyosin .

6. **Striations** are produced by alternating **light and dark** filaments .



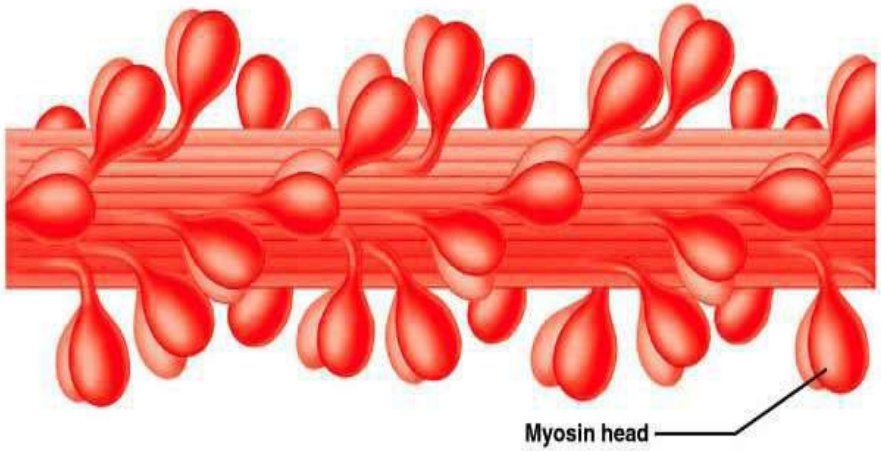
Arrangement of the Filaments in a Sarcomere



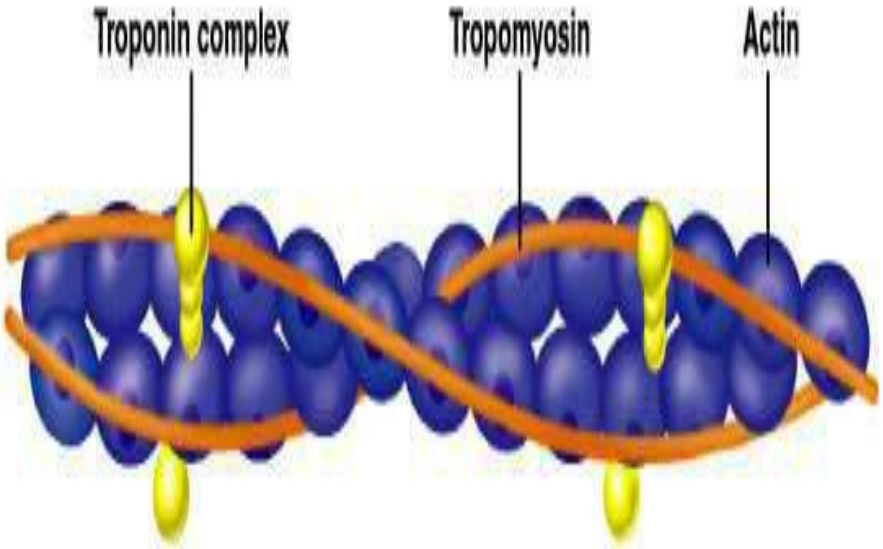
(d) Longitudinal section of filaments within one sarcomere of a myofibril

Thick (Myosin) & Thin (Actin) Filaments

(a) Myosin molecule



(b) Portion of a thick filament



(c) Portion of a thin filament

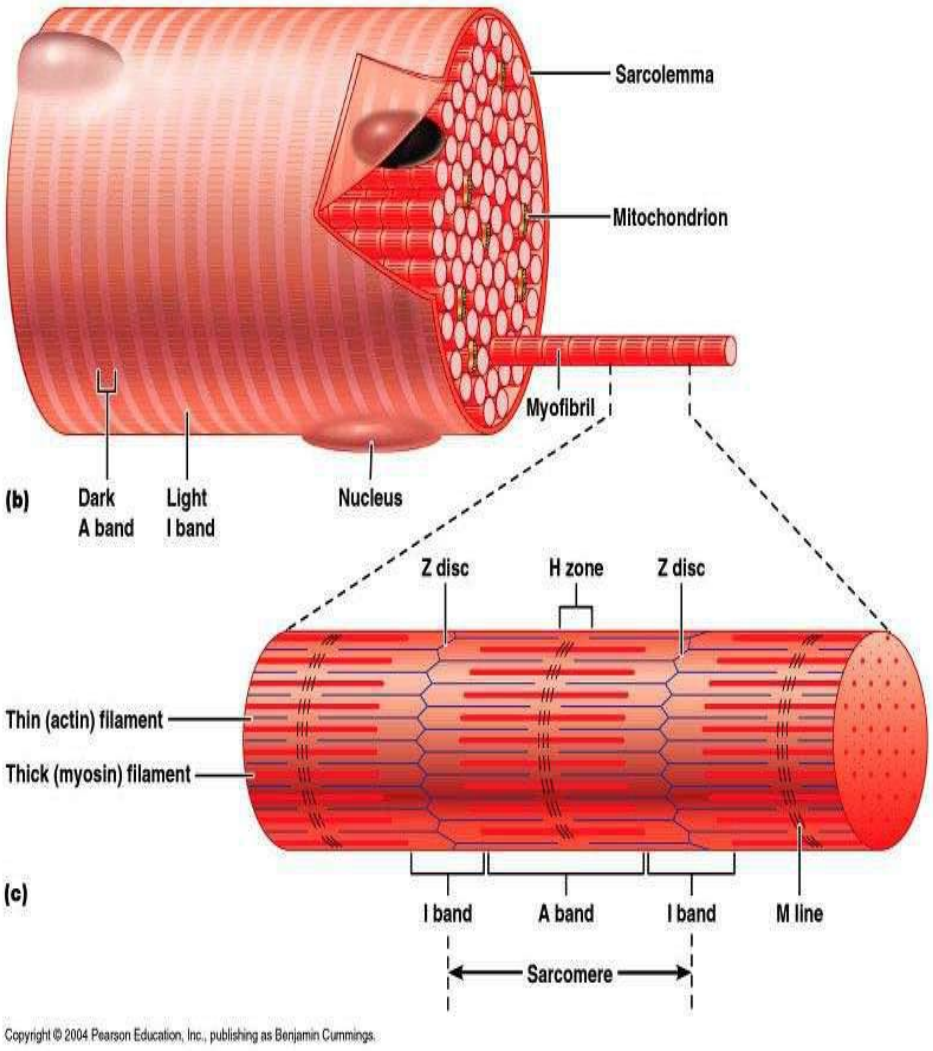
Striation pattern of skeletal muscles

1. **The I (light) bands** - Extends from the edge of one stack of thick filaments to the edge of next stack of thick filaments . The I band is composed of **thin actin** filaments.
2. **The A (dark) bands**– composed of **thick myosin** filaments **overlapping thin** filaments (actin) .

Myosin filaments are held together by **Z lines** (not attached) .

A band consist of a region where the thick and thin filaments overlap , and a region called **central** region (**H zone**) , consisting of **only thick** filaments.

In the center of A band is a **dark** band called the **M line**.



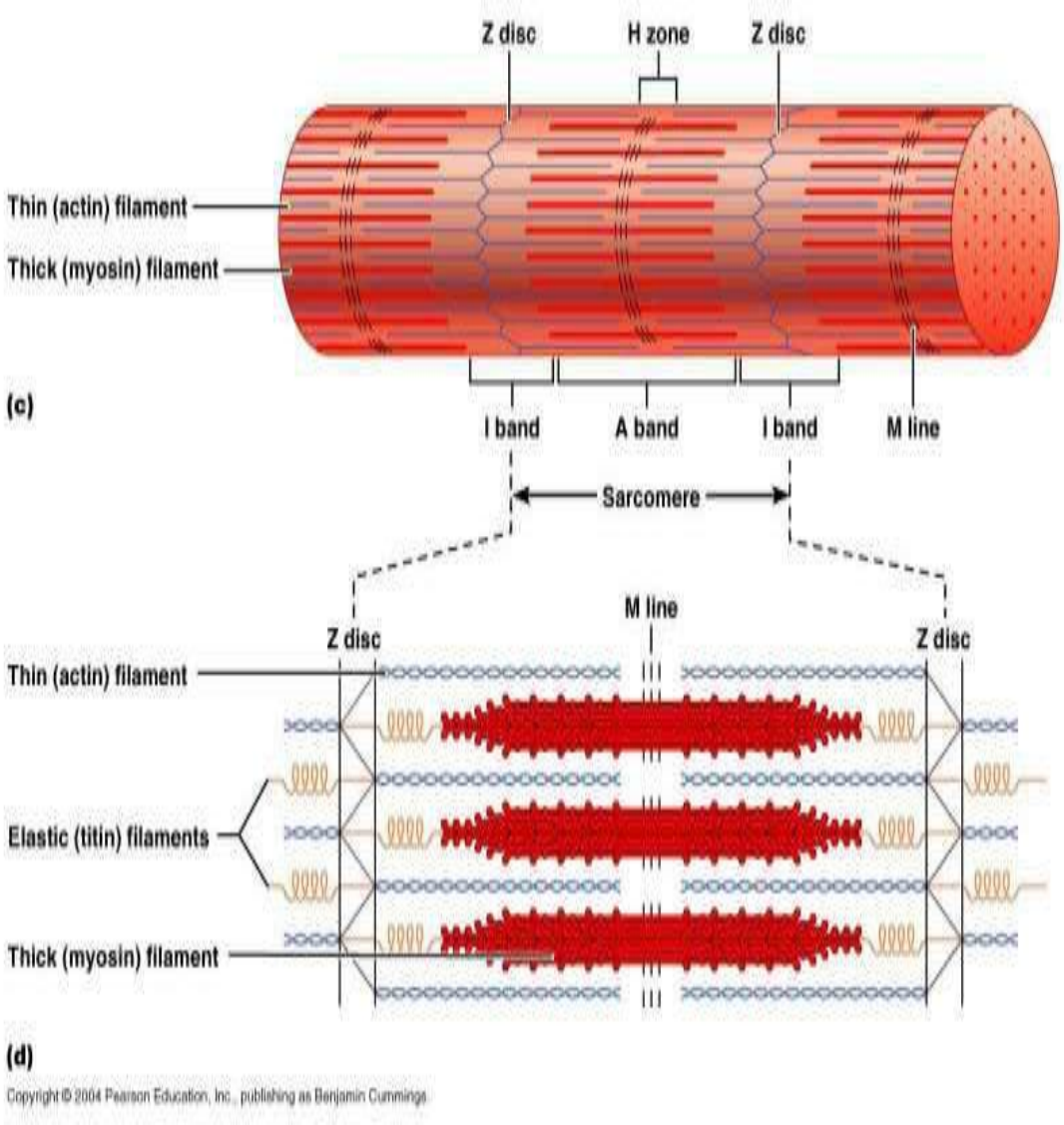
Striation pattern of skeletal muscles

Sarcomere : The segment of myofibrils that extends from one Z line to the next Z line.

