SYNAPSIS AND MUSCLE CONTRACTION

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Hyman physiology

First Semester

Week 5

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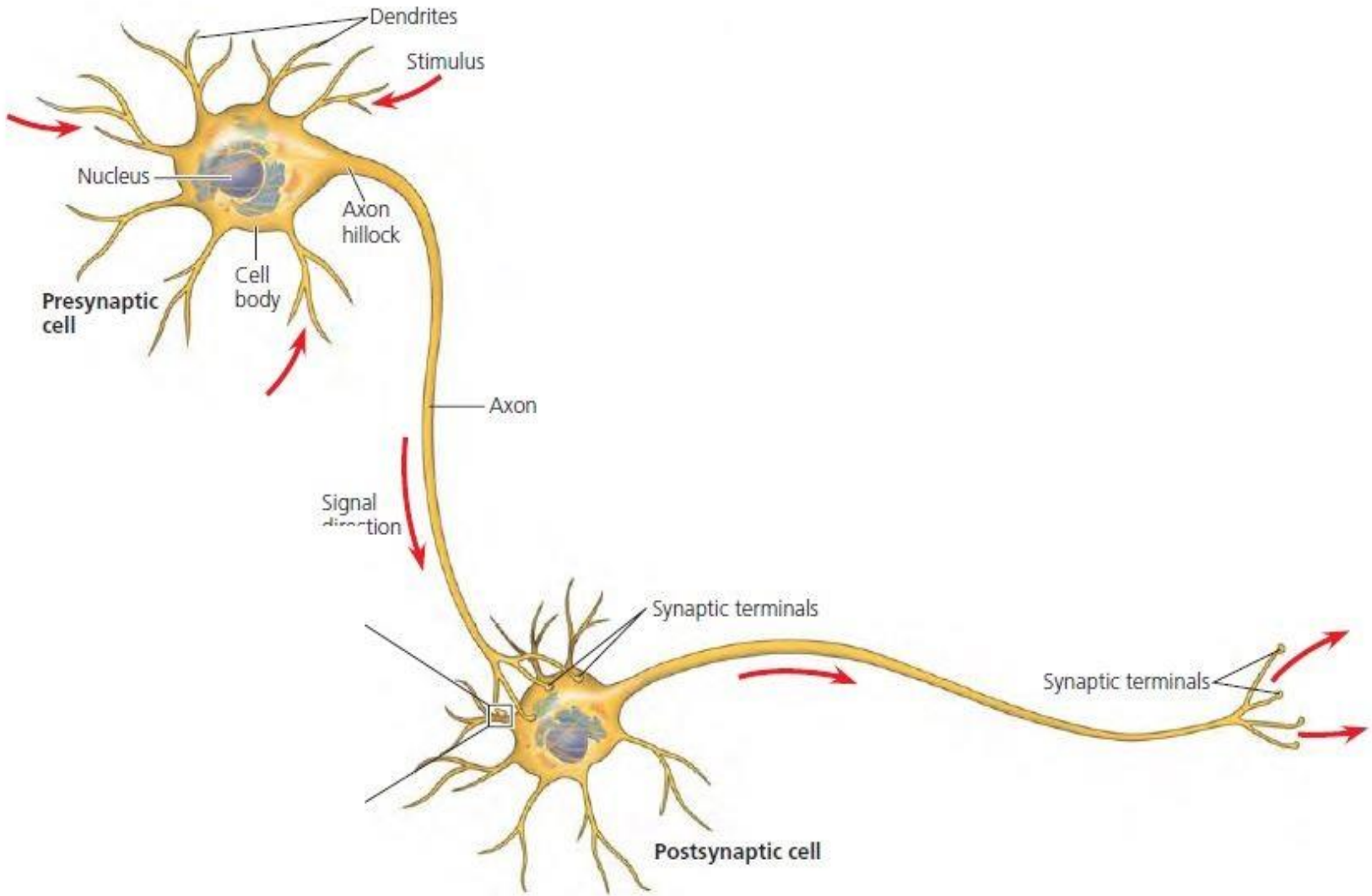
Outline

- Structure of Neuron
- Propagation of action potential
- Propagation of A.P. in myelinated neurons
- Discovery of action potential

Objectives

- Understanding structure of Neurons
- Understanding propagation of action potential
- Understanding why action potential not travelling backward
- Understanding saltatory conduction in myelinated neurons


Dendrites
Stimulus
Nucleus
Axon hillock
Cell body
Presynaptic cell
Axon
Signal
Synaptic terminals
Synaptic terminals
Postsynaptic cell

Conduction of Action Potentials or Action potential propagation

- **An unmyelinated fiber** has voltage-gated channels along its **entire** length.

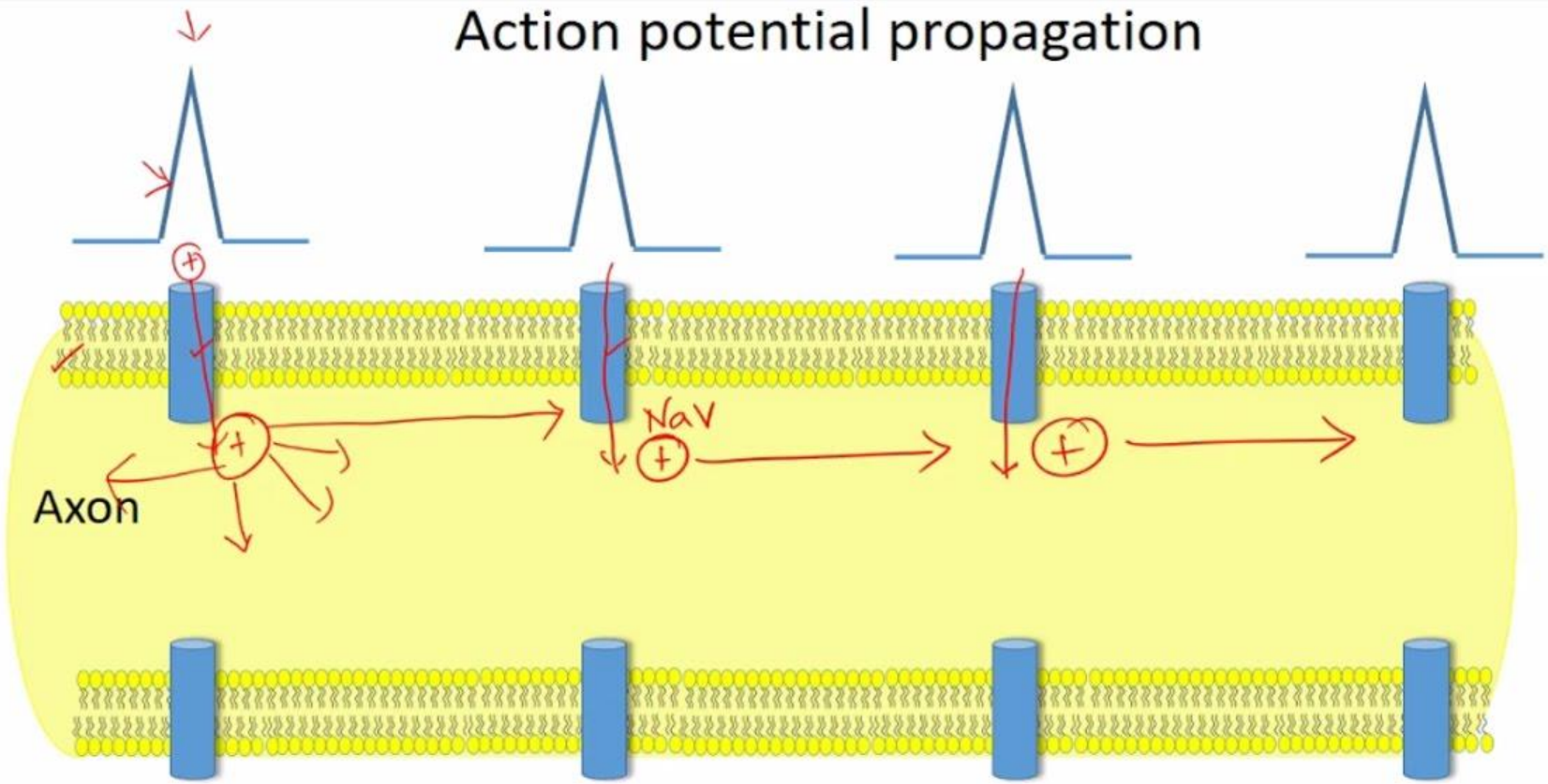
The result is the movement of a nerve impulse from the cell body to the synaptic terminals, much like the cascade of events triggered by knocking over the first domino in a line

- Note that an action potential itself doesn't travel along an axon; rather, it stimulates the production of a **new action potential** in the membrane just ahead of it.

- The **nerve signal** is a traveling wave of excitation produced by self-propagating action potentials It is like a line of falling dominoes.

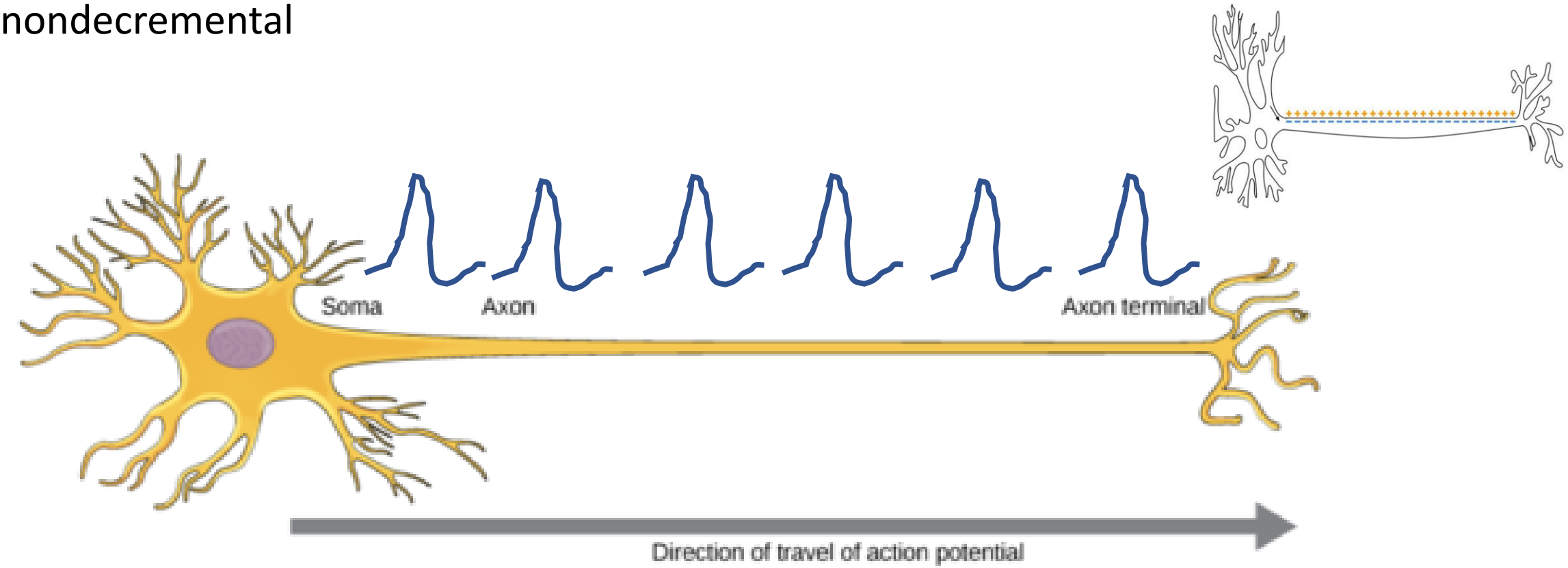
- No one domino travels to the end of the line, but each domino pushes over the next one and there is a transmission of energy from the first domino to the last. Similarly, no one action potential travels to the end of an axon; a nerve signal is a chain reaction of action potentials, each triggering the next one ahead of it.

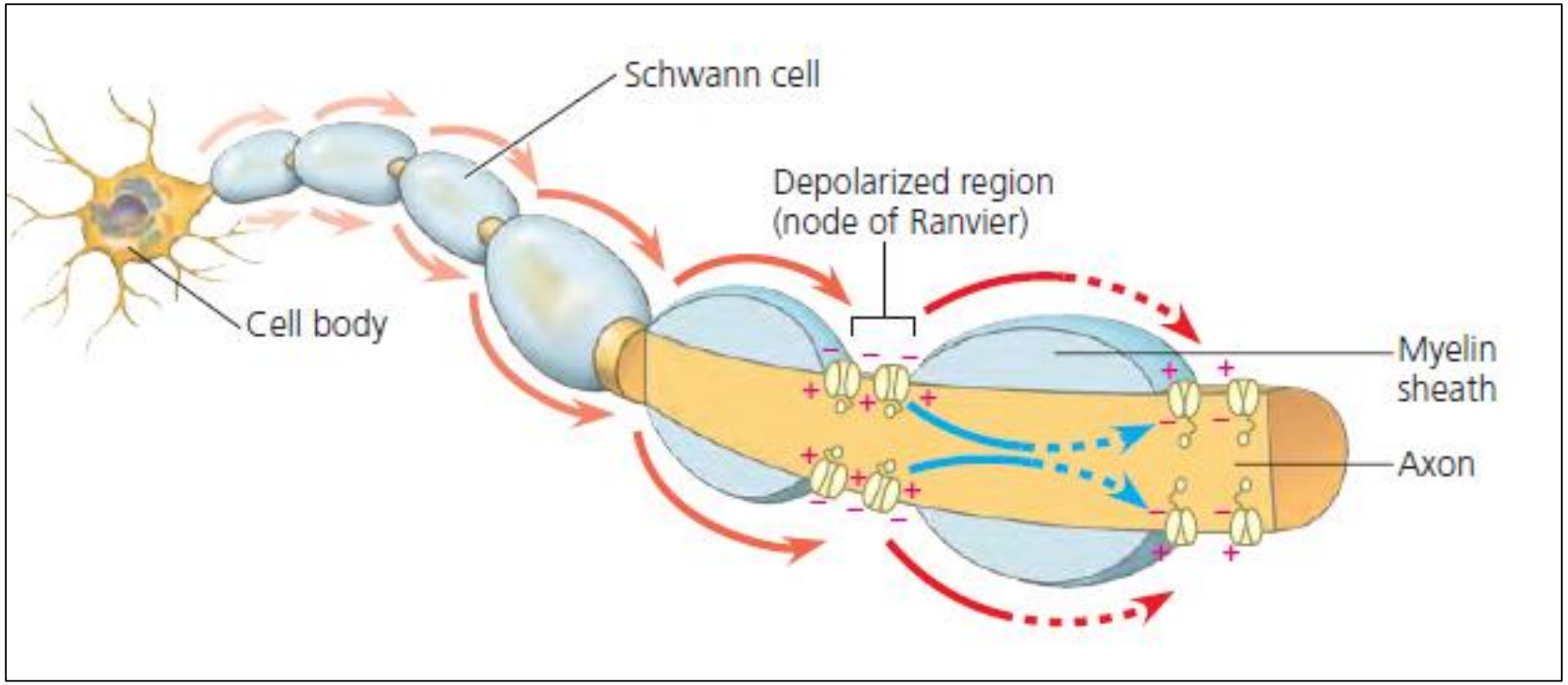
Action potential propagation



How far the charges spread...

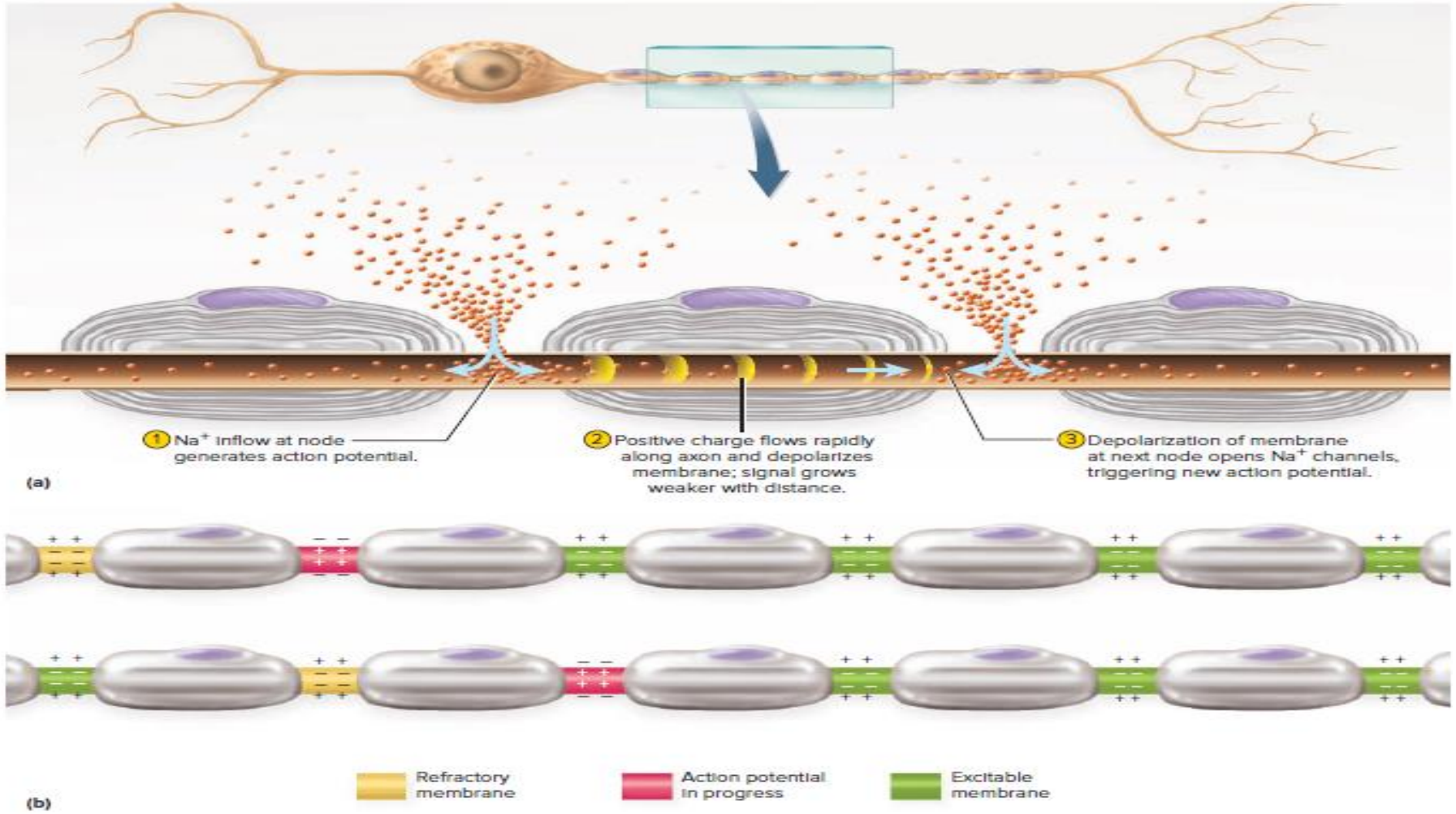
- A traveling nerve signal is an electrical current, but it isn't the same as a current traveling through a wire. A current in a wire travels millions of meters per second and is decremental—it get weaker with distance. A nerve signal is much slower (not more than2 m/s in unmyelinated fibers), but as already noted, it is nondecremental





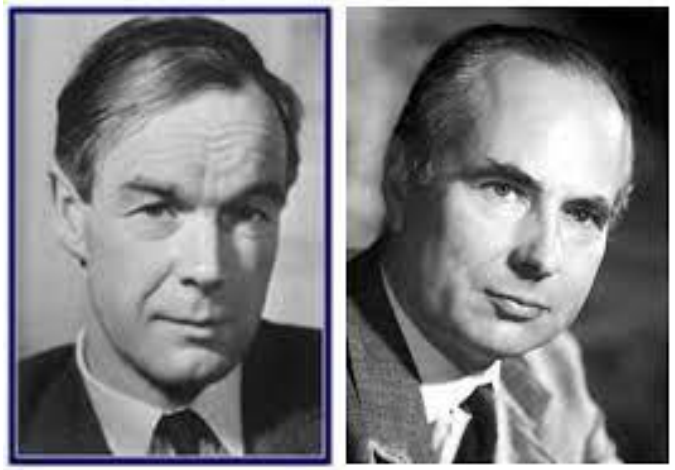
Saltatory conduction. Schwann cell In a myelinated axon, the depolarizing current during an action potential at one node of Ranvier spreads along the interior of the axon to the next node (blue arrows), where voltagegated sodium channels enable reinitiation. Thus, the action potential jumps from node to node as it travels along the axon (red arrows).

