MEDICAL UNIVERSITY – PLEVEN
FACULTY OF MEDICINE
DISTANCE LEARNING CENTER

Lecture №4

Skeletal muscles

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There Are 3 Basic Types of Muscle in the Body:

- **Skeletal muscle** attaches to bones which form levers- used for bodily movement
- **Cardiac muscle** forms the heart- used to pump blood through circulatory system
- **Smooth muscle** lines gut and blood vessels- controls diameter of these tubes and in gut helps to propel the digested food

Skeletal muscle:

- attached to bones & moves skeleton
- also called striated muscle (because of its appearance under the microscope)
- voluntary muscle

Characteristics of **Skeletal** muscle:

- excitability - responds to stimuli (e.g., nervous impulses)
- contractility - able to shorten in length
- extensibility - stretches when pulled
- elasticity - tends to return to original shape & length after contraction or extension

Functions of skeletal muscle:

- motion
- maintenance of posture
- heat production

Structure of Skeletal Muscle

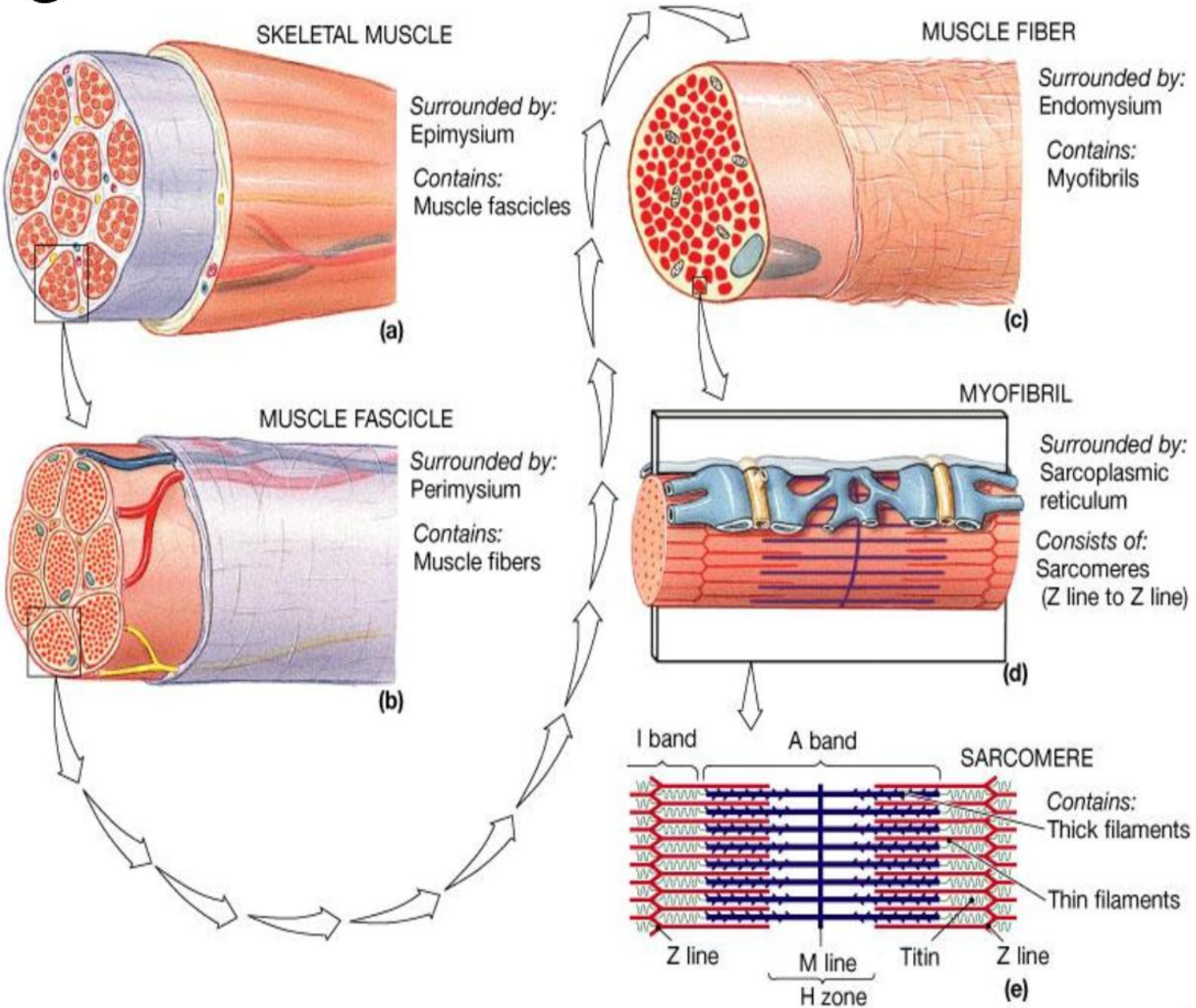
- Skeletal muscles consist of numerous subunits or bundles called fasicles (or **fascicles**). Fascicles are also surrounded by connective tissue (called the perimysium) and each fascicle is composed of numerous muscle fibers (or **muscle cells**). Muscle cells, consist of many fibrils (or **myofibrils**), and these myofibrils are made up of long protein molecules called myofilaments. There are two types of myofilaments in myofibrils: **thick myofilaments** and **thin myofilaments.**

Physiological anatomy

muscle fiber :

- * multinucleated long cylindrical cell
- * sarcolemma
- * sarcotulular system - transverse tubules; sarcoplasmic reticulum
- * myofibrils

Organization in Skeletal Muscle Fiber



Structure of muscle cells

- The cell membrane of a muscle cell is called the **sarcolemma**, and this membrane, like that of neurons, maintains a membrane potential. So, impulses travel along muscle cell membranes just as they do along nerve cell membranes. However, the 'function' of impulses in muscle cells is to cause contraction. To understand how a muscle contracts, you need to know a bit about the structure of muscle cells.

Structure of muscle cells

- The **SARCOLEMMA** has a unique feature: it has holes in it. These "holes" lead into tubes called **TRANSVERSE TUBULES** (or T-TUBULES for short). These tubules pass down into the muscle cell and go around the MYOFIBRILS. However, these tubules DO NOT open into the interior of the muscle cell; they pass completely through and open somewhere else on the sarcolemma (i.e., these tubules are not used to get things into and out of the muscle cell). The function of T-TUBULES is to conduct impulses from the surface of the cell (SARCOLEMMA) down into the cell and, specifically, to another structure in the cell called the SARCOPLASMIC RETICULUM.

Structure of muscle cells

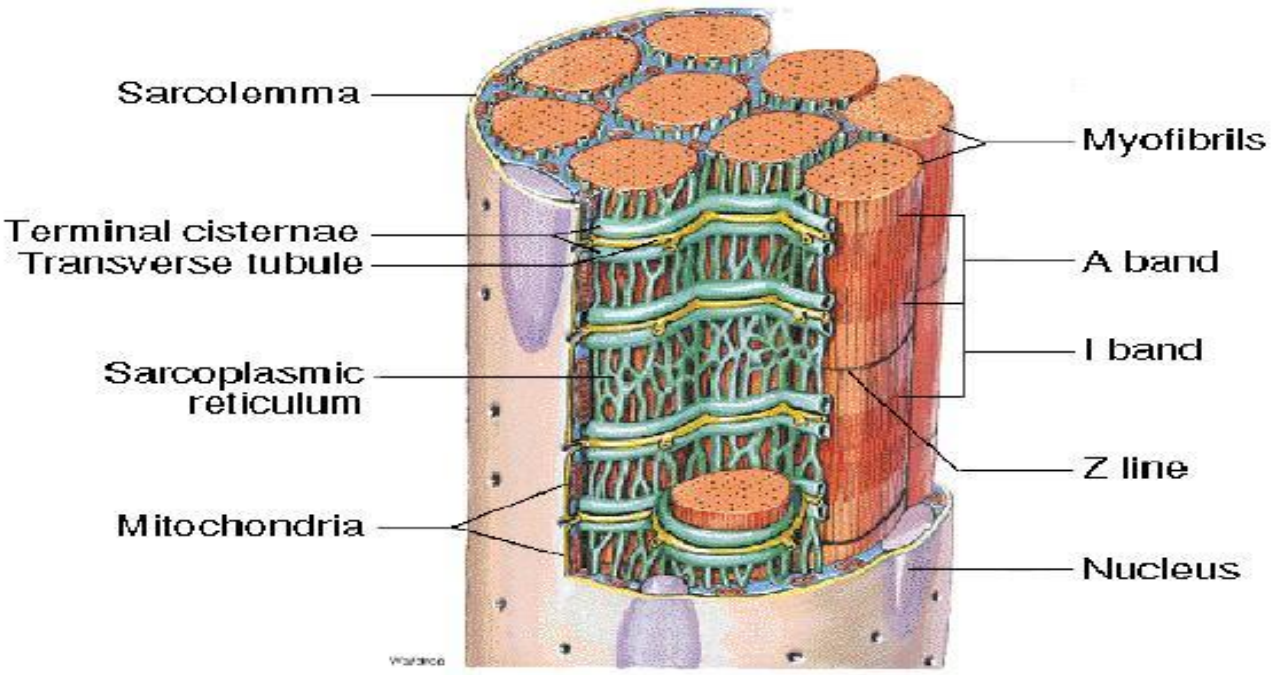
- The **SARCOPLASMIC RETICULUM** (SR) is a bit like the endoplasmic reticulum of other cells, e.g., it's hollow. But **the primary function of the SARCOPLASMIC RETICULUM is to STORE CALCIUM IONS.** Sarcoplasmic reticulum is very abundant in skeletal muscle cells and is closely associated with the MYOFIBRILS (and, therefore, the MYOFILAMENTS). The membrane of the SR is well-equipped to handle calcium: there are "pumps" (active transport) for calcium so that calcium is constantly being "pumped" into the SR from the cytoplasm of the muscle cell (called the SARCOPLASM).

Structure of muscle cells

- As a result, in a relaxed muscle, there is a very high concentration of calcium in the SR and a very low concentration in the **sarcoplasm** (and, therefore, among the myofibrils & myofilaments). In addition, the membrane has special openings, or "gates", for calcium. In a relaxed muscle, these gates are closed and calcium cannot pass through the membrane. So, the calcium remains in the SR. However, if an impulse travels along the membrane of the SR, the calcium "gates" open &, therefore, calcium diffuses rapidly out of the SR & into the sarcoplasm where the **myofibrils & myofilaments** are located. This, as you will see, is a key step in muscle contraction.

Structure of muscle cells

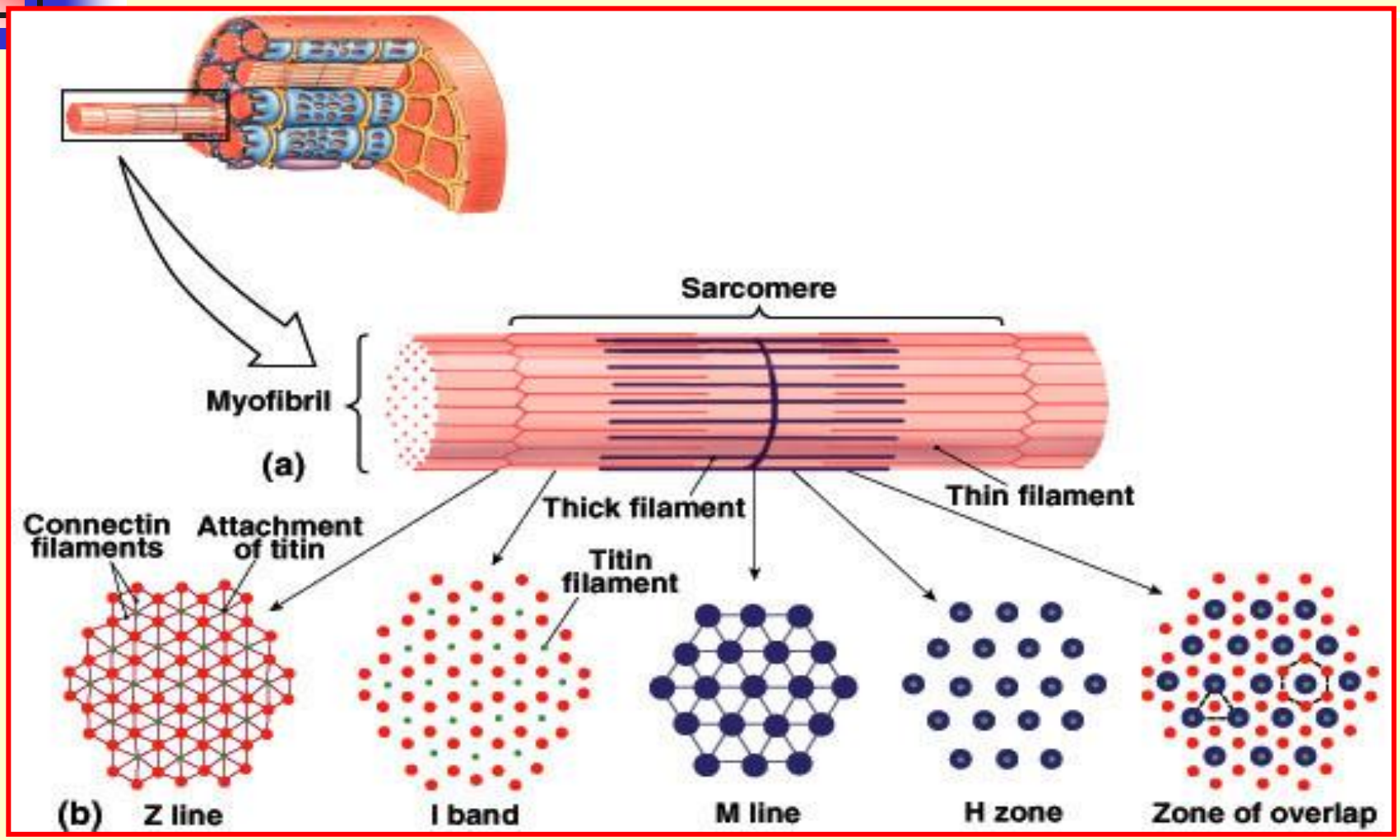
Sarcoplasmic Reticulum



Structure of muscle cells

- Myofibrils are composed of **2 types of myofilaments: thick and thin.** In skeletal muscle, these myofilaments are arranged in a very regular, precise pattern: thick myofilaments are always surrounded by 6 thin myofilaments. In a slide view, thin myofilaments can be seen above and below each thick myofilament.