Cross bridge Attachment:

The activated myosin heads are attracted to the exposed binding sites on actin and cross bridge attachment occurs.

Power stroke : The sliding action , which occurs at the same time for thousands of actin and myosin molecules is referred to as the power stroke .

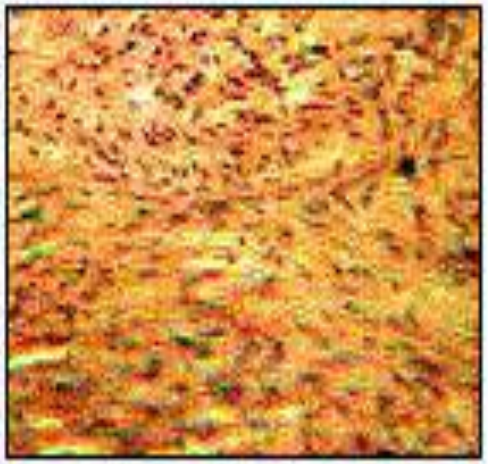


Muscle Contraction

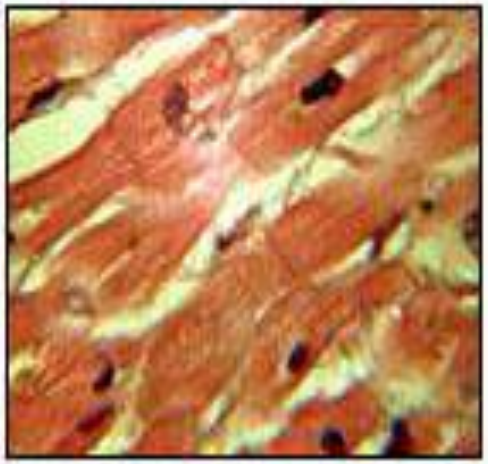
There are three general types of muscle contractions:

1. **Skeletal** muscle contractions.
2. **Heart** muscle contractions.
3. **Smooth** muscle contractions.

Skeletal muscle



Smooth muscle



Cardiac muscle

Muscle Response

- **All – or – none response**
- a. if a muscle fiber contracts at all , it will contract completely.
- b. motor units respond in an all – or – none manner .
- **Threshold stimulus** is the minimal stimulus needed to elicit a muscular contraction .
- **Twitch :** single , short contraction reflecting stimulation of some motor units in a muscle .
- **Latent period** is the time between stimulus and responding muscle contraction .
- **Refractory period** : During his period immediately following contraction , a muscle cannot respond .

General Types of Contractions

1. **Isometric** : when a muscle contracts but attachments do not move
2. **Isotonic** : when a muscle contracts and its ends are pulled together.
3. **Isokinetic** : when the force a muscle generates is less than that required to move or lift an object , the contraction is called isokinetic .

Detailed Types of Contractions

- 1. **Isometric contraction--** Muscle does not shorten during contraction and does not require the sliding of myofibrils but muscles are stiff.
- 2. **Isotonic contraction--** More energy is used by the muscle and contraction lasts longer than isometric contraction. Isotonic muscle contraction is divided into two categories:
- **2a. Concentric**, where the muscle fibers **shorten** as the muscle contracts (ie. biceps brachialis on the up phase of a biceps curl); and

  2b. Eccentric, where the muscle fibers **lengthen** as they contract (ie. biceps brachialis on the down phase of a biceps curl).
- 3. **Twitch**--Exciting the nerve to a muscle or by passing electrical stimulus through muscle itself. Some fibers contract quickly while others contract slowly.

Contraction and Relaxation

- For most muscles, contraction occurs as a result of conscious effort originating in **the brain**. The brain sends signals, in the form of **action potentials**, through the nervous system to the **motor neuron** that innervates the muscle fiber.
- However, some muscles (such as the **heart)** do not contract as a result of conscious effort. These are said to be **autonomic.**
- Also, it is not always necessary for the signals to originate from the brain. **Reflexes** are fast, unconscious muscular reactions that occur due to unexpected physical stimuli. The action potentials for reflexes originate in the **spinal cord** instead of the brain.

Principals of Contraction and Relaxation

1. While they differ in many regards, they all **use actin sliding against myosin** to create muscle contraction and relaxation.
2. A **motor nerve** and a **myofibril** form a **neuromuscular junction** where gap (called **synapse**) occurs between the two structures.
3. At the end of motor nerve, neurotransmitter (i.e. acetylcholine) is stored in **synaptic vesicles** which will release the neurotransmitter using exocytosis upon the stimulation of a nerve impulse.
4. In skeletal muscle, contraction is **stimulated** at each cell by **nervous impulses** that releases **acetylcholine** at the **neuromuscular junction**, creating **action potentials** along the cell membrane.
5. Across the synapse the surface the of myofibril contains **receptors** that can **bind** with the neurotransmitter.
6. All skeletal muscle and many smooth muscle contractions are **stimulated by the binding of the neurotransmitter acetylcholine.**

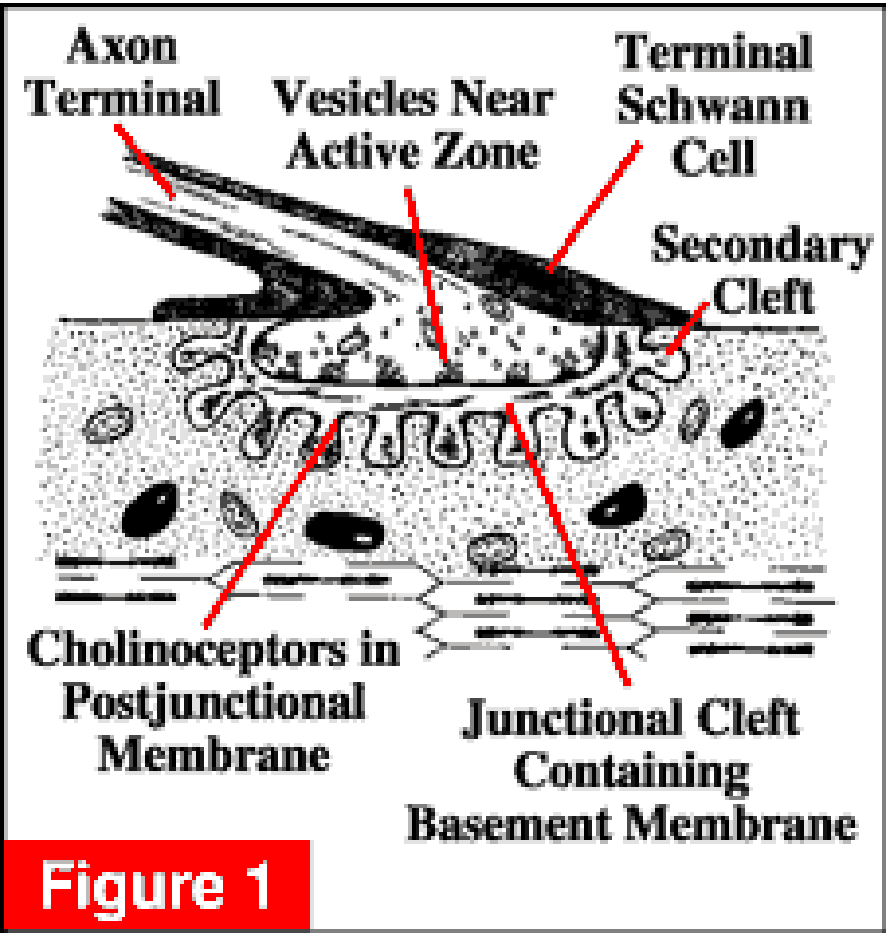
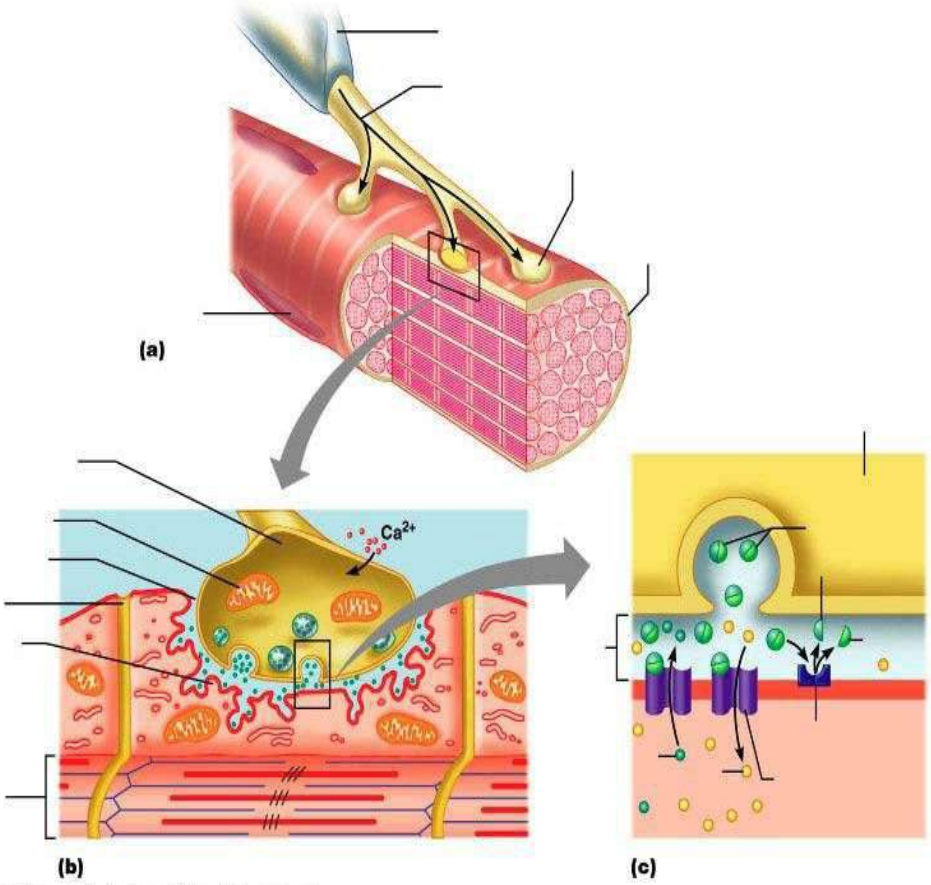