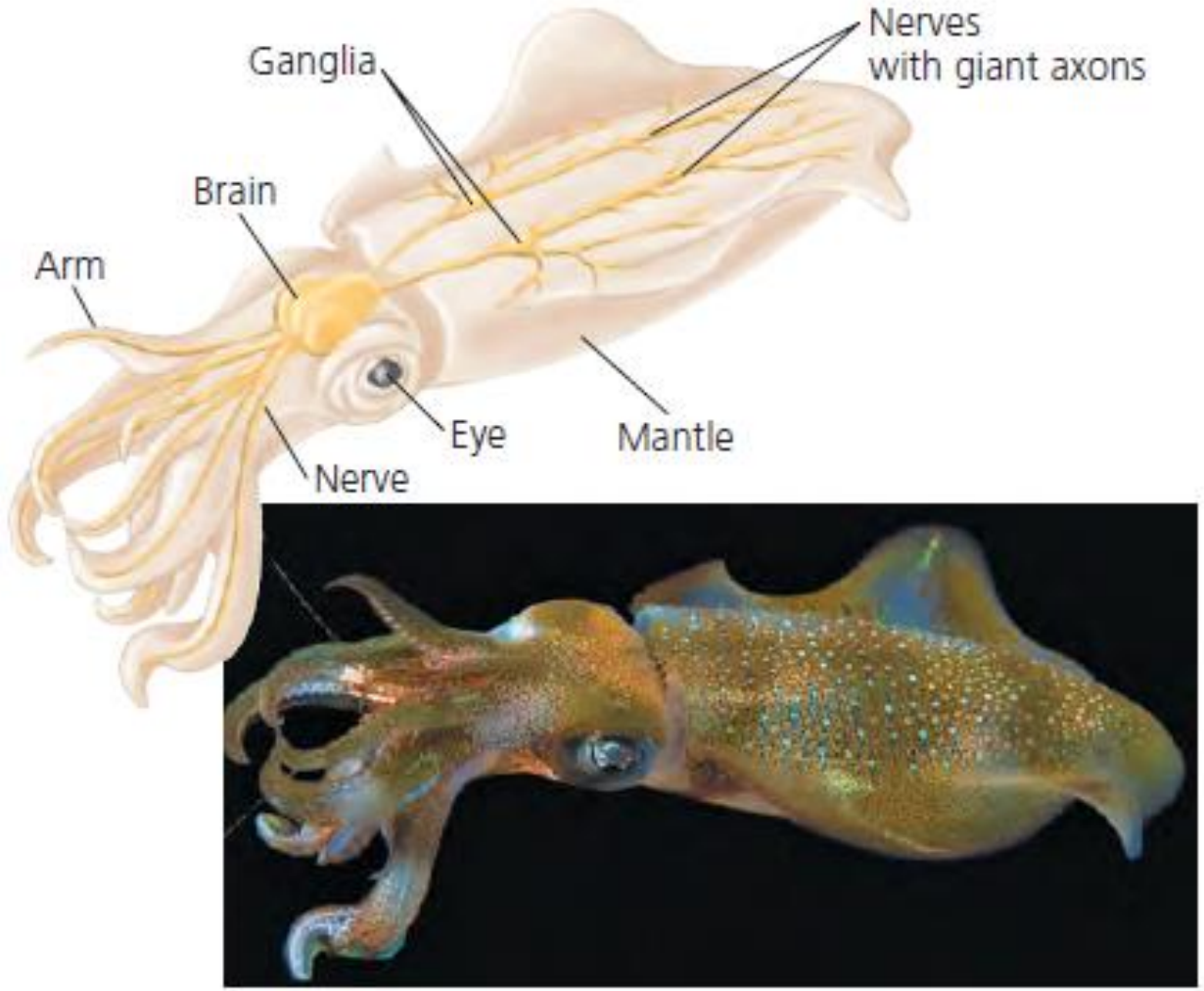
- In summary, myelinated fibers conduct signals much faster (up to 120 m/s) than unmyelinated ones (up to 2 m/s).



The Discovery of action potentials

- The discovery of how action potentials are generated dates to the 1940s and 1950s, with the work of British scientists Andrew Huxley and Alan Hodgkin.
- Because no techniques were available for studying electrical events in small cells, they took electrical recordings from the giant neurons of the squid (see Figure 48.2). Their experiments led to a model, presented in the next section, that earned them a Nobel Prize in 1963.



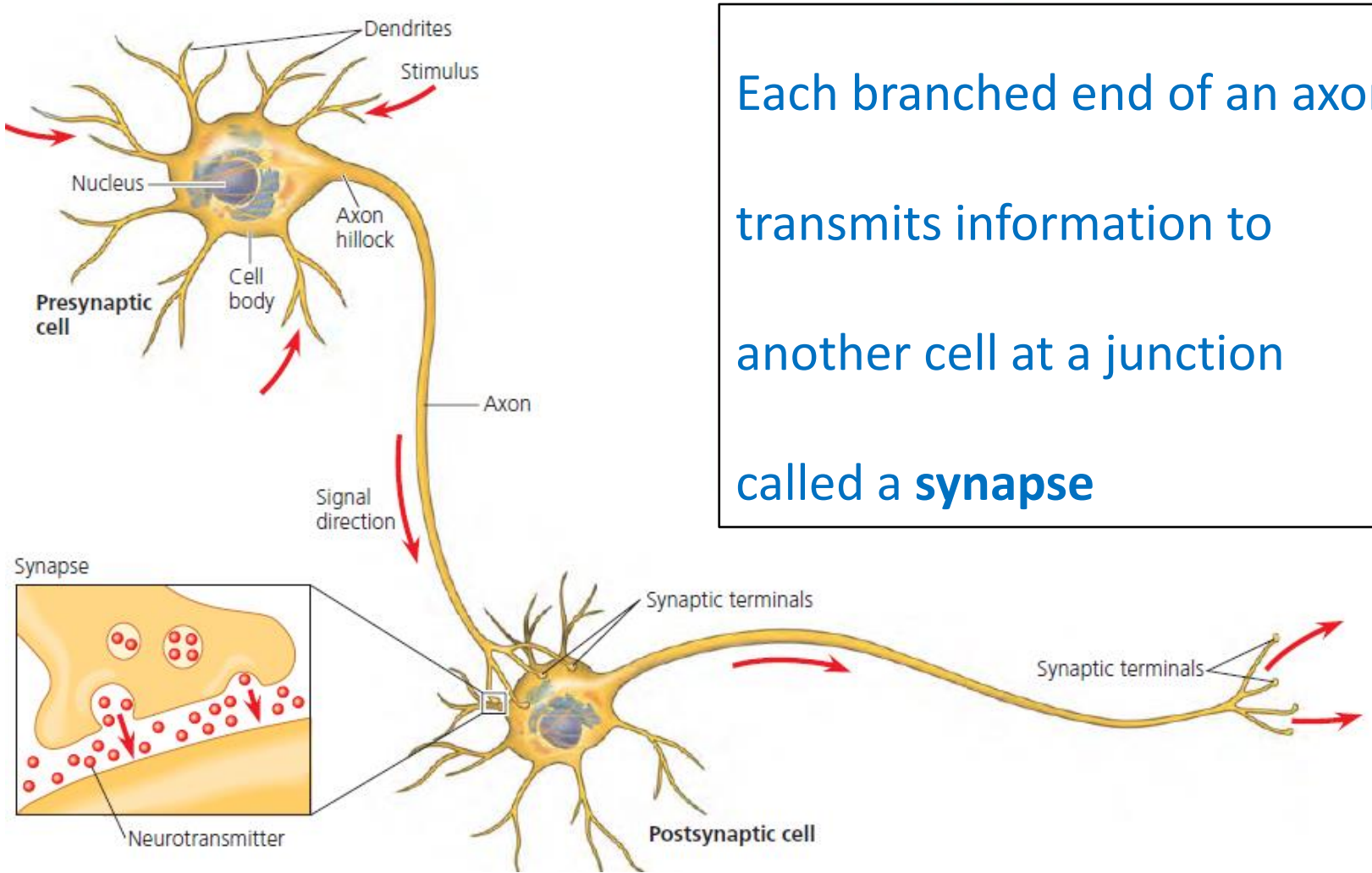


▲ **Figure 48.2 Overview of the squid nervous system.**
Signals travel from the brain to the muscular mantle along *giant axons*, nerve cell extensions of unusually large diameter.

Synapse

- The cone-shaped base of an axon, the *axon hillock*, is typically where signals that travel down the axon are generated.

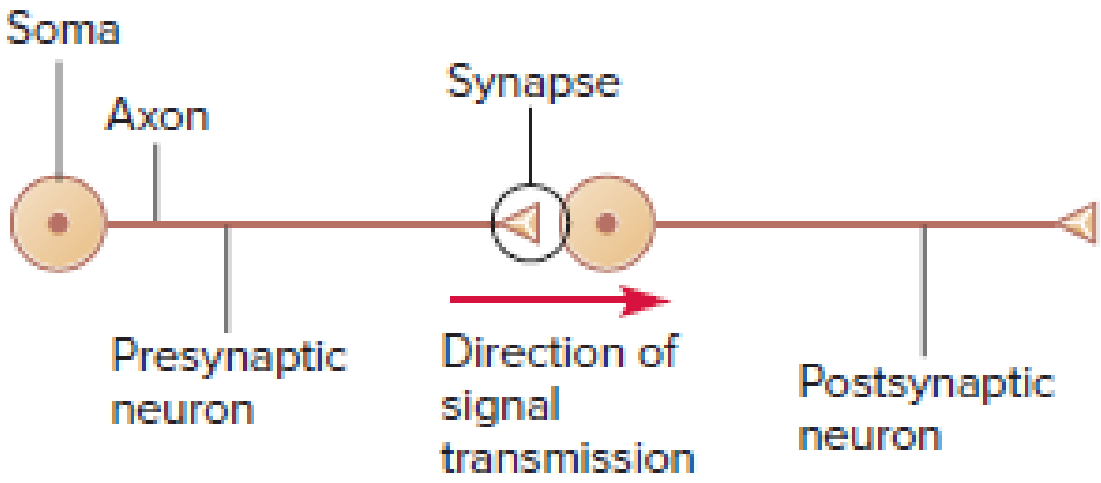
- Near its other end, an axon usually divides into many branches.



Each branched end of an axon transmits information to another cell at a junction called a **synapse**

- The part of each axon branch that forms this specialized junction is a *synaptic terminal*.
- At most synapses, chemical messengers called **neurotransmitters** pass information from the transmitting neuron to the receiving cell.
- In describing a synapse, we refer to the transmitting neuron as the ***presynaptic cell*** and the **neuron**, **muscle**, or **gland cell** that receives the signal as the ***postsynaptic cell***.
- **Highly branched axons can transmit information to many target cells. Similarly, neurons with highly branched dendrites can receive input through large numbers of synapses, as many as 100,000 in the case of some interneurons.**

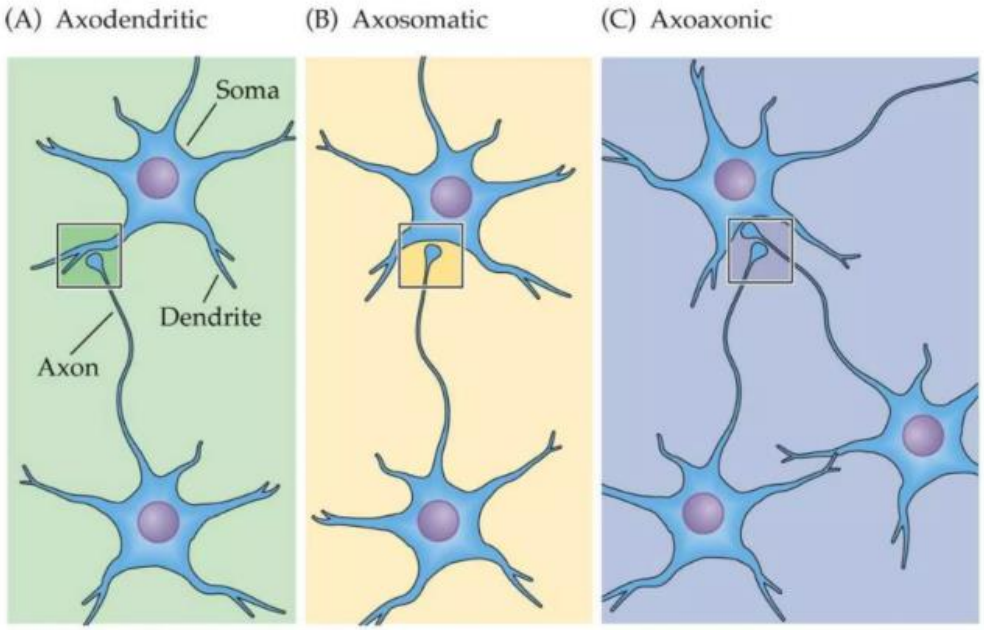
- A nerve signal soon reaches the end of an axon and can go no farther. But in most cases, it triggers the release of a **neurotransmitter** that stimulates a **new wave of electrical** activity in the next cell across the synapse
- Signals arrive at the synapse by way of the **presynaptic neuron,** which releases a **neurotransmitter**. The next neuron, which responds to it, is called the **postsynaptic neuron**

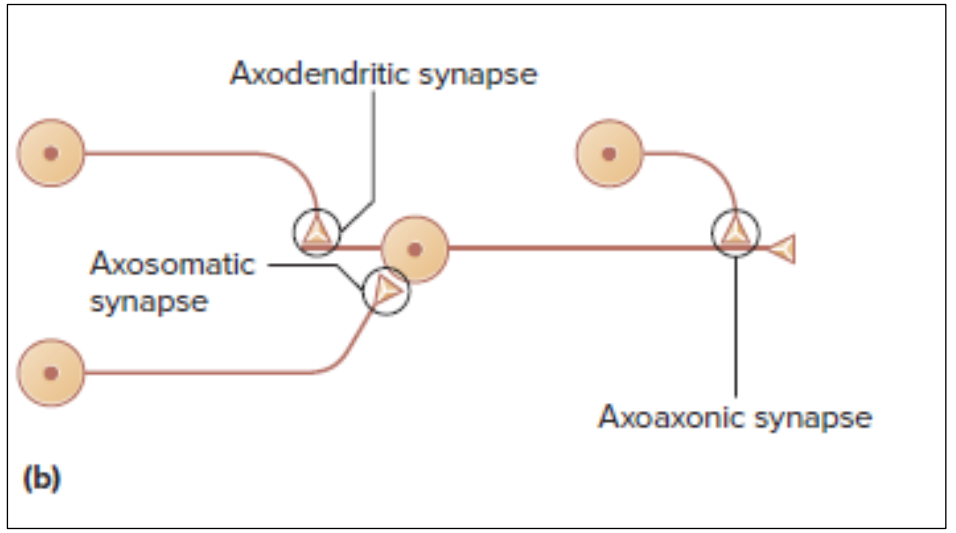


Types of synapses

- The presynaptic neuron may synapse to postsynaptic neuron through

1. A dendrite → *axodendritic*
2. Soma → *axosomatic*
3. Axon → *axoaxonic synapse,*





A neuron can have an enormous number of synapses

- For example, a spinal motor neuron is covered with about 10,000 axon terminals from other neurons—8,000 ending on its dendrites and another 2,000 on the soma.
- In a part of the brain called the cerebellum, one neuron can have as many as 100,000 synapses.

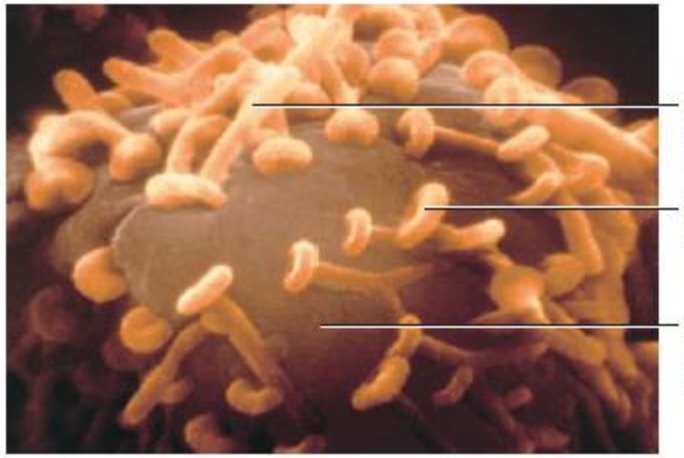


FIGURE 12.20 Axon Terminals Synapsing with the Soma of a Neuron in a Marine Slug, *Aplysia* (SEM).

Type of synapsis according to nature synaptic communication

1. **Chemical synapsis** in which neurons communicate by neurotransmitters.

2. **Electrical synapsis** where adjacent cells are joined by gap junctions and ions diffuse directly from one cell into the next. E. g Synapsis in cardiac muscle