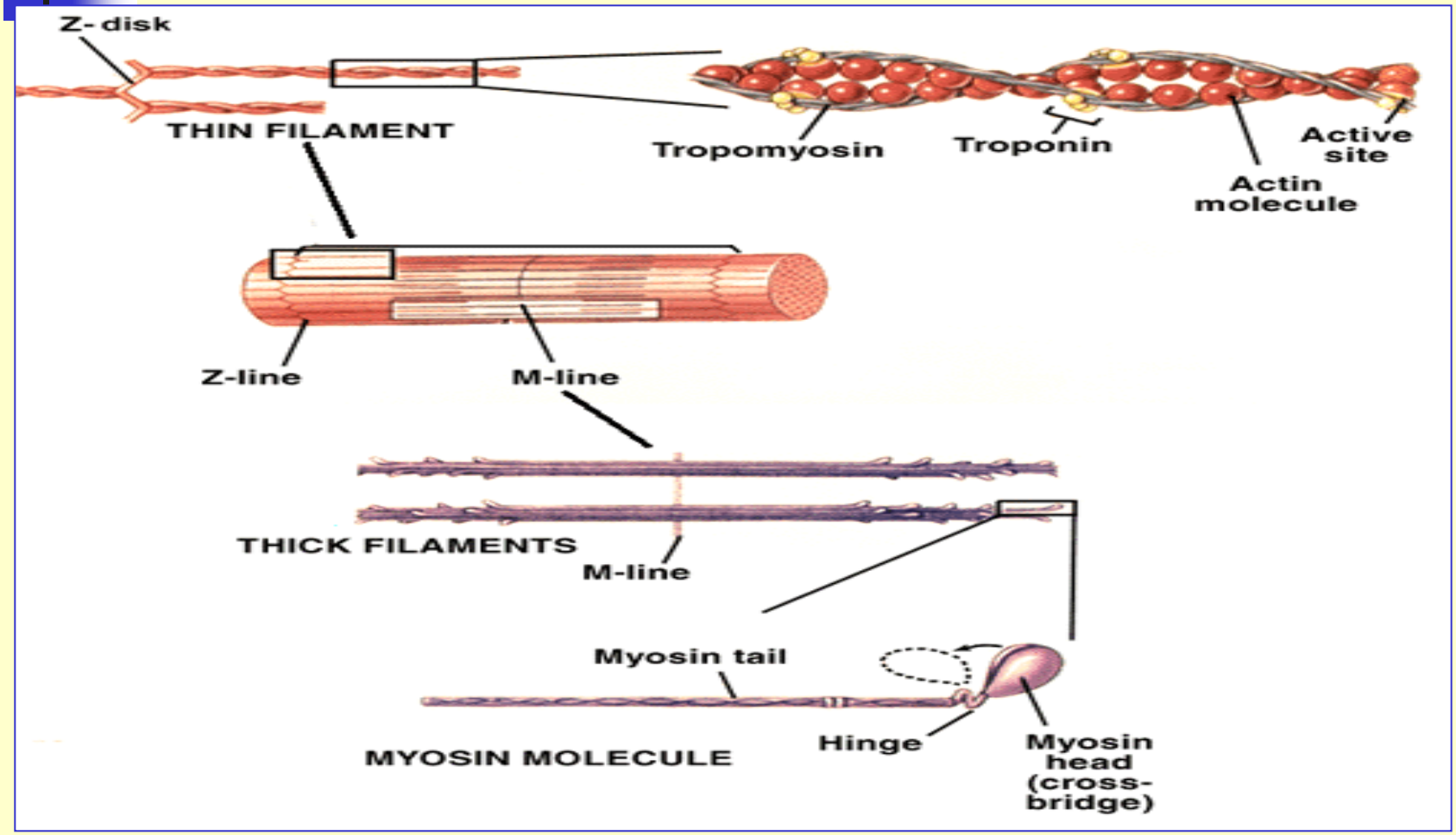
Structure of muscle cells



SARCOMERE

- **Each myofibril is composed of many subunits lined up end-to-end**. These subunits are, of course, composed of myofilaments and are **called SARCOMERES**. ***The basic contractile unit of skeletal muscle cells is a sarcomere*** the area between two successive Z discs.
- The drawings above & below show just a very small section of the entire length of a myofibril and so you can only see one complete SARCOMERE.

Sarcomere


Z- disk
THIN FILAMENT
Tropomyosin
Troponin
Active site
Actin molecule
Z-line
M-line
THICK FILAMENTS
M-line
Myosin tail
MYOSIN MOLECULE
Hinge
Myosin head (cross-bridge)

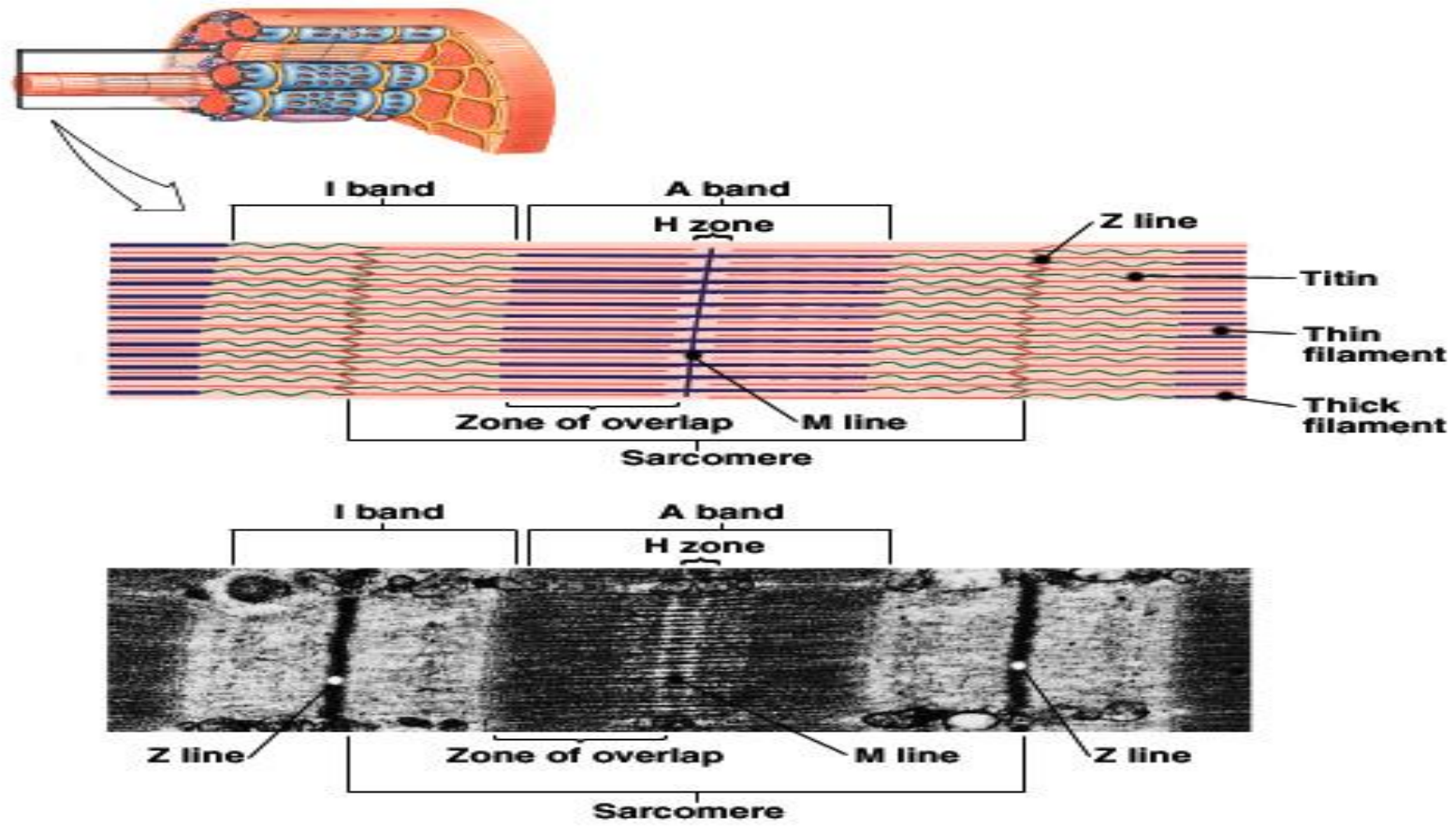
Sarcomere

- In each sarcomere, thin myofilaments extend in from each end. Thick myofilaments are found in the middle of the sarcomere and do not extend to the ends. Because of this arrangement, when skeletal muscle is viewed with a microscope, the ends of a sarcomere (where only thin myofilaments are found) appear lighter than the central section (which is dark because of the presence of the thick myofilaments).

Skeletal muscle

Thus, a myofibril has alternating light and dark areas because each consists of many sarcomeres lined up end-to-end. This is why skeletal muscle is called **STRIATED MUSCLE** (i.e., the alternating light and dark areas look like stripes or striations). The light areas are called the I-BANDS and the darker areas the A-BANDS. Near the center of each I-BAND is a thin dark line called the Z-LINE (or Z-membrane in the drawing below). The Z-LINE is where adjacent sarcomeres come together and the thin myofilaments of adjacent sarcomeres overlap slightly. Thus, a sarcomere can be defined as the area between Z-lines.