Figure 1

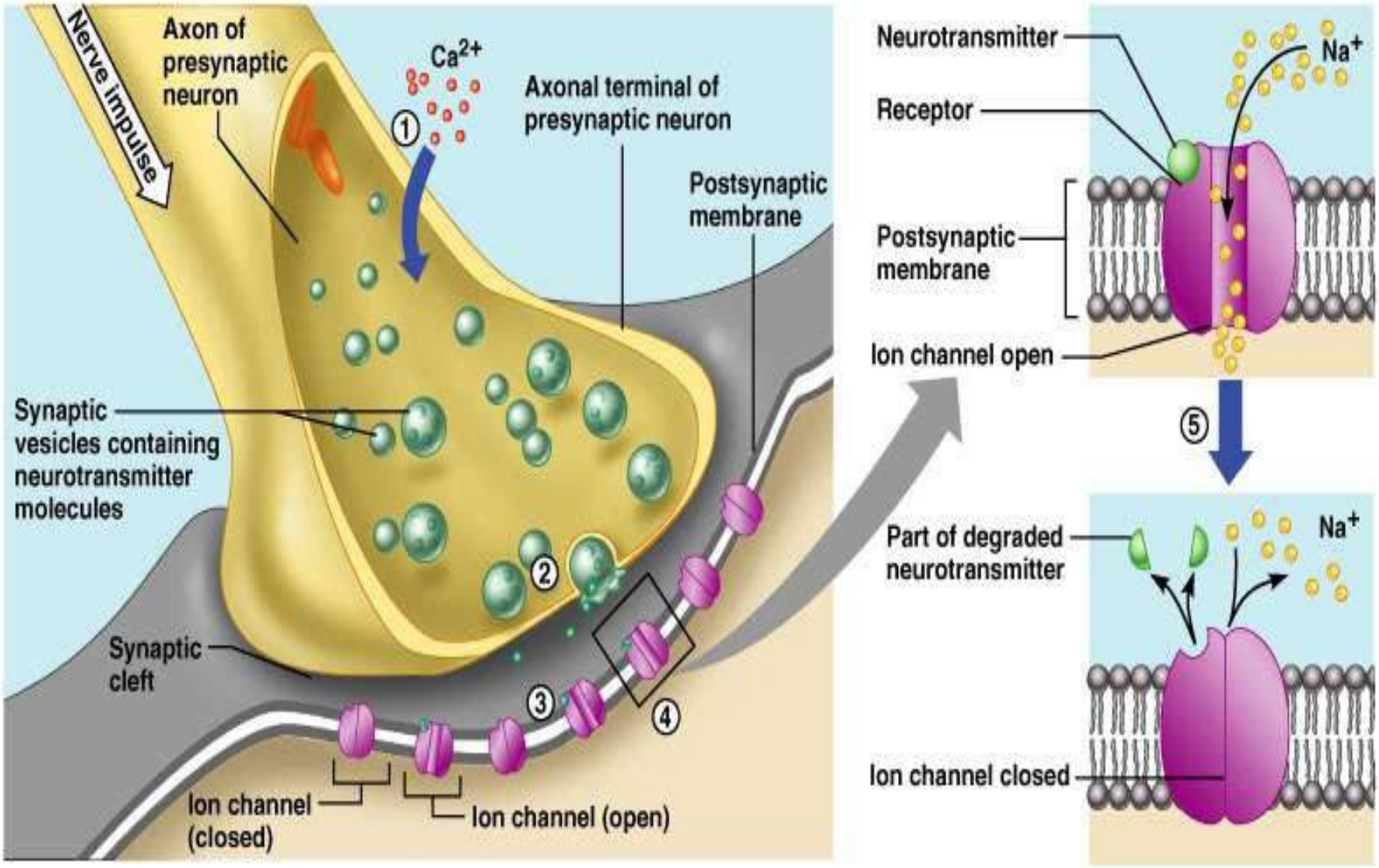


Summarized Steps of Skeletal Muscles Contraction

1. The distal end of a motor neuron releases Acetylcholine .
2. Acetylcholine diffuse across the gap at the neuromuscular junction .
3. The sarcolemma is stimulated , and a muscle impulse travels over the surface of the muscle fiber and deep into the fiber through the transverse tubules and reaches the sarcoplasmic reticulum .
4. Ca2+ ions diffuse from the sarcoplasmic reticulum into the sarcoplasm bind to troponin molecules .
5. Tropomyosin molecules move and expose specific sites on actin filament .
6. Actin and myosin filaments form linkages .
7. Actin filaments are pulled inward by myosin cross – bridges
8. Muscle fiber shortens as a contraction occurs .

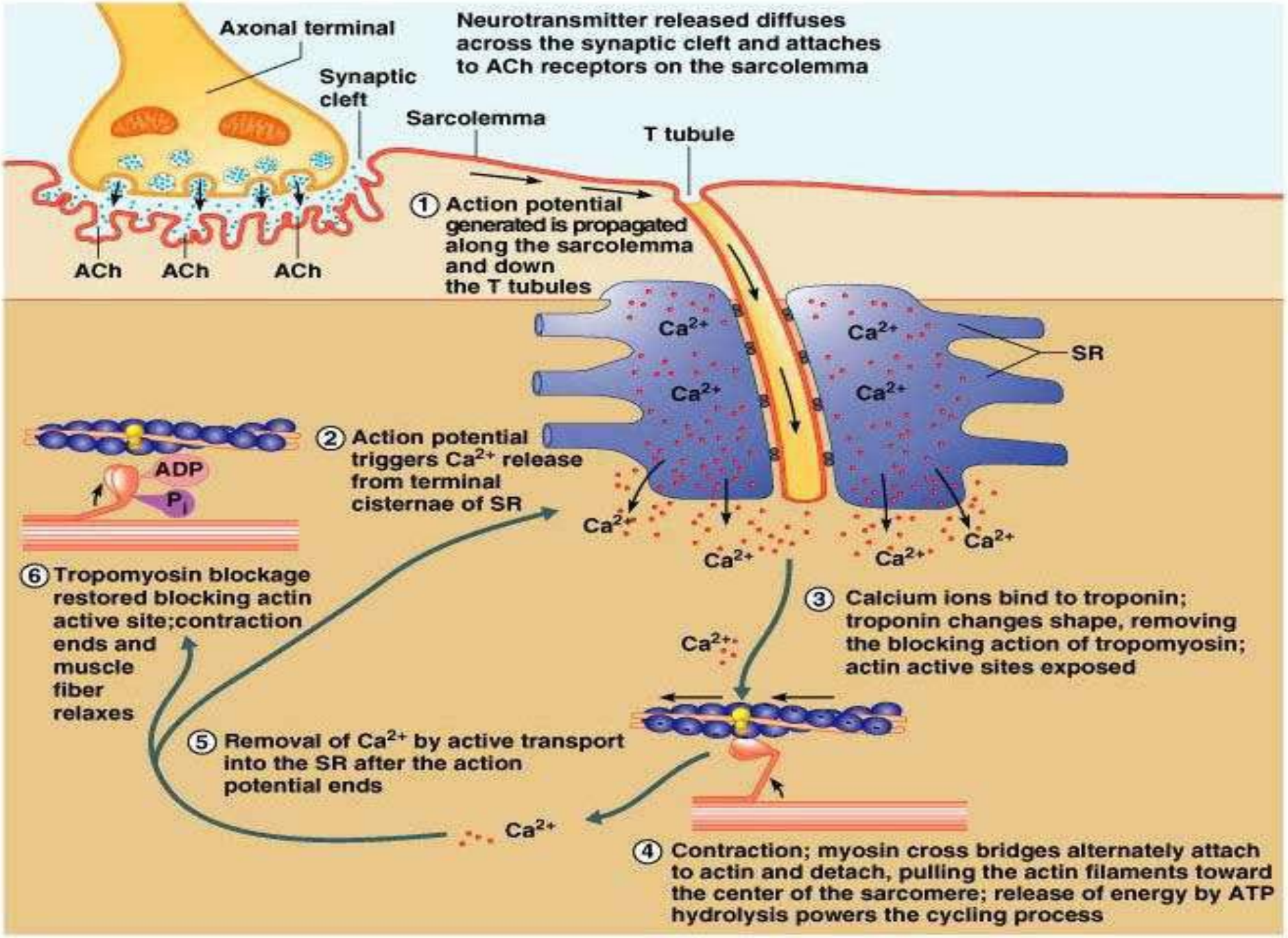
Detailed Steps of a skeletal muscle contraction