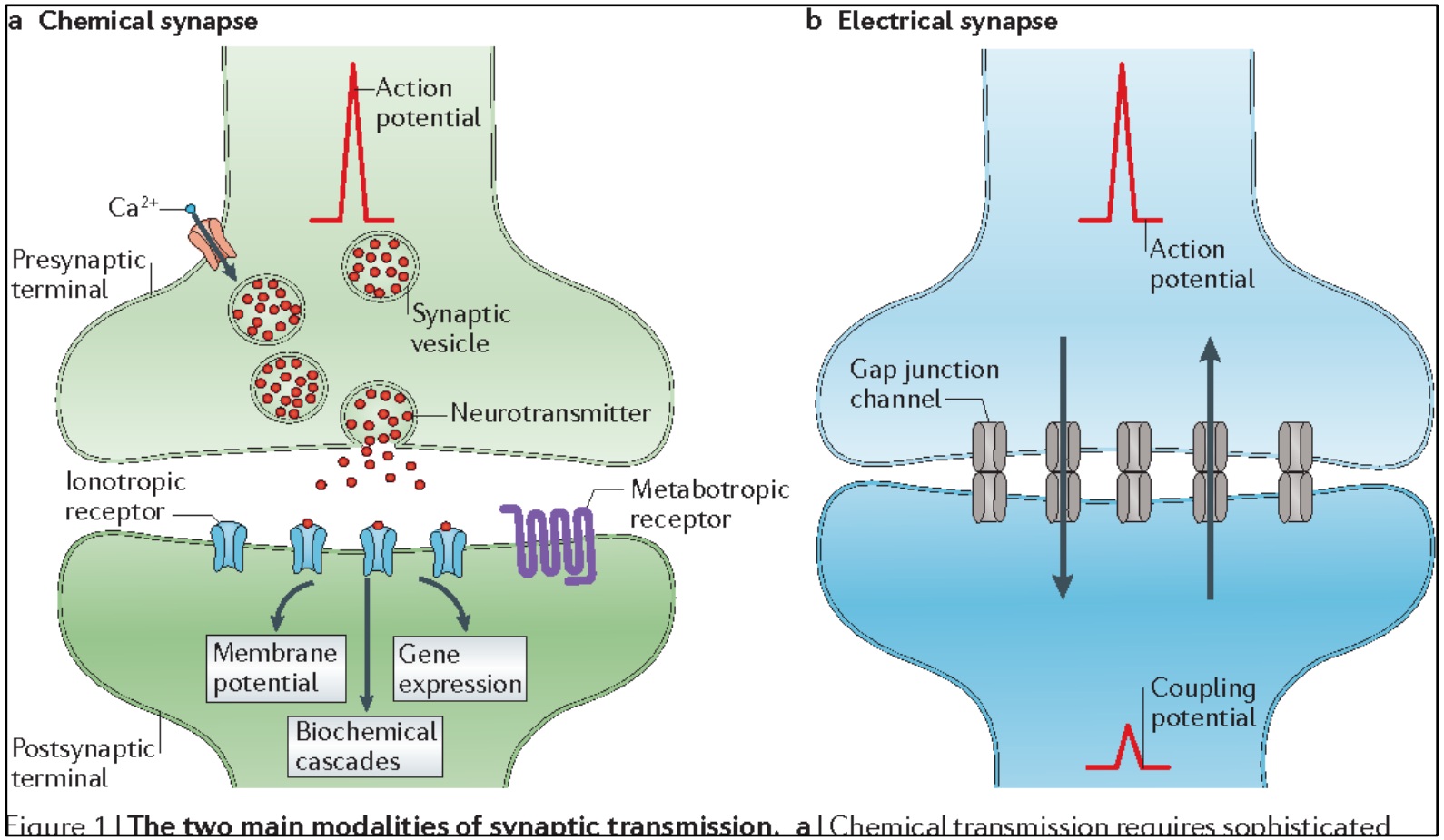
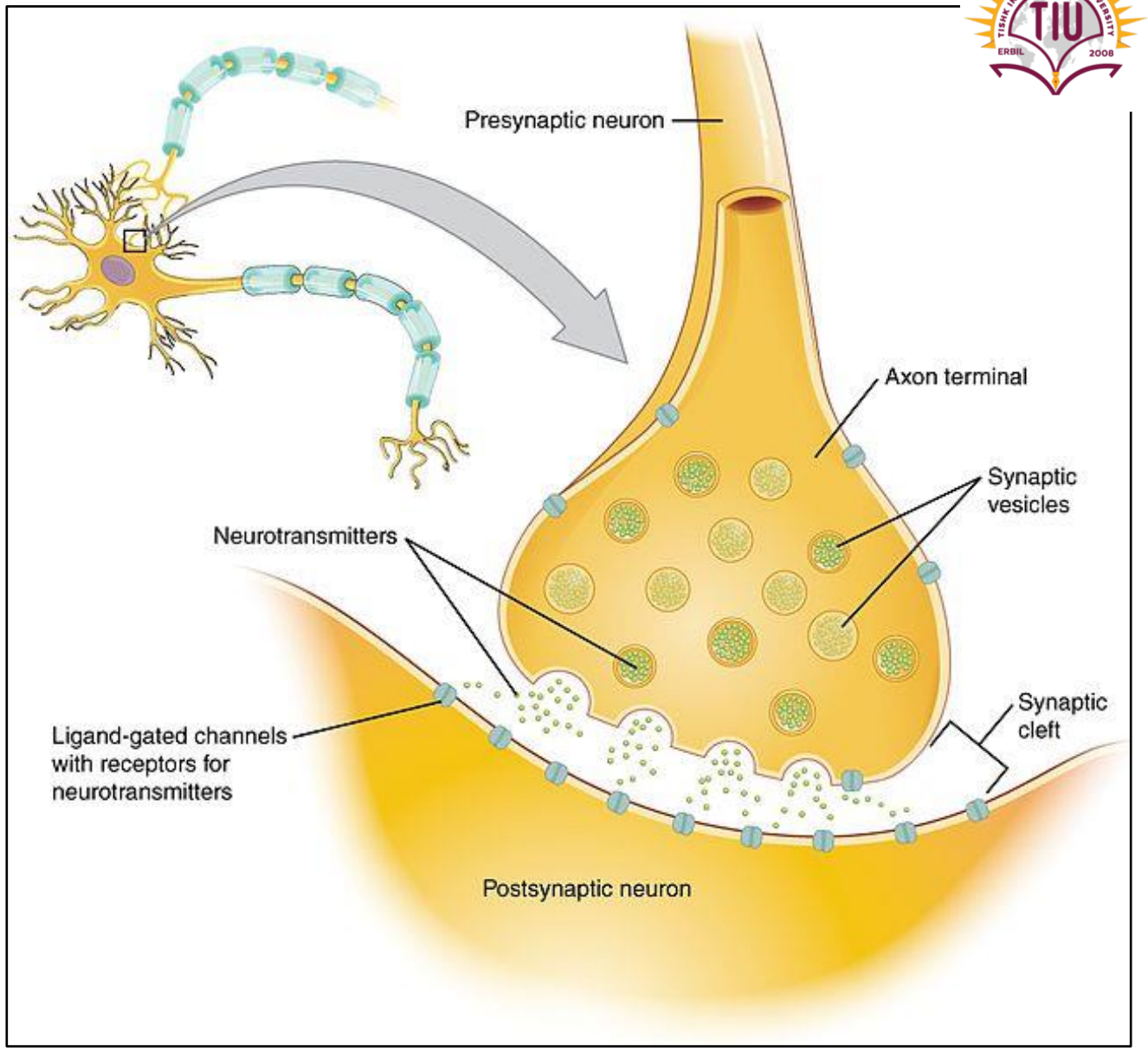


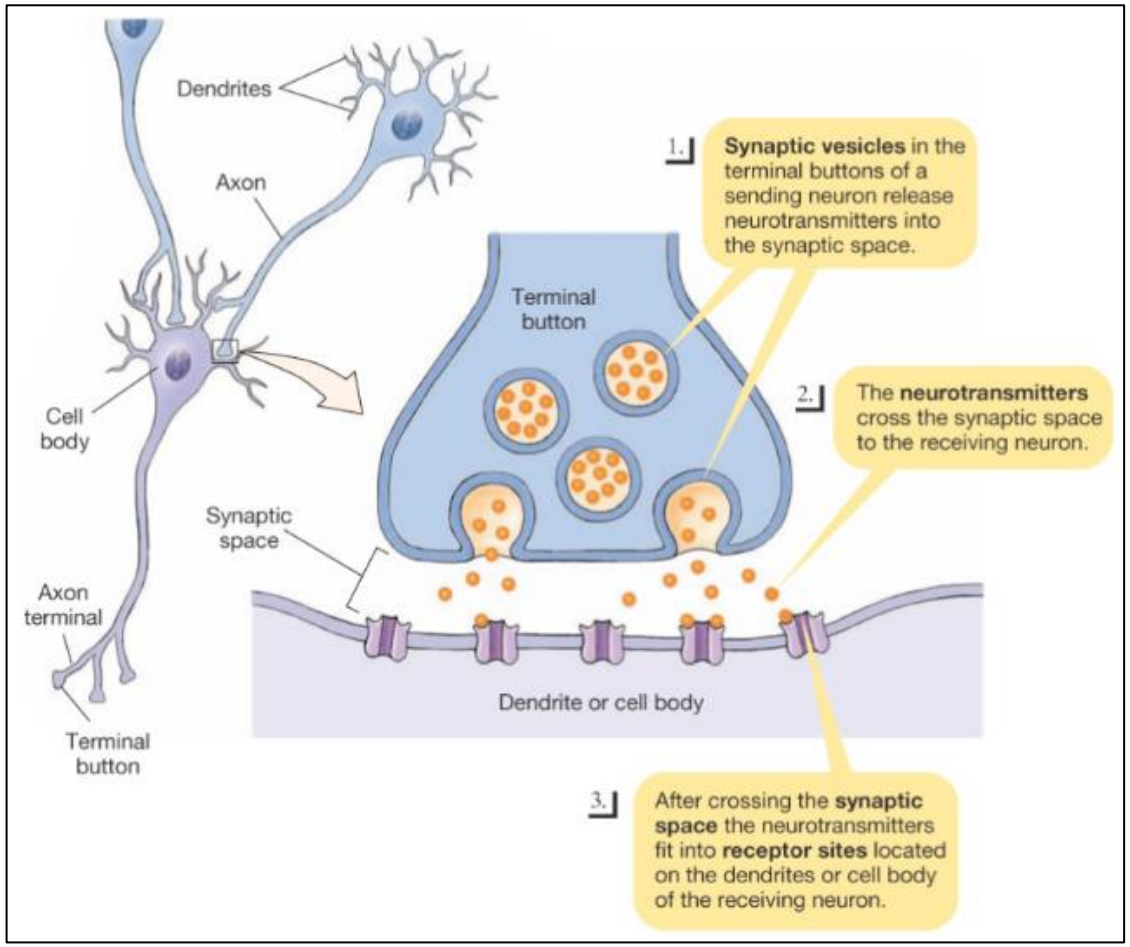
Figure 1 | **The two main modalities of synaptic transmission.** a | Chemical transmission requires sophisticated

- Neurotransmitters are chemical substances that secreted by axon terminal of presynaptic neuron to a synaptic cleft (20-40 nm) which then diffuse a very short distance to bind to receptors of postsynaptic neuron



Structure of a Chemical Synapse

- The **axon terminal** contains synaptic vesicles, many of which are “docked” at release sites on the plasma membrane, ready to release neurotransmitter on demand..
- **The postsynaptic neuron lacks** these conspicuous specializations. At this end, the neuron has no synaptic vesicles and cannot release neurotransmitter. Its membrane does, however, have neurotransmitter **receptors** and ligand-gated **ion channels**.



- More than 100 neurotransmitters have been identified
- **Neurotransmitters** can be defined as molecules that are synthesized by a neuron, released when a nerve signal reaches an **axon terminal**, and have a specific effect on a receiving cell's physiology.
- Most of them are small organic molecules that are released by exocytosis and bind to specific receptors on the receiving cell, but there are exceptions.

Classification of Neurotransmitters according to chemical structure

1. **Acetylcholine** is in a class by itself. It is formed from acetic acid (acetate) and choline.

2. **Amino acid** neurotransmitters include glycine, glutamate, aspartate, and γ-aminobutyric acid (GABA).

3. **Monoamines (biogenic amines)** are synthesized from amino acids by removal of the COOH group. They retain the NH_2 (amino group), hence their name. e.g epinephrine, norepinephrine, dopamine, serotonin (5-hydroxytryptamine, or 5-HT), and histamine.

4. **Purines** serving as neurotransmitters include adenosine and ATP (adenosine triphosphate).

5. **Gases,** specifically nitric oxide (NO) and carbon monoxide (CO), they are synthesized as needed rather than stored in synaptic vesicles; they simply diffuse out of the axon terminal rather than being released by exocytosis; and they diffuse into the postsynaptic neuron rather than bind to a surface receptor.

6. **Neuropeptides** are chains of 2 to 40 amino acids. Some examples are cholecystokinin (CCK) and the endorphins

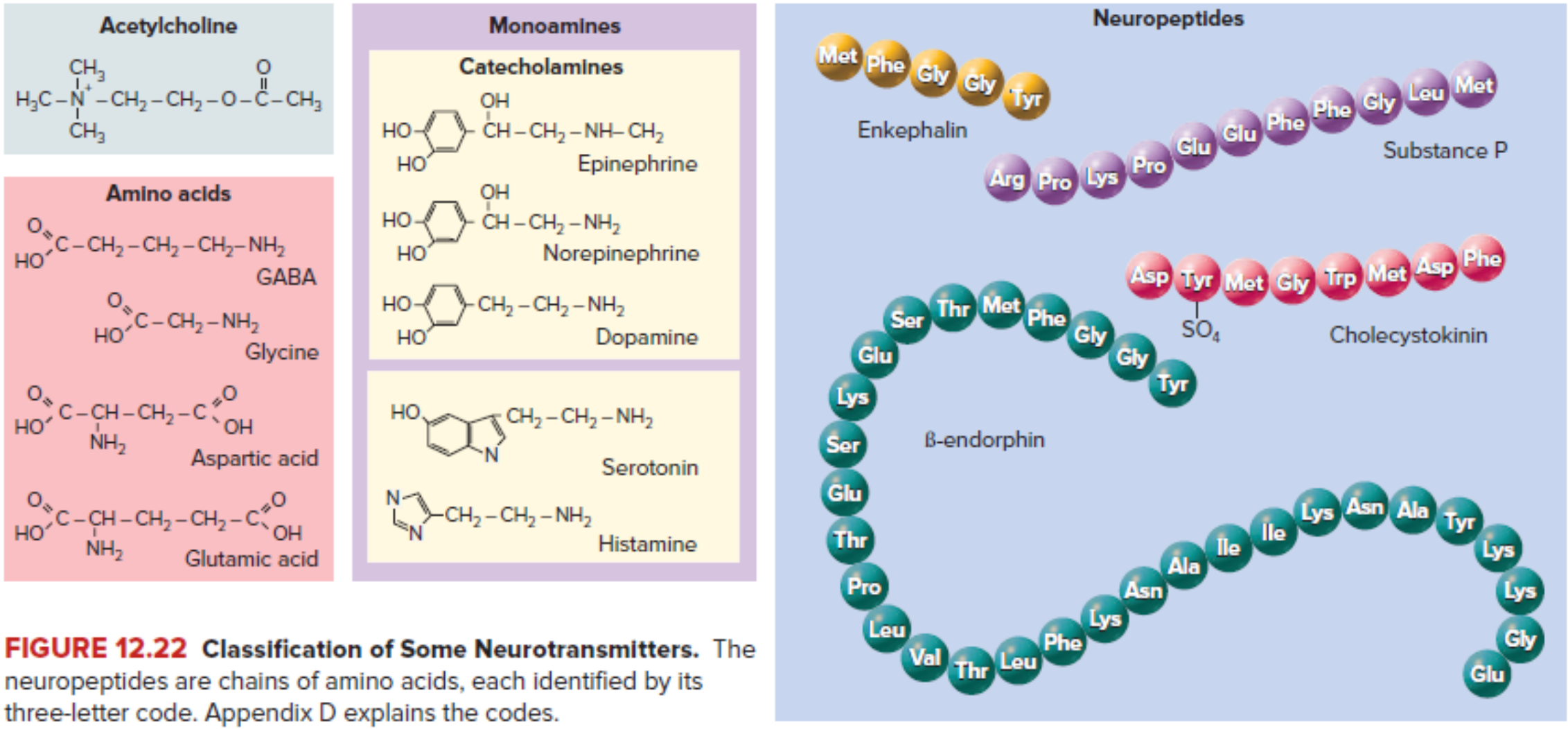
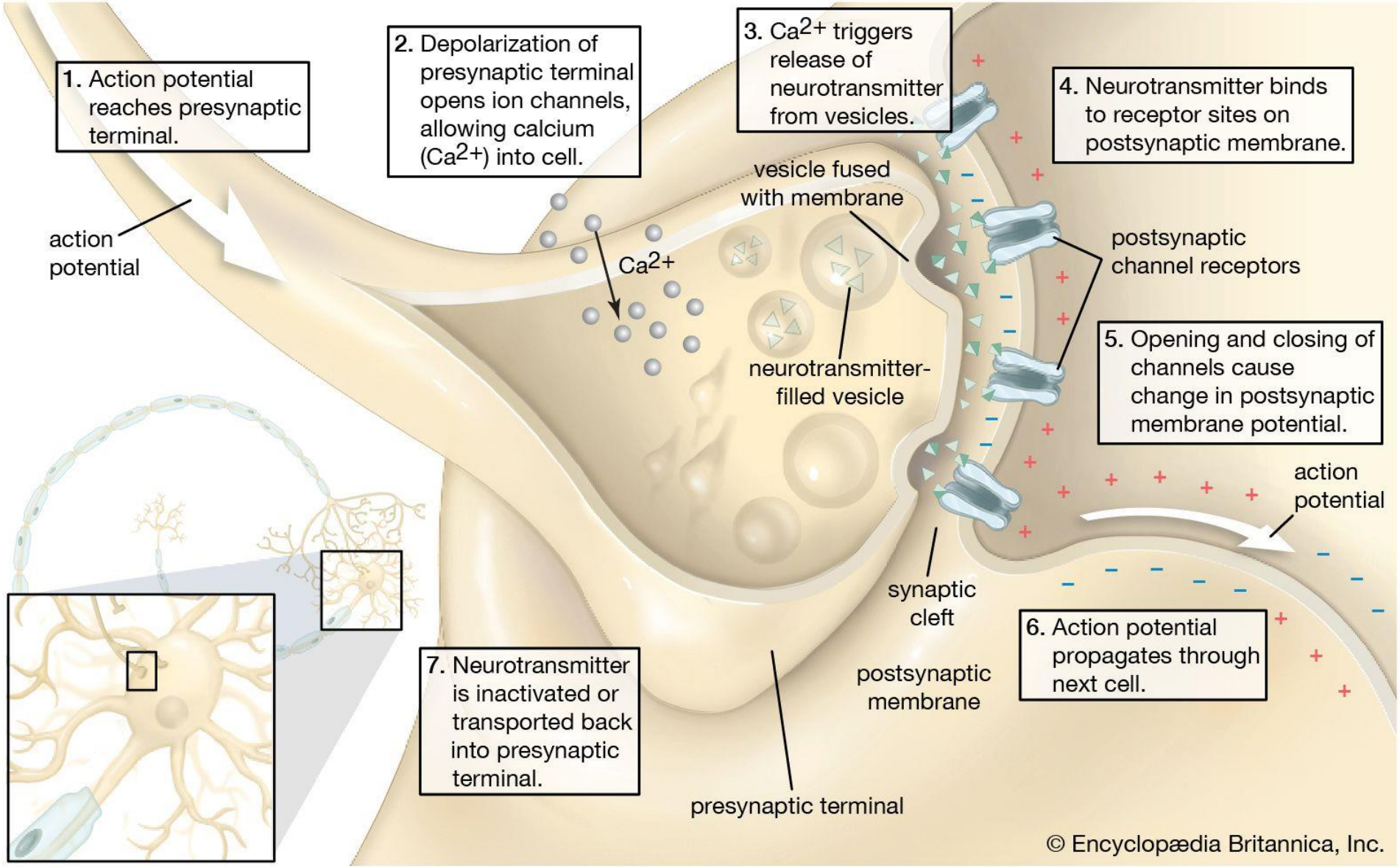


FIGURE 12.22 Classification of Some Neurotransmitters. The neuropeptides are chains of amino acids, each identified by its three-letter code. Appendix D explains the codes.

- A given neurotransmitter does **not** have the **same** effect everywhere in the body.
- There are **multiple receptor types** in the body for a particular neurotransmitter—over 14 receptor types for **serotonin**, for example—**and it is the receptor that governs what effect a neurotransmitter has on its target cell**.
- Most human and other mammalian neurons can secrete two or more neurotransmitters and can switch from one to another under different circumstances.