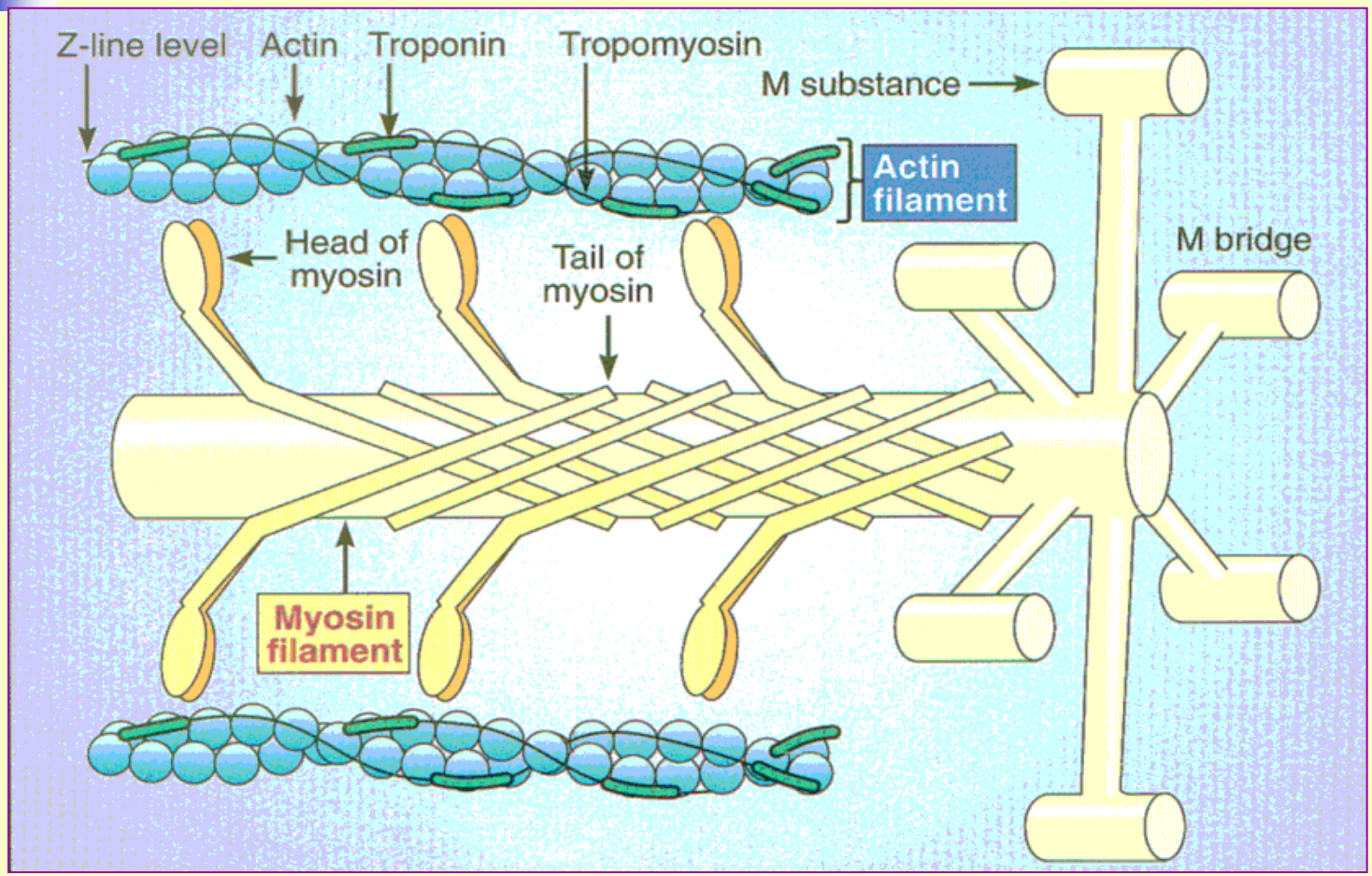
STRIATED MUSCLE



Thick myofilaments

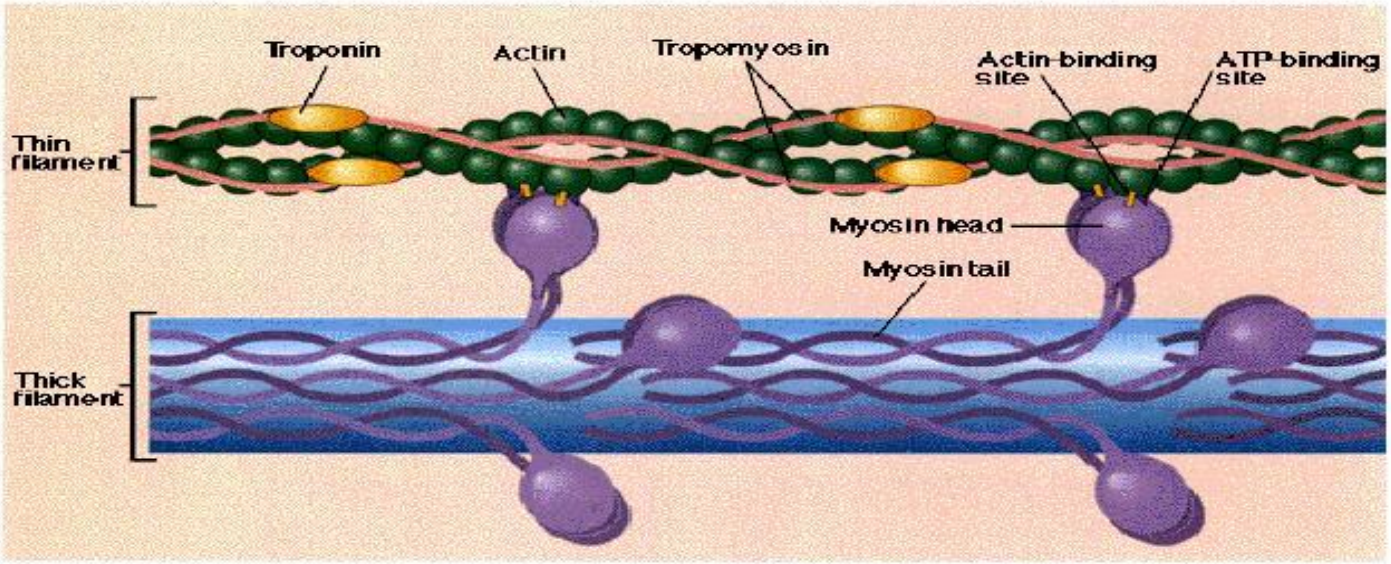
- Thick myofilaments are composed of a protein called MYOSIN. Each **MYOSIN molecule** has a tail which forms the core of the thick myofilament plus a head that projects out from the core of the filament. These MYOSIN heads are also commonly referred to as CROSS-BRIDGES.

Myofilaments



Myofilaments

Myosin & the Thick Filament



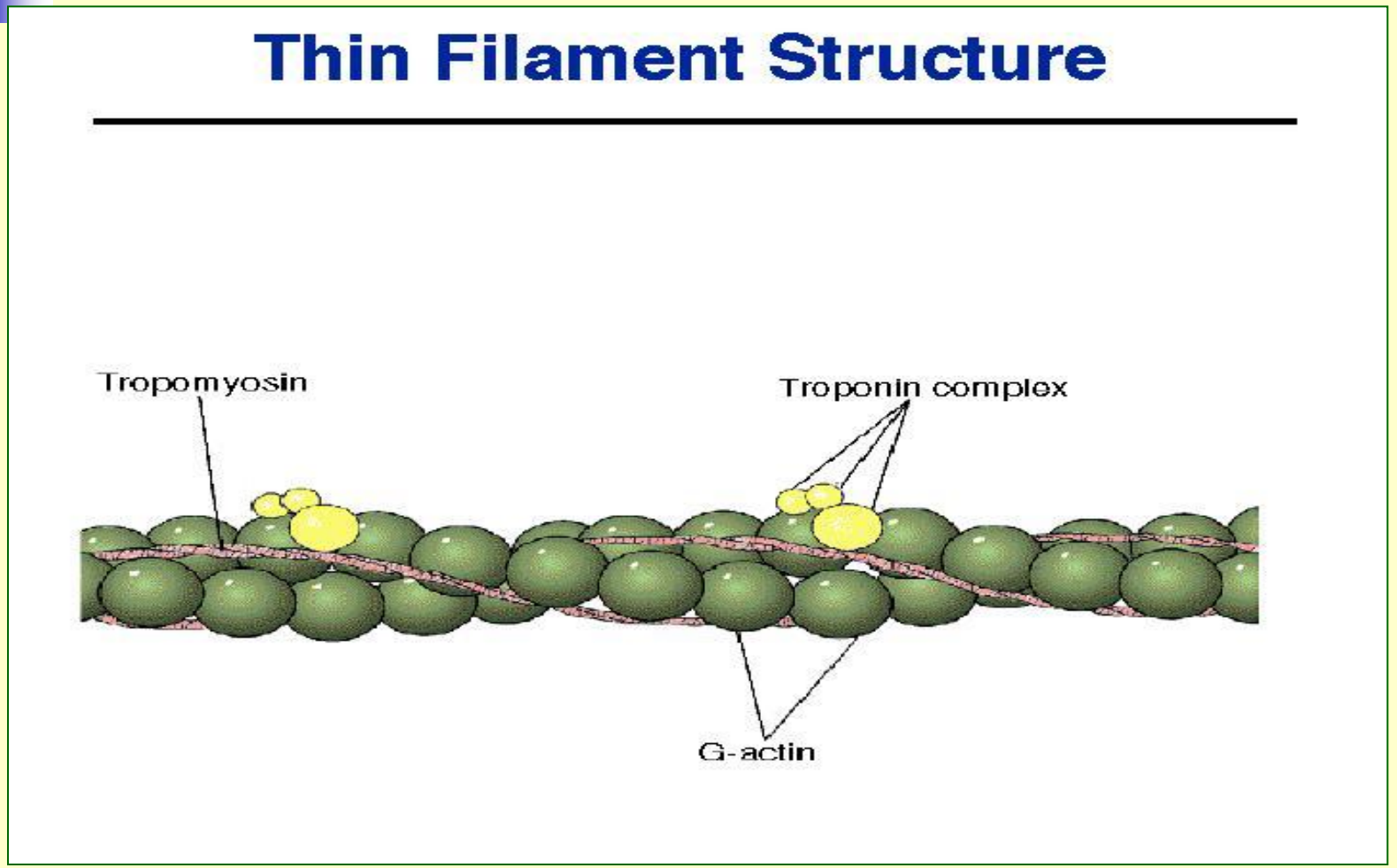
The MYOSIN HEAD has several important characteristics:

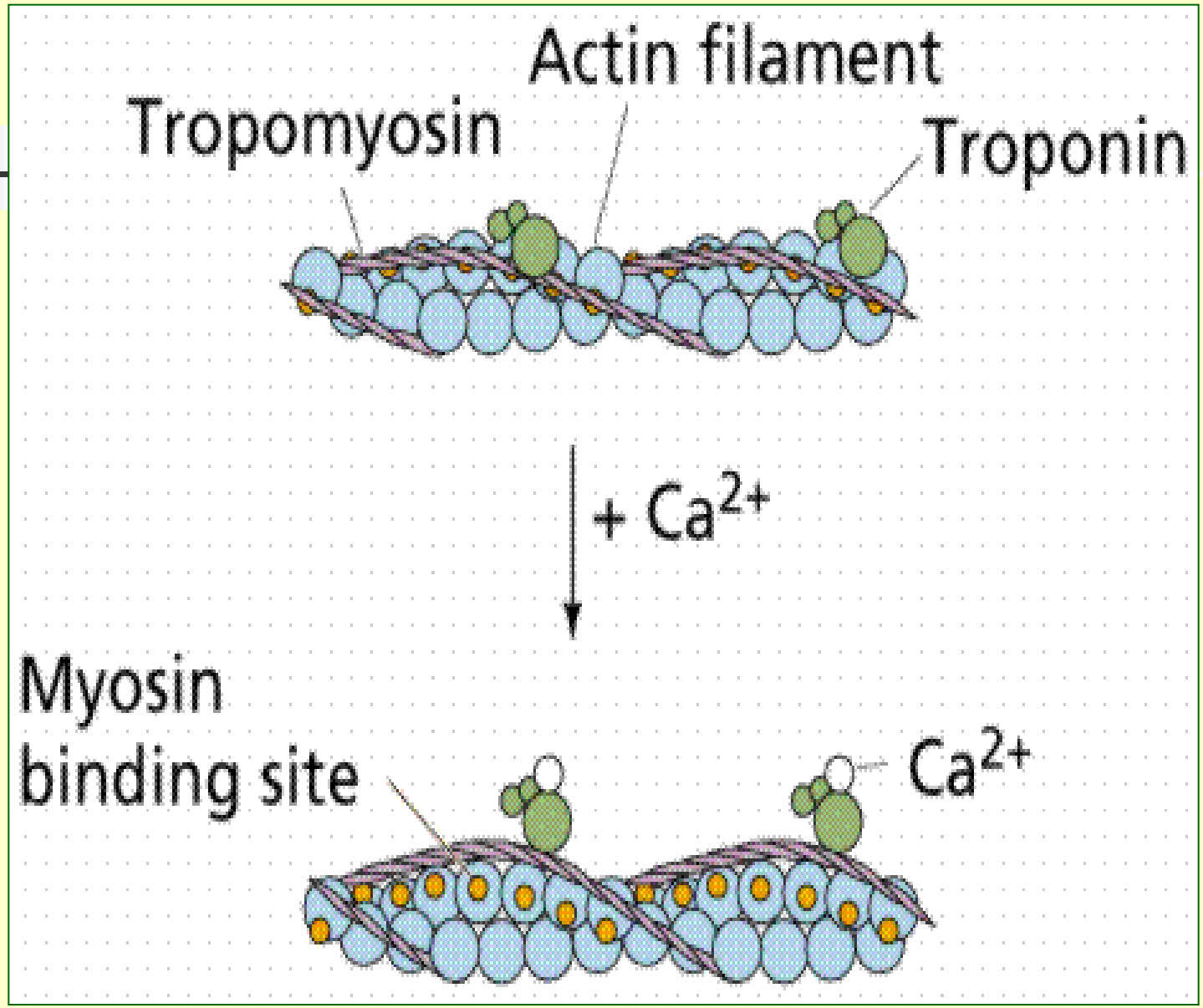
- it has ATP-binding sites into which fit molecules of ATP. ATP represents potential energy.
- it has ACTIN-binding sites into which fit molecules of ACTIN. Actin is part of the thin myofilament.
- it has a "hinge"at the point where it leaves the core of the thick myofilament. This allows the head to swivel back.

Thin myofilament contains:

- The **actin molecules** (or G-actin as above) are spherical and form long chains. Each thin myofilament contains two such chains that coil around each other. **TROPOMYOSIN molecules** are long, thin molecules that wrap around the chain of ACTIN. At the end of each tropomyosin is an **TROPONIN molecule**. The TROPOMYOSIN and TROPONIN molecules are connected to each other. Each of these 3 proteins plays a key role in muscle contraction:

Thin myofilament



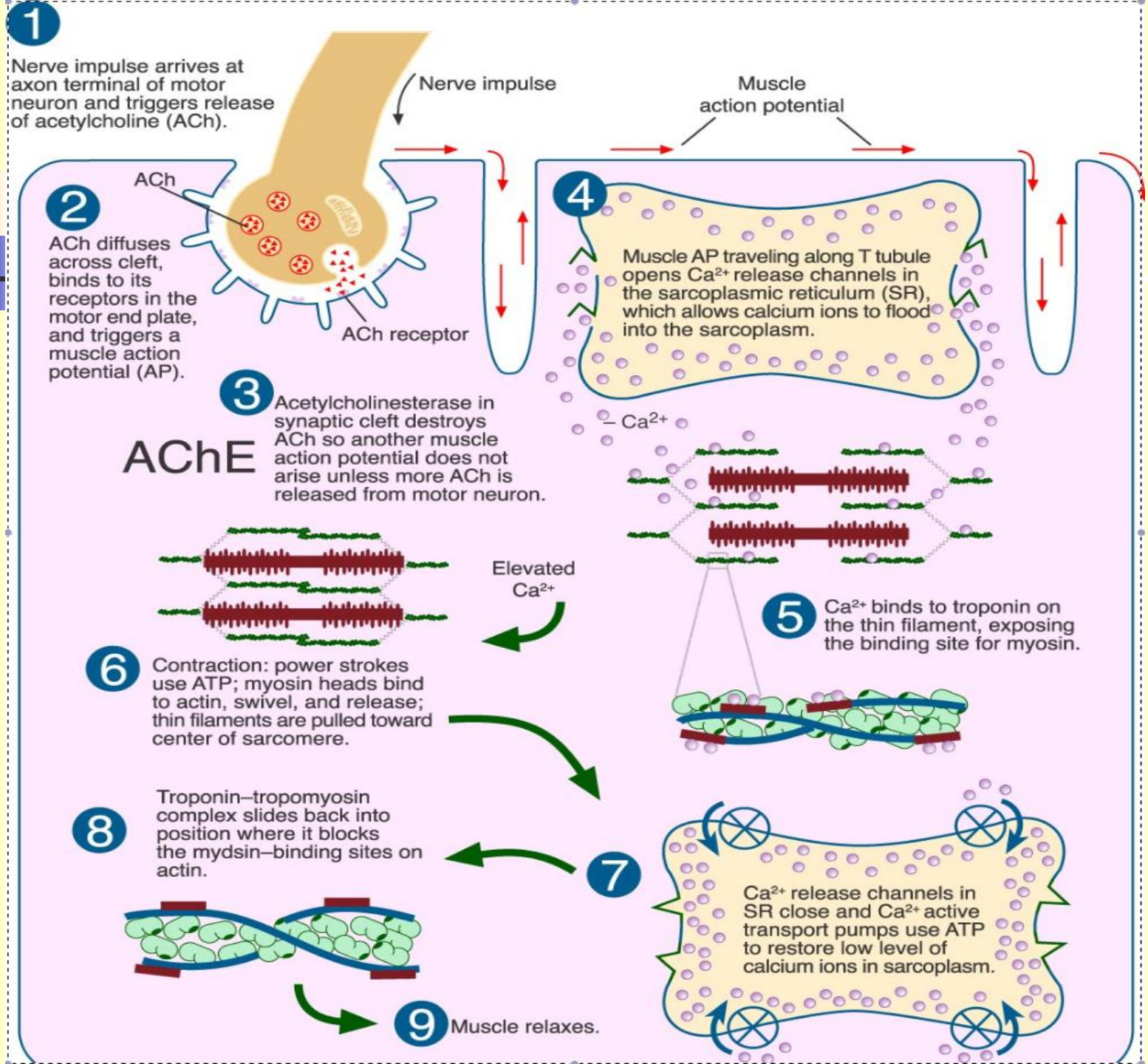

Actin filament
Tropomyosin
Troponin
+ Ca2+
Myosin
binding site
Ca2+

Thin myofilament

- ACTIN - when actin combines with MYOSIN HEAD the ATP associated with the head breaks down into ADP. This reaction released energy that causes the MYOSIN HEAD to SWIVEL.
- TROPOMYOSIN - In a relaxed muscle, the MYOSIN HEADS of the thick myofilament lie against TROPOMYOSIN molecules of the thin myofilament. As long as the MYOSIN HEADS remain in contact with TROPOMYOSIN nothing happens (i.e., a muscle remains relaxed).

Thin myofilament

- TROPONIN - Troponin molecules have binding sites for calcium ions. When a calcium ion fills this site it causes a change in the shape and position of TROPONIN. And, when TROPONIN shifts, it pulls the TROPOMYOSIN to which it is attached. When TROPOMYOSIN is moved, the MYOSIN HEAD that was touching the tropomyosin now comes in contact with an underlying ACTIN molecule.


1
Nerve impulse arrives at axon terminal of motor neuron and triggers release of acetylcholine (ACh).
Nerve impulse
Muscle action potential
ACh
2
ACh diffuses across cleft, binds to its receptors in the motor end plate, and triggers a muscle action potential (AP).
ACh receptor
4
Muscle AP traveling along T tubule opens Ca^{2+} release channels in the sarcoplasmic reticulum (SR), which allows calcium ions to flood into the sarcoplasm.
Ca^{2+}
3
AChE
Acetylcholinesterase in synaptic cleft destroys ACh so another muscle action potential does not arise unless more ACh is released from motor neuron.
Elevated Ca^{2+}
5
Ca^{2+} binds to troponin on the thin filament, exposing the binding site for myosin.
6
Contraction: power strokes use ATP; myosin heads bind to actin, swivel, and release; thin filaments are pulled toward center of sarcomere.
7
Ca^{2+} release channels in SR close and Ca^{2+} active transport pumps use ATP to restore low level of calcium ions in sarcoplasm.
8
Troponin–tropomyosin complex slides back into position where it blocks the mydsin–binding sites on actin.
9
Muscle relaxes.

Muscle Contractions

Steps:

- 1. Because skeletal muscle is voluntary muscle, contraction requires a nervous impulse. So, step 1 in contraction is when the impulse is transferred from a neuron to the SARCOLEMMA of a muscle cell.
- 2.The impulse travels along the SARCOLEMMA and down the T-TUBULES. From the T-TUBULES, the impulse passes to the SARCOPLASMIC RETICULUM.
- 3. As the impulse travels along the Sarcoplasmic Reticulum (SR), the calcium gates in the membrane of the SR open. As a result, CALCIUM diffuses out of the SR and among the myofilaments.

Muscle Contractions

Steps:

- 4. Calcium fills the binding sites in the TROPONIN molecules. As noted previously, this alters the shape and position of the TROPONIN which in turn causes movement of the attached TROPOMYOSIN molecule.
- 5. Movement of TROPOMYOSIN permits the MYOSIN HEAD to contact ACTIN.
- 6. Contact with ACTIN causes the MYOSIN HEAD to swivel.

Muscle Contractions

Steps:

- 7. During the swivel, the MYOSIN HEAD is firmly attached to ACTIN. So, when the HEAD swivels it pulls the ACTIN (and, therefore, the entire thin myofilament) forward. (Obviously, one MYOSIN HEAD cannot pull the entire thin myofilament. Many MYOSIN HEADS are swiveling simultaneously, or nearly so, and their collective efforts are enough to pull the entire thin myofilament).

Muscle Contractions

Steps:

- 8. At the end of the swivel, ATP fits into the binding site on the cross-bridge & this breaks the bond between the cross-bridge (myosin) and actin. The MYOSIN HEAD then swivels back. As it swivels back, the ATP breaks down to ADP & P and the cross-bridge again binds to an actin molecule.
- 9. As a result, the HEAD is once again bound firmly to ACTIN. However, because the HEAD was not attached to actin when it swiveled back, the HEAD will bind to a different ACTIN molecule (i.e., one further back on the thin myofilament). Once the HEAD is attached to ACTIN, the cross-bridge again swivels, SO STEP 7 IS REPEATED.

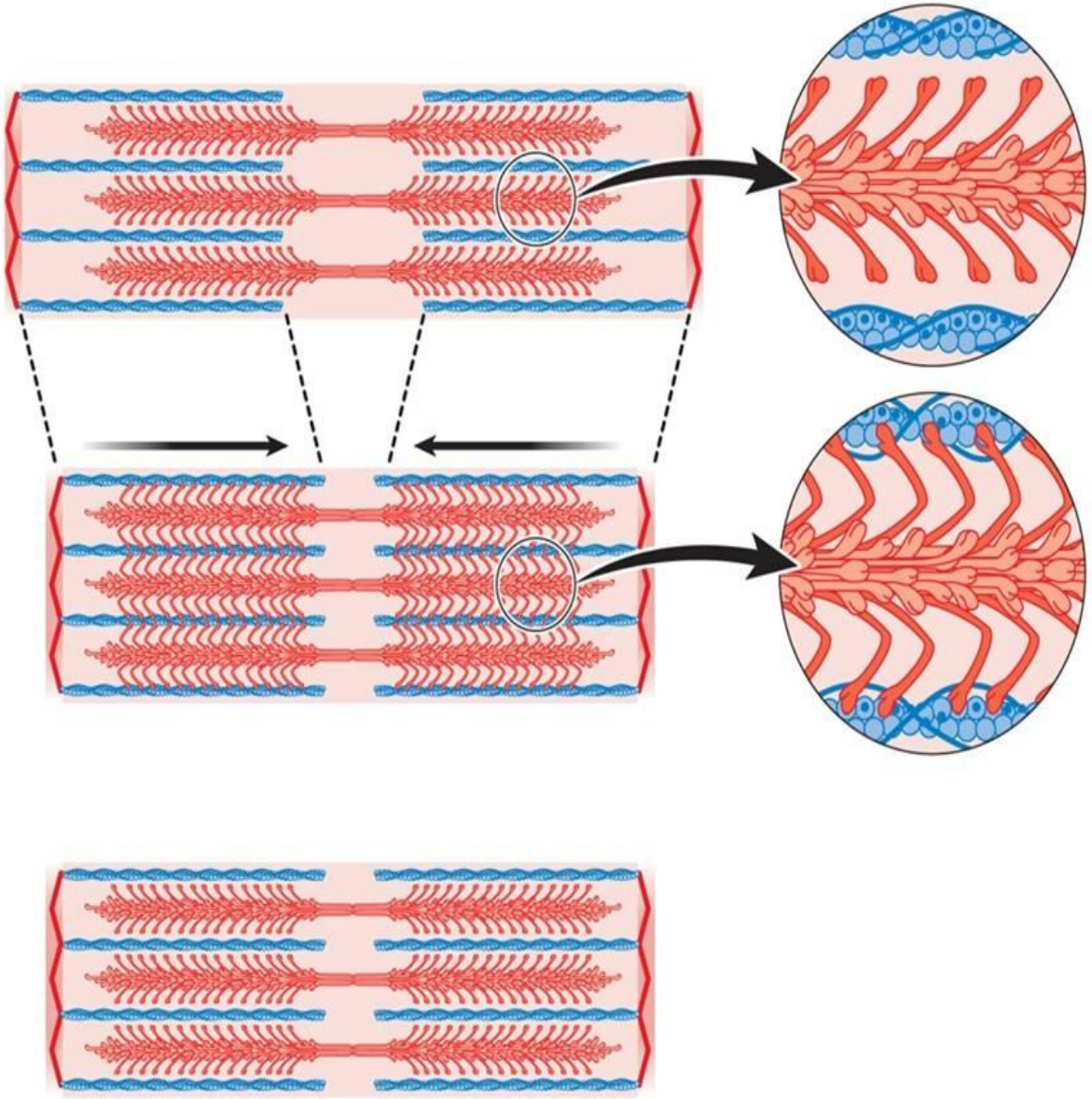
THE SLIDING FILAMENT THEORY

- When a skeletal muscle fiber contracts, (1) the H bands and I bands get smaller, (2) the zones of overlap get larger, (3) the Z lines move closer together, and (4) the width of the A bands remains constant. The contraction ends once the fiber has shortened by about 30 percent, which coincides with the elimination of the I bands. These observations make sense only if the thin filaments are sliding toward the center of the sarcomere, alongside the thick filaments

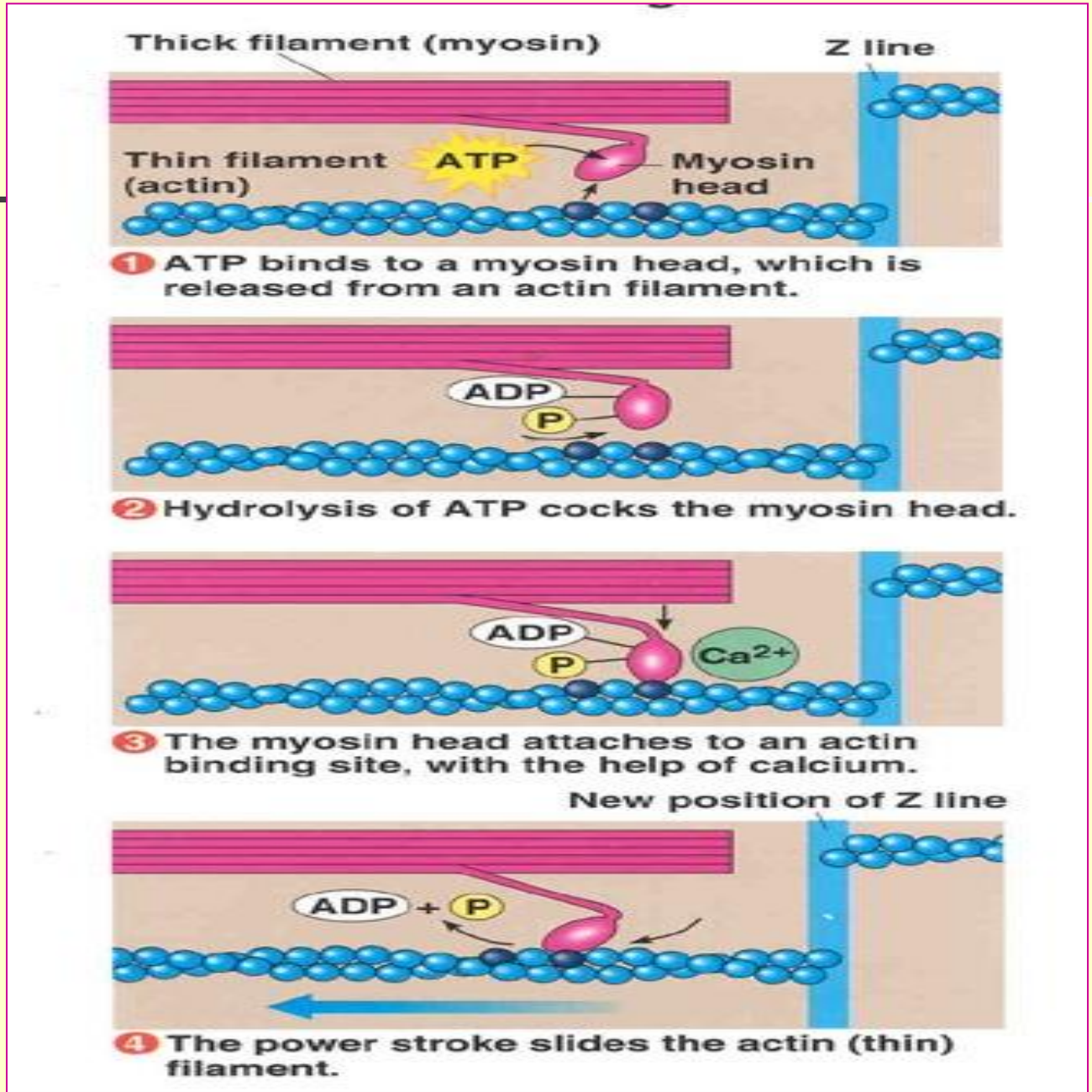
A Muscle relaxed– no contact between actin and myosin