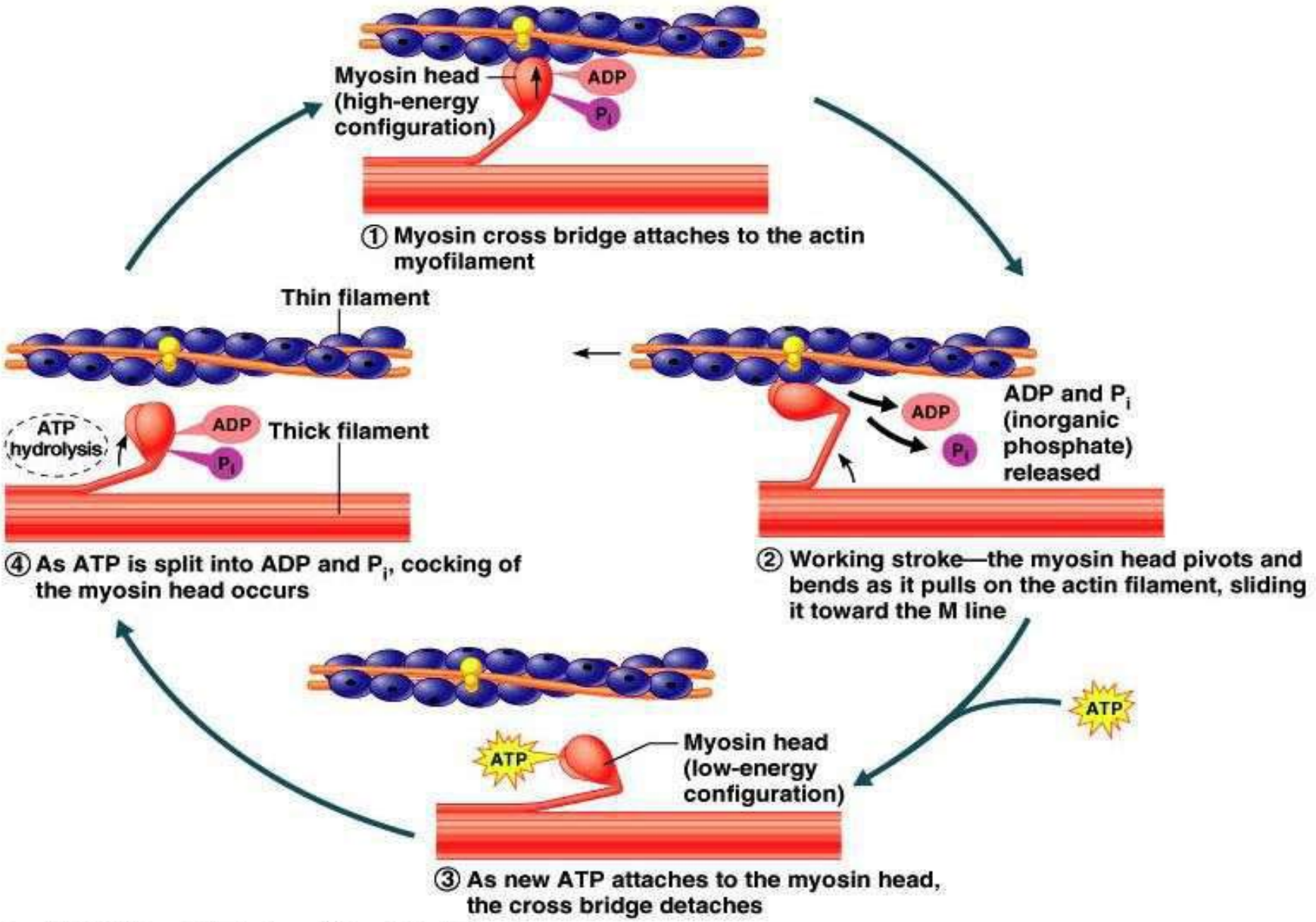
1. An action potential reaches the axon of the motor neuron.
2. The action potential activates voltage gated calcium ion channels on the axon, and calcium rushes in.
3. The calcium causes acetylcholine vesicles in the axon to fuse with the membrane, releasing the acetylcholine into the cleft between the axon and the motor end plate of the muscle fiber.
4. The skeletal muscle fiber is excited by large myelinated nerve fibers which attach to the neuromuscular junction.
5. The acetylcholine diffuses across the cleft and binds to nicotinic receptors on the motor end plate, opening channels in the membrane for sodium and potassium. Sodium rushes in, and potassium rushes out. However, because sodium is more permeable, the muscle fiber membrane becomes more positively charged, triggering an action potential.
6. The action potential on the muscle fiber causes the sarcoplasmic reticulum to release calcium ions (Ca++).

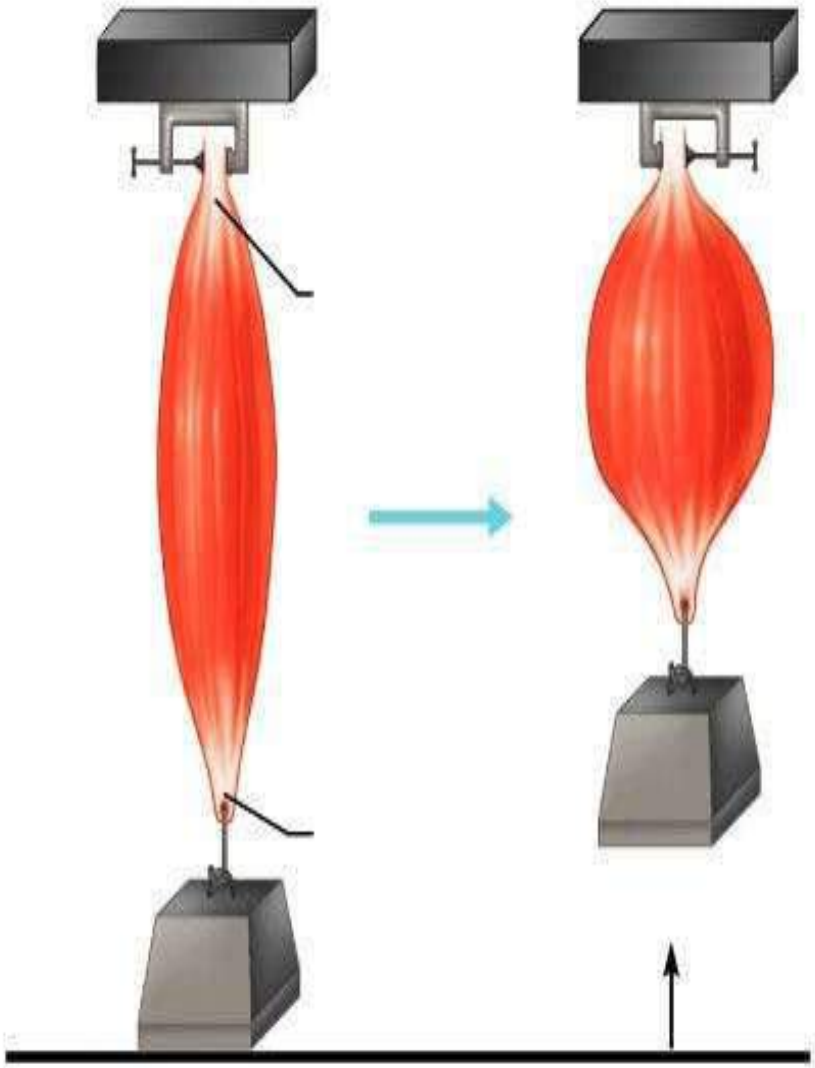


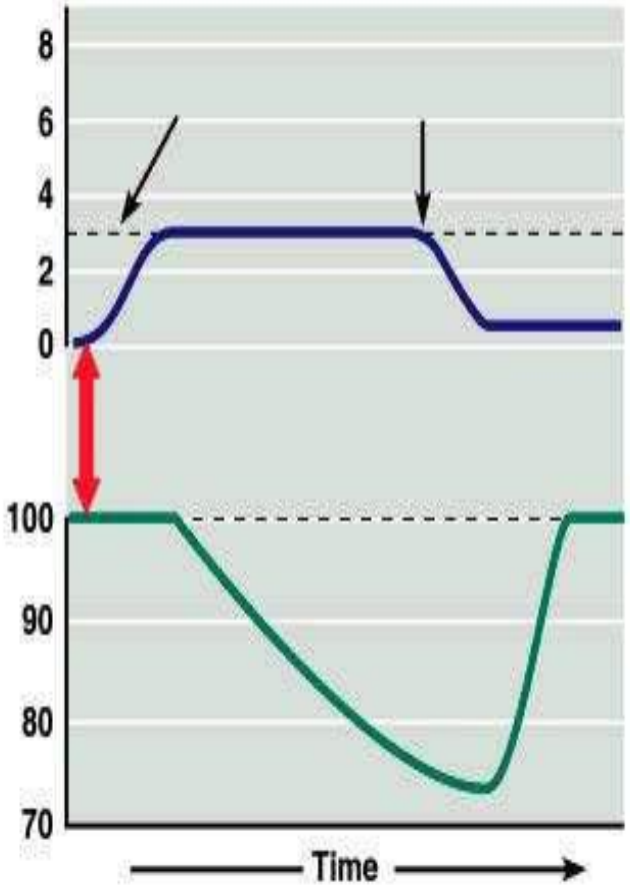
Detailed Steps of a skeletal muscle contraction

7. The calcium binds to the troponin present on the thin filaments of the myofibrils. The troponin then allosterically modulates the tropomyosin. Normally the tropomyosin physically obstructs binding sites for cross-bridge; once calcium binds to the troponin, the troponin forces the tropomyosin to move out of the way, unblocking the binding sites.
8. The cross-bridge (which is already in a ready-state) binds to the newly uncovered binding sites. It then delivers a power stroke.
9. ATP binds the cross-bridge, forcing it to conform in such a way as to break the actin-myosin bond. Another ATP is split to energize the cross bridge again.
10. Steps 7 and 8 repeat as long as calcium is present on thin filament.
11. Throughout this process, the calcium is actively pumped back into the sarcoplasmic reticulum. When no longer present on the thin filament, the tropomyosin changes back to its previous state, so as to block the binding sites again. The cross-bridge then ceases binding to the thin filament, and the contractions cease as well.
12. Muscle contraction remains as long as Ca++ is abundant in sarcoplasm.