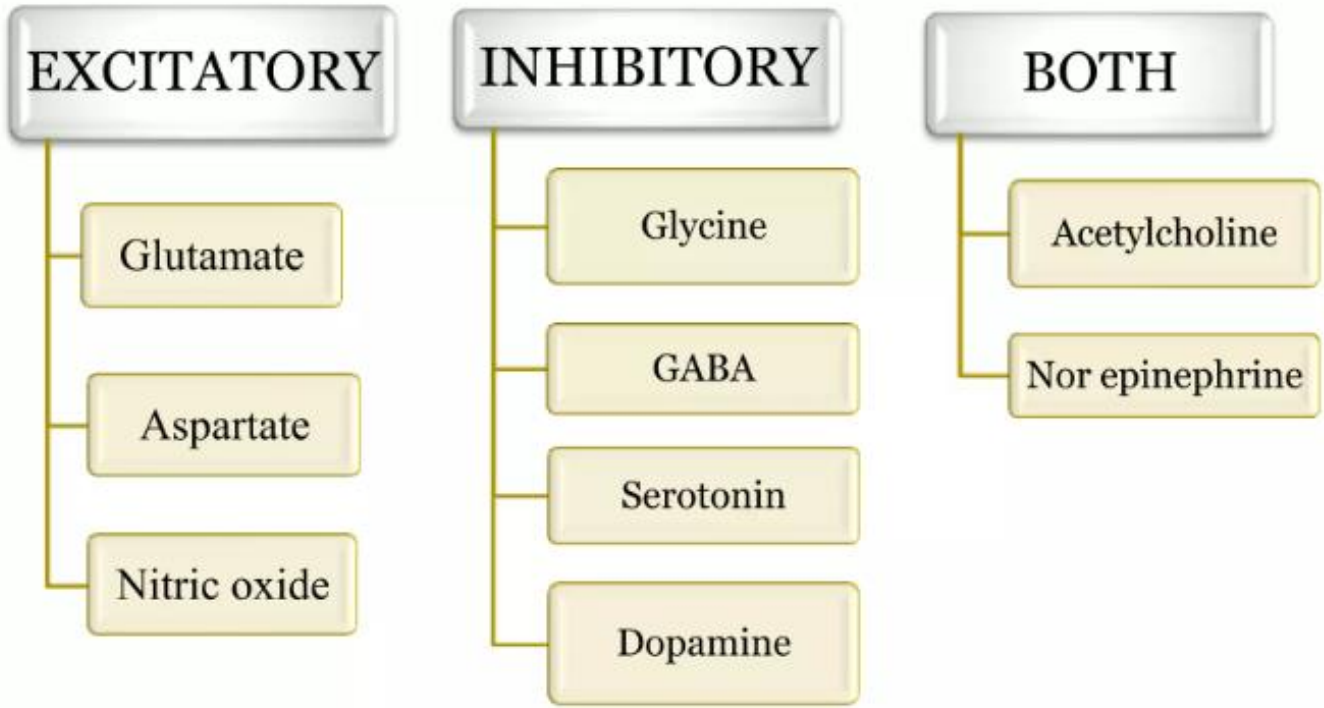
Steps in releases AND action of Neurotransmitters in Synapses



Mode of action of Neurotransmitters

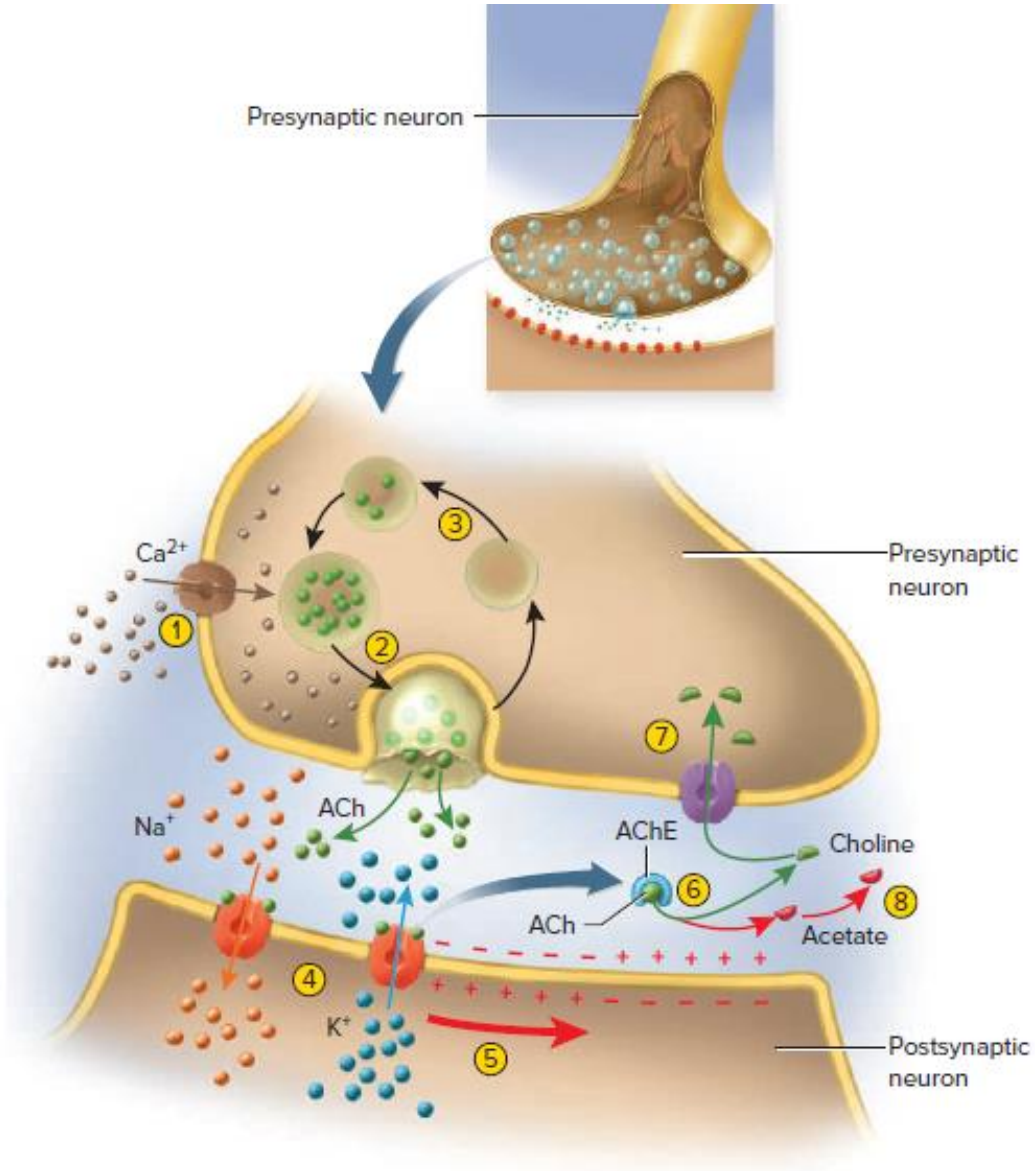
- Some neurotransmitters are excitatory, some are **inhibitory**, and for some the effect depends on what kind of receptor the postsynaptic cell has.
- Some open ligand-gated ion channels and others act through **second messengers** .
- **we will examine three kinds of synapses with different modes of action.**

TYPES OF NEUROTRANSMITTERS



Generation of Postsynaptic Potentials

- At many chemical synapses, the receptor protein that binds and responds to neurotransmitters is a **ligand-gated ion channel**
- Binding of the neurotransmitter (the receptor's ligand) to a particular part of the receptor opens the channel and allows specific ions to diffuse across the postsynaptic membrane. **The result is a *postsynaptic potential*, a graded potential in the postsynaptic cell.**
- At some synapses, the ligand-gated ion channel is permeable to both **Na^+ and K^+ channels**, when these channel are open depolarization will happen and action potential form in post synaptic neuron
- As Na+ enters, it spreads out along the inside of the plasma membrane and depolarizes it, producing a local voltage shift called the **postsynaptic potential**
- At other synapses, the ligand-gated ion channel is selectively permeable for only **K^+** or **Cl^-**. When such a channel opens, the postsynaptic membrane hyperpolarizes



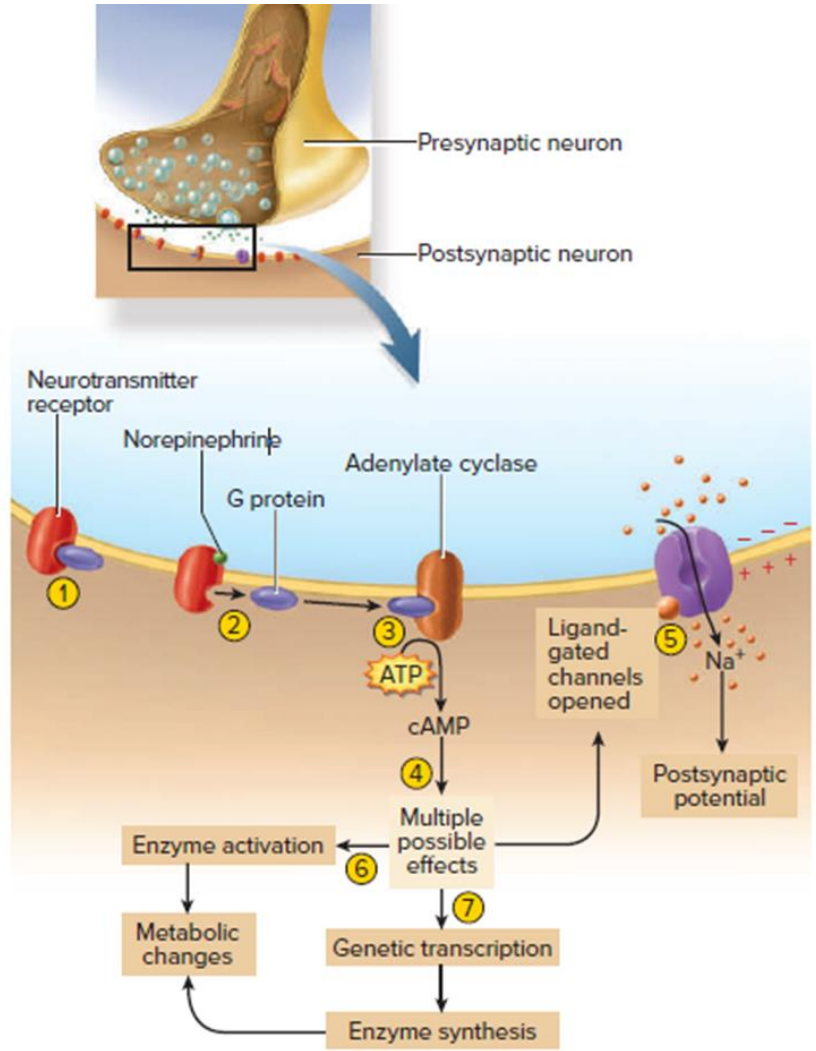


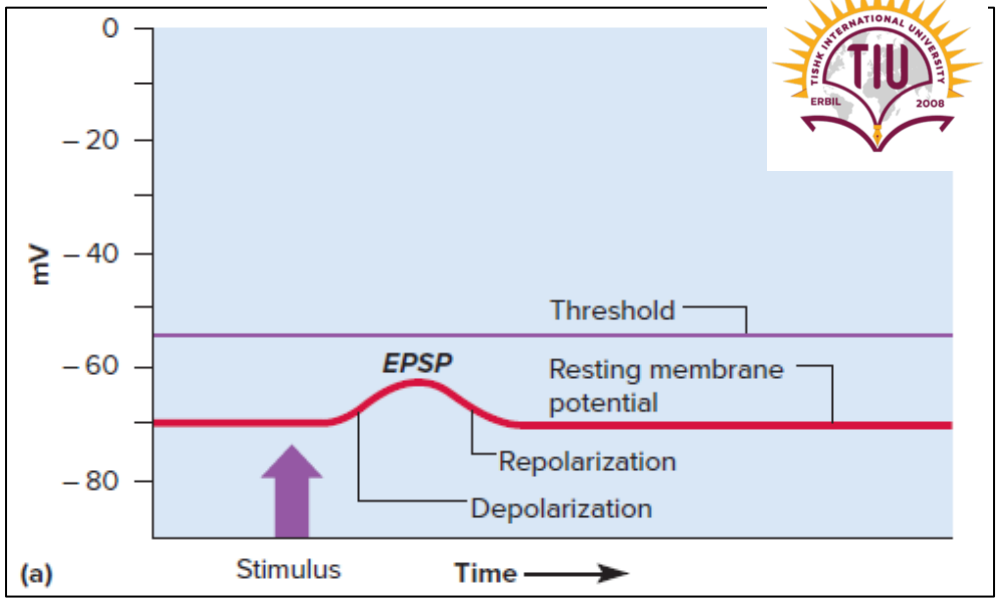
FIGURE 12.24 Transmission at an Adrenergic Synapse.
Numbered steps correspond to the description in nearby text.

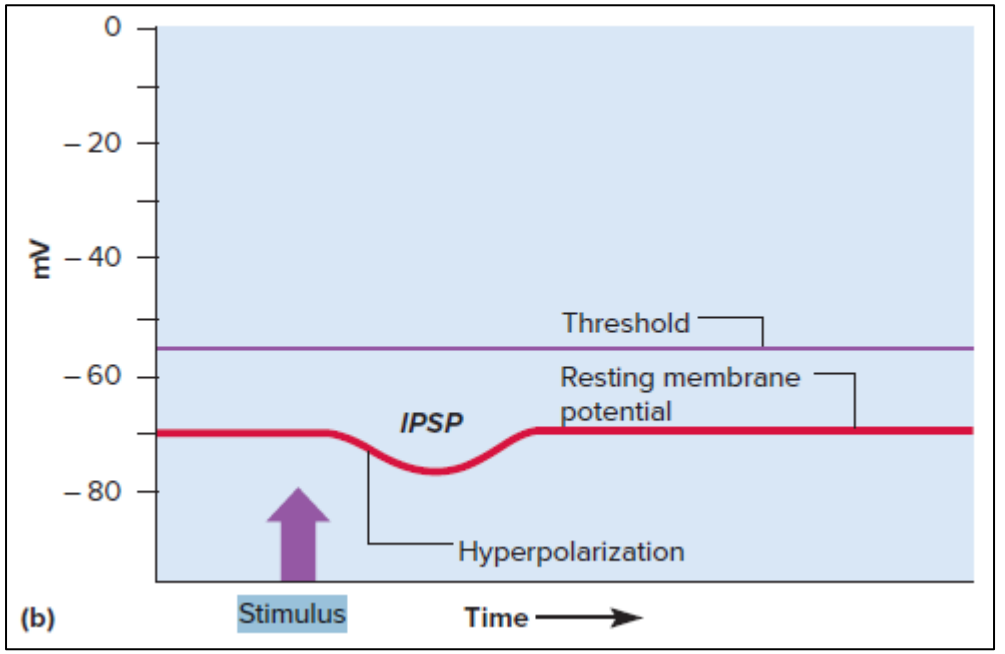
Excitatory post synaptic potential(EPSP)

A Graded potential that depolarize the postsynaptic neuron due to influx of positive ion thereby increasing likelihood of the firing action potential of postsynaptic cell

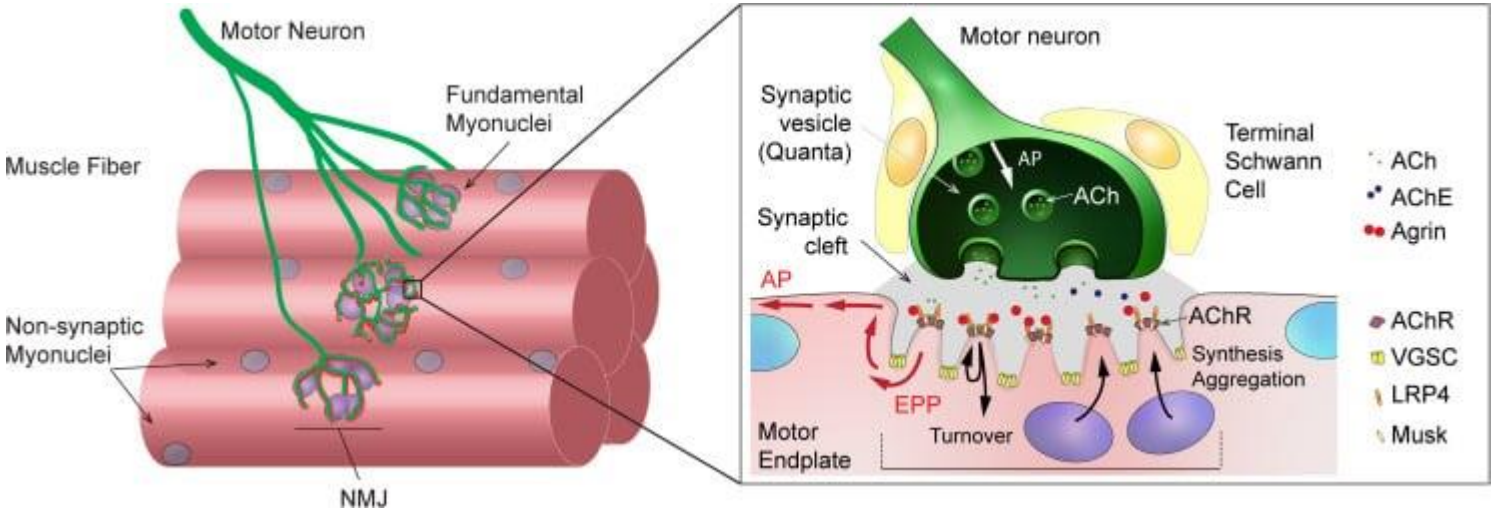
Inhibitory post synaptic potential(iPSP)

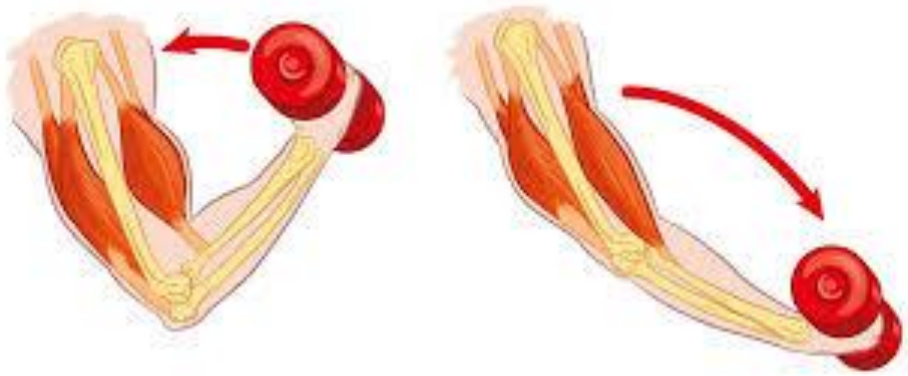
graded potential that hyperpolarize the postsynaptic neuron due to net influx of negative ion and net efflux of positive ion thereby decrease the likelihood of the firing action potential of a cell





Muscle contraction





Main Functions of Muscles

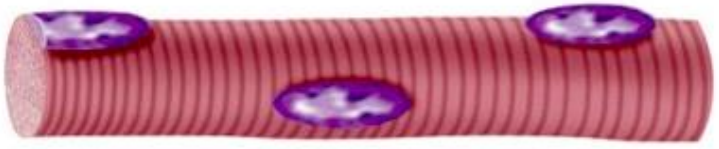
1. **Produce movement**
2. **Maintain posture & body position**
3. **Stabilize joints:** Many muscles also stabilize the joints by maintaining tension on tendons and bone
4. **Generate heat:** The skeletal muscles produce 20% to 30% of the body's heat at rest and up to 85% during exercise. This body heat is vital to the functioning of enzymes and therefore to all metabolism

Muscle special characteristics

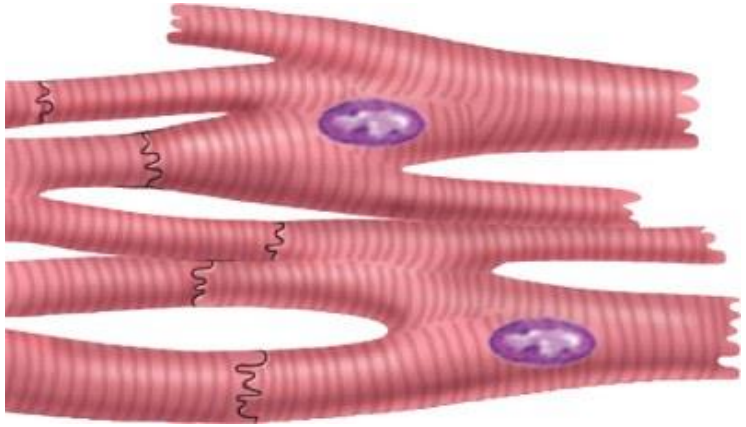
- **Excitability (responsiveness)**. When stimulated by chemical signals, stretch, and other stimuli, muscle
- cells respond with electrical changes across the plasma membrane.
- **Contractility.** Muscle cells are unique in their ability to shorten substantially when stimulated. This enables them to pull on bones and other organs to create movement.
- **Extensibility** – can be stretched or extended

  Elasticity. When a muscle cell is stretched and then released, it recoils to a shorter length.