B Cross-bridges form, actin filaments move closer together

C Cross-bridges return to normal postion, attach to new sites



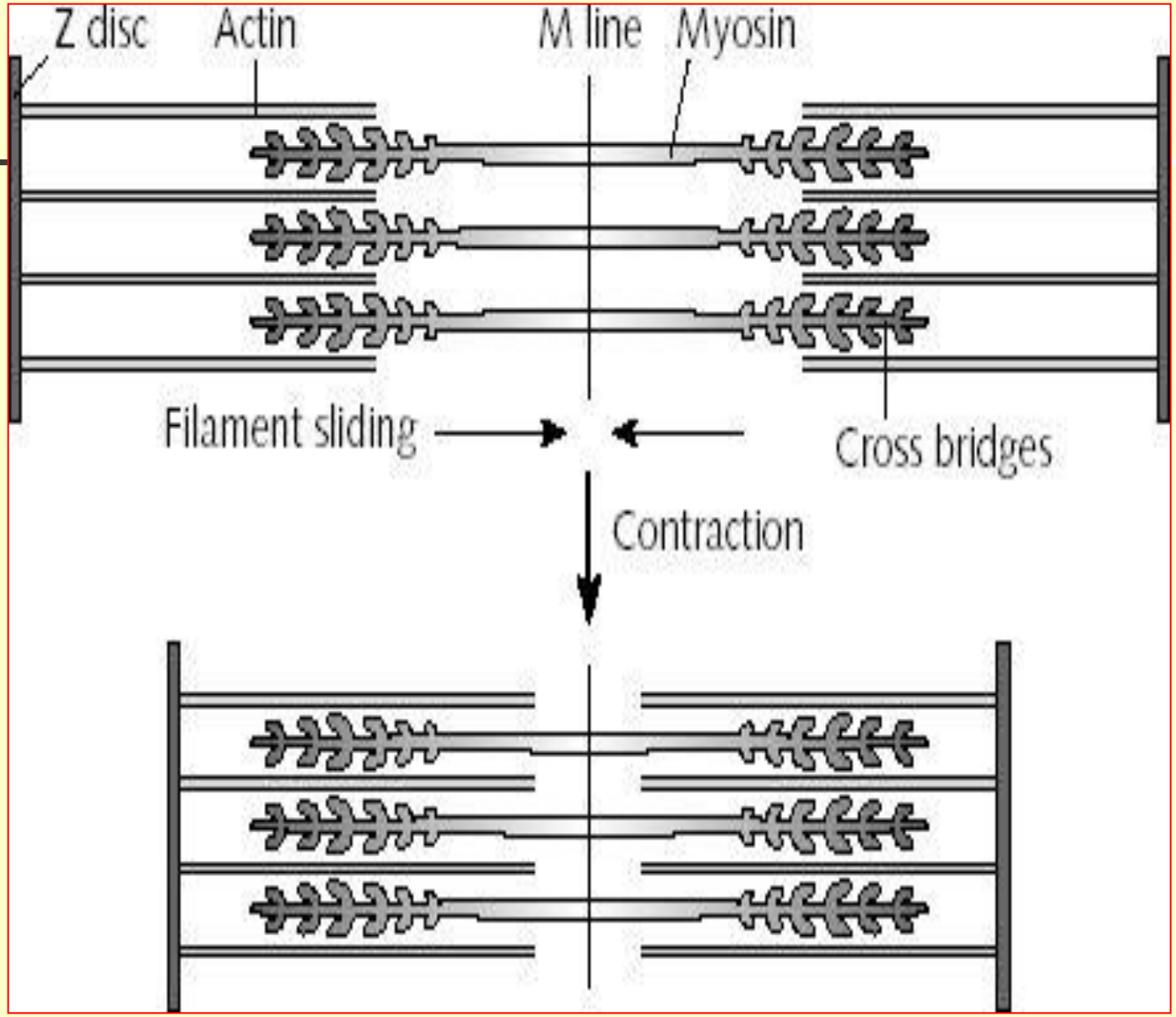
Muscle Contractions



Muscle Contractions
steps

- As long as calcium is present (attached to TROPONIN), steps 7 through 9 will continue. And, as they do, the thin myofilament is being "pulled" by the MYOSIN HEADS of the thick myofilament. Thus, the THICK & THIN myofilaments are actually sliding past each other. As this occurs, the distance between the Z-lines of the sarcomere decreases. As sarcomeres get shorter, the myofibril, of course, gets shorter. And, obviously, the muscle fibers (and entire muscle) get shorter.

Muscle contraction



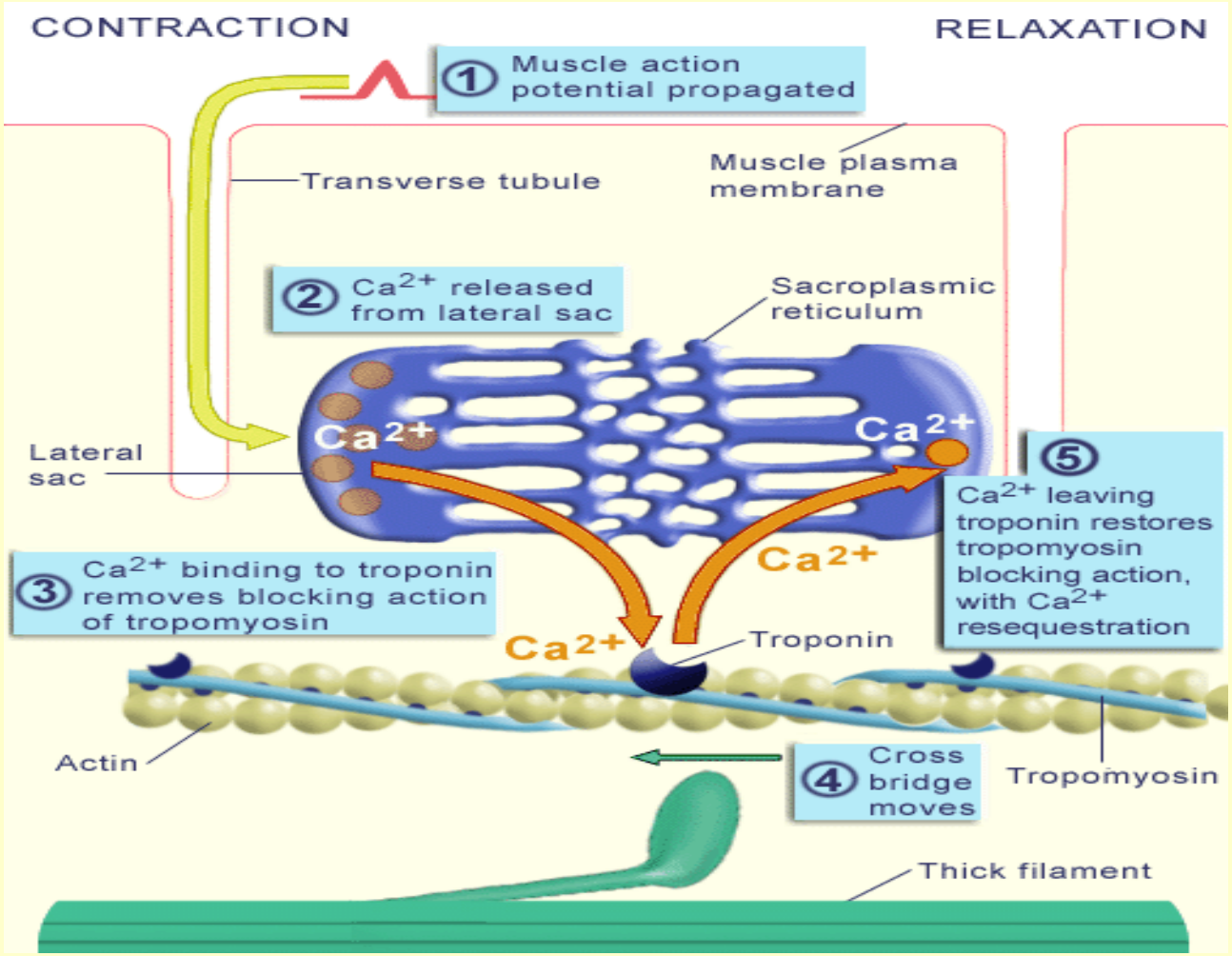
Muscle relaxation

- Skeletal muscle relaxes when the nervous impulse stops. No impulse means that the membrane of the SARCOPLASMIC RETICULUM is no longer permeable to calcium (i.e., no impulse means that the CALCIUM GATES close). So, calcium no longer diffuses out. The CALCIUM PUMP in the membrane will now transport the calcium back into the SR. As this occurs, calcium ions leave the binding sites on the TOPONIN MOLECULES.

Muscle relaxation

- Without calcium, troponin changes shape and allows tropomyosin to block binding sites for myosin on actin
- ATP bound to myosin heads
- So, the MYOSIN head is no longer in contact with ACTIN and, therefore, the muscle stops contracting (i.e., relaxes).

Contraction - relaxation



Contraction - relaxation

- So, under most circumstances, calcium is the "switch" that turns muscle "on and off" (contracting and relaxing). When a muscle is used for an extended period, ATP supplies can diminish. As ATP concentration in a muscle declines, the MYOSIN HEADS remain bound to actin and can no longer swivel. This decline in ATP levels in a muscle causes MUSCLE FATIGUE. Even though calcium is still present (and a nervous impulse is being transmitted to the muscle), contraction (or at least a strong contraction) is not possible.

Rigor mortis

- When death occurs, circulation ceases and the skeletal muscles are deprived of nutrients and oxygen.Within a few hours, the skeletal muscle fibers have run out of ATP and the sarcoplasmic reticulum becomes unable to pump Ca^{2+} out of the sarcoplasm. Calcium ions diffusing into the sarcoplasm from the extra cellular fluid or leaking out of the sarcoplasmic reticulum then trigger a sustained contraction. Without ATP, the cross-bridges cannot detach from the active sites. Skeletal muscles throughout the body become locked in the contracted position.

Rigor mortis

- Because all the skeletal muscles are involved, the individual becomes “stiff as a board.” This physical state, called **rigor mortis**, lasts until the lysosomal enzymes released by autolysis break down the myofilaments 15–25 hours later. The timing is dependent on environmental factors, such as temperature. Forensic pathologists can estimate the time of death on the basis of the degree of rigor mortis and the characteristics of the local environment.

Different Types of Skeletal Muscle Fibers Specialize for Endurance or Speed

Muscle cells (fibers) specialize for their type of activity

Endurance fibers (type I)

- Have many mitochondria- the mitochondria give these fibers a red appearance because one of the mitochondrial enzymes contains Fe.
- Also contain a red pigment called myoglobin which stores O_2.
- Contract slowly but resist fatigue

Fast twitch fibers (type II)

- Fibers specialized for fast contractions are white- they contain few mitochondria
- Relying on glycolysis to supply energy (glycolysis is faster than respiration).
- Contract rapidly but fatigue quickly

Excitation of skeletal muscle

- ***The resting membrane potential of skeletal muscle cell = - 90 mV.***
- ***It can be exited by signals of motor nerve.***

  Myoneural synapse

  *neurotransmitter – **acetylcholin***
- *postsynaptic receptors - **N cholinoreceptors***
- ***depolarizing PSP is generated***