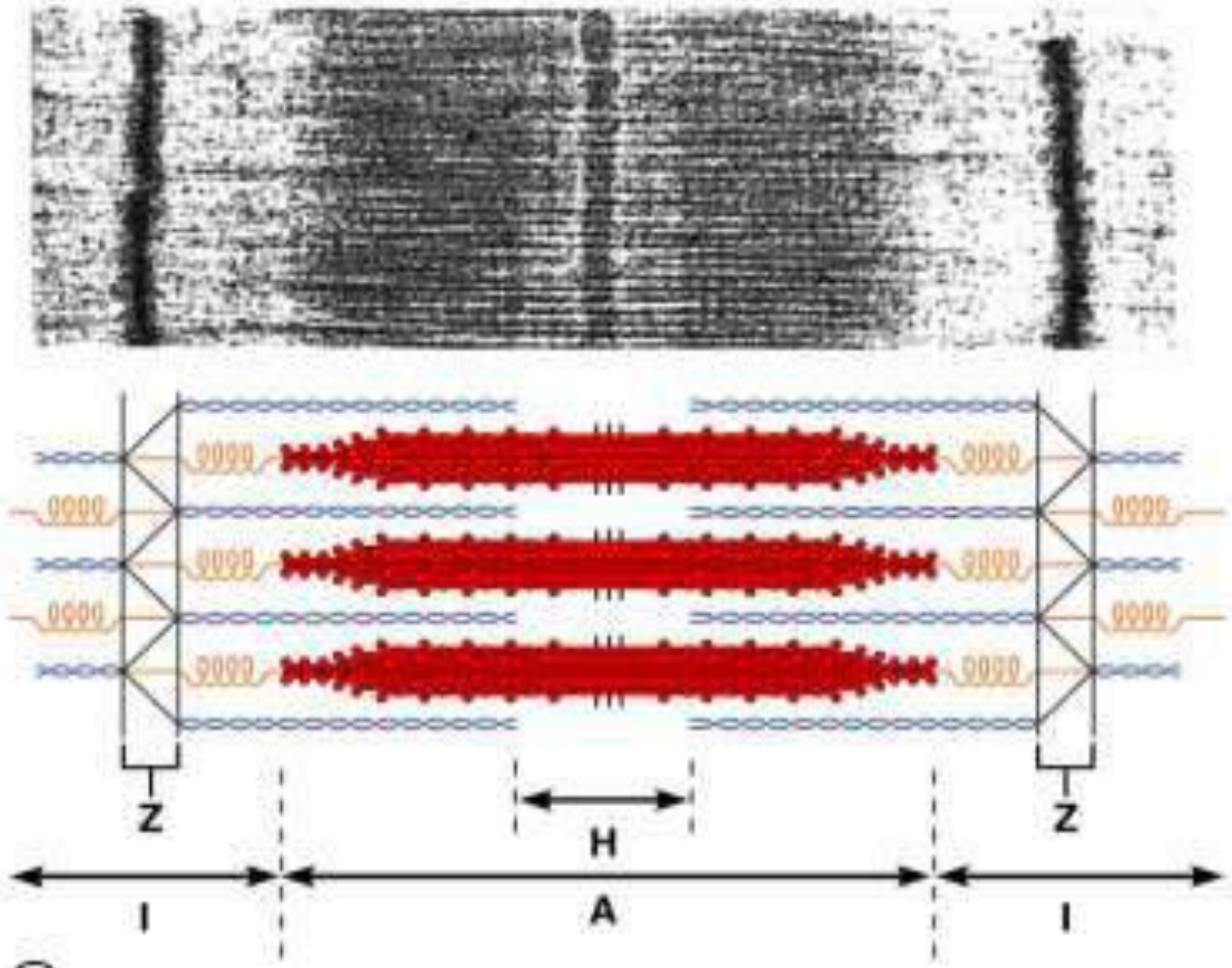
(a) Isotonic (concentric) contraction

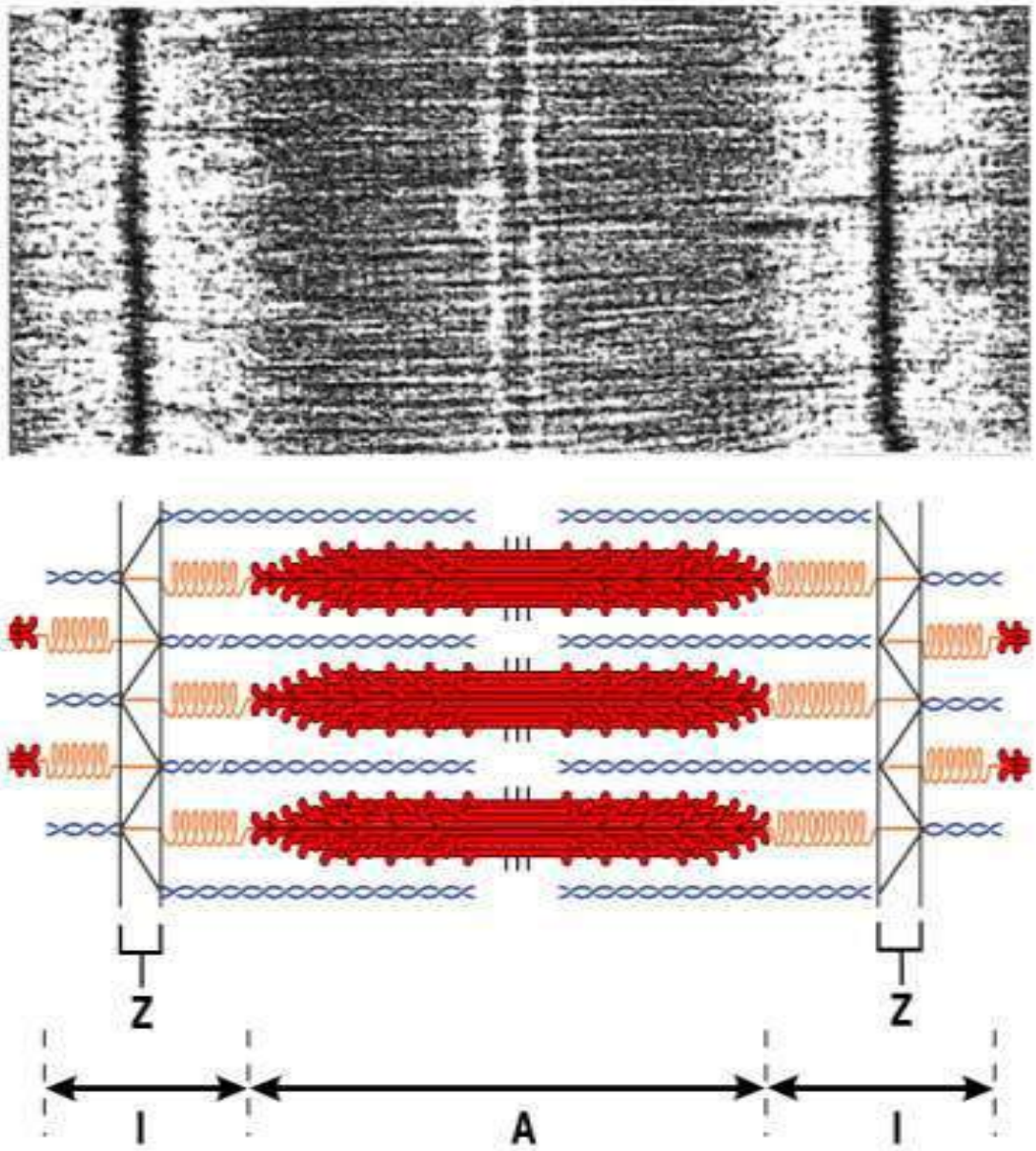
Sliding Filament Theory

- When a muscle contracts, the **actin is pulled along myosin toward the center** of the sarcomere until the actin and myosin filaments are completely overlapped.
- The **H zone becomes smaller** and smaller due to the increasing overlap of actin and myosin filaments, and the muscle shortens.
- Thus when the muscle is **fully contracted**, the **H zone is no longer visible.**
- The actin and myosin filaments themselves **do not actually change length**, but instead **slide past each other.**

Sliding Filament Theory

1. A myofiber , together with all of its myofibrils , shortens by movement of the insertion towards the origin of the muscle .
2. Shortening of the myofibrils is caused by shortening of the sarcomere (The distance between Z lines is reduced) .
3. Shortening of the sarcomere is accomplished by each filament remains the same during contraction .
4. sliding is produced by power strokes of myosin cross bridges ,which pull the thin actin over the thick myosin .
5. The A band remains the same length during contraction , but are pulled toward the origin of the muscle .
6. Adjacent A bands are pulled closer together as the I bands between them shorten .
7. The H band shorten during contraction as the thin filaments on the sides of the sarcomeres are pulled towards the middle .