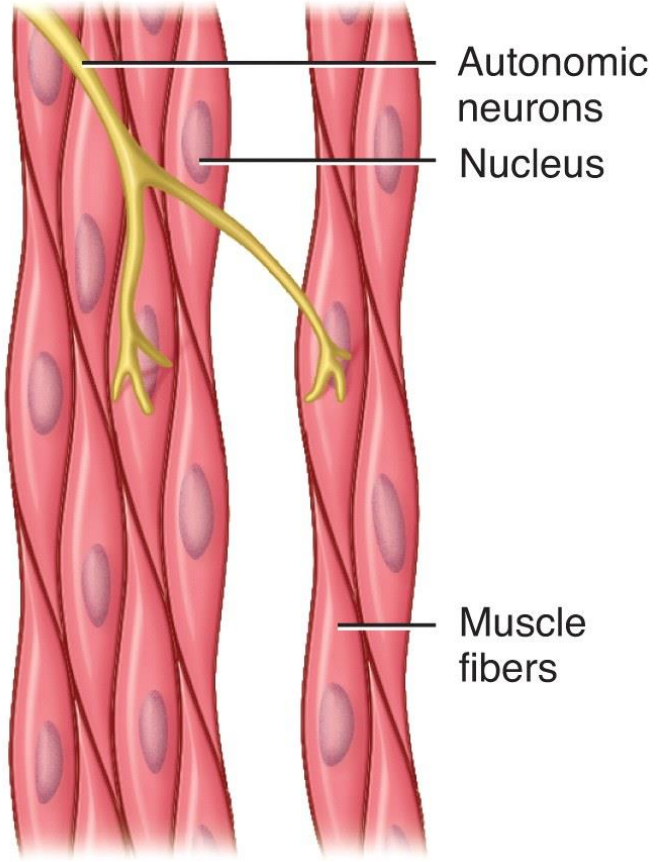
Three Types of Muscular Tissue



(a) Skeletal muscle

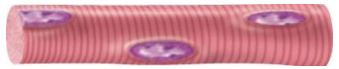
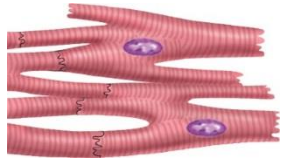


(b) Cardiac muscle



(c) Visceral smooth muscle

Three Types of Muscular Tissue

	Location	Function	Appearance	Control
Skeletal 	skeleton	movement, heat, posture	striated, multi-nucleated (eccentric), fibers parallel	voluntary
Cardiac 	heart	pump blood continuously	striated, one central nucleus	involuntary
Visceral (smooth muscle) 	G.I. tract, uterus, eye, blood vessels	Peristalsis, blood pressure, pupil size, erects hairs	no striations, one central nucleus	involuntary

Skeletal Muscle

- **Skeletal muscle** is composed of skeletal muscle tissue and also contains nervous tissue, blood vessels and connective tissue
- Half of the body's weight is muscle tissue
  - Skeletal muscle = 40% in males, 32% in females
  - Cardiac muscle = 10%

- It also contains an abundance of **glycogen**, a starchlike carbohydrate that provides energy for the cell during heightened levels of exercise, and the red oxygen binding pigment **myoglobin**, which provides some of the oxygen needed for muscular activity.
- A typical skeletal muscle cell is about 100 µm in diameter and 3 cm (30,000 µm) long; some are as thick as 500 µm and as long as 30 cm. Because of their extraordinary length, skeletal muscle cells are usually called **muscle fibers** or **myofibers**

Skeletal muscle fibers (cells) are arranged into bundles called fascicles
Fascicles are bound by connective tissue

Recall that a skeletal muscle is composed not only of muscular tissue, but also of fibrous connective tissue

Epimysium

Closely surrounds skeletal muscle, binds fascicles together

Perimysium

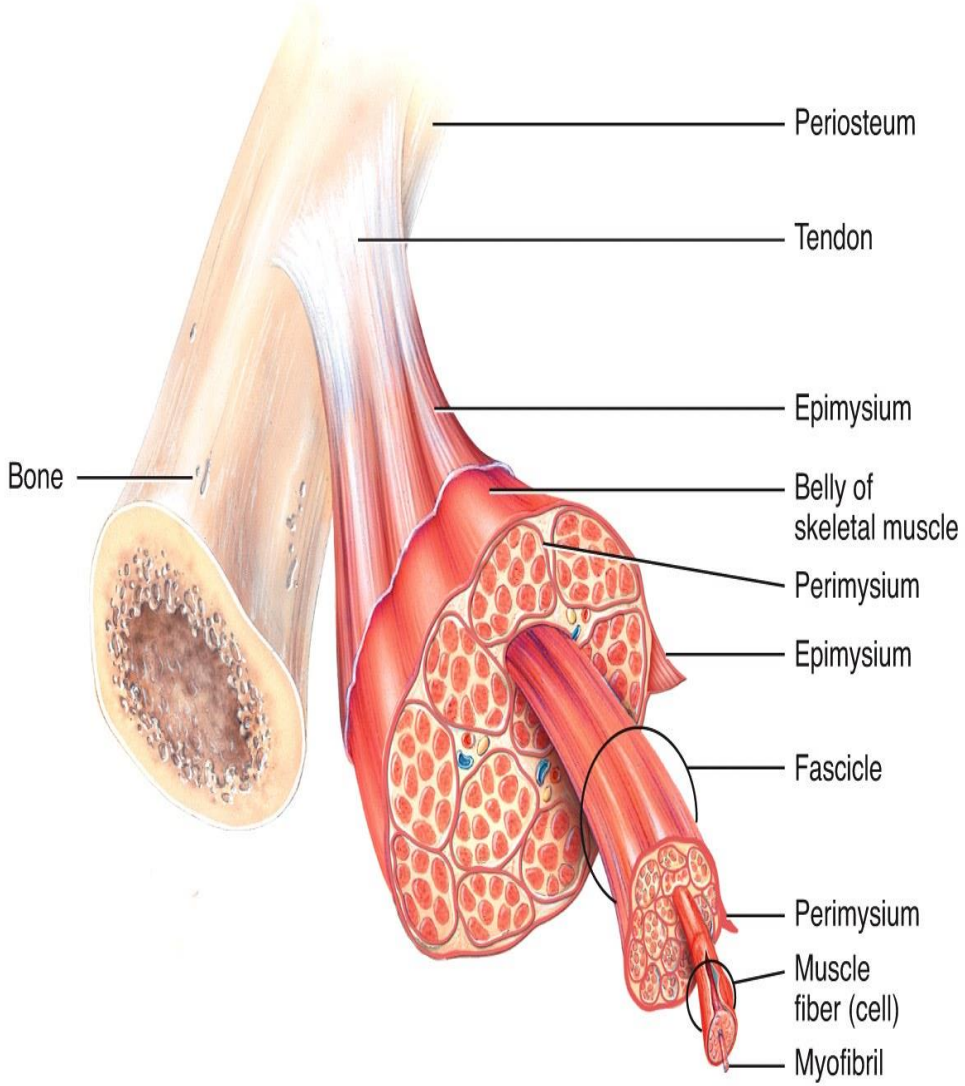
Surrounds each fascicle

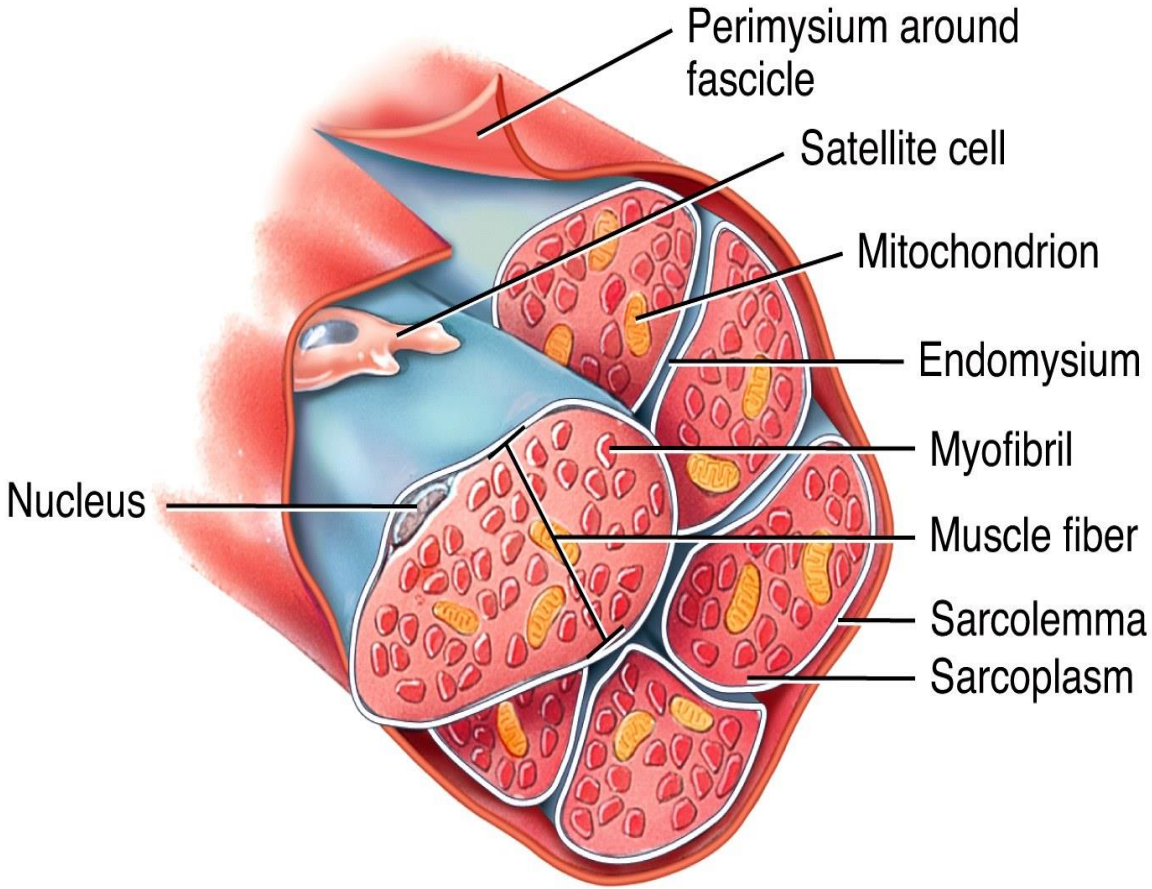
Endomysium

Surrounds each muscle fiber (cell)

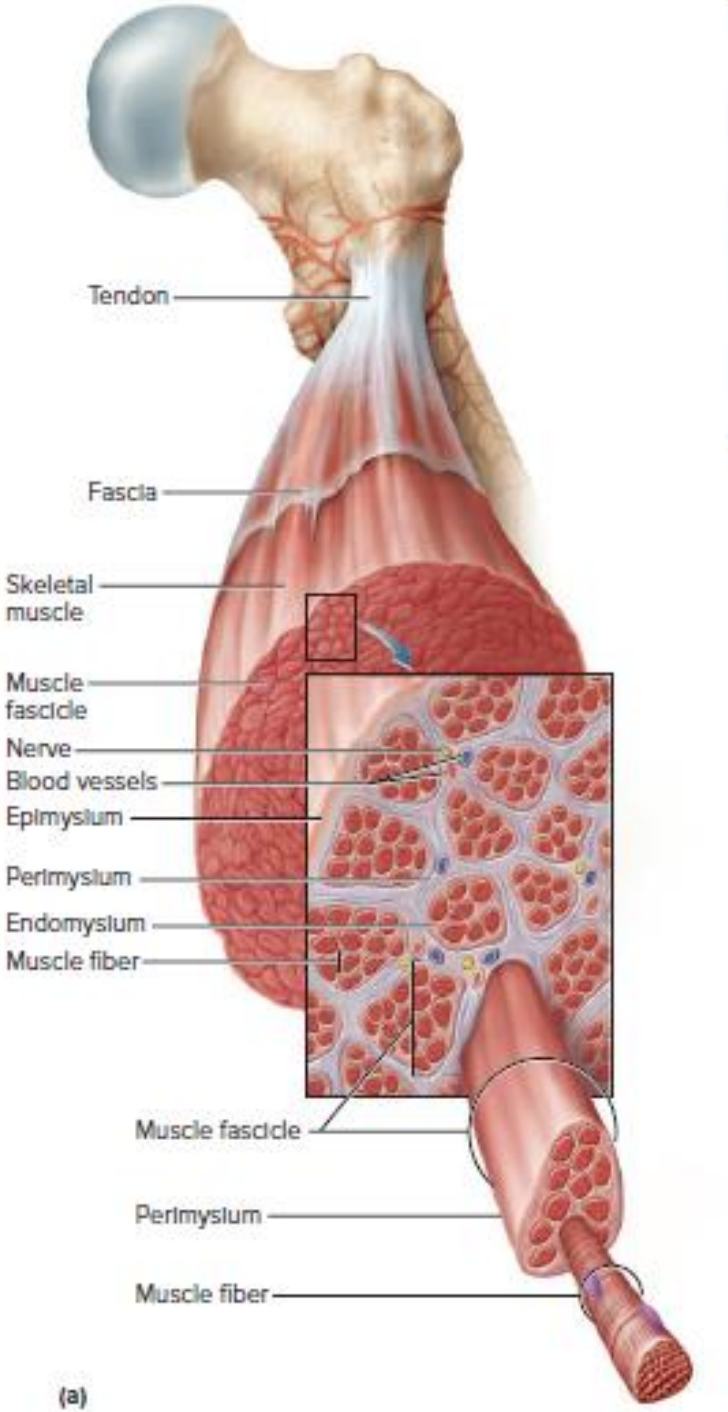
These connective tissues are continuous with the collagen fibers of tendons and those, in turn, with the collagen of the bone matrix. Thus, when a muscle fiber contracts, it pulls on these collagen fibers and typically moves a bone

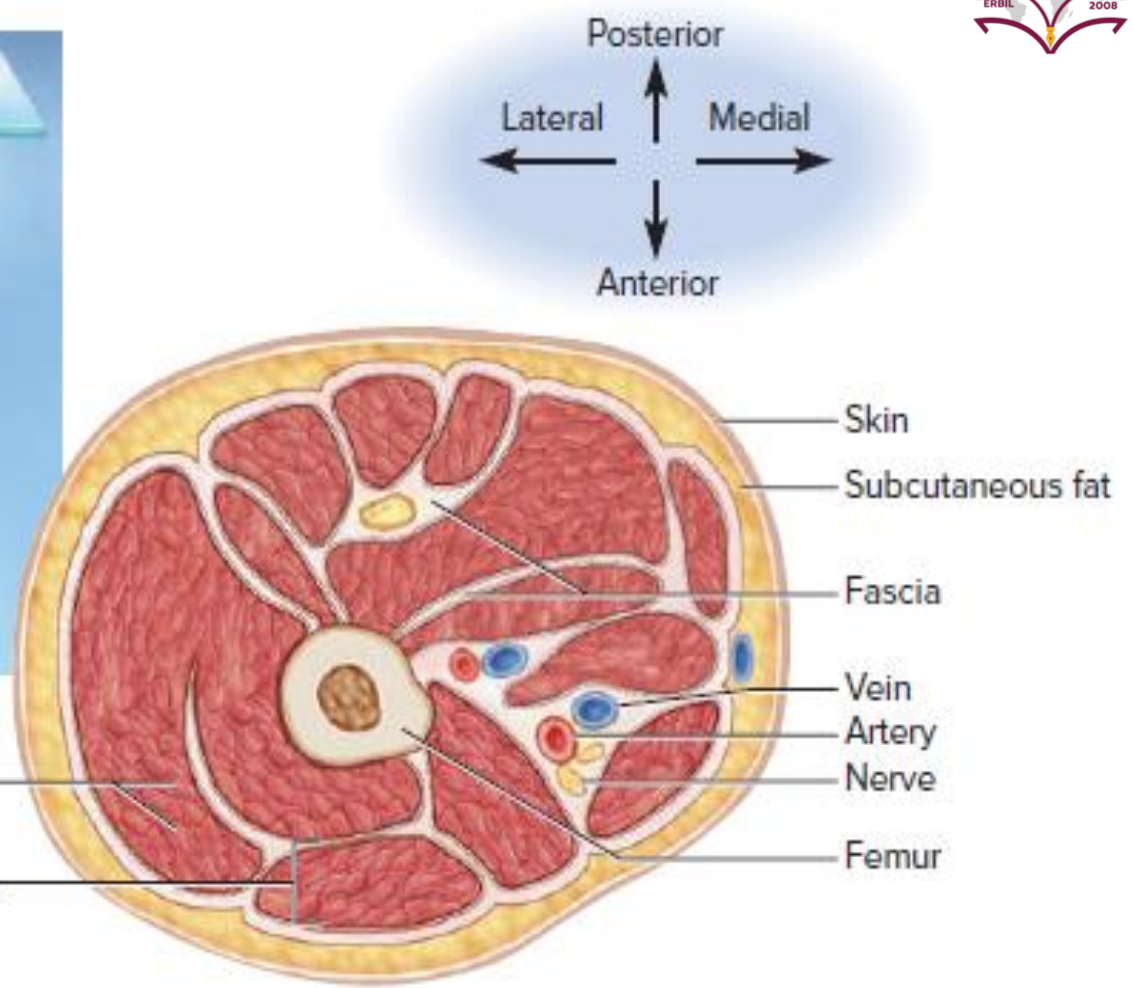
Organization of Muscle Tissue





A muscle, a fasciculus, and a fiber all visualized


Tendon
Fascia
Skeletal muscle
Muscle fascicle
Nerve
Blood vessels
Epimysium
Perimysium
Endomysium
Muscle fiber
Muscle fascicle
Perimysium
Muscle fiber
(a)

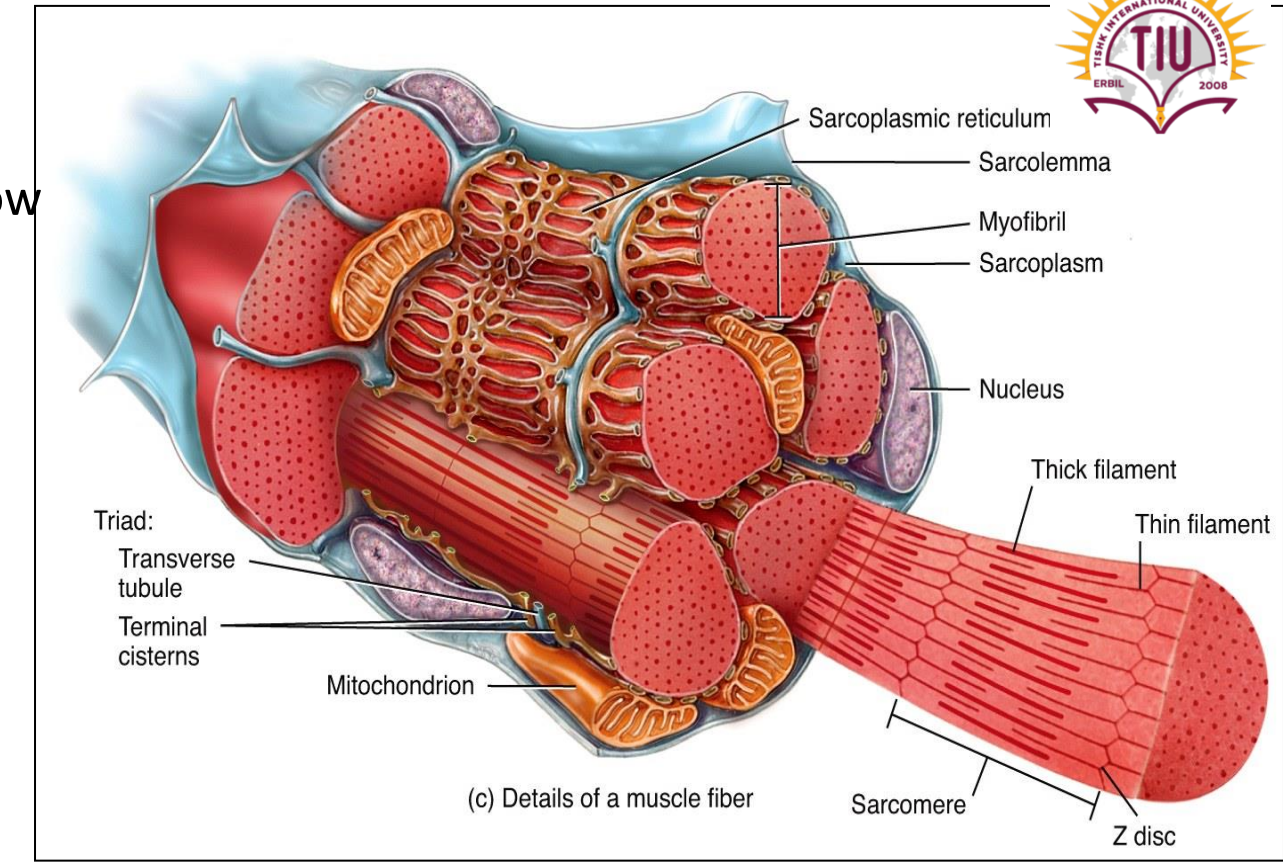

Posterior
Lateral
Medial
Anterior
Skin
Subcutaneous fat
Fascia
Vein
Artery
Nerve
Femur
Fascicles
Individual muscle
(b)

Skeletal Muscle Arrangement

In order to understand muscle function, you must know how the organelles and macromolecules of a muscle fiber are arranged

A single muscle cell is a muscle fiber

- Sarcolemma – muscle cell membrane
- Sarcoplasm = muscle cell cytoplasm
- Fibers are made up of myofibrils



- The sarcoplasm is occupied mainly by long protein cords called **myofibrils** about 1 µm in diameter
- Most other organelles of the cell, such as mitochondria, are packed into the spaces between the myofibrils

Specialized Organelles of Skeletal Muscle

- Sarcoplasmic Reticulum (SR) – a type of ER
  - Surrounds each myofibril, running parallel to it periodically exhibits dilated end sacs called terminal cisterns
  - Stores calcium, when stimulated, calcium diffuses into sarcoplasm