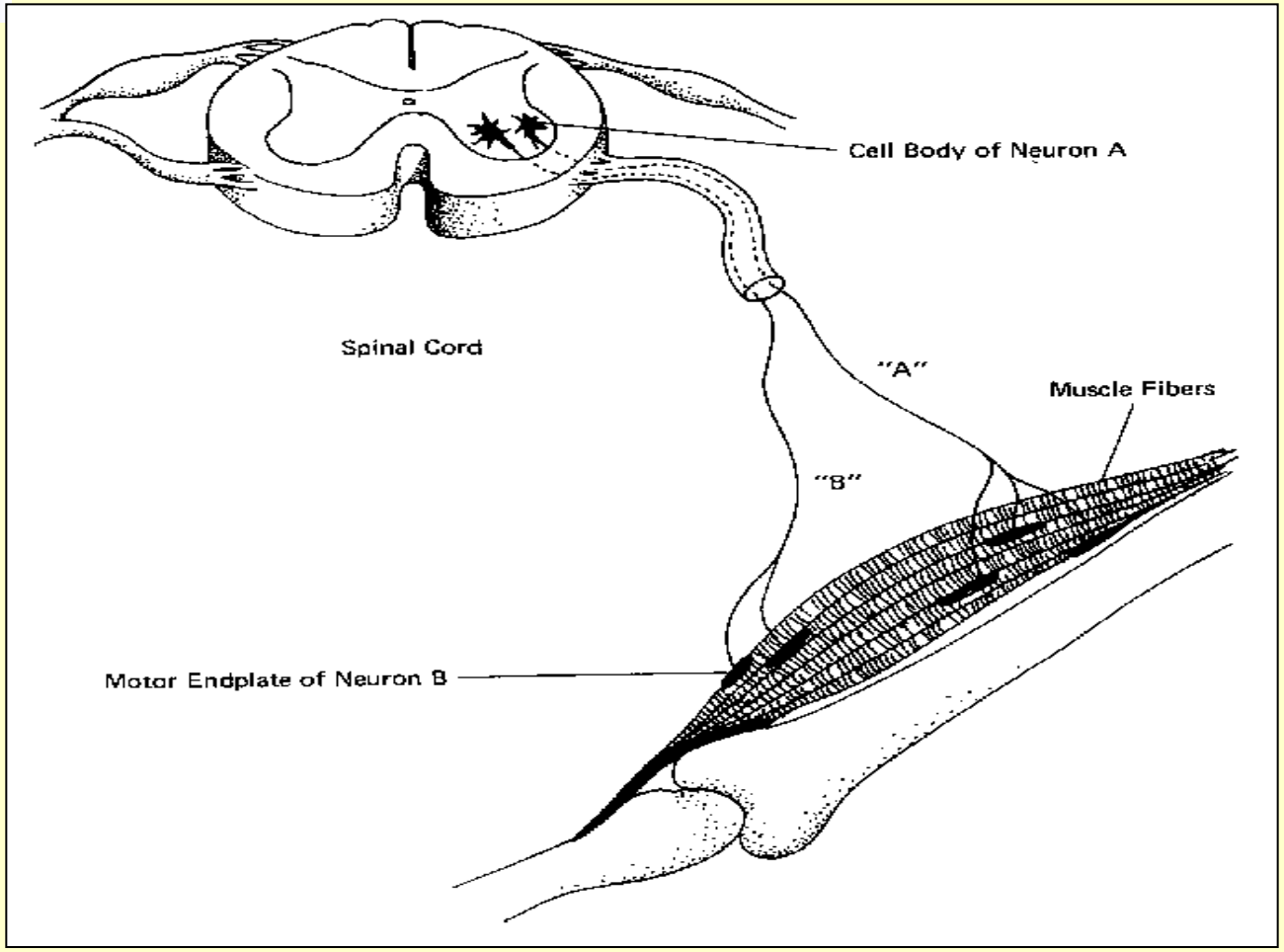
Excitation of skeletal muscle

- ***Action potential (AP) is generated and travels along sarcolemma.***

Excitation - contraction coupling- the process by which depolarization of muscle fiber initiates contraction

The AP is transmitted to all the fibrils of the fiber via the T- system. It triggers the release of Ca^{2+} ions from the terminal cisterns trough the Ca^{2+} channels*(ryanodine receptors).*

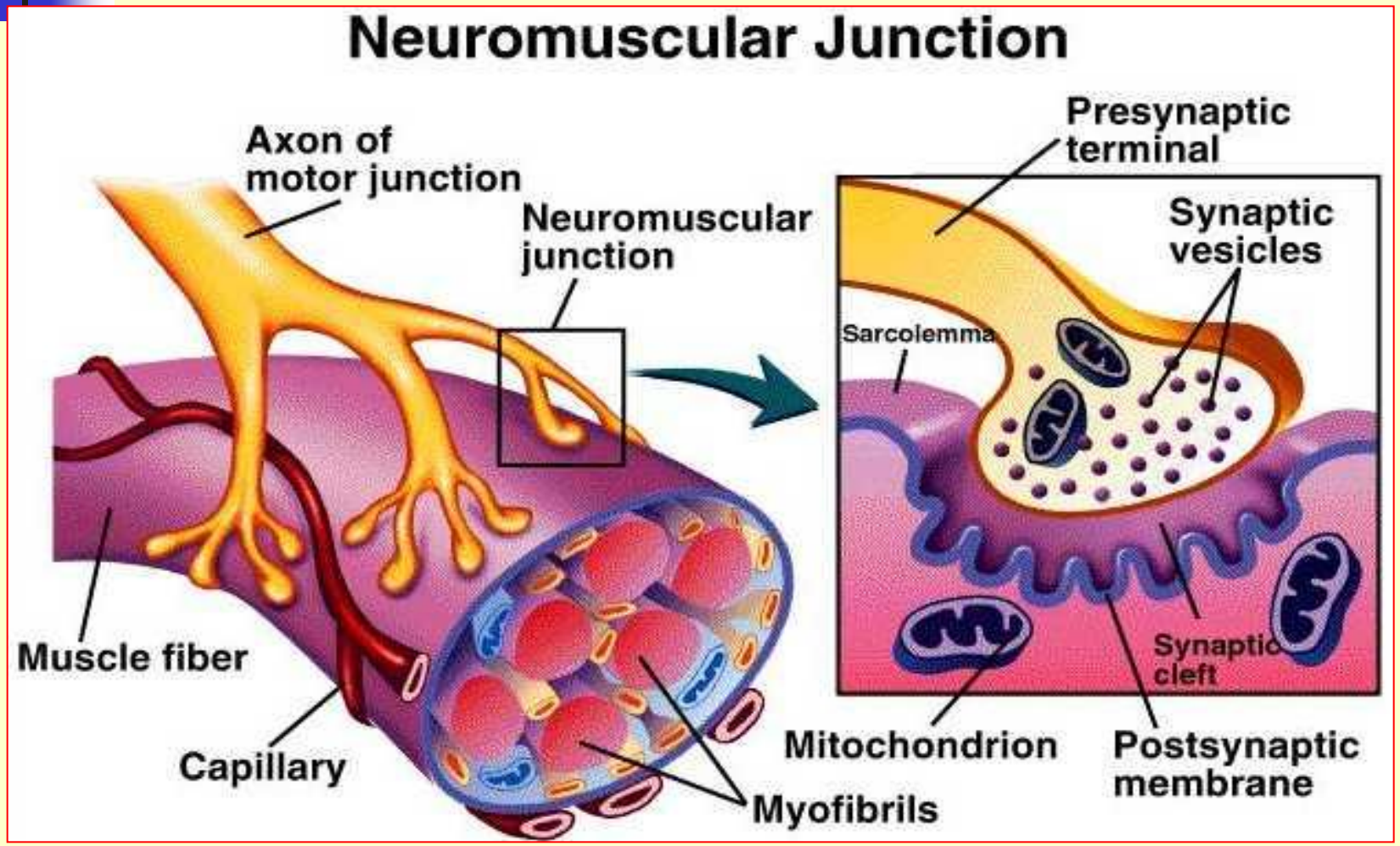
Neuromuscular junction



Neuromuscular junction

- The neuromuscular junction (NMJ) is the synapse between the presynaptic motor neuron and the postsynaptic muscle membrane. The axon divides into terminal buttons that invaginate into the muscle fiber. The synaptic cleft is 50-70 nm wide and filled with extra cellular fluid. The orifices lie opposite the release points for Ach and contain high concentrations of acetyl cholinesterase.

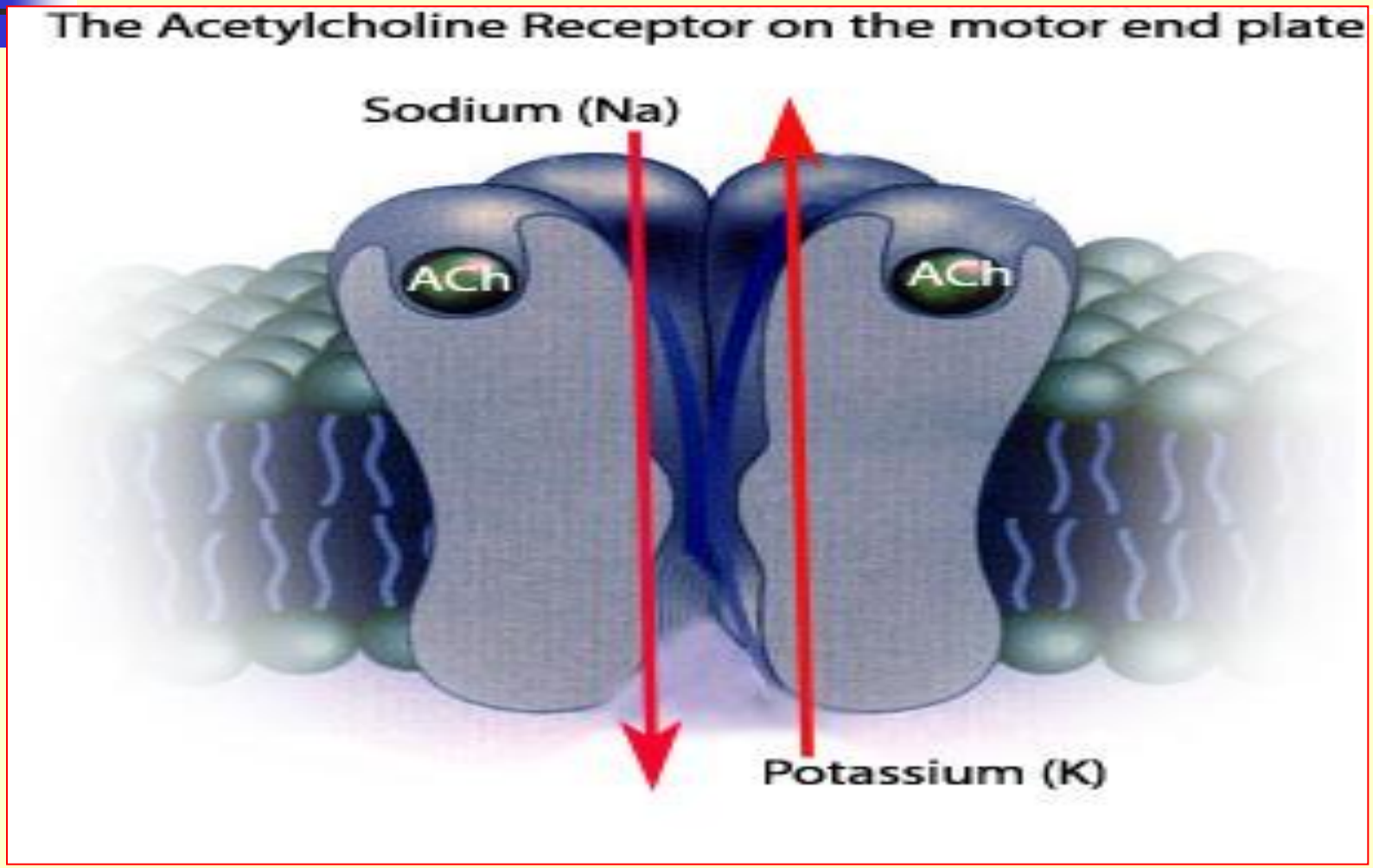
Neuromuscular junction



Neuromuscular junction

- The action potential conducted along the motor nerve causes depolarization and an influx of calcium. The influx of calcium stimulates the release of Ach from storage vesicles into the synapse. Ach binds to nicotinic receptors on the motor end plate. Stimulation of the Ach receptor results in opening of sodium channels (and some potassium channels), and influx of sodium and potassium into the cell results in depolarization. Depolarization is termed "end plate potential" (EPP). If the EPP is sufficiently large, an action potential is produced, muscle contraction occurs and Ach is metabolized by acetyl cholinesterase.

Neuromuscular junction



Muscle Contractions

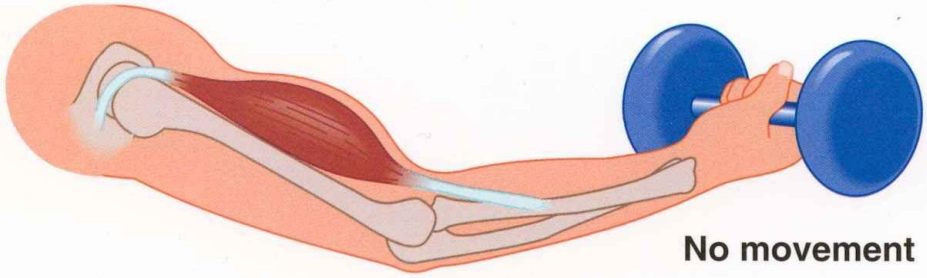
- The contraction of a muscle does not necessarily imply that the muscle shortens; it only means that tension has been generated. Muscles can contract in the following ways:
- "**isometric contraction**"

  This is a contraction in which no movement takes place, because the load on the muscle exceeds the tension generated by the contracting muscle. This occurs when a muscle attempts to push or pull an immovable object.

Isotonic contraction

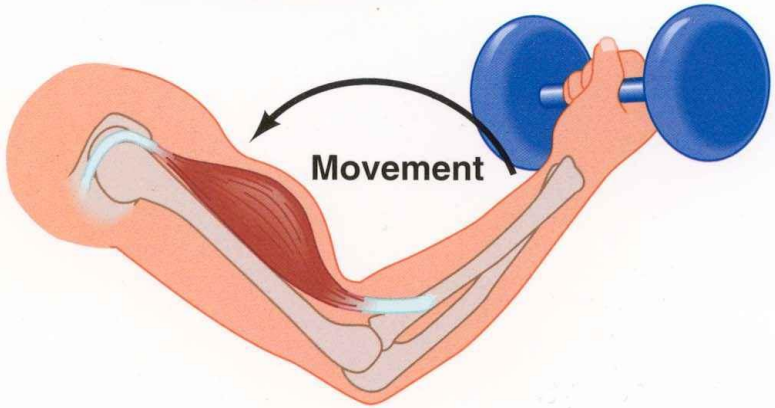
- **Isotonic contractions are further divided into two types**:
  - "concentric contraction" This is a contraction in which the muscle decreases in length (shortens) against an opposing load, such as lifting a weight up.
  - "eccentric contraction" This is a contraction in which the muscle increases in length (lengthens) as it resists a load, such as pushing something down.