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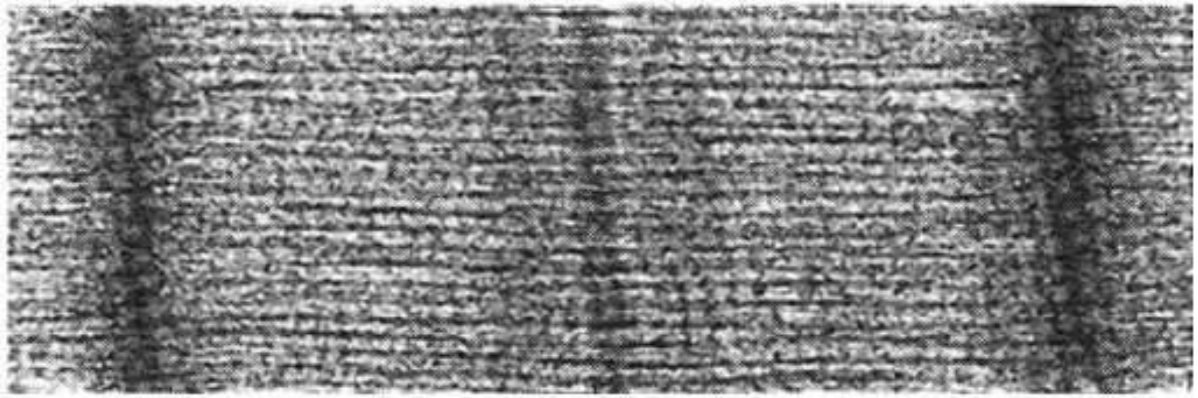
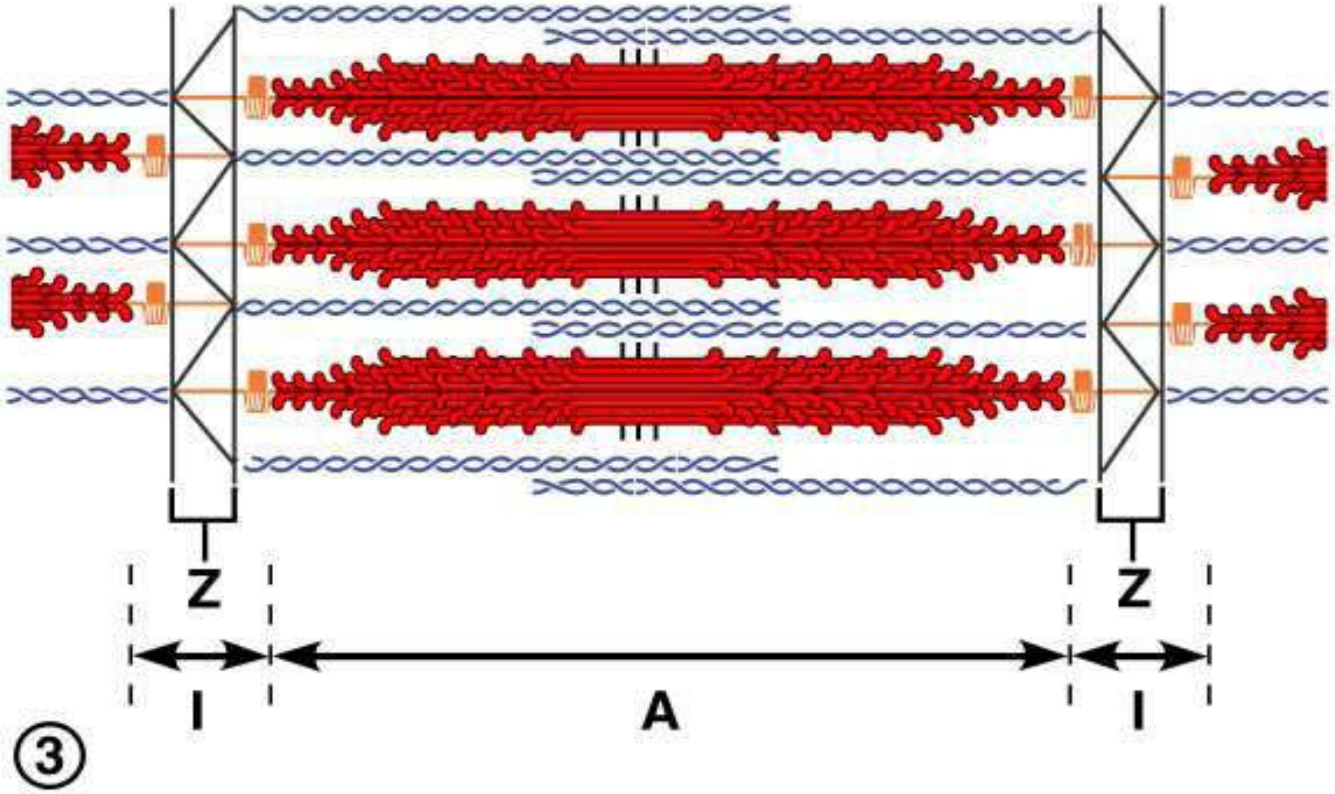
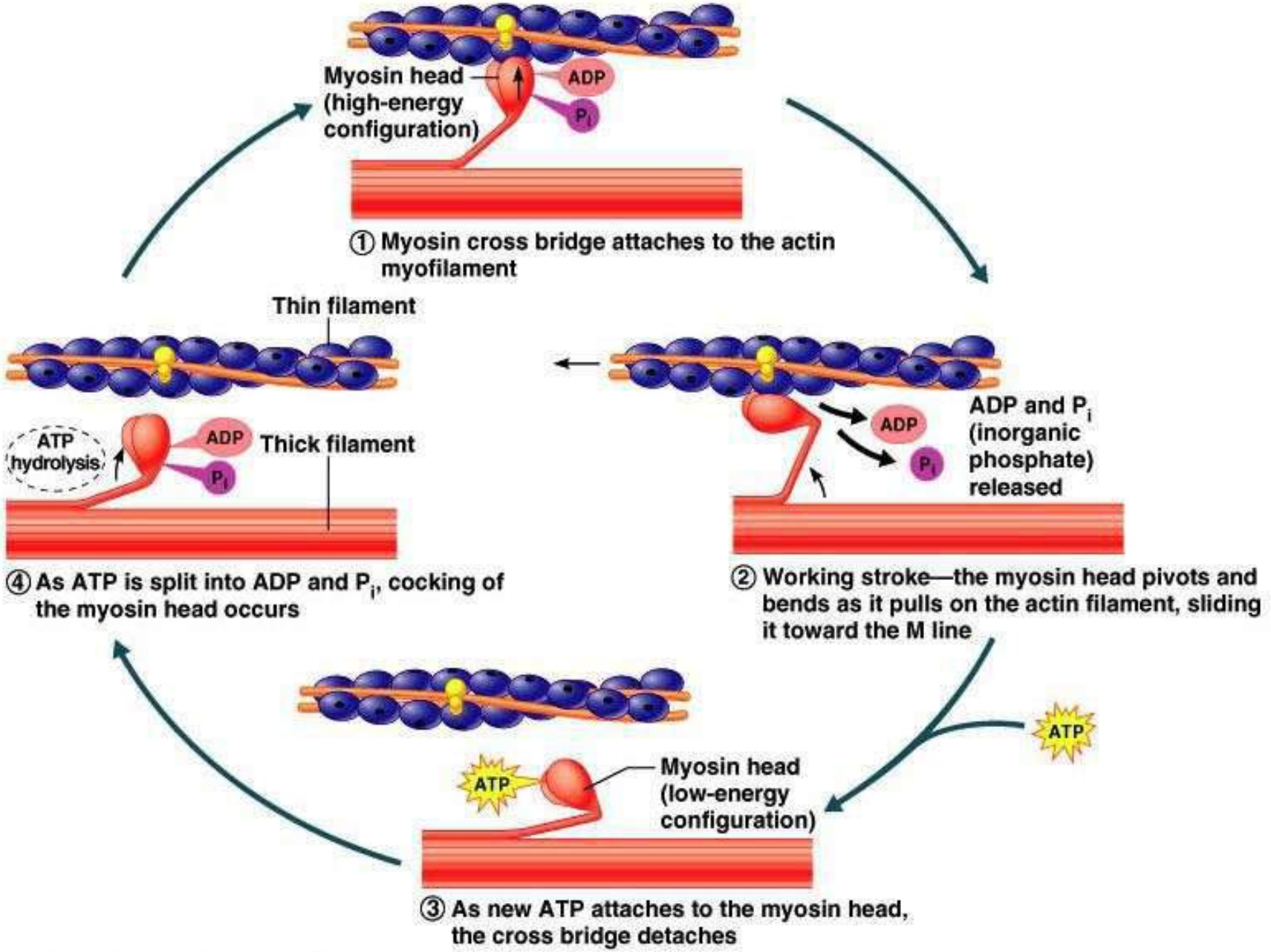




Major events of muscle relaxation :

1. Acetylcholinestrase decomposes acetylcholine , and the muscle fiber membrane is no longer stimulated .
2. Ca2+ ions are actively transported into the sarcoplasmic reticulum .
3. ATP causes linkage between actin and myosin filaments to break .
4. Cross–bridges re–open .
5. Troponin & tropomysin molecules inhibit the interaction between myosin and actin filaments .
6. Muscle fiber remain relaxed , yet ready until stimulated again .