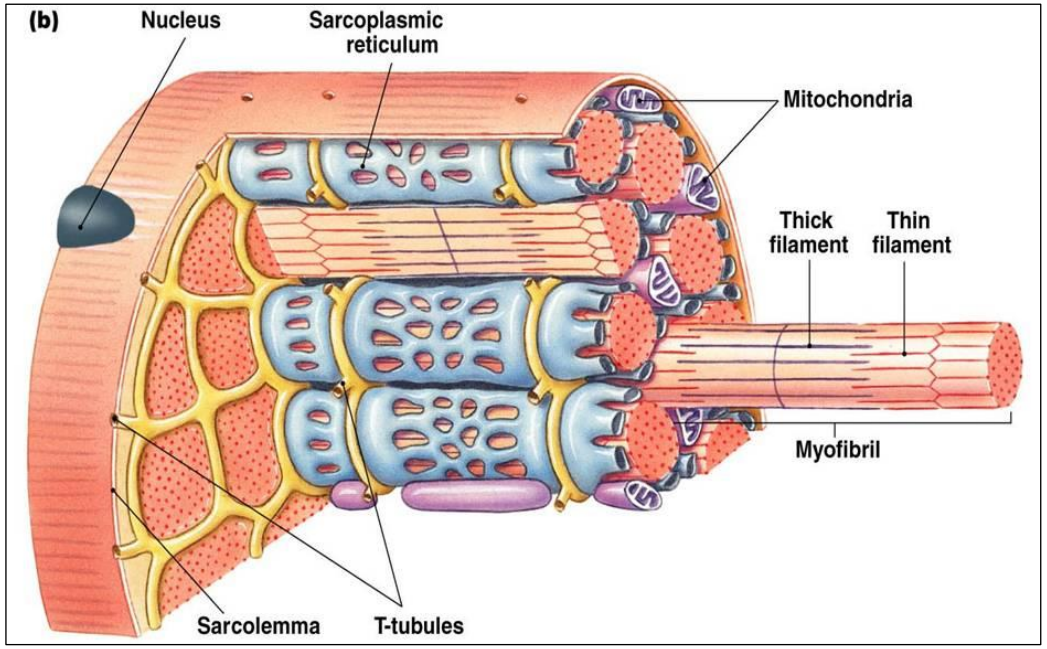
Transverse Tubules (TT)

Extends into sarcoplasm as invaginations continuous with sarcolemma

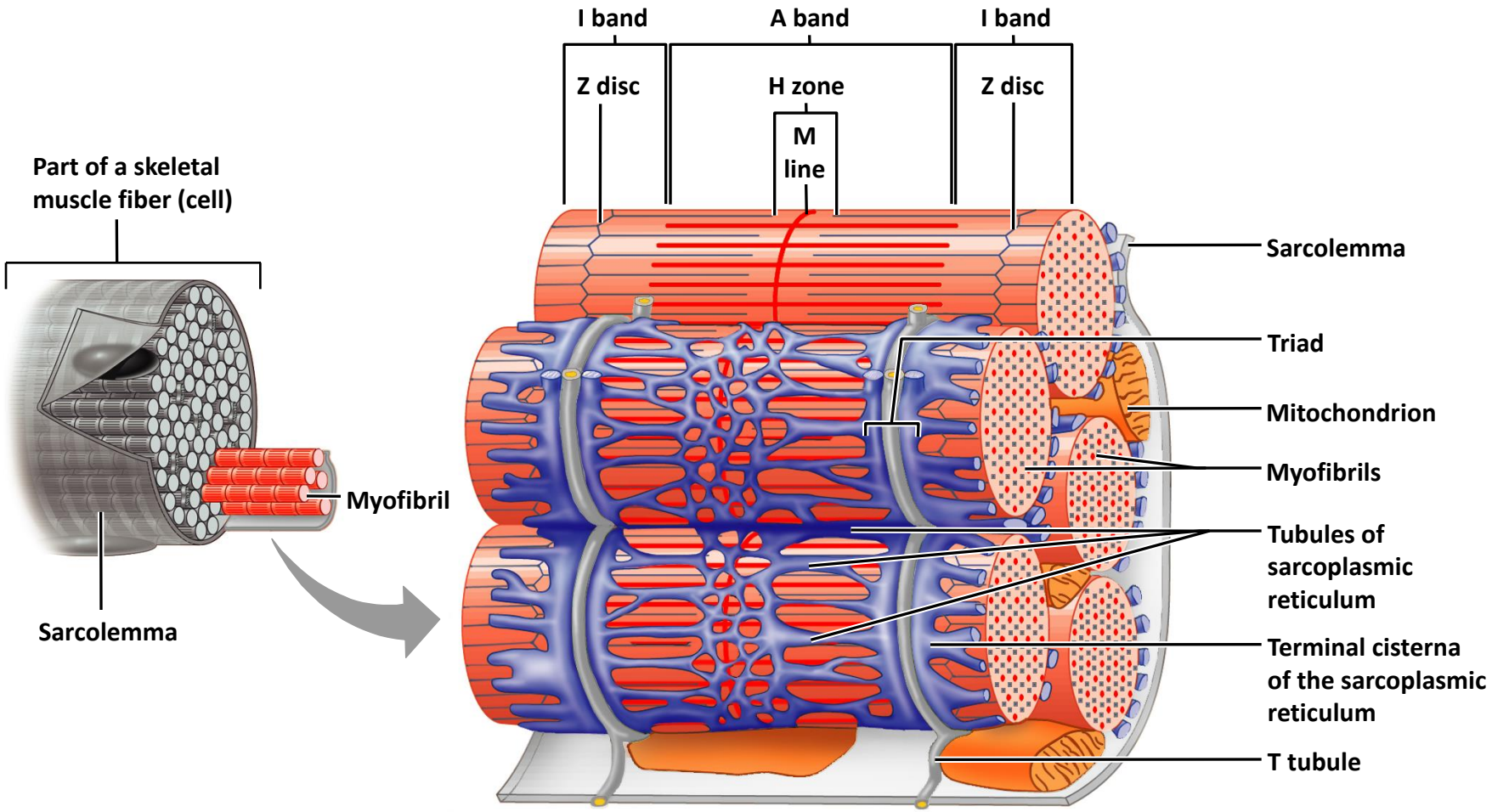
T tubules run between cisternae of SR

Filled with extracellular fluid

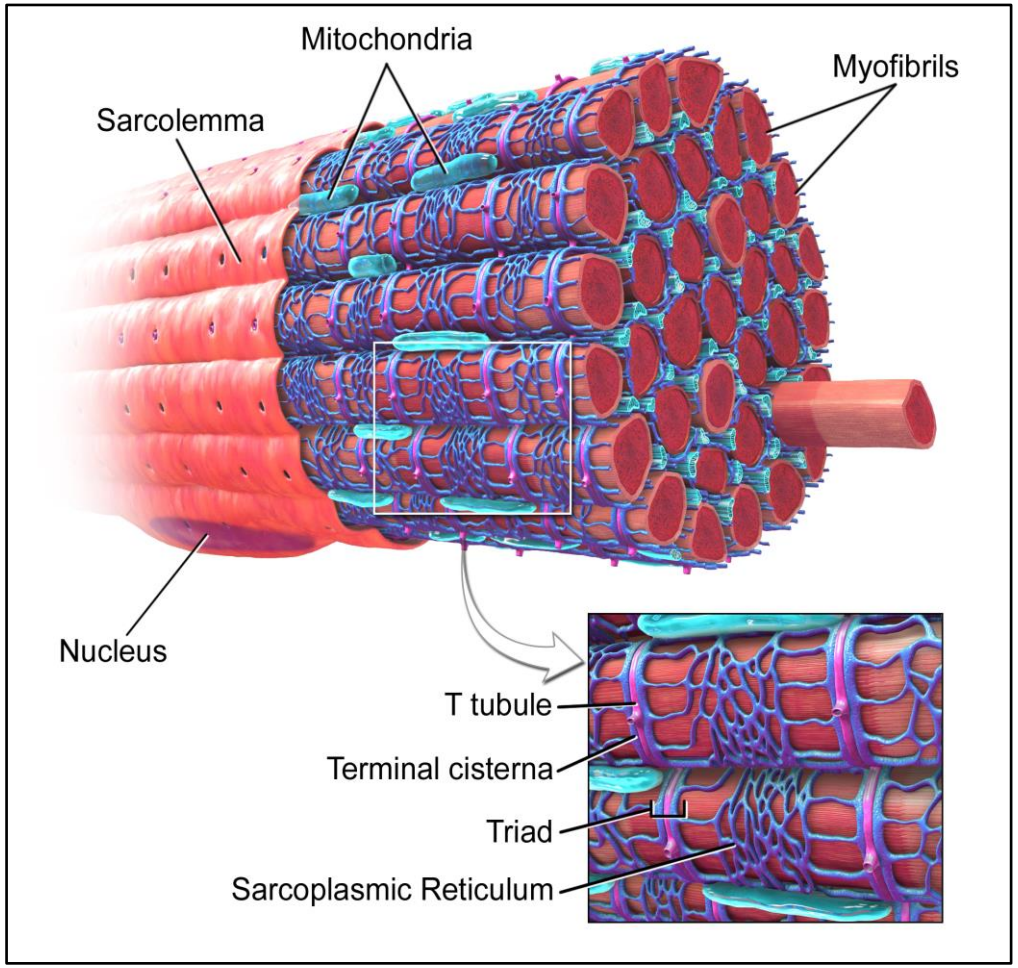
Cisternae of SR and TT form a triad near where thick and thin filaments overlap



Relationship of the sarcoplasmic reticulum and T tubules to myofibrils of skeletal muscle



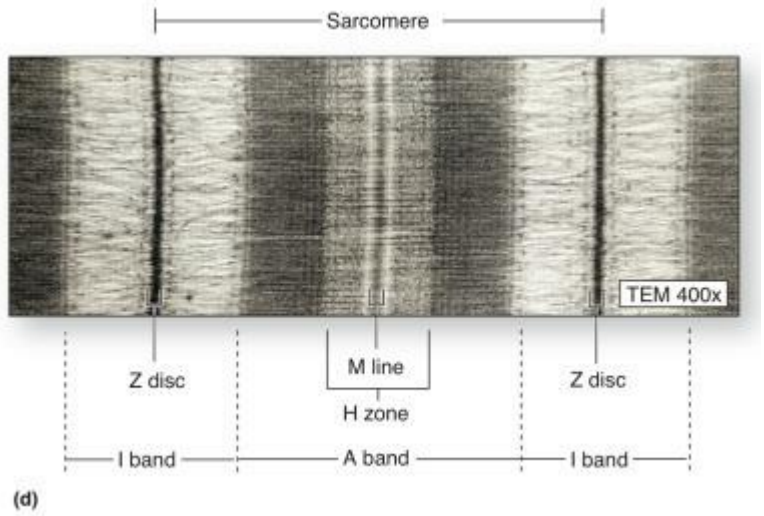
- Muscle has a high demand for ATP and therefore possesses an exceptionally large number of mitochondria wedged in between the myofibrils

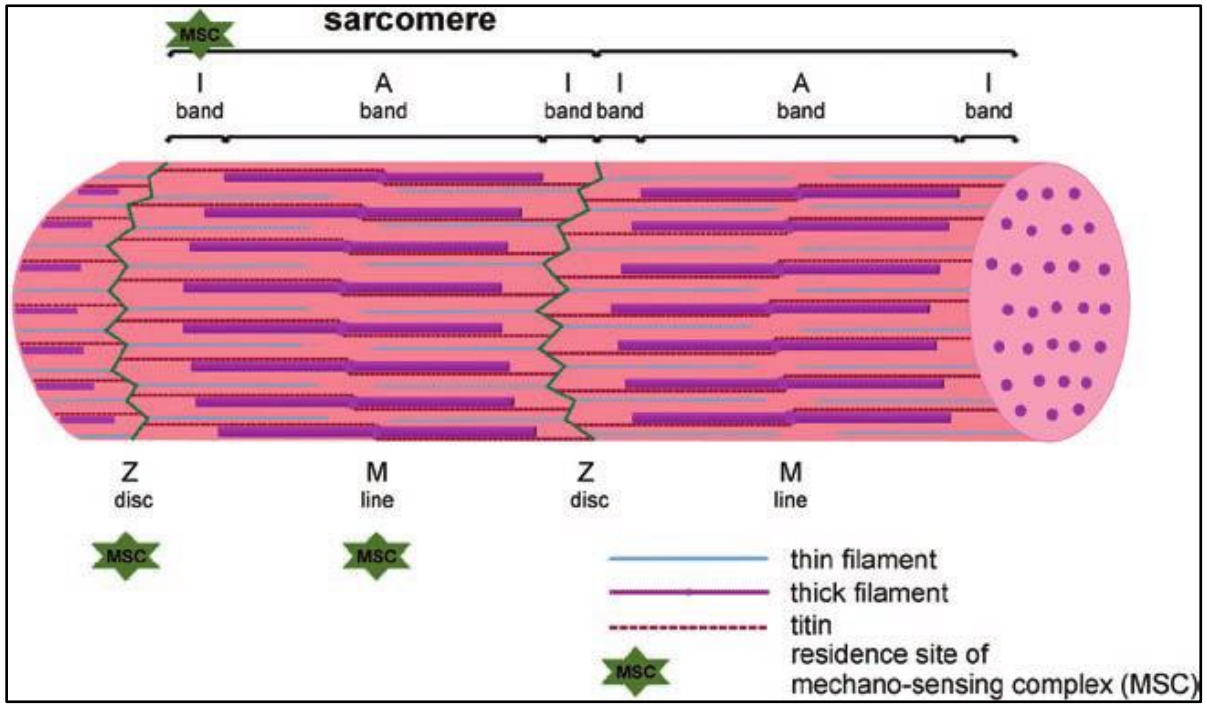


Myofibrils

- myofibrils just mentioned—the long protein cords that fill most of the muscle cell
- Each myofibril is a bundle of parallel proteins called **muscle filaments** or **myofilaments**

- Myofibrils are striated, Striations due to arrangement of thick and thin filaments, seen as alternating areas of **light** and **dark** bands.



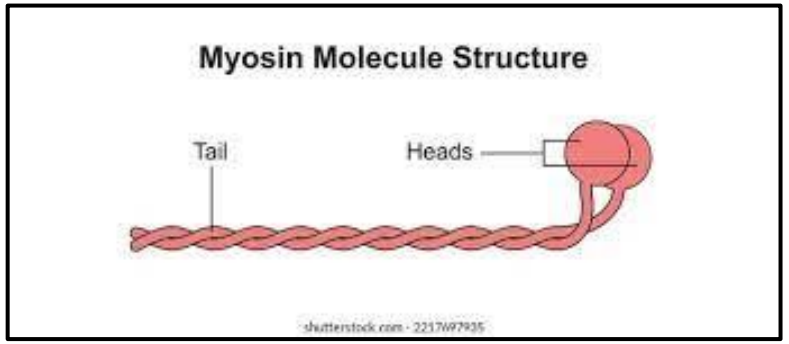


Myofilaments

1-Thick Filament (myosin)

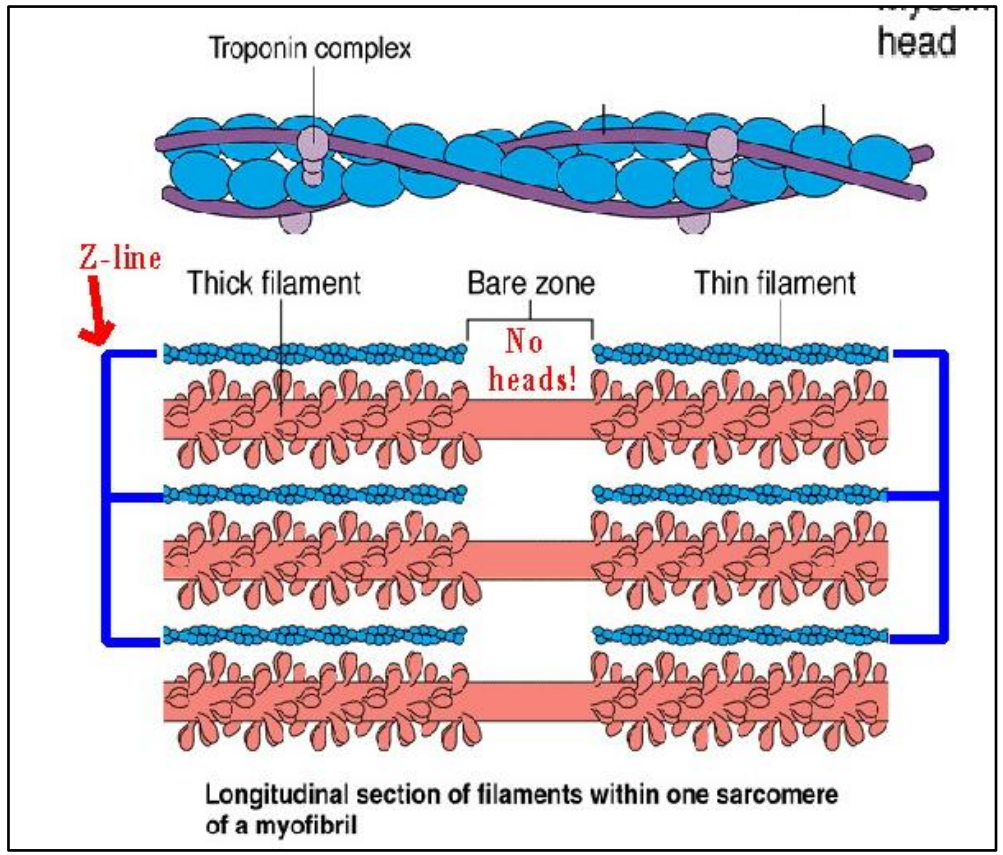
2- Thin Filament (Actin)

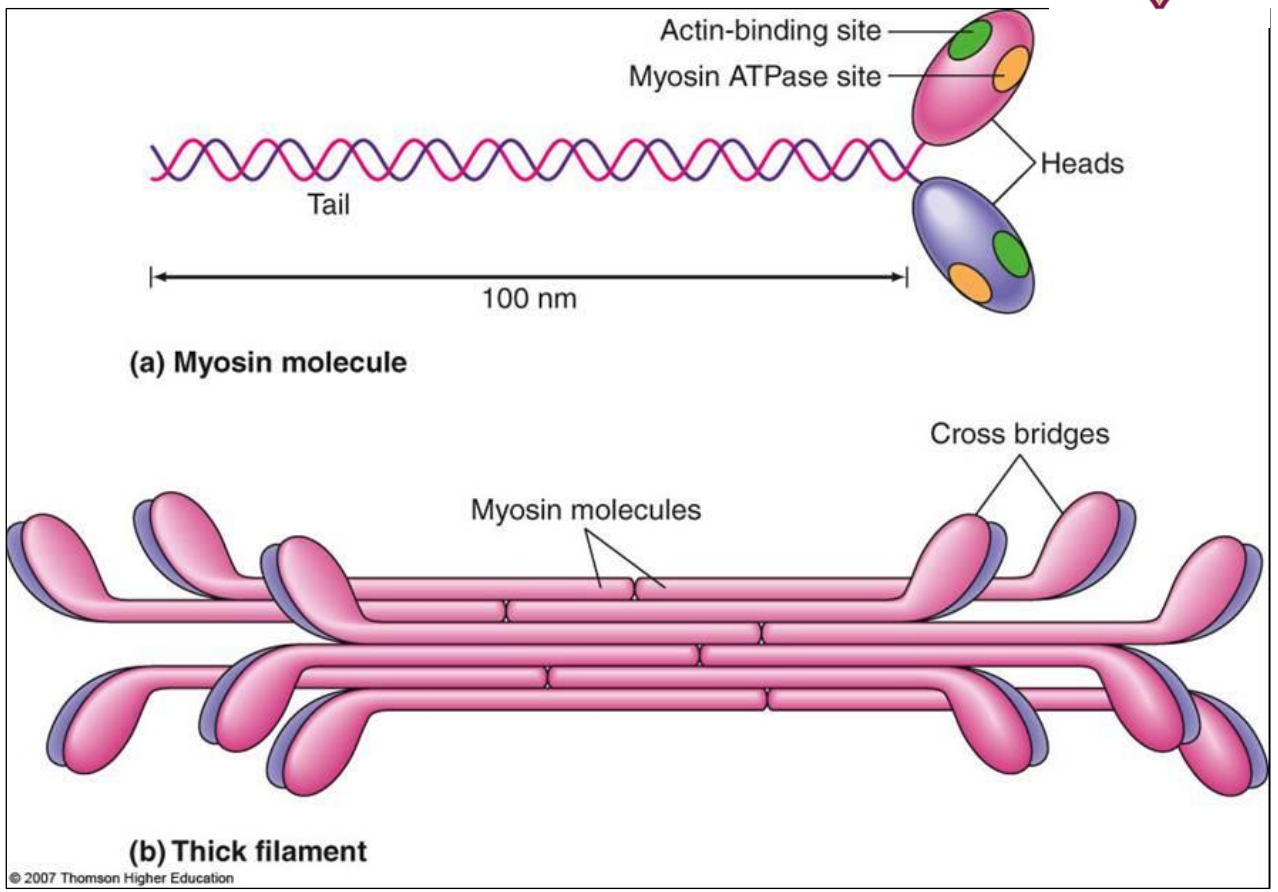
Myosin and actin are called **contractile proteins** because they do the work of shortening the muscle fiber