Isometric contraction
Muscle contracts
but does not shorten



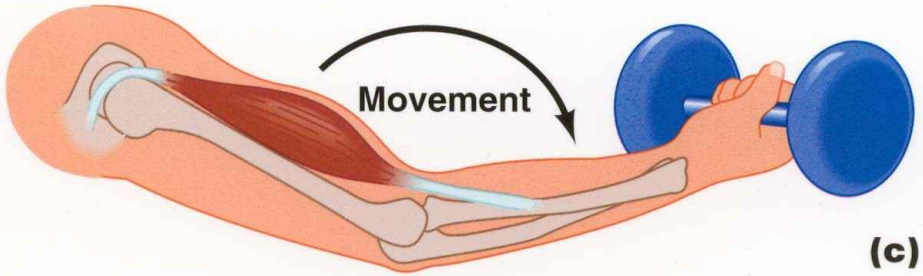
(a)

Concentric contraction



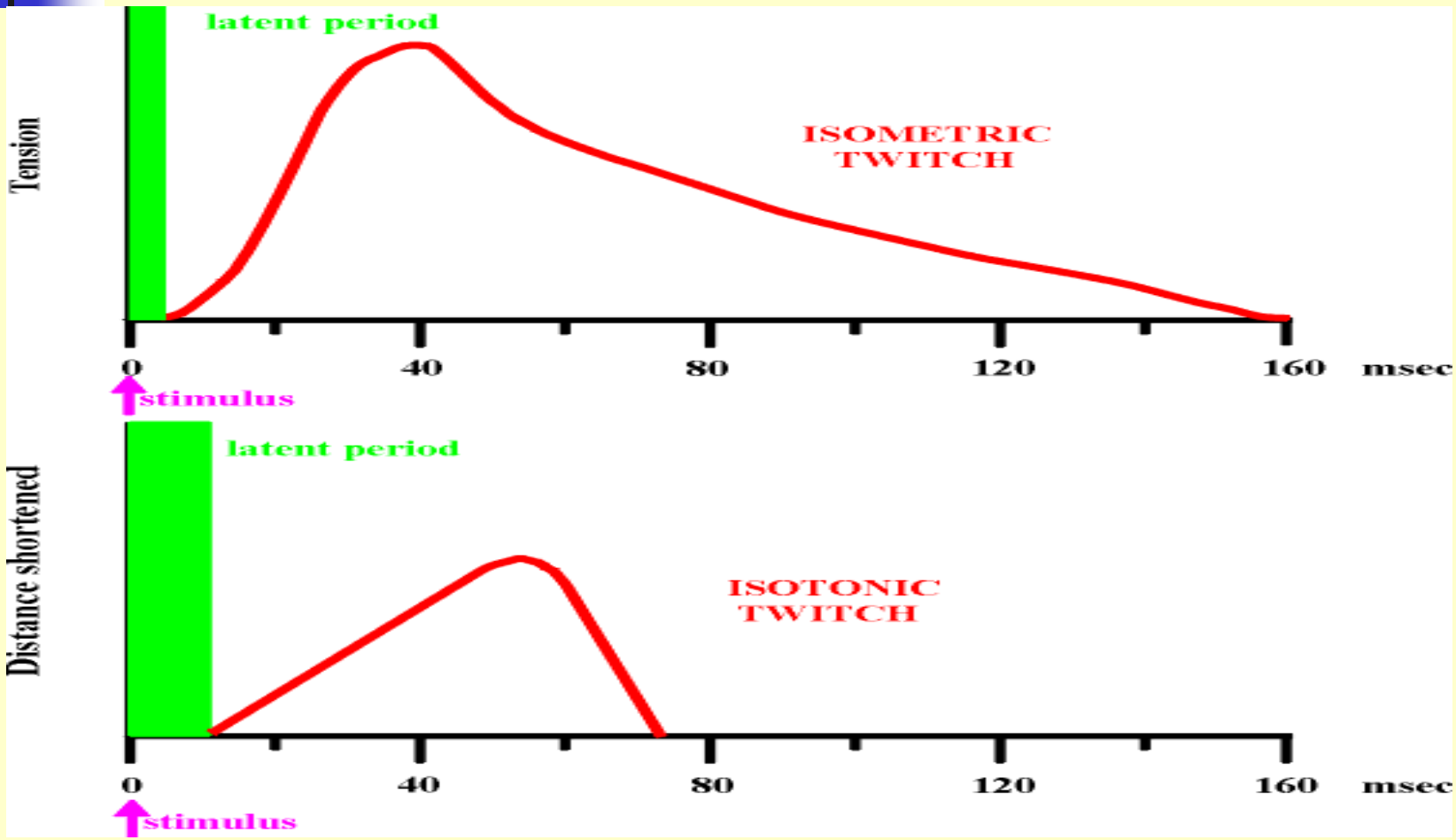
(b)

Eccentric contraction



(c)

Muscle Contractions

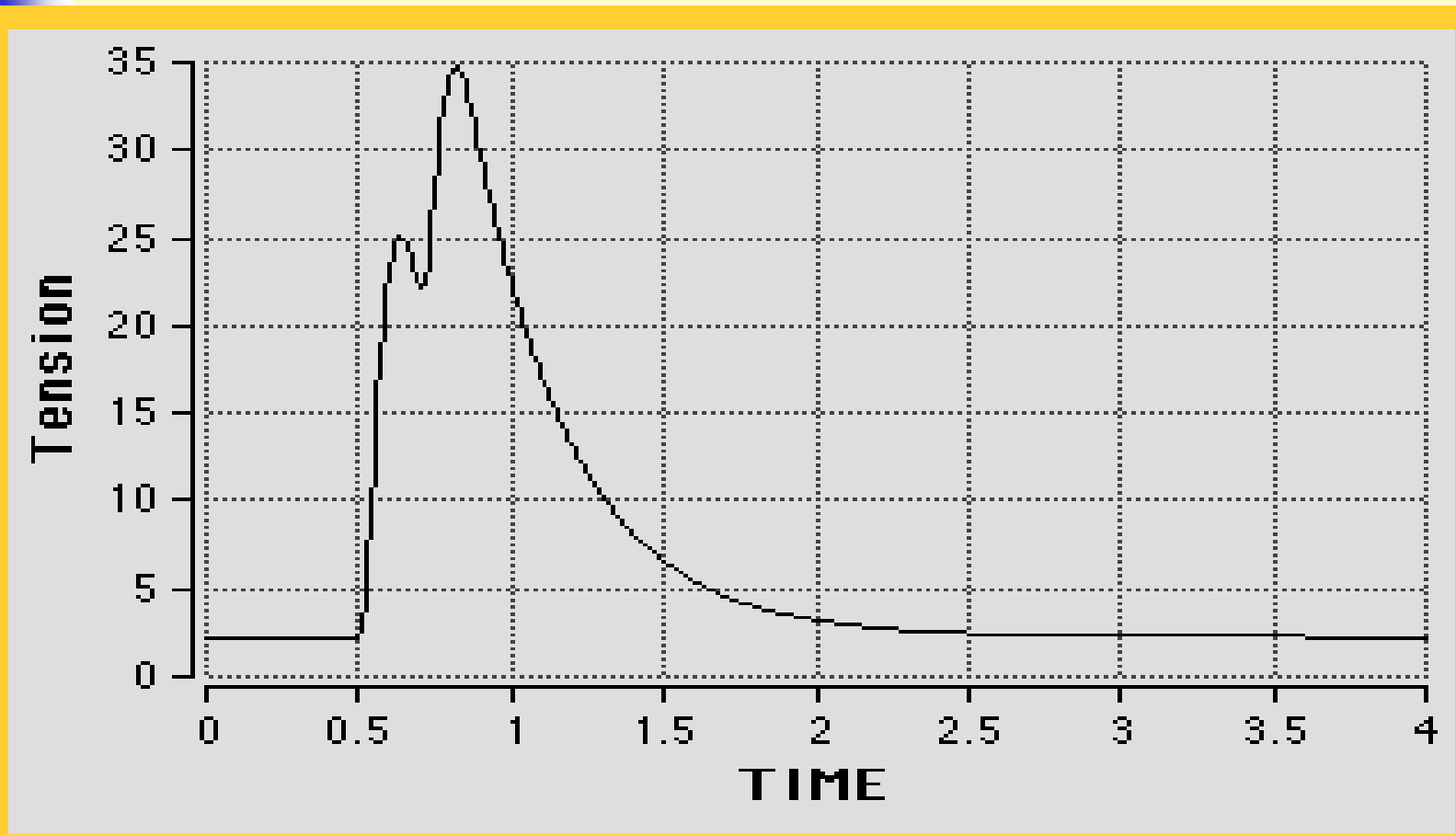


Single muscle twitch - the response of a skeletal muscle to a single stimulation (or action potential):

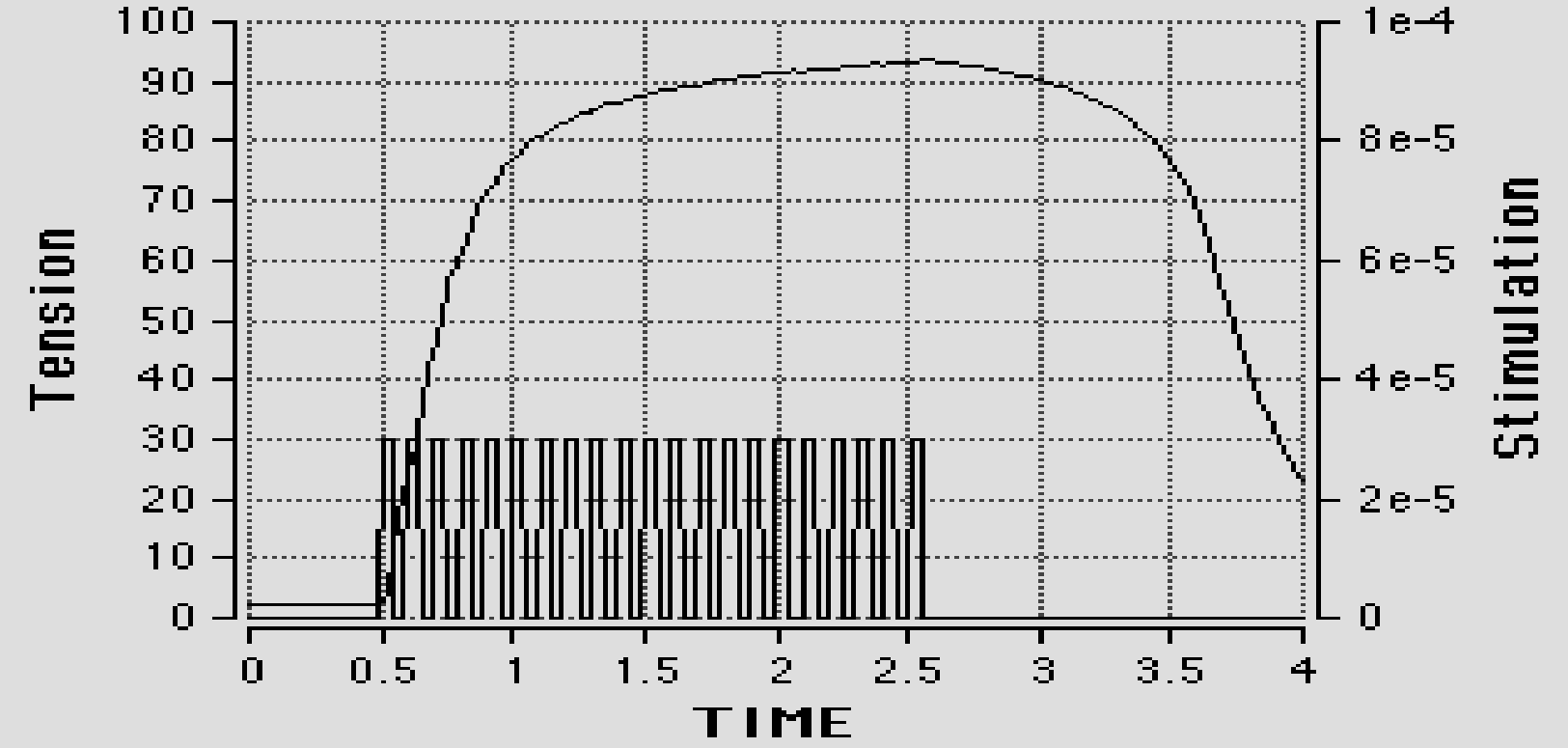
- **latent period** - no change in length; time during which impulse is traveling along sarcolemma & down t-tubules to sarcoplasmic reticulum, calcium is being released, and so on (in other words, muscle cannot contract instantaneously!)
- **contraction period** - tension increases (cross-bridges are swiveling)
- **relaxation period** - muscle relaxes (tension decreases) & tends to return to its original length

A simple twitch gives only 20-30% of the maximum tension possible- the muscle starts to relax before the maximum is reached

If a second stimulus is given before a muscle relaxes the muscle will shorten further, building up more tension than a simple twitch- this is called summation.



If many stimuli are given very close together the muscle will go into a smooth continuous contraction called tetanus.