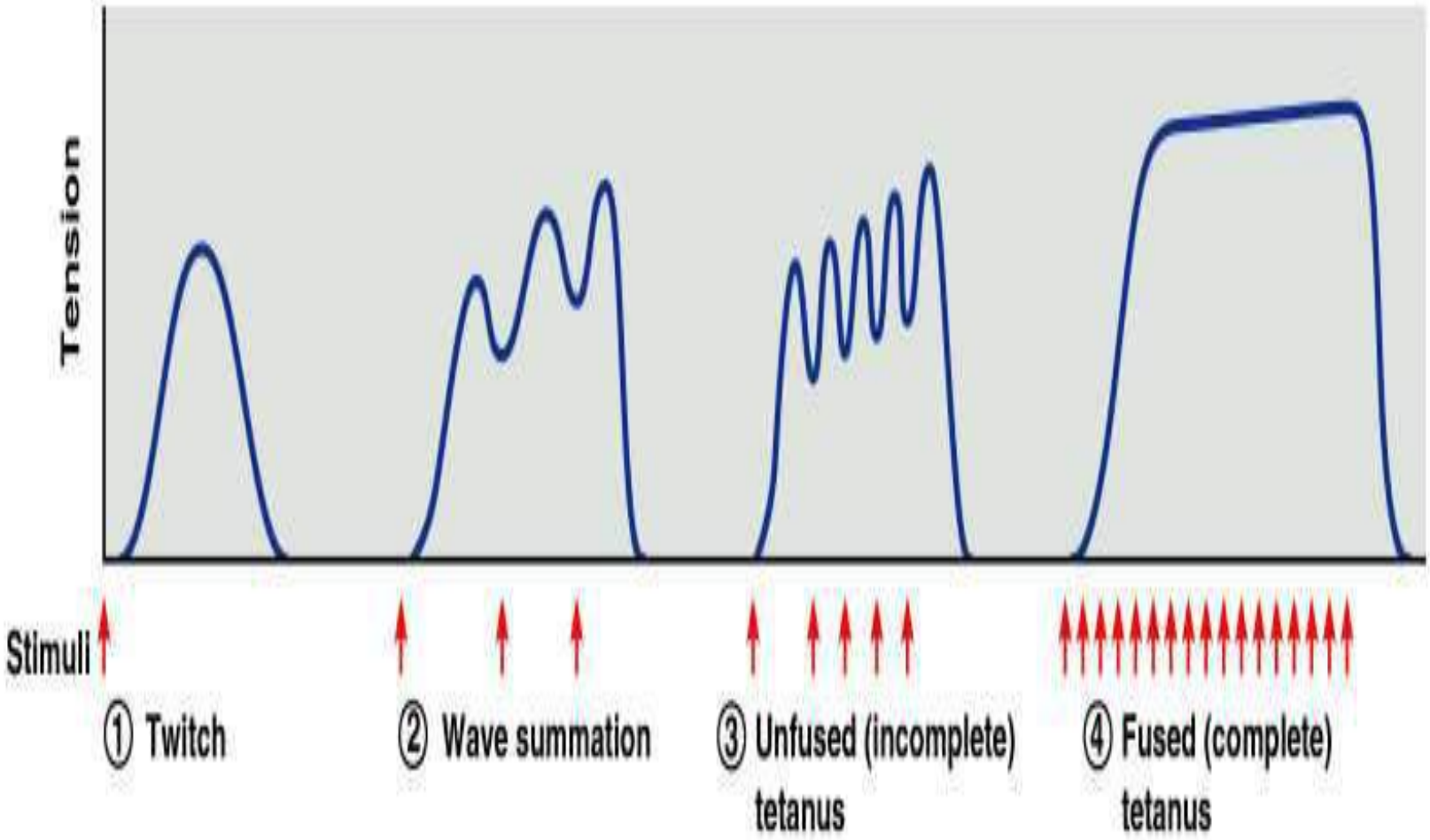


Summation of Muscle Contraction

- It is the **adding together** of individual muscle **twitches** to make strong muscle movements . **Rapid series** of stimuli may **produce summation** of twitches and a sustained contraction .
- **Titanic contraction:** It's a Forceful , sustained contraction without relaxation is a.
- **Tetany** is the result of **low Ca2+** concentrations .

Types of Summation

- 1. **Multiple motor unit summation** which means increasing number of motor units contracting simultaneously.
- 2.**Wave summation** which means increasing rapidity of contraction of individual motor units.
- 3.**Tetanization** which means higher frequency successive contractions fuse together and cannot be distinguished from one another.



Cellular Action of Skeletal Muscles

- During cellular respiration the mitochondria, within skeletal muscle cells, convert **glucose** from the blood to carbon dioxide and water in the process of **producing ATP** (see 1st Lecture).
- ATP is needed for all muscular movement. When the need of ATP in the muscle is higher than the cells can produce with **aerobic respiration**, the cells will produce extra ATP in a process called **anaerobic respiration**.
- The first step of aerobic respiration (**glycolysis)** produces two ATP per glucose molecule. When the rest of the aerobic respiration pathway is occupied the **pyruvate** molecule can be converted to **lactic acid**.
- This method produces much **less ATP than the aerobic** method, but it does it faster and allows the muscles to do a bit more than if they relied solely on ATP production from aerobic respiration.

The Efficiency of Muscle Contraction
Energy Consumption

Muscular activity accounts for **most** of the body's energy **consumption.** Muscles store energy for their own use in the form of glycogen, which represents about 1% of their mass. **Glycogen** can be rapidly converted to glucose when more energy is necessary.

- Only about **20%** of input energy converts into muscular work. The **rest** of the energy is **heat**. **50%** of energy from food is used in **ATP formation**.
- If a muscle contraction is **slow or without movement**, energy is lost as **maintenance heat**. If muscle **contraction is rapid**, energy is used to overcome **friction.**

Muscle Soreness & Fatigue

- **Lactic acid accumulates** and causes the muscles to fatigue.
- They will eventually stop contracting until the **breakdown** of lactic acid is sufficient to allow for movement once again.
- During **heavy breathing**, following exercise, the cells are **converting the lactic acid** either back into **glucose** or converting it to **pyruvate** and sending it through the additional steps of aerobic respiration.
- By the time a person is breathing normally again the lactic acid has been removed.
- Muscle soreness (pain) sometimes occurs after vigorous activity. It is actually from **small tears in the fibers** themselves.
- After the fibers heal they will increase in size. The number of mitochondria will also increase if there is continued demand for additional ATP.
- Hence, through **exercise** the muscles can **increase in both strength and endurance.**

Types of Muscle Pain

Spasms

When smooth and skeletal muscles go through multiple spasms it is referred either as seizure or convulsion.

Cramps

Strenuous activities can cause painful spasms that are long, this is referred to as cramps.

Sprain

An injury to a joint that involves a stretched or torn ligament.

Muscle Strain

A strain occurs when a muscle or the tendon that attaches it to the bone is overstretched or torn.

Muscle strains are also called pulled muscles.

Oxygen Debt

During **rest** or moderate exercise , **O2 is sufficient** to support **aerobic respiration** (using many ATP molecules).

During strenuous **exercise** , **O2 deficiency** may develop and lactic acid may accumulate as a result of **anaerobic respiration**.

The amount of O2 needed to **convert** accumulated **lactic acid to glucose** and restore **supplies of ATP** and creatine phosphate is called **oxygen dept** .

Smooth Muscle Contraction

1. Smooth muscles contain filaments of **actin and myosin** .
2. **Lack** transverse **tubules** and S.R. is not well developed .
3. Display **rhythmieity** (spontaneous repeated contractions) , responsible for peristalsis (alternate contraction and relaxation) .
4. **Lack troponin** (protein that **binds to $Ca^{2)}$,**) instead **calmodulin** binds to Ca^{2+} .
5. Both **Acetylcholine & norepinephrine** are **neurotransmitters** for smooth muscles .
6. Hormones and stretching affect smooth muscle contractions .
7. Can contract for a **long period** of time .

Steps of Contraction Smooth Muscles

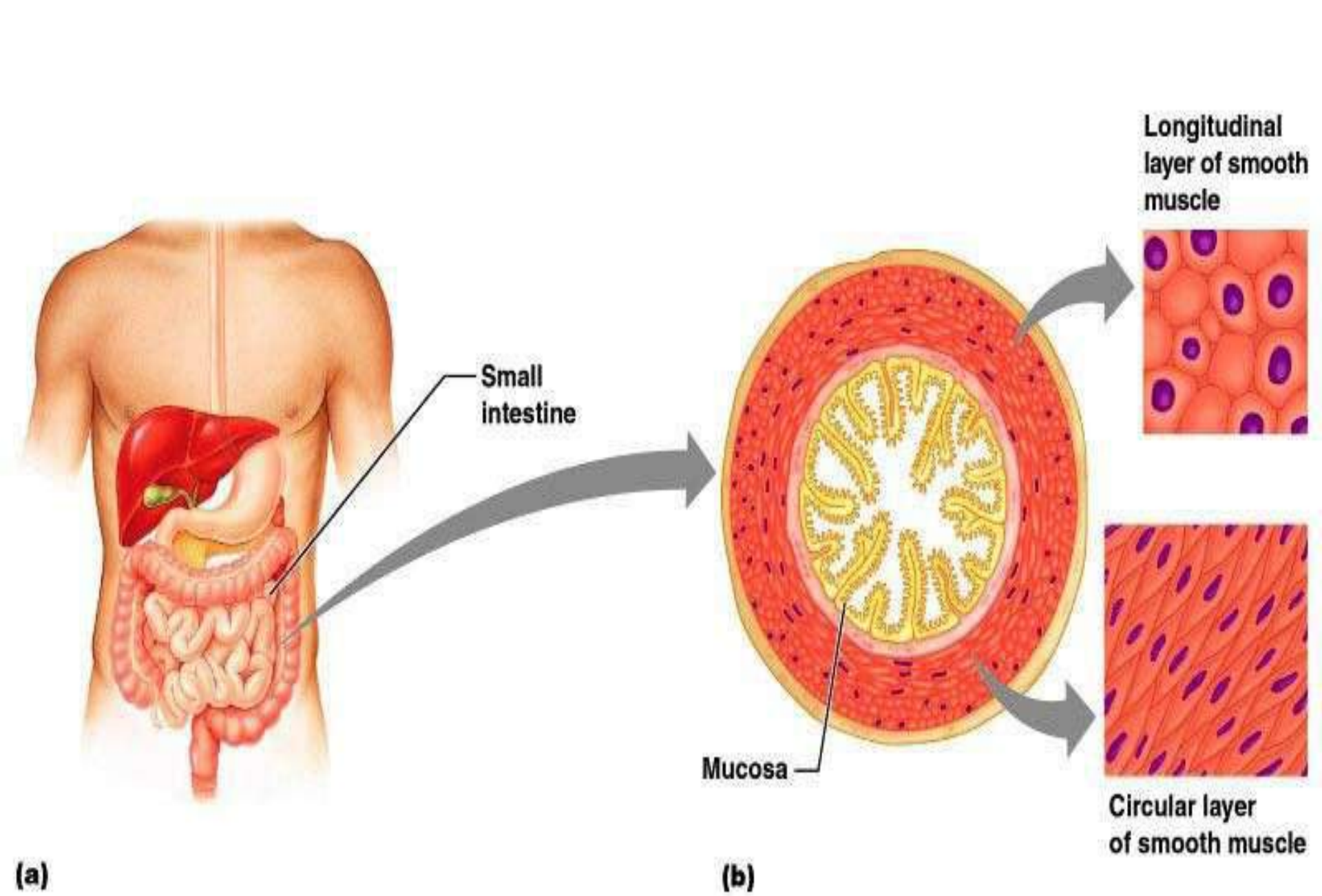
Contractions are initiated by an **influx of calcium** which binds to calmodulin to form calcium-calmodulin complex which binds to and activates myosin light-chain kinase.

Myosin light-chain kinase **phosphorylates** myosin light-chains using ATP, causing them to interact with actin filaments to make a Powerstroke.

Calcium is actively **pumped out** of the cell by receptor regulated channels. As calcium is **removed** the calcium-calmodulin complex breaks away from the myosin light-chain kinase, **stopping phosphorylation**.