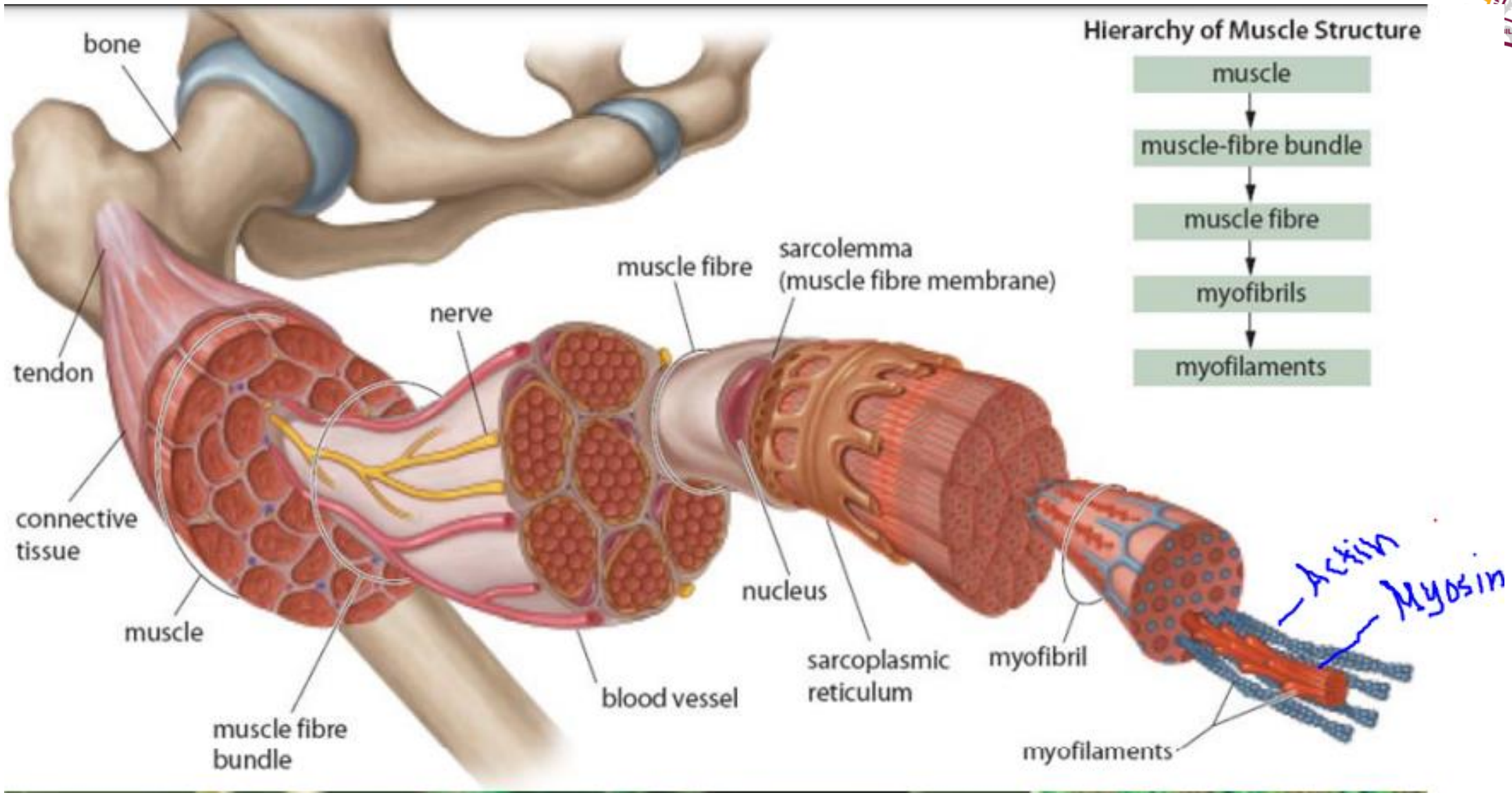


1-Thick Filament (myosin)

- **Composed of many myosin molecules**
- **Each myosin molecule has a tail region and 2 globular heads (crossbridges)**
- A thick filament consists of a bundle of 200 to 500 myosin molecules with their heads directed outward in a helical array around the bundle.
- The heads on one half of the thick filament angle to the left, and the heads on the other half angle to the right; in the middle is a *bare zone* with no heads.

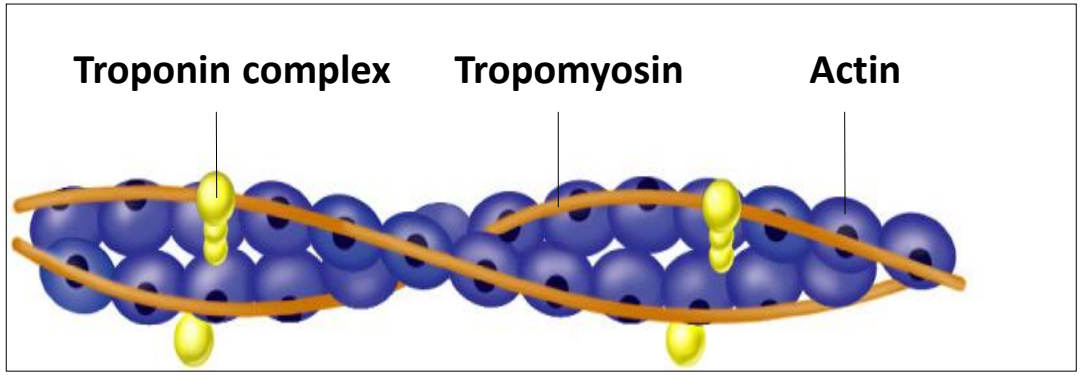

Troponin complex
head
Z-line
Thick filament
Bare zone
Thin filament
No heads!
Longitudinal section of filaments within one sarcomere of a myofibril


Actin-binding site
Myosin ATPase site
Heads
Tail
100 nm
(a) Myosin molecule
Cross bridges
Myosin molecules
(b) Thick filament
© 2007 Thomson Higher Education


Hierarchy of Muscle Structure
muscle
muscle-fibre bundle
muscle fibre
myofibrils
myofilaments
bone
tendon
connective tissue
muscle
muscle fibre bundle
nerve
blood vessel
muscle fibre
sarcolemma (muscle fibre membrane)
nucleus
sarcoplasmic reticulum
myofibril
myofilaments
Actin
Myosin

2- Thin Filament Structure

- Composed of actin protein
- 2 strands of globular actin molecules twisted into a helix
- Actin filaments have binding sites for myosin cross bridges



Regulatory proteins

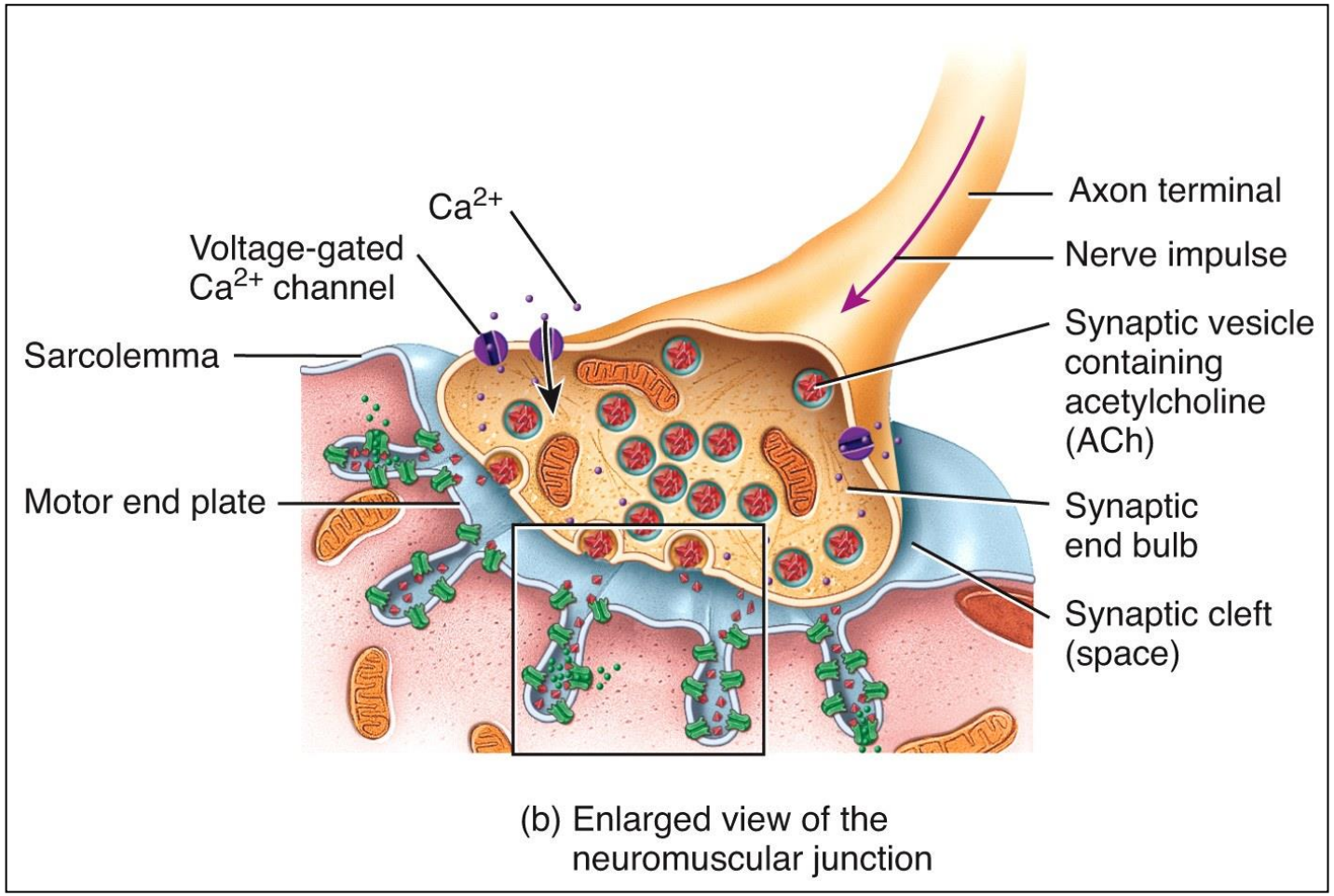
- Tropomyosin protein spirals around actin helix Troponin protein (3 subunits) is attached to actin and holds tropomyosin in place
- Call this the troponin-tropomyosin complex

Neuromuscular Junction

Motor end-plate

Sarcolemma of muscle fiber directly beneath motor nerve ending (axon trminal)

Contains an abundance of mitochondria and nuclei



(b) Enlarged view of the neuromuscular junction

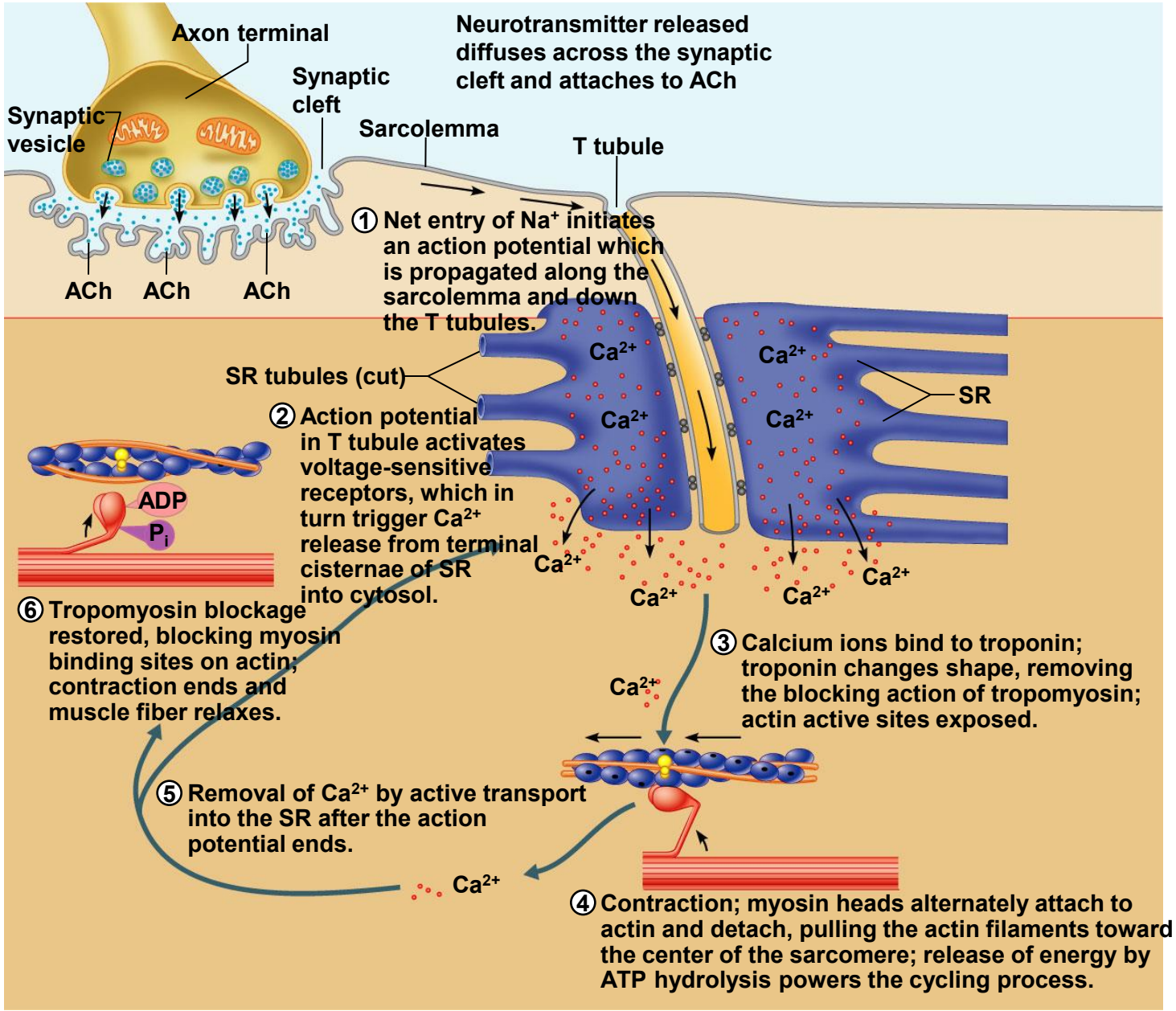
Physiology of Skeletal Muscle Contraction: Depolarization

- ACh binds receptors on motor end plate
- Depolarizes skeletal muscle fibers
- Reverses charge of membrane
- Impulse travels through transverse tubules to reach all of the muscle fibers
- Muscle depolarization causes release of calcium from the sarcoplasmic reticulum into the sarcoplasm

Physiology of Skeletal Muscle Contraction: Power Stroke

- Calcium binds troponin (which is attached to tropomyosin)
- Moves tropomyosin from the myosin binding sites on actin
- Myosin crossbridge (heads) bind to actin ATP hydrolysis supplies energy
- Actin is pulled inward towards the center of the sarcomere = POWER STROKE
- Power Stroke: The myosin heads undergo a conformational change, known as the **power stroke**. This change causes the myosin heads to pull the actin filaments toward the center of the sarcomere (the basic functional unit of a muscle).
- Sarcomeres shorten as muscle contracts