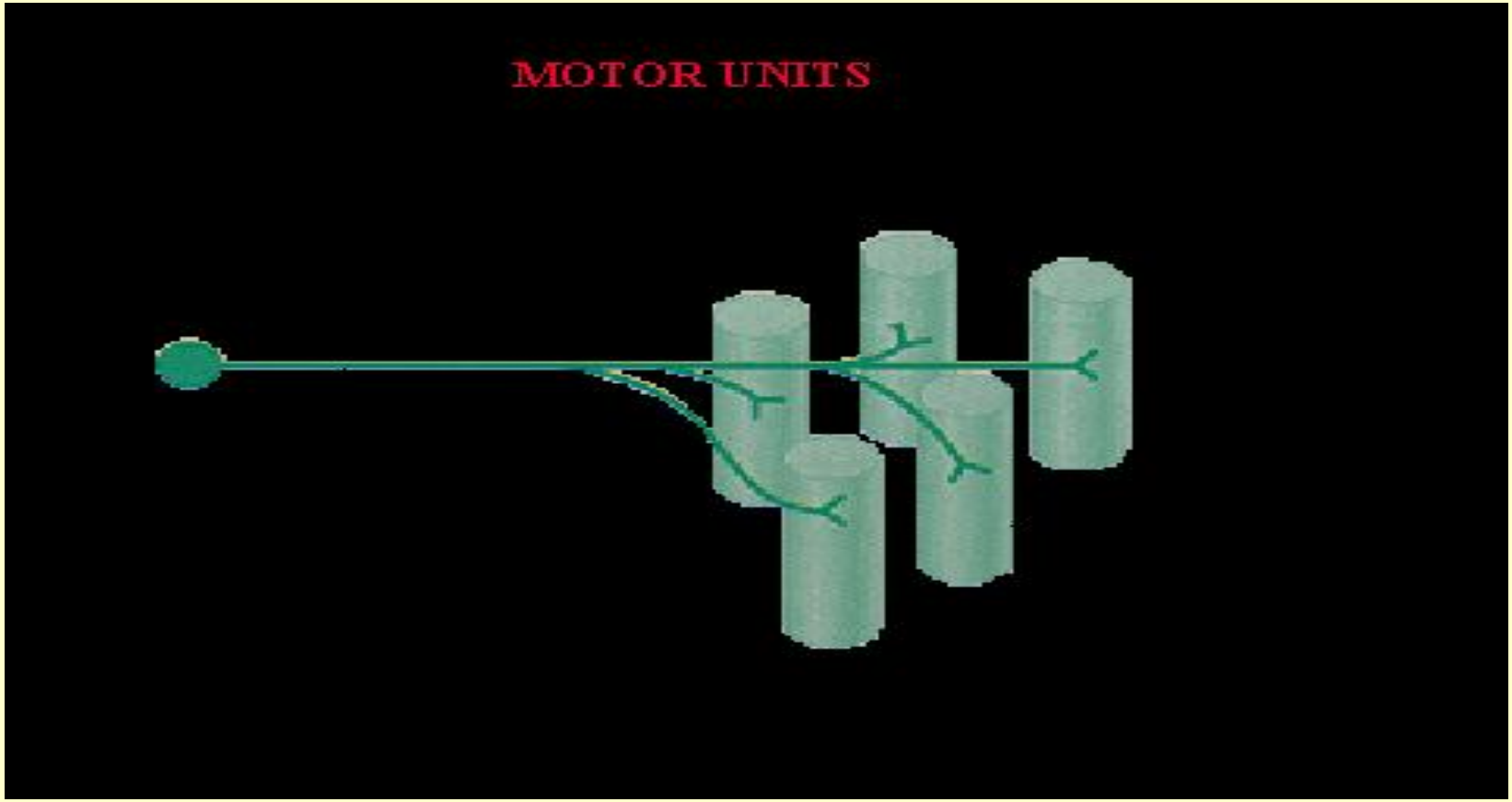
Mechanisms for control of force of contraction

- **Muscle Contractions Can Summate to Produce More Force,** when the frequency of signals of motoneurons increases
- **Another Way to Increase the Force of Contraction is to Recruit More Motor Units**
- Each muscle is made up of tens of thousands of motor units
- Force generated by a muscle can be increased by firing more and more motor units

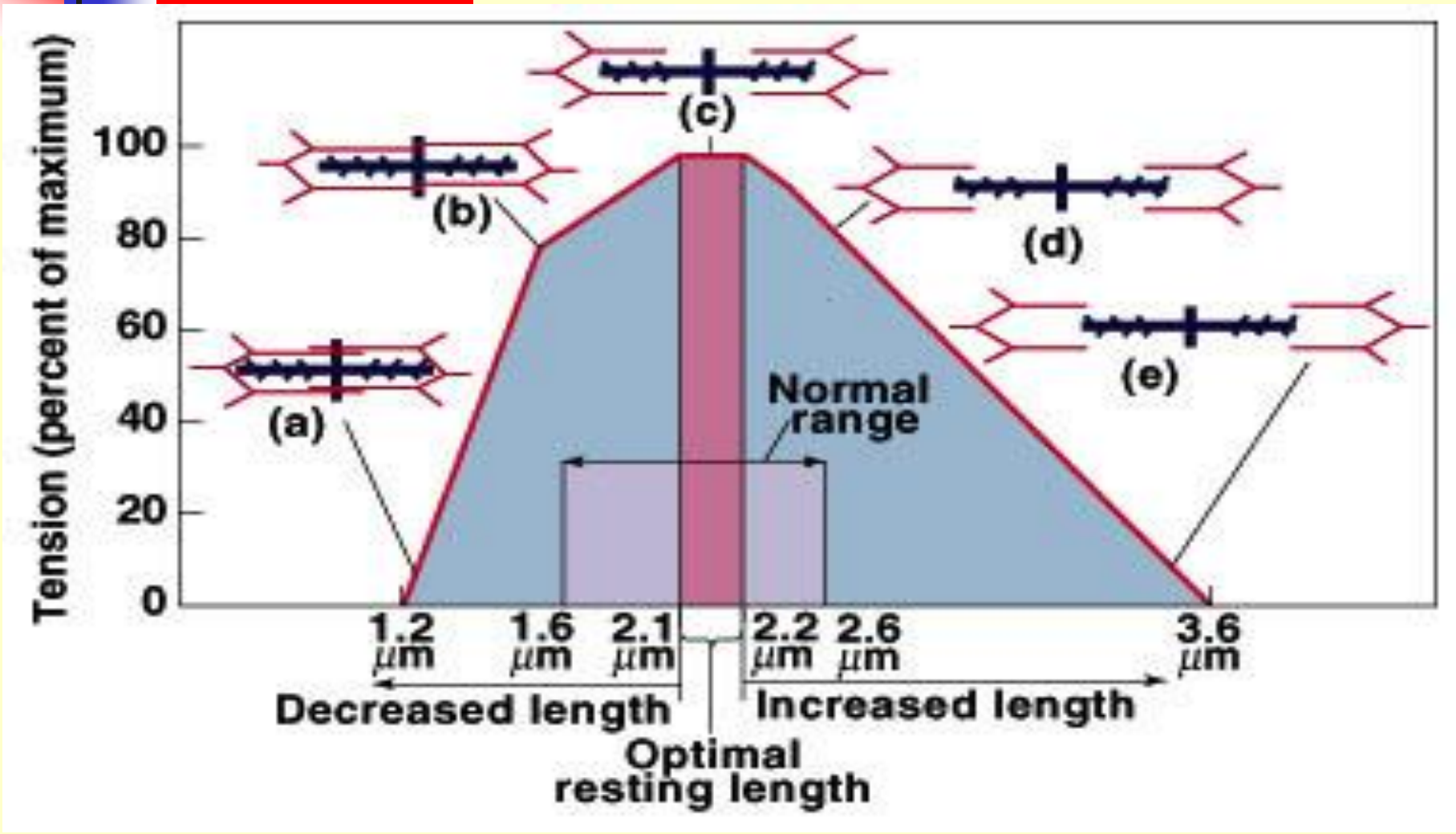
Motor unit

- **Motor unit - all the muscle fibers innervated by a single motoneuron.**
- Each muscle has many motor units. Each motor unit contains only one type of muscle fibers.

Motor unit



The Effect of Sarcomere Length on Tension.



The Effect of Sarcomere Length on Tension.

- At short resting lengths, thin filaments extending across the center of the sarcomere interfere with the normal orientation of thick and thin filaments, reducing tension production. In addition, very little contraction can occur before the thick filaments crash into the Z lines. **(c)** The maximum tension is produced when the zone of overlap is large but the thin filaments do not extend across the sarcomere's center. If the sarcomeres are stretched too far, the zone of overlap **(d)** is reduced or **(e)** disappears, and cross-bridge interactions are reduced or cannot occur. The light purple area represents the normal range of sarcomere lengths.

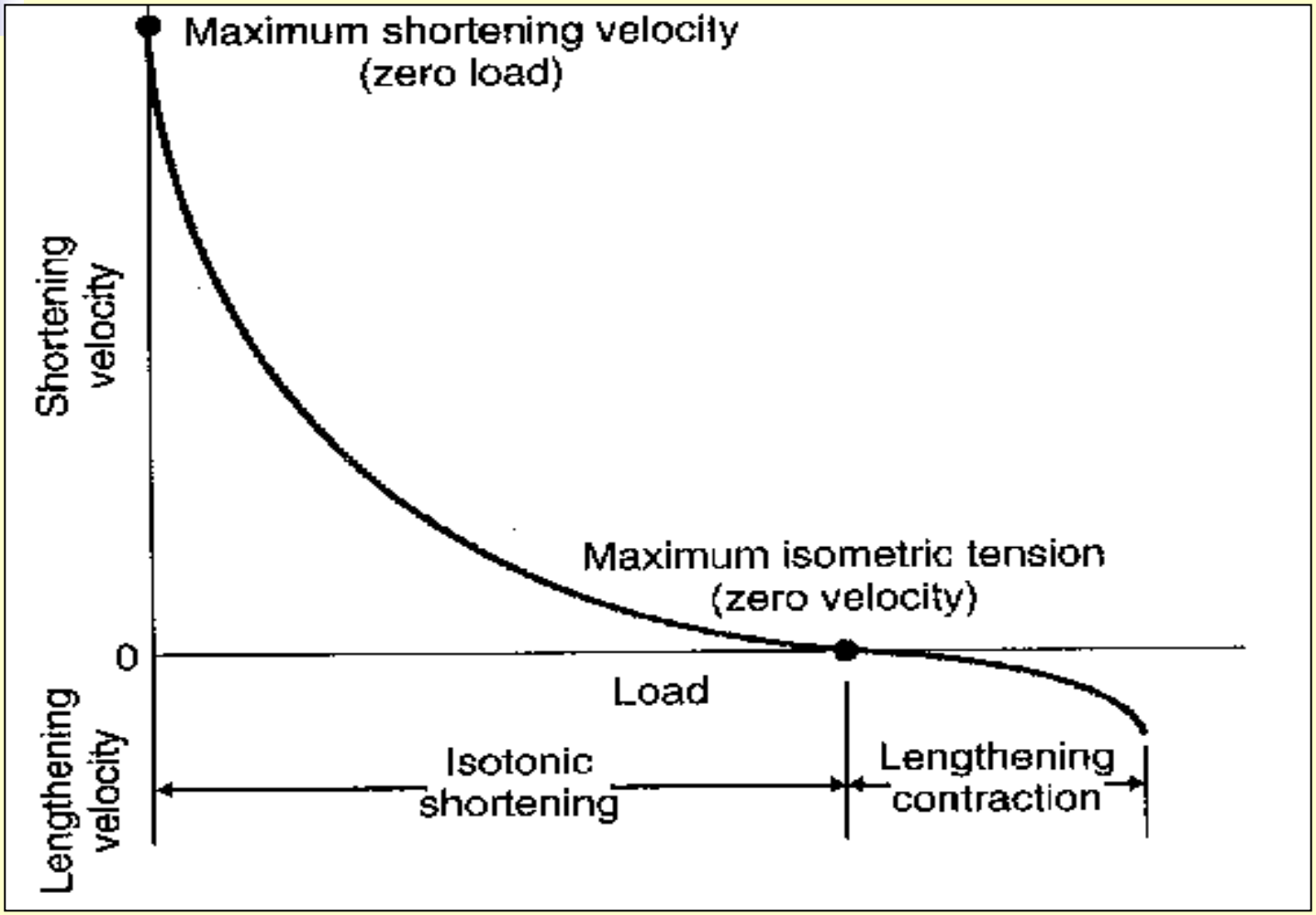
Force-velocity relationship

- What is the physiologic basis of the force-velocity relationship? The force generated by a muscle depends on the total number of cross-bridges attached. Because it takes a finite amount of time for cross-bridges to attach, as filaments slide past one another faster and faster (i.e., as the muscle shortens with increasing velocity), force decreases due to the lower number of cross-bridges attached. Conversely, as the relative filament velocity decreases (i.e., as muscle velocity decreases), more cross-bridges have time to attach and to generate force, and thus force increases.

Relation between muscle length, tension and velocity of contraction

- * Maximum strength of contraction - when the muscle has the resting length before activation
- * The velocity of muscle contraction is maximal at the resting length.
- * A muscle contracts extremely rapidly when no load is applied.
- *When load is applied the velocity of contraction decreases and becomes zero if this load equals the maximum force, that the muscle can exert.

Relation between muscle length, tension and velocity of contraction



Благодаря за вниманието!