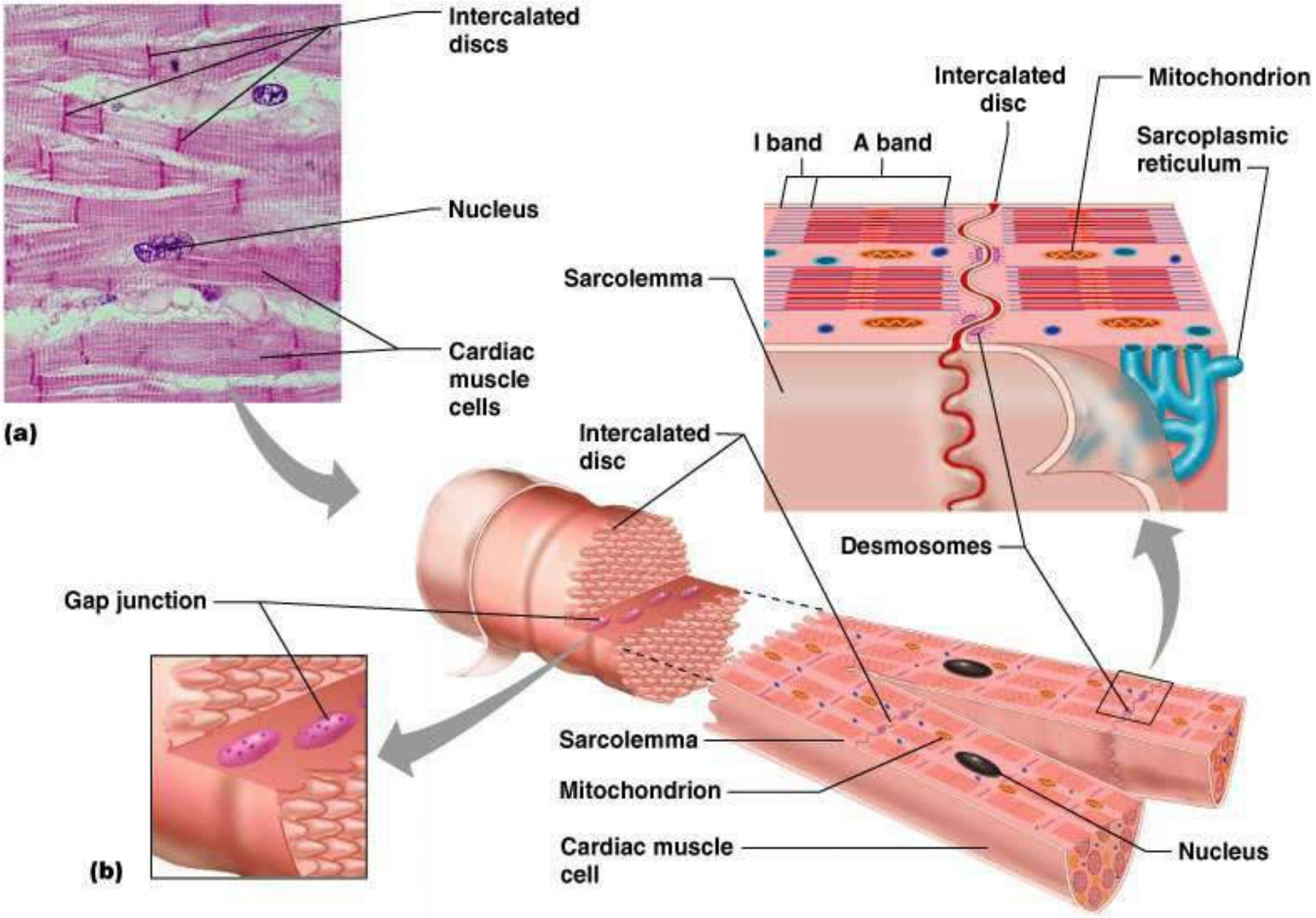
Myosin phophatase dephosphorylates the myosin. If the myosin was bound to an actin molecule, the release is slow, this is called a latch state. In this manner, smooth muscle is able to stay contracted for some time without the use of much ATP.

ATP is still needed for crossbridge cycling, and that there is no reserve, such as creatine phosphate, available. Most ATP is created from aerobic metabolism, however anaerobic production may take place in times of low oxygen concentrations.



Contraction of Cardiac muscle

1. **A unique arrangement** of actin and myosin filaments produces the cross- striations (an optical illusion the microscope), and rapid contraction with powerful forces involved.
2. Muscle cells are joined by **intercalated disks**, and allow muscle groups to form **branching networks** - both features are necessary for cardiac muscle to **function as a unit**.
3. **SR and T tubules are well developed**, so a large amount of calcium can be released rapidly through the T tubules. It contains **more mitochondria** in each muscle cell than skeletal and smooth muscles, providing **more ATP** energy for continuous contraction.
4. **Self- exciting** muscle fibers form "**pacemakers**" which initiate **spontaneous nerve impulses** for autorthymic contraction .These pacemakers can be influenced by the **autonomic nervous system** and hormones.



Characters of Cardiac Muscle Contraction

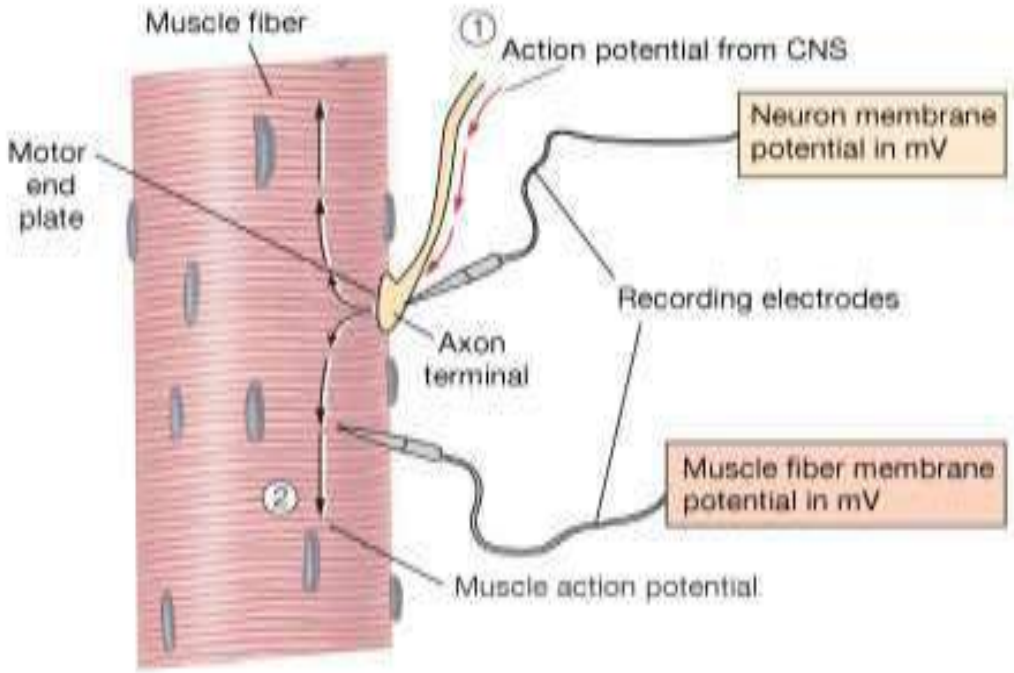
1. Contracts for a **longer time** than skeletal muscle because transverse tubules supply **extra Ca+2** ions .
2. **Intercalated disc** connects the ends of adjacent muscles and hold cells together as a unit (syncytium).
3. Fibers contracts as a unit .
4. Muscle fibers are **self – exiting** , rhythmic , and remain refractory until a contraction is completed.
5. **No Tetanic contractions**.

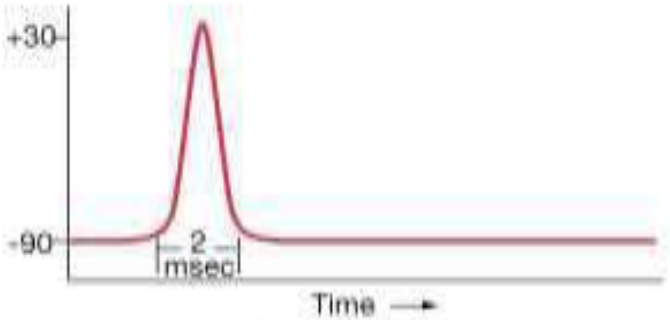
Electromyogram (EMG):

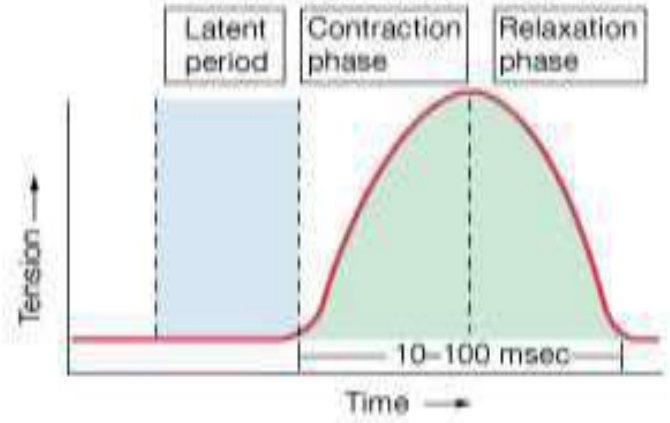
a) **Latent period –** chemical reactions and physical changes that occur preceding the actual contraction of a skeletal muscle.

b) **Period of contraction** – actin causing the shortening of macromere and the contraction of muscle.

c) **period of relaxation-** actin returns to its original position, causing the lengthening of sarcomeres and the relaxation of muscle.







3 Development of tension during one muscle twitch

FIGURE QUESTION

- Compare the resting membrane potential of the motor neuron and the muscle fiber.
- Movement of what ion(s) in what direction(s) creates the muscle action potential?

Clinical Terms

- Myopathy : Any muscular disease .
- Paralysis : loss of ability to move a body part .
- Myotonia : prolonged muscular spasm .
- Myositis : inflammation of skeletal muscle tissue .
- Spasm : A sudden , involuntary smooth or skeletal muscle twitch , can range from mild to very painful irritation .
- Tics : spasm of eye–lid or facial muscles .
- Cramp : a prolonged spasm that cause a muscle to become taut and painful .