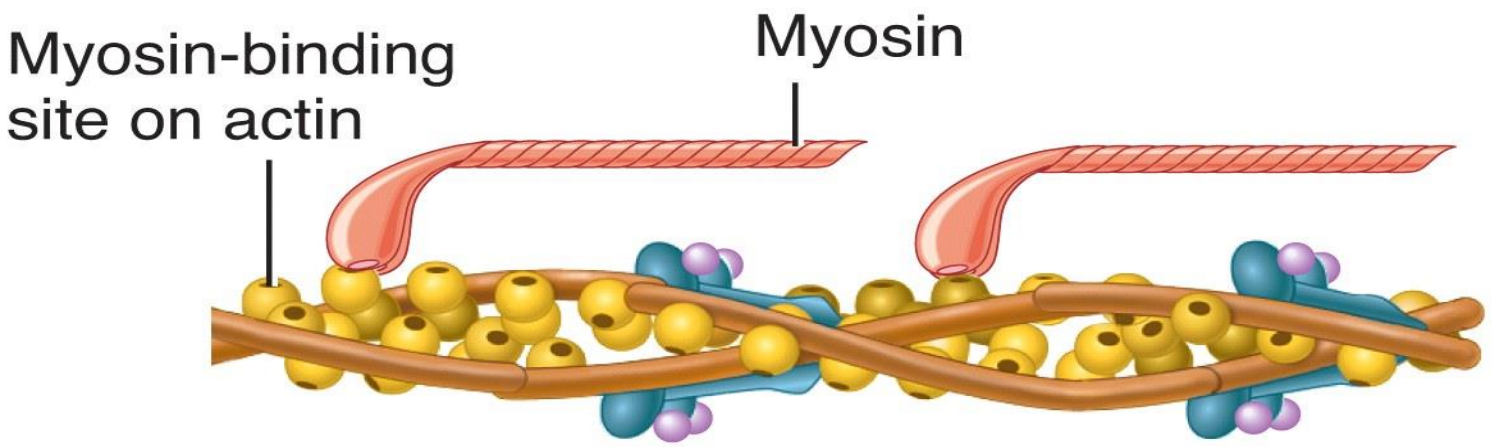
Excitation-Contraction Coupling



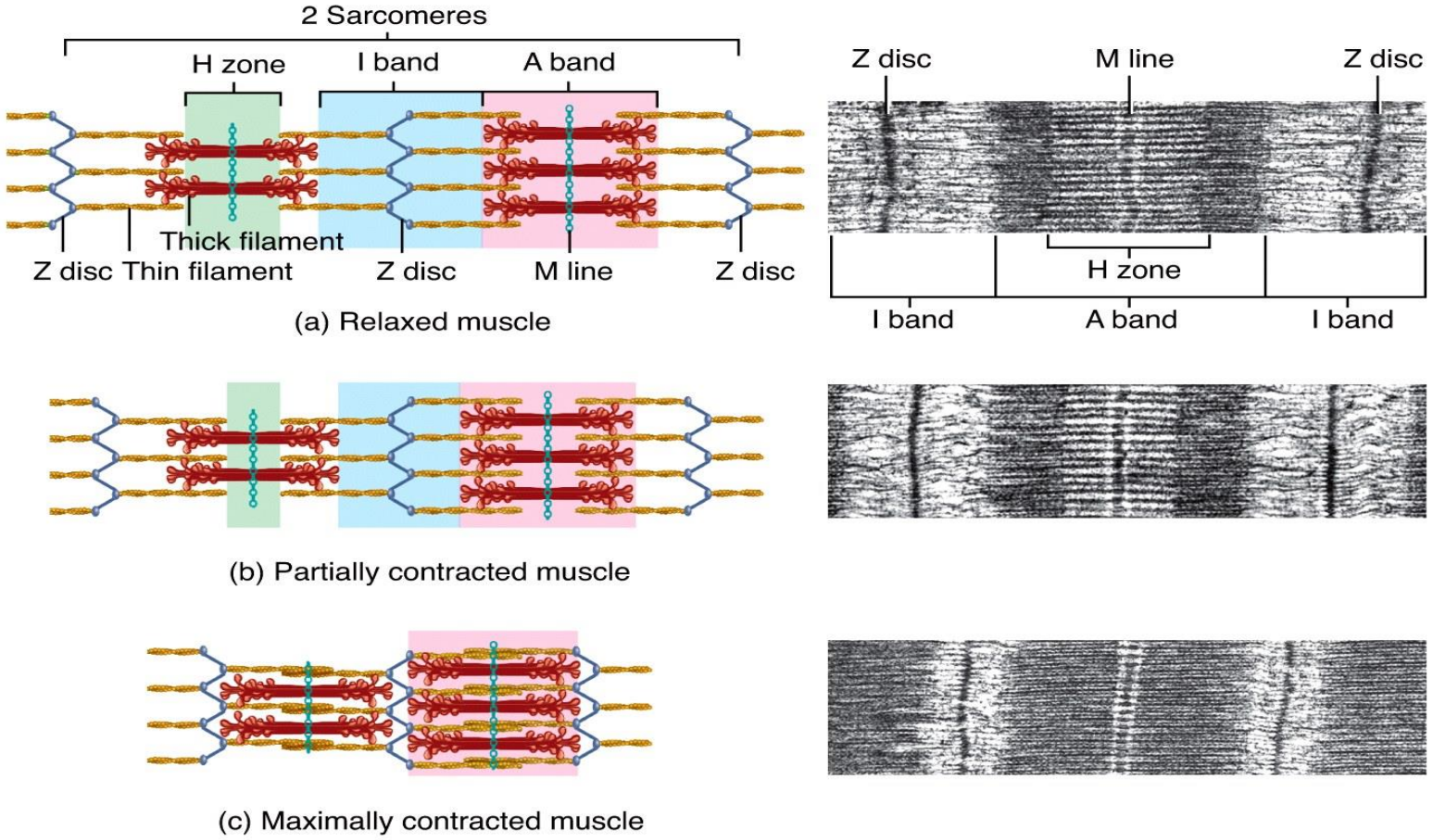
Sliding Filament Theory

- Sarcomeres shorten because thick and thin filaments slide past one another

- Thin filaments move towards the center of the sarcomere from both ends

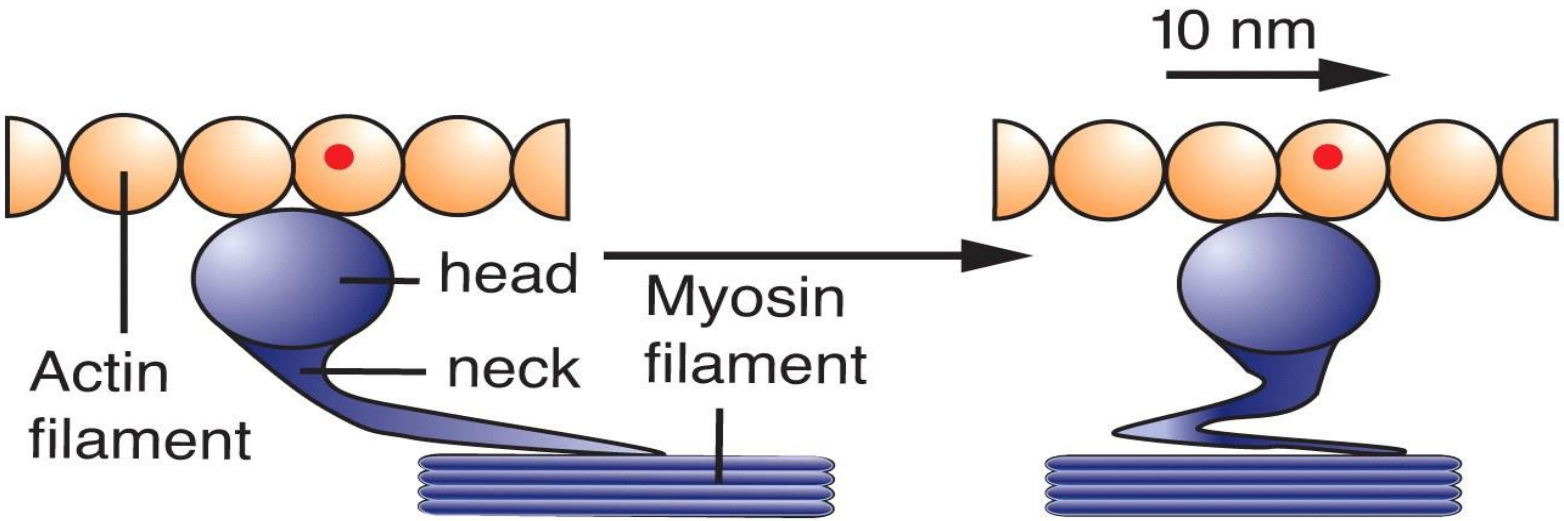


The Sliding-Filament Mechanism



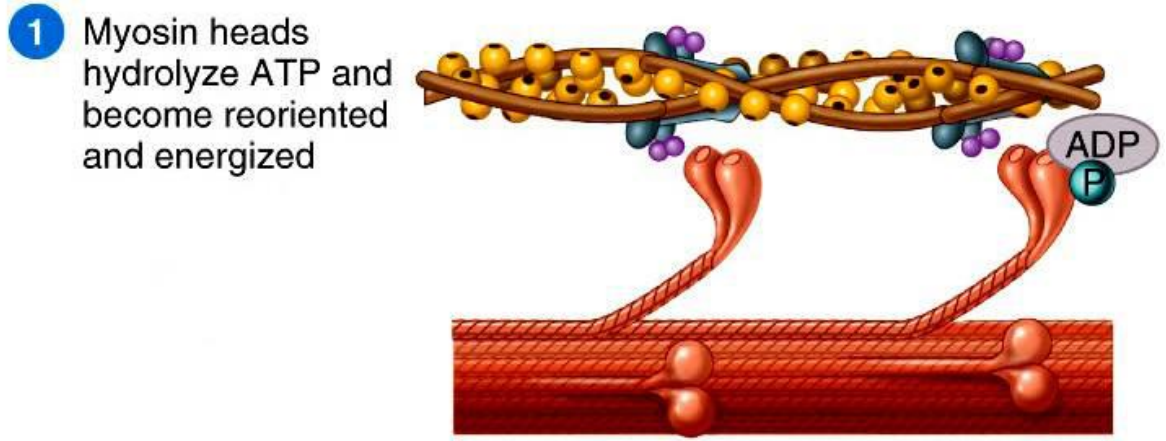
- The “sliding” of actin on myosin

The Sliding-Filament Mechanism

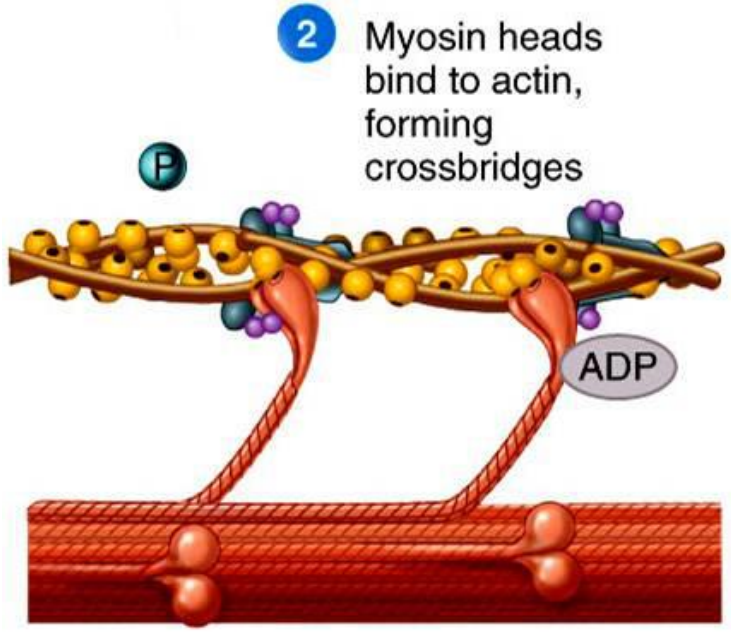


- With exposure of the myosin binding sites on actin (the thin filaments)—in the presence of Ca^{2+} and ATP—the thick and thin filaments "slide" on one another and the sarcomere is shortened

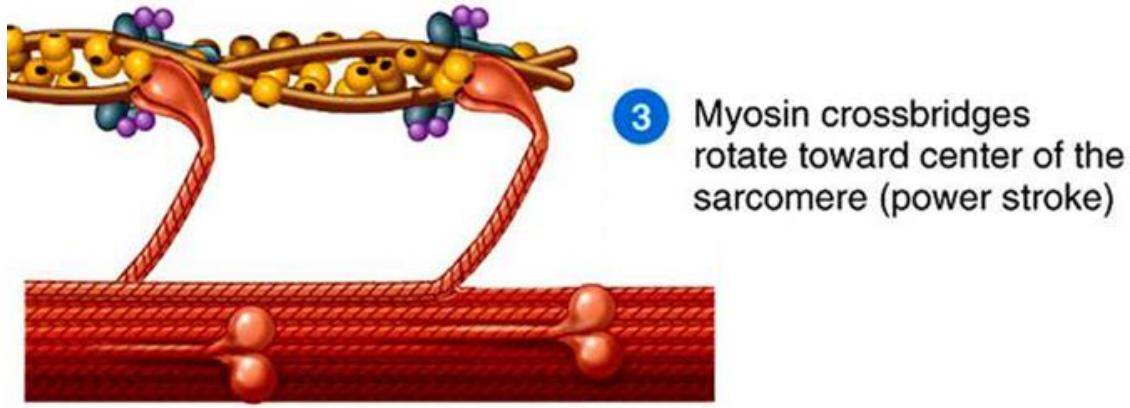
- **Step 1: ATP hydrolysis**



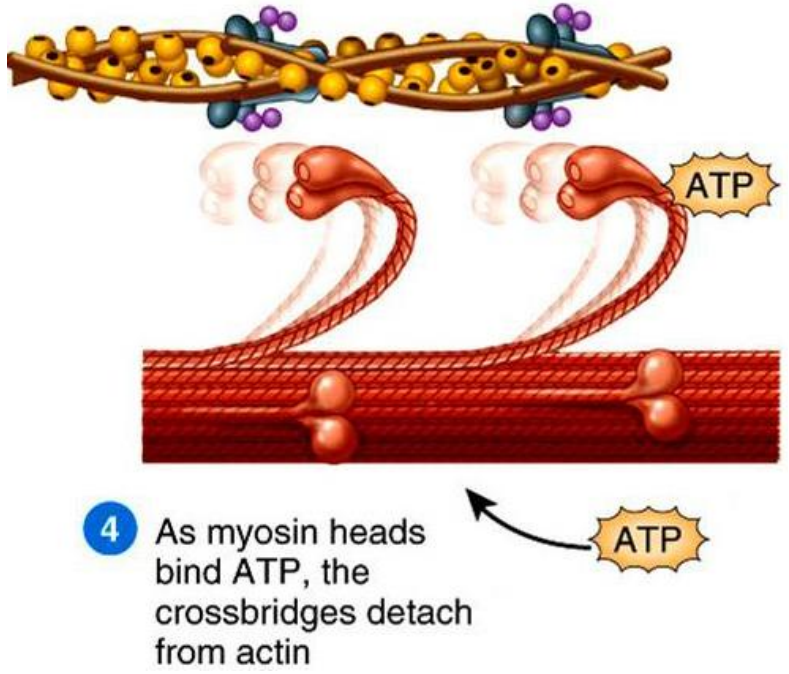
- **Step 2: Attachment**



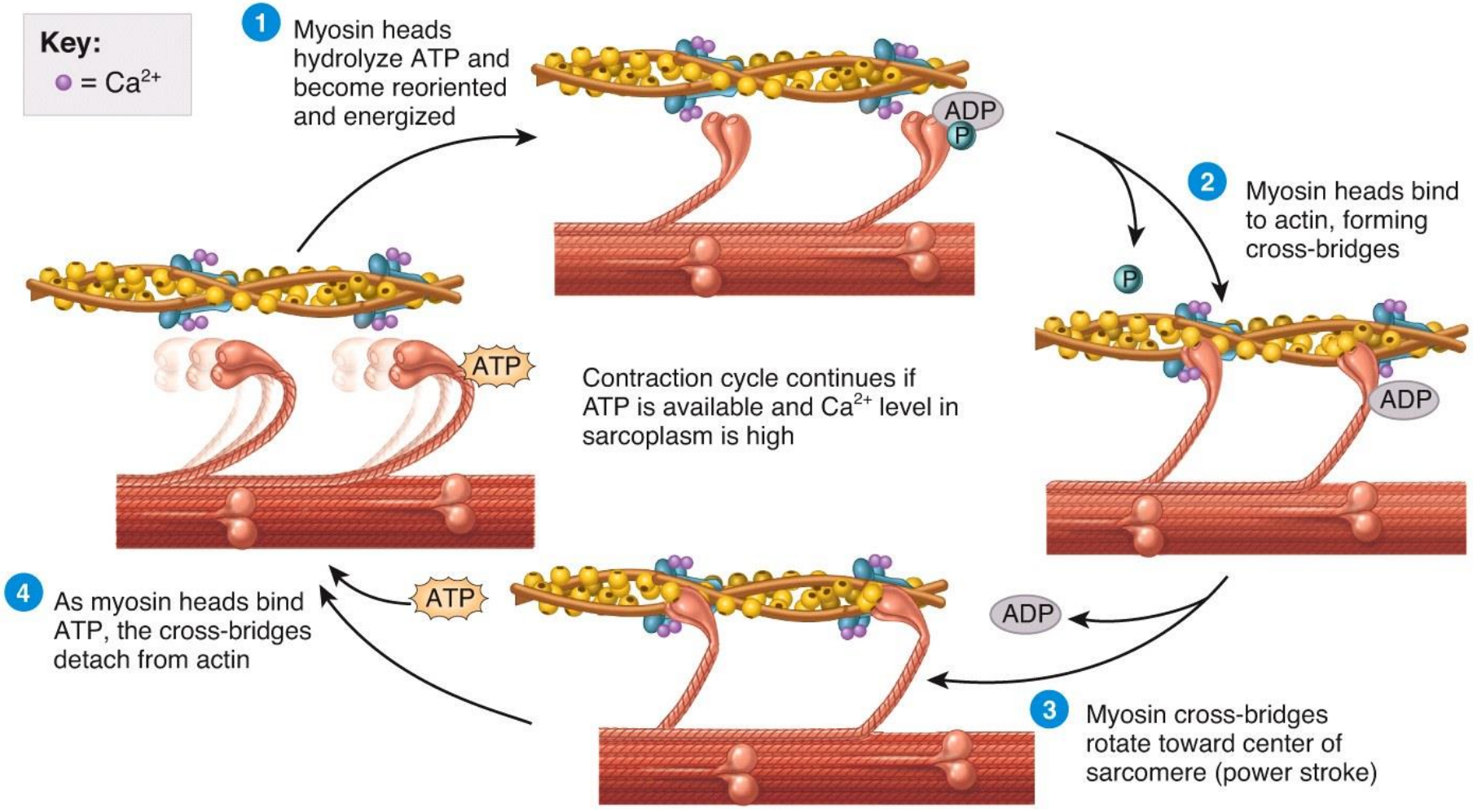
- **Step 3: Power Stroke**



- **Step 4: Detachment**



The Sliding-Filament Mechanism



Muscle Relaxation Mechanism

1. **Acetylcholinesterase present in the NMJ destroys ACh (preventing continual stimulation)**

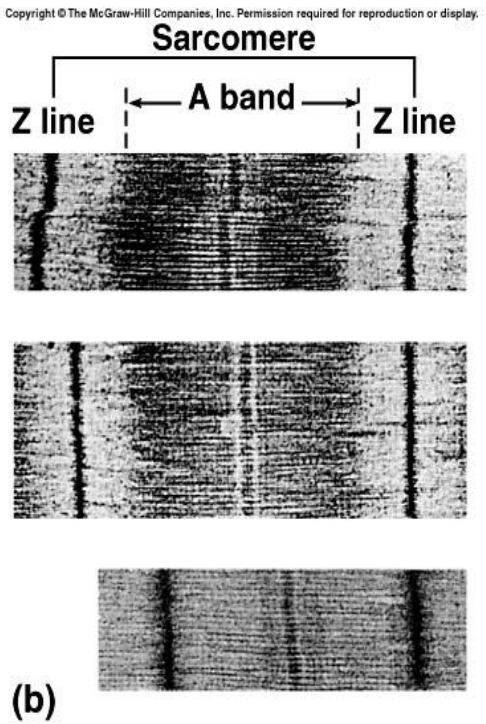
2. **Calcium ions are transported from the sarcoplasm back into the SR**

3. **Linkages between myosin and actin are broken**
   - **Requires ATP binding**

- **THEN: The muscle fiber relaxes**

Contraction in the Sarcomere

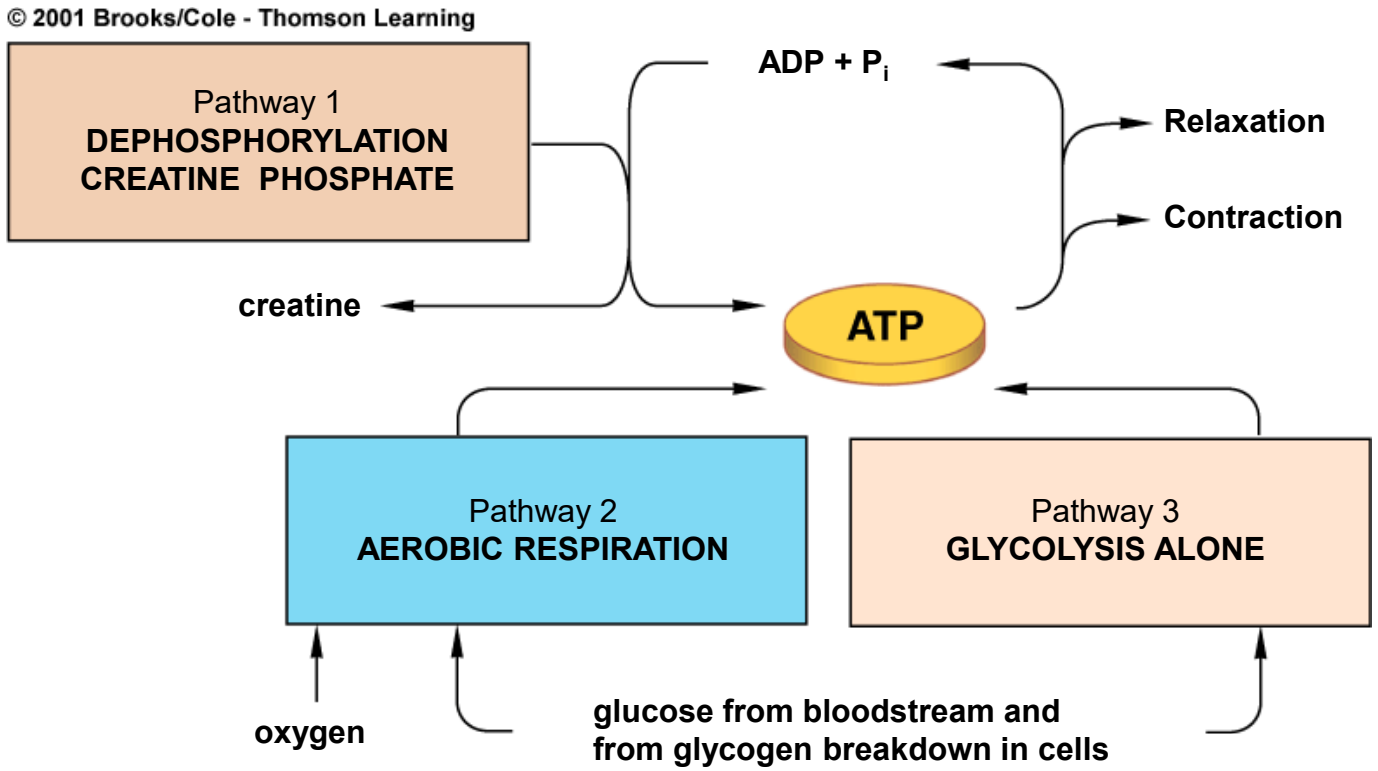
- **A band stays the same**
- **I band gets smaller**
- **H zone gets smaller**
- **Sarcomere shortens**



Energy for Contraction

- **Muscle cells require huge amounts of ATP energy to power contraction**
- **The cells have only a very small store of ATP**
- ***Three pathways supply ATP to power muscle contraction***

ATP Supply for Contraction



Heat Production

- Cellular respiration is only about 40% efficient
- About 60% of the energy found in a glucose is lost as heat during cellular respiration
- Muscle contraction generates heat because muscles use large amounts of nutrients to make ATP, generating large amounts of heat
- Heat is used to maintain body temperature

References

- Hall, J. E., & Hall, M. E. (2020). Guyton and Hall Textbook of Medical Physiology. Elsevier.
- Saladin, K. (2020). Anatomy & Physiology: The Unity of Form and Function. McGraw-Hill Education.

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- Hall, J. E., & Hall, M. E. (2020). Guyton and Hall Textbook of Medical Physiology. Elsevier.
- Saladin, K. (2020). Anatomy & Physiology: The Unity of Form and Function. McGraw-Hill Education.